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Aortography

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With rapid advances in vascular surgery, precise diagnosis of vascular lesions becomes a necessity. Since Dos Santos[1] published his work on aortography in 1929, the procedure has become recognized as a valuable clinical tool which can provide accurate anatomic information not available by any other means.

Many methods have been advocated to assure certain, safe visualization of the aorta and its branches; for example, 1-needle technics, 2-needle technics, and retrograde catheter technics.[2,3] Aortography by the intravenous route[4,5] is being developed and shows promise, especially for studying patients in whom previous aorta grafts have been placed.

We use direct percutaneous injection of the abdominal aorta through the patient's back. It is done on the x-ray table with the patient prone. The use of local or general anesthesia depends on how cooperative the patient is. A 17-gauge, 7-in. needle with a stylet is used for the injection. A plastic tube placed between the needle and syringe prevents inadvertent manipulation of the needle after it is in the aorta, and also keeps the injector from receiving so much radiation to his hands. Fifty per cent sodium diatrizoate (Hypaque) is the contrast material used. The total amount of Hypaque used during a single study is limited to not more than 40 cc. After the needle is inserted into the aorta, a small amount of Hypaque is injected to check the level of the needle and to assure that the end of the needle is well within the lumen of the aorta. The contrast material is injected rapidly and the exposure is made near the end of the injection.

Details of this general technic vary with the clinical situation. Complications are reported in the literature.[6,7] Although some of them are probably inherent in the procedure, the author believes that most complications can be avoided by individualizing each examination according to (1) the clinical information available about the patient, and (2) the information desired from the study.

The exact mechanism of renal and spinal cord complications resulting from injection of contrast material into the aorta is not entirely clear, but it seems to be related to the concentration of contrast material in the blood stream and to the quantity used. Therefore, in general, it is desirable to use a small amount of contrast material and to inject it as low into the aorta as is practical. Unnecessary ischemic and toxic reactions in the kidneys and spinal cord can thereby be minimized. For example, if aortic or iliac artery obstruction exists, use only 12 to 15 cc. of Hypaque. If greater quantities of dye are used, retrograde filling of the renal arteries will cer-

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tainly occur in large amounts. If it is not necessary to visualize the renal arteries, the aortogram needle can be placed into the aorta at a lower level; for example, at the level of the third lumbar vertebra. A test dose injection and exposure will prevent the complication of massive injection of a single branch of the aorta, and will also prevent traumatic dissection within the aorta wall.[8]

We perform aortography only on patients who are suitable candidates for surgical treatment. In spite of every precaution, aortography carries certain minimal risks. Therefore, the study is not done if, for medical reasons, the patient would never be able to survive an operation. Clinical applications of aortography are discussed below.

ANEURYSM

Aorta. It is now accepted that abdominal aortic aneurysms almost invariably arise below the renal arteries. In the presence of a clear-cut clinical diagnosis of abdominal aneurysm, especially when it is aided by roentgen evidence of bone erosion and calcification, aortography to determine operability is not generally done. Diagnosis of an abdominal mass, especially if a renal or suprarenal lesion is suspected, may be aided by an aortogram.[9]

Renal, splenic, and hepatic arteries. Aneurysms of these vessels are very uncommon. When they occur, there is usually characteristic calcification, so contrast visualization is not necessary.

ARTERIOVENOUS FISTULA

Diagnosis of an arteriovenous fistula can be made clinically, but angiography helps to determine the level of the fistula and size and number of communications.[10–12]

OCCLUSIVE DISEASE

Aorta. Leriche first described that syndrome of thrombotic occlusion of the distal aorta which bears his name. Such patients have an aching pain and weakness in the buttocks. Penile erections are absent or unstable. Pulsation is absent over the femoral arteries and lower aorta. Hypertension in the arms is common.

Aortography will visualize the level and extent of the obstruction and also the condition of the vessel wall above and below the obstruction. In this situation, it must be emphasized that use of a small amount of contrast material will prevent retrograde flooding of kidneys and spinal cord vessels with a toxic concentration of Hypaque.

Renal artery. This is discussed in the section on renal hypertension.

Iliac artery. Common iliac artery obstruction is characterized by pain in the hip, thigh, or even in the calf, which is brought on or aggravated by exercise. If the obstruction is of long-standing, there may be constant pain of ischemic neuritis in the foot, heel, or toes. The picture may be more confusing if the obstruction is high and segmental, since there may then be a palpable, though weak, femoral pulsation.

Aortography can confirm the diagnosis. It can help decide whether an operation is feasible and, if so, whether endarterectomy resection and grafting or bypass grafting will be the procedure of choice. It was formerly accepted that if no distal runoff was seen, direct arterial surgery was not indicated. However, on the basis of personal experience, the author tends to explore the distal arterial tree to determine directly whether or not patency exists. If a patent distal artery can be found, then proximal blood flow can be obtained by one means or another and benefit to the patient can be expected.

External iliac artery obstruction is accompanied by more physical evidence of ischemia in the foot; femoral pulsation will be absent. The following is a helpful adjunct to aortography in these cases: after placing a grid cassette under the legs, a second portable x-ray machine may be used to make a second exposure over the legs. The arterial tree from aorta to the tibial vessels can thus be visualized with 1 injection.

Femoral artery. For suspected femoral artery lesions, femoral arteriograms are done.

EMBOLISM

Acute embolism usually presents no diagnostic problems. The author has done an aortogram on one patient with embolism to a leg. In that case, the history was suggestive of a Leriche syndrome. It was important to ascertain this because embolectomy at the femoral level would have failed if there had been a proximal obstruction to prevent good blood flow.

RENAL HYPERTENSION

The most common cause of reversible renal hypertension is occlusive disease of the renal artery or of its main branches.[13] In the experimental laboratory, Goldblatt[14] demonstrated that constriction of 1 renal artery produced hypertension and that removal of the ischemic kidney resulted in disappearance of the hypertension. Thus the concept of the "Goldblatt kidney" originated; it was then loosely applied to any

unilateral kidney disease which caused elevation of blood pressure. In earlier years, urologists were principally interested in this problem. They found a variety of unilateral kidney lesions —mostly chronic pyelonephritis. After nephrectomy, occasional cures of hypertension were reported from among these cases. However, renal arteriograms done for various uropathies occasionally showed narrowing of the main renal artery by atheromatous changes or other changes in the vessel walls.

These sporadic reports and autopsy observations of plaques in the renal arteries of hypertensive patients, combined with the technical advances of vascular surgery, greatly stimulated the search for a vascular lesion in the renal arteries.[15,16] Poutasse[13] reported on 337 hypertensive patients who had aortograms performed. Eighty-seven of these patients were found to have occlusive disease of 1 or both renal arteries. During the period when these patients were studied, only 6 cases of pheochromocytoma were found. This indicates the relative frequencies of these 2 potentially reversible causes of hypertension.

On which hypertensive patients should one do renal arteriography? History, physical examination, blood chemistry studies, Regitine testing, and excretory urograms do not always yield an etiologic diagnosis in the work-up of a hypertensive patient. Significant occlusive disease in the renal arteries may exist even if all these studies are normal. We currently use the following criteria for performing renal arteriograms: (1) recent onset of hypertension; (2) malignant hypertension; (3) an intravenous pyelogram that shows such abnormalities as a small kidney or delayed excretion; and (4) a high diastolic blood pressure that is refractory to drugs.

Utilizing uretral catheterization to measure volume and sodium excretion by the individual kidneys is thought helpful by some writers and not helpful or unreliable by others.[18] We utilize individual renal function studies in equivocal situations.

The following reports demonstrate several clinical situations employing aortography.

CASE REPORTS

Case 1. K.Y., a 49-year-old white man, complained that for twenty-three years he had experienced constant pain in his left heel and the sensation of a vise being clamped on the heel. These symptoms were made worse by exercise; with exercise, he noted tightness of the muscle in the left calf. During this time, 2 operations had been performed on his back, presumably for a disk, and he had spent several months in a neuropsychiatric institution receiving psychiatric therapy.

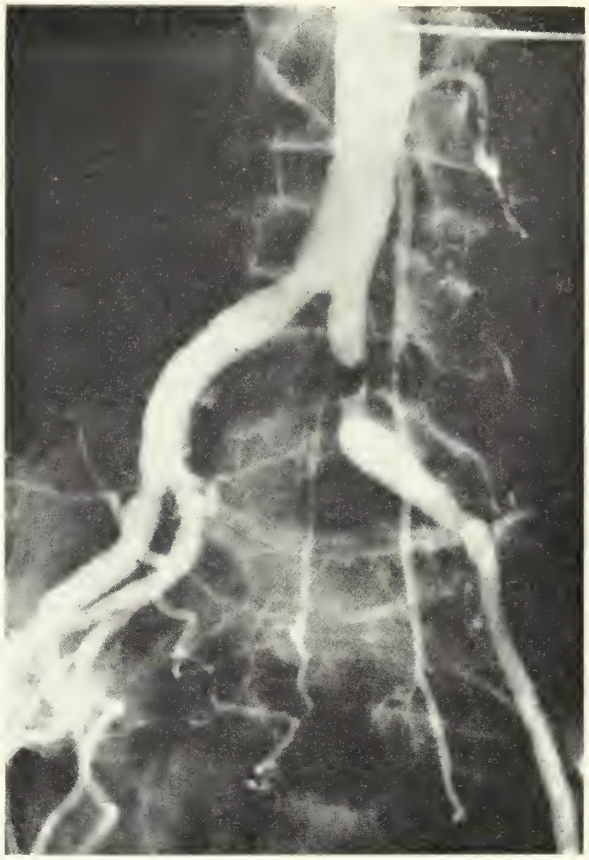


Fig. 1. *Case 1.* Note left common iliac artery obstruction.

The author's examination showed a cool left foot and a very weak left femoral artery pulsation.

Aortogram disclosed left common iliac artery obstruction (figure 1). Thromboendarterectomy was carried out, which gave complete relief of symptoms.

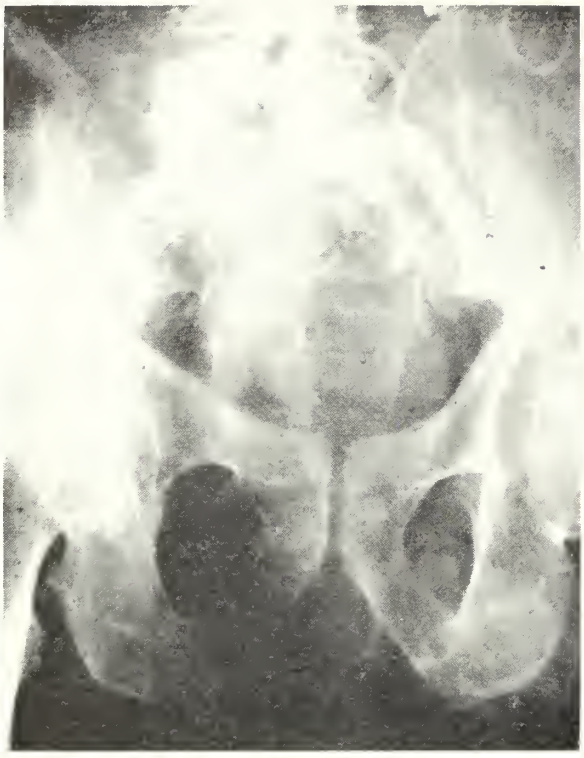
Case 2. T.H., a 67-year-old white man, complained of progressive intermittent claudication of the left calf during a two-year period. A left lumbar sympathectomy had been recently done, but it had not relieved his symptoms. Examination of the lower extremities showed a very weak left femoral artery pulsation and no arterial pulses palpable below the groin. The right femoral pulse was normal, but no arterial pulsations could be felt below the right groin. The left foot and leg were cooler than the right.

Aortogram disclosed an almost complete obstruction in the left external iliac artery (figure 2). The arteriogram shown in figure 3, which is a delayed exposure, shows filling of the iliac and femoral system distal to the obstruction.

Thromboendarterectomy was performed; this relieved the patient's claudication.

Case 3. V.A., a 51-year-old white man, had a fifteen-year history of cramping pain in the left calf; he first noted it while marching in the army. At that time, he also noted some swelling of the left foot and ankle. Since 1950, he had been unable to work because of pain, aggravated by exercise, in the entire left lower extremity, left hip, and left lumbar back region.

On admission to the hospital, examination of the left



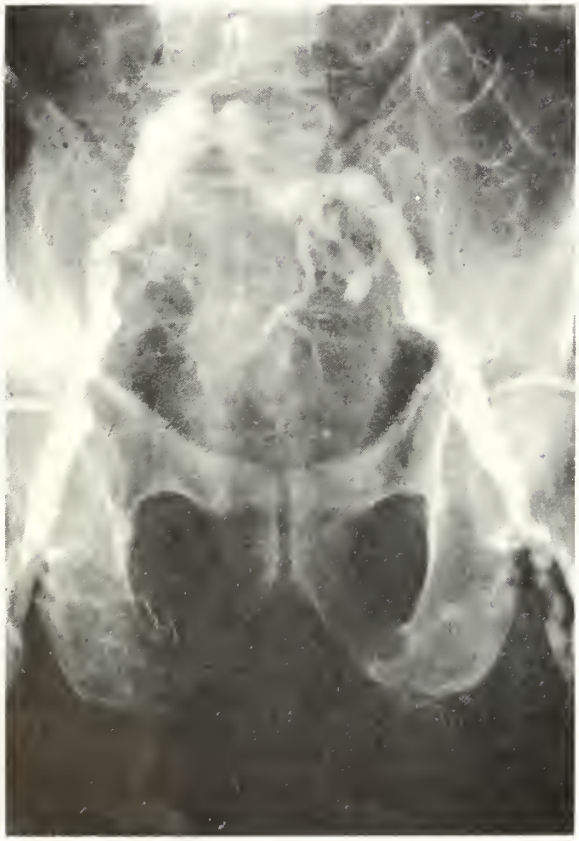


Fig. 3. *Case 2.* Delayed exposure shows filling of the arterial tree distal to the obstruction shown in figure 2.

Fig. 2. *Case 2.* Note obstruction in left external iliac artery.

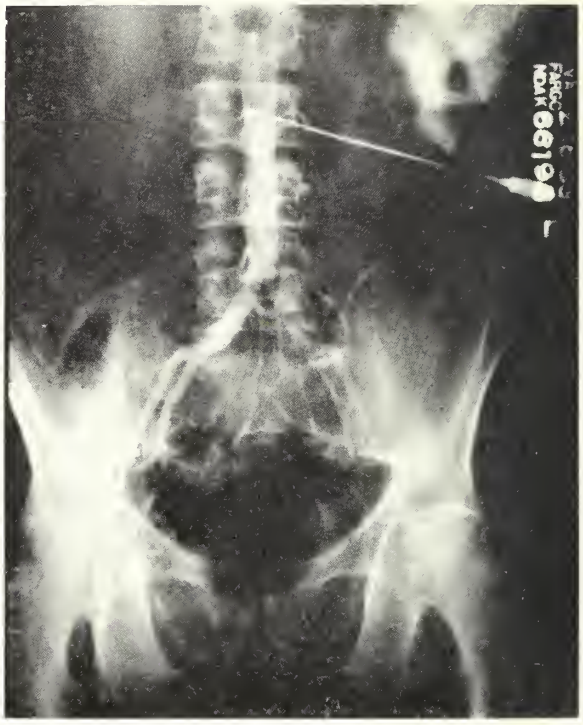


Fig. 4. *Case 3.* Note left common iliac artery obstruction.

lower extremity disclosed no arterial pulsations in the entire left lower extremity. There was pitting edema of the left leg to a point just above the knee and the leg was cool. It was thought that he had arterial disease and an acute and chronic iliofemoral thrombophlebitis. He was treated with anticoagulant therapy for approximately one month; the edema had then subsided. Aortogram (figure 4) showed left common iliac obstruction. Thromboendarterectomy was performed.

Case 4. R.G., a 50-year-old white man, was well until September 1957, when he fell and ruptured a blood vessel at the back of the left thigh. He was treated with physiotherapy. Shortly thereafter, he developed pain and prickling sensations in the toes of his left foot. In April 1958, he developed an ulcer on the left leg and was again treated with physiotherapy. In September 1958, he dropped an oil burner on his left second toe. The toe became cyanotic and painful and, in all toes of the left foot, the prickling sensations and occasional sharp pains became worse. At this time, he first noted numbness and tingling from the hips down when walking; this existed in both lower extremities, but was worse on the left. He did not have typical claudication. Instead, he complained of numbness in his leg. This was so severe that he would have to stop walking and rest until the numbness subsided. The injured second toe became ulcerated and would not heal. It was finally amputated in November 1958. However, coolness, mottled discoloration, and paresthesia persisted in the remaining toes until the patient had small ulcers at the tips of all toes of the left foot.

Fig. 5. *Case 4.* Aortogram, August 1959. Note bilateral common iliac artery obstruction.

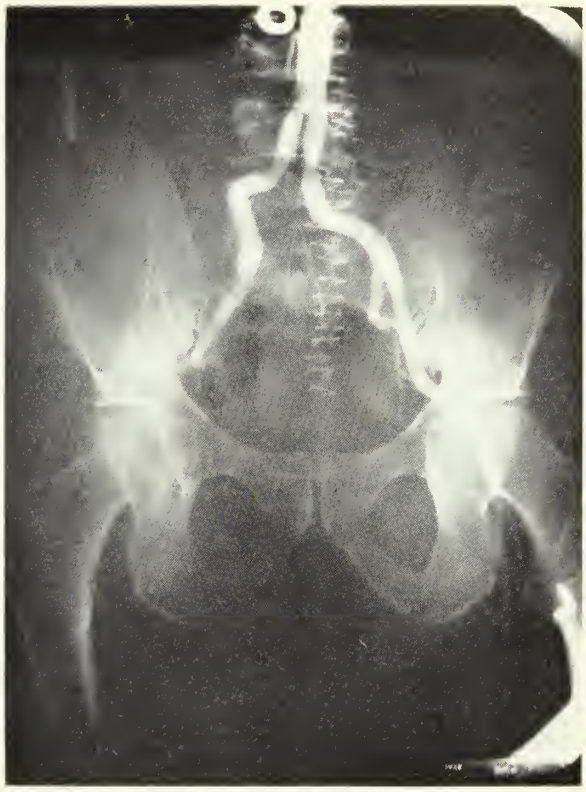


Fig. 6. *Case 4.* Aortogram, February 1960. Note complete obstruction of right external iliac artery.

The author first saw this patient in August 1959, when examination of the lower extremities showed the left foot to be slightly cooler than the right. Remaining toes of the left foot were dusky, cyanotic, and reddish in color, with small ulcerations on the tips. The left foot was sweating. Arterial pulsations on the left lower extremity showed only a very weak left femoral pulse. Arterial pulsations were all present and normal on the right lower extremity.

An aortogram (figure 5) performed in August 1959 disclosed a partial obstruction of both common iliac arteries immediately below the bifurcation of the aorta. It was more severe on the left side. On August 28, 1959, a bilateral common iliac thromboendarterectomy was performed. An excellent therapeutic result was obtained with restoration of all arterial pulses in both lower extremities and disappearance of all discoloration, sweating, pain, numbness, and so forth. Ulcers on the toes healed within a week. The patient was able to walk any distance without difficulty.

Approximately six weeks following this operation, the patient suddenly developed severe intermittent claudication in the right calf after walking only a short distance—approximately one-half block. Examination of the lower extremities showed an essentially normal left lower extremity, but this time the right foot was cooler than the left and no arterial pulsations were present in the right lower extremity (figures 6 and 7). Aortogram showed a complete obstruction of the right external iliac artery approximately 5 cm. distal to the bifurcation of the right common iliac artery. A delayed exposure showed no evidence of a runoff. It was thought that this patient was probably a poor candidate for direct arterial surgery

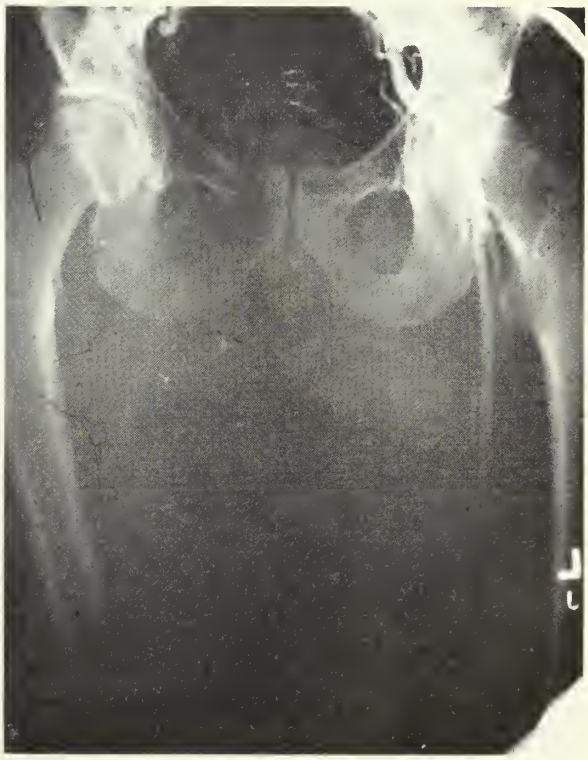


Fig. 7. *Case 4.* Aortogram, February 1960. Note lack of runoff in this delayed exposure.

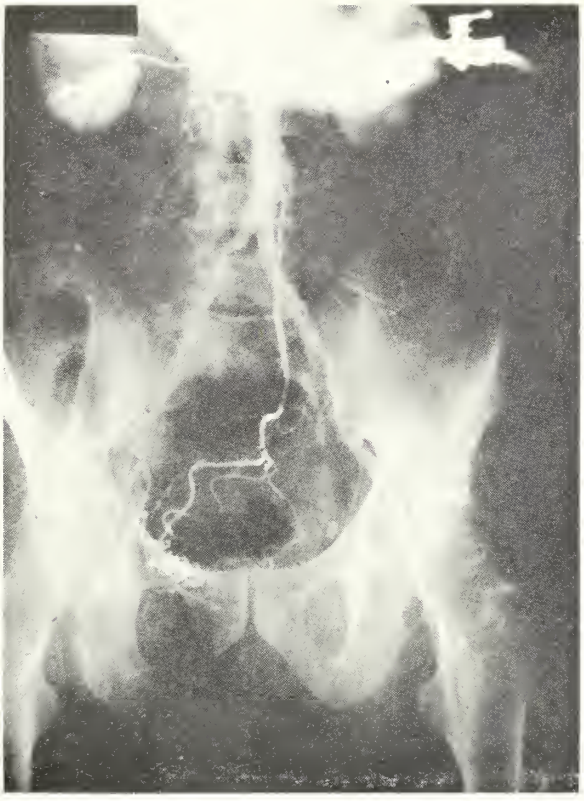


Fig. 8. *Case 5.* Aortogram, February 1957. Note obstruction in right common iliac artery.

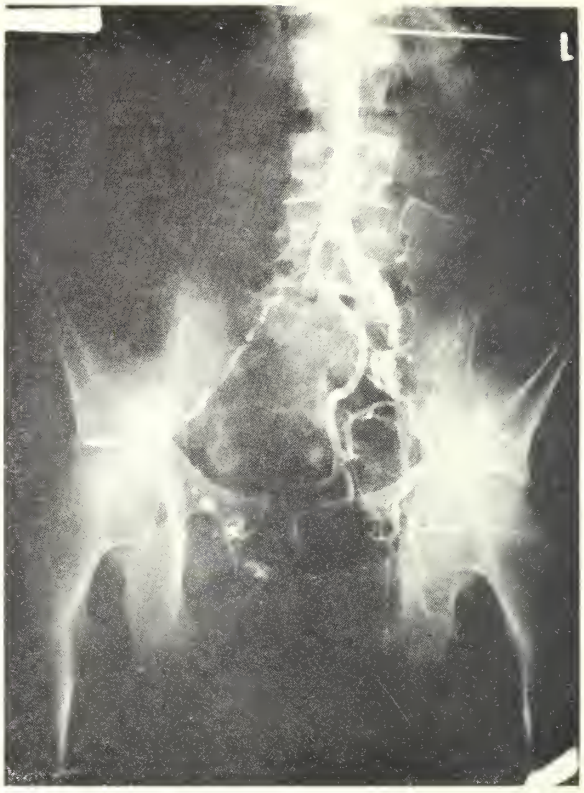


Fig. 9. *Case 5.* Aortogram, January 1959. Note occlusion of right common iliac artery and left external iliac artery.

but that exploration of the femoral system should be done.

Thromboendarterectomy was then performed from the point of obstruction in the right external iliac artery to the bifurcation of the popliteal artery. This resulted in complete restoration of all arterial pulsations in the right lower extremity and complete relief of all symptoms. Since that time, the patient has been completely well. He has continued to maintain all arterial pulsations in both lower extremities.

Case 5. G.F., a 47-year-old white man, was a salesman whose chief complaint was fatigue and heaviness of the right lower extremity. This condition had started several years before as a sensation of tiredness of the right leg. Tiredness had tended to extend down the leg to the foot and to be accompanied by numbness and heaviness, especially after walks of even a short distance. These symptoms were progressive until they extended all the way to the hip.

Examination of the lower extremities showed the right leg and foot to be cooler and paler than the left. A very weak right femoral pulsation was present, but there were no arterial pulses below the groin. Also noted was a very weak left femoral arterial pulse; no arterial pulsations were noted below the groin on the left leg. In February 1957, an aortogram showed obstruction in the right common iliac artery (figure 8). An operation was then performed; it consisted of a bypass crimped nylon artery graft placed from the distal aorta to the superficial femoral artery on the right. After this operation, the right foot and leg became warm. However, no popliteal or dorsalis pedis pulsations could be felt. Nevertheless, the patient was clinically much improved.

This patient was next seen in January 1959, when he complained of pain in both hips that extended down both legs after exercise. This time, pain was worse on the left. He could walk only a very short distance before being forced to stop and rest. Examination showed no arterial pulsations in either lower extremity. Both feet were cool and pale. Aortogram disclosed complete occlusion of the right common iliac artery at the bifurcation of the aorta and complete occlusion of the left external iliac artery (figure 9). There was no evidence of a runoff bed in either lower extremity. It was not thought at that time that direct arterial surgery was feasible; he was treated with vasodilator medications. After three months, pain in his legs—especially on the left side—became so severe that he was unable to work. Left lumbar sympathectomy was performed. After the operation, the left leg and foot were warmer than the right. The patient, although still quite incapacitated, was nevertheless able to resume his occupation as a salesman.

Shortly after the sympathectomy, the patient developed angina pectoris. This finally became so bad that he was unable to walk far enough to develop pains in his legs. In August 1959, the diagnosis was made of coronary artery disease with cardiac decompensation. Since then, the patient's pain problem has been his heart disease. His legs do not now cause significant symptoms.

Case 6. R.W., a 38-year-old white man, was admitted to the hospital in November 1958 because of hypertension. Hypertension had been first noted in the preceding spring. Treatment with antihypertensive drugs had no

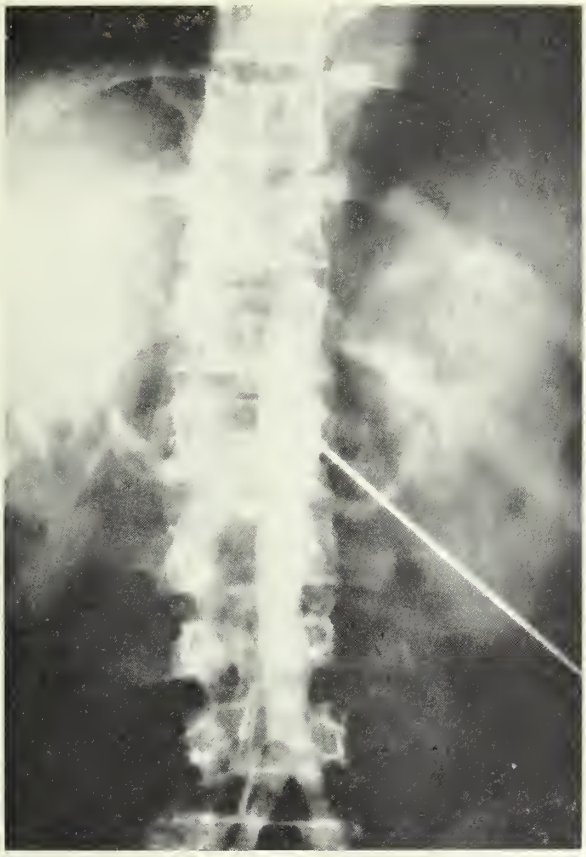


Fig. 10. *Case 6.* Note narrowing of right renal artery and poststenotic dilatation.

effect on his blood pressure. The usual studies were performed, including blood chemistries and Regitine testing. Excretory urogram showed good function of both kidneys, but a very slight delay of excretion of dye on the right side and, questionably, a smaller kidney on the right side. An aortogram done in November 1958 showed a narrowing of the right renal artery approximately 1 cm. from the aorta, with some poststenotic dilation of the right renal artery. The x-ray picture (figure 10) shows that this narrowed segment is immediately over the site of a spine injury which the patient had sustained a few years before. The relationship between the old injury and the patient's current disease is not known.

Exploration of the right renal artery was carried out. At the operating table, there was a marked differential of arterial pressure across the narrowed segment. Right nephrectomy was carried out. The patient had an almost immediate fall in blood pressure; while still in the recovery room, he required vasopressor substance to maintain a systolic blood pressure of 88 mm. of mercury. For twenty-four hours postoperatively, he continued to require fairly large amounts of vasopressor substance to maintain a systolic blood pressure close to 90 mm. During this time, the patient's pulse was of good quality, with a rate of approximately 72 beats per minute. Throughout the day after surgery, the patient required a vasopressor substance in somewhat smaller quantities. On the second postoperative day, the vasopressor substance could be discontinued entirely. Blood pressure was then stable at 130/80. His blood pressure has since been normal, with the most recent examination in January 1960.

Case 7. Mrs. H.W., a-69-year-old white woman, was admitted to the hospital in August 1959. Her chief complaint was of hypertensive vascular disease since at least 1955. She also complained that during the previous three to four weeks she had experienced sharp pains in the left flank region which radiated anteriorly. She was known to have had meningovascular syphilis for many years. An excretory urogram showed no renal function on the left side. Retrograde pyelogram could not be obtained on the left side. The patient's blood pressure ranged from 240/140 to 180/100.

A renal arteriogram was done in April 1959 (figure 11) and showed complete occlusion of the left renal artery where it branches off from the aorta. Exploration of the left renal artery and kidney was carried out. At operation, the left kidney was very small but was otherwise normal. The left renal artery was very small with a diameter no more than 2 or 3 mm.; it carried no arterial pulsations. Left nephrectomy was carried out. After the operation, the patient's blood pressure fell dramatically; since discharge, it has ranged from 134/70 to 150/90.

Case 8. Mrs. B.C., a 47-year-old housewife, was admitted to the hospital in July 1959 with the complaint of headache and dizziness of one month's duration. She also had an acute urinary tract infection with hematuria and pyuria. Her blood pressure on admission was 200/140. A chest film showed enlargement of the left ventricle. An intravenous pyelogram showed malrotation of the right kidney, although both kidneys function-

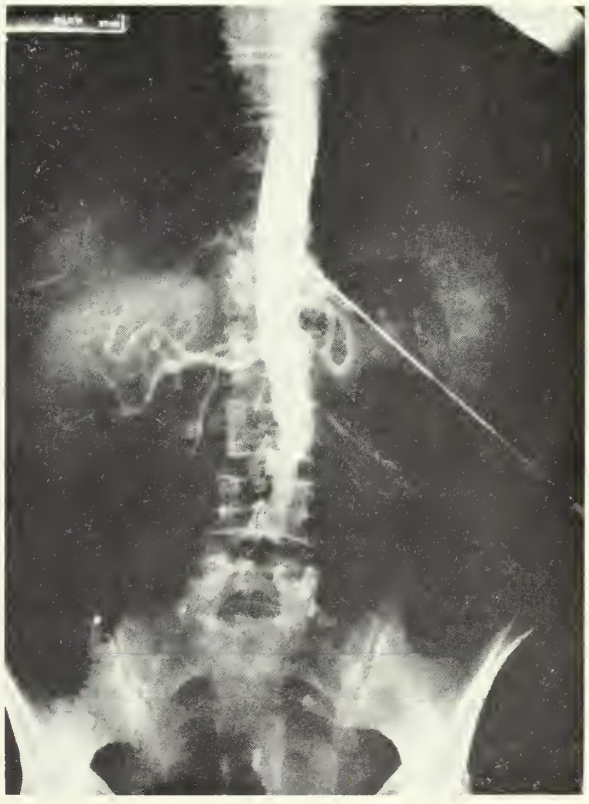


Fig. 11. *Case 7.* Note complete occlusion of left renal artery.

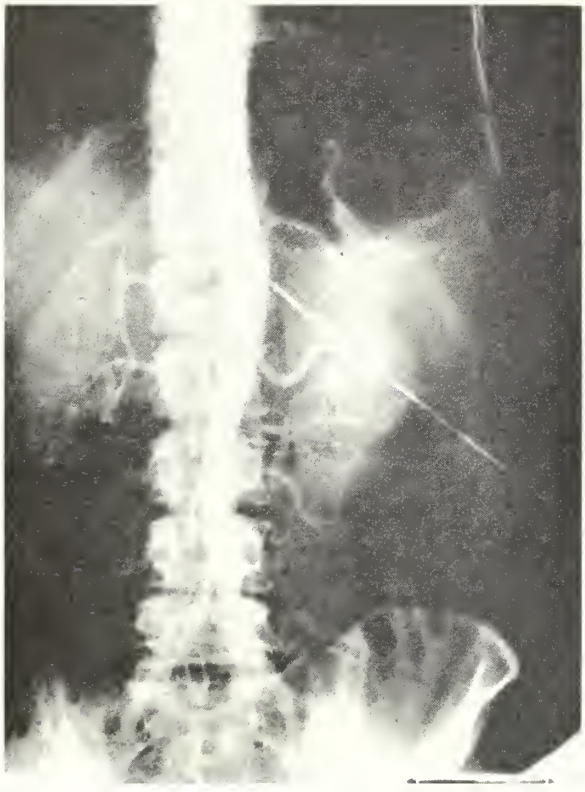


Fig. 12. *Case 8.* Aortogram, November 1959. Note slight narrowing of right renal artery and diminished vascularization of right kidney.

ed well. The Regitine test was negative. The urinary tract was treated with antibiotics, and she was started on a course of antihypertensive drugs.

She got a poor effect from her drugs, and so was readmitted in August 1959. A renal arteriogram was then done. This study showed that the right renal artery was slightly smaller than the left.

It was also thought that there was less vascularity in the right kidney. However, findings were not too definite on the basis of this one study, so the patient was placed on a more vigorous antihypertensive medical program.

Since her blood pressure did not respond to medical measures, another renal arteriogram was performed in November 1959. This study (figure 12) discloses essentially the same findings as before. Because of the severity of her headaches and dizziness and the high blood pressure level, an exploration was decided on. At operation, atheromatous changes were noted in both renal vessels with a hard calcified plaque located at the orifice of the right renal artery. The right kidney was surprisingly small with marked nephrosclerotic changes. Because we considered that we had nothing else to offer this patient, we did a right nephrectomy. Pathologic examination of the kidney showed severe nephrosclerosis. Since the operation, her headaches and dizziness have been completely relieved. Her blood pressure is still 180/100 while she takes Apresoline and Serpasil. The medical department considers that nephrectomy made her blood pressure amenable to medical therapy.

If a situation equivocal to this occurred today, we would probably do differential water and sodium excretion studies from the kidneys to help determine a course of action.

SUMMARY

Aortography is a safe and useful method for diagnosis of lesions of the aorta and its major branches, for selection of patients for surgery, and as an aid in determining the appropriate operative procedure. To avoid the complications of angiography, the technic must be individualized on the basis of each patient's clinical situation.

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MEDICAL GRAND ROUNDS
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Therapy of Pyogenic Meningitis in Adults

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Pyogenic meningitis occurs as a result of local invasion of bacteria from a neighboring focus or hematogenous spread from a distant focus of infection. With invasion of the central nervous system, there is, initially, hyperemia and edema of the meninges and, later, production of a fibrinous exudate that often accumulates at the base of the brain and along the fissures. Plaques of exudate may appear on the surfaces of the meninges, limiting absorption of cerebrospinal fluid, and may also obstruct the foramina of the fourth ventricle, producing spinal block. In untreated cases, organization of the exudate produces a thick membrane. In addition to pathology of the meninges and the effect on the dynamics of cerebrospinal fluid flow, there are irritative, toxemic, and necrotizing effects on the brain tissue and its vasculature.[1]

The prognosis in pyogenic meningitis is affected by the acuity of the disease and by complications in the central nervous system and in other organ systems. Both of these factors are influenced by the patient's age and previous health. The patient who is acutely ill or moribund when treatment is begun often dies before adequate therapy is established. In a recent series of 55 deaths from pyogenic meningitis, 36 occurred in the first twenty-four hours.[2] Of a group of 144 United States Army fatalities during World War II due to meningococcal meningitis, only 26 lived longer than ninety-six hours after onset of disease.[3]

Complications may occur in any patient but particularly in the elderly patient with associated chronic disease. Central nervous system complications include subdural accumulation of fluid, spinal block, encephalitis, and relapse of the acute meningeal reaction. Other complications are due to associated chronic disease outside the nervous system. It is common to find healing meningitis at autopsy with respiratory, cardiac, or renal disease as the cause of death.

Optimal therapy demands immediate use of an effective antibiotic that will control the focus of infection, eliminate bacteremia, and diffuse quickly into the central nervous system in bactericidal levels. Antibiotic therapy often must be started before an etiologic diagnosis is known. Also, therapy must prevent bacterial shock and fibrotic complications in the central nervous system. Other complications outside the nervous system must be anticipated, especially in the elderly patient, in whom coexistent chronic disease is most common.

GENERAL THERAPY

General supportive care of the meningitis patient is as important as the use of the proper antibiotic. This phase of treatment is often neglected because of reliance on the magic of antibiotics.

Each patient should be isolated until a diagnosis of meningococcic or tuberculous meningitis can be excluded. In addition to cerebrospinal fluid cultures, blood and nasopharyngeal cultures must be done. Possible associated cardiovascular, genitourinary, gastrointestinal, or pulmonary disease must be evaluated by the usual routine clinical studies, including at least electrocardiograms, renal function tests, and chest films. Complicating disease outside the nervous system often makes care of the adult meningitis patient more difficult than that of the pediatric patient. In many patients, skull roentgenograms are helpful in determining the focus of infection in paranasal sinuses or mastoids or in the area of a fracture.

Central nervous system symptoms, such as restlessness and convulsions, are treated with sedation and anticonvulsants when necessary. Hyperpyrexia should be treated vigorously with

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salicylates and body cooling by sponging or by use of a hypothermal blanket. Oxygen therapy and tracheotomy may be necessary for respiratory problems. Cardiac complications requiring treatment may include arrhythmias and decompensation. Prostatism in the older patient must be evaluated, and an exact measurement of urinary output is especially important when large doses of sulfonamides are being used. L-norepinephrine and corticoids have been found to be very useful in cases of shock.[4,5]

The search for foci of infection and their surgical treatment may be very necessary, as cases with prolonged courses, which finally resolved only after surgical drainage of an infected sinus or mastoid, have been reported.[6] Surgical relief of excessive intracranial pressure is necessary only rarely with current adequate therapy, and it is not necessary to perform a large number of lumbar punctures to reduce spinal fluid pressure or to follow the disease.[4]

STEROID THERAPY

Steroids have been advocated for any overwhelming bacterial infection, including the meningitides.[7,8] Theoretic values of steroids for infection are that they limit shock, reduce inflammation, decrease fever and anorexia, and give the patient a sense of well-being.

Nelson and Goldstein[9] used cortisone for meningococcic meningitis with adrenal hemorrhage in 1951, and it has been standard therapy for this complication since that time. Some writers[5] believe that steroids should be used prophylactically in every case of meningococcic meningitis; others[10] disagree. Ribble and Brande[11] reported only one fatality in 12 cases of pneumococcic meningitis when steroids were added to the usual treatment regimen. They and others[12] have been impressed with the use of steroids in this disease, which has carried a relatively poor prognosis despite antibiotic therapy. They believe that steroids reduce the inflammation which tends to limit antibiotic-bacteria contact and leads to spinal block. Reduction in bacterial hypersensitivity may be another effect of steroids.

Lepper and Spies[2] have been skeptical of the value of steroids in meningitis. They reviewed the records of 55 fatal cases of pyogenic meningitis and found that there was no demonstrable effect in the 25 cases in which steroids had been used. More recently, these investigators[13,14] treated alternate meningitis patients of all ages with steroids and found that, in 57 cases of Hemophilus influenzae meningitis, all patients survived. In 56 cases of meningococcic meningitis, only patients with adrenal collapse died, and, in 23 cases of pneumococcic meningitis, there was 1 death in both the steroid- and nonsteroid-treated groups. They also found that the complication rate was slightly higher in the steroid-treated group and that, in Hemophilus influenzae and meningococcic meningitis, the spinal fluid of the steroid-treated patient returned to normal more slowly. Their final conclusion was that, although steroids are not lifesaving, they do have a place in the treatment of shock, hyperpyrexia, and meningococcemia.

ANTIBIOTICS AND BLOOD-BRAIN BARRIER

A few general comments concerning the passage of antibiotics through the hematoencephalitic barrier are necessary before discussing the treatment of specific meningitides. Sulfadiazine and chloramphenicol appear in the cerebrospinal fluid in large amounts. It is estimated that sulfadiazine levels in the cerebrospinal fluid are two thirds to four fifths of the blood level.[15,16] Cerebrospinal fluid levels of chloramphenicol are 30 to 40 per cent of blood levels when the drug is given by mouth.[17] Streptomycin, chlortetracycline, and erythromycin diffuse poorly into the cerebrospinal fluid.[18-20] Cerebrospinal fluid levels of tetracycline are likewise low; however, Hansen and Koch[21] have shown that tetracycline has been found in bactericidal levels in children with meningitis after oral therapy.

Koch[22] found that oxytetracycline, like other antibiotics, crosses the inflamed blood-brain barrier in substantial amounts but in smaller amounts when there is no inflammation. Unless massive doses of penicillin are used, cerebrospinal fluid levels are very low. Boger and Wilson[23] have shown that penicillin diffuses more readily through the inflamed blood-brain barrier.

In an effort to compensate for the poor diffusion of penicillin across the blood-brain barrier, intrathecal therapy was advocated in the early years of penicillin use. When Dowling and associates[24] established the necessity of using massive doses of penicillin, they condemned intrathecal therapy because of complications of irritative arachnoiditis, myelitis, and radiculitis and failure to assure distribution of the antibiotic. Appelbaum and associates[25] reported that 4 per cent of patients had a reaction such as pyrexia, delirium, or spinal block after intrathecal therapy and that secondary pyogenic meningitis developed in 3 per cent. Because of these reports and improved knowledge of necessary antibiotic dosages, most current reports on the treatment of adult meningitis do not mention intrathecal therapy. An exception occurs when successful treatment depends on the use of a

single antibiotic that will not pass the blood-brain barrier, such as polymyxin B in the treatment of Pseudomonas pyocyanea meningitis. Weinstein,[26] however, favors a single intrathecal injection of streptomycin for H. influenzae meningitis and several injections of intrathecal aqueous penicillin for pneumococcal meningitis. Alexander[27] also advises intrathecal antibiotics for several types of pyogenic meningitis.

PNEUMOCOCCIC MENINGITIS

In the presulfonamide era, pneumococcic meningitis was universally fatal. With the use of sulfonamides, the mortality dropped to 60 to 80 per cent. Considering the dependable action of penicillin on the pneumococcus, it was surprising that Dowling and associates,[24] in 1949, found a 49.2 per cent fatality rate in 319 cases from the literature in which penicillin was the principal treatment.

The poor prognosis of this disease is generally accepted.[6,11,28-30] On the basis of observations by Schwemlein and associates,[31] Dowling and his associates[24] advocated use of 12 million units of penicillin daily in patients with pneumococcic meningitis. With this dose, they found cerebrospinal fluid levels of 0.08 to 1.25 units per cubic centimeter. Previously, it had been concluded that 0.03 units per cubic centimeter was the minimum necessary to sterilize the cerebrospinal fluid.

Currently, administration of 12 to 24 million units of penicillin the first day, with a maintenance dose of 10 to 12 million units daily, is recommended. This may be given according to Dowling's original schedule of 1 million units intramuscularly every two hours or by using aqueous penicillin in an intravenous continuous drip. In most recent reports, intrathecal therapy is not advised. However, Weinstein[26] uses 30,000 units of aqueous penicillin diluted in 10 cc. of saline intrathecally after 15 cc. of cerebrospinal fluid has been removed. He repeats this intrathecal dose twelve to twenty-four hours later.

In addition to penicillin, many clinicians favor use of sulfadiazine in the dose of 6 gm. initially by intravenous drip, followed by 1 gm. every four hours. Such treatment was based on early experience with small doses of penicillin and sulfonamides as combined therapy, which appeared to improve clinical results.[6,32] Experimental studies[33] with animals offer theoretic support for such combination therapy. Other authors[34] feel that the simultaneous use of sulfonamides and penicillin is contraindicated.

Use of probenecid to enhance penicillin blood levels is occasionally recommended.[35] As has been mentioned, use of steroids has been favored by some writers.[11,12] Recent reports, however, question the value of this therapy.

In an effort to reduce fibrotic complications in pneumococcic meningitis, Johnson and associates[36] have used intrathecal pancreatic desoxyribonuclease in 25 cases. Of these, 16 were over the age of 50. In the 25 cases, there were 3 deaths, 2 of which were not related to the meningitis. This therapy is experimental and is not advised for the average case at this time.

Typically, the treated patient is out of coma in two to four days and is afebrile in five to six days. Therapy probably can be discontinued when cerebrospinal fluid sugar rises and bacteria disappear. Some physicians prefer to wait for the disappearance of pleocytosis. Relapse, if it is to occur, will be evident within forty-eight hours after antibiotics have been discontinued.[37] Recent series[11,13,36] on the treatment of pneumococcic meningitis indicate a mortality of less than 15 per cent.

MENINGOCOCCIC MENINGITIS

Vieusseux first reported meningococcic meningitis in 1805,[38] and attention was immediately attracted to this fulminating disease because of its occurrence in epidemics. It is stated that adult cases are rarely seen except under unhygienic conditions favorable to epidemic spread. The highest recent morbidity occurred during World Wars I and II. Daniels[3] states that the death rate in World War I was 33 per cent of 2,466 United States Army cases and, in World War II, 3.6 per cent of 11,332 cases. In analyzing the pathology in 300 deaths from meningococcemia in World War II, he found that 48 per cent died of meningitis, 42 per cent died of fulminant meningococcic bacteremia with adrenal hemorrhage, and the remainder died of bacteremia without evidence of meningitis or adrenal hemorrhage.

Untreated cases showed a mortality of 75 per cent. Antiserum was first used in this country by Flexner[39] in 1906, and the mortality was reduced to 30 per cent. The antiserum, however, was not polyvalent, and the mortality in various epidemics was similar to that of the untreated cases. In 1939, Banks[40] reported 31 cases treated with sulfonamides without a death. In 1943, Beeson and Westerman[41] reviewed 3,575 cases treated with sulfonamides and found a fatality rate of 15 per cent.

Strains of meningococcus resistant to sulfonamides have not been found.[42] In spite of the advent of newer, more soluble sulfonamides, most clinicians favor the use of sulfadiazine. Initially, the dose can be 5 gm. of the sodium salt

intravenously, followed by 2.5 gm. intravenously every twelve hours.[26] When oral treatment can be started, the maintenance dose is 1 gm. every four hours. A comparable schedule is 8 to 10 gm. intravenously the first day, with one third given initially and the remainder throughout the day. The urine should be kept alkaline, and, if sulfadiazine levels are maintained at 10 to 15 mg. per 100 cc. of blood and 7 to 10 mg. per 100 cc. of cerebrospinal fluid, treatment should be adequate.[4] If more soluble sulfonamides are used, the dose should be slightly higher.

Some clinicians[5,27] prefer to augment sulfadiazine with penicillin early in the disease. The rationale for using penicillin is the reported delay before the maximum antimeningococcic effect is achieved. It is felt also that penicillin may have a more immediate though less decisive effect. It has been stated[34] that 1 to 2 million units of penicillin alone every two hours can be effective in meningococcemia.

Cortisone treatment of adrenal collapse in meningococcemia was established in 1951 by Nelson and Goldstein.[9] Many physicians feel that use of pressor amines is also very important. Cassidy[5] treated 17 young adults with meningococcic meningitis prophylactically with steroids and, in spite of the presence of meningococcemic petechiae in 10 patients, there were no fatalities. He used 300 mg. of hydrocortisone daily until there was no danger of insult to the adrenal glands. Others[10] do not favor the prophylactic use of steroids.

Therapy can be terminated after a rise in cerebrospinal fluid sugar and disappearance of bacteria. Renal complications of sulfadiazine therapy may include acute renal glomerular lesions and lower nephron nephrosis.[13] Ureteral obstruction due to sulfonamide precipitation has also been seen.[11]

HEMOPHILUS INFLUENZAE MENINGITIS

In 1958, Selman and Seides[15] reviewed 32 adult cases of H. influenzae meningitis in the literature and concluded that these cases were clinically indistinguishable from other pyogenic meningitides. Before the sulfonamide era, 8 of 16 adult patients recovered from H. influenzae meningitis; since 1937, all reported adult cases have recovered. It has been found that all antibiotics, including penicillin, are effective in vitro against H. influenzae.[16] In recent reports of adult meningitis,[17-19] various antibiotics have been used.

Appelbaum[4] prefers to use streptomycin and chloramphenicol. He continues the latter for five to seven days after the patient is afebrile. Others favor the combination of chloramphenicol and sulfadiazine. Weinstein[26] uses intramuscular streptomycin and sulfadiazine and also gives a single intrathecal injection of 35 mg. of streptomycin in 10 cc. of saline. He removes 15 cc. of cerebrospinal fluid and gives the intrathecal streptomycin slowly over a ten-minute period.

A majority of clinicians do not favor the use of intrathecal antibiotics in this disease. Also, in most case reports, the diagnosis was invariably missed until spinal fluid culture results were returned.

STAPHYLOCOCCIC MENINGITIS

Staphylococcic meningitis may be a complication of staphylococcic bacteremia or may be secondary to a facial infection or an osteomyelitis. An occasional case may follow a lumbar puncture. Penicillin is used on the basis of sensitivity tests. At the present time, it is estimated that only 25 per cent of staphylococci are penicillin-sensitive. If the staphylococci are sensitive, the dose of penicillin is 12 million units daily. If the bacteria are penicillin-resistant, 30 to 40 million units daily, plus an antibiotic indicated by sensitivity tests, is advised. Erythromycin, in doses of 2 to 4 gm. daily; chloramphenicol, 2 to 3 gm. daily; or Novobiocin, 2 gm. daily, are most frequently indicated.[4] Alexander[27] and Weinstein[26] favor the simultaneous use of penicillin, erythromycin, and chloramphenicol.

STREPTOCOCCIC MENINGITIS

Streptococcic meningitis is usually secondary to otitis, mastoiditis, sinusitis, bacterial endocarditis, or head injury. Usually, hemolytic streptococci cause the disease. Rarely, enterococci may be the etiologic agent. Petechiae may be present, and streptococcic meningitis may mimic other bacterial meningitides in other ways. Penicillin, in the dose used for pneumococcic meningitis, is the treatment of choice, and sulfonamides are added in some severe cases. Some physicians[27] prefer to use chloramphenicol in addition to penicillin and sulfadiazine. Since most strains of enterococci are penicillin-resistant, streptomycin should be added in these cases.

MENINGITIS DUE TO GRAM-NEGATIVE BACILLI

Bacteremia of gram-negative bacilli may cause vascular collapse due to effects of the endotoxin. Mortality is high in these meningitides for this reason and because of the poor diffusion of effective antibiotics into the cerebrospinal fluid. Therefore, for these meningitides, as for pneumococcic meningitis, steroids and intrathecal antibiotics have been advised.

Pseudomonas pyocyanea meningitis is best

treated with intrathecal polymyxin B. This agent does not pass the blood-brain barrier. The intrathecal dose is 2 to 5 mg. in 10 cc. saline, with simultaneous intramuscular administration of 25 to 50 mg. every six hours.[50] Successful treatment has been reported using streptomycin and sulfadiazine. Many cases of this disease have been attributed to contaminated intrathecal antibiotic or anesthetic solutions.

Escherichia coli meningitis is found primarily in newborn infants, but occasional adult cases have been reported. Treatment with intramuscular and intrathecal streptomycin combined with sulfadiazine and chloramphenicol is usually most successful.[4]

A review of 119 cases of Klebsiella pneumoniae meningitis, including 36 adult cases, showed a mortality of 50 per cent.[51] Therapy must be individualized, as all antibiotics have failed. The tetracyclines are of no value; sulfadiazine and streptomycin probably are the best agents. Weinstein[26] advises 1 gm. of streptomycin daily and 1 gm. of chloramphenicol every six hours.

SUMMARY

General and specific therapies of various etiologic types of pyogenic meningitis have been discussed. Mortality is frequently influenced by the acuity of the disease and the previous health of the patient, despite use of the proper antibiotic. Anticipation of complications outside the central nervous system is important.

Chloramphenicol and sulfonamides are the only antibiotics, except for isoniazid, which penetrate the blood-brain barrier in large amounts. Penicillin, when given in massive doses, is found in bactericidal levels in the cerebrospinal fluid. Intrathecal therapy is indicated only rarely. The value of the routine use of steroids in meningitis has not been established.

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Ischemic S-T segment depression is the only valid electrocardiographic evidence of coronary atherosclerosis and insufficiency after the double standard 2-step exercise test. The degree of such horizontal or sagging depression may reflect the seriousness of the coronary disease. Sagging S-T segments and diphasic or inverted T waves probably denote more serious insufficiency. S-T junction depression is a normal response. Among about 900 persons traced ten years after examination, the death rate from coronary disease was about 8 times higher for patients with ischemic S-T segment depression noted on recordings than for those with S-T junction depression or normal recordings.

G. P. Robb and H. H. Marks: Evaluation of type and degree of change in postexercise electrocardiogram in detecting coronary artery disease. Proc. Soc. Exper. Biol. & Med. 103:450-452, 1960.

Local injection of vasopressin significantly reduces blood loss during gynecologic operations. A dilute solution containing 4 units or less of the hormone was used at Cornell University Hospital, New York City, for procedures such as myomectomy, conization of the cervix, and vaginal hysterectomy for 80 women. Transfusion requirements were greatly reduced as compared with those in a similar number of controls. No cardiovascular complications or other side reactions were observed. The effect of vasopressin was the same whether the purified natural, synthetic, or commercially available form (Pitressin) was used.

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Concentrations of seromucoid (mucoprotein), the perchlorate-soluble, phosphotungstate-precipitable substance from serum, are reduced in patients with Marfan's syndrome as compared to controls. Acid mucopolysaccharide values, however, are increased. Seromucoid content of hexose, hexosamine, sialic acid, and fucose is generally the same in patients with the syndrome and in controls, as are results of seromucoid chromatography on diethylaminoethyl-cellulose columns. The pattern of increased acid mucopolysaccharide and decreased seromucoid values may have both diagnostic and pathogenetic significance.

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Degenerative Diseases of the Nervous System

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THERE ARE a large number of diseases of undetermined etiology that implicate the nervous system. At the present time, these are often classified as degenerative in nature. Fortunately, with a few exceptions, these conditions are relatively uncommon. Most of them seem to have specific predilection for different age groups and therefore will be discussed accordingly. Only the more frequent of this large group of diseases will be included in this paper.

INFANCY

Tay-Sachs disease (amaurotic familial idiocy). This is probably a familial metabolic disturbance of the nervous system which may affect many age groups. The best known type occurs in infancy.

The infant usually develops normally for the first six months of life. Often, visual impairment is first noticed when the infant loses his following reaction. Within a short time, most of the learned activities are lost, with a coincidental progressive weakness of the neck, trunk, and extremities. The limbs at first become flaccid but terminally are spastic with hyperactive reflexes. Myoclonic jerks and even convulsions may occur. Vision decreases and is soon completely lost. Terminally, the infant becomes vegetative and usually dies about one to two years after the onset of the illness.

The diagnosis can easily be established by examination of the fundi. There is a marked atrophy of the optic nerve and a *cherry-red spot in the center of an atrophic macula.*

Tuberous sclerosis. This is a herditofamilial disorder characterized clinically by *convulsions, facial nevi,* and *mental retardation.* Onset of this disease is usually before the age of 5 years, and both sexes are affected. The diagnosis should be suspected when seizures occur in the presence of various types of skin lesions. The most common skin manifestation is the so-called adenoma sebaceum, which consists of yellowish nevi distributed over the nose and cheeks in a butterfly fashion. Other types of skin lesions may also be present, such as café-au-lait spots (brownish discolored areas), shagreen patches (areas of fibrous hyperplasia of skin) in the lumbar region, and areas of vitiligo.

Any degree of mental retardation may be present, including complete idiocy. Visceral abnormalities are commonly encountered. Two thirds of the patients have renal tumors, and many have tumors of the heart, liver, pancreas, or ovaries. Occasionally, even skeletal abnormalities, such as polydactylism, spina bifida, and hydrocephalus, may be present.

Treatment is symptomatic. The seizures can be medicinally controlled. Usually, the mental retardation requires institutionalization.

Neurofibromatosis (von Recklinghausen's disease). This is a strongly hereditary disease characterized by the development of multiple tumors of the spinal and cranial nerves, *tumors of the skin,* and *cutaneous pigmentation.*

The skin lesions consist of scattered cutaneous tumors of varying size and consistency, which are often present at birth but increase during puberty. These tumors are usually soft fibromas but may also be angiomas and lipomas. In addition to these tumors, the skin contains numerous café-au-lait spots.

Involvement of the terminal distribution of the nerves may be accompanied by diffuse fibrosis and enlargement of the affected part, re-

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sulting in enlargement of the extremity or hypertrophy of one half of the face, lips, tongue, or ear (elephantiasis neuromatosa).

Skeletal defects are extremely common and consist of malformations of the fingers, congenital absence of bones, absence of roof of the orbit, rarefaction of bones of the pelvis, and so forth.

Tumors of the spinal nerves may result in spinal cord compression, while neuromas of the eighth nerve can cause brain stem symptoms.

Demyelinating diseases (Leukodystrophies). Progressive diseases usually occur early in life and are characterized by widespread demyelination of the white matter of the brain, manifested by *mental retardation* and, often, *spastic paralysis* and incoordination. Both sporadic and familial cases are encountered.

A strongly familial form that has been described in infants is often introduced by fever which subsides in a few weeks and is followed by such signs of regression as loss of learned activities, spasticity, convulsions, and loss of vision. As the disease progresses, decerebrate rigidity results, often accompanied by total blindness and deafness. Death usually occurs before the end of the first year (Krabbe's disease).

A more chronic form of the illness is seen in older children, often siblings, and produces chiefly cerebellar signs, such as a stiff, unsteady gait; tremor of the hands; and bizarre movements of the eyes. The incoordination of the limbs increases in severity and is finally accompanied by spasticity of the limbs and ataxia of the trunk (Pelizaeus-Merzbacher disease).

The life expectancy is a few years, although temporary arrest of the illness can occur.

In one form of this disease, metachromatic granules are deposited in the brain as well as in organs outside of the nervous system. This form of the illness can be diagnosed during life by finding the abnormal material in centrifuged urine sediment stained with certain aniline dyes such as toluidine blue.

Progressive muscular atrophy. The infantile form of this disease (Werdnig-Hoffmann disease) has its onset during the first year of life and is characterized by a *widespread weakness and atrophy of the musculature* due to involvement of the anterior horn cells of the spinal cord of unknown etiology. Both sexes are equally implicated.

Onset of symptoms usually occurs between the sixth and ninth month of life. The infant has trouble holding up its head and slowly loses previously developed motor activity. The muscles of the limbs and trunk become progressively weak and atrophic. The deep reflexes are absent but may be active. Cutaneous sensibility remains uninvolved. The bulbar musculature becomes affected terminally and is usually the cause of death. The course is progressive, with death usually occurring within a year or two after onset of illness.

Progressive muscular dystrophy. This is a *chronic*, progressive *wasting disease* of the *skeletal musculature* with a strong *familial tendency.* The disease usually begins early in childhood but occasionally may first appear late in adolescence. A pseudohypertrophic form of the illness begins as early as the second year of life and progresses slowly, terminating fatally before the age of 20 years.

The muscle weakness begins in the hip muscles, resulting in a waddling gait. The back muscles soon become weak and atrophic, so that the child has difficulty sitting up or getting up from a reclining position. A marked scoliosis develops. The calf muscles are hypertrophied but weak. The deep reflexes are absent. As the disease progresses, it spreads to involve the muscles of the upper limbs, chiefly those of the shoulder girdle. All of the involved muscles become weak and atrophic. Ultimately, the child becomes chair- or bedridden.

Treatment is symptomatic. Hydrotherapy, gentle massage, and mild exercise may be of help. No medication has proved of specific benefit.

YOUTH

Schilder's disease. This is a slowly progressive degenerative disease of the brain which occurs chiefly in children and young adults and results in *blindness*, *spasticity* of all limbs, and progressive *mental deterioration.* It is a disease of the white matter of the brain of unknown etiology and occurs as a sporadic illness.

The sequence of the clinical picture depends upon the areas of the brain first involved. In a typical case, visual impairment develops first and slowly progresses to complete blindness. However, the pupillary reflexes and the fundi remain normal. As vision is lost, spasticity of the limbs develops and becomes prominent. Mental deterioration soon sets in and progresses to dementia.

Since this process can begin in any part of the brain, many cases are not typical and early show quite variable symptoms and signs related to that part of the brain first involved. Occasionally, in children, the presenting symptoms are headache, vomiting, and convulsions. As the illness progresses, weakness and spasticity occur

and may remain unilateral for a long time. However, in all cases, the course characteristically is slowly progressive, with terminal visual impairment, mental deterioration, and spasticity. The disease lasts from a few months to several years. Treatment is strictly symptomatic.

Muscular dystrophy. This chronic, progressive wasting disease of the skeletal musculature appears most commonly in late childhood and youth and affects the sexes equally. In this form of the disease, the muscles of the face, arms, and shoulder girdle are first affected (facioscapulohumeral type of Landouzy-Déjerine dystrophy), resulting in *atrophic facial musculature* (myopathic facies), *winged scapulae*, and marked *wasting of the shoulder girdle* and *proximal muscles of the arms.*

The course of this illness is often very slow, and patients may live their full span of years, although partially incapacitated. Occasionally, the illness becomes arrested and may even improve a little. If the course is progressive, the lower extremities may become implicated, with the predominant involvement in the pelvic girdle muscles and those of the proximal part of the extremities.

Progressive muscular atrophy. This is a chronic degenerative disease of the motor cells of the spinal cord, beginning in the cervical cord and producing *flaccid weakness* of the limbs, marked *muscle wasting, fasciculations*, and *no sensory disturbances.* It is a sporadic disease that implicates young adults, with males being more frequently involved.

In the typical case (Aran-Duchenne type), the process begins in the small muscles of the hands, with wasting of the thenar and hypothenar eminences, deepening of the interosseous spaces, and a flattening of the entire hand due to muscle wasting. As the process progresses, it spreads to the forearm, arm, shoulder, and, later, to the back muscles, producing extreme weakness and muscle atrophy. The limb then hangs limply and there is a winging of the scapulae. The lower extremities are involved late in the disease, also beginning distally in the feet and spreading upward. Ultimately, the patient may have trouble walking or holding up his head. Terminally, the bulbar musculature may be implicated. Fasciculations are usually prominent in the muscles affected, and the deep reflexes disappear early in the disease. Sensation and the intellect are both spared.

Although the disease is usually progressive, it may remain stationary for years or may even show mild remissions. Usually this form of the disease, although progressive, tends to spare the bulbar musculature and causes little or no threat to life.

Treatment is limited. Vitamin therapy, chiefly B and E, may be tried. Rest and avoidance of exertion are helpful in making the patient more comfortable. Orthopedic appliances may improve the patient's usefulness.

Friedreich's ataxia. This is a progressive familial degenerative disease involving the spinal cord and cerebellum and producing a slowly increasing *ataxia* appearing in *siblings. Clubfoot* and *scoliosis* are present in a high percentage of cases.

The first indication of this illness is the gait disturbance, which manifests itself in stumbling, falling, and difficulty in climbing stairs. As the disease progresses, the upper limbs also become incoordinated and the speech is slow, scanning, and dysarthric.

The posterior columns of the spinal cord are invariably involved, resulting in a loss of deep sensation. Weakness of the muscles occurs but is rarely severe or extensive. Mentality is intact, but, in advanced cases, some progressive dementia may occur.

In the average case, the course is progressive, with complete incapacity by the age of 25 years. Death may result from intercurrent infection or bulbar involvement.

ADULT

Multiple sclerosis. This is one of the most common neurologic diseases of this age group. It is of unknown etiology and affects both sexes equally. It is characterized clinically by *exacerbations* and *remission of symptoms* and by the *scattered lesions* within the nervous system.

The exact age of onset is often difficult to determine because of the fleeting character of the early symptoms. These may be very vague and consist of episodes of giddiness, paresthesia, ill-defined visual complaints, and lability of emotions. The neurologic findings at this time are also too trivial for diagnosis, revealing absent abdominal reflexes, nonsymmetric reflexes, a few beats of clonus, and questionable toe signs.

Any of the cranial nerves may be involved and may be the presenting symptom. Optic nerve involvement produces retrobulbar neuritis with acute visual loss. Oculomotor weakness results in diplopia, and eighth nerve disturbance produces nystagmus. All of these cranial nerve complaints are transient and improve after a few weeks.

In the more obvious form of the illness, the patient develops clear-cut scattered neurologic disturbances that may implicate any part of the

nervous system. Spastic weakness of one or both limbs is one of the most common signs. Cerebellar involvement is frequently seen in the younger age group and results in bilateral incoordination of the limbs, unsteady gait, intention tremor, and dysarthric speech. Sensory disturbances are also common and consist of areas of hypesthesia, paresthesia, and impaired deep sensation. These neurologic disturbances usually appear dramatically and spontaneously improve, either completely or partially, within a few weeks or months. Similar or different neurologic disturbances may recur within a few weeks or months or may be delayed for years. Generally, each episode of involvement leaves some degree of residual effect, so that, in many cases, increasing disability results over a period of years. A neurologic examination carried out during an exacerbation of this illness usually reveals evidence of widespread scattered neurologic involvement in the form of vertical nystagmus, dysarthria, unequal deep reflexes, spasticity, intention tremor, sensory disturbances, optic atrophy, and so on.

Although cerebral involvement is common pathologically, clinical evidence of such lesions usually is not too apparent in most cases. Euphoria and depression may occur. Actual intellectual impairment occurs in less than 20 per cent of the patients.

Since multiple sclerosis can resemble a number of other neurologic illnesses, certain precautions should be taken in making this diagnosis. One should hesitate to make a diagnosis of this disease in the following situations: (1) if onset of the illness occurs after the age of 45 years; (2) if there is evidence of only a single lesion within the nervous system; (3) if the course of the illness is progressive without remissions and exacerbations; (4) if true papilledema is present (occurs in less than 1 per cent of cases); (5) if convulsions occur; and (6) if a true mononeuritis is present.

There is no specific treatment for this disease. The acute illness often responds well to a course of intravenous ACTH. Intravenous histamine also has been advocated for the acute illness. During the phase of remission, these patients can be treated with intramuscular liver, various vitamin combinations, and vasodilators. Most popular in the treatment is niacin, which is available in a number of forms, such as Roniacol and Nemase (niacin plus large doses of vitamins). Chilling and overfatigue should be avoided. If severe neurologic disabilities occur, physical and corrective therapy may prove helpful.

Syringomyelia. This condition consists typically of a cavitation occurring in the center of the spinal cord. It begins as a slowly progressive, relatively benign type of glial increase, which breaks down into a cystic cavity. This cavitation usually involves the lower cervical cord, with primary implication of the upper extremities. Although centrally located, it tends to extend irregularly throughout the cord.

The earliest and most characteristic clinical manifestation is a *segmental loss* of *pain and temperature* with *preservation of light touch.* At onset, the patient may be unaware of this involvement and frequently burns or injures his hands without knowing it. Spread of the lesion to the motor cells soon produces *weakness* and *atrophy of the hand muscles,* resembling a progressive muscular atrophy. Trophic and vasomotor disturbances are very common; the skin becomes hard and thick and perforating ulcers may occur. A *Charcot joint* in the upper extremities is very suggestive of this illness. Horner's syndrome (miosis, ptosis, and enophthalmos) also is frequently seen. If the condition extends to the medulla (syringobulbia), there may be the additional findings of atrophy and fasciculation of the tongue, dysphagia, and sensory disturbances over the face.

The course of this disease is prolonged over many years, although remissions may occur. Eventually these patients become bedridden and are plagued by severe pains.

Treatment is limited. Deep x-ray therapy occasionally stops the progression of symptoms. Surgery may be instituted to evacuate the cyst and decompress the spinal cord.

Hereditary ataxia. This is a strongly hereditary or familial form of ataxia that occurs in an older age group than does Friedreich's ataxia. It shows *no spinal cord involvement nor* the presence of *skeletal abnormalities.*

The initial symptom is ataxia of gait, followed later by involvement of the upper limbs. Optic atrophy, oculomotor palsies, and dysarthria may occur. The deep reflexes are hyperactive. The course is progressive but very slow, so that incapacitation does not occur until very late in the illness.

MIDDLE AGE

Combined degeneration of spinal cord. This is a chronic disease implicating chiefly the posterior and lateral columns of the cord. In some cases, only the pyramidal tracts are involved, producing *bilateral lower limb spasticity* manifested by a slowing of gait and great difficulty in going down stairs. More commonly, however, both the pyramidal as well as the posterior columns are involved, resulting in a subacute combined

syndrome with an *ataxic* as well as a *spastic gait*. The deep reflexes are often absent, and vibration and sense of position are impaired.

Many intrinsic as well as extrinsic conditions may produce a progressive spastic diplegia. A careful survey of the possible etiologic factors is necessary before concluding that the condition is of an unknown degenerative nature.

1. Pernicious anemia frequently produces a subacute combined degeneration of the cord. This form of the disease is often introduced by dysesthesia of the hands and feet, which persists throughout the illness. Diagnosis of this form of the disease can be verified by the associated achlorhydria, glossitis, macrocytic anemia, and megaloblasts in the peripheral smear. Treatment consists of vitamin B_{12} or crude liver extract.

2. Vitamin deficiency secondary to a gastric carcinoma, bowel obstruction, dysentery, or bowel resection may produce a mild progressive combined degeneration of the spinal cord. Large doses of intramuscular vitamins, chiefly B and C, will arrest the progress of the illness.

3. Pellagra is occasionally seen in individuals who have had a diet deficient in thiamine chloride and nicotinic acid, often associated with high carbohydrate intake. In prolonged cases, a typical subacute combined degeneration of the spinal cord results and is often accompanied by confusion, delusions, and even dementia. The diagnosis should be suspected from the associated findings of a symmetric dermatitis of the hands, wrist, elbows, and neck (exposed parts); pigmentation and thickening of the skin; glossitis; and stomatitis.

4. Extramedullary tumors, such as meningiomas and neuromas that compress the thoracic cord, may produce the typical picture of a slowly progressive, subacute combined degeneration of the spinal cord. The diagnosis can often be established only by myelography.

5. Certain poisons, such as arsenic, lead, and ergot, can occasionally produce the syndrome of combined degeneration of the spinal cord.

6. After all of the foregoing diagnostic possibilities have been eliminated, the physician is often left with a diagnosis of combined degeneration of undetermined etiology. Many feel that this form of the disease should be classified with multiple sclerosis. However, the later onset of this disease, the progressive course without remissions, and the limitation of the lesion to specific segments of the spinal cord suggest that this process is probably not multiple sclerosis but some other form of degenerative disease, the etiology of which has not as yet been discovered.

Amyotrophic lateral sclerosis. This is probably a symptom complex in which both upper and lower motor neurons are affected by a number of different etiologic agents.

The clinical picture varies, depending upon which area of the spinal axis is first implicated. There is often a *progressive muscular weakness* and atrophy implicating the *limbs* or the *bulbar musculature* in a somewhat asymmetric distribution. *Fasciculations* occur early and at the onset may be limited to the hands, tongue, and shoulder musculature. In spite of the progressive and often marked weakness and atrophy, the *deep reflexes* are present and often *hyperactive*, indicating involvement of the pyramidal system. Sensory disturbances are entirely absent.

As the disease progresses, the limbs become more atrophic and finally completely paralyzed and the deep reflexes may terminally disappear. Speech becomes indistinct and swallowing is difficult. Death usually occurs within a few years after the onset from bulbar palsy or an intercurrent infection. No treatment procedures have proved of value.

Spondylosis with spinal cord disease. This condition usually occurs in individuals in the middle and older age groups. It is basically an osteoarthritis of the cervical vertebrae in which the cervical cord is slowly compressed by the arthritic bony proliferations.

Clinically, the symptoms develop very insidiously, with a slowly *progressive spasticity* of *both lower extremities* associated with hyperreflexia. Occasionally the posterior columns are also involved, resulting in a disturbed sense of position and some incoordination. *Atrophy* and *fasciculations* are frequently seen in the upper extremities, with weakness being most marked in the hand musculature. Often pain or paresthesia is present, chiefly in the upper limbs radiating to the outer aspect of the hands.

Spinal fluid examination is usually normal but may show an increase in protein. The diagnosis is established by myelography, which will reveal the bony proliferation and the spinal cord compression.

Treatment consists of decompression of the cervical region and section of the dentate ligaments. This often alleviates the symptoms and prevents further progression of the illness.

Presenile deterioration (Psychosis). This condition is a *progressive dementia,* occurring most frequently between the *ages of 40 and 60* years. It is of unknown etiology and often has a hereditary tendency. It occurs in two forms known as Alzheimer's disease and Pick's disease.

Onset of the illness is gradual, with a pro-

gressive intellectual deterioration often associated with scattered focal neurologic findings. One of the first manifestations is memory impairment, with a definite slowness in cerebration. The patient loses his ability to perform his routine duties efficiently and may become slovenly in habit and dress. This disease progresses to a profound deterioration involving all components of the intellectual sphere associated with widespread neurologic signs, such as aphasia, tremor, scattered motor weakness, incoordination, unequal reflexes, and, occasionally, seizures. Death results from some intercurrent infection when the state of physical debility is reached.

Laboratory studies are usually normal. An air encephalogram often reveals cortical atrophy of the brain substance and enlargement of the ventricles. No treatment is available. These patients usually require institutionalization when the dementia becomes far advanced.

Senile dementia. This condition occurs in the elderly age group and is due either to primary degeneration of the brain elements or to diffuse vascular changes resulting in a secondary degenerative process. In either group of cases, the clinical manifestations are similar and the exact etiologic mechanism cannot be determined prior to death.

Onset is gradual over several years. The first symptoms consist of minor personality changes, such as loss of energy, nervousness, and hypochondriac complaints. Soon the patient shows minor defects in judgment, slowing of the thinking process, and defects in abstract thinking. He becomes obstinate and fixed in his patterns of behavior. Trivial happenings may precipitate emotional outbursts. He begins to misplace articles and show marked memory defects, particularly for recent events. With progression of the illness, the intellectual disturbance is accentuated. The patient lives largely in the past, appears childish, and has marked emotional instability with rapid mood swings. Gaps in memory are filled with fabrication. With further deterioration, he may become aggressive, antisocial, immoral with a loss of all previous moral and ethical standards, and increasingly restless and may wander and become lost. Delusional trends often develop and may be paranoid, depressive, or hypochondriac.

With the mental deterioration, there is often evidence of physical deterioration, manifested by headaches, vertigo, scattered weakness, convulsions, weight loss, gait disturbance, and skin changes.

The mental deterioration usually progresses to a state of complete vegetation and requires institutional care terminally.

Parenchymatous cerebellar degeneration. This disease occurs sporadically and consists of a progressive atrophy of the cerebellar cortex in individuals between the fourth and sixth decades.

Onset of this illness is gradual, with a progressive gait disturbance. The *ataxia* appears to remain *localized to the lower limbs* but, in some cases, may implicate the upper extremities and even speech. The course of the disease is slowly progressive, and treatment is symptomatic.

In the treatment of acute gouty arthritis, desacetylmethylcolchicine (DMC), desacetylthiocolchicine (DTC), and trimethylcolchicinic acid (TMCA) are effective; colchicoside is somewhat beneficial; and colchiceine is ineffective. DMC and DTC may produce agranulocytosis, but TMCA apparently does not have such toxicity. Antigout and antimitotic effects of colchicine and some of its analogues can be distinguished by changes in the molecular structure. The specific configuration of the side chains on the third ring of the colchicine molecule seems to be necessary in order to elicit the antigout effect.

S. L. Wallace. Colchicine analogues in the treatment of acute gout. Arthritis & Rheumatism 2:389-395, 1959.

Corticosteroid Hormones in the Treatment of Pleurisy with Effusion

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It has long been held that pleurisy with effusion usually is of tuberculous origin. Roper and Waring[1] recently outlined with great accuracy the historic review of that opinion. It is true that bacteriologic evidence of the tuberculous origin is not always detectable. The test is not performed in some cases, and bacteriologic findings in the pleural fluid are negative in others in spite of the specific etiology. In a series of 141 patients, these authors found 51 positive, 48 negative, and 42 who did not undergo laboratory procedures. Skaggs and Smiley,[2] dealing with a series of 50 patients, performed the test in 29 with 7 positive results. When more objective evaluation is possible, for instance, by pleural biopsy, the incidence of positive cases increases, as shown by Stead and associates[3] with 15 positive results in 24 patients observed by direct pleural exploration and Sutliff and co-workers[4] with 17 positive results in 21 patients. Schless and associates[5] found 38 positive and 25 nontuberculous patients in a series of 63 with effusion who had undergone thoracotomy. They point out the minor diagnostic significance of bacteriologic evaluations of pleural effusion owing to the low incidence of positive results, as well of the tuberculin test which is only valuable when negative because it then excludes tuberculosis. Douglass and co-workers[6] present an account of 21 surgically treated patients with only 5 cases of tuberculosis, which shows that there is always a certain number of pleurisy cases of a different etiology.

On the other hand, we should always keep in mind that the incidence of pulmonary tuberculosis in patients who have previously had pleurisy with effusion is very high. In the 141 patients of Roper and Waring,[1] the incidence of relapse after pleurisy was 65.2 per cent, including bacilli-negative effusion (60.4 per cent) and those not submitted to tests (71.4 per cent). In a series of 49 patients with pleural effusion, Ibiapina[7] found 57 per cent in whom pulmonary tuberculosis developed or who already suffered from that infection. He believes that this relationship is so important that he considers primary pleurisy an initial feature of tuberculous disease of the lungs. That relationship was also established by Scheel[8] and Wallgren[9] in primary infection of childhood. Malmros and Hedvall[10] found pleurisy in 23 per cent of adults with tuberculous primary infection.

These findings do not support the opinion that pleurisy with effusion is a benign affair; on the contrary, it is a grave complication frequently tuberculous in its nature and part of a generalized infectious process. This was evidenced by Soltys and Jennings,[11] who found a rapid dissemination of tubercle bacilli after infection and hepatic tuberculous lesions, as demonstrated by liver biopsies in 3 of 8 young adults with primary pleurisy with effusion.[1]

The pleura may be involved by direct propagation from a parenchymal focus not detectable by the usual means of investigation or by lymphohematogenic dissemination from a distant focus, as is stressed by Redeker.[12] The occurrence of effusion depends, however, upon the intensity of the reactivation of the host through pleural hypersensitivity evinced by exudation. Experimental evidence of this fact was supplied by Paterson,[13] who was able to induce effusion only in guinea pigs previously sensitized by inoculation of avirulent bacilli. In the control group, there was no incidence of effusion.

During a long period of time, in spite of knowledge of the relationship between pleurisy with effusion and pulmonary tuberculosis, the treatment of that pathologic condition was restricted to a policy of expectancy. According to general belief, pleurisy was a benign illness and

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effusion would resorb spontaneously. As a matter of fact, that resorption occurred in some instances, but the patients were handicapped by a multitude of adverse sequelae, among which were suppuration and functional disorders of the underlying lung, with pleural thickening and thoracic deformity. The inauguration of the chemotherapeutic era afforded the opportunity to prescribe such agents in the treatment of pleurisy, which was considered analogous to minimal tuberculosis and required, therefore, medical treatment for at least a year, even though confirmatory bacteriologic evidence could not be obtained. This policy is salutary insofar as it considers the possibility of an early or future reactivation of pulmonary tuberculosis, as demonstrated by Falk and Stead,[14] who found 4 per cent of tuberculous complications in patients with pleurisy who were receiving chemotherapy as against 19 per cent in the untreated group. The rate with which the effusion is resorbed, however, is not influenced by chemotherapeutic agents, so that the hazard of remote functional disturbances persists. Mackay-Dick and Rothnie[15] made a comparative analysis of 140 patients submitted to routine conservative procedures and 50 cases treated with frequent aspiration, physiotherapy, and chemotherapy with isoniazide and streptomycin, in which the results of this second technic were the more favorable. Nevertheless, the most favorable cases took at least three and a half months to be resorbed. Of large effusions, 60 per cent cleared in six and a half months. Neither complications from aspiration nor thoracic deformities occurred, but still the time of resorption was very long.

With the introduction of adrenopituitary hormones, hastening the resorption of the exudate has been tried, taking advantage of the specific activity of the hormone in modifying the reactional capacity of the host. In fact, those hormones show a striking antiallergic and anti-inflammatory activity and are also able to accelerate the process of resorption by modifying the pleural reactivation. These alterations of hypersensitivity have been carefully scrutinized by Ebert.[16] Several authors, mostly Europeans[17–19] gathered a reasonable amount of experience with fairly encouraging results. Although there is convincing evidence that such hormones may adversely affect active or silent tuberculosis,[20] it is also well known that the concurrent use of specific chemotherapy will protect the patient from those deleterious effects.[21,22] In spite of this fact, the use of corticosteroids in pulmonary tuberculosis has been fairly restricted in the United States.[23]

For the foregoing reasons, we found it interesting to report the results achieved in 15 patients with primary pleurisy with effusion treated with prednisone and specific chemotherapy.

MATERIAL AND METHODS

The material analyzed is represented by a group of 15 patients, 10 females and 5 males, of whom 11 were white and 4 were nonwhite. The ages of the 15 patients ranged from 18 to 60 years; the pleural effusion was on the right side in 8 and on the left in 7. All patients had effusion established prior to the first medical examination, and only in 1 case was the coexistence of pulmonary tuberculosis evident. In no instance was the fluid aspirated, so that there was no bacteriologic evidence of the tubercular nature of the exudate. Even in instances of total effusion of one hemithorax with dyspnea and marked shift of the mediastinum, the pleural fluid was not removed. All patients showed the clinical and roentgenographic picture of pleural effusion. Treatment consisted of daily doses of 1 gm. of streptomycin, 10 mg. of isoniazide per kilogram of body weight, and 30 mg. of prednisone for about fifteen days, the latter dosage being lowered progressively to 5 mg. daily at the end of forty-five to sixty days. After withdrawal of prednisone, specific chemotherapy was sustained for a minimal period of one year. So far, this term has been reached by only 4 patients. The remainder are still under treatment. The pulse rate, temperature, blood pressure, and weight of hospitalized patients were recorded daily and, of outpatients, weekly. All patients in this series were previously submitted to laboratory and roentgenographic tests, consisting of blood count, blood sedimentation rate, analysis of urine and feces, and radiography and tomography of both lungs. Thoracic roentgenography was repeated every seven days during the first three weeks and every fifteen days thereafter. Other tests were repeated at monthly intervals.

RESULTS

Results were uniformly excellent. Clinically, the response was dramatic, as fever subsided in the majority of patients in a few days. In 2 patients (cases 1 and 2) with large effusions and severe dyspnea, symptoms rapidly ceased so that aspiration was unnecessary for removal of the effusion. In 1 female patient with concomitant pulmonary tuberculosis (case 3), pleural effusion resorbed without the parenchymal disease becoming worse; on the contrary, the tuberculous lesion of the lung improved. In the 4 patients who underwent chemotherapy for

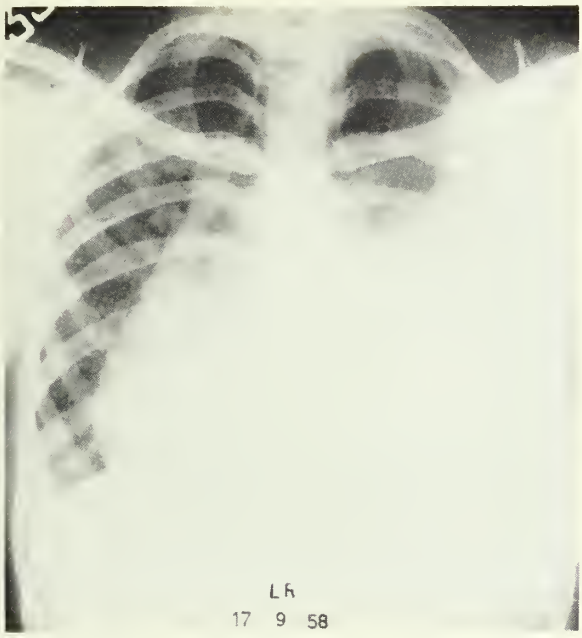

Fig. 1. *(Case 1)* Chest roentgenogram made September 17, 1958, showing pleural effusion on left side, with marked mediastinal shift to the right.

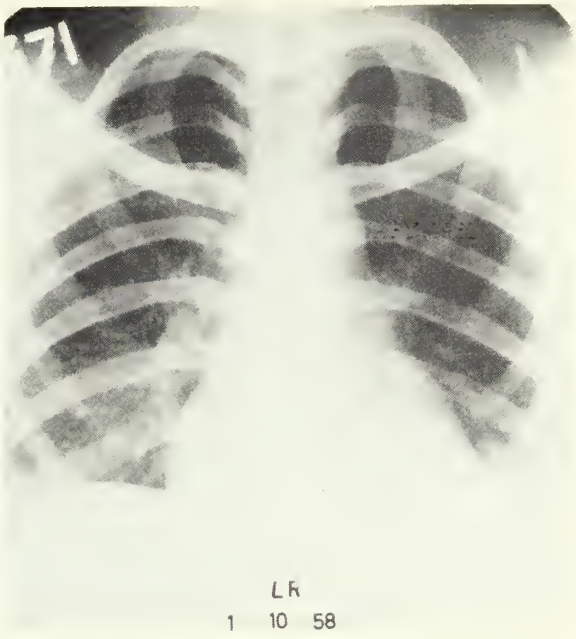

Fig. 2 *(Case 1)* Chest roentgenogram two weeks later shows the centralization of mediastinum with practically total resorption of the effusion.

one year, there have been no flare-up recurrences of tuberculous lesions. Those still under treatment are in excellent condition, although we must agree that the period of observation is very short.

Chest roentgenograms taken after treatment showed absolute normality without any thoracic deformity in nearly all cases. Only in 2 patients did slight blurring of the costophrenic angle remain.

It has been impossible to establish an accurate correlation between the duration of the disease and the rate of resorption, as all patients represented fresh cases with only thirty days of illness. We believe, though, that chronic cases will show a poor response. The great volume of the effusion was not an impeding factor to the resorption. In 2 cases, total effusion cleared in fifteen and twenty days, respectively, as did medium effusion in case 4.

CASE REPORTS

Case 1. L.R., a 20-year-old unmarried Negro woman who was a Brazilian servant, was admitted on September 17, 1958. Onset one month previously was characterized by hyperpyrexia, pain in the left hemithorax, emaciation, progressively increasing dyspnea, and asthenia. Laboratory findings showed no abnormalities. Physical examination evinced effusion in the left pleural cavity, which was confirmed by roentgenogram (figure 1), which showed marked mediastinal shift to the right. The patient was started immediately on daily doses of 1 gm. of streptomycin, 10 mg. of isoniazid per kilogram of body weight, and 30 mg. of prednisone. Pyrexia subsided the next day and dyspnea three days later. After two weeks of this therapeutic program, the chest roentgenogram showed that the effusion had completely cleared (figure 2).

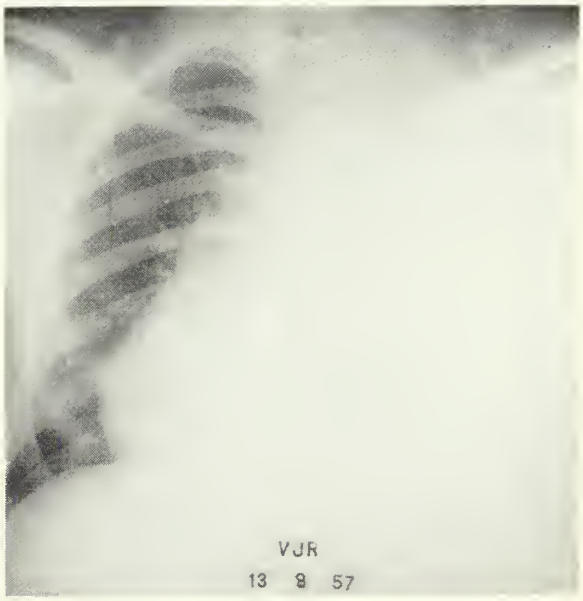

Fig. 3. *(Case 2)* Chest roentgenogram made August 13, 1957, showing total opacity of the left hemithorax with mediastinal shift to the right.

Case 2. V.J.R., a 32-year-old Brazilian mulatto laborer, was first seen August 13, 1957, because of a history of pyrexia, thoracic pain, and progressive dyspnea. Physical examination revealed intense exertional dyspnea and left pleural effusion, radiologically confirmed the same day (figure 3). Moreover, the roentgenogram showed marked mediastinal shift to the right. The patient was at once placed on the therapeutic schedule of streptomycin, isoniazid, and prednisone in routine dosage with excellent clinical response. Three days later, the patient was symptom-free, and the chest roentgenogram made twenty days later (figure 4) showed almost complete clearing of the effusion. The patient has completed one year of treatment and continues in excellent condition.

Case 3. I.L.S., a 17-year-old Brazilian mulatto servant, was admitted June 3, 1958, with moderately advanced pulmonary tuberculosis and pleural effusion on the right side. The patient underwent the therapeutic course of streptomycin, isoniazid, and prednisone in the usual dosage. Results were excellent. Twelve days later (figures 5 and 6), the pleural effusion had cleared and pulmonary lesions showed marked improvement. Treatment continues.

Case 4. A.D.M., a 28-year-old white Brazilian airman, was first seen January 2, 1958, with history of fever for fifteen days, dry cough, pain in the left hemithorax, and fatigue on exertion. Physical inspection revealed pleural effusion on the left side, which was substantiated by roentgenogram (figure 7). The rest of the tests were normal. Treatment with streptomycin, isoniazid, and prednisone was prescribed in the usual dosage. After twenty days, the patient was in perfect condition. A chest roentgenogram made on January 21 (figure 8) showed almost complete resorption of the effusion.

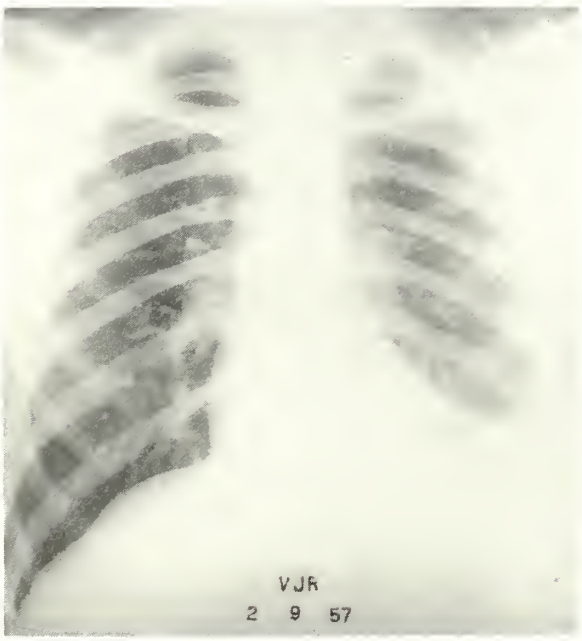

Fig. 4. *(Case 2)* Chest roentgenogram made September 2, 1957, showing slight blurring at the left pulmonary base.

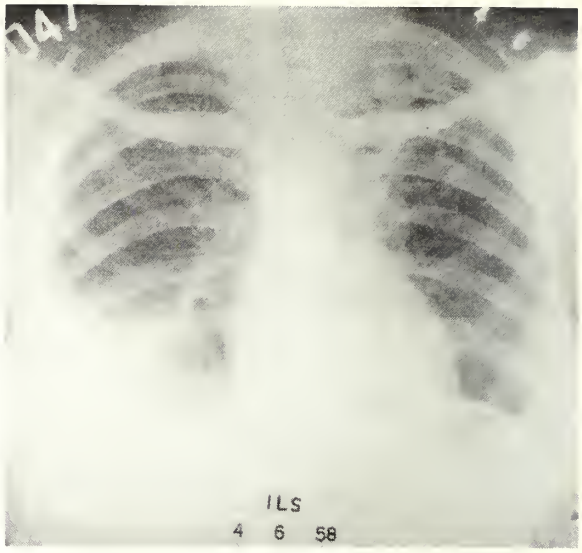

Fig. 5 *(Case 3)* Chest roentgenogram made June 4, 1958, shows pleural effusion on right side and both infiltrate and cavitary lesion in the left upper lobe.

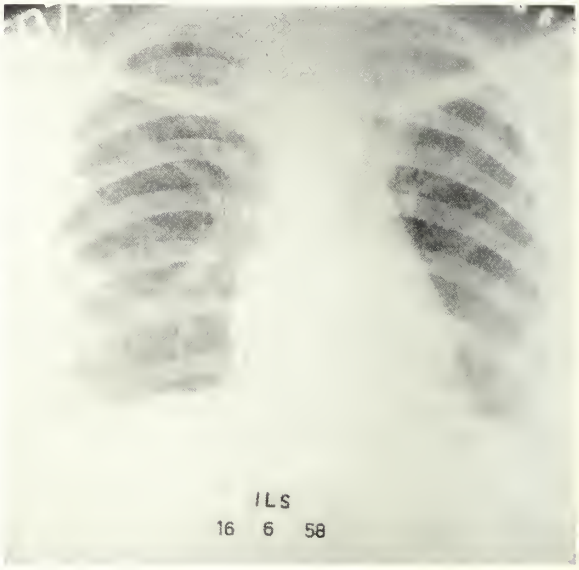

Fig. 6 *(Case 3)* Chest roentgenogram made June 16, 1958, showing complete resorption of pleural effusion and improvement of the radiographic findings on the left side.

DISCUSSION

So-called primary pleurisy with effusion cannot be considered a benign affair with a favorable outcome in all cases. Several clinical entities may be responsible for the effusion, but clinical evidence supports its tuberculous origin in a fair proportion of cases.

Such is Roper and Waring's[1] opinion after a thorough observation of a great number of cases,

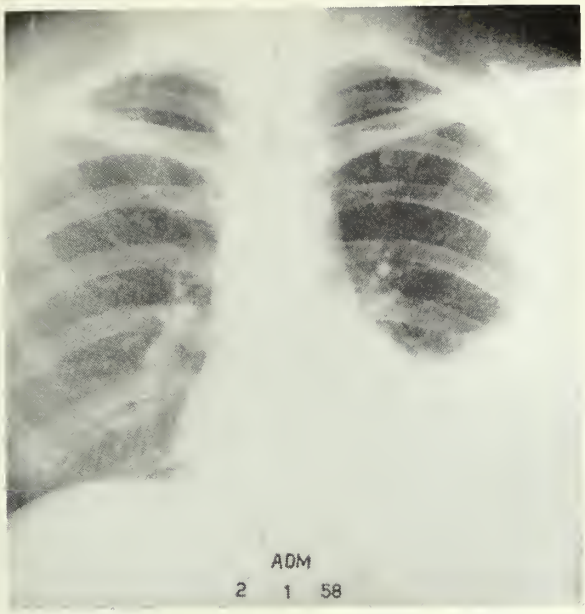

Fig. 7 *(Case 4)* Chest roentgenogram made January 2, 1958, shows moderate pleural effusion at left.

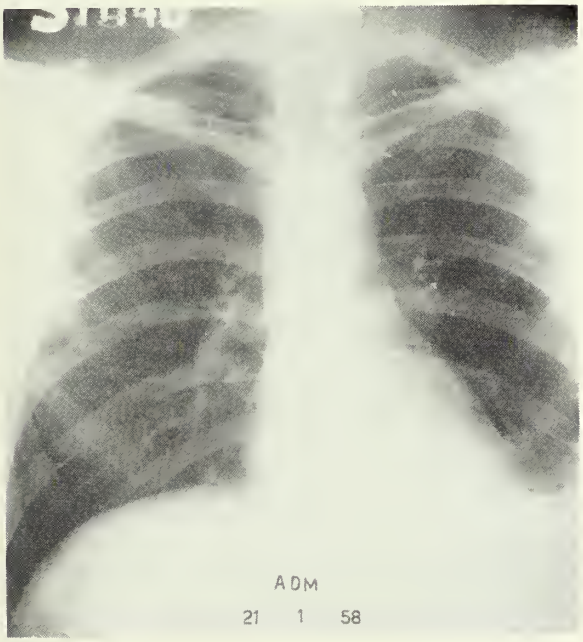

Fig. 8 *(Case 4)* Chest roentgenogram made January 21, 1958, shows only a slight blurring of the left pulmonary base.

when they say that "acute serofibrinous pleurisy with effusion in the vast majority of cases is of tuberculous origin." Even in the instances when effusion is resorbed and outcome tends to be favorable, it is a very grave condition, and the remote prognosis is always serious insofar as tuberculous morbidity or functional capacity are concerned.

Farber,[24] in a 13-year follow-up observation of 111 patients, found 34 who developed tuberculosis, with 71 per cent resulting in death. Jones and Dooley[25] found similar figures. Roper and Waring[1] corroborate these findings, showing that 87.2 per cent of army personnel who resumed military duty after effusion subsequently relapsed with pulmonary tuberculosis, while reactivation developed in only 23.2 per cent of those who retired.

Another aspect of the problem concerns the impairment of the functional condition of lungs. It has been demonstrated that after the resorption of the effusion,[26] there may appear a marked pleural thickening[26] accounting for ventilatory insufficiency which chiefly impairs the diaphragmatic mobility.[27] Bronchospirometric studies of Pinner and associates[28] as well as those of Bruce[29] after pneumothorax, show the importance of the ventilatory insufficiency resulting from pleurisy. Several therapeutic procedures have been devised in order to hasten the resorption of pleural effusion and to prevent organization of the fluid with consequent fibrous adhesions bearing detrimental functional repercussions. Frequent pleural aspiration and therapy with specific antimicrobial agents[15] concurrent with breathing exercises[27] have been tried with encouraging results. Therapy with corticosteroids shows that it is possible to achieve a much greater resorption rate in a safer way.[17–19,30] In fact, in our series, the effusion cleared in a period of ten to sixty days in all patients. Furthermore, combined antimicrobial coverage will overcome the deleterious effect of prednisone and will ensure, we hope, a lower incidence of early or remote pulmonary or extrathoracic tuberculosis.

Although it was not possible in our series to assess bacteriologic evidence of tuberculosis, except in 1 case, we feel that our procedure is justifiable. Actually, in the presence of pleurisy with effusion, once discarding the possibility of other causes, we are entitled to admit its tuberculous character and to prescribe a test treatment. Semiotic procedures will, of course, be continued until they substantiate or invalidate the presumptive diagnosis. Therapeutic response will manifest itself in the majority of cases in about thirty days without any detrimental effect upon the patients. Hence, it seems unwise in many instances to wait thirty to forty days for the result of the culture of pleural aspirate or bronchial and gastric washings, which are frequently negative, in order to institute therapeu-

tic measures. Normally, the patient subject to treatment from the beginning would have his effusion totally resorbed by then.

The number of such cases is small, but therapeutic response is so consistently favorable that such a policy seems sound and will be worth a trial.

SUMMARY

The present study is a report of 15 cases of pleural effusion, probably of tuberculous origin, subjected to a combined therapy of streptomycin, isoniazide, and prednisone.

The great incidence of the tuberculous etiology of such instances is discussed and the advisability of specific treatment in order to avoid relapse is advocated, especially of pulmonary localizations. The paramount importance of prompt resorption of the exudate as a prophylaxis of subsequent functional disorders is stressed. According to the authors' point of view, both requirements are fulfilled by the therapeutic procedure they used. The resorption of pleural effusion took place in the whole series in sixty days: namely, in 2 patients, between ten and fifteen days; in 8, between sixteen and thirty days; in 3, between thirty-one and forty-five days, and in 2 at the end of the above period of time. In spite of the small number of patients treated, the authors suggest combined treatment with prednisone and specific antimicrobial drugs in cases of pleural effusion of confirmed or suspected tuberculous etiology.

The drugs employed in the present study (Streptomix, Ditubin, and Meticorten) were generously supplied by Schering Indústria Quimica e Farmacêutica S/A.

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Carcinoma of the Lung

A Study of Five-Year Survival After Surgery

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An analysis of five-year cures after surgery for carcinoma of the lung was undertaken to ascertain significant factors that may be responsible for long-term survival.

A review was made of 724 patients with carcinoma of the lung who had been seen between January 1941 and April 1955 at 3 local institutions. For reasons of inadequate diagnosis or follow-up study, 63 of these cases were eliminated. Thus a total of 661 cases was studied, of which 563 were males and 98 were females. Records, including personal records, produced a meager yield of 25 five-year survivals.

Thoracotomy had been performed on 265 patients, or 40 per cent, and resection had been done on 151, or 57 per cent, of those explored. The resectability rate was 22.9 per cent of the entire group. The 25 long-term survivors represent 16.6 per cent of those resected or 3.8 per cent of the total of 661 cases (table 1).

Although the number of five-year cures was small—in itself a significant finding—the observations abstracted from them stress the need for a more extensive and intensive review of the problem. This is particularly true in view of significant variations from similar studies by other investigators.[1-4]

In the five-year survivors, 19, or 76 per cent, were males and 6, or 24 per cent, were females —a ratio of 3:1. Ages ranged from 38 to 84. The youngest female was 42, the oldest 63; the youngest male was 38, the oldest 84 (table 2).

DIAGNOSIS AND TREATMENT

Twenty patients presented a variety of symptoms and 5 were asymptomatic (table 3). Cough —the most common complaint—was prominent in 15 patients. Other symptoms reported were as follows: weight loss—7 cases, hemoptysis—6 cases, wheezing — 6 cases, fever — 5 cases, dyspnea — 4 cases, weakness — 3 cases, pulmonary osteoarthropathy—2 cases, and pain—only 2 cases.

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Duration of symptoms before diagnosis and treatment varied from no symptoms in 5 instances to a period of two years for 1 case. The average length of time was five and one-half months.

Roentgenograms were an aid to diagnosis in 24 of the 25 cases. They failed to demonstrate a lesion in only 1 patient.

Bronchoscopy was performed in 17 cases. Of these, a positive biopsy was obtained in 5 cases, a suspicious area was seen in 3 cases, and a negative report was given in 9 cases.

Sputum and bronchial cytology disclosed malignant cells in 4 of 10 patients studied.

The site of involvement was reported as follows: right lung—18 cases, left lung—7. Upper lobes were the site in 12 cases (8 on the right, 4 on the left), lower lobes were involved in 11 patients (8 on the right, 3 on the left), and, in 2 instances, the right middle lobe was involved.

A definitive diagnosis was established in 10 patients before surgery. In the remaining 15 patients, it was determined by exploratory thoracotomy and resection. In 1 instance, a frozen section was interpreted as probably benign and a wedge resection was performed. Subsequent studies revealed an alveolar cell carcinoma; a lobectomy was done one week after the wedge resection.

All survivors were treated by pulmonary resection, with pneumonectomy in 14 subjects and lobectomy in 11. Supplemental x-ray therapy was administered in only 2 instances.

Histologic diagnosis showed epidermoid carcinoma in 13 cases. Of these, 3 were poorly differentiated. Adenocarcinoma was found in 8 cases; 1 case was poorly differentiated. There were 3 alveolar cell carcinomas with only 1 report of undifferentiated cell type (table 4).

None of the survivors had hilar nodes or hilar vascular involvement. However, intrapulmonary nodes were positive in 3 instances; metastases to another lobe in the same lung were present in 1 of these.

TABLE 1

SURVEY OF CARCINOMAS OF THE LUNG
JANUARY 1941 to APRIL 1955

	Number of patients	*Per cent of total patients*	*Per cent of total patients explored*	*Per cent of total patients resected*
Clinical diagnosis	661	100	———	———
Thoracotomy	265	40	———	———
Resection	151	22.9	57	———
Five-year survival	25	3.8	9.4	16.6

The largest lesion was an epidermoid carcinoma, which was 10 cm. in size with a 6 cm. area of central necrosis. The smallest lesion was also an epidermoid carcinoma, which was 1 cm. in size.

DISCUSSION

Examination of these documented facts gives rise to interesting interpretations and leaves room for considerable speculation.

It immediately becomes apparent that bronchogenic carcinoma is more kind to women than to men. Not only were women attacked less frequently than men—a ratio of 6:1 in this survey—but once afflicted, women evidenced a far better prognosis and decreased the ratio to 3:1 in the group of five-year survivors.

Detection and treatment of neoplasms before the appearance of symptoms favor longevity after surgery. However, delay in diagnosis, as measured by duration of symptomatology, does not mitigate against the possibility of five-year survival. The case previously mentioned—that of a five-year cure which occurred after a history of symptoms lasting two years—stands as dramatic testimony to this contention.

Absence of bronchoscopic findings suggests a favorable outlook; this reflects the more lethal nature of the disease when it is visible and centrally located.

Limited resections were performed on 11 of the five-year survivals in this series. Considering this number, the trend toward performing lobectomy wherever possible in lieu of routine pneumonectomy certainly deserves more favorable consideration. This study reaffirms the indications for lobectomy outlined by Robinson and associates,[3] namely, (1) peripheral localized lesions, (2) compromise procedure in poor-risk patients, and (3) incurable cases in which such symptoms as hemoptysis, infection, and intractable cough are best controlled or relieved by excisional measures.

However, it is imperative to note that, in the face of intrapulmonary lymph node involvement, lobectomy may produce a cure. This occurred in 2 of the 25 cases studied. It is not impossible, therefore, to consider extending the indications for lobectomy.

Prognosis on the basis of cell type deserves comment. The incidence of 13, or 52 per cent, survivors with epidermoid carcinoma reflects the

TABLE 2

FIVE-YEAR SURVIVALS OF CARCINOMA OF THE LUNG

Age	*Number of males*	*Number of females*	*Total number*
30 to 40	1		1
40 to 50	5	2	7
50 to 60	7	3	10
60 to 70	5	1	6
70 to 80			
80 to 90	1		1
Total for all ages	19	6	25

TABLE 3

SYMPTOMS OF CARCINOMA OF THE LUNG PRESENTED BY FIVE-YEAR SURVIVALS

Symptoms	*Number of patients*
Cough	15
Weight loss	7
Hemoptysis	6
Wheeze	6
Fever	5
Dyspnea	4
Weakness	3
Pulmonary osteoarthropathy	2
Pain	2
None	5

TABLE 4

HISTOLOGY OF CARCINOMAS OF THE LUNG IN FIVE-YEAR SURVIVALS

Cell type	*Number of patients*	*Per cent of total patients*
Squamous	13	52
Adenocarcinoma	8	32
Undifferentiated	1	4
Alveolar cell	3	12
Total	25	100

somewhat more favorable outlook in this group. Noteworthy is the presence of 8, or 32 per cent, survivors with adenocarcinoma. This high rate is even more striking because adenocarcinoma made its appearance in only 98, or 15 per cent, of the total number of cases. The fate of those patients with alveolar cell carcinoma cannot be adequately evaluated. In this series, 3, or 12 per cent, survived five years, but the total number of patients with carcinoma of this cell type was very small—12, or 0.15 per cent. It would be unwise to draw conclusions from such limited incidence. However, the survival rate in the undifferentiated carcinoma group was only 4 per cent —1 patient. This small rate reflects an unfavorable prognosis, particularly considering its overall 29.7 per cent occurrence in the total group.

Our study does not bear out the reviews of others[1-6] who have reported that as high as 34 per cent of those surviving five years managed to do so despite extension to mediastinal lymph nodes, chest wall, or pulmonary vein. On the contrary, our study fails to uncover a single five-year survivor with hilar adenopathy or hilar vascular invasion!

SUMMARY

1. A survey was made of 661 cases of carcinoma of the lung that had been seen between January 1941 and April 1955. The rate of five-year survivals was found to be 16.6 per cent subsequent to resection and 0 per cent in cases not treated by surgery. For the total group, the five-year survival rate was 3.6 per cent.

2. Women present a more favorable prognosis than men.

3. Adenocarcinoma of the lung may not be so lethal a cell type as has been universally reported.

4. Delay in diagnosis does not contraindicate surgery nor obviate the possibility of a five-year cure.

5. Whenever possible, lobectomy is believed to be the procedure of choice.

6. Advanced age, per se, should not be a contraindication to surgery—as noted by the five-year survival of one male in the ninth decade of life.

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Determination of serum hexosamine content may aid in diagnosing Hodgkin's disease. In 5 of 6 patients with untreated disease, the value was at least twice as high as the mean of 101.5 mg. per 100 cc. for healthy subjects. Content was 160 mg. or lower in treated patients. Hexosamine values were elevated only moderately in patients with active infections, such as pneumonia, and were high with rheumatoid arthritis, cancer, and macroglobulinemia.

S. Weiden: Serum hexosamine level in the diagnosis of Hodgkin's disease. M. J. Australia 1:207-209, 1960.

Medical Illustrating in Minnesota

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Although there are examples of illustrations used in Minnesota medical journals before 1905, it was at about that time that medical illustrations began to be given serious consideration. Dr. William J. Mayo, who was keenly interested in medical illustration, was among the first to employ an artist to illustrate surgical technics. Among the early examples are drawings made for a paper on pancreatitis (figures 1 and 2). These drawings were made by Florence Byrnes, who I presume had had no formal training in the field. The first school of medical illustrating, conducted by Max Brödel, was not started until 1905. Florence Byrnes was no doubt counseled by Dr. Mayo to assure that the drawings would be anatomically correct. Such an arrangement must have represented working under a serious handicap, and it must have been time-consuming for both surgeon and artist. Because of the lack of trained illustrators, many physicians made their own drawings—with varying results.

Today's medical illustrator is trained as an artist and then receives special training in a school of medical illustrating. In such a school, the artist receives training in anatomy and in the technics best suited to medical drawing and becomes familiar with the operating room. Without this training, an artist should not attempt medical drawing.

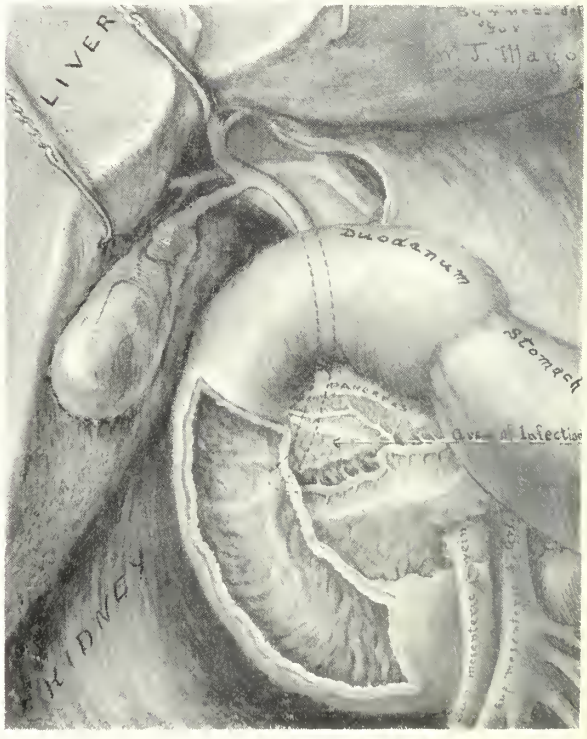
EARLY MEDICAL ILLUSTRATORS

In 1905, however, there was little choice in such matters. After that time, trained medical illustrators became available. It cannot be definitely stated as a fact, but surely Dorothy Peters, who took a full-time position with the Mayo Clinic in 1908, was among the first full-time medical illustrators in Minnesota. To the best of my knowledge, she worked in what was the first department of medical illustration established in Minnesota (figure 3).

There was much to be illustrated at that time, because surgical technics were developing rapidly. A need for medical drawing was keenly felt, for without it the reporting and recording of surgical and medical findings would have to be neglected. Even if this type of reporting and recording could have been done by the written or spoken word, understanding would not have been as good and, without visual examples, the time required for review of this material would have been infinitely greater. Da Vinci realized this long ago when he said ". . . and do not busy yourself in making enter by the ears things which have to do with the eyes, for in this you will be surpassed by the work of the painter."

A very early example of illustrating, taken from the *Northwestern Lancet* of 1885, is shown in figure 4. Figure 5 also is taken from an early

Fig. 1. An early drawing by Florence Byrnes to show pancreatitis. (Reproduced with permission from: Mayo, W. J.: Pancreatitis resulting from gallstone disease. J.A.M.A. 50:1161-1164, 1908.)



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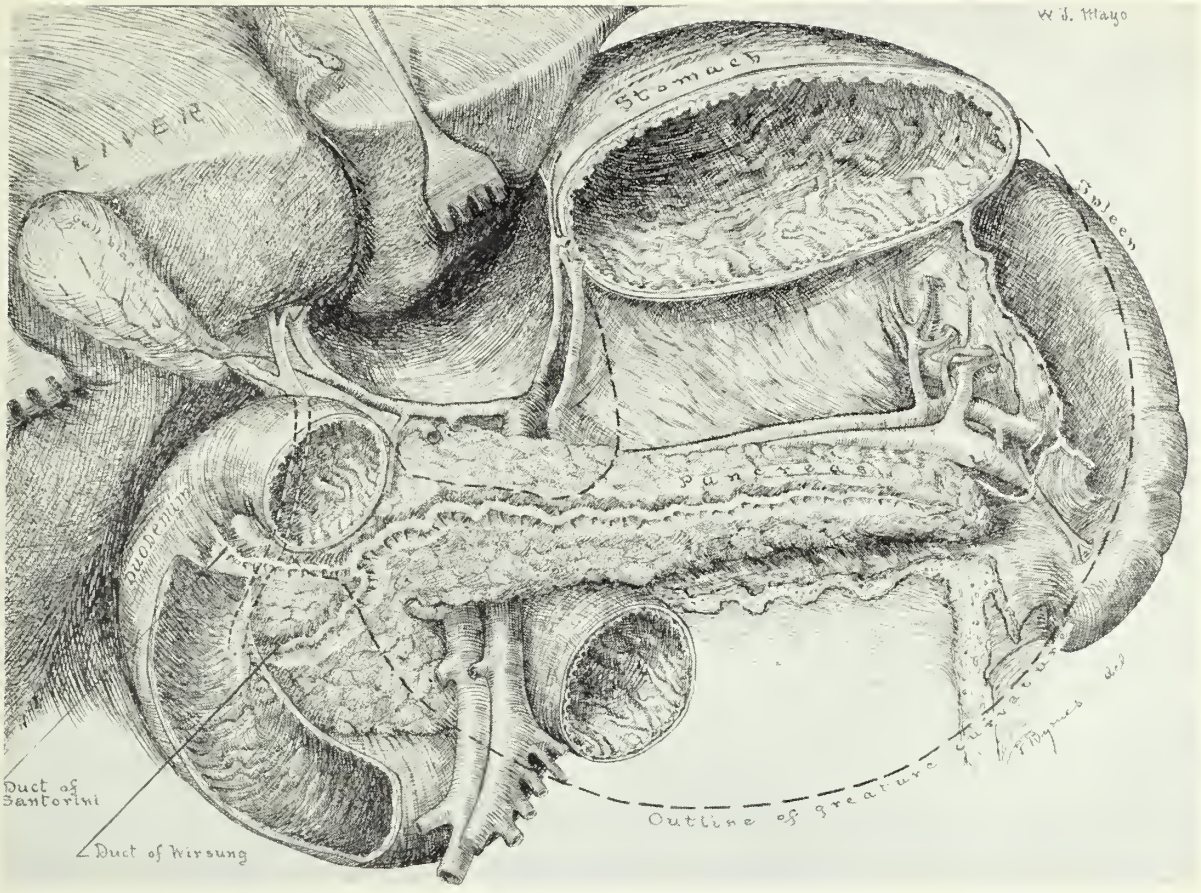


Fig. 2. Another early drawing by Florence Byrnes, also showing pancreatitis. (Reproduced with permission from: Mayo, W. J.: The surgical treatment of pancreatitis. Surg., Gynec. & Obst. 7:607-613, 1908.)

issue of the same journal. This type of illustrating, that is, drawings of specific conditions, could be done by an artist untrained in medical illustration. Drawings depicting surgical technics, however, require knowledge of anatomy and familiarity with the appearance of normal and abnormal tissues. This special training is so important that it can be said that art training and skill in drawing, although absolutely necessary, are really incidental to medical illustrating. It is after some studies in a college or university and some training in art that the artist is ready to start special training for medical illustration. This sort of background is required for entrance into schools of medical illustration.

As the need for drawings of medical and surgical findings increased, schools for the training of medical illustrators graduated students qualified for this work. In 1912, Miss Eleanora Fry assumed the post of medical illustrator at the Mayo Clinic. Miss Fry was adept in both black-and-white (halftone drawings) and line drawings. Figure 6 is an example of line drawing.

A few years later, another illustrator, Ralph Sweet, was added to the staff (figure 7). He left in 1917, when the author began his long association with the Section of Medical Illustration. It was at about this time that a department of medical illustration was started at the University of Minnesota. Known as the "Medical Art Shop," it was headed by Miss Jean Hirsch. Early part-time artists were Pearl Sanders, Mrs. J. Payne, Esther Pardee, and K. Whiting. Miss Hirsch remained at the university until 1951 (figure 8). During that time, she was assisted by Miss Evelyn Erickson, who has since left Minnesota and is practicing medical illustration elsewhere. Other illustrators at the University of Minnesota were Bill Holmes and Alvin Shamish. Bob Smith did some medical illustrating in Minneapolis. Elton Hoff at present is doing medical illustrating in Minneapolis, as are Mrs. Inga Platou at the University of Minnesota, and Robert Benassi.

Rochester has seen many medical illustrators in the past fifty-five years. Nineteen trained people have been employed during that time.

Fig. 3. A drawing made by Dorothy Peters in 1910 to illustrate dissection for tuberculous glands of the neck. (Reproduced with permission from: Judd, E. S.: Treatment of tuberculous glands of the neck: a study of 649 operated cases. Ann. Surg. 52:758-766, 1910.)

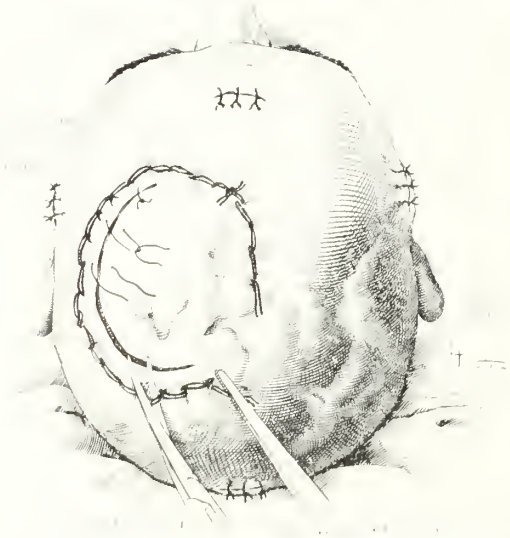


Fig. 6. A line drawing made by Eleanora Fry in 1921 to illustrate the surgical treatment of arteriovenous aneurysms.

Fig. 4. A drawing prepared for the printer by cutting the illustration on a wood block. (Reproduced from: Thompson, J. W.: Diseases of the frontal sinuses. Northw. Lancet 4:284-286, 1885.)

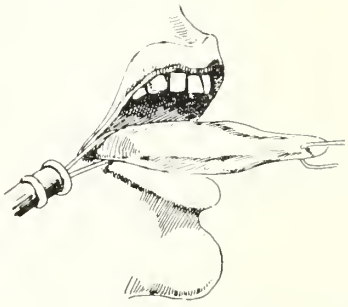


Fig. 5. A drawing made to illustrate a paper on carcinoma of the tongue. (Reproduced from: Wheaton, C. A.: Cancer of the tongue considered from a diagnostic and surgical standpoint. Northwestern Lancet 13:62-66, 1893.)

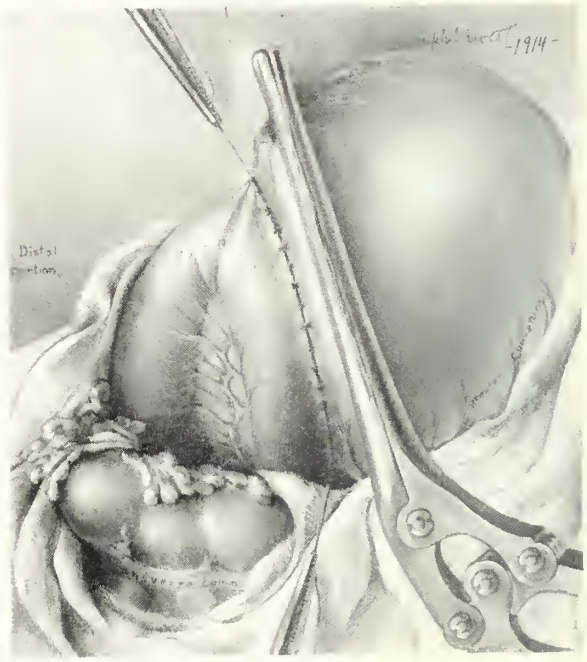


Fig. 7. A halftone drawing made in 1914 by Ralph Sweet to show the surgical treatment of carcinoma of the pyloric end of the stomach. (Reprodneed with permission from: Mayo, W. J.: The radical operation for cancer of the pyloric end of the stomach. Surg., Gynec. & Obst. 19:683-691, 1914.)

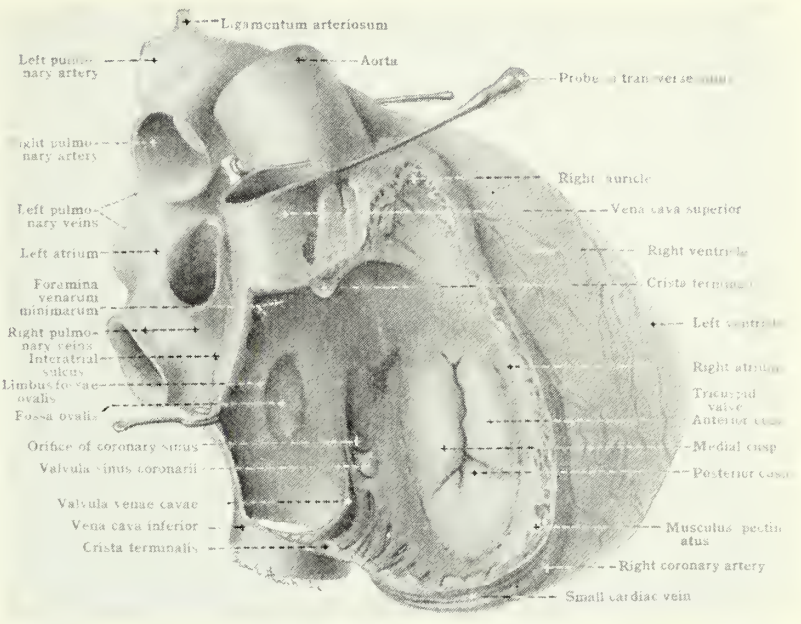


Fig. 8. A drawing by Jean E. Hirsch to show the interior of the right atrium of the heart, superior view. (Reproduced with permission of the publishers from: Morris' Human Anatomy: A Complete Systematic Treatise, ed. 10. Edited by J. P. Schaeffer. Philadelphia: The Blakiston Co., 1942, p. 587.)

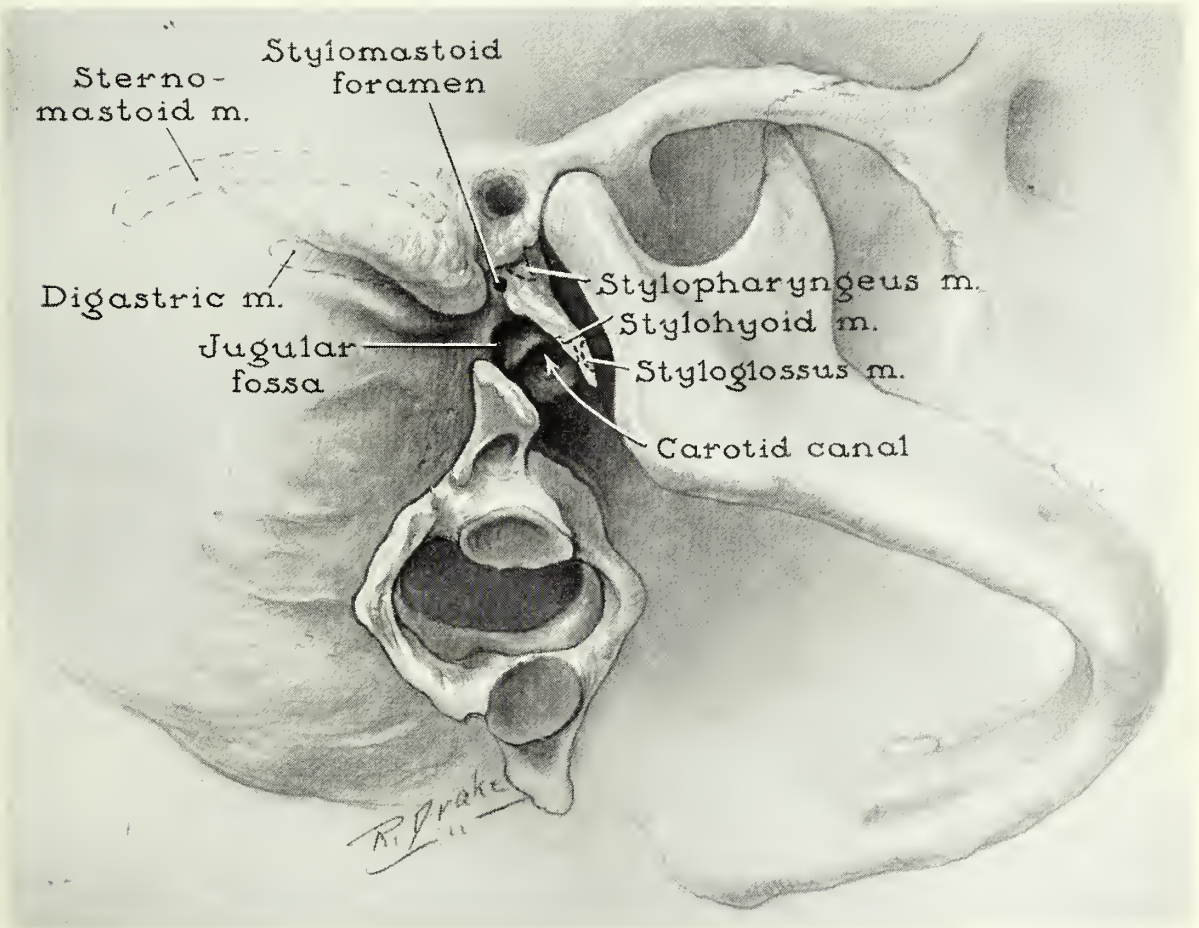


Fig. 9. A drawing made by the author to accompany a paper on parotidectomy. (Reproduced with permission from: Beahrs, O. H., and Adson, M. A.: The surgical anatomy and technic of parotidectomy. Am. J. Surg. 95:885-896, 1958.)

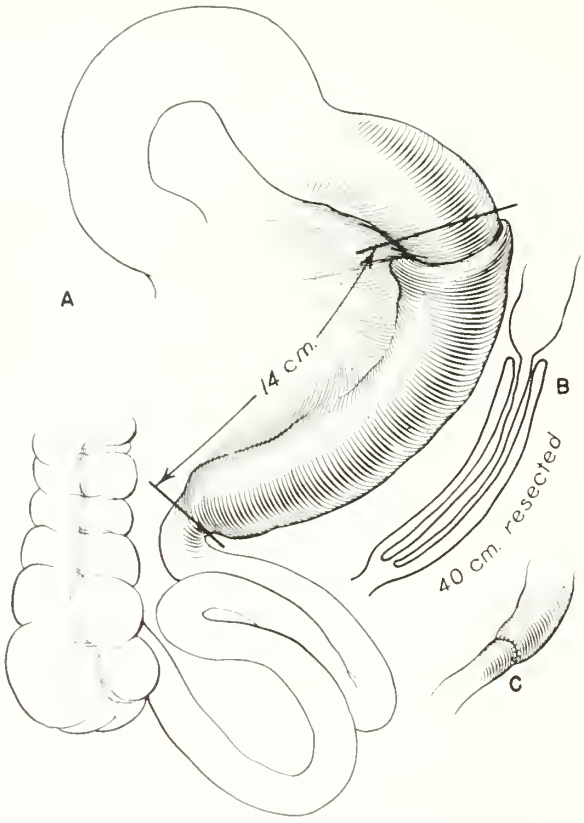


Fig. 10. Another drawing by the author to show partial gastrectomy and intestinal anastomosis. (Reproduced with permission from: Chance, D. P., Keith, H. M., and ReMine, W. H.: Recurrent ileoileal intussusception: report of unusual case. Proc. Staff Meet. Mayo Clin. 29:241-246, 1954.)

Among those not previously mentioned, were Myra Warner, Margaret Whiting Phillips, Kenneth Phillips, Theodora Bergsland Ewing, Clarice Ashworth Francone, Gladys McHugh, Jean Young, Jessie Phillips, Kathleen Mackay, Harriet Carpenter MacCarty, Dorothy Booth, William Osborn, Aileen Young, Jane Allen Destro, and Vince P. Destro. During this period more than 32,000 original illustrations have been filed in the Section of Medical Illustration of the Mayo Clinic. With a few exceptions, all these illustrators are still active.

Changing Demands in Illustration

The medical illustrator has seen many changes in the demands upon him and the type of drawings he makes. It will be noticed that in the earlier drawings much care was taken to include great detail in the over-all aspects of a scene, in contrast to the modern practice of concentrating interest with more freedom of treatment (figures 9 and 10). In 1905, the field of medical illustration was new. Almost all the classic surgical technics were yet to be illustrated. Every time an abdomen was opened, there seemed to be something new to illustrate. Neurosurgery was coming into its own; it would require many drawings to illustrate new technics and findings—not to mention the other branches of surgery which were also arising or expanding.

So much was being added to medical knowledge that colleges of medicine found it necessary to increase the time required for the study of medicine. This knowledge, of course, is ever-increasing, but the practicability of further increasing the time required for the study of medicine is doubtful. The answer is to be found in methods of teaching other than academic which will impart knowledge in less time.

It is in this field that visual aid is called upon, and the medical illustrator is the person trained to aid in solving this problem. A drawing or diagram conveys an idea or a fundamental concept in a fraction of the time required to read an account of the same matter, and that which is thus presented will be better remembered. Medical writings have become so voluminous that a physician has not time to read the current literature, even in his own specialty. He is greatly helped in this respect by illustrations, which save countless hours of reading and also quickly interpret the meaning of a text.

Contemporary demands have changed somewhat the type of work required of the medical illustrator. Drawings are being made for lantern slides, films, television presentations, and exhibits. Demands are such that a medical group, school, or writer can ill afford to operate without the services of a medical illustrator, and to do so is surely false economy.

Medical journals of note are asking increasingly for illustrations. In many instances, publishers have medical illustrators on their staffs or can inform medical authors of where illustrators may be reached. Publishers are well aware of the value and power of good illustrations.

Medical illustration has progressed greatly in Minnesota during the last ninety years. Many illustrators working during this period have been mentioned in this paper. Others of equal importance may have been overlooked through inadvertence or lack of information. Many new names will be added in the future, because the need for drawings made by trained medical illustrators will ever increase.

Editor's note: A biographical sketch of Henry W. Morris, pioneer in medical photography, will appear in a future issue.

Medical Education in Minnesota

J. ARTHUR MYERS, M.D.

Minneapolis

DURING THE PRETERRITORIAL and territorial periods, as well as the early years of Minnesota's statehood, not enough physicians migrated to Minnesota to provide adequate medical care for the American Indian and Caucasian populations. The Philadelphia Medical College, which was the first medical institution in the United States, was established in 1765. During the remainder of the eighteenth and the first half of the nineteenth centuries, several other medical schools came into existence. The one nearest Minnesota was the Rush Medical College in Chicago, established in 1843.

From 1840 to 1870, the preceptor system was in vogue in Minnesota. According to this system, the practitioner of medicine chose a pupil, who really became his servant and assistant. By working in the physician's office, reading his books, and making house calls with him, the student learned, and thus the practice of medicine was perpetuated in the community.

MEDICAL SCHOOLS

In 1871, the St. Paul Medical School announced its opening as a private institution, with Dr. A. J. Stone as president. This was only a preparatory school, and its students, for the most part, completed their medical courses in Chicago.

In 1872, a similar private preparatory school was opened in Winona, Minnesota, but, like the St. Paul school, did not graduate students or confer diplomas. This school closed in 1879. The same year, the St. Paul school was elevated to college standing, and it became the medical department of Hamline University in 1880, when Dr. A. J. Stone was dean. However, this department closed in 1881, and its faculty combined with a group of Minneapolis and St. Paul physicians to form the Minnesota Hospital College, situated in Minneapolis.

In 1882, Dr. C. N. Hewitt, secretary of the State Board of Health, proposed to the Board of Regents that a department of medicine be organized at the University of Minnesota. The board appointed a committee, whose report received favorable action in January 1883, and the first faculty was appointed. However, no provision had been made for teaching. Therefore, an act to regulate the practice of medicine in Minnesota, requiring all physicians to be licensed and conferring upon the University's medical faculty the function of an examining board, with power to approve and accept diplomas of recognized medical colleges as evidence of fitness to practice or to require the applicant for license to be examined by the board was passed.

The same year the faculty was appointed, another private medical college was organized, under the name of the Minnesota College of Physicians and Surgeons, which became the Hamline University Department of Medicine twelve years later. In 1885, this new private school and the formerly organized Minnesota Hospital College received recognition of the faculty of medicine of the University of Minnesota as satisfactory schools for instruction. That year, the St. Paul Medical College was reorganized and was soon recognized by the University examining faculty.

The Minnesota Homeopathic Medical College was established in Minneapolis in 1886. In 1887, the legislature passed a new medical practice act, which created an independent state board of medical examiners. The same year, the Board of Regents of the University was petitioned to establish a high-grade teaching department of medicine at the University of Minnesota.

In February 1888, the faculties of the Minnesota Hospital College and the St. Paul Medical College appeared before the Board of Regents in support of the petition, with the offer to surrender their charters and with the tender of their properties for the temporary use of the state. Soon thereafter, the Minnesota College of Homeopathic Medicine made a similar offer.

UNIVERSITY OF MINNESOTA

In October 1888, the first entrance examinations were held for the Medical School of the University of Minnesota. The faculty consisted of 29 members, who occupied a leased building on the corner of Sixth Street and Ninth Avenue South. Teaching was done in this building until 1893, when the Board of Regents constructed a small building, known as Medical Hall, on the campus. In 1895, the laboratory of the medical sciences building was added.

Dr. P. H. Millard practiced medicine in Still-

water and took an active part in medical education. He was one of the first nonteaching faculty of 5 members of the College of Medicine and Surgery of the University, appointed in 1883. In fact, he was secretary of that organization. On May 4, 1887, Dr. Millard resigned. However, when the teaching faculty was appointed in 1888, he was made dean. When his death was announced on February 2, 1897, the president of the University requested Dr. R. O. Beard to write the memorial. In this he said:

> His most signal service was rendered in the projection, organization, and development of the Department of Medicine of the University of Minnesota. It was in his brain that this institution, which has taken rank among the foremost professional schools of America, first took shape. It was his influence which secured the surrender of the charters of those private colleges which united in its establishment. It was largely through his unceasing labors and his persistent enthusiasm that it was placed on the University Campus under the roof of Medical Hall. It was his first ambition, his daily duty, his well-justified pride to forward its interests throughout the years of his fatherhood of its faculty.

Dr. H. Parks Ritchie was appointed dean May 28, 1897.

The need for more information was recognized as the twentieth century opened. Moreover, it was important that all facts then known or later established be widely disseminated so as to have the best possible informed professional workers as well as an understanding public.

Two schools of medicine were still in operation, one at Hamline University, and the other at the University of Minnesota. Following Dean Ritchie's death in 1906, Dr. F. F. Wesbrook was appointed dean. On February 20, 1908, Hamline University presented a plan whereby its department of medicine would be taken over by the University of Minnesota. This was approved by the faculty and ratified by the Board of Regents on March 4, 1908. Since that time, only the University of Minnesota has operated a school of medicine.

Under Dr. Wesbrook's deanship, a building program resulted in the Institute of Pathology and Public Health, 1907; Elliot Memorial Hospital, 1911; Millard Hall, 1912; and Institute of Anatomy, now Jackson Hall, 1912. When Dr. Wesbrook died in 1913, Dr. E. P. Lyon was appointed dean.

Dr. William J. Mayo early conceived the idea of a permanently endowed institution at Rochester connected with some university, preferably the University of Minnesota. In 1907, he was appointed regent of the University. Seven years later, he received letters from 3 members of the University Medical School faculty pertaining to graduate education and "relations with the Mayo Clinic." The subject was discussed by appropriate groups in Rochester and at the University. On June 9, 1915, the Board of Regents entered into an agreement with Dr. William J. Mayo, Dr. Charles H. Mayo, and others whereby the Mayo Foundation for Medical Education and Research became a definite part of the University of Minnesota. This affiliation, however, applied only to graduate work.

Establishment of the Mayo Foundation for Medical Education and Research was a boon to all branches of medicine and surgery because it provided for a large number of fellowships, for a stipulated period of time and with an annual stipened, which permitted many physicians to undertake graduate training. From the establishment of the Foundation until today, many physicians have received excellent instruction. Dean Lyon's administration was one of significant advance in medical education until he retired in 1935. During the last five years of his administration, Dr. R. E. Scammon served as dean of Medical Sciences.

Harold S. Diehl was elected Dean of Medical Sciences in 1935. His tenure was characterized by a marked increase in teaching and research activities. During the latter part of Dean Diehl's administration, construction of building and acquiring of equipment reached previously undreamed-of heights, including the Variety Club Heart Hospital; a new Student's Health Service building; the Mayo Memorial Building, which nearly doubled the capacity of the school and housed the new School of Public Health; the Lyon Laboratories; the Medical School Library Building, which his colleagues named Diehl Hall; and the Masonic Memorial Hospital. From a nonteaching faculty of 5 in 1883 and a teaching faculty of 29 in 1888, 114 in 1908, and 541 in 1948, the faculty of the University of Minnesota Medical School has grown to a membership of 800 in 1960. When an affiliation was established between the School of Medicine and the Veterans Administration Hospital in 1945, a provision was made whereby physicians of the two institutions taught in both places.

When Dean Diehl retired in 1957, Dr. Robert B. Howard, then associate dean, was elected Dean of Medical Sciences without a single objection having been voiced by any person, on the faculty or otherwise, throughout a period of several months of considering applicants. Dr. Howard is conducting the institution, with all its ramifications, admirably.

In 1874, Dr. Charles N. Hewitt was appointed

nonresident professor of public health at the University of Minnesota. Apparently, this was the first appointment of its kind in the United States. For more than twenty years, he gave a course of lectures each year to the entering classes of the whole student body of the University. Dr. John Sundwall became professor of preventive medicine and public health in 1918. He was succeeded by Dr. Harold S. Diehl in 1920. The Department of Preventive Medicine and Public Health was established in 1922, with Dr. Diehl as head. Two years after Dr. Diehl was elected to the deanship of the medical sciences, in 1937, Dr. Gaylord W. Anderson was made head of this Department.

The School of Public Health was established in 1944, with Dr. Anderson as director. This school has become the largest from the standpoint of numbers of students of any school of public health in the United States. The superb teaching of a staff of approximately 200 members, along with important research activities, has attracted students from practically every nation in the world.

MEDICAL JOURNALS

Journals also have played an important part in medical education. Until 1870, physicians were dependent upon a few national journals. On February 1, 1870, Dr. A. J. Stone of St. Paul proposed a medical journal, which was approved by the Minnesota State Medical Association. The first issue appeared in June of that year under the title, *Northwestern Medical and Surgical Journal*. In 1881, the *Northwestern Lancet*, successor of the original journal, appeared. This magazine, THE JOURNAL-LANCET, is now in its ninety-second year.

In 1899, the *St. Paul Medical Journal*, an excellent magazine, was established. In December 1917, this journal yielded to the establishment of a new journal, *Minnesota Medicine*, which has continued as a medical magazine of high quality.

Papers read at the weekly staff meetings of the University Hospitals have long been published in the University of Minnesota Medical Bulletin, which is the official publication of the University of Minnesota Hospitals, the Minnesota Medical Foundation, and the Minnesota Medical Alumni Association. This bulletin was first a mimeographed publication. It has evolved into a dignified printed magazine under the managing editorship of Eivind Hoff, Jr., Executive Director, Minnesota Medical Foundation. The bulletin is widely distributed among graduates and many other physicians.

OTHER PHASES OF MEDICAL EDUCATION

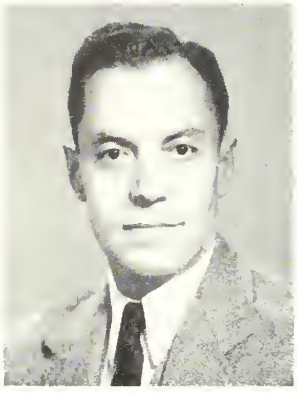
Another important part of medical education has been conducted by the State Department of Health. On March 4, 1872, a Board of Health was established by the legislature. It was the third such organization in the United States, having been preceded only by one in Massachusetts in 1869 and one in California in 1871. From then until now, the members of the State Board of Health and its staff of workers have participated significantly in medical education.

As President of the University of Minnesota, Lotus Delta Coffman conceived the idea of establishing a center for adult continuation study, which would permit adults in various activities of life to register for short courses in their fields of special interest. Since 1937, this program has been in continuous operation. Approximately 400 courses for physicians have been presented with a registration of 18,710. These courses have covered practically every medical subject requested by groups of physicians. Some have been for specialists in various fields, but the majority have been directed toward physicians in general practice. In addition to these courses, each of which has occupied the greater part of a week, three-month courses also have been offered in the basic sciences and in their clinical correlation. Also, courses of one month or more have been offered in medicine, surgery, pediatrics, and so forth. Evening extension courses in various subjects also have been given.

Regional seminars for physicians have been presented throughout the state. They usually have consisted of 6 or 8 consecutive weekly sessions of two hours each and dealt with topics requested by physicians of the areas in which they were held. Dr. W. Albert Sullivan has admirably directed the Department of Continuation Medical Education since 1958.

Thus, from the preceptor days before 1870, medical education in Minnesota has evolved into one of the best systems in the world, not only from the standpoint of training students to become physicians, general practitioners as well as specialists, but also from the standpoint of contributing much new information through numerous research projects. Long-term graduate medical education through fellowships and residencies has been provided in abundance.

This department of Continuation Medical Education has been directed by: Drs. William A. O'Brien, 1938-1947; George N. Aagaard, 1948-1951; Robert B. Howard, 1952-1957; N. L. Gault, Jr., 1957-1958; and W. Albert Sullivan, Jr., since 1958.



Notes from a Medical Journey

Bucharest, Rumania
15 September 1960

Dear Jay:

Here at Bucharest I recall a trip from Vienna long ago, when I shared a train compartment with a swarthy fellow who plied me with chocolates, Turkish cigarets, and endless talk that revealed only familiarity with every corner of the Balkans and a great variety of "droll," that is, dirty, stories. His ticket read "Bucharest," but he left the train escorted by Hungarian officials who had slit open the lining of his suitcase to reveal packet after packet of Rumanian bank notes.

I never went beyond Budapest then, but thereafter it seemed that most tales of international adventure I read reached high points in Bucharest, where men in opera cloaks concealing lethal weapons were seduced by exotic beauties in transparent negligees who extracted state secrets in 6 languages. In short, Rumania was a mysterious unreality to me until a few days ago.

From Copenhagen last Sunday, I was the sole passenger in a plane labeled "Roumanian Airlines Special," rereading the page in my passport covered with a visa: "Official Invitation -- Roumanian Ministry of Health." I recalled, too, that my travel insurance does not cover nonscheduled flights. But the first leg of the flight was mostly dull, and I was delighted at East Berlin's dingy little airport when Drs. Paul D. White, E. Cowles Andrus, Michael deBakey, Luther Terry, and John Turner, a young protégé of Paul's, came aboard. We were going to Rumania to break some cardiologic ice, hoping to promote professional cooperation and exchange and to learn something about local medical affairs before going on to the European Congress of Cardiology in Rome.

We were cordially greeted at Bucharest Airport -- no customs inspection -- and big black Russian cars were waiting. Paul's bag was not to be found, and, as we stood around, we watched a plane-load of the return-

ing Rumanian Olympic Team go through customs -- every bag searched from top to bottom and magazines opened page by page. Still no bag (it hasn't been found yet, four days later), so off we went along wide, tree-lined boulevards into the brightly lighted city. The biggest and most ornate building (in the Stalin-Gothic style of Moscow University) we passed proved to be the Headquarters of the Government Press.

Our rooms at the Lido Hotel overlook a huge garden and terrace with dining tables around a blue-tiled swimming pool, the whole prettily illuminated. Hospitality was underscored in each of our rooms by plates of fancy cookies, bowls of fruit, flowers, and bottles of mineral water. After thirty-plus hours of travel, we would have been content to collapse, but of course there was a dinner with our friends Professor Iliescu, Dr. Ionescu, the assistant minister, and several others. Very pleasant, too many courses of good food and drink, but finally to bed with mounting hyperlipemia and too tired to care.

Professor Iliescu, director of a big, new cardiovascular center, ASCAR, was some years with Sir Thomas Lewis in London in the early twenties and, though now aged 70, he is full of charm and a great deal of energy. ASCAR has 120 beds and a big outpatient department, to which cardiac patients are referred from a dozen secondary centers in the city as well as from all over Rumania. Everything was spotless, and rooms and corridors were full of asters and chrysanthemums. The patients seemed well cared for and presented a full variety of cardiovascular disorders, including plenty of unquestionable myocardial infarctions and a man aged 34 so labeled but about whom we had much debate.

ASCAR is planned as a research as well as a diagnostic center and has a considerable group engaged in experimental work. Dr. Ionescu has much new equipment, including a big pump-oxygenator from the States now being tried with dogs before the expected application to man. The Rumanians are doing an increasing amount of cardiovascular surgery, using hypothermia at present.

The biggest show of equipment is at a center for work capacity evaluation and rehabilitation, where a vast battery of tests and examinations is applied to persons of all ages and disabilities -- circulatory, sensory, orthopedic, and so forth. This again is a center of centers, and we were told that subordinate units for such medical care for the workers are operating all over the country. "Social medicine," with stress on prevention and rehabilitation, is much emphasized here, though it is difficult to know how far hopeful theory and plans are actually put into practice.

Paul White has been keen to learn about the local attitude toward the claims of Dr. Anna Aslan for the value of procaine injections to retard aging and its associated disabilities. None of the local physicians could be induced to give more than noncommittal comments. Dr. Aslan is away at present, and we were discouraged from spending the time to pay a visit to her G.I. Parhon Geriatric Institute. But she must be officially in favor,

not only as evidenced by the support of the Institute but, perhaps more significant, by her frequent recent appearances in Congresses outside Rumania. Permission and provision of funds for travel to the capitalist countries are not available to many Rumanian doctors.

Our lectures, slowed by translation, were applauded by overflow audiences, and we have been kept busy here in Bucharest and on an auto trip to the Carpathian Mountains. We are not restricted, but we do have such a full program that there is no time for just wandering around. An evening in the marvelous new Symphony Hall was relaxing. The huge audience seemed to be both better dressed and more sophisticated in music than I recalled on similar occasions in the country of the Big Brother. Afterwards, yet another elaborate dinner tested our capacities. Our usual day's quota here seems to average 4,000 or more calories, not counting the contribution of alcohol which comes in at least 4 varieties at every meal. And we have 2 elegant multicourse meals every day. Such are the hazards of trying to promote international cooperation in medical research.

In a few hours (at 7 a.m.), I must be ready to take off for Rome via Vienna. The others go by way of Sophia for a day, but I am on the program of a preconvention Colloquium for Arteriosclerosis in Rome. As usual, "all roads lead to Rome."

As ever,

Ancel Keys

AK:mn

George D. Haggard, M.D.

C. A. MC KINLAY, M.D.

Minneapolis

THREE YEARS BEFORE the start of the Civil War, and before large parts of the West were settled, during a year of great financial depression and of grasshopper pestilence, George Delaney Haggard, who is the oldest living member of the Minnesota State and Hennepin County medical societies, was born in an unroofed log cabin in sub zero weather in Fairpoint, Goodhue County, Minnesota Territory.

The date was January 18, 1857. He was the fourth son of David M. Haggard and his wife, Mary Ann, who migrated from Iowa to the Minnesota town of Fairpoint, a place that no longer exists. At one point during the hazardous move, the family camped where Rochester, Minnesota, is now located. The father had to leave the family at this camp while he continued to Fairpoint to prepare a place for them. He left his wife armed with an axe as protection against possible attack from wolves. Dr. Haggard's mother's brother was a physician in the area of Fairpoint; it was his love for Minnesota that was a stimulating influence in the Haggards' move from Iowa.

What was life in Minnesota Territory like in 1857? The rugged pioneer days of his childhood are well remembered by Dr. Haggard, and he recalls his uncle-physician recounting many instances of amputations of extremities in the severe and, to the pioneer, unrelenting winter. Survival in those days made it compulsory for people to know the principles of health care and to be able to apply these principles until professional help arrived. Dr. Haggard recounts that this knowledge often meant life or death to the patient, as physicians were scarce and often had to travel great distances to care for the ill. The telegraph was not in common use, and the telephone was not to be invented by Alexander Graham Bell until eighteen years later. Horseback, buggy, and stagecoach were the only available methods of transportation in many sections; railroads had not yet come into their own; river transportation was just developing.

To visualize, even partially, the contrast between the practice of medicine in Dr. Haggard's early days and in the present time, one needs to recall only a few of the great changes that have occurred within the span of his memory. In the field of preventive medicine, typhoid and tuberculosis were the great killers. Practically all the great specific therapies have appeared during his century. The organized teaching of clinical bedside medicine and of basic sciences is now an essential feature of medical training. Life expectancy in the United States increased from 38.3 years in 1850 to 67.1 years in 1957. Truly, Dr. Haggard has lived during a golden age of medicine.

Dr. Haggard was one of 6 boys and 4 girls. He recalls that "there was always a patient to take care of, either one of us or a neighbor." The parents were deeply religious and followed the Christian way of life; thus the home became, with the school and church, the main molder of character.

Dr. Haggard was motivated to study medicine largely by the examples of his mother and doctor-uncle. His mother, the former Mary Ann Schmid, was a woman of great courage and intelligence. Like other pioneer mothers, Mrs. Haggard had a resourcefulness in preparing and using remedies supplied by Mother Nature. She supplemented this skill with help from current medical literature that she obtained from various parts of the country—literature that George read and digested in his early years. Some of the things I have used with great success came from my mother," Dr. Haggard chuckles.

For a time, the family lived in Eau Claire, Wis-

consin, where George attended and was graduated from high school. He attended college in Oskaloosa, Iowa, and was graduated with a Ph.B. degree in 1880. He was now a mechanical engineer and, as such, entered upon his first career—a master mechanic for the Milwaukee Railroad. He became known as their expert pump man. He was also a heating engineer for the pioneer Minneapolis firm, The Martin Heating Engineers.

On September 20, 1880, he married Miss Lucina M. Headlee, who had attended the same college.

Not until 1893 did George Haggard receive his M.D. degree from the University of Minnesota and enter upon his second career. He was president of his class of 38 members, all of whom he credits with being leading physicians of their day, and is the only survivor.

Dr. Haggard recalls some of the less serious events that happened on the medical campus. During their senior year, by reason of a slight infraction of the rules by one of the students, the dean of the medical school suspended the whole class. As class president, Dr. Haggard saw to it that there was "class as usual," after they obtained permission to meet in one of the buildings. This informal class, under the leadership of medical student Haggard, went on for three weeks without an instructor. "Dr. Cyrus Northrop, president of the University," relates Dr. Haggard, "noticed us and our diligent efforts to keep up and intervened with the Dean on our behalf and said 'you better take the boys back.'"

After graduation, Dr. Haggard served his internship from 1893 to 1894 in Minneapolis City Hospital, now the Minneapolis General Hospital. His first medical appointment was assistant City Physician, a post he held from 1900 to 1904. The way this came about is an interesting story. Dr. C. G. Weston had come from Boston to assume the duties of City Physician at the Minneapolis City Hospital. He sought out young Haggard when he was a senior in medical school and offered him the position of assistant City Physician. Dr. Haggard was pleased, but, as president of his class, he was loathe to accept because, as he told the doctor, he knew some of his classmates had applied for the job. Dr. Weston's reply was, "The position is mine to give." At that time, the job was what might be called "the only paying residency in the Twin Cities." Dr. Haggard's duties were to take care of the poor.

Dr. Weston once said that he wished more medical students were older when they started, as was Dr. Haggard, because the manual dexterity he had developed during his career as a mechanical engineer had proved to be of great assistance in the operating room.

Dr. Haggard served as epidemiologist for the Minnesota State Board of Health and the Minneapolis City Health Department during the time Dr. Albert J. Chesley was executive secretary of the State Board of Health. Their lifelong friendship had begun when Dr. Chesley was a student in a physiology class taught by Dr. Haggard.

Dr. Haggard did the first medical field work in Minnesota, conducting a survey of poliomyelitis, going from farm to farm and town to town throughout the state. Years later, Dr. Haggard heard, at a conference in research studies, that his field work study had been put on charts and exhibited.

Through epidemics of typhoid, diphtheria, smallpox, and poliomyelitis, he carried on his private general practice. He maintained an office in downtown Minneapolis until, in 1903, he built a home at 2400 Chicago Avenue, the first residence in that part of the city. The office space provided in his new home made possible more time with his family.

During these days, Dr. Haggard used a bicycle to make his calls to all parts of the city at all hours and in all kinds of weather. He admits to one traffic accident! In front of the City Hospital on a muddy dirt road, he ran into and knocked down a policeman. There were no fines in those days, and the policeman even helped the good doctor to remount his bicycle and continue on his way. Later on, after his horse-and-buggy days, Dr. Haggard built his own first automobile; it had a marine motor and a speedometer of his own construction.

Dr. Haggard's early training as an expert machinist made it possible for him to install the plumbing and heating in his home. Such skills were not uncommon among the settlers who first populated the West and Minnesota and helped to develop self-reliance, a personal quality essential in those days to the maintenance of one's self and family. The pioneer settlers who were the background for the establishment of the present American way of life were resourceful and also had high ideals of personal, religious, and community responsibilities. Religious faith was and is fundamental to Dr. Haggard and his family and linked them closely to the community and its needs.

About 1916, at the request of the State Board of Health, Dr. Haggard was granted a leave of absence from the University, where he was then teaching. He went to Baudette, Minnesota and Spooner, Wisconsin, after fires that all but destroyed both towns. Poor sanitary conditions favored the development of typhoid fever, and an epidemic ensued. Dr. Haggard started a hospital, set up a fresh water system, and took care of sewage disposal. Within a few months the danger was over, and the townspeople were so grateful that they wanted him to make his home there and become the mayor of Baudette. However, the doctor had to tell the people that he was only on leave from the University.

During World War I, Dr. Haggard served as medical examiner for the Selective Service System and received a commission as First Lieutenant in the Army Medical Corps.

In 1917, Mrs. Haggard died as a result of an accident. On a severe winter day, she hurried out to help a man whose horse had fallen in the alley. Upon returning to the house after they had rescued the horse, Mrs. Haggard fell on the ice and suffered a fatal head injury.

Dr. Haggard and his daughter, Mildreth, still live in the home he built in 1903. His shingle of a practicing physician still hangs at the doorway. It is interesting to note that the barn which housed his horse and buggy is one of the few remaining barns in the city, still standing as it was built, in the back of his home. Dr. Haggard tells of one favorite horse, Nellie, who served him faithfully. "I never found that horse lying down when I went to the barn to leave on a call. She always heard the creak of the back door and never missed being up and ready."

It is because of the unselfish and loving care of Miss Mildreth that Dr. Haggard is able to live so fully. Their days are filled with visitors, including the doctor's professional associates, fellow church members, personal friends, and former patients.

The Haggards have been members of the First Christian Church in Minneapolis all through the years. Dr. Haggard has served as an elder and is now an elder emeritus. He never missed a church service if it was possible for him to get there.

It has been the writer's privilege to know Dr. Haggard during the last quarter of a century and to attend him professionally. Dr. Haggard symbolizes the term "family physician" in all its ramifications. He knew his patients and their families and served them through three and four generations. His daughter says, "My father was always very good at helping with solutions of family problems, because he knew every member of the household well." He was interested in guiding the youths of his neighborhood, and, when one was in trouble, he was there to lend a helping hand.

Dr. Haggard has been the recipient of many honors and awards and has carried many official responsibilities. He was one of the early presidents of the Minneapolis Medical Club, a group of young physicians organized about 1895. The group included Drs. R. E. Farr, J. C. Litzenberg, A. T. Mann, Henry L. Ulrich, and S. Marx White. It is interesting to note that the first tuberculosis clinic in the state was founded about this time at Hamline University School of Medicine, and a similar clinic was founded at the University of Minnesota, with Dr. Ulrich as chairman, a few months later.

Dr. Haggard has served on the medical staffs of Asbury, St. Barnabas, Deaconess, Northwestern, and other hospitals. He has served the Hennepin County Medical Society as president and as member of the executive committee and was made vice-president for life. He is a member of the Fifty-Year Club of both the Minnesota State Medical Association and the American Medical Association. He received the title of emeritus from the staff of Asbury (Methodist) Hospital and an honorary membership on the staff of Northwestern Hospital. He is also a member of the American Academy of General Practice.

Dr. Haggard gave up his active practice in 1953 at the age of 96. He led a life that was long in effective practice because he had the heart of the true physician and gave himself freely to his patients. He served his profession in many capacities—as practicing physician, public health officer, and teacher. Dr. Haggard's idealism, sense of responsibility, integrity, and skills identify him as an outstanding physician in the community.

We salute you, Dr. Haggard, because you have used your talents for the honor of your profession and for the good of those about you. You have healed the sick; you have comforted those in distress; and you have fulfilled your duties as physician and citizen to the honor of your profession, and school, community, home, church, and country. We are thankful that we have known you. We look forward to helping you celebrate your birthday on January 18, 1961, when you will be 104 years old.

Thanks are due to Miss Dorothy Riley for assistance in obtaining material for this manuscript.

THE OCULOGLANDULAR FORM of cat-scratch disease, although rare, can occur in children. Conjunctival ulcer and preauricular lymph node enlargement developed in an 11-year-old girl after facial contact with a cat. Dermal reaction to cat-scratch antigen was positive. The lesions persisted for about two and one-half months.

G. VAN LEEUWEN and C. E. BROOKE: Oculoglandular cat-scratch disease. J. Dis. Child 99:667-668, 1960.

Book Reviews . . .

Coronary Heart Disease

JOHN WILLIAM GOFMAN, M.D., *1959. Springfield, Ill.: Charles C Thomas. 353 pages. $8.00.*

Dr. Gofman is primarily involved with the relationship of plasma lipoproteins to coronary sclerosis. He is particularly interested in those fractions as determined by ultracentrifugal processes. His studies are detailed and well presented.

The author suggests an atherogenic index, which he believes can be a measure of an individual's likelihood to coronary attacks. Unfortunately, other able investigators do not agree with his conclusions, particularly concerning the controversial value of blood cholesterol levels as related to coronary disease.

The book contains many statistical studies relating to other areas in coronary disease. The bibliography is extensive and well selected.

The format is excellent, and the book reflects the excellent craftsmanship of the Charles C Thomas Company.

The book documents Dr. Gofman's beliefs and, for those interested in this feature of coronary disease, is well worth reading. It offers little, however, to those who are interested in the clinical features of coronary artery disease.

JOHN BRIGGS, M.D.
St. Paul

Anatomy of the Human Body

HENRY GRAY, *F.R.S.; edited by* CHARLES MAYO GOSS, M.D., *1959. 27th edition. Philadelphia: Lea & Febiger. 1,458 pages. Illustrated. $17.50.*

The centennial edition, as indicated in Dr. Goss' preface, "finds Gray's *Anatomy* in its hundredth year with its popularity undiminished." The book is still dominated by the genius of Henry Gray and of Gray's friend, H. Van Dyke Carter, who made the woodcuts for the first edition.

In preparing the present edition, Dr. Goss sought suggestions from colleagues. Finding two types of opinion, one demanding deletion and the other amplification, he decided upon certain compromises. He kept the chapter on embryology, because it is "popular and frequently used for preliminary reading and review." He resisted the demand to expand the section on x-ray anatomy and left the roentgenograms where they were, that is, in a chapter on surface and topographic anatomy. He shortened the chapter on the central nervous system by about 50 pages. He modernized the chapter on the heart, thus reflecting his own research interest in the development of the mammalian heart. He added new references to the bibliography, which now has 125 citations, *all complete!*

Gray's *Anatomy* is useful as a text and reference, though it scarcely measures up to Morris' *Human Anatomy*. It cannot be mastered, of course, by freshman medical students or graduate students in one year, but what thick text can?

The *Nomina Anatomica* (Paris, 1955) is adopted in the text. It is not always used, however, in the labels of figures. Relabeling of these figures might have justified the extra cost.

A supplement to the centennial edition has been published and distributed gratis to students (*A Brief Account of Henry Gray F.R.S. and his Anatomy, Descriptive and Surgical, during a Century of its Publication in America*, by Charles Mayo Goss, M.D., Philadelphia: Lea & Febiger, 51 pages, 1959).

LEMEN J. WELLS, M.D.
Minneapolis

The Anatomy of the Nervous System: Its Development and Function

STEPHEN WALTER RANSON, M.D.; *Revised by* SAM LILLARD CLARK, M.D., *1959. Philadelphia: W. B. Saunders Co. 622 pages. Illustrated. $9.50.*

Of the several texts available on neuroanatomy, that of Ranson, first published in 1920, is the best known. Its well-deserved popularity rests on its good balance of embryology, gross anatomy, simple diagrams, and generous illustrations of labeled transverse sections. From the first edition, the late Dr. Ranson endeavored to liven the text with reference to physiologic function. It is manifestly difficult to keep such discussions brief and to avoid controversial matter in a book that is primarily an anatomic text, particularly since, in the last ten years, electrophysiologic methods have enormously expanded available data on the patterns of representation in various parts of the central nervous system.

In the latest edition, Dr. Clark has succeeded admirably in providing summaries of such data. The discussions of the functional significance of the thalamus and of the limbic lobe are particularly well done in this tenth edition. The discussion of evidence for localization in the cerebral cortex is less successful, because there is at present no satisfactory over-all philosophic concept that can pull together the many conflicting statements in the literature. It is questionable if such contradictory material is of value to the average student of anatomy. Discussions of such controversial material as the significance of area 18 could well be omitted. The simplified pattern of cortical cytoarchitectonics of Bailey and Bonin and simple diagrams of nuclear patterns of human thalamus and its cortical connections would be welcome.

The book should continue to be a favorite with those specializing in clinical neurology, as well as with students of anatomy.

D. DENNY-BROWN, M.D.
Boston

The Thyroid Hormones

ROSALIND PITT RIVERS *and* J. R. TATA, *1959. New York: Pergamon Press. 250 pages. Illustrated. $7.50.*

This well-authenticated (over 1,700 references) text on the thyroid begins with the isolation by Kendall in 1915 and identification by Harington in 1926 of the first of these, thyroxine, containing four atoms of iodine per

(Continued on page 21A)

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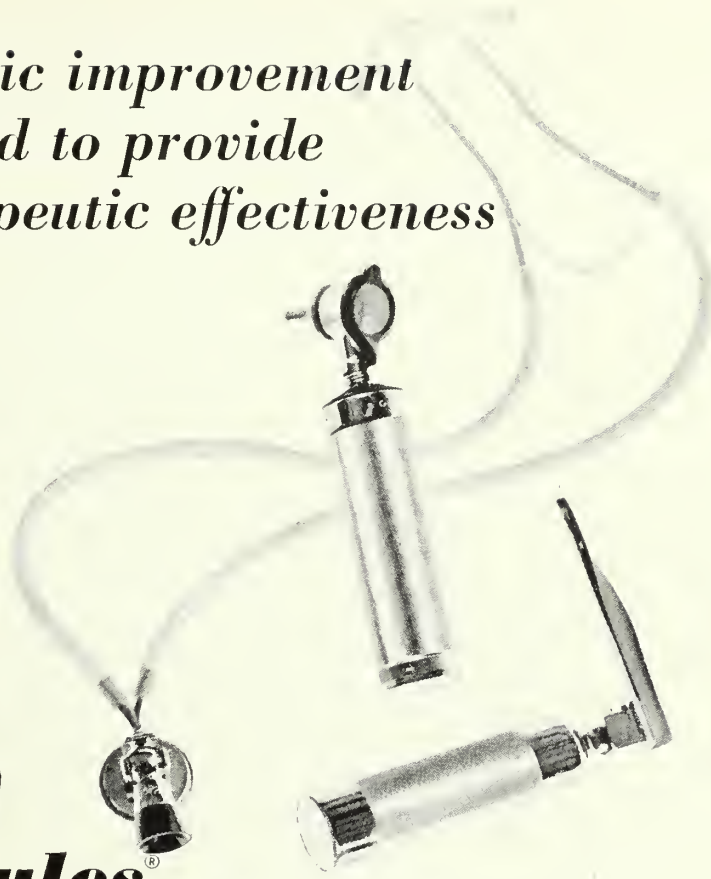

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1. Stephens, V. C., *et al.*: J. Am. Pharm. A. (Scient. Ed.), *48*:620, 1959.
2. Salitsky, S., *et al.*: Antibiotics Annual, p. 893, 1959-1960.
3. Reichelderfer, T. E., *et al.*: Antibiotics Annual, p. 899, 1959-1960.
4. Kuder, H. V.: Clin. Pharmacol. & Therap., in press.

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(Continued from page 44)

molecule. This book is written by a student of Harington's with the same thoroughness, precision, and conciseness that has long made the reading of Harington's papers strongly recommended by the reviewer to his graduate students. It also seems fitting that the isolation and characterization of the second thyroid hormone, triiodothyronine, should have been accomplished in Harington's laboratory.

The work covered in this book attempts to get at the reasons behind the effects of the hormones rather than at what the effects are and to clarify the etiology of various thyroid disturbances rather than to describe their symptoms. As methodology advanced in this field, it permitted an ever-increasing search into the finer details of action of the thyroid hormones. Thus, the work discussed by Pitt-Rivers and Tata can be divided chronologically into the three decades since thyroxine was first identified. During the first of these, the background was laid: (1) the effects of thyroxine were quantitated, (2) its relationship with the pituitary; the importance of thyroidal and blood protein, glucuronide, and sulphate combination in its transport; and its release to tissue and excretion via bile and urine were evaluated, and (3) the etiology of thyroid diseases was roughly defined. The second decade was marked by the introduction of 2 new weapons in methodology: the discovery of the antithyroid drugs and the use of radioactive iodine. The antithyroid drugs are of 2 types, those which, like thiocyanate, interfere with the uptake of iodine by the thyroid gland and those, including the sulfonamides and thioureas, which inhibit the organic incorporation of iodine into the hormone molecule. The former type but not the latter can be overcome by increasing the iodine intake. The inhibition of the goitrogenic activity of thiouracil is used as an assay for thyroxine activity. These drugs have also been used in the treatment of hyperthyroidism. Radioactive iodine is used for studying the metabolism of iodine and of the thyroid hormones. It may be incorporated selectively in the structure of the hormones chemically or throughout the whole hormone molecule by biologic procedures. This has permitted a study of the distribution and rate of uptake of iodine and the thyroid hormones by tissues and cells. Finally, this past decade has seen the application of paper chromatography to thyroid hormone studies. This, particularly when used together with radioactive iodine, permitted the investigation of finer details of iodine hormone metabolism, such as distribution among different parts of the cell. It was the following of an unknown spot of radioactivity, in studies on the blood iodinated hormone metabolites on a paper chromatogram, that led to the isolation of the second thyroid hormone, triiodothyronine. This hormone has one less iodine atom per molecule than thyroxine. A great deal of work has been done during the past few years in comparing the relative potencies of the 2 hormones. While considerable species variation has been demonstrated, in some of these, including man, it appears that triiodothyronine is about five times as active as thyroxine and has a much shorter latent period and shorter duration of activity than thyroxine but the same total activity.

The interdependency of the various branches of science is manifested by the fact that antibodies against thyroglobulin antigen may be involved in many cases of myxedema and in increasing genetic considerations in the etiology of thyroid diseases.

This book is strongly recommended for the growing number of endocrinologists with biochemical orientation and for those interested in the why and wherefore of biologic problems related to the thyroid gland.

SAUL COHEN, M.D.
Toronto

Physiology of the Eye

FRANCIS HEED ADLER, M.D., *1959. St. Louis: C. V. Mosby Co. 780 pages. $9.00.*

This is the third edition of a text which first appeared in 1950. Its purpose is to present the experimental facts gathered in the laboratory regarding the physiology of the eye and to give them practical application.

The text consists of 22 chapters covering each anatomic as well as each physiologic section of the ocular system. This new edition contains recent advances reported both in ophthalmology publications and basic science journals. Dr. Adler has added a section on tonography, which has taken on increased importance in the clinical study of glaucoma in recent years. He refers to the work of Grant and Becker and describes the determination of facility of outflow. The author emphasizes the modern concept of narrow-angle and open or normal-angle glaucoma. In surgery for glaucoma, he adds cyclodiathermy and Scheie's fistulizing operation to the armamentarium described in his 1953 text.

Dr. Adler has added a description by Duane of the retina during a blackout. Retinal ischemia was the cause of the blackout.

The chapter on ocular motility was rewritten. He refers to the relatively new field of electromyography of ocular muscles, in which the electric activity in the ocular muscles is measured and recorded. He describes the contributions of Goodwin and Breinin. The electric activity in agonist and antagonist muscles were studied in various cardinal rotations and vergences. Many electromyograms from Breinin's papers are copied in the text.

The tracings are informative in myasthenia gravis, where the effects of Tensilon can be measured in electric response before the improvement in muscle function is grossly discernible. The electromyogram can help to differentiate a true paralysis of an eye muscle from a mechanical block.

Dr. Adler briefly describes evidence for efferent fibers in the optic nerve. To entoptic phenomena previously noted in his text, Dr. Adler has added Moore's lightening streaks, as well as the phosphene of quick eye movement recently described by Nebel, which may represent an early senescent sign of normal vitreous shrinkage. The author refers to Haidinger's brushes and its possible use in detecting anything which may interfere with the macular pigment, such as edema.

In the chapter on binocular vision, a discussion of the horopters and of Panum's fusional area is included.

There is a section on retinal rivalry, as in presenting dissimilar targets in a test for binocular simultaneous macular perception. Dr. Adler reiterates that the amblyopia of strabismus is selective inhibition.

A bibliography is included at the end of each chapter.

It is quite evident that this text is a very worthwhile addition to the library of the ophthalmologist and ophthalmology residents and is of interest to physiologists. I do not feel that it would greatly appeal to men in other fields of medicine.

HARRY S. FRIEDMAN, M.D.
Minneapolis

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PROGRESS IN NEUROSURGERY

A COMPILATION OF PAPERS IN HONOR OF WILLIAM T. PEYTON

For some time, the physicians who have trained in neurologic surgery under Dr. William T. Peyton have considered ways of honoring him at the time of his retirement as director of the Division of Neurological Surgery at the University of Minnesota. Last fall, 100 per cent of the former residents and several of his close neurosurgical associates attended an informal meeting in his honor. Reports were given by these men on the investigative or clinical projects in which they were specifically interested. It was considered an excellent meeting, and Dr. Peyton seemed to enjoy it very much. But this was a rather personal affair. How could one best express to the physicians throughout the state of Minnesota this same recognition of him? Many worthwhile suggestions were made. Then, in March of this year, Dr. Owen H. Wangensteen suggested to me that the men in the Division of Neurological Surgery collaborate in honoring Dr. Peyton by dedicating an issue of The Journal-Lancet to him. Was this the appropriate way to honor such a man as Dr. Peyton? The more thought that was put to the idea, the more acceptable it became. The more I realized that the most competent way of paying tribute to a man whom we all consider a scholar in the truest sense was to publish a group of papers written by men who have trained under Dr. Peyton and written on investigative and clinical problems in progress at the time of his retirement.

No one ever questioned Dr. Peyton's interest in teaching—and giving to others the fruit of his extensive knowledge and experience. No one ever questioned Dr. Peyton's clinical ability—his natural surgical judgment and his cool and effortless technical skill. What many don't realize is that he always has manifested an intense interest in research problems. He has tried to engender and foster in his students a need to question presumed established fact. He usually answered questions put to him by asking questions. He tried to instill into his students, undergraduates as well as graduates, the need to think a problem out themselves—to apply known data. He has been strong in requiring his students to know and understand thoroughly the basic material so that they can apply it in time of need. He has heeded very little the minutia—the isolated or unrelated item—and he has always felt that, if one knows how to apply basic concepts, the details will take care of themselves. His every productive hour has taught somebody something about medicine in general and about neurosurgery in particular.

Is it, therefore, not manifestly evident that it is with genuine respect and appreciation that the task of helping to publish this issue of The Journal-Lancet was accepted, and why it was felt that the issue should be compiled of reports on work in progress at the time of his retirement?

By the same token, this may be the proper place to announce that the men who have trained with him, either directly as residents in neurologic surgery or by close association in the practice of neurologic surgery, have established by contribution a perpetuating fund in his honor—The William T. Peyton Research and Training Fund in Neurological Surgery. All of these men, as do I, feel a deep sense of gratitude to Dr. Peyton. With this feeling, we dedicate this journal.

Lyle A. French, M.D.
Minneapolis

Use of Dexamethasone in Treatment of Cerebral Edema Associated with Brain Tumors

JOSEPH H. GALICICH, M.D., LYLE A. FRENCH, M.D., and JAMES C. MELBY, M.D.

Minneapolis

This study was prompted by observations made in the course of an earlier investigation to determine the concentration of adrenal corticoids that could be achieved in gliomas as compared to surrounding brain. Patients suspected of harboring gliomas were given large intravenous doses of either cortisol or dexamethasone just before craniotomy, and it soon became apparent that they had unusually smooth postoperative courses. Upon recovery from anesthesia, they were remarkably alert and active, considering the extent of the operative procedures. Furthermore, in those patients receiving maintenance corticoid therapy for several days after surgery, there was no depression of the sensorium or temporary increase in neurologic deficit often observed during the first or second postoperative day and usually attributed to cerebral edema.

More clear-cut evidence of the efficacy of glucocorticoids in relieving symptoms generally attributed to cerebral edema came as a result of treating 2 patients having recurrent glioblastomas with large doses of dexamethasone but without surgical decompression. Improvement in the neurologic status of these patients was impressive. All signs and symptoms of increased intracranial pressure, including papilledema, disappeared, and motor and sensory deficits were either completely alleviated or markedly improved. In an attempt to demonstrate graphically the effect of the drug in these 2 patients, carotid angiography was carried out immediately before treatment and again after maximum improvement had taken place. Comparison of the 2 studies showed reduction of the pretreatment displacement of the cerebral vasculature (figures 1 and 2).

It is well known that many intracerebral tumors, especially fast-growing gliomas and metastatic tumors, are surrounded by edematous brain tissue that may extend for a considerable distance from the tumor and, on occasion, even into the opposite hemisphere.[1,2] It was felt that the reduction in the size of the mass lesion in these 2 patients as evidenced by angiography could be best explained on the basis of relief of such edema. The early onset of improvement, clearly evident eight to twelve hours after initiating therapy, and the achievement of maximum improvement within four to five days after starting treatment would seem to indicate that the corticoid was not affecting the tumor itself. With these encouraging results, a more comprehensive evaluation of the treatment of cerebral edema with dexamethasone has been undertaken. It is the purpose of this paper to report the response of a series of patients with verified brain tumors to this drug.

MATERIALS AND METHODS

Fourteen patients with brain tumors having obvious evidence of increased intracranial pressure were studied. In 13 cases, histologic diagnosis of tumor type was obtained; the exception had a histologically verified adenocarcinoma of the lung, with presence of an intracranial lesion established by angiography. Of the tumors, 12 were located intracerebrally and 1 was in the cerebellum; 1 patient had diffuse meningeal carcinomatosis. Six patients, of whom 5 had recurrent gliomas and 1 a metastatic tumor, were treated with dexamethasone only during their hospital stay. Response to treatment was evaluated in the remaining 8 patients before surgery.

Dexamethasone (16α methyl-9α fluoroprednisolone) was used exclusively in this study. This synthetic glucosteroid was chosen because of its marked antiinflammatory potency and low salt-retaining activity.[3,4] Before the use of this drug in human beings, a preliminary study was made in animals. Doses of dexamethasone phosphate, 2 to 4 mg. per kilogram of body weight, far exceeding those used in this study were injected

JOSEPH H. GALICICH *and* LYLE A. FRENCH *are with the Department of Surgery, Division of Neurosurgery, University of Minnesota Medical School, Minneapolis.* JAMES C. MELBY *is with the Department of Medicine, Medical Center, University of Arkansas, Little Rock.*

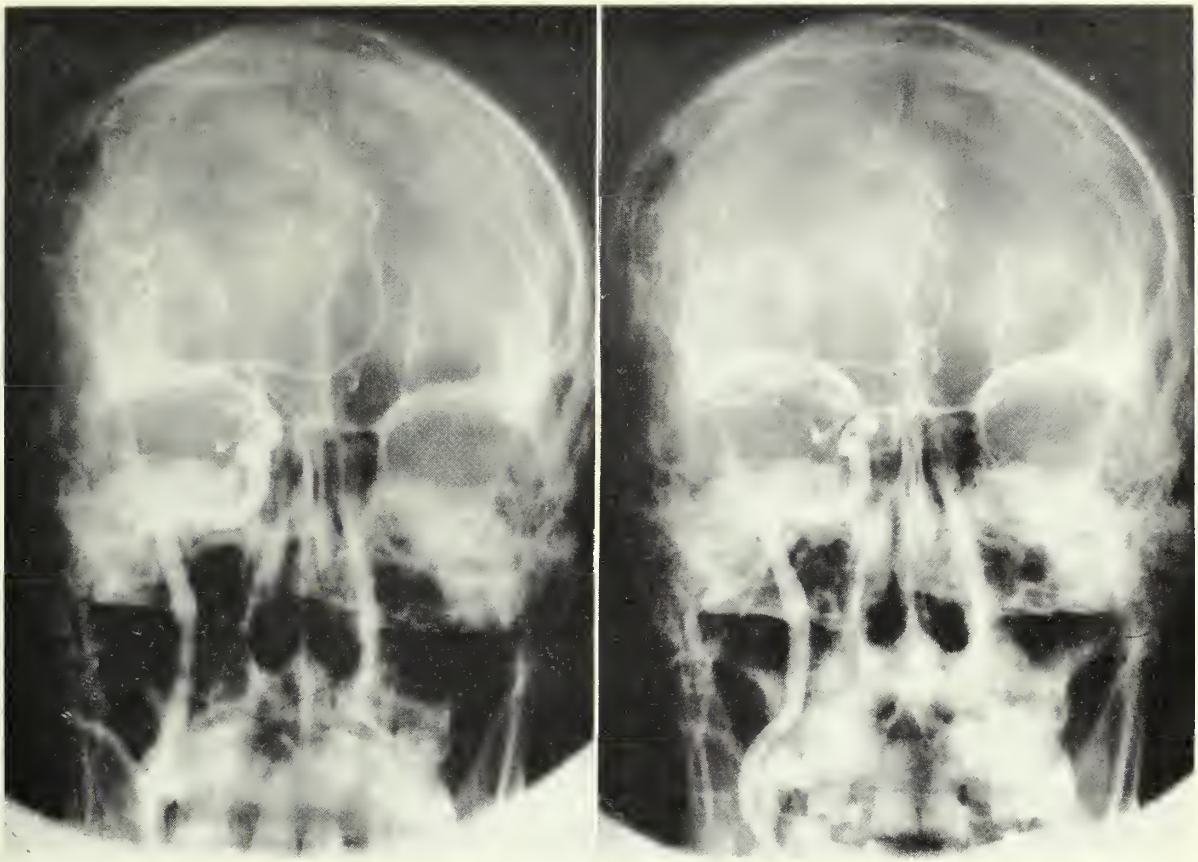

Fig. 1. L. S. Recurrent glioblastoma multiforme, right temporal lobe (see text). *(Left)* Carotid angiogram done immediately before treatment with dexamethasone. Note marked shift of anterior cerebral artery across midline caused by tumor and edema of surrounding brain. *(Right)* Sixth day of treatment. Note return of anterior cerebral artery toward midline.

intravenously and intra-arterially (carotid) in dogs. No ill effects were observed.

In 2 patients, therapy was started with an injection of 40 mg. of dexamethasone phosphate into the carotid artery at the time of angiography. However, intravenous and intramuscular routes proved to be equally effective, and therapy in the majority of cases was initiated with a 10 mg. intravenous injection of the phosphate ester followed by 4 mg. intramuscularly every six hours until a maximum response had been achieved. In those patients subsequently undergoing surgery, this schedule was continued for two to four days postoperatively. As a rule, dosage was then tapered over a period of five to seven days, using the oral, free alcohol form of the drug. In several patients, therapy was continued by the oral route for prolonged periods —up to five weeks.

Aluminum hydroxide gel and various anticholinergic agents were given to the patients to combat any possible ulcerogenic effect of corticoid therapy. The anticholinergic agents were given only after the maximum effect of dexamethasone seemed to have been obtained in order to obviate any possible contribution that these medications might have in reducing cerebral edema. No other medications were given during the observation period.

Response to therapy was evaluated by frequent neurologic examinations and, in the 2 cases mentioned above, by cerebral angiography performed before and after treatment. Serum Na, K, and chlorides were obtained frequently to ascertain any gross disturbance in electrolyte metabolism that might be associated with the use of large doses of corticoids. Accurate recording of fluid intake and output was obtained in 6 patients in an attempt to assess any diuretic action of the drug.

RESULTS

Response to treatment with dexamethasone in 14 patients with brain tumors is given in the

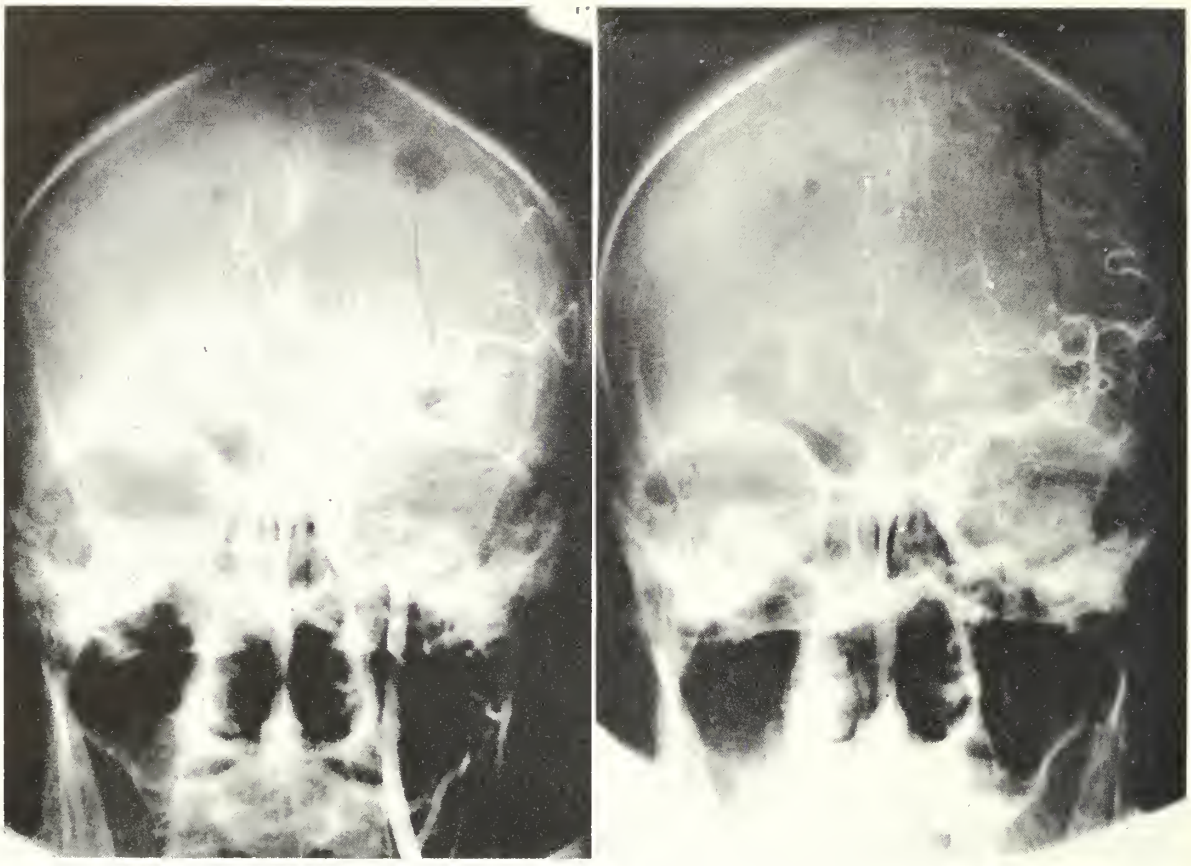

Fig. 2. J. T. Recurrent ghioblastoma multiforme, left temporal lobe (see text). *(Left)* Carotid angiogram done on first day of treatment. *(Right)* Fifth day of treatment. Note return of anterior cerebral artery toward midline. Difference in rotation of head in pre- and post-treatment angiograms in both figures 1 and 2 tends to minimize observed decrease in shift.

table. This series represents all the tumor patients on whom we have thus far (since July 1959) been able to evaluate the effect of dexamethasone alone for any appreciable interval, that is, without any other known beneficial form of therapy given. All patients were evaluated for at least one week, with the exception of 4 patients who underwent surgery two to three days after treatment with dexamethasone was initiated. Since 3 of these patients were still improving up to the time of surgery, no estimate of the time taken to obtain maximum benefit could be established. It is mentioned that, with one exception (K.H.), all patients were in critical condition at the beginning of treatment and, judging from experience with similar cases, would definitely not have improved without relief of intracranial hypertension.

Prompt and continued relief, for the duration of therapy, of signs and symptoms of increased intracranial pressure was taken as evidence of reduction of cerebral edema. Using this criterion, edema was reduced in 13 of the 14 patients in this series. In addition, 8 of these patients showed definite alleviation of neurologic deficit. Onset of response was invariably evident within twelve to eighteen hours after initial therapy, and maximum neurologic improvement was attained within one week in most patients. However, further improvement of varying degree was observed for up to two weeks after this period in several patients.

As might be expected, general symptoms of increased intracranial pressure–that is, nausea, vomiting, and depression of the sensorium, which ranged from lethargy and confusion to coma–were the first to be completely alleviated, usually within twenty-four hours. Further evidence of relief of intracranial hypertension was shown by complete subsidence of a tense, protruding craniotomy flap within forty-eight hours in 1 patient with a recurrent glioma and disappearance of papilledema after one to two weeks of treatment in 5 patients.

Improvement in neurologic function, of course, was related to the location and, to some extent, to the type of tumor. In general, patients with metastatic tumors showed more improvement than those with glioblastomas, and these in turn showed more improvement than 2 patients with infiltrating astrocytomas. This correlates well with the severity of edema usually associated with these tumors.[2]

In this series, 11 patients were hemiplegic or hemiparetic. Of these, 5 responded with greatly improved motor function and 2 others had easily detectable improvement in the strength of their affected extremities. Of the 4 patients who showed no improvement in motor strength, 2 (K.H. and M.K.) had slowly growing astrocytomas and only barely detectable hemiparesis before treatment. Of 5 patients with aphasia, 4 showed definite improvement. The aphasia continued to regress for several days after the patients had become completely alert and oriented; hence the improvement in aphasia was not simply a function of improved sensorium. Homonymous hemianopsia, evident even on confrontation tests, disappeared in 2 patients. Each had a small metastatic tumor, located in the occipital lobe in one patient and in the temporal lobe in the other. In the patient with a suspected cerebellar lesion (A.H.), the cerebellar signs cleared up completely. In another patient with intractable temporal lobe seizures, the seizures stopped during the period of treatment with dexamethasone.

The one patient who failed to show improvement was E.M., a 54-year-old woman with mental deterioration and lethargy of six weeks' duration. Physical examination revealed extreme papilledema, hypoactive deep tendon reflexes, and bilateral Babinski signs. After all other tests, including carotid angiograms and 2 ventriculograms, failed to reveal the cause of her increased intracranial pressure, she was treated with large doses of dexamethasone for one week without improvement. Bilateral subtemporal decompressions proved to be of only temporary benefit, and the patient eventually died. Autopsy showed diffuse carcinomatosis of the meninges, no intracerebral metastases, and no parenchymal edema. Pressure symptoms in this case undoubtedly were caused by failure of absorption of cerebrospinal fluid as a result of a block in the subarachnoid space.

Case summaries of 3 patients, including the 2 having angiograms immediately before and after six days of treatment, are presented below.

Case 1. L. S., a 51-year-old man, did very well for two months after subtotal removal of a large right temporoparietal glioblastoma multiforme. Headaches, episodes of confusion, increasing lethargy, and progressive weakness of the extremities then developed. On admission on June 1, 1959, the patient was stuporous, disoriented, and unable to walk, even with assistance. Examination revealed left homonymous hemianopsia; papilledema; extreme left hemiparesis, most marked in the upper extremity; and probably left astereognosis, although this latter was difficult to assess. A right carotid angiogram was done and showed a shift of the anterior cerebral artery across the midline, with elevation of the middle cerebral group of vessels. Therapy was begun immediately with a 40-mg. injection of dexamethasone into the right carotid artery. The patient was then placed on a maintenance dose of 7.5 mg. of dexamethasone every six hours intramuscularly. Approximately eight hours after the first injection, the patient was considerably less lethargic and took an interest in his surroundings for the first time since admission. By the next morning, he was completely alert and oriented. He could walk with slight assistance and had regained considerable function in his left hand and arm. On the second day of treatment, he walked unaided, with an almost normal gait. On the fourth day, the dose was decreased to 5 mg. every six hours. The patient continued to improve, and a repeat carotid angiogram was done on the sixth day of therapy. At the time of angiogram, the only persisting neurologic deficits were left homonymous hemianopsia, slight weakness of grip in the left hand, and left hyperreflexia. There was no measurable elevation of the optic disk, and the margins were distinct. The angiogram showed marked reduction of shift in the cerebral vasculature (figure 1). The dosage was then tapered over a ten-day period and, because of persistence of improvement, the patient was discharged on 1 mg. of dexamethasone, to be taken twice a day.

The patient was admitted one week later for reoperation. Examination revealed that he had retained the improvement manifested during the previous admission. A repeat right carotid angiogram also disclosed no evidence of exacerbation of edema. However, after the dosage of dexamethasone had been cut to 0.5 mg. two times a day, the patient became increasingly more lethargic and within six days was barely arousable. The dosage of dexamethasone was then increased to 10 mg. four times a day intramuscularly. Within forty-eight hours, he had improved markedly and was again up and about. A repeat craniotomy was carried out on July 10, 1959, with gross removal of the recurrent tumor. Postoperatively, the patient had difficulty with secretions, and aspiration pneumonia developed, resulting in death four weeks later.

Autopsy revealed massive infiltration of both hemispheres and the brain stem with tumor, lung abscess, and blood in the large bowel. Careful examination of the gastrointestinal tract revealed no source of bleeding.

Case 2. A. H., a 58-year-old man, was admitted on August 13, 1959, with headaches and impaired memory of several months' duration. For three weeks, he had experienced progressive weakness of the left extremities and episodes of vertigo. Six months earlier, he had had pneumonectomy for adenocarcinoma of the lung. On examination, he had slurred speech, bilateral papilledema, left homonymous hemianopsia, left central facial paresis, almost total paralysis of the left arm, marked paresis of the left leg with left hyperreflexia, and positive

Romberg and left Babinski signs. Carotid angiography revealed a mass deep in the temporal lobe. During the next several days, the patient became increasingly lethargic and confused, and the slurring of his speech became more pronounced. He was then started on dexamethasone, 4 mg. every six hours intramuscularly. On reexamination eighteen hours later, he was alert and spoke much more distinctly. Strength in his left extremities was greatly increased, and facial paresis was less notable. After the third day, dosage was decreased to 0.75 mg. every six hours orally. Improvement continued, and the patient was discharged from the hospital on the seventh day of treatment. By that time, he was completely alert, spoke distinctly, and walked with a normal gait. He had only minimal weakness of the left arm and slight left hyperreflexia. Papilledema and Romberg and Babinski signs had completely disappeared, and no visual field deficit could be detected by careful confrontation examination.

Case 3. J. T., a 56-year-old man, had fairly extensive removal of a glioblastoma multiforme in the left temporoparietal region two months before admission, after which he had no detectable motor deficit, although he did have homonymous hemianopsia and moderately severe expressive aphasia. On July 27, 1959, he was admitted for the second time because of rapidly progressive right hemiparesis. Examination showed almost total and receptive aphasia, 2-diopter papilledema, right homonymous hemianopsia, right central facial paresis, and total right hemiplegia. After a left carotid angiogram that revealed evidence of a large left cerebral mass lesion, he was given 10 mg. of dexamethasone intravenously; 4 mg. was given intramuscularly every six hours thereafter. Twelve hours after the first dose, he began moving his right extremities. He continued to improve; by the fourth day, there was no detectable weakness of his right extremities and his aphasia was approximately the same as it had been at the time of previous discharge. The next day, a repeat carotid angiogram showed decrease in displacement of the cerebral vasculature (figure 2). The dosage was tapered, and the patient was sent home on 0.75 mg. of dexamethasone three times a day. At the time of discharge, the patient had slightly increased deep tendon reflexes in the right lower extremities and slight right facial paresis but no other motor deficits. Papilledema was no longer present, and the Babinski sign was negative.

Case	*Age*	*Sex*	*Diagnosis*
L.S.	51	M	Recurrent left temporoparietal glioblastoma multiforme
T.T.	56	M	Recurrent left temporal glioblastoma multiforme
M.K.	4	F	Recurrent third ventricular astrocytoma
E.M.	54	F	Diffuse meningeal carcinomatosis
K.H.	30	F	Recurrent astrocytoma, right front temporal region
A.H.	58	M	Metastatic adenocarcinoma, left temporal and(?) cerebellum
T.A.	72	M	Glioblastoma multiforme, both hemispheres
H.L.	65	M	Metastatic squamous cell carcinoma, left occipital lobe
M.R.	38	M	Recurrent left frontotemporal glioblastoma multiforme
E.L.	23	F	Recurrent right parietal glioblastoma multiforme
M.K.	71	F	Metastatic hypernephroma, left temporal lobe
M.B.	68	M	Metastatic adenocarcinoma, left frontal lobe
C.R.	66	M	Left frontotemporal glioblastoma multiforme
C.B.	53	M	Metastatic adenocarcinoma, cerebellum

DISCUSSION

Benignity of the postoperative course in craniotomy patients receiving corticoids has been noted by others.[5,6,7] With the exception of Rassmussen, this observation was made in patients with craniopharyngiomas who received cortisone as prophylaxis against possible preexisting or operatively induced pituitary hypofunction. These authors emphasize the role of cortisone as replacement therapy in these patients but mention the likelihood of reduction of cerebral edema by cortisone as contributing to their good results.

Marked improvement of the condition of patients with cerebrovascular accidents treated with glucocorticoids has been reported. In the series of Russek and associates,[8] 9 out of 12 patients with hemiplegia resulting from cerebral thrombosis or embolism showed improvement in mental status and decrease in neurologic deficit within twenty-four hours after start of cortisone therapy. Greatest improvement occurred within the first twenty-four to forty-eight hours, with gradual improvement thereafter. Roberts[9] used cortisone, cortisol, prednisolone, and prednisone with marked success in treating patients with cerebral infarction. These workers attributed

TABLE 1

RESPONSE TO DEXAMETHASONE IN 14 PATIENTS WITH BRAIN TUMORS

Major signs and symptoms before treatment	*Response to treatment*	*Onset of response (hours)*	*Achievement of maximum neurologic improvement (days)*	*Observation period (days)*
nicoma, papilledema, hemihypes-sia, hemiastereognosis	Alert, oriented; no papilledema or parietal lobe signs; marked return of motor function	12	6	37
nfusion, aphasia, papilledema, ho-nymous hemianopsia, hemihypes-sia, hemiplegia	Oriented; complete disappearance of papilledema, hemiplegia and hemi-hypesthesia; aphasia improved	12	4	10
usea, vomiting, headache, papille-na, slight hemiparesis	Relief of all evidence of increased intracranial pressure including pa-pilledema; hemiparesis unaltered	24	–	36
na, papilledema, bilateral Babin-reflexes	No improvement	—	–	8
nstant headache, frontal lobe syn-me, intractable temporal lobe sei-es, slight hemiparesis	No headaches or seizures; personali-ty improved; hemiparesis unaltered	48	–	20
por, papilledema, homonymous nianopsia, cerebellar signs, hemi-gia	Alert; no papilledema, visual defect, or cerebellar signs; marked improve-ment in strength	18	5	7
npletely unresponsive for six ks, pneumonia, hemiplegia	Awake, talking, eating	24	3	10
fusion, lethargy, papilledema, nonymous hemianopsia	Alert, cooperative; disappearance of papilledema and homonymous hemi-anopsia	12	5	27
adache, nausea, vomiting, papille-na, hemiplegia, slight aphasia	Complete relief of all symptoms of increased intracranial pressure; neu-rologic status essentially unchanged	24	–	14
adache, nausea, vomiting, hemi-gia, parietal lobe signs, marked ging over craniectomy	Relief of headache, nausea, vomit-ing; improvement in motor and sen-sory functions; scalp depressed over craniectomy	24	7	26
nieoma, hemiplegia, aphasia	Alert, oriented; improvement in aphasia; good return of strength	12	*	3
hargy, complete aphasia, hemi-gia	Alert, oriented; speaking in sen-tences; walking unassisted	12	*	3
por, uncooperative, aphasia, hemi-gia, papilledema	Alert, oriented; speaking in sen-tences; good return of strength in leg	12	*	3
hargy, disorientation, papillede-, cerebellar signs	Alert, oriented	18	–	2

*Since patients were still improving up to time of surgery, no estimate of time taken to obtain maximum benefit was established.

their results to relief of the interstitial edema so often prominent in this type of lesion.

Hume and Moore[10] have reported relief of signs and symptoms of increased intracranial pressure with ACTH therapy in a patient with a secondary tumor of the brain. That cerebral edema may be reduced to some degree even by levels of endogenous glucosteroids within the physiologic range is suggested by the quite common observation that the condition of patients with space-occupying brain lesions is often appreciably better each morning and worsens as the day progresses. Studies of the circadian (diurnal) rhythm of circulating 17-hydroxycorticosteroids in human beings have shown that they reach their peak levels early in the morning, fall rapidly until about noon and then more slowly, with the lowest values being obtained

at night. Daily variations in the severity of the symptomatology of some brain tumor patients, especially with regard to the sensorium, hold an inverse relationship to this normal rise and fall of adrenal steroids.

Several studies have shown that experimentally produced cerebral edema can be suppressed by ACTH and a variety of glucosteroids. Prados and associates[12] showed that cerebral edema, measured as an increased permeability to trypan blue, produced in cats by exposure of the cerebrum to air for long periods could be inhibited by ACTH and adrenal cortical extract. This work was confirmed and extended by Grenell and his collaborators,[13,14] who reported that cortisol was more active in preventing edema than either ACTH or cortisone. Desoxycorticosterone in contrast to 11-oxysteroids increased edema and permeability to trypan blue. Foley and associates[15] reported that cortisone inhibited edema and extravasation of serum in tissue adjacent to stab wounds in brains of guinea pigs.

The mechanism of action of glucocorticoids in inhibiting or decreasing brain edema is uncertain. Indeed, the pathogenesis of brain edema is obscure. The brain seems to be able to react to injury in a limited fashion, and the edema caused by a variety of insults is histologically similar.[2] The fact that corticoids influence brain edema resulting from many different types of injury supports the concept of the nonspecificity of brain edema. A prominent feature of edematous brain is its increased vascular permeability. Whereas normal brain tissue excludes, to a great extent, larger molecules such as albumin and various dye stuffs and its rate of exchange with common electrolytes is very slow as compared to other body tissues, edematous brain has lost, to a varying extent, both this discriminatory capacity and impediment to exchange with substances within the vascular system. Irrespective of the exact mechanism of the development of cerebral edema, the phenomenon can be prevented by the administration of glucosteroids in experimentally produced brain edema. It is our feeling that glucocorticoids may reduce edema by restoring the integrity of the cerebrovascular brain barrier.

The diuretic effect of the glucocorticoids seems to play little part in the relief of brain edema. Although 3 patients exhibiting improvement in response to dexamethasone therapy in this study showed moderate diuresis, that is, urine output was equal to or up to 1 liter more than fluid intake for one to three days, marked improvement always preceded any significant water loss, the height of the diuretic effect being twenty-four to forty-eight hours after the beginning of treatment. Furthermore, diuresis was not detected in 3 patients successfully treated.

Sodium diuresis has been reported[4] with large doses of the glucocorticoids and could conceivably decrease brain edema. No alterations in serum electrolytes were detected in this series. However, urinary electrolyte excretion studies done on 1 patient (E.L.) revealed that the patient actually retained sodium during the period in which relief of cerebral edema was evidenced by the transition of a tense, 2-cm. bulging of the scalp over a craniectomy to a scaphoid depression. This finding would suggest that the mechanism of action of dexamethasone in relieving cerebral edema is not via a decrease in total body sodium. Accurate water and electrolyte balance studies are needed to confirm the foregoing impressions and are now in progress.

With the exception of the one possible but unproved case of gastrointestinal bleeding mentioned previously, no detrimental side effects often associated with the use of large doses of corticoids were met in this study. One patient (M.K.) had a typical Cushinoid facies after one month of treatment but did not exhibit hypertension. There were no infections or delayed healing of wounds in those undergoing surgery, and there was no indication of adrenal suppression upon discontinuance of dexamethasone.

SUMMARY AND CONCLUSION

1. Fourteen patients with increased intracranial pressure as a result of brain tumors were treated with dexamethasone, a potent synthetic glucosteroid, to determine its effect on localized cerebral edema.

2. Of the 14 patients, 13 showed dramatic improvement as evidenced by relief of signs and symptoms of increased intracranial pressure and decrease in neurologic deficit. In 2 cases, angiographic proof of a decrease in the size of the intracranial mass was obtained.

3. Improvement in these cases is undoubtedly a result of decrease in the edema surrounding the tumor and illustrates the surprisingly great contribution of localized cerebral edema to the neurologic deficit in such patients.

4. It is our impression that patients receiving glucocorticoids before or immediately after surgery generally have an unusually benign postoperative course.

5. With the exception of 1 possible case of gastrointestinal bleeding, no detrimental complications attributable to dexamethasone therapy were observed.

6. A discussion of the possible mechanism of action in decreasing brain edema is presented.

7. It is concluded that treatment of localized brain edema with dexamethasone is safe and highly effective.

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Incidence of electroencephalographic abnormalities is high after whiplash injuries sustained in automobile accidents. Therefore, apparently psychoneurotic reactions after such injury may actually reflect underlying brain damage. Treatment of patients with psychoneurotic symptoms and persistent electroencephalographic abnormalities is less successful than that of subjects without such abnormalities.

Injury to the brain may result from (1) the sudden contact of the organ with the skull, (2) accelerating or decelerating forces on the brain tissue, or (3) vascular insufficiency associated with involvement of the vertebral artery.

Moderate to notable electroencephalographic abnormalities were found in 21 of 47 patients with whiplash injuries but without head trauma. In 4 patients, abnormalities have persisted longer than eighteen months, signifying probable permanent brain damage.

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Chemopallidectomy and Chemothalamectomy in the Treatment of Parkinsonism

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The disability of advanced parkinsonism is well known. The increasing tremor and muscular spasticity that cripples the patient while he retains good intellectual function provides extreme frustration. Drug treatment, inefficacious except in mild cases, has now found a welcome aid in cerebral basal ganglion surgery.

Personal observation of such patients before and after chemopallidectomy and chemothalamectomy has been gratified by the results obtained. For the most part, the surgical technic outlined by Cooper and Bravo[1–3] was followed by the author. Tables 1, 2, and 3 summarize the clinical data of the patients operated upon. Table 3 is concerned with other basal ganglion diseases treated with the same method as parkinsonism.

Method

The patients treated had progressed to a state of appreciable disability, during which time various medications and extensive physiotherapy had been used. The patients selected for this surgical treatment should always have appreciable disability from a slowly progressive disease and be sufficiently mentally vigorous to make good rehabilitation prospects. These requirements place most of these surgical candidates below the age of 60 years.

The beneficial result gained is the reduction of muscle spasticity and tremor of the side of the body opposite to the side of the brain operated upon; there also is often less but definite reduction of spasticity and tremor on the same side. Mental impairment does not occur. Muscle tension distress or pain in newly relaxed parts of the body is immediately relieved. Relaxation of tightness in the face and throat permits easier smiling, chewing, talking, and swallowing, with reduced salivary distress. Body posture becomes more erect, walking steps are longer, with less stumbling; and swinging of the arms returns. The patients also claim that their minds become relaxed and thinking is easier. Nervousness has been reduced, appetite increased, weight gained, and body strength increased. Extremities improve in dexterity. Greater benefit is derived from reduction of spasticity than from reduction of tremor. Various medications employed to reduce spasticity and tremor have an enhanced effect after chemopallidectomy.

Certain unusual occurrences follow alcohol injections into the basal ganglion regions. Lethargy and reduced mental alertness and awareness that may last several hours have been observed. Spasticity and tremor may actually increase for several minutes or even an hour or more after injection; then reduction in spasticity and tremor usually occurs. Frequently, transient motor paresis of the contralateral face and arm, and occasionally of the leg, occurs after the alcohol injections and ordinarily decreases after a few days or weeks. Expressive aphasia or mutism sometimes develops at about the time of the third alcohol injection, which is usually about a week after the original placement of the catheter in the globus pallidus or in the thalamus. Ordinarily, speech returns after a few days. A general state of apathy and weakness may last for several days after the alcohol injections. Mental acuity and memory may even be decreased for several days after the procedure. These disturbances are, for the most part, temporary and are definitely outweighed by the benefits derived.

Figures 1 and 2 demonstrate the intraventricular air of the pneumoencephalogram used during the procedure to give anatomic landmarks for placement of the catheter, which is carried out with local anesthesia to enable better evaluation of the patient's response to the procedure. Figures 1 and 2 show the position of the cavity in the medial part of the globus pallidus after Pantopaque has filled a small balloon at the end of the tube. About 1 cc. of absolute alcohol is

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TABLE 1

UNILATERAL CHEMOPALLIDECTOMY AND CHEMOTHALAMECTOMY FOR PARKINSONISM

Patient	*Age*	*Sex*	*Disability*	*Duration (years)*	*Surgery*	*Result*
M. J.	59	F	Moderately marked right rigidity, little tremor	25	8/28/58, left chemopallidectomy	Fairly good
G. K.	56	F	Marked rigidity, little tremor, right more than left	5	12/3/58, left chemopallidectomy	Fairly good
R. K.	56	M	Marked rigidity, little tremor, right more than left	15	12/5/58, left chemopallidectomy	Excellent and bilateral improvement
G. M.	56	M	Moderately marked rigidity, less tremor bilaterally	5	4/1/58, left chemopallidectomy	Excellent and bilateral improvement
N. J. H.	60	M	Moderate marked tremor, less rigidity, left more than right	10	9/5/57, right chemopallidectomy	Fair
E. N. O.	47	M	Marked rigidity, less tremor, mostly right	5	4/8/59, left chemothalamectomy	Excellent
H. C. T.	52	M	Moderate tremor, less rigidity, right more than left	13	8/6/58, left chemopallidectomy	Very good
E. H. A.	58	M	Moderately marked right tremor, less rigidity, less on left	6	11/19/58, left chemopallidectomy	Very good
A. D.	65	F	Marked rigidity, tremor bilaterally	12	8/20/58, left chemopallidectomy	Good

TABLE 2

BILATERAL CHEMOPALLIDECTOMY AND CHEMOTHALAMECTOMY FOR PARKINSONISM

Patient	*Age*	*Sex*	*Disability*	*Duration (years)*	*Surgery*	*Result*
A. J. A.	50	M	Marked bilateral rigidity, tremor	8	11/—/54, left premotor cortex excised 6/27/58, rt. chemopallidectomy 9/4/58, left chemopallidectomy	Rt. arm and leg paresis Improved for two weeks, then regressed Gradual regression Died 10/13/58
I. S. C.	40	F	Marked rigidity on left, then on right after right chemopallidectomy	10	2/5/58, rt. chemopallidectomy 10/10/58, left chemothalamectomy	Good relaxation on left Excellent bilateral improvement
V. M. C.	57	F	Moderately marked bilateral tremor, some rigidity	6	10/1/57, left chemopallidectomy 5/5/59, rt. chemothalamectomy	Good Good
H. L. F.	48	F	Marked bilateral rigidity, some tremor	5	12/28/57, left chemopallidectomy 4/9/58, rt. chemopallidectomy	Good Excellent
M. P. R.	59	M	Marked rigidity, tremor of both arms, less of legs	11	5/29/58, left chemopallidectomy 8/7/58, rt. chemopallidectomy	Very good Fair

TABLE 3

CEREBRAL PALSY

Patient	*Age*	*Sex*	*Diagnosis*	*Disability*	*Operation*	*Result*
R. K.	20	M	Kernicterus	Marked bilateral muscle spasticity	9/30/59, left chemothalamectomy	Good
M. N.	19	F	Kernicterus	Marked bilateral muscle spasticity, athetosis	7/3/58, left chemothalamectomy	Improvement good bilaterally
H. N.	37	M	Dystonia musculorum deformans	Marked bilateral muscle spasticity	8/28/59, left chemothalamectomy	Good bilateral improvement for 6 days postoperatively, then deteriorated and died 15 days postoperatively
L. O.	20	F	Cerebral palsy	Marked spasticity, athetosis of left arm and leg, much less of right	7/30/59, right chemothalamectomy	Very good

injected into this small, balloon-made cavity at two- or three-day intervals and usually in 3 separate injections, after which the catheter is removed.

Figures 3 and 4 show the Pantopaque-filled area where alcohol has been injected into the ventrolateral region of the thalamus during a chemothalamectomy. The essential difference between the region of the lesion in chemothalamectomy and that in chemopallidectomy is that the former is slightly more superior and posterior. The lateral distance from the midline is about the same in both procedures.

A lesion in the medial part of the globus pallidus eliminates rigidity better than tremor, whereas a lesion in the ventrolateral part of the thalamus serves to eliminate both spasticity and tremor. This was pointed out by Bravo and Cooper[3] and was observed in this study also. A substantial persisting benefit seems to result from these surgical procedures, as seen among these patients, many of whom have been followed for a two-year period. The cerebral palsy group does not generally enjoy the same degree of benefit as the parkinsonian, perhaps because of more extensive basal ganglion pathologic involvement.

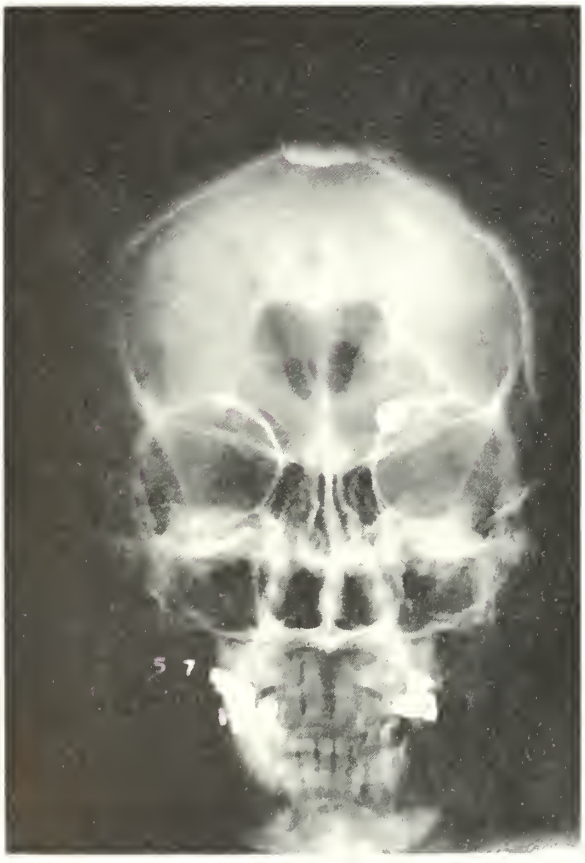

Fig. 1.

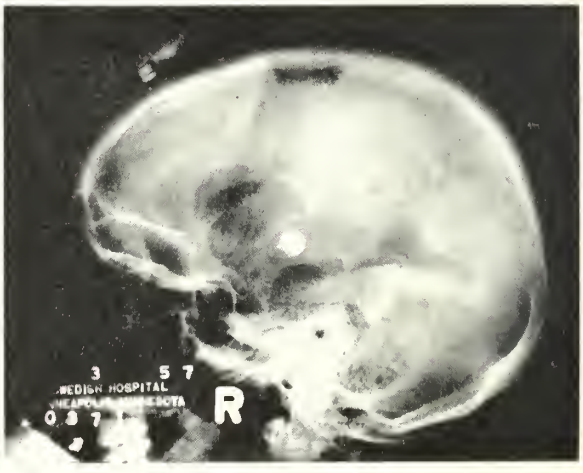

Fig. 2.

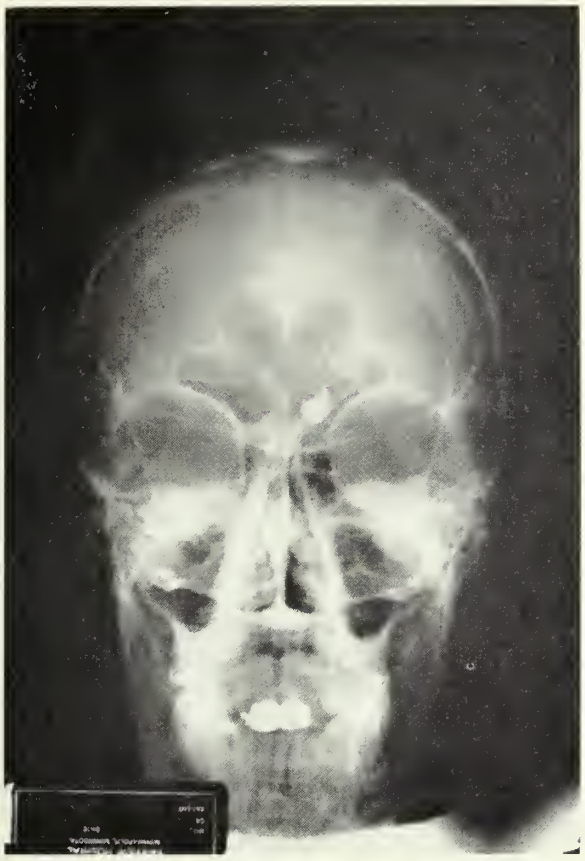

Fig. 3.

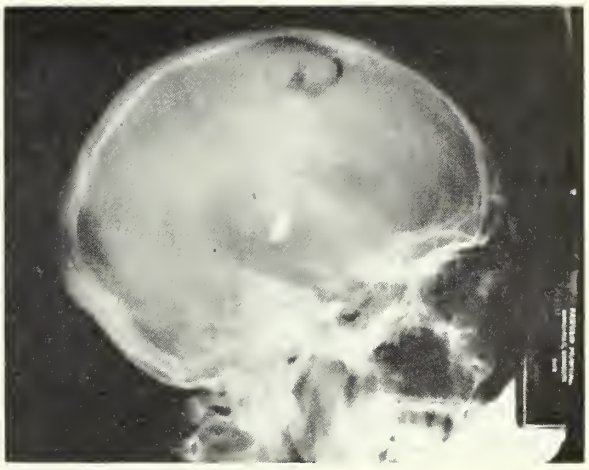

Fig. 4.

SUMMARY

Chemothalamectomy, at present, appears to be a practical neurosurgical procedure, employable in general clinical practice in most hospitals, that affords substantial reduction of the crippling rigidity and tremor of basal ganglion disease. Morbidity and mortality incidence has been very low. The patients selected should have sufficient disability to warrant the operation. Their mental and physical status should be vigorous enough to make them good rehabilitation candidates.

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Children with congenital or early brain damage are shorter and lighter than would be expected when compared with healthy siblings and graded on standard anthropometric charts. Persons acquiring brain damage later in childhood apparently do not differ greatly from predicted height and weight. Degree of impairment of speech and self-help correlates well with extent of growth retardation. More careful study of metabolic needs, intake, and incidence of fever or infection is needed before such retardation can be explained satisfactorily.

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Cerebral Hemispherectomy for Intractable Seizures . . . A Long-Term Follow-up

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THE PURPOSE of this report is to present long-term follow-up studies on patients who have had cerebral hemispherectomies for intractable seizures, personality disturbances, and hemipareses. A report in 1955[1] presented follow-up data on this series of patients up to that date. The longest follow-up then was approximately four and a half years. The patients have been seen subsequently on a number of occasions, and the longest follow-up period now is ten years. No reports in the literature, to our knowledge, give data on a series of comparable patients.

SELECTION OF CASES AND PREOPERATIVE STUDIES

Patients in this series were selected mainly from the population of the Cambridge State School and Hospital, Cambridge, Minnesota. Criteria used in the selection were hemiparesis since infancy or early childhood and grand mal seizures uncontrolled by what is generally considered adequate anticonvulsant medication. Hemiparesis alone was never considered sufficient indication for operation. At the time of selection of these patients, a disturbance in personality and in adjustment to environment also was not considered an indication. In retrospect, however, after following the postoperative course of the patients, it became apparent that not only did they have aberrations of personality and adjustment but also that these aberrations became less obvious postoperatively. Following surgery, most of the patients began to adjust very satisfactorily.

The group was selected from the population of the Cambridge Hospital because it was possible to obtain long preoperative care data on the number and character of observed seizures in each twenty-four hour period as well as the type and quantity of anticonvulsant drugs given during these periods. Preoperative work-up included history, physical examination, neurologic evaluation, carotid angiographic studies, pneumoencephalographic and electroencephalographic studies, and an extensive battery of psychologic tests.

OPERATIVE PROCEDURE

All patients were operated upon under thiopental-curare-nitrous oxide-oxygen anesthesia. A large craniotomy flap was turned down to expose a maximum of the involved cerebral hemisphere. The medial edge of the bone flap, in fact, went across the midline, so that the sagittal sinus was well exposed in all cases. Thus it was possible to turn the dural flap with the closed end toward the midline and then to place traction on this flap so that the large veins entering the sinus were more readily exposed. Cortical electrography was carried out under various experimental conditions.[2] The hemisphere was then excised. This was accomplished by first ligating the middle and posterior cerebral arteries immediately beyond their origin. Both vessels were cut at this time to prevent, in the process of removal of the hemisphere, traction on the proximal portion of the vessel which might secondarily induce ischemia of the basal ganglia or hypothalamus. However, in 2 patients, it was unusually difficult to expose the posterior cerebral artery, so it was cut in these patients immediately before the final removal of the hemisphere. The veins entering the sagittal sinus were then severed; the corpus callosum was incised longitudinally and the lateral ventricle entered. The anterior cerebral artery was severed immediately distal to the anterior communicating branch after it was ascertained that the contralateral anterior cerebral artery was present and arising from the contralateral internal carotid artery. Dissection from this point varied with the amount of basal ganglia that was to be removed. Generally, the stria terminalis was visualized and an incision was made along the stria so that

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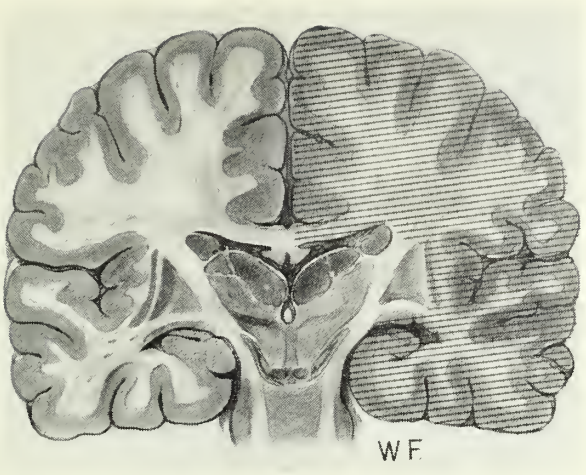

Fig. 1. Drawing to show extent of resection of brain tissue. Hemisphere is resected down to caudate nucleus, thalamus, globus pallidus, and putamen.

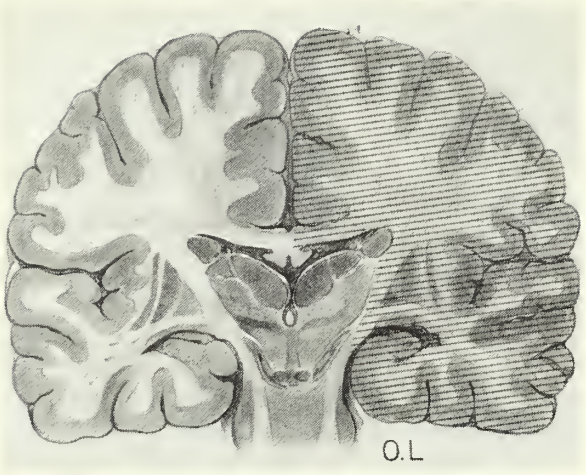

Fig. 2. Drawing to show extent of resection of brain tissue. Caudate nucleus and thalamus are left intact, but globus pallidus and putamen have been removed.

the caudate nucleus was separated from the thalamus. The line of dissection was then carried down the internal capsule to emerge at the incisura tentorii. During this latter dissection, the posterior cerebral artery occasionally was cut. The choroid plexus was excised. A wedge of the tentorium often was removed in order to expose the cerebellum for stimulation studies. In some patients, not included in this study, the thalamus also was removed. In this event, instead of the incision being made at the stria terminalis, the third ventricle was entered and the lateral incision was made at the upper margin of the third ventricle.

After electrographic and stimulation studies were made on the exposed remaining part of the hemisphere, the cavity was filled with saline solution and closure obtained in the usual fashion.

The extent of the hemispherectomy varied slightly from case to case. In all patients, the entire cerebral cortex, including the insula, hippocampus, amygdala, and inferior orbital gyri, was removed. In 2 patients, all the basal ganglia were left intact (figure 1). In 1 patient (figure 2), the caudate nucleus and thalamus were left intact but the globus pallidus and putamen were removed. In 2 patients, the caudate nucleus, globus pallidus, and putamen were removed but the thalamus was left intact (figure 3). The reason for this varied amount of resection was primarily investigative.

Gross abnormalities seen at operation were extensive in all cases and included such diverse abnormalities as high areas of severe leptomeningeal scarring, subarachnoid cysts that had replaced huge areas of the brain, and extensive vascular malformation. One patient had a Sturge-Weber syndrome (figure 4). Figure 5 shows an operative field. It is apparent that this is a fairly extensive resection of cerebral tissue.

CASE REPORTS

A short report on each of the patients included in this series is given in order to familiarize one with the clinical problem. In table 1 is given a summary of the patients, with data on diagnosis and results.

Case 1. H. P. was 38 years old at the time of hemispherectomy. Twelve years previously, a glioma had been removed from his left cerebral hemisphere, after which he had moderate right hemiparesis and slight expressive

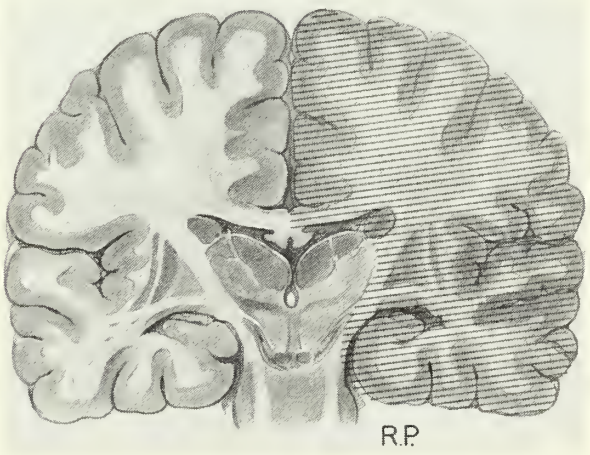

Fig. 3. Drawing to show extent of resection of brain tissue. Everything, including caudate nucleus, putamen, and globus pallidus, is removed down to thalamus.

TABLE 1
SUMMARY OF PATIENTS PRESENTED IN THIS REPORT

Number	*Patient*	*Diagnosis*	*Follow-up in years*	*Preoperative seizures per year*	*Postoperative seizures*	*Behavior*
1	H. P.	Gliosis	10	Status epilepticus	0	Improved
2	C. K.	Sturge-Weber	8	300-500 grand mal	1	Improved
3	O. L.	Meningo-encephalitis	8	300-500 grand mal	5	Improved
4	C. B.	Microcephaly, meningoencephalitis	13¼ mo. (died)	700-800 grand mal	75	No change
5	K. W. F.	Birth injury	8	165 grand mal	6	Improved
6	R. P.	Birth injury	7	50 grand mal, 1,800-3,600 petit mal	1	Improved
7	D. S.	Birth injury	7	50-100 grand mal	1	Improved
8	D. G.	Birth injury	6	65-160 grand mal	0	Improved

aphasia. He progressed reasonably well except for recurrent convulsive seizures (figure 6). He had been in status intermittently for a period of six weeks, controlled only when under thiopental sodium anesthesia, at the time of hemispherectomy. Since removal of the left cerebral hemisphere down to the thalamus on March 1, 1950, he has had no seizures. He is on no anticonvulsant medication. Spastic right hemiparesis and the same aphasia that was present preoperatively have continued. Neurologic loss postoperatively did not exceed the preoperative status. Removed brain tissue contained a diffusely infiltrative glial scar. There was no evidence of recurrent neoplasm. The patients personality and environmental adjustment were adequate both before and after surgery. Although he is not self-supporting, he is appreciated in his family group.

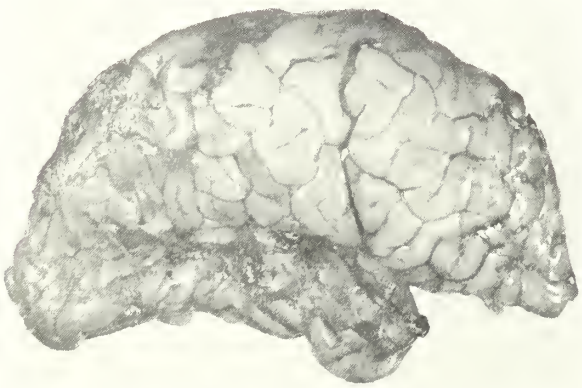

Fig. 4. Photograph of excised brain tissue from patient with intractable seizures associated with intracerebral vascular malformation, primarily in occipital and temporal areas, cerebral cortical calcium deposits, and facial angioma consistent with Sturge-Weber syndrome. Extensive involvement of excised hemisphere is apparent. Frontal lobe appears normal grossly, but histologic examination revealed extensive gliotic changes.

Case 2. C. K. was 13 years old at the time of surgery. She had an obvious Sturge-Weber syndrome (figure 4). Neurologically, she had extreme spastic left hemiparesis, marked athetoid movements of the involved arm, and almost continuous bobbing of the head. For several years before surgery, she had had 300 to 500 grand mal seizures per year (figure 7). Hemispherectomy was done, with the exception that the thalamus, caudate nucleus, globus pallidus, and putamen were left intact. Approximately five days after surgery, she had 1 grand mal convulsive seizure. Hemiparesis has continued, but the athetoid movements and bobbing of the head have ceased. From the standpoint of ward administration, there was unquestionable immediate improvement, which has been maintained. Before surgery, the patient needed much help in feeding herself, was subject to frequent temper tantrums, was enuretic, and was confined to the ward because of frequent seizures. Since surgery, she has taken more responsibility for feeding herself; handles toilet needs satisfactorily; is amenable except for occasional striking out when her hair is combed; and can go for walks because of freedom from seizures. She has been maintained on phenobarbital, ¾ gr. once a day.

Case 3. O. L. was 34 years old at the time of surgery. Birth and immediate postnatal development were normal. At the age of 2 years, she had severe meningoencephalitis. During the illness, a left hemiplegia developed. After the illness, she continued to have spastic left hemiparesis, was moderately mentally retarded, and had recurrent grand mal convulsive seizures. She was committed to the State School and Hospital at 15 years of age. She continued to have 300 to 500 major seizures yearly in spite of anticonvulsant medication. On July 9, 1952, right-sided craniotomy was performed. The exposed hemisphere revealed atrophic gyri and widened sulci. Arachnoid and pia were almost opaque. The hemisphere was excised, leaving the caudate nucleus, thalamus, globus pallidus, and putamen intact. Postoperatively, the patient has had 5 seizures (figure 8), all occurring in

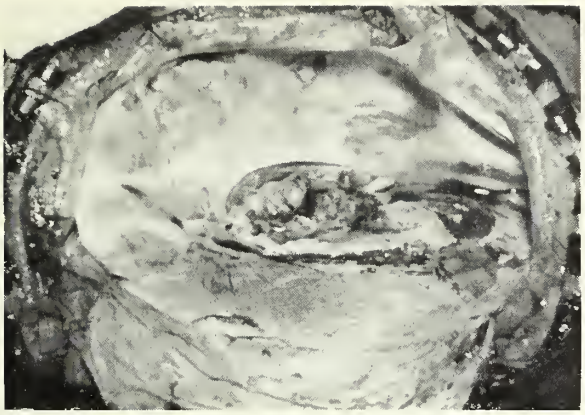

Fig. 5. Photograph of operative field after excision of cerebral hemisphere. Thalamus, caudate nucleus, globus pallidus, and putamen are intact. Falx and tentorium are plainly visible. Optic chiasm, optic nerve, oculomotor nerve, and carotid artery are visible anteriorly along incisura of tentorium.

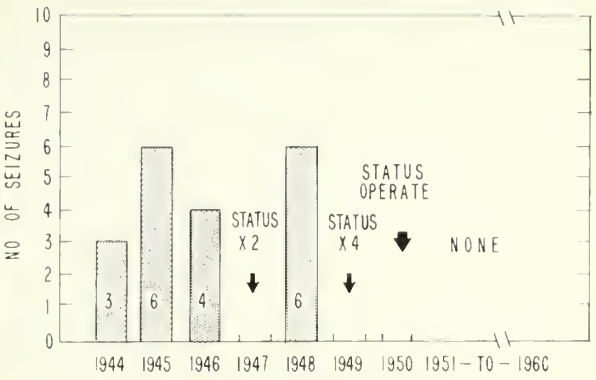

Fig. 6. Graph showing comparative seizure frequency before surgery (March 1, 1950) and absence of seizures postoperatively.

the immediate postoperative recovery phase. From the standpoint of the hospital administrator, remarkable benefit has been obtained. Before surgery, institutionalization for an indefinite period seemed inevitable on the basis of frequent severe seizures and aggressive and disturbed behavior—stubbornness, noisiness, fighting, attacking aides, and refusing food. Plans are now under way to separate her to a nursing or rest home environment because of exemplary behavior—neatness, quietness, never quarrelsome, orderly, helping with simple ward chores, and liking to draw.

Case 4. C. B. was 19 years old at the time of operation. Her birth was a full-term delivery. Sudden onset of grand mal convulsive seizures at the age of 5 weeks was followed by paralysis of the right arm and leg. Seizures present during infancy were severe and nu-

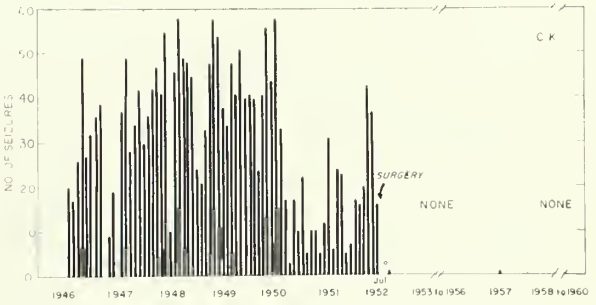

Fig. 7. Graph revealing comparative seizure frequency before and after surgery (July 1952). One bona fide attack occurred during immediate postoperative period. Seizure occurring in 1957 was only suspected because, when patient awakened in the morning, her pillow was damp, suggestive of nocturnal attack with salivation.

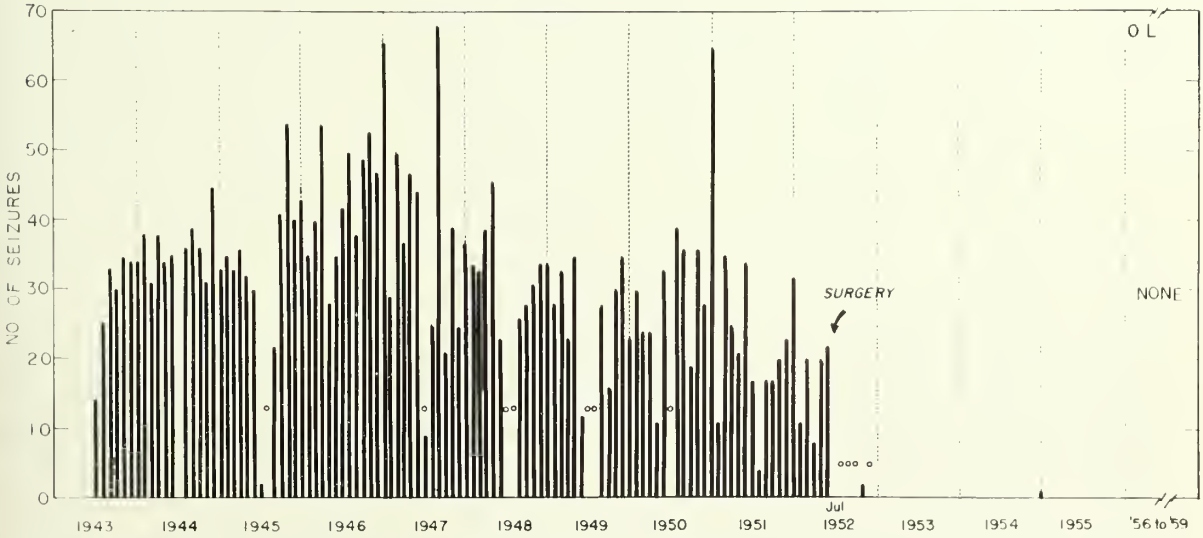

Fig. 8. Graph revealing seizure frequency before surgery (July 1952), five seizures that occurred during the immediate postoperative period, and long subsequent seizure-free period.

merous. Examination at 3 years of age revealed that the patient could walk a few steps and could speak a few words. Because of very retarded physical and mental development, as well as the great frequency of seizures, she was committed to the Cambridge State School and Hospital at the age of 4 years. She averaged 700 to 800 grand mal seizures each year for a period of almost seventeen years.

On December 21, 1952, a large left-sided craniotomy was performed. Throughout the left cerebral hemisphere were atrophic gyri with enlargement of the sulci. A large porencephalic cyst was found in the posterior part of the hemisphere. The overlying pia arachnoid was very thick, as though the patient had had meningoencephalitis. Hemispherectomy was carried down to the thalamus; all other basal ganglia were removed. Immediate postoperative convalescence was uneventful, although the girl had about 10 grand mal seizures originating on the right side of the body on the second or third postoperative day. She was continued on medication and, during the succeeding thirteen and one-fourth months before she died of diphtheria, had a total of 75 grand mal seizures. She is classified as a poor result, although reduction in seizures was almost 90 per cent.

In retrospect, this patient had had definite microcephaly, as well as severe meningoencephalitis at the age of 5 weeks. It is our opinion that she was a poorly chosen candidate, although there is no question that she was greatly improved after the operative procedure. From the viewpoint of ward administration, she presented slightly increased problems postoperatively compared to preoperatively because her general mental retardation was such that she simply was not able to dress herself, care for her duties, or get about the ward. This, of course, had been true before operation, but it seemed a bit more apparent after operation. The patient, however, continued to feed herself and, with improvement, evidenced none of her preoperative temper tantrums. Her over-all personality adjustment apparently was improved, although from a physical point of view she was unimproved.

Case 5. W. F. was 13 years old at the time of surgery. He had a normal birth and progressed satisfactorily until 5 weeks of age. At that time, he had pertussis, following which his development was retarded. At the age of 6 months, he had a grand mal convulsive seizure, after which he was comatose for three weeks; on recovery, he appeared to be deaf and blind for several more months. Gradually, he started to walk and, by the age of 2 years, could say a few words and had bowel and bladder control. At the age of 3 years, spasticity in the left arm and leg was observed. Because of continued seizures and apparent mental retardation, the boy was committed at 11 years of age to the Cambridge State School and Hospital. He had extreme left spastic hemiparesis and a seizure record preoperatively (figure 9).

On November 5, 1952, a craniotomy was performed. There were extensive adhesions between the cortex and meninges. Hemispherectomy was accomplished, removing all tissue down to the basal ganglia. The caudate nucleus, putamen, globus pallidus, and thalamus remained intact.

Neurologic loss postoperatively was no greater than preoperatively. In fact, the patient was able to use the involved spastic hemiparetic side more effectively after surgery because "it moved easier," according to him. The effect on seizure control is shown in figure 9. From a ward administration standpoint, this patient definitely

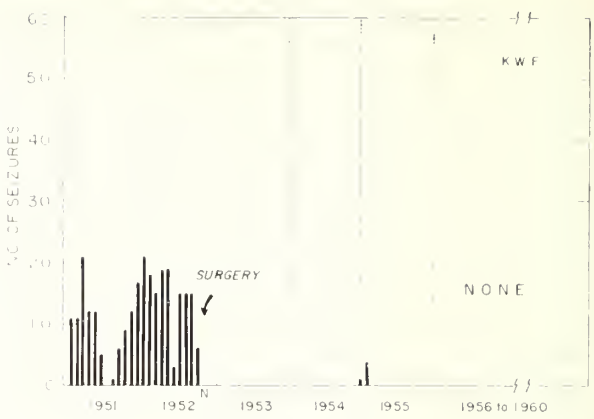

Fig. 9. Graph revealing seizure frequency before and after surgery (November 5, 1952). Patient went seizure-free for twenty-six months, had 6 grand mal attacks within twenty-one days, and has been seizure-free for the past five years.

benefited from surgery. He could not have approached his present level had he not had relief from seizures. Preoperatively he presented no special problem, except that he was labeled as being extremely retarded and needed much care, and progressive deterioration was apparent. After surgery, he became more alert, has continued to be alert, and is now able to care for his total needs satisfactorily. He helps feed and handle the wheel chair of another patient, attends all social functions, and relates well with patients and employees. He is on no medication.

Case 6. R. P. was 36 years old at the time of surgery. Immediately after birth, left hemiparesis was noted. Otherwise, the patient's development appeared normal until the age of 2 years, when she fell off a couch, striking her head. Immediately thereafter, she began to have grand mal seizures, which continued throughout infancy and childhood. At the age of 20, her seizures greatly increased in frequency and severity. About this time, an extreme personality disturbance was observed. Care for the patient at home became increasingly difficult. At the age of 30, she was committed to the Cambridge State School and Hospital. After admission, she noted numerous psychosomatic conditions and her seizures continued. The seizures were of 2 types: (1) minor spells, described by the patient as blackouts, which were preceded by a feeling of pressure in the back of her head, dizziness, and a gripping sensation in her abdomen. They lasted from a few seconds to five minutes, occurring about five to ten times per day and (2) typical grand mal convulsive seizures, which occurred over a period of years. Anticonvulsant medications had not influenced the attacks (figure 10). Because of hemiparesis, personality disturbance, and uncontrolled seizures, the patient was considered a candidate for cerebral hemispherectomy. Preoperative neurologic examination revealed her to be reasonably alert, fully oriented, and cooperative. A Wechsler-Bellevue test revealed a verbal scale of 78. A Stanford-Binet Form L was 70. Examination revealed bilateral optic atrophy; left homonymous hemianopsia; left sixth nerve palsy; bilateral horizontal nystagmus, with a slight rotatory component; pronounced

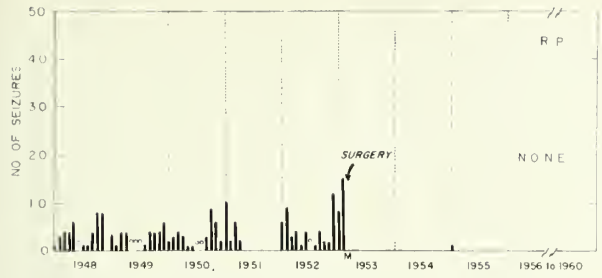

Fig. 10. Graph revealing seizure frequency before operation (March 23, 1953) and single brief akinetic type seizure that occurred almost two years after surgery. Since this attack, patient has been seizure-free.

left hyperreflexia, with positive Babinski sign; and moderate spastic hemiparesis, mainly involving the arm. There was a severe loss of all sensory modalities on the left side.

On March 23, 1953, the entire right cerebral hemisphere, including the insula, hippocampal gyrus, and part of the caudate nucleus, was removed. One-half hour after completion of the operation, the patient was alert and rational. She could move both her left arm and leg and could feel pain and light touch as well as before operation. Left arm and leg were flaccid. There was marked left hyperreflexia and a positive Babinski sign. Postoperative course was completely uneventful. At examination one month after surgery, the patient was walking as well as she did preoperatively, had had no convulsions, and was on no anticonvulsant medication. At a routine follow-up examination seventeen months postoperatively, her gait and reflexes were the same as on previous examinations. She had some finger movement in the left hand at least as good as the preoperative level. Nystagmus present before surgery was gone. Her Wechsler-Bellevue verbal scale was 82, and the Stanford-Binet Form L was 74—both slightly higher than preoperatively. She had one brief akinetic seizure, so she was placed on Mebroin therapy. Both the patient and her mother were more than satisfied with the result of the operation.

Seven years have passed since her surgery, and she has had only that one brief seizure. Her neurologic status is essentially unchanged from the preoperative status. From a hospital administrator's standpoint, a most satisfactory result has been obtained. Before admission, the woman presented problems of a moderate nature in personality, behavioral, and occupational spheres. She did not get along well with people ("people do things behind by back and I'll get even with them"), used vile language, and was argumentative, bossy, and lazy. Since surgery, she has been consistently pleasant; is considered to have a good sense of humor; participates fully in the vocational, educational, and industrial program; and is in an open ward with full privileges. Separation to a community facility is contemplated. She has been maintained on Mebroin, 1 tablet three times a day.

Case 7. D. S. was 30 years old at the time of surgery. Shortly after birth, spastic right paresis involving the face, arm, and leg was noted. The man walked with a marked gait disturbance. In addition, he had had multiple generalized convulsive seizures, most of which began on the right side of his body. Frequency varied from 50 to 100 grand mal attacks each year. In addition, he had frequent attacks of aggressive hostility toward his parents, other patients in his ward, and hospital personnel. Clinically, he presented the appearance of a hebephrenic schizophrenic. He had gone through high school, but, when he was first seen in the Cambridge Hospital, he seemed to be very deteriorated, and there was considerable doubt whether his presumed high school education could be used as a valid assessment of his intellectual abilities. The Wechsler-Bellevue score of 86 was obtained preoperatively. At the time of surgery, a large cystic area, 12 cm. long and 6 cm. wide, was found in the sylvian region. The adjacent brain was scarred and adherent to the arachnoid. The temporal lobe was extremely hard and firm on palpation. The only grossly normal appearing brain was in the anterior part of the frontal lobe. Left hemispherectomy, down to but not including the thalamus, was performed. Caudate nucleus, globus pallidus, and putamen were removed. Postoperatively, the patient progressed well, although he had one grand mal convulsive seizure (figure 11). Therefore, he was kept on anticonvulsant medication. From the hospital administration's standpoint, surgery meant the difference between a patient who would need indefinite hospitalization, probably never to be separated from the institution, and one who was discharged to his community within months after the surgical procedure. The previously aggressively hostile person had changed to one who was cooperative and well adjusted. Interestingly, over a period of many months after operation, a Minnesota Multiphasic Personality Index scale changed from strongly schizophrenic to within normal limits.

Case 8. D. G. was 15 years old at the time of surgery. At the age of 3 months, he began to have jerking spells and, at approximately 6 months of age, typical grand mal convulsive seizures developed. Shortly thereafter, the parents noted weakness of the right arm and leg following the seizures; eventually, the right hemiparesis became spastic and was persistent. The parents noted that the boy, practically from birth, did not have normal mental development. At the age of 4 years, he became a distinct behavior problem. He was extremely distractive and refractory to suggestion. He started grade school in a special school but could not continue because of his inability to get along with the other children. He therefore was institutionalized at the Cambridge State School and Hospital. He averaged between 65 and 160 grand mal seizures per year. He was also

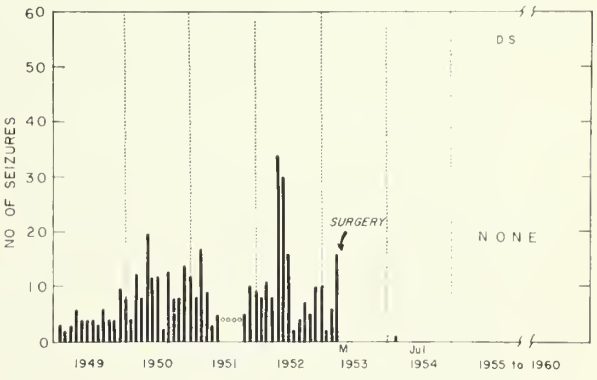

Fig. 11. Graph revealing seizure frequency before and after surgery (March 1953). Patient has had 1 grand mal seizure since surgery and has made remarkable social adaptation since hemispherectomy.

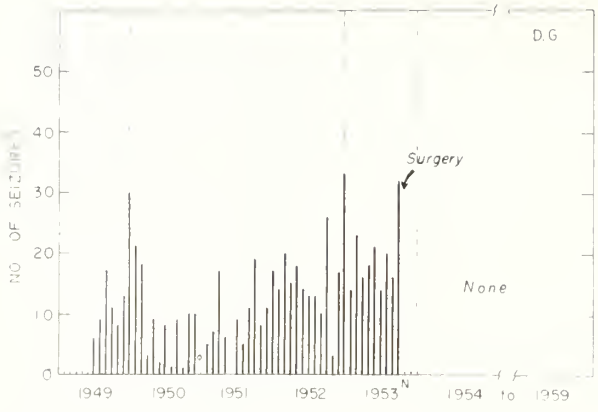

Fig. 12. Graph revealing seizure frequency before surgery (November 1953). Since surgery, patient has not had any convulsive attacks. He is not on any medication.

known to have a definite personality aberration. Because of the intractableness of his seizures and the fact that he had a right hemiplegia, hemispherectomy was done in an attempt to control the convulsive disorder. Electroencephalographic abnormalities over the entire left cerebral hemisphere were noted at that time.

All of the cerebral hemisphere was removed. In addition, the globus pallidus, putamen, and part of the thalamus were removed. Postoperatively, the boy progressed satisfactorily. Since surgery, he has had no seizures (figure 12). From the hospital administrator's viewpoint, the benefit is definite. It is felt that the patient's high level of institutional adjustment could not have been reached without freedom from seizures and their concomitants. He now cares for all of his needs; is meticulous about his personal appearance; gets along well with patients and aides; helps with feeding, bathing, and pushing wheelchairs of other patients; and attends dances, church, and movies. Separation to a community placement is envisioned. He is on no medication.

EFFECT ON CONTROL OF SEIZURES

All patients except one who had a glioma followed by gliotic scarring had had seizures since infancy or childhood. With the exception of this man, all others had uncontrolled seizures that made institutionalization necessary. Postoperative follow-up now ranges from six to ten years. Of the 8 patients, 7 have had excellent results so far; 2 have had no seizures of any kind and are on no medication, and 3 others have had one seizure each—all occurring in the first few months after operation—and are now on small doses of anticonvulsant medication. One patient had 5 seizures in the immediate postoperative period but none in the last eight years and now is on no medication. One case is classified as a poor result, although reduction in seizures was almost 90 per cent. In retrospect, this patient, with definite microcephaly and a history of severe meningoencephalitis at the age of 5 weeks, was probably poorly chosen. She had averaged 700 to 800 grand mal seizures for each year for a period of almost seventeen years of institutional custody. She lived thirteen and one-fourth months postoperatively and then died of diphtheria in the state institution. In the postoperative survival period, she had 75 grand mal attacks.

This effect on seizure control has several very interesting features. First, there is no question that the operative procedure has been an effective means of controlling these severe convulsions, whether grand mal or petit mal in character. It also has been possible to do so without any aggravation of neurologic status; in fact, if there is any change in the neurologic status, it is toward improvement. Patients are able to use the involved extremities more readily and without conscious thought. The same is true relative to any potential sensory deficit.

Secondly, it is interesting that these patients often will go for a period of two or three years without attacks, then have one or possibly two major seizures, and then have none for the succeeding two, three, or four years. A review has been made of possible precipitating factors for these seldom-occurring attacks, but no consistent factor was found. The question then arises, is it feasible to keep these people on anticonvulsant medication? It has been our feeling that, since the program was originally set up to give anticonvulsant medication to any of those who had some epileptic phenomena, this regime should be continued; however, the total dosage schedule has been greatly lowered from the preoperative level on these patients. This procedure has permitted immeasurably better functional response on their part. In the group of patients operated on subsequent to this series of 8, all anticonvulsant medication was discontinued two years after surgery.

EFFECT ON PERSONALITY AND ADJUSTMENT TO ENVIRONMENT

A previous report[3] has been made on psychometric evaluation of the patients in this series. Furthermore, a much more intensive and extensive series of tests is being administered to them at this five- to ten-year period.[4] Results of this testing will be the basis of another report. Hospital adjustment of these patients unquestionably is immeasurably better since surgery. As a general rule, they were hostile, aggressive individuals who tended to have temper tantrums preoperatively but who, after the operative pro-

cedure, adjusted fairly well to their environment. The fact that some of the group have left the environment of the hospital and are well adjusted outside speaks well for this change in personality and social adjustment. This procedure definitely reduces greatly the cost of hospitalization as well as the sociopsychologic production of these patients.

CONCLUSION

It is felt that, in selected cases, surgery as major as that described above is well advised. Not only should intractable seizures associated with hemiparesis be indications for surgery but also patients with pronounced personality aberrations but with fewer seizures probably should be strongly considered for operation. The experience gained with this group certainly testifies to the fact that, after removal of the abnormally discharging hemisphere, improved personality adjustment is obtained. Whether or not a personality disturbance without intractable seizures is sufficient indication for this type of surgical intervention is questionable.[5] Nevertheless, the response in this series has been gratifying.

During the ten-year period from 1950 to 1960, there have been an additional 16 patients subjected to hemispherectomy. Although the follow-up period is of shorter duration than in the series here reported, the results seem to be conforming to those in this longer follow-up group.

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To avoid renal damage in human beings, every effort should be made to keep the serum calcium concentration within the normal range.

Hypercalcemia was induced in 9 dogs by subcutaneous administration of 60 to 97 units of parathyroid extract per kilogram of body weight during a twenty-four-hour period. Serum calcium values returned to normal in forty-eight to seventy-two hours. The animals were sacrificed at intervals up to forty-four days.

Anatomic alterations were located in the ascending limb of Henle, distal convoluted tubule, and collecting tubule. The lesions were patchy and consisted of epithelial degeneration, calcification, and necrosis. The more proximal damage usually healed by epithelial regeneration, but the medullary collecting tubule damage often remained as fixed intratubular calcific casts. These casts produced proximal tubule dilation and, sometimes, atrophy.

Functional changes included impaired renal concentrating ability, decreased glomerular filtration rate, and elevated blood urea nitrogen concentration.

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Long-Term Electroencephalography in Patients with Hemispherectomies

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THE PURPOSE of this report is to give the electroencephalographic findings in a series of 7 patients undergoing hemispherectomies for intractable seizures. The surgery was performed in 1952 and 1953 and, with the exception of one patient who expired 13¼ months following surgery, this represents a follow-up period of seven to eight years. The patients included in this series were part of a study made on the effect of cerebral hemispherectomy in patients with an intractable convulsive disorder associated with hemiparesis or hemiplegia. The preoperative electroencephalographic studies were made at the Cambridge State School and Hospital; the electrocorticograms and surgical procedures were done at the University of Minnesota hospitals; and the postoperative electroencephalograms were obtained, in the main, at the Cambridge Hospital. Previous studies of a somewhat similar nature have been made but none has included patients with this long follow-up period. Some of these patients have gone for several years postoperatively without a seizure. Others have had one or more recurrent attacks within a period of a month or two but none in the subsequent four or five years.

CASE REPORTS

The electroencephalographic interpretations are represented in tabular form according to the specific cases. In order to insure proper interpretation of these tables, we should like to designate what is meant by the various abbreviations as well as the various other terms used. Alpha refers to the background pattern frequencies of 8 to 12 cycles per second (c.p.s.) that are most noticeable in the occipital area and are obliterated by visual attention. Also included under this heading is the low voltage fast activity (l.v.f.) when it occurs on a predominantly normal background activity. Theta and delta refer to frequencies of 4 to 7 cycles per second and 1 to 4 cycles per second, respectively. Spikes refer to bursts of activity of higher voltage and faster frequency. These are at least 50 microvolts or more in amplitude than the background activity, and their frequency is greater than 15 c.p.s. The term, electrographic foci, refers to abnormalities found in specific anatomic areas—frontal, temporal, parietal, and occipital. In this report, primary bilateral synchrony (1° bil. syn.) refers to synchronous and symmetric paroxysmal or continuous activity presumably originating from deep midline sources. Secondary bilateral synchrony (2° bil. syn.) refers to relatively synchronous and symmetric activity that represents a unilateral source from a medial structure or interior or deep areas of the temporal lobe. Under miscellaneous are included observations made but not classified under any of the above groups.

Case 1. C. K., a girl who was 13 years of age at the time of surgery, had a Sturge-Weber syndrome involving the right cerebral hemisphere and the right side of her face. She was hemiparetic on the left, had a severe behavior disorder, and had 300 to 500 generalized convulsive seizures per year. The operative procedure was done in July 1952. Postoperatively, she has had only 2 seizures in more than seven years. One of these attacks occurred shortly following surgery and the other took place in 1957, five years after surgery. Her postoperative neurologic status reveals no deficit greater than that which she had preoperatively. In addition to improvement in seizure control, she has had marked improvement in behavior.

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EEG Summary (C. K.)

	Preop.	*E.Co.G.*	*Postop.* 12/10/52	*Postop.* 6/9/60
Alpha			5/sec.	l.v.f.
Theta & delta	high voltage, diffuse, bilateral		3/sec.	4 to 6/sec.
Spikes	high voltage, l. front	over entire exposed area	l. temp. -par.	l. fronto-central
Foci			l. temp. -par.	
1° bil. syn.				
2° bil. syn.				
Misc.			sleep spindles on l. only	

Abbreviations:
Frontal—front.
Temporal—temp.
Parietal—par.
Occipital—occip.
Miscellaneous—Misc.
Left—l.
Right—r.
Low voltage fast activity—l.v.f.
Electrocorticogram—E.Co.G.

Case 2. O. L. This woman had had 300 to 500 convulsive seizures per year, left hemiparesis, and mental retardation. Right cerebral hemispherectomy was performed on July 9, 1952, when she was 34 years old. She had 5 seizures shortly after surgery and 1 seizure two years later, in 1954. Neurologic examination revealed no abnormality that was not present before operation except for some slight diminution in two-point discrimination on the left. This was involved to some extent before operation but more so following surgery.

EEG Summary (O. L.)

	Preop. 6/1/52	*E.Co.G.* 7/9/52	*Postop.* 12/17/52	*Postop.* 2/12/59
Alpha	10 c.p.s.		9 to 11 c.p.s. l. only	7 to 8 c.p.s. l.v.f.
Theta & delta	3 to 4 c.p.s. l. hemisphere			5 to 7/sec.
Spikes	l. occip., diffuse	multiple		
Foci		diffuse		sharp waves l. ant. temp.
1° bil. syn.				
2° bil. syn.	l. & r. occip.			
Misc.			slowing with hyperventilation	

Case 3. C. B. was 19 years old at the time of surgery. This girl had right hemiparesis, severe mental deficieney, and 700 to 800 seizures per year. She was also microcephalic, and had meningo-encephalitis at the age of five weeks. Left hemispherectomy was done. Before her death from diphtheria 13¼ months later, she had 75 seizures. No additional neurologic deficit was noted postoperatively.

EEG Summary (C. B.)

	Preop. 4/4/51	*E.Co.G.* 12/21/52	*Postop.* 10/15/53
Alpha	8 to 10 c.p.s. bilat.		l.v.f.
Theta & delta	5 c.p.s.		bifrontal 5 to 7 c.p.s.
Spikes		diffuse	
Foci	entire l. hemisphere		
1° bil. syn.			
2° bil. syn.			
Misc.			

Case 4. W. F. was 13 years old at the time of surgery. This boy had left hemiplegia and mental retardation, and averaged 100 seizures per year. Right cerebral hemispherectomy was performed on November 5, 1952. Postoperatively, he has had 6 seizures, occurring in 1955. Two-point discrimination is decreased on the left, but position sense is present. He is able to talk some, understands quite well, and is ambulatory.

EEG Summary (W. F.)

	Preop. 3/6/52	*E.Co.G.* 11/5/52	*Postop.* 4/9/52	*Postop.* 1/19/59
Alpha				l.v.f.
Theta & delta	5 to 8 c.p.s. 3 to 5 c.p.s., diffuse	multiple	5 to 7 c.p.s., l.	l.v.f. 4 to 6/bil.
Spikes	entire l. hemisphere			
Foci	l. temp., mirror focus r. temp.			
1° bil. syn.				
2° bil. syn.	temp. areas			
Misc.			sleep spindles on l. only	

Case 5. R. P. was 36 years of age at the time that surgery was performed. Preoperatively she had a spastic-type left hemiparesis, a rather severe behavior disturbance, and intractable major and minor convulsive seizures. A right cerebral hemispherectomy was done on March 22, 1953. Postoperatively, she has had only 1 convulsive seizure and that was in 1955. There has been no neurologic deficit additional to that present before operation. She moves her left arm quite well, walks well, and has almost intact sensory ability on the left except for a definite diminution in two-point discrimination.

EEG Summary (R. P.)

	Preop. 5/10/51	*E.Co.G.* 3/2/53	*Postop.* 2/22/59
Alpha	8 to 10 c.p.s., l.		8 to 10 c.p.s., l. only
Theta & delta	5 to 7 c.p.s. r. greater than l.		rare 2 to 3 c.p.s., 5 to 7 c.p.s. on l.
Spikes		random spikes at cyst edge	
Foci			
1° bil. syn.			
2° bil. syn.			
Misc.	alpha absent on r.		

Case 6. Patient D. S. had a right hemiparesis, personality disturbance, and 50 to 100 seizures per year, mostly manifested first by movement of the right side of his body. A left hemispherectomy was done in March

1953, when he was 30 years old. The patient had 1 postoperative seizure in 1954. He was discharged from the Cambridge State School in 1954 and has had no seizures at home. He takes care of yard work, shops, and banks for his mother. He converses very well and his gait is excellent. The right hand has the same poor function that was present before surgery. Two-point discrimination is impaired on the right. Stereognosis and position sense are intact.

EEG Summary (D. S.)

	Precop. 6/1/51 & 3/24/52	*E.Co.G.*	*Postop.* 3/6/53	*Postop.* 6/18/60
Alpha	8 to 10 c.p.s., l.v.f.			15 to 20 c.p.s.
Theta & delta	diffuse high voltage		diffuse 4 to 6 c.p.s., l.	
Spikes		diffuse		
Foci	bitemp. sharp waves, l. greater than r.		r. front & par. sharp waves	
1° bil. syn.				
2° bil. syn.				
Misc.				slight bifront. slowing with hyperventilation

Case 7. D. G. was 15 years of age at the time of surgery. This boy had spastic right hemiparesis, mental deficiency, a profound behavior disorder, and seizures varying from 65 to 160 per year. These were grand mal in type. On November 29, 1953, left cerebral hemispherectomy was performed. Postoperatively, he walks fairly well, is able to converse well, and has the ability to use his right hand in manipulating small as well as light objects. Two-point discrimination, however, is greatly diminished to absent over the right side of his body. He has had no seizures since surgery.

EEG Summary (D. G.)

	Precop. 2/22/52	*E.Co.G.* 11/29/53	*Postop.* 12/3/53 & 1/22/54	*Postop.* 2/20/59
Alpha	8 to 10 c.p.s.		8 to 10 c.p.s., r. only	10 to 12 c.p.s. l.v.f.
Theta & delta	1 to 5 c.p.s. diffuse	1 to 3 c.p.s.	rare 4 to 6 c.p.s.	rare 5 to 7 c.p.s.
Spikes	random, diffuse, l. greater than r.	diffuse		
Foci	l. occip., r. occip., l. temp., mirror r. temp.			
1° bil. syn.	spike & wave, occip.			
2° bil. syn.	bifrontal			
Misc.				only 25 microvolts difference r.-l.

DISCUSSION

All of the preoperative electroencephalographic studies in this series were abnormal. In 1 patient, the abnormality was moderate only. All records showed bilateral abnormalities with definite unilateral localization. Hemispheric abnormalities were in various and multiple anatomic areas and were of all types, characteristic of large lesions. Contralateral abnormalities included independent foci of spikes, slow waves, and sharp waves. Temporal lobe mirror foci were seen in 2 patients. Secondary bilateral synchrony was present in 3 patients, in the occipital area in 2 and in the temporal area in 1. Primary bilateral synchrony was present in 1 case and presented as 3 c.p.s. spike and slow wave activity in both frontal areas. Unilateral absence of alpha rhythm was seen in 1 patient.

Reports from the literature on patients who have had hemispherectomies and on those with large cortical lesions[1–9] have noted all of these types of abnormalities, both unilaterally and contralaterally. The contralateral findings have been interpreted as being both independent abnormalities, in the case of spikes and slow waves, and as projected abnormalities when mirror foci and secondary bilateral synchrony were found. Pronounced EEG abnormalities on the relatively normal side were considered to be contra-indications to hemispherectomy. The one patient with a poor result in our series had a moderately abnormal electroencephalogram with mild slowing maximally but not exclusively on the side opposite the patient's hemiparesis.

Electrocorticograms obtained from the exposed cerebral cortex all showed multiple spike activity. High voltage slow waves were seen in some. The patients with cerebral cysts had no activity over the surface of the cyst with maximal spiking at the edges of cortex surrounding the cyst. In cases where the hippocampus was exposed for electrocorticographic recordings, spikes were recorded from this area. In one patient 6 and 14 c.p.s. activity was recorded from the hippocampus.

Electroencephalograms were obtained within a year postoperatively and again in 1959 or 1960. Generally, the early postoperative electroencephalogram revealed marked improvement over the preoperative series. The late postoperative records showed further improvement with 4 records considered within normal limits on the unoperated side. This improvement corresponds to the experience of others.[3, 9] One exception was present, again in the patient with frequent postoperative seizures. The postoperative record

was slightly more abnormal than the preoperative record. There was little normal alpha activity and bilateral slow activity.

All the records showed depressed activity on the operated side but none of the late records had a so-called flat electroencephalogram.[4] The alpha activity voltage difference was 25 microvolts or less in 2 cases.

All postoperative records showed slow activity of varying degrees of severity.

Spike and sharp wave activity was greatly decreased in the electroencephalograms obtained in the early postoperative period and absent in the late recordings.

Previously noted mirror foci and primary and secondary bilateral synchronous activity were not seen after surgery.

When electroencephalograms were recorded during sleep, spindles were seen on the unoperated side only. This may be related to poor transmission or to damage of the thalamus on the side of the hemispherectomy. Other clinicians have reported either a general increase or a decrease in voltage on the unoperated side. In this series this was also true. A depression of activity on the operated side has been reported in all series[3–9] and this finding was also present in this series.

The disappearance of spike activity is interpreted as evidence of adequate excision of the major cortical and subcortical electrographic abnormalities. The absence of mirror foci and secondary bilateral synchronous activity concurs with the postulate that these abnormalities are projected from the opposite side. The continued presence in some of the recordings of slow waves on the unoperated side is consistent with the presence in those patients of a deep midline abnormality. This may be the explanation of the seizures occurring either immediately postoperatively or late (two to four years) after surgery.

There does not seem to be any correlation between the degree of abnormality seen on the postoperative electroencephalograms and the presence of postoperative seizures with the exception of the 1 patient who had relatively frequent seizures. One of the patients who had no seizures postoperatively had in the early postoperative period a few specific electrographic abnormalities not dissimilar to the patients who did have postoperative seizures. However, his late record was within normal limits. The patient who has been home for six years still shows a slightly abnormal record. There was no particular electroencephalographic pattern that suggested the probable occurrence of postoperative seizures. However, the evidence of a greatly improved electroencephalogram probably suggests a good prognosis.

Reports in the literature on local or restricted excisions of epileptogenic foci[10] have indicated that seizures occurring in the early postoperative period have portended poor prognosis; this was not noted in this series in which a much more major excision of tissue was done.

It is believed that this series can be considered to show excellent results both from clinical as well as electrographic standards. The best results of local excisions for seizures, although certainly done for entirely different types of problems, have been 54 per cent good (frontal lobe lesions)—good being a 75 per cent or greater decrease in seizure frequency.[10] No seizures have occurred in the patients in the series presented here in the past three years.

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Quantitative Effects of Basal Ganglia Surgery on Handwriting and Gait

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In recent years, psychologists have endeavored to develop technics to objectify precisely the performance capacities of the human system in terms of the intrinsic properties which define their functional significance in particular tasks. Through the utilization of electronic methods of motion analysis, research has focused upon a variety of human performance variables such as gait, handwriting, assembly skill, panel-control operations, and different patterns of uni- and bimanual dexterity.[1-3]

Human motions may be conceived of as organized into functionally defined component movements, psychologic and physiologic dimensions, and quantitative characteristics, such as rate, frequency, duration, accuracy, and efficiency.[4] Psychologic variables of import in assessing performance are motivation, perception, learning, personality function, and development. Some critical physiologic dimensions would include water and caloric restriction, pharmacologic agents, and central nervous system changes induced by stereotactic procedures.

From the behavioral point of view, all human motions can be thought of in terms of functionally differentiated components within larger patterns of organized motions, such as handwriting and gait. At least 3 components of a functionally distinct kind can be isolated behaviorally: postural, or supportive movements; travel, or transportive movements; and manipulative, or contact movements. Travel movements involve the transport of limbs through space, while manipulative components enhance the manipulation of hard space and the interaction of the organism with the changing space and time characteristics of environmental objects and surfaces.

The purposes of this investigation are (1) to determine the applicability of electronic methods of motion analysis to the assessment of manipulative and travel components of handwriting and gait in individuals with known abnormalities of motion and (2) to present preoperative and six-month postoperative handwriting and gait data for a patient who underwent stereotactic surgery involving the ventrollateral nucleus of the thalamus.

METHODOLOGY

Apparatus. A 2-channel electronic motion analyzer was used for obtaining manipulation and travel time data in handwriting and gait.[1] For handwriting tasks, the subject used a metallic pencil filled with electrographic lead and wrote on conductive paper. When his pencil came in contact with the paper, a subthreshold current passed through the operator's body and closed a relay that activated an electric timer to .01 second. This clock remained activated for the duration of the manipulative movement involved in a handwriting task. The circuit also contained a flip-flop circuit so that, when the pencil was lifted from the paper and the hand traveled through space toward another contact point, the first contact was broken, thus stopping the manipulation time clock, and a second clock, the travel time clock, was activated. The recording system included a stop circuit that was activated by a plate at the end of the area through which a repetitive handwriting motion pattern had been carried out. In making the stop contact, all clocks were stopped, and a precise summation of the manipulative and travel components in writing a series of 10 figure 8's was obtained.

For gait measurement, the apparatus operated in a similar manner. The subject walked on a copper screen 1 ft. in diameter and 11 ft. in

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length. At the end of the runway was a stop plate 3 ft. long. Each leg was measured separately during walking, and summations of the contact and stride times for traversing the runway were obtained.

Assessment conditions. The patient was run on all procedures in a single session.

Handwriting. The task was writing the figure 8 ten times at maximum pace. Markers were provided on the writing board for placing each figure so that counting was unnecessary for the subject. A trial consisted of 1 such patterned series of manipulative and travel movements. Measures of these components were obtained for a series of 15 distributed practice trials, with a one-minute rest period between each trial. Then, 10 more trials were run under massed practice conditions, with only a short interval between trials to allow the observer to record the manipulation and travel times. These were followed by a five-minute rest period and 5 more massed practice trials. Thus, 30 manipulation and travel time measures were obtained in blocks for distributed and massed conditions of practice.

Gait. Contact and stride movement times were recorded for each leg independently in traversing the 11-ft. runway and stepping on the stop circuit. Initially, the right leg motion components were measured for 5 trips (trials) down the runway under regular pacing; 5 trials under regular pacing were then run with the left leg. Then, the subject was instructed to walk at maximum pace, 5 trips, for left leg measurement and 5 trials for right leg assessment of contact and stride time in gait. Thus, the above components were quantified for each leg under regular and fast pacing conditions.

CASE REPORT AND RESULTS

C. S., a 53-year-old man, had onset of a parkinsonian syndrome in 1950. At that time, he noted a tremor in the right hand, which gradually increased in severity. By 1954, the right leg was similarly involved. In the same year, tremors also appeared in the left arm and left leg. During this same period, 1950 to 1954, the patient was aware of a progressively developing rigidity that was much more pronounced on the right than on the left. He did office work until July 1958 but by then was sufficiently incapacitated so that he no longer could carry out his occupation. He had tried almost all of the usual antiparkinsonian drugs, with only minimal benefit. No etiologic or causative agent to account for the symptoms was uncovered; there had been no influenza, past hospitalizations, or serious illness.

On examination, this patient seemed to be well motivated, although a definite poverty of spontaneous movement was present. There was dryness of the skin, masked facies, and a mild problem of excessive salivation. His voice was monotonous in character. He walked with small steps and tended to lose his balance when walking either forward or backward. Kyphosis of thoracic and cervical spines was present. An alternating tremor, 6 to 8 per second, in all extremities was much more prominent on the right than on the left. The tremor was accentuated with excitement and diminished with intention. Cogwheel-type rigidity was present, again more pronounced on the right than on the left. Deep tendon reflexes were definitely hyperactive on the right and normal on the left. Ability to perform repetitive and alternating movements was markedly decreased.

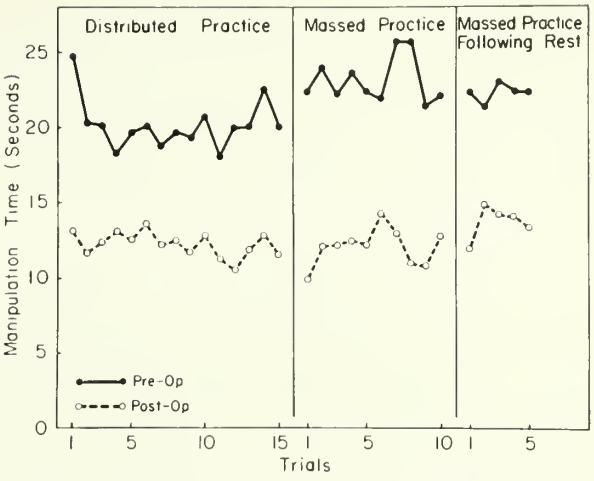

Fig. 1. Manipulation times in handwriting before and after stereotactic surgery.

The first stage of a left ventrolateral thalamotomy was done on November 16, 1959, after the various investigative procedures done on the patients in this program.[5] The second stage was done on November 19, 1959. The patient's rigidity was definitely and quite satisfactorily reduced, but the tremor was only minimally reduced. Therefore, using the stereotactic coordinates previously calculated, the electrolytic lesion was increased in size. After this, good motor function was maintained and the tremor was reduced significantly.

The patient was examined in the outpatient clinic on May 10, 1960; he was much improved over his preoperative status. He could dress himself, button his own clothes, eat by himself, walk much better, and was immeasurably more animated and spontaneous in his movements and over-all activities. He was considered a very satisfactory result.

The following figures reveal the results on this patient of the various procedures outlined above.

Figure 1 shows the distributions of manipulation time measures for handwriting across the distributed practice series of trials, the massed practice trials, and the massed practice trials after rest. Comparison of pre- and postoperative measures indicates sizable reduction of the manipulative component in handwriting for both distributed and massed conditions of practice. Furthermore, the relatively increased times exhibited under massed conditions preoperatively are not manifest postoperatively. Massed prac-

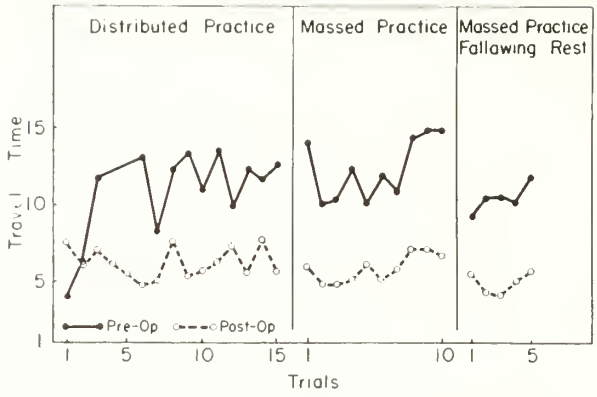

Fig. 2. Travel times in handwriting before and after stereotactic surgery.

tice can be regarded as a stress condition with rather remarkable slowing of response preoperatively. Thus, performance stress produces no relative negative changes in manipulation time postoperatively. However, a normal level of performance, according to the norms available for non-neurologic samples,[6] is not reached.

Comparable data for the travel times across conditions pre- and postoperatively are found in figure 2. Some reduction in travel time for handwriting is seen with more dramatic changes under massed or stress practice conditions. Postoperative travel times appear less variable and more stable from trial to trial.

Data for contact time in gait for each leg under regular and fast pacing are represented in figure 3. Relatively greater improvement is suggested for both legs under regular pacing. Performance is more stable and approaches that of normal persons from earlier studies.[6] Under fast pacing, a full-second reduction in contact time is seen across all trials for both legs—a considerable change under pacing conditions of stress level for persons with gait disturbances. Considerable improvement is seen in that component of gait mediating contact with hard space.

Pre- and postoperative stride time comparisons for gait under regular and fast pacing conditions are shown in figure 4. Improvement, as measured by a reduction in the travel component in gait, is evident across both legs and conditions, with relatively more extensive change for the right leg under regular pacing. Although bilateral improvement in function is present, more sizable gains are shown for the right leg—an expected finding for left-sided stereotactic coagulation. That such a result did not arise for the contact measures in gait suggests a greater interaction, compensatory or otherwise, between both legs in the contact component of the gait cycle.

The above results, though limited in their generality to a single case, afford evidence for the efficacy of applying electronic motion analytic technics to quantify patterned motion cycles in clinical groups with known locomotor, handwriting, and other motion abnormalities. The convenient and rapid quantification of the temporal aspects of patterned motions affords an economic operational approach to performance assessment in contrast to the stop watch and fast motion picture technics. This level of analysis seems appropriate for evaluating the effects of drugs, rehabilitation measures, systemic stress, and stereotactic procedures on temporal aspects of behavior. The results appear to justify a long-term follow-up investigation of the effects of stereotactic surgery on the motor behavior of Parkinson's disease patients. In addition to handwriting and gait, studies of simple and complex reaction time, ballistic tapping movements, and 2-handed coordination are planned to follow this exploratory effort.

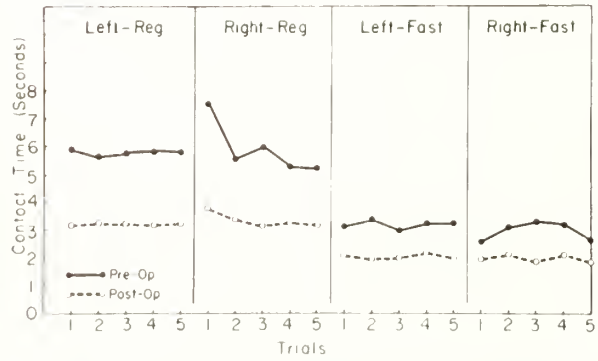

Fig. 3. Contact times in gait before and after stereotactic surgery.

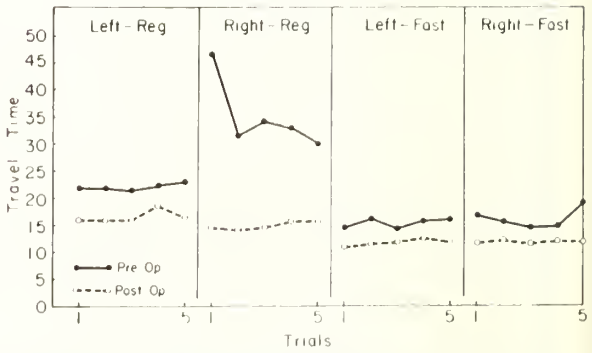

Fig. 4. Stride times in gait before and after stereotactic surgery.

SUMMARY

An exploratory study into the application of electronic motion analysis in assessing change in patterned motion cycles as a function of stereotactic surgery was carried out.

Measures of the manipulation and travel components in handwriting and gait were obtained preoperatively and six months postoperatively for a patient subjected to electrothalamotomy of the ventrollateral nucleus.

Findings were presented and lent encouraging support to the utilization of time-sensing technics in the investigation of long-term effects of stereotactic procedures on quantitative aspects of patterned motion cycles.

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Diagnosis of blunt trauma to the abdomen, especially in unconscious patients with multiple injuries, is often difficult. Repeated physical examination is the main diagnostic aid, although observation of hematologic changes, radiographic examinations, and peritoneal aspiration are also valuable.

Manifestations of peritoneal irritation include abdominal pain, rebound tenderness, umbilical and rectal tenderness, and lack of peristalsis. Elevation of pulse rate and temperature are of little help in making a diagnosis. Leukocytosis above 20,000 accompanies injury to solid viscera but not hollow viscera wounds and is uncommon six hours after extraabdominal injury.

Solid viscera are more vulnerable than hollow organs. Kidney injury is commonest but often is slight and does not require operation. The bladder and neck are frequently damaged by severe compression. Severe crushing is required to impair the intestines. Injuries to the pancreas and gallbladder are rare.

During surgery, a systematic exploration of the entire abdomen should be made. Suppression of bleeding is the first concern. Resection of the intestine may be necessary when viability is in doubt. Each loop of intestine must be inspected for perforation.

More than half of patients have concomitant injuries in other parts of the body, the thorax being the most common location. Significant head injuries accompany about 20 per cent of blunt abdominal wounds.

Driving accidents account for a large share of injuries and deaths, with drivers more exposed to injuries than passengers. Young men are the most frequent victims, but the mortality rate is significantly higher at the extremes of life.

Over-all mortality rate in a series of 271 cases of intraabdominal visceral injuries was 14 per cent. The death rate was about 40 per cent with multiple abdominal injuries, 20 per cent with combined abdominal and extraabdominal injuries, and 3 per cent when only 1 abdominal organ was injured.

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Report of a Case

Clostridium Perfringens Infection of the Brain

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INFECTION OF THE central nervous system by Clostridium perfringens is very unusual. Because of the seriousness of this infection in general body tissues, it was our impression that a similar serious outlook was present with Cl. perfringens infection of the brain. Certainly, gas gangrene of brain tissue connotes a morbid outlook. Without appropriate therapy, it carries a very high mortality rate. However, with debridement and antibiotic therapy, prognosis is greatly improved. The purpose of this report is to present a summary of a patient who survived a proved Cl. perfringens infection and also to present a general summary of this problem.

CASE REPORT

A 19-year-old soldier was admitted to a local community hospital on December 20, 1959. The history obtained was that while encouraging a calf to move into a barn by striking it on the buttock with the handle of a pitchfork, the pitchfork handle broke, and one of the tines was driven into the patient's skull in the region of the right supraorbital ridge. The accident occurred at 4:30 P.M. on December 20. The man pulled the tine out, staggered into the house, and fainted. He regained consciousness at 4:45 P.M. but was observed to be very lethargic. He vomited, and, as he did this, blood extruded from the site of the entrance of the tine. He was hospitalized immediately. Cerebrospinal fluid and necrotic debris were noted to be extruding from the wound. The drainage persisted from December 20 to December 21 and then abated. The patient received 0.5 cc. of tetanus toxoid intramuscularly immediately on arrival at the hospital and then 1,000,000 units of penicillin and 250 mg. of Chloromycetin intramuscularly every sixth hour. During that hospitalization, he had a temperature elevation to 99 to 100° F. There were intermittent bouts of vomiting. He was lethargic and confused. There were no seizures, chills, nor focal neurologic findings. The patient was transferred to the Minneapolis Veterans Administration Hospital on December 22.

Physical examination at the time of admission revealed the patient to be confused and lethargic. His blood pressure was 180/95; pulse, 120 per minute; respirations, 24 per minute; and temperature, 100° F. A small puncture wound was evident over the medial part of the right supraorbital ridge. There was pronounced ecchymosis and edema about the right eye, which was almost closed. There was no evidence of drainage from the wound, nor were there any crepitations in the surrounding soft tissue. Extraocular muscle movements were normal. Pupils were equal and reacted promptly to light and accomodation. There was bilateral papilledema. Nuchal rigidity was present. The left patellar tendon reflex was increased and there was unsustained left ankle clonus.

Hemoglobin was 16.2 gm. White cell count was 12,450 per cubic millimeter, with a shift to the left. Erythrocyte sedimentation rate was 18 mm. per hour. Serum electrolytes were within normal limits. Blood serology was negative.

Lumbar puncture revealed a pressure of 330 mm. H_2O; cerebrospinal fluid contained 1,400 white blood cells per cubic millimeter—90 per cent polymorphonuclear leukocytes and 10 per cent monocytes. Protein was 115 mg. per cent, and chlorides and glucose contents were normal. Serology was negative and the colloidal gold curve was normal. Cerebrospinal fluid was sterile.

Skull roentgenograms (figure 1) revealed evidence of a gas shadow in the right frontal lobe extending across the midline to the left frontal lobe area. A small perforating hole was present in the frontal bone and went through the frontal sinus.

After a culture of the wound, which revealed coagulase-negative staphylococci, had been taken, intravenous penicillin—2,000,000 units every sixth hour—and Chloromycetin—500 mg. every sixth hour—was initiated. The following day, lethargy and mental confusion were increased and temperature was 101° F., but otherwise the neurologic picture had not changed. On December 23, three days after the injury, the site of entrance of the pitchfork tine was explored surgically. As the tract was followed, it was noted that the right frontal sinus had been perforated and that the tine had gone through the posterior wall of the sinus into the tip of the right frontal lobe. In this area, grossly purulent material was encountered and cultured. The necrotic brain tissue and debris were removed, along with the mucous membrane of the right frontal sinus. The area was thoroughly irrigated with sterile saline and hydrogen peroxide, and primary closure obtained.

Immediately after surgery, 21,500 units of polyvalent gas-gangrene antitoxin was given intramuscularly. The

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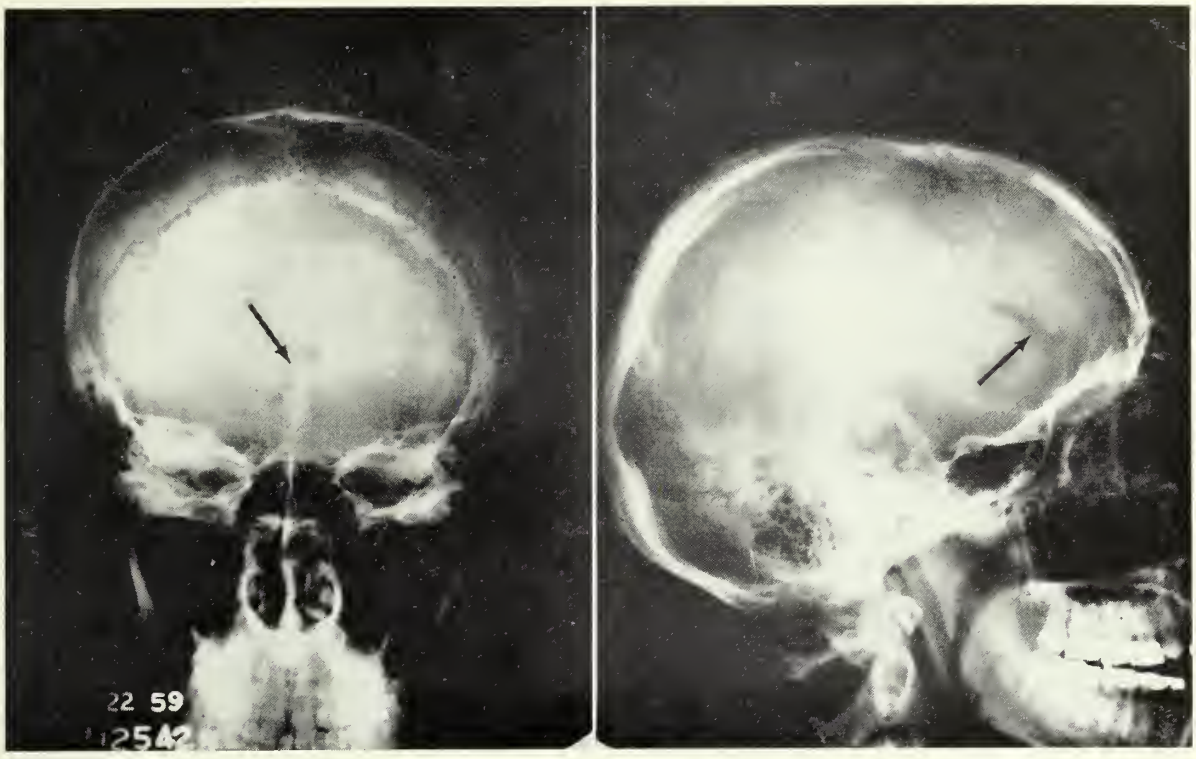

Fig. 1. Roentgenograms of skull in the anteroposterior and lateral projections illustrating a gas shadow (arrow) in frontal lobes.

following day, baeteriologie studies of the purulent material revealed Cl. perfringens and Escherichia coli. Thereafter, the patient received intravenously 43,000 units of polyvalent gas-gangrene antitoxin daily for four days, 5,000,000 units of penieillin every sixth day, and 500 mg. of Chloromyeetin every sixth day. The intravenous antibiotics were eontinued for fifteen days.

After surgery, the patient improved markedly, and on December 26, he was afebrile and alert. Neurologic examination revealed no abnormality. The wound healed by primary intention, and the patient was discharged on January 19, 1960. Repeat skull roentgenograms (figure 2) revealed the previously noted gas shadow in the frontal area to be absent.

DISCUSSION

Cl. perfringens is a saprophyte rather than a true parasite; it is capable of growing and thriving only in those body tissues that have first been injured by some mechanical or chemical means. Gas gangrene cannot result solely from the presence of these bacteria; there must also be extreme cellular damage and impairment of circulation in the involved area.[1] The mere presence of Cl. perfringens does not imply clinical gas gangrenc. It is recognized that clostridia can often be cultured from contaminated wounds without overt signs of gas gangrene. Also, because of their ubiquitous nature in the gastrointestinal tract of man, clostridia may spread rapidly via the bloodstream to any organ after death. Taking these facts into account, Bagley[2] stated that a diagnosis of intracranial gas infection is justified only if, in addition to the intracranial lesion, there are in vivo demonstrations of clostridia and clinical signs of gas gangrene. There have been only 11 civilian cases reported in the literature that fulfill these requirements.[2–7]

It is believed that this case report satisfies these criteria. In addition to Cl. perfringens, E. coli was also found in the culture of the purulent material. It is known that E. coli, under anaerobic conditions, can ferment glucose with the production of gas. Taking this fact into account, it may be argued that the gas shadow was secondary to the fermentative powers of E. coli in this anaerobic environment. However, many cases of E. coli meningitis have been reported and no evidence of gas formation has been mentioned. If such gas formation were a common phenomenon with E. coli infection, it should occur quite frequently with that form of meningitis. Consequently, it is felt that the gas shadow was secondary to the Cl. perfringens and not the E. coli.

Cairns and associates and MacLennan[8,9] summarized the World War II experience of the British with clostridial infection of the central

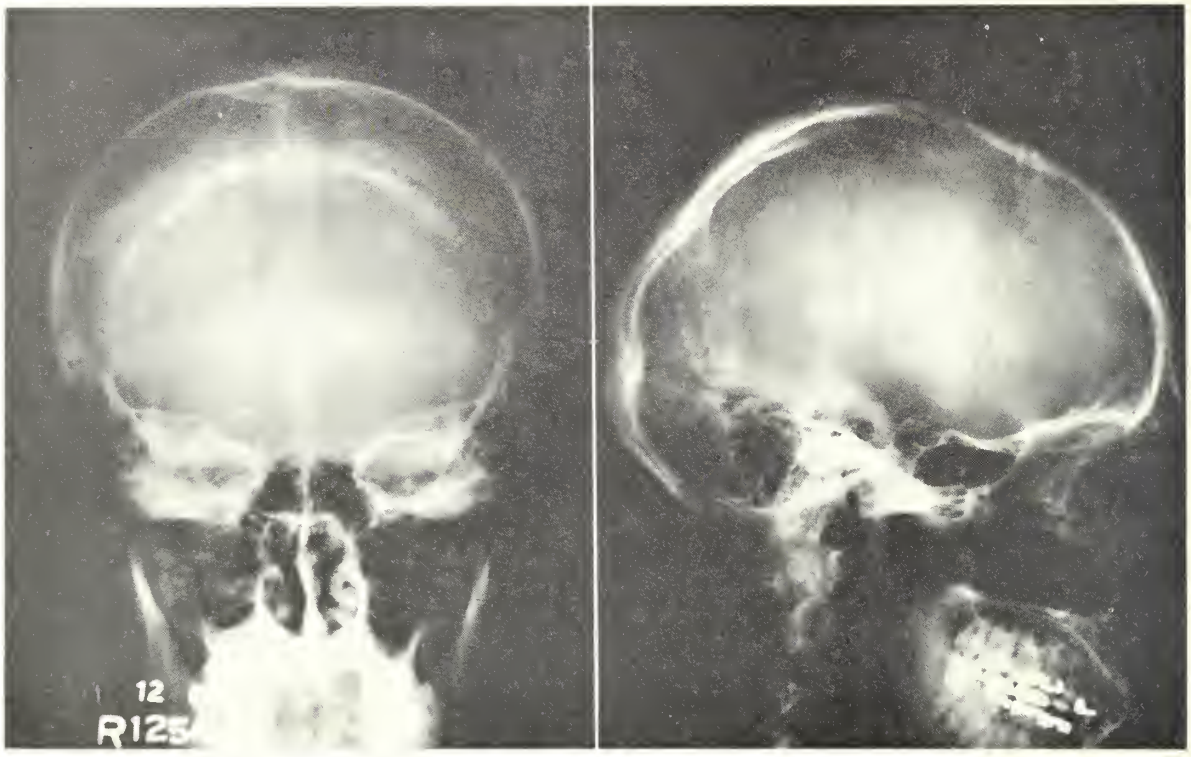

Fig. 2. Roentgenograms of skull in the anteroposterior and lateral projections after surgical debridement. No gas shadow present.

nervous system. It was their opinion that this infection, although it tended to become established unusually early after wounding and could be the sole pathogen in a brain abscess, was generally remarkably benign. In fact, they felt it was much less virulent and more easily treated than brain abscesses secondary to Staphylococcus aureus. The British felt that adequate debridement and chemotherapy without the use of antigas-gangrene serum was usually sufficient in dealing with this type of infection.

Grashchenkov,[10] on the other hand, felt that infection of the central nervous system by pathogenic clostridia was an extremely serious and virulent entity. He reported, in a series of 607 penetrating skull wounds, an incidence of 2.3 per cent of gas gangrene. This was comparable to the 1.6 to 2 per cent incidence of gas gangrene occurring in wounds of the extremities. He cited the work of Sakharov and Gudkova, who were able to produce a high incidence of severe anaerobic infection of mice brains only if inoculation with pathogenic clostridia penetrated the dura. They concluded that the susceptibility of the brain to infection, particularly with pathogenic anaerobes, is exceptionally high.

In a review of 300 cases of craniocerebral war injuries in Russia,[11] 11.2 per cent were infected with gas-producing anaerobic organisms. Of these organisms, 94 per cent were found to be Clostridium perfringens. These organisms were usually found in combination with putrefactive anaerobes, aerobes, and streptococci. In this review, 4 forms of the clinical picture of clostridial infection of the central nervous system are given:

Acute form, manifest by gas formation in the wound, discharge of necrotic brain and debris, putrid odor, edema, extreme headache, and frequent septic complications, with the great majority terminating in death within nine or ten days.

Subacute and chronic forms, manifest by gas formation in the wound, watery discharge, putrid odor, edema, and gangrene. Later, after treatment of the wound and apparent cure, formation of metastatic abscesses of anaerobic etiology and meningitis was followed, in some cases, by death.

Latent form, manifest by delayed healing of the wound but without development of the characteristic symptoms of gas anaerobic infection. To this group belonged all carriers of clostridia, particularly Clostridium perfringens.

In this same report, the distinguishing features of gas infection of the brain were given: pro-

lapse or herniation of cerebral tissue, "bursting" headache, meningitis, and absence of crepitations.

In agreement with the Russian viewpoint is the experience[2–7] with these lesions in the civilian population. Of the 11 reported cases, 7 survived and 4 died. Most of these cases occurred after small puncture wounds involving the scalp and skull. Although Cairns and associates[8] stated that no "small wound of the central nervous system" infected with clostridia can be regarded as severe, this has not been borne out in the above-mentioned experience, in which the mortality rate was 36 per cent.

The case given in this report tends to support the impression that intracranial gas bacillus infection is, indeed, a serious entity. The marked improvement and eventual recovery following adequate debridement, treatment with massive doses of antibiotics, and administration of anti-gas-gangrene serum in this case have permitted the conclusion that this is the preferred method of treatment. It is emphasized that thorough and careful examination of all superficial head wounds is necessary. Radiographic studies should be obtained and, if penetration of the skull is in evidence, thorough exploration and debridement of the area are mandatory.

SUMMARY

1. A case of Clostridium perfringens infection of the brain with subsequent recovery is reported.

2. Adequate wound debridement; antimicrobial therapy, including massive doses of penicillin; and gas-gangrene antitoxin are indicated in clostridial infections of the central nervous system.

3. Small, penetrating wounds of the scalp and skull are particularly prone to clostridial infection, and it is stressed that this entity should be kept in mind when dealing with this type of injury.

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Experimental Brain Tumors in Rabbits and Associated Cerebral Edema

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This report concerns an investigation into cerebral edema associated with experimental brain tumors in rabbits. These tumors grow in the majority of animals in which they have been transplanted. Furthermore, these tumors are associated with considerable surrounding cerebral edema. The edema so produced is thought to be comparable to that associated with primary or metastatic cerebral tumors in human beings, unlike the acute cerebral edema produced by intracarotid injection of noxious agents or by local application of physical irritants.[1–4] Cerebrovascular permeability studies in these animals, using vital dye and radioisotope technics as investigative tools, are presented.

MATERIAL AND METHOD

New Zealand white rabbits were used. The tumor selected was that of the Brown-Pearce variety,[5] which was carried in colonies of donor rabbits by periodic intratesticular transplantations. In this series of experiments, 67 rabbits were used. Each was anesthetized with barbital sodium via the marginal vein of the ear. The head was shaved, and a stab wound was made into the scalp under aseptic conditions. A drill opening was then placed in the skull immediately anterior to the coronal suture line, care being taken not to perforate the dura. Using a short bevel No. 18 needle that had been previously attached to a 1-cc. syringe containing 0.2 to 0.3 cc. of freshly prepared saline emulsion of the tumor, an intracerebral puncture was made via the drill opening in the skull. The needle was gently rotated through 360°, and then the tumor emulsion was slowly injected. The puncture was made perpendicular to the plane of the skull, and the tip of the needle was maintained at a depth of 0.6 cm. from the cortical surface. After injection, the needle was held in the wound for about three minutes to minimize possible extracerebral leakage of the emulsion. The needle was then withdrawn, and the drill opening was sealed with bone wax. The scalp was approximated with 1 or 2 sutures. The rabbits were replaced in their cages; no special postoperative care or feed was needed.

Animals usually were sacrificed from nine to twelve days after transplantation, because of high mortality beyond that time. In the beginning, complete autopsies were carried out, but, because of lack of metastatic sites extracranially, this procedure was abandoned and examination was limited to the head.

In those instances in which cerebrovascular permeability was studied, either 0.5 cc. of 20 per cent sodium fluorescein was given intravenously about thirty to forty-five minutes before the sacrifice or approximately 30 μc. of radioactive iodinated serum albumin (RISA) was injected via the marginal vein twenty-four hours before the sacrifice. In the former case, examination of the brain was made with a CH_4 mercury lamp with a Wood's filter. Fluorescence of the tissue would indicate increased cerebrovascular permeability to sodium fluorescein. In the latter case, removal of the brain was made after sacrifice of the animal by cardiac puncture to pool the blood in the thorax and injection with normal saline of the carotid system to remove any radioactive element contained therein. Specimens of tumor tissue, obviously edematous adjacent cerebral tissue, and normal brain from the opposite hemisphere were obtained. These specimens were assessed by counting in an end window counter, and specific activities were determined. In some rabbits, cerebrospinal fluid, usually no more than 0.7 cc., was aspirated by cisternal puncture twenty-four hours after intravenous injection of RISA. Blood samples also were obtained at the same time. The blood was withdrawn with a heparinized syringe to prevent clotting. Using burets, 0.5 cc. each of blood and cerebrospinal fluid thus removed were delivered separately into specially calibrated

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curetts; specific activity of RISA was determined by counting these specimens in a well counter.

CLINICAL COURSE

For the first two days after transplantation, these rabbits behaved normally. They did not show any lack of appetite or become inactive. Their body weights remained stable. Beginning on the fifth or sixth day, there was evidence of increasing irritability. Respiratory rates became accelerated and appetites decreased. Thereafter, lethargy developed slowly but steadily. Some animals would just sit, usually in the corner of a cage, with their eyes closed, breathing rapidly, and suddenly jumping up, as if greatly startled, when evoked in any way. Most of them would not survive twenty-four to forty-eight hours beyond that stage. Before their deaths, many showed signs of hemiplegia. However, a considerable number of animals died before becoming hemiplegic. No convulsive episodes were observed in these animals, but such may have escaped detection because twenty-four-hour observation was not maintained.

In those animals in which the transplant did not grow, there was no detectable general or neurologic deficit.

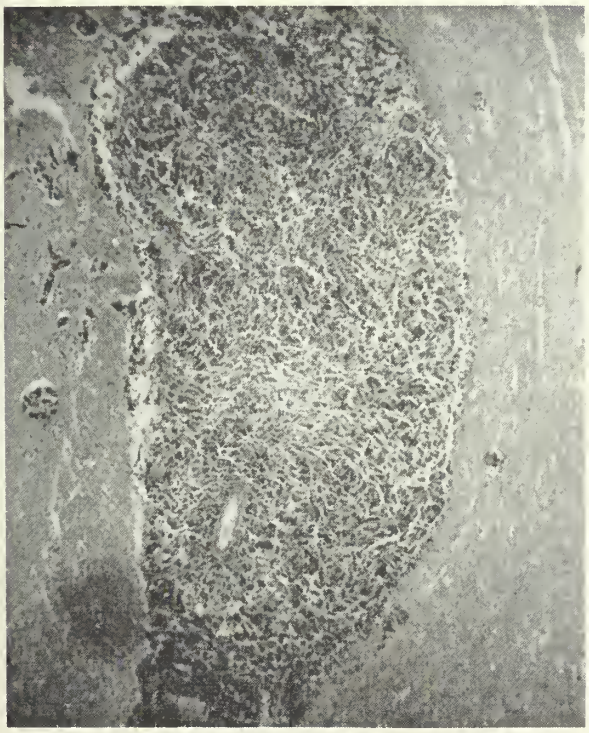

Fig. 1. Photomicrograph of tumor, low magnification; area showing large blood vessel in right lower field shown in figure 2.

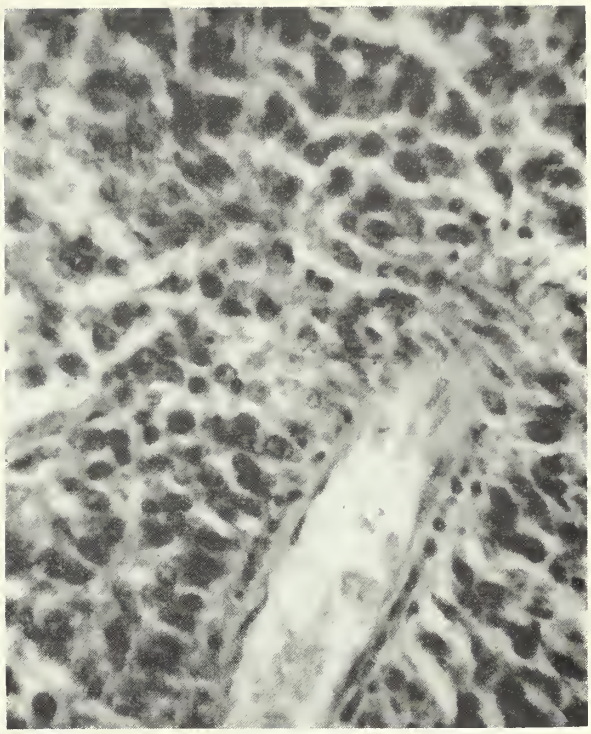

Fig. 2. Photomicrograph of tumor, high magnification.

POSTMORTEM EXAMINATION

Of 67 rabbits in which transplantation was made, 54, or 80 per cent, showed unquestionable tumor mass in the cranium; 32 animals had intracerebral tumors which extended externally to involve the leptomeninges, and 3 had en plaque tumor masses presenting into the epidural space. In 1 rabbit, leptomeninges covering the entire anterior cranial fossa were involved in a similar en plaque tumor growth. In general, those animals that had large leptomeningeal lesions presented small intracerebral tumor masses, probably due not to any tissue specificity but to unavoidable leakage of tumor emulsion into the subarachnoid space at time of transplantation.

Tumors confined to the hemisphere at the site of transplantation developed in 22 animals. These were obviously the animals in which extracerebral leakage of tumor emulsion at the site of transplantation was minimal.

Intraventricular extension of the tumor developed in 15 of the animals in association with either primary intracerebral masses or hemispheral and leptomeningeal involvement. When intraventricular growth developed, the tumor likewise presented an en plaque extension on the ventricular surface, much like that involving the leptomeninges. These extensions were usually smaller than the leptomeningeal plaques, per-

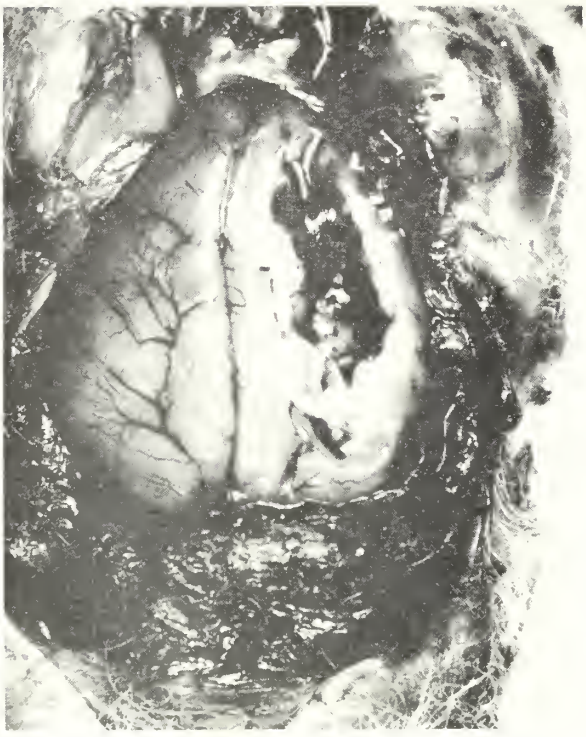

Fig. 3. Intracerebral tumor mass in right hemisphere.

haps due to paucity of blood supply of the ependymal lining compared to that of the leptomeninges.

In addition to tumor masses, associated cerebral edema and even hemorrhages could be seen. The involved hemisphere sometimes became so necrotic that very little normal-appearing cortical tissue was left. The edema, as a rule, was in the white matter closely related to the tumor site.

In those animals with fairly large tumors, there was definite widening of the cranial sutures. The coronal suture on the transplanted side was involved most frequently. In some rabbits, there was even definite elevation of the bone edges.

Histologically, the tumors appeared densely cellular and usually sharply demarcated from the cerebral tissue. The adjacent brain showed some loss of staining properties and vacuolation consistent with cerebral edema. Low-power photomicrographs of an island of the tumor is shown in figure 1, and a part of it surrounding the blood vessel is shown in high-power magnification in figure 2.

Outside of the central nervous system, the only significant autopsy findings were pulmonary edema and infection. The gastrointestinal tract was found to be normal in all animals.

Figure 3 is a photograph of the brain in situ. The right hemisphere is enlarged, especially in the frontal region. A part of the cortex has been removed to show the tumor mass and the adjacent cerebral tissue. The darkened area is mostly necrotic tumor tissue, together with several small hemorrhages. Figure 4 is a photograph of the same specimen taken with ultraviolet illumination. It can be seen that most of the tumor mass, except the necrotic area, fluoresced brilliantly. In addition, brain tissue medial to the tumor, particularly in the subcortical matter, also showed marked fluorescence. Sometimes, if the opposite hemisphere were compressed, fluorescence was present also along the sagittal plane (figure 4). This fluorescence is believed to be due to the presence of sodium fluorescein, which obviously had crossed the blood-brain barrier that had been damaged by the tumor or its accompanying pressure.

Table 1 presents data indicating specific activity of normal, edematous, and tumor tissues. These data were obtained from animals which had been given about 30 μc. of RISA twenty-four hours before sacrifice. The average ratio of the specific activities contained in these 3 types of tissues are 1:4:24.3, respectively.

Fig. 4. Same as figure 3, except taken under ultraviolet illumination. Note fluorescence of tumor mass and adjacent tissue.

TABLE 1

SPECIFIC ACTIVITY OF NORMAL, EDEMATOUS, AND TUMOR TISSUES, EXPRESSED IN COUNTS PER MINUTE PER GRAM OF TISSUE

Rabbit	*Normal*	*Edematous*	*Tumor*
8	58	208	987
9	61	262	1,680
10	54	168	1,042
13	48	218	1,475
15	59	240	1,380
16	70	318	2,008
27	42	188	1,042
28	65	264	1,238
29	69	196	708
32	73	284	2,403
34	48	196	1,128
35	59	300	1,970
40	40	180	784
42	77	208	1,306
45	58	208	1,087
54	69	216	1,142
58	71	378	2,594
59	48	210	1,459
65	54	240	1,432
66	50	180	2,679
Totals	1,183	4,752	29,544
Mean	59.3	237.6	1,477.2
Ratio	1	4	24.3

Table 2 shows the data on permeability indexes in 11 animals. The permeability index is the ratio of specific activity of RISA in the blood compared to that in cerebrospinal fluid. Thus, the index becomes lower when specific activity in cerebrospinal fluid is increased. In this experiment with intracerebral tumors, the average index was 32.52, the range being from 43.48 to 17.19. These figures compare well with those of Haines and associates[9] in a similar study of human beings with various types of primary brain tumors.

To precipitate the protein component, several cerebrospinal fluid specimens were treated with trichloroacetic acid after counting. It was found that almost all the radioactivity could be recovered from the precipitate, indicating that the isotope was still bound to the protein fraction. Because of the small volume of cerebrospinal fluid involved, further analysis of protein fraction either by electrophoresis or by paper chromatography was not pursued. It would seem from these trichloroacetic acid precipitation studies that the permeability index is merely a measure of the protein level in the cerebrospinal fluid.

DISCUSSION

Production of cerebral edema by implanted experimental brain tumors is not new. Using methylcholanthrene, primary brain tumors resembling gliomas have been successfully produced and transplanted in several generations of mice.[6,7] However, these tumors are usually infiltrating and consequently a clear line of demarcation between neoplastic and normal tissue is lacking. Because of this, cerebral edema associated with this type of space-occupying lesion is not entirely ideal. Another theoretical method of producing cerebral edema is to produce brain abscesses. This procedure has been tried in dogs with experimentally produced arteriovenous fistulas. Dogs with such fistulas are susceptible to spontaneous bacterial endocarditis, which may theoretically cause metastatic brain abscesses.[8] Our experience in this regard has been disappointing.

Acute cerebral edema can be produced by local application of heat or cold or by intracarotid injection of noxious agents.[1–4] Application of heat or cold produces local edema of various degrees, which gradually progresses and then regresses. Edema fluid thus accumulated has been shown to exhibit an electrophoretic pattern identical with that of the plasma, indicating that this edema was due to extravasation of plasma into the edematous area.[4] This presumably occurred because the cerebrovascular permeability had been altered by the injurious physical agents. The data presented herein indicate an abnormal accumulation of tagged albumin in the edematous cerebral tissue as well as in the tumor. It is felt that the normal cere-

TABLE 2

PERMEABILITY INDEXES, EXPRESSED IN COUNTS PER MINUTE PER CUBIC CENTIMETER OF BLOOD AND COUNTS PER MINUTE PER CUBIC CENTIMETER OF CEREBROSPINAL FLUID

Rabbit	*Blood*	*CSF*	*Index*
9	19,578	487	40.2
13	15,842	387	40.94
16	24,872	572	43.48
28	20,475	798	25.66
34	17,480	597	29.28
35	21,075	490	43.0
42	27,470	846	32.45
45	23,415	974	23.73
58	27,068	1,574	17.19
59	12,487	374	35.98
64	17,425	675	25.81
		Mean	32.52

brovascular permeability must have been disrupted either by the tumor or by some accompanying process to cause extravasation and accumulation of protein-rich fluid in the tissue.

Cerebral edema produced by intracarotid injection of noxious agents is usually an acute and generalized process dissimilar to that in human beings with primary or metastatic tumors of the brain. Other than an acute study of disruption of normal cerebrovascular permeability, there is very limited experimental use of such preparations.

The need for further study of the permeability of the cerebrovascular structure is obvious. Such studies ultimately will require more histochemical or electron-microscopic methods or both. Already, cerebral edema has been shown to be due to swelling of certain brain cells, that is, intracellular, not extracellular fluid. Luce[10] feels that these involved cells are oligodendroglial cells, but others[4,11] believe them to be astrocytes.

The method described herein to produce experimental brain tumors and associated cerebral edema appears simple and attains a high yield. Furthermore, the areas of cerebral edema are well demarcated from the neoplasm, so that the edematous tissue can be used for further investigation without contamination.

SUMMARY

Brown-Pearce tumors were transplanted intracerebrally in a series of 67 rabbits, of which 54 developed experimental brain tumors. Most animals also developed edema in the cerebral tissue surrounding the neoplasm. There was a fairly well demarcated differential between neoplastic, edematous, and normal tissue. Disruptions of normal cerebrovascular permeability, determined by the sodium fluorescein technic and an isotopic tracer method using RISA, have been described. It has been concluded that the method described herein appears to be simple and fruitful in producing chronic and progressive cerebral edema. Such edematous tissue can be used for further investigations of the problems related to the physiology and pathology of the blood-brain barrier.

This investigation was supported in part by Public Health Service Grant B-665(C4) from the National Institute of Neurological Diseases and Blindness.

The author is grateful to Dr. Otto Saphir, Department of Pathology, Michael Reese Hospital, Chicago, for his kindness in supplying the tumor.

The radioactive iodinated serum albumin was obtained from Abbott Laboratories, North Chicago, Illinois.

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Diffusates from burned skin circumventing the circulation of rats contain a toxin that is lethal to mice and rats when given subcutaneously, intravenously, intraperitoneally, or intracerebrally. Total dose and route of administration determine rapidity of death.

The toxin is dialyzable, heat stable, and partially precipitated by 80 per cent ethanol. Chemical composition is not known. The toxin contains peptides, polynucleotides, hexoses, and pentoses. Histamine, bradykinin, adenyl compounds, and salts are independent of the burn toxin but may contribute to the lethal effect.

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Report of a Case

Pregnancy After Successful Treatment of a Patient with a Chromophobe Adenoma

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That endocrine disturbances are important in the natural history of chromophobe adenomas has been long recognized. Disturbances related to sexual function are most commonly observed. Younghusband and associates[1] state that the diagnosis of a chromophobe adenoma must be seriously doubted in the presence of normal menstruation in the woman or undiminished libido in the man. Most authors are not so emphatic, but amenorrhea and loss of sexual potency are important and common symptoms of the disease.

Results of therapy of these tumors are uniformly based upon survival and visual reclamation. Improvement of endocrine function has been both inconstant and disappointing. Cushing[2] reported that occasionally menses did occur in the previously amenorrheic patient after adequate therapy. Bakay's analysis of Olivecrona's series[3] revealed 61 woman between the ages of 15 and 50 with chromophobe adenomas, of whom only 9 had regular menstruation before operation; 10 regained their menses after operation, but in only 5 of these were the menses of normal frequency and duration. In the same series, 19 of 30 women with acidophilic adenomas had amenorrhea. Of these 19 patients, 3 regained regular menses after removal of the tumor; 1 became pregnant several years later and had a normal delivery.

But this was a patient with an acidophilic, not a chromophobe, adenoma—really an entirely different problem, for seldom, if ever, do pure acidophilic adenomas enlarge sufficiently to compress or to destroy the pituitary gland. Only if there is an overgrowth of the chromophobe elements in the tumor is the gland compressed. More recently, Mogensen[4] has studied the problem and found return of menses in 1 of 22 women treated for chromophobe adenomas. Whether surgery or irradiation has been used seems to make little difference in the frequency of return of menses.

Pregnancy after treatment for chromophobe adenoma is rare indeed. One case of conception subsequent to therapy is reported in the analysis of Cushing's series.[5,6] Olivecrona,[3] likewise, had 1 such case in his experience. Kaplan[7] reported the successful treatment of a suspected chromophobe adenoma by irradiation, with the patient's first pregnancy occurring at the age of 40. In the series from the Lahey Clinic,[1] the first report of multiple pregnancies after therapy is given.

The purpose of this report is to present another case of remission of hypopituitarism and occurrence of multiple pregnancies subsequent to treatment of a chromophobe adenoma with surgery and deep roentgen irradiation.

CASE REPORT

K.B., a 19-year-old woman, was admitted to the University Hospitals on October 10, 1949. For sixteen months before admission, she had not menstruated, although her menses had always been normal up to that time. She had also noticed an increase in shoe and glove size and a tendency for swelling of the hands and feet. For six months before admission, she had persistent, generalized headaches and intermittent nausea and vomiting. Diplopia had been present for about two months.

Menarche had occurred at the age of 11, with normal menstrual periods thereafter. The patient had been married fifteen months without becoming pregnant.

Physical examination upon admission revealed a well-developed, well-nourished woman with normal vital signs. There was a 4-mm. proptosis of the right eye. Funduscopic examination revealed minimal optic atrophy on the right and venous engorgement on the left. There were third, fourth, and sixth cranial nerve paralyses on the right and bitemporal hemianopsia. Other

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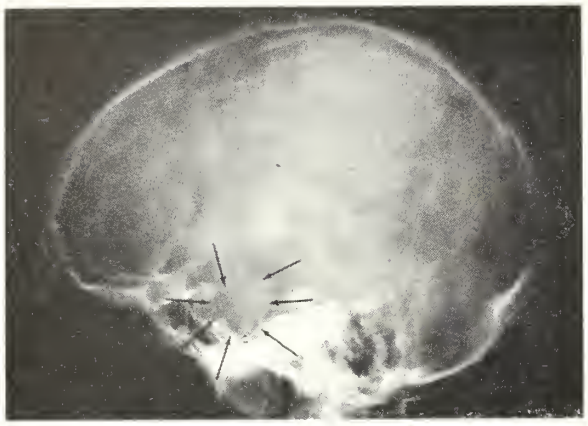

Fig. 1. Roentgenogram of skull showing enlarged, ballooned-out sella. Arrows outline decalcified bony margin.

cranial nerves were intact. A bruit was present over the right eye. Deep tendon reflexes were hyperactive on the left, and the left Babinski sign was positive.

Laboratory studies were entirely normal. Roentgen examination of the skull revealed an enlarged sella with thinning of the dorsum sellae and a depression of the floor of the sella into the sphenoid sinus. The appearance of the sella was quite characteristic of an intrasella tumor (figure 1).

On December 24, 1949, right transfrontal craniotomy was performed, and a large cystic tumor of the pituitary gland was encountered. Contents of the cyst were aspirated and adenomatous tissue curetted. Approximately one third of the capsule was removed. That portion adherent over the right carotid artery and to the hypothalamic region was not extirpated.

Pathologic diagnosis was chromophobe adenoma.

Postoperative course was uneventful except for a transient episode of diabetes insipidus of one week's duration, which relented spontaneously. Visual fields were normal by confrontation examination at the time of discharge from the hospital.

One month after discharge, a twenty-one-day course of deep roentgen therapy to the pituitary fossa was begun. A total of 2,160 tissue r was delivered through 3 ports.

Examination two months after surgery revealed the patient's visual fields to be normal, with a vision of 20/20 in both eyes. The patient was then entirely normal neurologically. Right extraocular palsies had cleared by six weeks after surgery.

Menses resumed in May 1950. The patient became pregnant in May 1951. Pregnancy was complicated only by mild polyuria, which disappeared after delivery.

It is noteworthy that, with the last menstrual period on April 20, 1951, the expected date of confinement would be January 27, 1952. Attempts were made to induce labor with enemas, castor oil, Upsher-Smith ergot routine, and Pitocin given intravenously and intramuscularly, all with no effect. Roentgenograms revealed a large, well-developed fetus. Finally, at an estimated period of gestation of forty-four weeks, a low cervical cesarean section was performed. The infant was a normal male, weighing 9 lb. Menstruation resumed after pregnancy. The patient remained symptom-free. A second child was conceived in 1953. This pregnancy was entirely uncomplicated. The child was delivered by cesarean section in March 1954. This was an elective procedure done at thirty-nine weeks' gestation. The child was a normal male infant who weighed 7 lb., 11 oz.

In 1955, the patient returned, noting blurred vision and headaches. Visual fields were normal and skull films revealed evidence of the right transfrontal craniotomy. The sella was smaller than on the previous (1949) examination. The dorsum sella was recalcified (figure 2). During June and July 1955, a second course of roentgen therapy of 2,940 tissue r was given, with complete remission of symptoms. The patient continued to do well until 1957, when persistent alarming menorrhagia required hysterectomy for control, which was done after control could not be obtained by dilation and curettage and various types of endocrine therapy. No causative lesion was found. The pathology report was as follows: "The uterus contained no myomas. The cavity of the uterus was smooth. The cervix showed no ulceration."

COMMENT

It is believed that endocrine dysfunction observed in patients with chromophobe adenomas is due to compression of the normal pituitary cells by the tumor. Often, much of the remaining secretory tissue is destroyed by surgery and deep radiation. Consequently, seldom is return of function sufficient to permit the return of normal menses or of pregnancy. In this regard, the case presented is extremely unusual. Perhaps the reason that intact cells were present is that this adenoma broke through the diaphragm sella early in its growth and thereafter extended extrasellarly to produce extreme visual field defect and extraocular palsies rather than permanent endocrine defects.

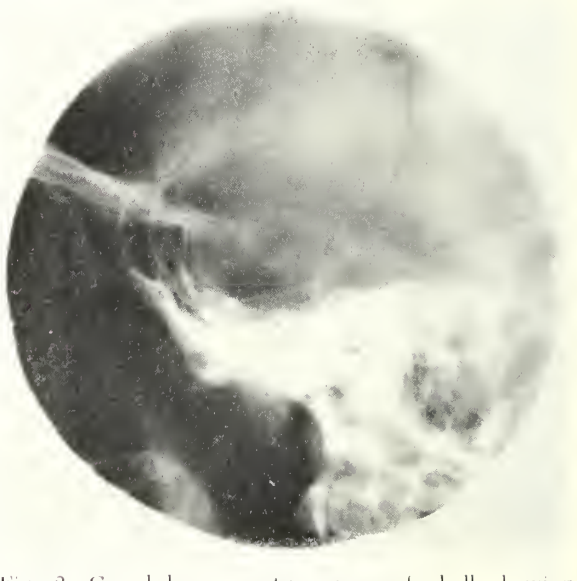

Fig. 2. Coned-down roentgenogram of skull showing sella in detail, taken in December 1955, five years after surgery and deep roentgen therapy for the chromophobe adenoma. Sella is now normal in size and considerable recalcification has taken place.

SUMMARY

A brief review of the subject of pregnancy after treatment of chromophobe adenoma is undertaken. An additional case of multiple pregnancies in such a situation is presented.

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In chronically fatigued women with depleted bone marrow iron but without anemia, iron therapy increases the average hemoglobin value and may alleviate iron deficiency symptoms.

Symptomatic iron deficiency is possible even when hemoglobin values are normal. For a time after decline from the individual norm, hemoglobin values for a patient with a normal or high normal content will continue to be in the normal range. Iron deficiency in such patients can be detected by examination of bone marrow for stainable iron.

Iron and a placebo were given for alternate three-month periods to 29 chronically fatigued women with hemoglobin content of more than 12 gm. per cent. Iron therapy increased the average hemoglobin value in the group deficient in marrow iron, but significant changes did not occur during placebo administration or in patients with adequate iron stores. Of 18 iron-depleted patients, 13 reported more symptomatic improvement with iron therapy, while 5 improved more with a placebo. Of 11 women with normal or slightly reduced iron stores, 4 improved more with iron and 5 with a placebo; 2 did not improve.

E. Beutler, S. E. Larsh, and C. W. Gurney: Iron therapy in chronically fatigued nonanemic women: a double-blind study. Ann. Int. Med. 52:378-394, 1960.

Approximately one-third of patients with renal cancer seek medical attention because of nonurologic symptoms. Recognition of this fact and diagnostic use of intravenous urograms in atypical cases should speed diagnosis and improve the presently poor end results of renal cancer.

The classic triad of gross hematuria, pain in the flank, and flank mass was lacking in 183 of 577 patients with renal cancer. In 138 of the 183 patients, the presenting symptom was fever, weight loss, pain other than in the flank, unexplained weakness, or painless abdominal mass. In 45 patients, the renal tumor was silent and discovered incidentally by autopsy or during examination for prostatism, hypertension, polycythemia, nephrolithiasis, or other unrelated conditions.

Only 4 of the 183 patients had gross hematuria; significant hematuria was noted microscopically in 18.

Metastasis was observed in 80 of the 183 patients at the time the tumor was discovered. The skeletal system was affected almost as frequently as were the internal organs, including the soft tissues. The lungs were the most commonly affected organs. In no instance was excision of metastatic lesions curative.

M. M. Melicow and A. C. Uson: Nonurologic symptoms in patients with renal cancer. J.A.M.A. 172:146-151, 1960.

Experimental Production of Tremor

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PARKINSON'S DISEASE, first described by James Parkinson in 1817, is actually a complex of symptoms or a syndrome. Clinically, the symptoms include alternating tremor, cogwheel rigidity, mask-like facies, dysarthria, kyphosis, gait disturbance, poverty of movement, and disturbances in autonomic function. The 3 cardinal features, however, are tremor, rigidity, and akinesia; most other features can be explained on the basis of these. The pathologic changes associated with parkinsonism are widespread; they involve the central nervous system structures from the subthalamic nucleus caudally upward through the brain stem to the cortex. Of all these structures, the globus pallidus and substantia nigra are most frequently involved or, at least, the characteristic degenerative lesions seem to be found there most often.[1]

There is no specific site in which a lesion can be placed or in which one has been found that can account for the entire clinical picture. This clinical complexity should indicate the likelihood that a single anatomic and physiologic basis for all the stigmata of parkinsonism may not be found. Even the etiology has remained a controversial point up to this time.[2] Inflammatory and toxic encephalitis, cerebral arteriosclerosis, posttraumatic encephalopathy, and a number of other causes have been implicated.

In spite of these complexities, an understanding of the pathophysiology is now beginning to emerge. Within the past few years, several laboratories have demonstrated that an alternating tremor can be produced in the experimental animal either by stimulation of the basal ganglia or by discrete destructive lesions within the bulbar reticular formation.[3,4] Moreover, stimulation or coagulation within certain of the basal ganglia, particularly the globus pallidus and thalamus, effectively alters the tremor thus produced. The purpose of this report is to give the results of further investigation into experimental production of tremor and rigidity, as well as into surgical methods that might be used for altering this experimentally produced parkinsonian syndrome.

Extensive systematic experimental investigation has not been made into the effects of ablating various subcortical brain structures in animals that exhibit tremor or other involuntary movements. This is primarily because of the comparative lack of reliable methods for producing involuntary movements in laboratory animals. In 1940, Kennard and Fulton[5] reported the production of tremor in animals subjected to bilateral surgical ablation of the premotor cortex and head of the caudate nucleus. More recently, tremor and athetosis have been produced in animals by placement of destructive lesions into the tegmentum of the midbrain, the subthalamic nucleus, and into other brain stem areas. Each of these methods, however, involves surgical ablation of 1 or more brain structures; consequently, they are not well adapted for appraising the results of further surgically produced destructive lesions.

However, abnormal movements have also been produced in experimental animals through the use of such chemical agents as Thorazine, Serpasil, and some others. This latter approach seemed to be suitable for investigating the effects of destructive surgical lesions on induced tremor. Therefore, these methods were first appraised in an effort to establish reliability of the chemical agents. The obvious advantage in producing a parkinsonian syndrome by this technic is that no electrode or probe of any type needs to be placed through the brain substance. Damage to brain tissue is thereby avoided. Chemical agents can produce tremor and rigidity which closely parallel the tremor and rigidity observed in human beings with Parkinson's disease.

The second part of this investigative program was (1) to produce lesions in the basal ganglia by the insertion of an electrode under careful stereotactic procedures and (2) to produce discrete well-defined lesions by electrocoagulation.

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The parameters of the current used to produce these lesions obviously must be closely monitored. It is believed that further knowledge useful for the understanding of Parkinson's disease can be obtained only by the use of comparable, carefully controlled, precisely located discrete lesions.

It is appreciated that both tremor and rigidity can be altered clinically by placing necrotizing solutions into various areas of the brain. Such lesions are unquestionably quite variable in size because the solutions tend to spread along the fiber tracts. From the point of view of investigation into the basic mechanisms, this variable size of the lesions does not permit entirely reliable conclusions to be obtained. For example, White and others[6] reported the passage of a mixture of alcohol in ethyl cellulose, which is the solution commonly used to produce destructive lesions, from the region of the globus pallidus across the anterior commissure to the medial part of the contralateral globus pallidus. Bertrand[7] reported similar results with the use of other agents. In a study of the directional growth of neoplastic diseases done in this laboratory, it was found to be utterly impossible to effectively confine various injected substances to a discrete brain area. For these reasons, the technic of stereotactic placement of electrodes and electrocoagulation, as developed by Spiegel and associates,[8,9] was modified and used.

PRODUCTION OF TREMOR

In the first phase of this study, various substances were used in an attempt to produce a syndrome in experimental animals that would be akin to the syndrome observed in human beings with Parkinson's disease. The most consistent results were obtained with the use of Thorazine or Serpasil. Both cats and dogs were used as experimental animals. Following are some of the results obtained; they show the general reliability of this technic.

Thorazine

1. A series of 10 dogs was given intramuscular injections of Thorazine, 20 mg. per kilogram, at daily intervals for at least three days. In 5 animals, tremor never developed at any time. In the 5 remaining dogs, tremor appeared 9 times after 15 injections.

2. A series of 10 cats was given intramuscular injections of Thorazine, 15 or 25 mg. per kilogram, at daily intervals for at least three days. Tremor never developed in 9 animals. In 1 animal tremor developed on 1 occasion.

Serpasil

1. A series of 10 dogs was given subcutaneous injections of Serpasil, .2 mg. per kilogram, at varying intervals. Tremor developed in every animal for durations varying from three to twenty days. Associated autonomic phenomena, such as excessive salivation, diarrhea, and hypokinesia, also appeared.

2. A series of 25 cats was given subcutaneous injections of Serpasil, .2 to .4 mg. per kilogram, at varying intervals. Tremor never developed in 40 per cent of the animals tested. In 60 per cent of the animals, tremor did develop, but not consistently.

3. A series of 10 cats was given intraperitoneal injections of Serpasil, 2.5 mg. per kilogram, at varying intervals. In 8 animals, a good symmetrical tremor developed in all 4 extremities after every injection. In 2 animals, tremor developed which, although symmetrical, was considered too mild for evaluation.

The most reliable method of tremor production, as determined in this study, involved the use of Serpasil injected subcutaneously in dogs. The use of Serpasil injected intraperitoneally in cats appeared almost equally reliable. Cats are much more readily adaptable to stereotaxis because of their uniform skull architecture. Therefore, the intraperitoneal Serpasil method, with cats as the experimental animal, was the technic finally selected.

METHOD OF PRODUCTION OF ELECTROLYTIC LESIONS

The second phase of this study involved altering these Serpasil-induced tremors by means of

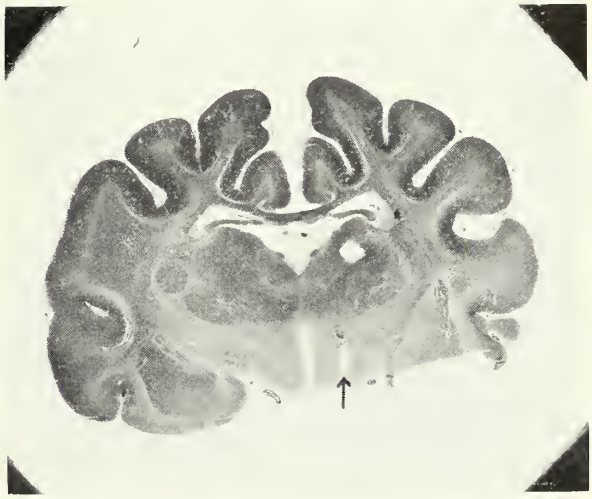

Fig. 1. Photograph of cat's brain under hematoxylin and eosin stain showing lesion produced electrolytically in the region of Forel's area H_2.

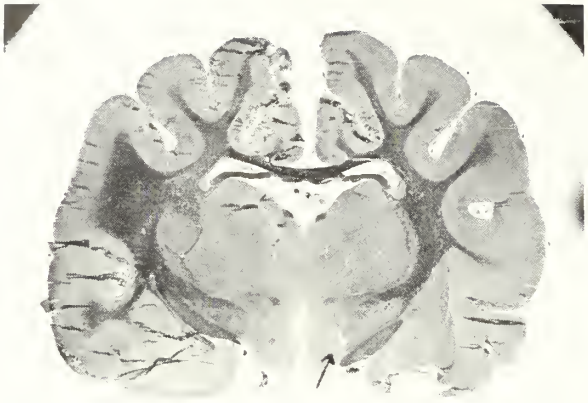

Fig. 2. Photograph of cat's brain under Nissl's stain revealing lesion produced electrolytically in region of Forel's area H.

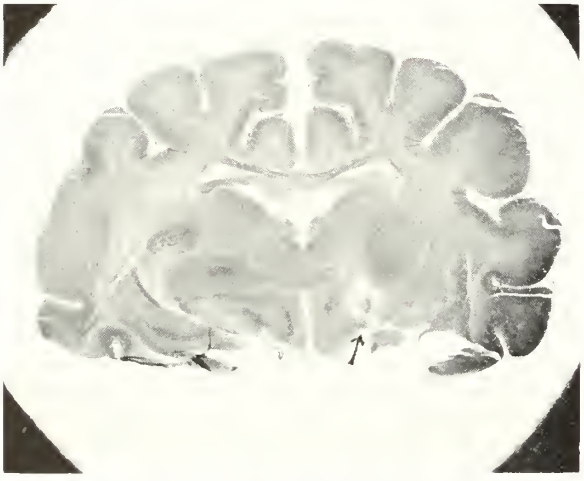

Fig. 3. Photograph of cat's brain stained with hematoxylin and eosin showing electrolytically produced lesion in region of Forel's area H.

stereotactically placed, subcortical electrolytic lesions.

Mature cats were used. They were anesthetized with intraperitoneal Nembutal sodium, using 30 mg. per kilogram of body weight. A standard stereotactic device was used, and lesions were produced with direct, anodal current —3 ma. for thirty seconds. Single lesions were unilaterally placed in a variety of structures, and a period of recovery that varied from seven to fifteen days was allowed. The recovery period was considered to be terminated when the animal exhibited normal behavior and normal neurologic status. When there was an apparent neurologic deficit in an animal subsequent to placement of the electrolytic lesion, the animal was not used in this series.

After each cat had recovered to preoperative status, it was given an intraperitoneal injection of Serpasil, as previously described. The resultant tremor was carefully observed for symmetry, rate, and intensity. Significant alteration of tremor in the extremities contralateral to the electrolytic lesion was considered to have taken place when the tremor in opposing sides exhibited a ratio of 2:1 or greater in intensity. Rarely was a change in rate seen. Each animal was followed by 2 observers, and unanimity of opinion was required.

Finally, each animal was sacrificed and intracerebral lesions were verified histologically with hematoxylin and eosin and by Nissl's sections (figure 1 through 5). Only those animals in which the lesion was confined to a specific subcortical nuclear structure are included in table 1. The tremor referred to in the table was a postural alternating tremor of 6 to 8 per second in frequency.

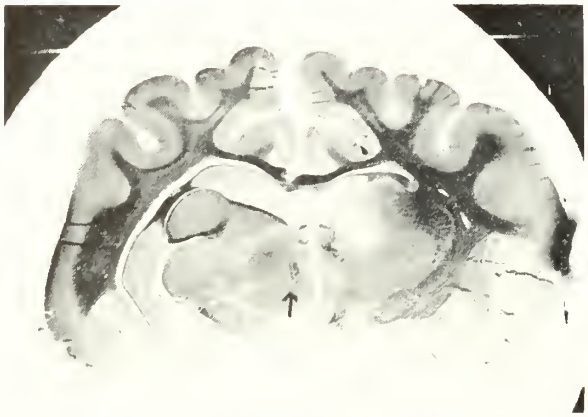

Fig. 4. Photograph of cat's brain stained with Nissl's stain revealing electrolytically produced lesion in ventrolateral nucleus of the thalamus.

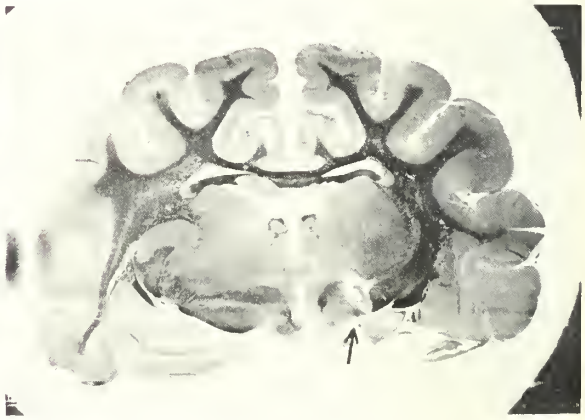

Fig. 5. Photograph of cat's brain under Nissl's stain revealing electroytically produced lesion in the region of Forel's area H.

TABLE 1

EFFECT OF LESIONS ON TREMOR PRODUCED BY DRUGS

Structure	*Tremor altered*	*Tremor not altered*	*Questionable*
Caudate nucleus	0	1	—
Globus pallidus	5	2	2
Nucleus ventralis anterior	2	3	—
Nucleus ventralis lateralis	3	1	—
Field H_2	6	1	1
Nucleus ruber	2	4	—

COMMENT

Lesions in 3 specific structures appeared to alter significantly the appearance of induced tremor in the contralateral extremities; namely, the globus pallidus, nucleus ventralis lateralis, and field H_2. Of these, the most profound alterations resulted from lesions in field H_2, where ratios of 4:1 and 6:1 were obtained and where, in a few instances, no tremor at all appeared in the contralateral extremities. Alterations resulting from lesions in the globus pallidus and nucleus ventralis lateralis, although quite definite, were less profound. Lesions in the remainder of the structures that were studied provided no consistently significant alteration in tremor.

DISCUSSION

A method of producing tremor in laboratory animals by using drugs is outlined. This is not a unique method. Tremor has been produced before by other investigators using similar drugs and also using other drugs, such as Tremorine.[10–12] Other drugs have also been used in this laboratory, and some have successfully produced tremor. But, for this series of investigations, it was thought that the tremor produced by Thorazine or Serpasil seemed to relate most closely to the tremor observed in human beings with parkinsonism. The effects of stereotactically placed lesions in a variety of subcortical nuclear structures were then studied in a series of animals with induced tremor. The results are presented.

As a result of these and other investigations, this clinic has altered the site of the lesion in an attempt to relieve the symptomatology of patients with parkinsonism; the site now includes a quadrangular area centered around Forel's field H_2. Whether or not lesions placed in this area in human beings will be more proficient clinically than those in the medial part of the globus pallidus or in the ventrolateral nucleus of the thalamus cannot yet be shown. Because lesions in Forel's field H_2 have been made only during this past year, insufficient time has elapsed to verify the persistence of results.

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William Thomas Peyton, M.D.

Educator, Surgeon, Investigator

J. ARTHUR MYERS, M.D.
Minneapolis

When one of its most prominent figures for more than a third of a century retires from the University of Minnesota faculty, the evaluation of his contributions to the institution and to his fellowmen tells the story of the significance of his career. Such a man is William Thomas Peyton, professor and director of the Division of Neurosurgery, University of Minnesota School of Medicine. His outstanding achievements and service to mankind will be remembered as long as there is a University. An illuminating insight into the character of this dedicated man was clearly illustrated when Dr. Peyton was asked why he chose to devote his life to the medical profession. He answered that he loved teaching and desired to help others.

CHILDHOOD

Bill Peyton, as he is called by his colleagues, is a native son of Minnesota and one who never succumbed to the temptation of "the greener grass on the other side of the fence." He has spent his entire professional life within the boundaries of his state, never straying far or for very long, and then only in response to the demands of his position.

Born January 11, 1892, to Michael Peyton, a Traverse County farmer, and his wife Katherine, Bill was one of 6 children, 2 of whom are living. His childhood was happily spent in a family in which kindness toward one another and the community were considered important.

The Traverse county farm was typical of American households at the turn of the century, when every family was pretty much a unit and survival sometimes depended on the "home talent" and tenacity of its members. Practicing physicians were few, and distances were great between the doctor and the patient. William's family, as did many of their neighbors, possessed a "doctor book," from which they sought guidance in illness emergencies, large or small, while sending for the doctor. William and his elder sister, Agnes, were immensely intrigued with this book, in which so vast a store of medical knowledge was to be found. When illness occurred, William and Agnes raced for the book, with symptoms to search for well in mind, and from its pages made prompt diagnoses. Dr. Peyton, when nostalgically recalling his boyhood days, tells, "We often made some pretty good diagnoses." This brother-and-sister team developed a talent which reached far beyond the confines of their own farm. Agnes has long been called "Doc" in her home community, while William, home on vacations, is still "Billy," although he has achieved fame as one of the great modern surgeons and an outstanding leader in neurosurgery, not only in his home state but everywhere. Those early experiences on the farm may have motivated his desire to enter the medical profession.

William helped his father on the farm, doing the many chores of the average boy, and he grew to love the soil and to respect the people who spent their lives in providing food and sustenance for their families and the nation. His knowledge of farming held him in good stead during World War II, when he obtained a plot of ground near the University campus and grew vegetables and fruits

not only for his own family but also for colleagues and friends. He continues gardening as a hobby that provides exercise and keeps him "a dirt farmer."

YOUTH

Dr. Peyton's elementary education was received in the public school of Traverse County. He attended Wheaton High School from 1907 to 1908. The next three years he was enrolled in St. John's High School at Collegeville, Minnesota, where he graduated in 1911. He matriculated at St. John's College, Collegeville, in the fall of 1911.

He entered medical school at the University of Minnesota in the fall of 1914, and by 1918 he had received B.S. and B.M. degrees. He always stood high in his class scholastically and was awarded membership in Alpha Omega Alpha fraternity. Since then, his connection with the University as gradnate student and staff member has been practically continuous; he retired in June 1960.

Dr. Peyton's has been distinctly a Minnesota career. He served his internship at Minneapolis General Hospital from July 1, 1918, to June 30, 1919, and his M.D. degree was conferred in 1919.

His graduate training included anatomy, University of Minnesota, 1922 to 1926, resulting in a Ph.D. degree; a fellowship in surgery, University of Minnesota, July 1 to December 31, 1926; a fellowship in surgery and neurology, Mayo Foundation, Rochester, Minnesota, January 1, 1927, to January 1, 1928; and a fellowship in surgery, University of Minnesota, January 1, 1928, to January 1, 1929. His major field as a graduate student was surgery, in which he was awarded the Ph.D. degree in 1930.

As he became deeply immersed in his work over the years, his recreational reading understandably gave way to the reading required in the field of medicine to keep up with the rapidly increasing advances. He contends that he has no library, as the medical literature published so prolifically soon becomes obsolete. Instead, he depends on the medical school library. This amuses Mrs. Peyton, as she wonders just what to call the room in their home whose four walls are bulging with books.

Dr. Peyton first joined the staff of the University of Minnesota as an instructor in anatomy in 1922. He was appointed instructor in surgery in 1929 and became assistant professor in 1930. He served in this capacity until 1934, when he was promoted to associate professor. In July 1937, he was appointed director of the Division of Neurosurgery, which was established at that time by Dr. O. H. Wangensteen, professor and director of the Department of Surgery. The switch marked the change in his career from general to neurosurgery.

At that time, when the Division was in its infancy, there were relatively few neurosurgical patients. Dr. Peyton's interest and knowledge in the field was utilized to advantage in the development of the Division. Before 1937, he was identified as a general surgeon whose reputation had already been established to the point that many of his patients were doctors, their relatives and nurses. He had a special interest in general surgery and in neoplastic diseases of the head and neck. He was advanced to the rank of professor in July 1940.

In 1920, Dr. Peyton married Miss Clara Krapp of St. Paul. They have 4 children, now married. Both Dr. and Mrs. Peyton are deeply devoted and extremely proud of their 15 grandchildren, whose photographs dot the walls of his office.

Mrs. Peyton always has been interested in her husband's work at the University. The couple met during their college days. They have made their home for many years at 64 Barton Avenue S.E., Minneapolis, where their family was reared and where the children and grandchildren now come for visits.

ADULTHOOD

Dr. Peyton has been described by his colleagues as a "quiet man with positive ideas." When the tall, distinguished man with a quick step is seen walking in the hospital corridors, he gives the appearance of an austere personage. That image is soon forgotten when students refer to him as "Uncle Bill," whom they know and love. He became a teacher to help others and he has taken his self-assignment literally. No matter how weighted he has been with executive responsibilities of his office, he has never been known to refuse to take time out to hear a student's problem. He has a way about him which suggests that he is completely relaxed and that the problem at hand is the only one worth considering. His every effort has been spent in the service of his fellow creatures. He has always tried to obtain the best for his students and has been generous in sharing his profound technical knowledge with them. His wise diplomacy in the teaching and surgical fields has proved the inspiration for many young men seeking guidance. He continues to maintain that nothing could be better than to help young people become proficient in their chosen fields.

No flowery language could picture as dramatically the high esteem in which he is held by his former pupils as did the reunion of all of his resident students, who returned to the campus in 1959 to pay tribute to their teacher and friend. They came from all parts of the country and honored him as few persons have been during their lifetime. They climaxed the festivity with a banquet at which Dr. and Mrs. Peyton were honored guests.

Dr. Peyton was certified to the American Board of Surgery in 1937 and the American Board of

Neurological Surgery in 1940. He holds memberships in many medical and affiliated organizations, including the county, state and American medical associations; Western Surgical Association; Minnesota Surgical Society; Minneapolis Surgical Society; St. Paul Surgical Society (Honorary Member); Minnesota Society of Neurology and Psychiatry; American Academy of Neurology; Harvey Cushing Society; and Society of Neurological Surgeons. He is a prolific writer.

It seldom happens to any individual that whenever or wherever his name is mentioned, something good is always heard. Dr. Peyton is such a man. Colleagues, hospital employees, and friends all agree that everybody "loves Dr. Peyton." Before joining the University staff, he was in private practice. It was during this period that he recognized his desire to devote his professional life to teaching and helping others rather than to what might have been a more lucrative career.

Dr. Peyton is a man's man, and his short vacation jaunts have been hunting and fishing trips with colleagues and friends. One group with whom he has gone on hunting trips for many years includes Drs. Baxter Smith, Richard L. Varco, Donald and Bernard Lamnin, Harry Hall, Logan Levin, and others. With Dr. Lyle A. French and others of the staff, he frequently goes on fishing trips and is a real fly-fisherman. Following retirement, he plans to take a vacation trip south, where he and a group of physicians will try their luck at deep sea fishing.

TRIBUTES

Dr. Peyton is held in high reverence by all who have had the privilege of associating with him. Space permits expressions of a few of the large number who hold him in the same high regard.

When Dr. Richard E. Scammon came to assume the administrative responsibilities of the Dean's office in 1932, Dr. Peyton occupied a key position in the Department of Surgery. Because Dr. Peyton's primary training had been in anatomy, he was asked to take over Dean Scammon's lectures in embryology until someone in the Department of Anatomy could be found to discharge the responsibility.

Versatile and skilled in many operations of general surgery, Dr. Peyton assumed direction of the Division of Neurosurgery in 1937 and was the first to occupy this important post. A large number of neurosurgeons in this and other communities owe their training to Dr. Peyton. His successor, Dr. Lyle A. French, is one of Dr. Peyton's most distinguished pupils.

No member of the Department of Surgery in my day has been as popular with students, undergraduate and graduate alike, as has Dr. Peyton. He is affectionately known as 'Uncle Bill' to a host of young surgeons to whom he has been and continues to be 'one of the boys.'

O. H. Wangensteen, M.D.
Chief, Department of Surgery
University of Minnesota

For many years Dr. Peyton has served the University of Minnesota Hospitals and its patients in a very distinct and unusual manner. His professional solicitude for the well-being of the patient, as well as of all those who worked on the patient's behalf, is well known to all of us.

However, behind this unusual man's modest outward appearance of strict behavior is a great feeling of warmth and humor. For many years, with the late Dr. O'Brien, he invited his friends for a 'sour dough, buckwheat pancake breakfast,' in which he was the expert on the batter—frying and serving unusual stacks of "blankets" to his friends.

His prowess as a hunter is also well known to members of the staff, and, as an outdoor man, he is an ardent Nimrod and teacher in the field of conservation, especially of wildlife.

To know him has been my great pleasure, and I think that no one is more universally well liked in the College of Medical Sciences than Dr. 'Bill' Peyton.

Ray M. Amberg
Director, University Hospitals
University of Minnesota

It has been my good fortune to have been associated with Dr. William Peyton throughout the period of expansion and rapid growth of medical neurology at the University of Minnesota Medical School. His wise counsel and good judgment have been a definite guiding influence in this development. He has always shown a deep understanding of the needs and contributions of medical neurology to the entire field of medicine and through his stature has aided greatly in cultivating general faculty acceptance of this field, thus making my position as head of medical neurology much more enjoyable. His critical but well directed questions have always acted as a caution for our younger staff to avoid superficial examination and thinking about neurologic problems; his conservation and willingness at all times, day or night, to consider a patient problem has focused for our staff the importance of the patient's welfare in the practice of good medicine; and his kindness and tolerance for the faults and inadequacies of others have been a constant lesson to us that a physician should aspire to be a gentleman as well as a scholar.

In Minnesota neurology, I am sure Dr. Peyton's influence will subtly play a role for many years to come, for he has taught us some of the key assets of being a good physician, namely, kindness, tolerance, open-mindedness, and critical evaluation. I, personally, shall always be grateful to him for his help, encouragement, and guidance and shall cherish the memories of our pleasant associations academically, socially, and in our travels.

One could supplement such statements with many personal examples which have been vividly recorded in my memory over a period of years. But they would only substantiate the fact that Dr. William Peyton has been endowed with all those virtues which make for a fine physician, an exceptional surgeon, and a wonderful friend.

A. B. Baker, M.D.
Director, Division of Neurology
University of Minnesota

A truly modest man does not willingly accept praise from his fellow beings. Doctor Peyton is such a person. I trust he will forgive his many friends for doing what

is against his nature and realize it is for their benefit that they are taking this opportunity to express their affection, admiration, and loyalty to him.

Those of us who have had the unusual opportunity of learning the science of neurosurgery from him have equally benefited by absorbing the art of medicine from a man who has had that rare combination of both of these important aspects of medicine.

We can be forever grateful for the influence he has had upon us.

Wallace P. Ritchie, M.D.
Clinical Professor, Neurosurgery
University of Minnesota

Bill Peyton may be said to have invented neurosurgery at the University of Minnesota. I have always had a very high regard for him and his work. It seems unfortunate that he should have to retire at this juncture while in the midst of achieving such spendid accomplishments in teaching, surgical technic, and research.

C. D. Creevy, M.D.
Director, Division of Urology
University of Minnesota

One who is not acquainted with Dr. Peyton might regard him as a bit firm. His friends, and they are many, know he is steadfast. Moreover, they applaud him for it.

Colleagues openly, and students quietly, call him "Uncle Bill." The nickname is used with admiration and respect. To his associates, "Uncle Bill" is the good counsellor. To his students, he is the instructive teacher. To his patients, Dr. Peyton is the kind physician. We all wish him well.

R. C. Gray, M.D.
Professor of Neurology
University of Minnesota

To have known and worked with Dr. William T. Peyton is to have enjoyed that stimulating experience of learning surgical principles and technics from a thoughtful technician utterly familiar with the anatomical basis of each operation. Whether seeking counsel about a new procedure designed to improve upon existing methods or merely desiring to acquire seasoned advice on an already time-tested standard operation, one could expect to receive from Dr. Peyton clear and effective guidance. In a corresponding fashion, his discourses in the crassroom or at less formal gatherings throughout the hospital were uniformly lucid, stimulating, and revealed evidence that this surgeon had earned and proudly wore the hallmark of a practicing clinical anatomist. Indeed, his advice on such problems, so frequently sought by those less experienced than he (and very few were not), was always sage and considerate of the other man's feelings. I am personally grateful both for these instructive hours in the operating room and elsewhere in the hospital and for those spent in a hunting blind where Bill Peyton tried to share with me (upon request) his abundance of surgical wisdom.

Richard L. Varco, M.D.
Professor of Surgery
University of Minnesota

It is a pleasant privilege to add my words to those of other pupils and colleagues on the occasion of Dr. William T. Peyton's retirement. The splendid nationwide reputation of his service and the accomplishments of his pupils in many parts of the country are eloquent testimonials to the success of his efforts.

To me, Dr. Peyton's outstanding quality has been his complete intellectual honesty and objectivity in evaluating clinical problems and in judging the results of his treatment.

I consider it a real privilege to have known Dr. Peyton for approximately thirty years. As a junior medical student I was tremendously impressed with his detailed, accurate, and lucid expositions in anatomy which he presented to us in weekly clinics in applied surgical anatomy. As a senior medical student I had the opportunity of "scrubbing in" with Dr. Peyton on several occasions and was treated as though I was really an important part of the team. There was no doubt in the medical student's mind that here was a skillful surgeon who was also a gentleman as well as a teacher.

In 1937, when Dr. Peyton started to limit his practice to neurosurgery, I began a long and rewarding association with him. He firmly believed that many heads working together on a problem was desirable. To this end he cultivated and developed many associates by constantly seeking their opinions and advice. Furthermore, he had great respect for these opinions and freely gave them credit. In 1938 he inaugurated a weekly Neuroradiological Conference, attended by neurologists, neurosurgeons, and radiologists, as well as graduate and medical students, which continues today as an active group. As for himself, Dr. Peyton has always been modest, humble, and unassuming, content with honest scientific and intellectual achievements. He has avoided publicity and personal aggrandizement. By his good works he has become well known, respected, and loved by his colleagues both in the University and in private practice. There is no Town or Gown problem for Dr. Peyton.

Although he has made many contributions to medical literature, his greatest accomplishments include the development of the Division of Neurosurgery from its infancy to its present prominent status and the training of many fine neurosurgeons. I am sure that, as the years pass, these men who have worked with him will agree that the many fine qualities which have made Dr. Peyton a great man have influenced their own lives as much or more than the excellent technical training they received from him.

Harold O. Peterson, M.D.
Professor and Head
Department of Radiology
University of Minnesota

In a field where enthusiasm and optimism have often colored others' opinions, he has maintained an open mind, ever ready to advance but requiring sound reason for change.

Always generous with his time and counsel, he has been a continuing source of support to his younger colleagues in their practice of neurosurgery.

Harold F. Buchstein, M.D.
Clinical Associate Professor
Neurosurgery
University of Minnesota

Dr. William Peyton's quiet philosophy might be described as a business-like "go ahead and do the job." His approach to clinical matters embodies full appreciation of the human and emotional side of the patient's problem. The clarity and simplicity with which he expresses his view have made him a good teacher. His medical excellence and his steady, consistent personal qualities, without bias, have made him a source of sound counsel and have inspired confidence and admiration. Under his guidance the Division of Neurosurgery has attained a fine record.

Bertram C. Schiele, M.D.
Professor of Psychiatry
University of Minnesota

According to the calendar, which I feel must somehow or other be wrong, it was forty-six years ago this fall that Bill Peyton and I first met as freshmen entering the University of Minnesota Medical School. Little did we then think that for almost forty years we would be colleagues on the faculty of our medical school; or that in this relationship we would be privileged to be associated with Jay Myers, our beloved instructor in anatomy and the author of this article.

The intervening years have been interesting and rewarding ones for us both. To me, however, as senior administrative officer of the medical school during most of this period, they provided a unique opportunity to observe and to appraise the work of the individual members of the medical faculty. Bill Peyton was one of those, one who quietly and modestly was continuously doing distinguished work, first in anatomy, then in neurology and neurosurgery, as a scholar, as a scientist, as a teacher, and as superb practitioner of medicine. In each of these roles he inspired confidence and instilled enthusiasm on the part of his students and colleagues by his thorough mastery of everything he undertook.

Bill Peyton not only has brought distinction to our medical school and taught thousands of medical students but, in addition, has trained a large group of outstanding neurosurgeons who can be relied upon to continue the same high standards of proficiency which he set for himself and for all associated with him. What more in the way of achievement or satisfaction could anyone desire.

As for me, I am proud to have had Bill Peyton as classmate, a friend and an esteemed colleague over these many years. The University of Minnesota Medical School is truly a better institution for having had him on our faculty. For his superb contributions over many years we are thankful and eternally indebted to him.

Harold S. Diehl, M.D.
Former Dean, College of Medical Sciences, University of Minnesota; now Senior Vice President for Research and Medical Affairs and Deputy Executive Vice-President, American Cancer Society, Inc.
New York

My acquaintance with Bill Peyton began in 1914, when he registered for the course in anatomy as a freshman in the medical school of the University of Minnesota. Throughout the medical school course, he was admired by the students and faculty alike because of his fine scholarship, sincerity, and dependability in every respect.

About the time I transferred from anatomy to medicine, Dr. Peyton began teaching anatomy, so we still were rather closely associated. After he joined the hospital staff in general surgery, it was a pleasure to refer patients to him because of the thoroughness of his work, his splendid reports, and the confidence he inspired in his patients. For example, in 1936, a senior medical resident developed a cold abscess over the anterior surface of one side of his chest. He was referred to Dr. Peyton, who found tuberculous involvement of a rib. He removed the focus and the sinus tract so completely that periodic examinations of this physician, the last in October 1960, have revealed no recurrence—this in the absence of antituberculosis drugs! He did thoracoplasty and other procedures on a number of tuberculous patients, as well as numerous operations for various conditions in the field of general surgery.

His colleagues have already written glowingly about Dr. Peyton's accomplishments in all aspects of neurosurgery. It was not until he became my personal physician on three occasions that I fully understood why everyone manifested so much confidence in him and why his entire career has been so successful.

Although he has retired from active neurosurgery and teaching at the University of Minnesota, his love for teaching and desire to help others are abiding. He recently accepted invitations to serve as consultant in neurosurgery at the General Hospital and the Veterans Administration Hospital in Minneapolis. In this capacity, students will learn from him, and his "help to others" will include not only patients but also experts in his field. Thus the number of former students engaged in practice, teaching, research, and numerous other medical activities, as well as his patients and many others, who are so deeply indebted to him for his teaching, encouragement, restoration to health, and the fine influence he has had on our lives, continues to grow.

The author wishes to thank Miss Dorothy Riley for her assistance in the preparation of this manuscript.

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Many patients with disseminated lupus erythematosus and some with rheumatoid arthritis have delayed cutaneous reactions to intradermally injected autologous and homologous leukocytes. Local erythema and induration were noted in 16 of 20 lupus erythematosus and 2 of 7 rheumatoid arthritis patients. Sensitivity was noted in only 1 of 52 patients with various conditions, including 2 with active rheumatic fever and 1 with allergic vasculitis. Of the 4 lupus erythematosus patients with negative results, 3 were receiving large doses of prednisone. The reactions may be caused by cellular or humoral antibodies to nucleoprotein.

E. A. Friedman, W. A. Bardawil, J. P. Merrill, and C. Hanan: "Delayed" cutaneous hypersensitivity to leukocytes in disseminated lupus erythematosus. New England J. Med. 262:486-491,

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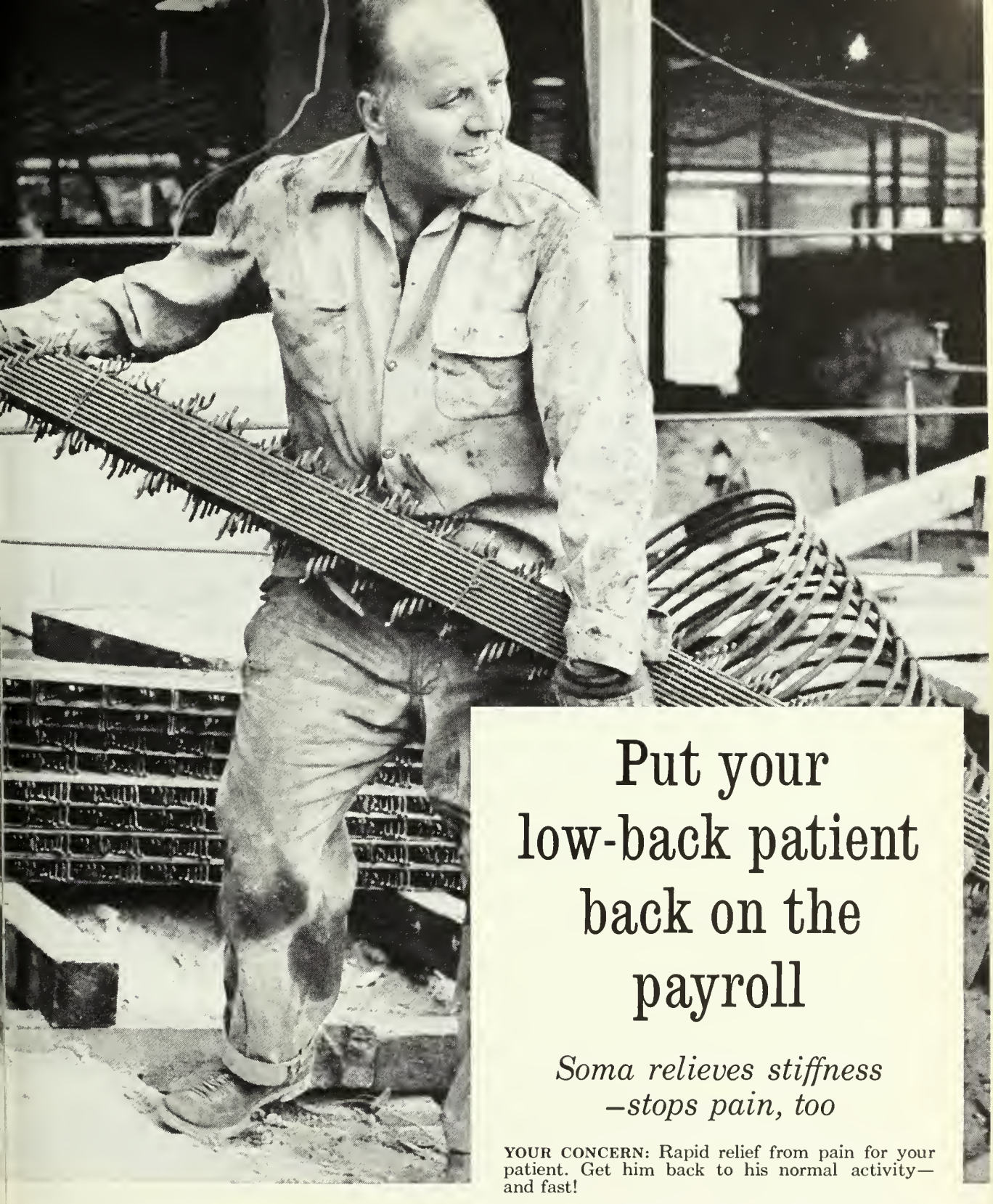
K. S. Mullard: Carcinoma of oesophagus treated by excision. Lancet 1:677-679, 1960.



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Book Reviews . . .

Textbook of Otolaryngology

DAVID D. DE WEESE, M.D., and WILLIAM H. SAUNDERS, M.D., *1960. St. Louis: C. V. Mosby Co. 480 pages. Illustrated. $8.00.*

In the preface to this text, the authors state that it is written for students and general practitioners. Both will find that their problems have been recognized and treated with great clarity. Descriptions and a profusion of excellent illustrations enable the reader to follow the details of diagnosis with such assurance that he may be induced to broaden his field of investigation.

Nationwide, more ear, nose, and throat pathology is seen in the offices of the general practioner than in the clinics of the city. To a large degree, those engaged in general practice have never been taught the refinements of diagnostic procedures, either in school or in their internships.

This text spans the gap between general practice and specialization. Experienced otolaryngologists will also find it profitable reading. Inasmuch as 24 per cent of bodily ills are referable to conditions encountered in the ear, nose, and throat, this book assumes considerable importance.

Common conditions and those less frequently encountered are thoroughly covered. Questions, such as what to look for, the interpretation of what is seen, what to do, and how to do it, are anticipated and answered in detail.

The book is attractively designed. The paper, illustrations, and printing are of excellent quality. The index is complete, so that references to the text are readily found. At the end of each chapter, there is a valuable reference to additional reading.

The authors are to be congratulated on writing a valuable addition to any medical library.

DAVID HIGBEE, M.D.
San Diego

Notes of a Soviet Doctor

C. S. PONDOEV, *1959. New York: Consultants Bureau, Inc. 238 pages. $4.95.*

This book could have been written by an American doctor but for its political flavor.

It is primarily written for the medical student and the young doctor and deals with the exercise of such virtues as kindness, understanding, tact, honesty, and humility in the care of patients.

The ideas, as voiced, are excellent and form a good foundation for the young doctor's concept of how medicine should be viewed and practiced. This, however, is nothing new. It is more of a reiteration of what doctors have always been taught to accept as the high ideals of our profession. It does show us that, in this world, political systems may differ, but the idealistic doctor, wherever he may be, holds in highest esteem the noblest virtues in life.

The book is well written and timely, and the only criticism that can be voiced is the injection of politics into medical ideas. For instance, in the conclusion of the book, there is this statement: "The forty years of existence of Soviet public health with its great accomplishments and perspectives leaves no doubt that in its achievements it has exceeded everything which has been done in this respect by mankind in a thousand years."

I cannot resist saying that the exercise of the human qualities as practiced in medicine does not require tutoring by political philosophy. Medicine has stood on its own two feet for too many centuries to suddenly require a group of politicians to teach it how to best exercise kindness, understanding, humility, honesty, and a reverence for life.

Can one think of two greater opposites than the practice of medicine and the practice of politics? One is dedicated to the relief of suffering, the other to the acquisition of political power. In our search for peace, the Soviet doctor and the doctors of the rest of the world must forget about their political systems and work for peaceful coexistence on the honest foundations of good medicine and not on the shaky foundations of different political systems.

Everything considered, this book is worth reading by the American doctor. It will give him a better understanding of the Soviet doctor, but I am sure it will not convert him to Communism.

ARNOLD S. ANDERSON, M.D.
St. Petersburg, Florida

Typical Gynecological Operations

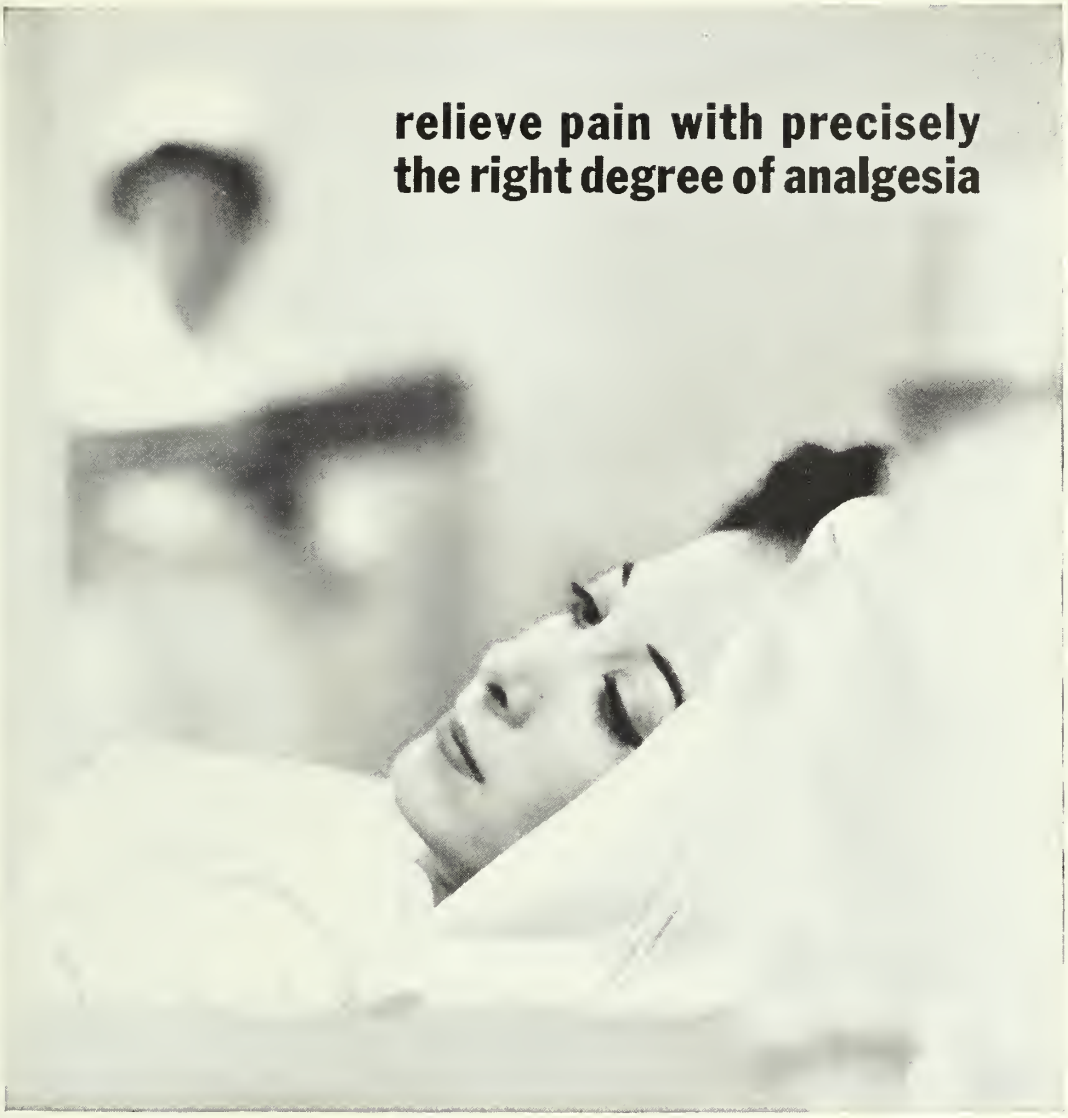
SIEGFRIED TAPFER, M.D., *1960. Philadelphia: J. B. Lippincott Co. 76 pages. Illustrated. $9.00.*

This publication represents a compendium of some of the major abdominal and vaginal operations performed in the field of gynecology. Although the original work was written in German, the author and his collaborator and translator present a clear and graphic description of some of the technical variations in the usual gynecologic procedures. The book creates interest since it is a compilation of technics gained by observation, study, and trial in several European schools. In addition to the written text, there is a complement of 168 drawings which in themselves have an educational value. They are well executed and accompanied by explicit subtitles.

The author notes the importance of anatomic relationship, careful dissection of tissues, care in avoiding injury to vital structures, adequate hemostasis, and meticulous reperitonization. Essentially, the operative technics described are similar to any that are seen wherever gynecology is practiced. We view with favor the lifting of the bladder from the cervix as the initial step in performing an abdominal hysterectomy. However, this is not new, as it has already been advocated by others. It matters little to the practiced surgeon whether further dissection is carried out by the scissors, as employed by the author, or scalpel or by blunt manipulation, as long as tissues are handled gently.

The value of this book as an adjunct to the gynecologic library lies in the description of radical, abdominal, and vaginal operations. The author chose to omit the controversy over use of surgery or radium inasmuch as he is dealing solely with operative technics.

(Continued on page 22A)



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(Continued from 20A)

Of particular merit is the portion that describes the radical vaginal operation for carcinoma of the cervix. Another point of interest is the method of opening the vaginal mucous membrane by sharp dissection in a vaginal procedure. This particular method may be foreign to some, yet mastery of it could prove superior to other known technics. We call attention to the plication of the bladder wall by a purse-string suture and the emphasis placed upon the exacting repair of the poneh of Douglas to prevent enterocele.

As a whole, this book may serve as a valuable supplement to the standard gynecologic text. The strongest portions are those that describe the vaginal and abdominal radical hysterectomies; the weakest are the descriptions of operations for vulvar lesions. The latter topic has been dealt with somewhat superficially. The necessity for a radical procedure in this area has assumed increasing importance in view of the fact that modern concepts reveal that less radical surgery is accompanied by a high mortality.

I would heartily recommend this book to those physicians whose prime interest is gynecology. A thorough knowledge of the technics illustrated could prove helpful in furthering their operative know-how.

H. MELVIN RADMAN, M.D.
Baltimore

Medical Aspects of Flight Safety

E. EVRARD, P. BERGERET, *and* P. M. VAN WULFFENTENPALTHE, *1959. New York: Pergamon Press. 308 pages. Illustrated. $11.00.*

This extensive undertaking is a compilation of papers presented at two international symposia held in Oslo and Copenhagen in 1956 and Paris in 1957 and sponsored by the AGARD aeromedical panel. This book could more properly be referred to as an "AGARDograph." The material compiled was presented by 36 specialists from the United States, Canada, and several European countries. Eight of the papers are written in French.

The book is especially well organized and is produced on fine grade paper. It contains many tables and diagrams. In general, it is replete with excellent illustrations. The reports are arranged in 5 chapters, with English and French summaries at the end of each. The chapters are organized as follows:

Chapter I—Flight Safety and Aircraft Accidents—Generalities
Chapter II—Unexplained Aircraft Accidents
Chapter III—Use of Pathology in Crash Injuries
Chapter IV—In-Flight Protection
Chapter V—Some Special Problems

Chapter I discusses the psychophysiologic mechanisms associated with high altitude flights. It further discusses the measures that should be taken in the preventive aeromedical aspects of aircraft accidents. It is pointed out in one of the reports that there are not enough career flight surgeons. Because of the rapid turnover of doctors entering and leaving the services and the heavy medical work load, the program of preventive medicine in aviation is handicapped. In general, this chapter is the essential part of the book.

Chapter II deals with accidents of unknown causes. It brings forth quite clearly that the flight surgeon must participate actively in flight safety problems, particularly

in the investigation of both explained and unexplained accidents. The flight surgeon should be on guard against the abuse of the hypothesis of human failure, which is used too often with insufficient cause. Due to the rapid evolution of modern aviation, the adaptation of man to the aircraft will remain a perennial problem..

Chapter III is devoted to pathologic investigations of aircraft accidents. It should be recognized that, in the event of a fatal aircraft accident, investigation may no longer be considered complete without an autopsy. The cause of death in this connection is interpreted to mean any correlation between pathologic evidence and factors contributory to the accident. It should be remembered that there are a large number of pathologic conditions, demonstrable only by autopsy, that might arise in a pilot during flight and precipitate an aircraft accident.

Chapter IV is an excellent survey of the in-flight protection of flying personnel. In essence, this portion of the book discusses problems of higher speeds and altitudes and suggests solutions for protection.

Chapter V is a catchall for papers indirectly related to the main subject. One of the papers, on crash-injury research as a means for greater safety in accidents, is well written and easy to read.

It should be noted that the opinions expressed by the authors are solely their own and not necessarily those of the aeromedical panel of AGARD. This research-oriented book has excellent reference value not only for the flight surgeon and flight examiner but also for the curious clinician.

CAPTAIN A. P. RUSH, M. C.
Washington, D. C.

Medicine and Society in America 1660-1860

RICHARD HARRISON SHRYOCK, *1960. New York: New York University Press. 174 pages. $4.00.*

Among the finest books published in medicine are those which result from series of lectures such as the Harvey Lectures, the Anson G. Phelps Lectures, and, at Princeton, the Vanexum Lectures. There must be a score or more of such series of lectures, which yield fine, permanent contributions to medical philosophy.

The history of the past often gives guidance to the present. In the Anson G. Phelps Lectures on early American history at New York University, Richard Harrison Shryock, who registers himself as "of the Library of the American Philosophical Society," considered medicine and society in America from 1660 to 1860. Such strange facts as a 1:600 ratio of physicians to population in the revolutionary era become apparent. Actually, there was 1 doctor for 350 people in New York in 1750, and 1 doctor for 135 people in Williamsburg in 1730.

Doctors in those days probably made more from the sale of drugs than from their practice. Practically all practice was on the fee-for-service basis, although some contract practice was already in effect. The first medical school in the colonies was that of the College of Philadelphia in 1765, second was Kings College Medical School in New York in 1768. The great Dr. John Morgan, even in those days, recommended that surgery and pharmacy be separated from medicine.

The book by Dr. Shryock offers innumerable facts about the development of medical thought and the lives of the leaders, such as Benjamin Rush, who dominated it. Dr. Shryock sees a similarity between Rush's concept

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of the relationship of external causes to disease modified by the body's behavior and the current views of Browne and Selye.

In the third chapter, health and disease are discussed. Improvements in health were largely credited to hygiene and rising living standards. Indeed, Dr. Shryoek feels that the risks peculiar to the United States in 1800 were those involved in bleeding and purging—in too ready use of the knife and of medicaments. His final sentence is barbed satire. He says, "But no one will ever know just what impact heroic practice had on American vital statistics: therapy was never listed among the causes of death."

The final chapter is entitled "Medicine and Society in Transition." He sees in the contract practice of the first part of the nineteenth century the beginning of organized concern about the causes of medical care for the masses. Concepts of health insurance were launched as early as the 1700's. Medical costs were low, but specialization had hardly begun. Cults, such as homeopathy and eclecticism, occupied a prominent place in American medical practice. The number of physicians in proportion to population was already excessive; in fact, in 1848, the ratio of physicians to population was 5 times as high in America as in France. In 1860, there was 1 doctor for every 572 people, contrasted with 1 for every 750 now.

In this chapter, Dr. Shryock outlines the development of the American Medical Association, which began to correct the scandalous conditions which prevailed from 1820 to 1860. Dentistry was the first full-time specialty in American medical practice. Dr. Shryock believes that dentistry broke off from medicine because of the reluctance of doctors to recognize specialization of any sort.

Altogether, the view of medicine and society in America over the two hundred founding years is most thought-provoking in regard to the trends that developed and persisted and the trends that concern us today. If there is any real value to the work of the historian, it lies in the broad and sound basis that he establishes for the guidance of future action.

MORRIS FISHBEIN, M.D.
Chicago

Cholinesterases

M. V. CEREBTZOFF, *1959. New York: Pergamon Press. 188 pages. Illustrated. $8.50.*

This book, divided into an introduction and 3 parts, is a contribution to the study of the cholinesterases from the histochemical viewpoint. The introduction gives a brief outline of the scope and limitations of the histochemical methods and a description of the technic used by the author in his studies. The 3 parts deal with the humoral cholinesterases, the cholinesterases in the nervous system, and the cholinesterases in tissues outside the nervous system.

The positive part of the work, as stated by the author, is that concerned with the localization of acetylcholinesterase in the nervous system. The results presented in the book are compatible with the hypothesis that acetylcholine and acetylcholinesterase play their roles in the transmission of the nervous impulse at the synaptic junctions. The results also indicate that cholinergic transmission exists in both central and peripheral nervous tissue.

On the other hand, the results presented in part III indicate localizations of the cholinesterases outside the

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(Continued from page 24A)

nervous system with no physiologic explanation at present. In this part, the data pertaining to the hepatic secretion of plasma cholinesterase and its relations to food assimilation are of particular interest.

The book is clearly written, is easy to read, and has a large number of excellent illustrations and a very complete and up-to-date list of references. In the reviewer's opinion, this is an excellent book and will be useful to those interested in the functional aspects of the cholinesterases and in the mechanisms of nervous transmission.

FRANCISCO GRANDE, M.D.
Minneapolis

Diseases of the Skin

JAMES MARSHALL, M.D., *1960. Baltimore: Williams & Wilkins. 919 pages. Illustrated. $15.00.*

The author of this new textbook of dermatology is head of the Department of Dermatology at the University of Stellenbosch, South Africa. He was trained in dermatology in England and France. These biographical data are recounted to place the viewpoints of this textbook in proper perspective. Some of its approach is refreshingly new to one whose medical background is entirely American.

This book is thoroughly up-to-date. Treatment recommendations are modern; there is even a chapter on griseofulvin. The book does not attempt to be encyclopedic, and there is no bibliography—only a list of recommended books for additional reading. It is a well-presented expression of the personal views of Dr. Marshall and therefore highly readable to the medical student and general physician, for whom it was written. Specialists in dermatology will find it particularly interesting because of its unique coverage of cutaneous diseases in Africa. Where else would one learn that there is a form of scleroderma endemic among the underground miners in the Witwatersrand?

The section on diseases of malnutrition is especially good, and there is an excellent chapter on parasitic diseases. As befits a South African textbook, there is an excellent discussion of porphyria. Porphyria in the Bantu population is quite different from that in Caucasians, and Bantu patients with chronic porphyria often demonstrate a fine, velvety, verrucose hyperkeratosis of the 2 terminal finger joints.

The chapter on the treponematoses is outstanding. There are striking photographs of extreme lesions of syphilis, both venereal and nonvenereal, and yaws. Throughout the book, many of the illustrations are of Negro patients, an instructive display for northern physicians who have little opportunity to observe cutaneous diseases as they appear in dark-skinned individuals.

While generally good, the book does have its weaknesses and omissions. For example, the only rickettsial disease discussed is South African tick-bite fever. The reviewer found the views of Dr. Marshall on some subjects, such as the classification of sarcoidosis as one of the reticuloses, to be quite different from his own.

Technically, the printing and illustrations are good. The book is recommended to anyone interested in increasing his knowledge of diseases of the skin.

ROBERT W. GOLTZ, M.D.
Minneapolis

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Current Plastic Surgical Concepts of General Interest

JOHN K. GROTTING, M.D., and
LYLE V. KRAGH, M.D.
Minneapolis

With the ever increasing number of persons with severe accidental injuries and with the greater efforts that are being made to rehabilitate patients with congenital deformities, the plastic surgeon's principles in the management of these patients are being used more extensively. In this discussion, we do not attempt to go into detail in the treatment of these problems but wish to review briefly some of the more common problems and their management and to emphasize some newer concepts and their application in this field.

EMERGENCY CARE OF FACIAL INJURIES

Although injuries to the facial skeleton are not often emergency problems, the best final result will be obtained if the wounds are cared for early and adequately. Occasionally, with severe facial injuries, considerable soft tissue swelling may develop, as in a comminuted mandibular fracture with loss of bony support, and tracheotomy may be necessary. Sometimes, bleeding from the nose associated with nasal and facial bone fractures may be persistent and result in significant depletion of the blood volume until the hemorrhage is controlled. However, the majority of patients with maxillofacial injuries do not present these serious signs. Usually, pressure will control the hemorrhage until the bleeding points are ligated and the wound sutured. Many of these soft tissue injuries can be treated under local anesthesia, which, of course, is preferable if significant head injury is suspected. If the patient is unconscious or has had a severe head injury, suturing the facial soft tissue lacerations under local anesthesia will not add insult to his already serious problem.

Following infiltration of the wound edges with an appropriate local anesthetic to which a vasoconstrictor has been added, the wounds should be thoroughly inspected and cleansed. Deep inspection of the wounds may reveal a fracture of the underlying skull or facial bones that was not evident on the roentgenograms. With lacerations about the lips, a thorough search should be made for tooth or denture fragments. Thorough cleansing and irrigation with copious amounts of normal saline will rid the wound of most of the particulate matter. Occasionally, foreign material will be literally ground into the depths of the skin. The longer the time interval between the injury and the repair, the more tightly embedded the particles become. If not removed, they may result in a permanent traumatic tattoo. This can almost always be pre-

JOHN K. GROTTING *and* LYLE V. KRAGH *are plastic surgeons with offices in Minneapolis.*

Abridgement of a paper presented at the meeting of the North Dakota State Medical Association, Grand Forks, May 3, 1960.

vented by thoroughly removing the dirt particles with a stiff scrub brush at the time of repair. Occasionally, a traumatic tattoo in which the pigment particles are not too deeply embedded can be removed by dermabrasion.

Debridement of traumatized facial tissues should be minimal. Facial tissues have an abundant vascular supply, and necrosis of traumatized facial skin is infrequent. Eyebrows should not be shaved in preparation of the wound, since the eyebrows grow back slowly and irregularly, and, if the eyebrow skin is shaved of hair, correct alignment of these structures is difficult.

Mandible fractures can usually be diagnosed by the clinical examination of the patient. Tenderness is present over the fracture site, the teeth may not occlude as they did prior to the accident, and there may be compounding of the fracture site into the mouth through a break in the oral mucosa. With pain in the ear region, especially with jaw motion, a subcondylar fracture should be suspected. And, with any mandibular fracture, a search should be made for a second fracture somewhere else in the mandible. Most of these fractures will be demonstrable on the mandible roentgenograms. With severe injury to the condyle and temporomandibular joint, special roentgenographic examinations directed to that region may be indicated.

With suspected fractures of the middle third of the face, the most useful single roentgenographic examination is the Waters' view of the facial bones. Even in this view, the exact status of the facial bones is somewhat difficult to interpret, but fortunately, most facial bone fractures can be accurately diagnosed by the clinical examination alone.

With maxillary fractures, the upper jaw may be freely movable. If the upper jaw has been forced posteriorly, the patient may have a relative prognathism and the narrowed nasopharyngeal airway may obstruct nasal breathing. Often, the fracture line may involve the midline of the palate, so that half of the upper jaw is stable and half is loose.

Fractures of the zygoma, or malar bone, can usually be diagnosed on clinical examination. These fractures, like those of other areas of the mid-third of the face, usually occur through the thin and weak areas of the bones. The main features of malar fractures are: (1) flattening of the cheek due to inward and downward depression of the bone, (2) numbness of the upper lip due to impingement of the infraorbital nerve in the line of fracture, (3) diplopia due to depression of the infraorbital ridge and floor of orbit, (4) unilateral epistaxis due to fracture lines involving the lateral wall of the antrum causing intraantral hemorrhage, and (5) possible difficulty in closing the jaw due to impingement of the coronoid process on the inwardly displaced zygomatic arch. On the Waters' projection, the infraorbital ridge irregularity may be noted as well as fractures of the lateral wall of the antrum and opacity of the involved antrum.

Most facial bone fractures are not real emergencies, and treatment may be delayed for a few days until the patient's general condition improves or until the correct plan of management of the facial fracture can be determined. Fractures of the zygoma are best reduced within the first forty-eight hours after the accident, but the procedure can sometimes be delayed ten to fourteen days. These fractures can usually be reduced by one of the direct approaches through the cheek overlying the bone, through the intraoral route, or through the temporal route. The markedly comminuted malar fractures and fractures that will not stay reduced by one of these methods may require in addition a Caldwell-Luc antrotomy and antral packing. If the orbital floor is disturbed, open reduction is often the treatment of choice.

With acute nasal injuries, the external and internal examination of the nose is usually more informative than roentgenographic examination. The roentgenographic examination of the nasal framework is often inconclusive, and, if the external nasal contour has not been changed and if, on internal examination, the septum is unchanged, one can be quite certain that no serious nasal injury exists that needs specific treatment.

With nasal injuries that are several days or a week old, the problem is more difficult. The nose will probably still be very swollen, and, therefore, exact determination of any change in its contour is difficult. Also, the interpretation of the roentgenographic examination may be inconclusive. This problem is especially serious in children. In some of these patients, as the soft tissue swelling recedes, a residual nasal deformity may be present. In children, this deformity may become more marked as growth proceeds. These cases may then require a corrective rhinoplastic operation to correct the nasal obstruction and improve the contour of the nose. Even at an early age, this procedure may be necessary in order to prevent the adenoid type of facial deformity.

Most nasal fractures can be reduced satisfactorily, the nasal contour returned to near normal, and the nasal obstruction improved. With very

severe injuries in which there is marked comminution of both the bony and cartilaginous framework, it may be impossible to completely restore the nasal framework and contour. In these cases, a corrective rhinoplastic operation, which includes a bone graft to the nose, may be required later.

CLEFT LIP AND PALATE

In this presentation, we will not attempt to cover the whole problem of cleft lip and palate, but we wish to point out that progress has been made in the past few years in the treatment and rehabilitation of patients with this condition. Following the initial surgical evaluation and repair, there is an increasing trend to utilize the team approach in recommending further treatment for these patients. These teams may consist of a plastic surgeon, a dentist, an orthodontist, a prosthodontist, and a speech therapist. This group examines the patient simultaneously and makes recommendations for further coordinated care of the patient. The panel may reexamine him periodically to review the progress and to make additional recommendations for the future.

We believe that the cleft lip should be repaired in the first month or two of life, when the baby is gaining weight. Soon after, at age 2 to 3 months, the anterior part of the palate may be repaired by a vomer flap technic. The repair of the remainder of the palate should be deferred until the child is about 2 years old in order to prevent interruption of the growth of the maxilla that may occur if the rest of the palate is repaired too early.

Much of the new stimulus in cleft lip surgery has come recently from the modification by LeMesurier[1] of an old method of primary repair of the unilateral cleft lip. This repair involves the principle of making a step-type or Z-type square flap from the lateral side of the cleft and suturing it into a prepared notch on the medial side of the cleft. This type of repair usually results in a lip with a more normal vermillion portion and a better cupid's bow. A somewhat similar type of operation was presented by Tennison.[2] These operative repairs obviate the problem of contraction of the operative scar, which, in the case of straight-line repairs, may shorten the vertical height of the upper lip or produce a notching of the upper lip. Older repairs made it impossible to close a short lip over the upper teeth, so that the teeth were constantly exposed on the side of the repair. Secondary repair of these tight short lips, utilizing the foregoing principles, has produced considerable improvement in the patient's appearance.

Following repair of the lip and palate, the patient may need the assistance of an orthodontist to correct malocclusions or to expand a contracted upper dental arch. Special dental prostheses are often helpful in improving the function and appearance of the teeth or in helping to build out the contour of a dished-in upper lip. Occasionally, a special dental prosthesis with a pharyngeal extension, or speech bulb, is used to partially occlude the area of velopharyngeal insufficiency and minimize the escape of nasal air. This prosthesis often does improve the speech in these patients but it has 2 disadvantages: (1) these special dental appliances must be remodeled as the dental arch changes with growth and (2) these large appliances apply considerable pressure on the anchoring molar teeth. Because a dental prosthesis may play a very important role in the rehabilitation of these patients, who often have poor teeth initially, they should be especially encouraged to try to preserve their teeth by good dental hygiene and periodic dental examinations. The large tonsils and adenoids that are often present in these children help to occlude the velopharyngeal space, and patients often note that more nasal air escapes in their speech following tonsillectomy. Therefore, the tonsils and adenoids should be preserved if to do so is at all compatible with the general health of the patient.

The child with a cleft palate often profits greatly from the help of a speech therapist in the prevention and correction of faulty speech habits. Though the patient may have inadequate velopharyngeal closure from shortening of the palate, part of his poor speech is often related to bad speech habits totally unrelated to the anatomic velopharyngeal insufficiency.

In the past few years, there has been a return to the use of a pharyngeal flap to partially close the insufficient velopharyngeal region in some of these patients with poor speech due to escape of nasal air. This operation involves elevating a flap of tissue from the posterior wall of the pharynx and suturing it to the soft palate. Nasal air then passes lateral to the flap, and the flap decreases the escape of nasal air. This operation often results in considerable improvement in speech defects related to nasal escape of air.

EXTERNAL EAR DEFORMITIES

A common ear deformity that plastic surgeons are asked to correct because of the embarrassment it causes is the protruding ear, which is usually congenital and bilateral but may be unilateral. The deformity is usually due to a poorly developed or absent anthelix fold. In boys, the

deformity is especially conspicuous, and, in girls, although it can be covered by hair styling, the number of such hair styles is limited. The deformity can be corrected by making an incision behind the ear and making incisions through the cartilage, thereby restoring the anthelix fold and suturing the ear framework in this new corrected position. This operation can be done under local anesthesia even in very young children.

A less frequent but more perplexing reconstructive task is the problem of the congenitally absent external ear. This deformity may be unilateral or bilateral. Usually, only a small nubbin of soft tissue is present, representing what should have been the normal ear. This ear remnant is usually considerably lower on the head than normal. Total reconstruction of the congenitally absent external ear has always been a most difficult task, requiring many operations and often yielding only a fair result. Thus, many plastic surgeons were satisfied to have these patients fitted with a prosthetic ear, which was attached daily.

Recently, a different approach to this old problem was introduced.[3] First, the small remnants of the malformed ear are rotated as flaps into the normal position on the side of the head. Later, the cartilaginous framework of the ear is fabricated from the patient's own costal cartilage, and the framework is inserted under the aural skin through an incision in the tragus region. Autogenous cartilage is preferred, as gradual resorption of homologous cartilage often occurs. At later stages, the ear and its cartilaginous framework is elevated from the head, and the raw surface behind the ear is covered with a free skin graft. With this new surgical procedure, an external ear can be constructed with fewer operations and with more chance of being cosmetically acceptable. We feel that this operation should be offered to children with this distressing handicap.

RADIODERMATITIS

Although fortunately of infrequent occurrence, radiodermatitis is a difficult and perplexing problem. In the past, it has been an occupational hazard to those dealing with radiation, such as dermatologists and dentists. The skin may be damaged to such an extent that only very slight trauma produces a sore that will not heal.

Occasionally, some of these chronic ulcerations can be covered successfully with a free skin graft, but, in others, a flap of normal tissue must be used to cover the defect. In cases in which radiodermatitis and ulceration are severe, the local tissues may be so damaged by irradiation that a flap from a more distant part of the body must be utilized to repair the defect.

With less severe radiodermatitis, ulceration may not be present, but the possibility of malignancy forming in the permanently damaged skin is a real danger. The involved skin is also very tight and inelastic. Replacement of this involved skin with an appropriate free skin graft or, if necessary, a skin flap will remove the offending tissue, which is a potential site of malignant degeneration.

RHINOPHYMA

Rhinophyma, the later stage of acne rosacea, may grow to enormous size. With this condition, the nose, particularly the tip and alar regions, becomes markedly enlarged due to benign hypertrophy of the cutaneous sebaceous glands and blood vessels. This produces the characteristic red nodular nose. It is more commonly found in men and is thought to be associated with alcoholism; however, it is seen not infrequently both in women and in men who abstain from alcohol.

Decortication, or shaving down the nose to more normal proportions, is usually satisfactory treatment for this condition. This can be done with an ordinary scalpel, but some physicians prefer to use an electric scalpel. As the nose is sculptured to more normal proportions, care must be taken to retain a sufficient amount of sebaceous gland elements in the wound to allow epithelial regeneration over the surface. The epithelium regenerates and usually provides a satisfactory cutaneous covering for the nose. When considerable scarring is present in the nasal skin and the sebaceous gland elements are insufficient to provide satisfactory epithelial regeneration after the nose is pared, a skin graft to the nasal skin surface may be required.

SUMMARY

In this presentation, we have reviewed some of the more common plastic and reconstructive problems that are encountered by physicians. Discussion on the diagnosis and treatment of some of these conditions is presented as well as some of the more recent views on treatment and rehabilitation of these patients.

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Some Aspects of Allergy

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ALLERGY AND IMMUNITY may be said to be mirror images of one another. Allergy is the sensitivity to an antigen to which other persons are unsusceptible; immunity is the power to resist an antigen to which other persons are susceptible. Both conditions are very specific, and both require previous contact with the substance in question. A person may be allergic to one antigen and immune to another, and a specific antigen may cause an allergic symptom at one time and an immune condition at another time. If a person is allergic to a substance, contact causes distressing, if not dangerous, symptoms, whereas if he is immune to it, contact causes no evident harm.

The widespread incidence of allergy is not generally realized. There are 16,500,000 cases of allergy in the United States today, and from 15 to 24 per cent of these are cases of urticaria; 1 in 20 Americans has hay fever, and, of these, 1 in 3 develop asthma.[1–4]

Virtually everyone gets at least one cold a year.[5] Any cold lasting longer than four days is one with complications[6] and definitely calls for the tools of the allergist.

Anyone claiming to have a cold or sinus trouble should be suspected of having hay fever, with or without the secondary bacterial infection to which the hay fever patient is prone. In either case, allergy treatment is indicated. If sneezing is absent, the patient does not have allergic rhinitis. Other cardinal symptoms or signs of hay fever are found in the nose. Vasodilation, increased capillary permeability, and edema are all manifestations of antigen-antibody reaction.

Obtaining an adequate history is the most important step of the first clinic visit. If the hay fever is seasonal, pollens, mold spores, or both are probably the causes. If the allergic rhinitis is worse in the morning, wind-borne pollinating plants are probably the cause, as they shed their pollen in the morning as soon as the dew dries.[3] If the symptoms are nonseasonal and exaggerated during the night or in the early morning, a feather pillow or a dust-catching mattress is the probable cause. Other common causes of an itchy, runny nose are cooking odors, animal hair, hay, certain foods and medications, articles of clothing, and so on.

Having determined the situations which usually provoke the allergy symptoms, the specific items may be tracked down by skin testing. Scratch tests for foods are less accurate than for inhalants but still are worthwhile for confirming the history.[7] If there is a history of a very definite allergy to a specific food, a marked reaction will result from a test for that aliment.

The patient should not be desensitized against his food sensitivities by a series of shots containing extracts of these nutriments but instead should avoid eating or handling these foods at all times for at least three months. He then has an excellent chance of losing his sensitivity and may tolerate the pabulums in small, occasional amounts. Cooked or boiled foods are much less likely to cause allergic symptoms than are the same foods eaten raw. During hay fever season; during a cold or sinus infection; or while suffering from urticaria, asthma, or allergic dermatitis, certain foods may cause symptoms in a patient which would not bother him at all when he is free from allergic manifestations.

In intradermal testing, a reaction is harder to control than in scratch or patch testing. A tourniquet above the site if on the arm, adrenalin injected locally and centrally, antihistamine injections, or an ice bag to the site may control the reaction.[8] In intracutaneous or scratch testing, if ascending lymphangitis is noted, the drop should be wiped clean.

Tests should be given for all suspicious antigens, including inhalants. Fabrics, such as cotton, wool, rayon, nylon, and silk; household lints, such as house dust, kapok, mohair, goat hair, upholstery dust, grain mill dust, Kleenex, jute, sisal, and chicken, duck, and goose feathers; and epidermals, such as cat, cattle, horse, dog, and human hair and furs, should be routinely scratch-tested. Miscellaneous inhalants, such as animal glue, cottonseed, cascara, karaya gum, soybean, orris root, pyrethrum, and tobacco and its smoke, should also be remembered. No matter how many allergens the patient is warned about and

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avoids, a single overlooked antigen will cause his discomfort to continue, and he will feel that the treatment is faulty.

Several methods may be used for diagnosis and treatment of food allergy. With one method, the patient eats all the foods most likely to cause trouble; if there is no reaction, these foods are assumed to be innocent. Another method is to have the patient avoid all suspected foods until he is symptom-free, then deliberately add the allergenic foods in sequence. The nutriments eaten immediately before symptoms appear are the offenders. One such initial diet of relatively innocent foods includes only cooked fruits, cereal, scrambled eggs, coffee, and evaporated milk for breakfast and lunch. For dinner, broiled meat is added to this menu. Then one new food at a time is added. A third method is to continue the patient's usual menu but to omit 4 suspected foods every two weeks. This time period is used because symptoms may take as long as two weeks to disappear.

Whatever the method employed, the patient must be warned not to eat the particular aliment unwittingly. In these days of packaged foods, food mixtures, blends, flavorings, and additives, he must be very careful to read the labels, for even a trace of the offending food will keep the symptoms from disappearing. Also, in tracing the allergen, the physician must note the patient's preferences and dislikes in foods.

Foods vary greatly in their tendencies to cause allergic manifestations. The most common offenders are wheat, milk, eggs, potatoes, oranges, chocolate, tomatoes, navy beans, string beans, corn, pork, and spinach, and these should be avoided if a remission in symptoms is desired or eaten if an exacerbation is desired.

Some of these foods, such as spinach, are easy to avoid. However, wheat, milk, and eggs are in so many foods, as the main component or as trace ingredients, that complete sustained avoidance is a great challenge. Fortunately, there are diets already available in allergy textbooks and from commercial firms handling foods and catering to the physician which avoid them. A few of these also include an occasional helpful recipe to make the diet more palatable and interesting.[9,10] More such recipes are always welcome, however, for the patient must look long and hard before he can find a recipe not calling for wheat, an egg, or milk. The following recipes are offered so that the physician may make the diet more varied for the allergy patient who is restricted in choice of food.

General hints. In a cake recipe, ¾ rye flour and ¼ rice flour can be substituted for wheat flour. In a gravy recipe, half as much cornstarch as prescribed flour can be used for thickening. The gravy must be thickened over a low flame, as too intense heat will cause it to become lumpy. Meats should be turned in very finely crushed Corn Flakes, Rice Krispies, or Cream of Rice cereal instead of flour. Sliced bananas sprinkled over dry cereals help compensate for the lack of toast at breakfast.

Recipes:

Wheat-free Banana Bread

1 cup white sugar
½ cup melted butter
2 eggs, well beaten
1 cup finely mashed banana (2 large or 3 small)
3 tbsp. milk
1½ tsp. soda, added to milk
½ tsp. salt
1½ cup rye flour
½ cup rice flour

If rice flour is not available, 2 cups of rye flour may be used. However, 2 rounded tablespoons of cornstarch should be substituted for 2 rounded tablespoons of the flour.

Beat the sugar, melted butter, and eggs well. Add fruit. Next, add flour, alternating with the milk-and-soda mixture. Bake in 325° oven for one hour.

This recipe makes 2 small loaves, 3½ by 7½ in. Since rye products do not keep well in hot weather, 1 loaf may be frozen.

One-half cup finely chopped nuts may be added. In place of bananas, any fruit of equal consistency, such as several raw apples, with ½ tsp. cinnamon, or pumpkin, with ¼ tsp. nutmeg, may be used.

Wheat-free Ice Box Cookies

½ cup brown sugar
½ cup white sugar
½ cup melted butter (cooled)
1 unbeaten egg
½ tsp. vanilla
½ tsp. baking powder
½ tsp. salt
1½ cup rye flour
¼ cup rice flour or cornstarch

Mix butter and sugar and add egg. Mix dry ingredients and add to first mixture slowly. Add ½ cup finely ground nuts. Roll and put in refrigerator overnight. Cut in thin slices. Bake in 375° oven seven minutes on a greased cookie sheet.

Wheat-free Ginger Snaps

1 cup sugar
1 cup shortening
1 cup molasses
1 egg, well beaten
1 tsp. soda
1 tsp. ginger
3 cups rye flour
1 cup rice flour

Roll in small balls. Turn in sugar. Press flat and bake on greased cookie sheet. If a half batch is made, use the whole egg. If rice flour is not available, use 3½ cups rye flour and ½ cup cornstarch. This is a crisp cookie, so press thin. Bake for twelve to fifteen minutes in a 400° oven.

The recipes included in this paper are the creations of Mrs. Esther Delzer, R.N.

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Combined use of Dicumarol and quinidine is an effective and safe method of treating chronic atrial fibrillation. Bundle-branch block and cardiomegaly do not affect results.

Patients are hospitalized and treated for cardiac decompensation with salt restriction, digitalis, and diuretics. Dicumarol is administered for two weeks before attempted conversion to normal sinus rhythm. Prolongation of the prothrombin time to twice normal reduces the risk of embolization at the time of conversion by preventing formation of new thrombi and permitting organization of existing thrombi. Conversion is attempted by oral administration of quinidine sulfate in doses of 0.2 gm. every two hours for 6 doses. An electrocardiogram is made after the fourth dose. The drug is discontinued if extreme nausea, diarrhea, tinnitus, or prolongation of the QRS complex beyond 25 per cent of the control occurs. If no untoward effects are noted, the schedule is repeated on the succeeding days with an increment of 0.2 gm. per dose per day until normal rhythm is restored, toxic reactions appear, or a dose of 1 gm. every two hours is reached. After conversion, a maintenance dose of 0.2 to 0.4 gm. of quinidine is given every six hours. Dicumarol is continued for three days after conversion.

Of 100 patients treated for chronic atrial fibrillation with Dicumarol and quinidine, 57 converted to normal sinus rhythm; only 1 patient died, and no thromboembolic complications were noted. In contrast, only 1 of 100 controls converted spontaneously; 18 died, and 4 had nonfatal thromboembolic complications.

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Progressive Intellectual Deterioration

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One of the most common forms of brain involvement is the type that interferes diffusely with its function, resulting in a progressive deterioration of intellectual function with or without associated focal findings. In the absence of definite focal symptomatology, such a gradual diffuse cerebral involvement may be overlooked for long period of time or may be falsely diagnosed as a functional disturbance. Careful attention to the presenting symptoms often will leave no doubt as to the exact nature of the cerebral dysfunction.

The presenting symptoms are often strikingly different in different age groups. In infancy and early childhood, it may be difficult to differentiate a progressive brain damage from congenital mental defects in which a certain level of mental development is reached and beyond which the child does not progress. Generally, in the infant, careful attention must be given to the early stage of development, since changes or regression of behavior must be based on the stage of development already achieved. Hence, a child who has already begun to walk and talk and then slowly loses these functions must be showing evidence of progressive brain damage. In addition, these children often show signs of emotional instability with rapid mood changes to the slightest stimuli and restlessness, temper tantrums, and marked overactivity. Some infants, by contrast, become apathetic, unresponsive, and completely disinterested and unreactive to environmental stimuli.

In older children, intellectual impairment is manifested primarily by mental deterioration, changes in personality, and emotional instability. The mental changes are noted in the inability to handle school work, impaired memory, preoccupation, inattentiveness, and failure to retain and to learn the necessary social habits. Reaction time is slow and thinking is dulled. Often, the intellectual impairment is covered by the marked changes in personality. The child may become irritable, restless, and overactive. He misbehaves and cannot be disciplined by an available means. He often lies, steals, and fails to observe social regulations. Emotional liability and changes in response to the slightest stimulus are common. There are often outbursts of unmotivated anger and periods of depression. Throughout the behavior pattern, one can detect the impaired intellect by the unusual and bizarre pattern of the disturbances.

In the adult, slowly progressive diffuse brain damage can also be detected by intellectual impairment, changes in personality, and alterations in mood and behavior. These changes may occur with or without evidence of focal brain damage and are apt to develop slowly and insidiously over a period of months or years. The dementia may be manifested at the onset by poor judgment; impaired memory, particularly for recent events; slowness of reaction time; dullness in thinking; and inability to follow abstract logic. When mild, these changes may merely interfere with the efficiency of activity, while, later, routine functions may be impossible. These patients may manifest inappropriate playfulness, petulance, irritability, coquettishness, erotcism of either normal or perverted sex behavior, and neurotic trends. The combination of intellectual loss and defective self-control may lead to disorders of conduct, such as carelessness of dress, uncleanliness, neglect of duty, violence, or indecent behavior. Emotional disorders may be common, with disturbances of mood in the form of elation, depression, apathy, or excitement. With severe involvement, the patient usually becomes more apathetic with gross disturbance of memory, insight, and orientation and ultimately may terminate as a totally unresponsive, helpless individual.

The cause of such diffuse brain damage with

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this type of organic picture is dependent chiefly upon the age of the patient (Table 1). There are many unusual causes of such brain damage. However, at this time, only the more common causes encountered by the physician will be discussed.

INFANCY, 5 YEARS AND UNDER

Subdural hematoma. This is one of the more common causes of brain damage in infants under 1 year of age and usually follows a head injury. Often, however, the history of injury may be absent. This diagnosis must always be considered in any healthy infant in whom evidence of restlessness, somnolence, or convulsions, develop or who loses functions which have already developed. The diagnosis is strengthened by the appearance of a gradual enlargement of the head or tense fontanels.

TABLE 1

CAUSES OF PROGRESSIVE INTELLECTUAL DETERIORATION

I. Infancy—5 years and under
   1. Subdural hematoma
   2. Craniostenosis
   3. Metabolic disturbances (cretinism, phenylpyruvic oligophrenia, hypoglycemia)
   4. Anomalies (hydrocephalus, aqueduct stenosis, porencephalia)
   5. Chronic infections (meningitis, encephalitis)
   6. Degenerative diseases (Tay-Sachs disease, tuberous sclerosis)
   7. Intoxications (lead, arsenic, aspirin)

II. Childhood—6 through 16 years
   1. Chronic infections (viral)
   2. Diffuse sclerosis (Schilder's disease)
   3. Juvenile diabetes

III. Adulthood—17 through 40 years
   1. Head injury
   2. Chronic intoxication (industrial poisons, drugs)
   3. Brain tumor

IV. Middle age—41 through 65 years
   1. Head injury
   2. Brain tumor (frontal lobe, temporal lobe)
   3. Toxins (alcohol, industrial poisons, drugs)
   4. Subdural hematoma (trauma, alcohol)
   5. Cerebrovascular disease (hypertension, diabetes)
   6. Syphilis (paresis, meningovascular)
   7. Presenile deterioration (Alzheimer's disease, Pick's disease)
   8. Thrombosis internal carotid artery

V. Senescence—over 66 years
   1. Cerebral arteriosclerosis (diffuse)
   2. Senile degeneration of brain
   3. Subdural hematoma
   4. Syphilis
   5. Tumor

Treatment consists of evacuating the blood and removing the hematoma surgically.

Craniostenosis. This is a relatively uncommon condition which results from a premature closure of the cranial sutures. If all the sutures close early, the skull remains small and the fontanels cannot be felt. If there is a premature closure of only the lambdoid and coronal sutures, the skull expands in a vertical direction (turricephaly), while closure of the sagittal suture results in expansion of the skull in an anteroposterior direction (scaphocephaly).

Evidence of increased intracranial pressure (headache and papilledema), exophthalmos, optic atrophy, and progressive loss or impairment of cerebral development is often associated with the skull changes. The diagnosis is readily verified by a roentgenogram of the skull.

Treatment is surgical and consists of cutting channels through the cranial bones to allow for proper brain development.

Metabolic disturbances. *Cretinism.* This condition generally appears during the sixth month of life with evidence of retarded physical and mental development. The diagnosis is made by the physical appearance. The lips are thick, the eyelids thickened, the cheeks baggy, and the tongue thickened. The forehead is low, and the base of the nose is broadened. The body remains small with a protruding abdomen. The skin is thick, dry, and scaly; the extremities are cold and cyanotic. Roentgenograms of the bones reveal delayed development of the centers of ossification, and the carpal and tarsal bones may not appear until late. These children are always intellectually retarded. Their behavior is sluggish and they appear quiet, contented, and good natured, often never learning to walk or talk.

These children are very sensitive to thyroid. The administration of small doses of oral thyroid produces prompt improvement in symptoms but does not cure the disease.

Phenylpyruvic oligophrenia. This is a form of mental deterioration in which phenylpyruvic acid is found in the urine. This substance is a product of incomplete oxidation of phenylalanine, one of the amino acids of which proteins are composed. There is nothing distinctive about the nature of the mental deficiency. However, the diagnosis can readily be made by adding a few drops of 5 per cent solution of ferric chloride to acid urine. If phenylpyruvic acid is present, a dark green color appears and fades away in a few minutes.

Treatment consists of a phenylalanine free diet. Under such a regime, improvement may result.

Hypoglycemia. Severe hypoglycemia almost invariably produces extensive brain damage. Hypoglycemia may be due to dietary causes, such as inadequate carbohydrates due to vomiting, diarrhea, and so forth; hyperplasia of the islands of Langerhans; or to functional causes without specific etiology. Recurrent paroxysms occur during the course of the illness from which the patient recovers. These paroxysms are preceded by pallor, weakness, restlessness, irritability, and marked sweating. They terminate in convulsions, confusion, or coma. During these episodes, the blood sugar is low. These attacks can be relieved by the administration of glucose. As a result of these episodes, progressive mental deterioration occurs and is often associated with focal findings.

Treatment consists of proper diet and the prevention of the paroxysms by the use of glucose. Regulation of the metabolic defect should be considered in idiopathic hypoglycemia of infants. Corticotropin may be effective in such cases.

Congenital anomalies. *Hydrocephalus.* In infancy, this condition is due to obstruction of the circulation of the cerebrospinal fluid at any part of its course as a result of gliosis of the aqueduct or occlusion of the foramen at the base of the fourth ventricle.

In most cases, the head is normal size at birth but begins to enlarge after a number of months. The fontanels become tense and fail to close, and the cranial sutures become widened. The scalp veins are distended. The child often becomes lethargic and fails to develop properly. In many cases, optic atrophy and spasticity of the limbs are present. The diagnosis is usually readily established by a skull roentgenogram, often supplemented by an air encephalogram.

The treatment consists of surgically relieving the increased pressure by placing a polyethylene catheter between the lateral ventricle and the cisterna magna, thus bypassing the area of spinal fluid block.

Porencephaly. True porencephaly is a funnel-shaped cavity in the cerebral hemisphere which communicates either with the ventricle or the subarachnoid space. It is attributed to some developmental defect. Often, the lesion may be asymptomatic for many years and then begin to be manifested by the development of focal symptoms, seizures, or retarded mental development. The diagnosis can often be suspected by the thinning of the overlying skull on roentgenograms. Air studies will fill the cavity and reveal the nature of the process.

Chronic infections. *Purulent meningitis.* Purulent meningitis is not an uncommon cause of progressive mental deterioration. With the advent of antibiotic therapy, many infants are surviving the acute illness only to manifest, at a later date, evidence of brain damage. In most cases of purulent meningitis, the inflammatory process penetrates the superficial layers of the cortex, resulting in small cortical abscesses. If the infectious process persists for any period of time, meningeal thickening and meningeal cerebral adhesions will result. These associated pathologic processes result in the chronic mental changes which often occur years after apparent recovery from the acute illness.

The diagnosis in these cases is made from the clinical history. Cerebral complications may be expected (1) if the illness is severe, (2) when the illness occurs in infants under 1 year of age, and (3) in cases in which the responses to treatment are delayed or incomplete.

Once cerebral complications have developed, treatment procedures are of little value. To avoid such complications, the treatment of meningitis in children should be instituted promptly and vigorously.

Encephalitis. In this age group, this condition generally follows the infectious diseases of childhood; namely, whooping cough, measles, chicken pox, mumps, scarlet fever. It has been estimated that less than 0.5 per cent of infectious diseases are accompanied by a recognizable cerebral complication. However, when one considers the tremendous number of children who have these diseases, then even 0.5 per cent becomes a large number. In children under 2 years of age whooping cough produces the greatest number of cerebral complications, while measles is the greatest offender in children in the older age group. Actually, there is no correlation between the severity of the infectious disease and the cerebral involvement.

The diagnosis is made by means of a good history of the existing or preceding illness. In all such cases, the prognosis must be guarded. Treatment during the acute illness consists of corticoids.

Degenerative diseases. *Tay-Sach's disease.* This is a progressive fatal degenerative disease of the nervous system appearing about the fifth to the eighth month of life. The child ceases to fix objects with the eyes and shows evidence of regression. Functions once acquired are lost. The child becomes unable to hold up his head, his

muscles become flabby, and he becomes demented and helpless. Terminally, the muscles become spastic. The diagnosis is readily verified by ophthalmoscopic examination. The region of the fovea contains a bright red area called a "cherry red spot." Death invariably occurs at the end of the second to the fourth year.

Tuberous sclerosis. This disease manifests itself by multiple tumors and malformations of the brain, skin, and viscera. It is a hereditary-familial disease affecting children up to the age of about 8 years. The disease frequently begins with seizures followed by evidences of mental deterioration. Cutaneous lesions are fairly characteristic of this disease, the most common of which is adenoma sebaceum, a red papular rash that involves the cheeks and nose. Other skin lesions consist of areas of thickening, particularly in the lumbosacral region.

The diagnosis is readily made by the clinical picture. It can be verified by an air encephalogram which will permit visualization of the intracerebral tumor nodules. Treatment is symptomatic.

Intoxications. *Lead poisoning.* Chronic lead poisoning in children is still fairly common in certain areas in the country. The ingestion of small amounts of lead over a long period of time produces no acute symptoms, but there is evidence of progressive intellectual retardation. The diagnosis is based on the history of lead infection and can be verified by the presence of anemia, basophilic stippling of the red cells, lead line of the gums, the dense zone shown in the roentgenograms of the bones, and the demonstration of lead in the blood by spectroscope.

Treatment in chronic lead poisoning consists of deleading the patient by means of a low calcium diet deficient in vitamin D and administration of potassium iodide and intramuscular or oral Calcium Disodium Versenate.

Arsenic poisoning. When arsenic is ingested in small amounts over a long period of time, signs of chronic intoxication may result. The arsenic may be obtained by accidental ingestion from sprays or insecticides or in the form of medication. In chronic poisoning, gastrointestinal symptoms are infrequent and mild. However, pain, numbness, weakness, and wasting of the limbs often occur, which are indicative of a peripheral neuropathy. The skin of the palms and soles becomes thickened and scaly and a brown pigmentation may develop over the trunk. If the diagnosis is in doubt, it can be verified by chemical testing of the hair, nails, and urine for arsenic.

Treatment consists of removal of the source of intoxication and the use of BAL to remove the arsenic from the body.

Drug poisoning. A number of drugs accidentally ingested produce intoxication in children. The clinical picture, however, is acute and rarely produces the picture of chronic mental deterioration. There is usually no characteristic clinical finding; the diagnosis is made from the history.

CHILDHOOD, 6 THROUGH 16 YEARS

Chronic infections. In this age group, the most common source of infection is the virus—namely, equine, the St. Louis and the Japanese forms. These infections occur in sporadic or epidemic forms and often have a seasonal incidence. The acute infection varies in severity and does not present any characteristic clinical features. The acute illness may be severe and associated with coma, convulsions, or focal symptoms or may be so mild as to escape attention. In either case, permanent and often progressive brain damage may occur, so that, at varying times after recovery from the acute illness, the child develops evidence of mental retardation, personality alterations, or even convulsions. A youngster who has been well behaved and getting along well in school begins to show scholastic difficulty and may become a definite personality problem.

The diagnosis often can be suspected by the presence of a high antibody titer against one of the specific viruses. However, unless the antibody level was available at the onset of the acute illness, an absolute diagnosis cannot be made.

Treatment is symptomatic. There are no means of halting or treating the damage already present within the brain.

Diffuse sclerosis (Schilder's disease). This is a degenerative disease involving the myelin sheaths throught the cerebral hemispheres. It develops usually late in childhood and shows a progressive course, resulting after a few years in bilateral spastic weakness of all limbs, cortical blindness, central deafness, and mental deterioration. The diagnosis is determined by the presence of progressive bilateral diffuse cerebral damage in the absence of any evidence of increased pressure or a cerebral mass. The prognosis is poor. No known treatment is available.

Occasionally, in this same age group, a strongly familial degenerative disease is encountered, which invariably implicates many members of a family and is known as Merzbacher-Pelizaeus disease. Symptoms begin early in life at about 6 months of age with rotary movements of head and nystagmus. These are followed later by

spasticity of the limbs, cerebellar ataxia, intention tremor, and scanning speech. After several years, mental deterioration appears. This condition is progressive, but life often is not shortened. No treatment is available.

Juvenile diabetes. When severe, this condition is usually difficult to control. Even with the best supervision, these patients show a rapidly fluctuating blood sugar and suffer repeated episodes of hypoglycemia. The latter results in diffuse brain damage, which, in turn, makes the diabetes even more difficult to control. These repeated episodes of hypoglycemia ultimately result in progressive mental involvement or personality changes. The diagnosis is usually not difficult. In most cases, the history of diabetes and the fact that the patient requires insulin is known. The real problem is to maintain a carefully regulated diet and an insulin intake sufficiently adequate to control the diabetes and prevent further hypoglycemic episodes. This may be difficult in a young patient who may have already suffered considerable brain damage from previous episodes.

ADULTHOOD, 17 THROUGH 40 YEARS

Head injury. Following a head injury, many patients complain of headaches, postural vertigo, insomnia, progressive failure of memory, depression, and personality changes. These complaints are not closely correlated with the severity of the injury although it appears that the more severe the injury and the more prolonged the unconsciousness, the more frequent and progressive the posttraumatic complaints. In many of these patients, the involvement persists and appears to be progressive. Memory becomes more impaired, efficiency decreases, and the patient shows marked personality changes with restlessness, irritability, temper outbursts, and poor social adjustment. He is unable to work or to adjust in the home. In some of these patients, the electroencephalogram shows diffuse abnormalities, and an air encephalogram may reveal dilated ventricles.

The prognosis in cases that show progression of symptoms is poor. Papaverine hydrochloride may improve the headaches and vertigo. However, all treatment remains symptomatic, and some of these patients may ultimately have to be institutionalized.

Chronic intoxication. The three groups of toxins encountered in this age group are medicinal drugs, industrial poisons, and alcohol. The latter will be discussed under middle age.

Drugs. Most drugs produce relatively acute symptoms of delirium and confusion, which subside when the drugs are discontinued. Chronic mental deterioration rarely occurs and only after prolonged dosage over a period of many years. Even then, permanent and progressive involvement is uncommon. Such chronic disturbances have been reported after chronic barbiturate intoxication and, a few cases, with overdosage of some of the anticonvulstant and sedative drugs, such as bromides and Mesantoin.

Industrial poison. In many cases, these substances result in chronic brain damage. Such involvement has been reported from lead, mercury, carbon monoxide, carbon disulfide, carbon tetrachloride, trichloroethylene, and many of the other industrial solvents. As a rule, the clinical picture produced by these toxins has no special diagnostic features. In all cases, the patients may show only a slowly progressive intellectual deterioration. The diagnosis can only be suspected by obtaining a careful occupational history which may suggest exposure. Hence, in discussing these toxic processes, the nature of exposure will be listed in order to aid in the proper diagnostic evaluation of the process.

1. Lead. The diagnosis of lead poisoning can be suspected when the following findings are present: (a) lead lines in the gingiva near the border of the teeth; (b) lead colic; (c) secondary anemia, with the red cell characteristically showing basophilic stippling; (d) lead in the urine, stools, and cerebrospinal fluid; (e) roentgenograms of long bones showing dense bands at the growing margins; (f) black discoloration of the skin after scarification with 25 per cent sodium sulfite sol; and (g) increased urinary porphyrins.

2. Mercury. Metallic mercury is used in making thermometers, barometers, vacuum pumps, incandescent lights, x-ray lights, and mirrors. It volatalizes at room temperature and condenses on exposed surfaces, such as skin and respiratory mucous membranes. Mercury in the form of Scrisan is used by farmers to sterilize seed before planting and frequently results in chronic intoxication. Chronic intoxication is characterized by tremor, dyskinetic movements, insomnia, and lethargy. The diagnosis can often be verified by the isolation of mercury in the urine.

3. Carbon monoxide. This is a treacherous gas because it is nonirritating and has no characteristic odor. The clinical course depends upon the length and degree of exposure. Chronic exposure occurs in traffic policemen, garage workers, welders, or individuals living in old gas or coal heated homes. The presence of polycythemia or

the detection of carboxyhemoglobin in the blood assists in making the diagnosis.

4. Carbon disulfide. This product is used as an insecticide, as a fat solvent, and as a constituent of varnishes and enamels. It is used in the manufacture of rubber, rayon, and certain chemicals. It is frequently used in vulcanizing plants. In addition to the cerebral damage, chronic exposure to carbon disulfide frequently results in a peripheral neuritis.

5. Carbon tetrachloride. This substance is widely used in industry as a dry cleaning fluid, as a fat solvent, as a "dry" shampoo for hair and in fire extinguishers, insecticides, and sprays. It has been employed as an anthelminthic against Ascaris and tapeworm.

6. Trichloroethylene. This product is used in industry as a solvent for fats and gums, as a dry cleaning agent, as a rubber solvent, and, more recently, as a degreaser for mechanical parts in industry. Its analgesic and anesthetic effects have led to its being used in medicine for trigeminal neuralgia, anginal pain, and migraine.

Brain tumors. In this age group, some of the more benign brain tumors are frequently encountered; namely, meningioma and astrocytoma. Because of their relatively slow growth, these tumors may not produce focal symptoms. If they occur in the frontal or temporal region, they may manifest themselves by the development of progressive mental changes, such as personality alterations and mental deterioration. The diagnosis should be suspected if the foregoing intellectual involvement is associated with seizures, focal findings on neurologic examination, evidence of increased intracranial pressure, or focal abnormalities on the electroencephalogram. When such a diagnosis is entertained, further diagnostic procedures are indicated, such as an air encephalogram, an angiogram, or even a ventriculogram. It is important to make a correct diagnosis, since these lesions can be helped by surgical removal.

MIDDLE AGE, 41 THROUGH 65 YEARS

Head injury. With the increasing mechanization of this country, head injuries secondary to automobile accidents have greatly increased in frequency. Chronic residual symptomatology in the form of progressive memory impairment, lack of drive, and progressive intellectual impairment occurs fairly frequently in this age group even after relatively minor injuries. The longer the period of unconsciousness or the more extensive the retrograde amnesia, the greater the possibility that mental deterioration will occur. Often months after the injury, the ventricles will be dilated if studied by air encephalogram, indicating the presence of some diffuse progressive process.

There is no specific treatment for such cases and no method of arresting the process.

Brain tumors. The most common tumors occuring in this age group are the glioblastoma multiforme and the metastatic brain tumors. Both types are rapidly progressive and generally produce focal symptoms and a short clinical course. However, the more slowly growing gliomas as well as the more benign tumors, such as meningiomas and angiomas, may also occur in this age group. If they implicate the frontal and temporal lobes, they may be relatively silent and result in progressive intellectual deterioration. The occurrence of seizures or of progressive focal findings associated with the mental involvement should make one suspect the possibility of a neoplastic process.

Toxins. Most toxins producing progressive mental deterioration have already been discussed under adulthood. These same toxins implicate middle age. In addition, alcohol poisoning must be seriously considered.

Alcohol is one of the most widely ingested of the organic solvents and, as such, has the potential of producing brain damage. The precise mechanism of its toxic action on the nervous system is not fully known. Aside from any direct action upon the brain tissue, there is the additional possibility of an associated vitamin deprivation due to poor diet and incomplete absorption because of gastritis and intestinal changes caused by the alcohol.

The most common and best known effects of alcohol on the nervous system consist of the psychotic manifestations resulting in Korsakoff's psychosis, alcoholic hallucinosis, and delirium tremens. However, chronic alcoholic intake can also result in diffuse and permanent brain damage which manifests itself in a progressive intellectual deterioration. Because of the slowly progressive manifestations, this type of involvement is often overlooked and the diagnosis delayed. The diagnosis can only be established by the history of chronic alcoholic intake with frequent bouts of intoxication. This often must be obtained from the relatives, as the patient tends to minimize the actual alcoholic intake. Head trauma associated with chronic alcoholism tends to accentuate the intellectual deterioration.

Subdural hematoma. In many cases of subdural hematoma, particularly in adults, the mental picture predominates. The patient shows

progressive intellectual impairment and becomes forgetful, clouded, morose, and even severely retarded. A history of trauma may not be obtained until after removal of the hematoma. The diagnosis should be considered in any patient in whom the foregoing symptoms develop in the presence of a history of trauma or alcoholism. Confirmation of the diagnosis can be established by the appearance of a pineal shift on skull films, air studies, angiography, or trephine exploration.

Treatment is specific and consists of surgical evacuation of the hematoma.

Cerebrovascular disease. The cerebral vessels are generally well preserved in middle age except in the presence of severe hypertension or diabetes. In such cases, a diffuse narrowing of the cerebral blood vessels may occur with a decreased cerebral circulation, which is expressed clinically as a slowly progressive dementia. Other signs and symptoms of vascular disturbances in the nervous system usually precede the personality and mental changes by years. These consist of headaches, postural vertigo, faintness, weakness, tinnitis, and, occasionally, transient focal neurologic symptoms. The mental and personality changes appear insidiously over a period of months or years. The earliest changes consist of restlessness, loss of efficiency, narrowing of interests, and impaired memory for recent events. Sleep disorders may also be present. Irritability may become marked and be accompanied by emotional instability and unpredictable behavior. Delusions of a persecutory nature are common. The mental decline slowly continues with loss of inhibitions that lead to irregularities in behavior. Ultimately, the patient may deteriorate to a state of vegetation with loss of bowel and bladder control.

The course of the illness may be punctuated by focal neurologic findings, such as paresis; sensory disturbances; vertigo; cranial nerve palsies; speech disturbances; and, rarely, seizures.

Syphilis. Within recent years, the frequency of severe central nervous system syphilis has definitely decreased. However, neurosyphilis is still regularly seen in the practice of medicine and characteristically may manifest itself by mental symptoms often many years after a primary infection or after apparent adequate therapy for such an infection. For this reason, in every case of intellectual deterioration in this age group, a careful history should be obtained covering (1) possible history of luetic infection, (2) treatment for syphilis or "bad blood," and (3) history of positive blood studies. Progressive mental alterations are caused primarily by general paresis but may occur also in meningovascular syphilis.

General paresis. The beginning of this mental disorder is often difficult to ascertain. In cultured individuals the esthetic sense may disintegrate first, accompanied by discourteous and rude behavior. Memory soon becomes affected, particularly for recent events, with fleeting disorientation as to time, place, or person. A disturbance of affect occurs early, with the patient becoming apathetic and dull or extremely euphoric. As the illness progresses, gross impairment of memory and judgement develops. Disorientation is present in all spheres, and gross mental abnormalities may appear. Some patients continue to show an intellectual regression with no hallucinations or delusions; the patient is content to vegetate and finally becomes bedfast. Frank psychoses with grandiose bizarre delusions or persecutory nihilistic ideas with definite paranoid reactions may develop in other patients.

The diagnosis can be suspected by the presence of certain physical findings often characteristic of paresis, which consist of hyperactive reflexes with positive toe signs; pupillary abnormalities, often with Argyll Robertson pupils; optic atrophy; slurred, careless speech; and circumoral tremor. The diagnosis can be further substantiated by blood and spinal fluid serology and spinal fluid changes. The spinal fluid serology is positive in 98 per cent of untreated cases and shows an increased cell count and a first zone colloidal gold curve.

Meningovascular neurosyphilis. The mental symptoms in this disease are usually not prominent, but personality alterations, intellectual dullness, or confusional states may occur. Generally, this type of neurosyphilis is associated with transient focal neurologic findings suggestive of a vascular component, such as motor weakness, cranial nerve palsy, speech disturbances, hemianopsia, and extrapyramidal involvement.

The diagnosis is suspected by the history and the possible presence of pupillary abnormalities. Serologic studies may be helpful in about 75 per cent of the cases.

Penicillin therapy in a dosage of 15,000,000 units is specifically indicated in both forms of neurosyphilis. In cases of paresis that fail to respond, a combination of penicillin and fever therapy should be considered.

Presenile deterioration. Clinically, this condition is diagnosed by exclusion. It refers to a group of conditions probably degenerative in nature, in which the brain tissues undergo senescent changes relatively early in life, resulting

in a clinical picture of dementia in individuals of middle age. This term then implies intellectual deterioration occurring in the presenium *in which all other causes for such a clinical picture have been ruled out.* If the cerebral changes are diffuse, the condition is labeled Alzheimer's disease; if limited to the frontal regions, it is called Pick's disease.

There are no clinical features that identify these conditions. The patients manifest slowly progressive mental changes that result in a state of profound dementia. The course and nature of the symptoms do not differ from the other causes of dementia in this age group.

The diagnosis can be established only after eliminating all other causes for the mental picture. An air encephalogram may help verify the diagnosis by revealing no focal lesions and by showing extensive diffuse cerebral atrophy.

Treatment consists of simplifying the environment so that the patient may make a suitable social adjustment. Milder cases may be cared for in the home, while more advanced cases require institutional care.

Thrombosis of internal carotid artery. This condition usually produces acute focal symptoms. Occasionally, however, because of poor collateral circulation, progressive intellectual changes may occur with impaired memory, poor judgment, reduced efficiency, and a general decrease of activity on a productive level.

Mild, one-sided hyperreflexia may be present and, in some cases, even mild hemiparesis may be found. The diagnosis is very difficult because of the atypical clinical picture. Palpitation of the internal carotids in the neck may be helpful by demonstrating reduced pulsations on the involved side. The diagnosis can be established by angiography.

In such cases, Dicumerol therapy is indicated to prevent further thrombosis. Such therapy may be continued for an indefinite period of time.

SENESCENCE

In this age group, conditions producing progressive mental deterioration are similar to those already discussed under middle age. The relative order of frequency, however, is somewhat different, although the clinical characteristics are similar. In the older age groups, cerebral arteriosclerosis and senile deterioration of the brain most commonly result in progressive mental changes. Such a diagnosis offers a very poor prognosis, since no treatment procedures are available, and these individuals ultimately must be institutionalized. Therefore, before one accepts such a diagnosis, extreme care must be exerted to be sure that the patient's symptoms are not the result of some other pathologic process which is more amenable to therapy. The three conditions which must be eliminated in every case are subdural hematoma, neurosyphilis, and brain tumor. Careful history supplemented by laboratory and special x-ray studies should enable the physician to definitely establish the proper diagnosis.

DESPITE PREVIOUS IMMUNIZATION with Salk polio vaccine, children can be infected readily with Sabin's L Se live attenuated-type 1 poliovirus, either by oral administration or by exposure to infected individuals. Children with comparable antibody levels acquired by previous natural infection are somewhat more resistant. Circulating antibodies protect the central nervous system against invasion, but some form of local immunity, acquired only by previous topical experience with poliovirus, is necessary to prevent intestinal infection.

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Isosorbide Dinitrate in Treatment of Angina Pectoris

Preliminary Clinical Impression

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THE CLINICAL PHYSICIAN has a responsibility to evaluate any marketed new drug which, on the basis of data presented, appears to possess desirable pharmacologic actions. In other words, he must learn how to use the drug properly and then confirm or reject for himself the claims made for it. Only a few clinicians have the time or facilities to carry out intricately designed studies. They must rely on past clinical experience and careful observation. In almost every instance, these accumulated clinical data are responsible for the final assessment of the efficacy of a drug.

Isosorbide dinitrate (Isordil) is one of many available drugs for which therapeutic potential has not yet been established. The drug is a potent coronary vasodilator and requires some effort on the part of the physician before it can be used successfully. Although it is a member of the homologous series of nitrated sugars, its action is different from that of other existing derivatives. As with most drugs with new modalities of action, the significance of this mode of therapy of coronary vascular disease probably will not be assessed for several years.

Isosorbide dinitrate was selected from a series of nitrates for clinical investigation in patients with angina pectoris because of high aqueous solubility and a low rate of metabolism.[1] In the laboratory, small concentrations of the drug increased coronary blood flow in the dog heart from 40 to 100 per cent. Isosorbide dinitrate compared favorably with nitroglycerin in this respect and was more potent than any of the other nitrates tested.[2]

This clinical investigation is presented mainly to stimulate interest in and additional study of the drug rather than to attest to efficacy. The data represent initial investigations by the author. The results have been confirmed by other investigators.[3,4,5]

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MATERIALS AND METHODS

Early evaluation of isosorbide dinitrate was carried out in 29 patients who had coronary insufficiency with associated angina pectoris. The average observation period was three months. The usual dose of the nitrate was 10 mg. four times a day.

All 29 patients, 17 men and 12 women, had arteriosclerotic heart disease. Chest roentgenograms generally showed a widened or calcified aortic knob. Evidence of coronary insufficiency could be detected by examination of the electrocardiograms of the patients. Most of the group had associated organic disease of vascular or degenerative origin. The age range was from 46 to 83 years, with an average age of 66 years.

Previous medication included nitroglycerin in 27 of the 29 patients, as well as other long-acting vasodilators. The other 2 patients were new to the clinic and had not received coronary vasodilators previously. All patients were requested to keep a careful record of the frequency and extremity of anginal attacks and the number of nitroglycerin tablets consumed.

RESULTS

The results obtained in this study may be noted in figure 1. Of the 29 patients, response was graded as good in 24; fair in 1, a patient with acute rheumatoid arthritis in whom coronary symptoms may well have been aggravated by concomitant corticoid therapy; and poor in 1, an uncontrolled and unreliable diabetic. The diabetic patient died from a coronary occlusion during the first week of the investigation, and he may not have taken the medication. Extreme vascular headaches caused 3 patients to discontinue the medication. Patients are now forewarned about the possibility of headaches, and

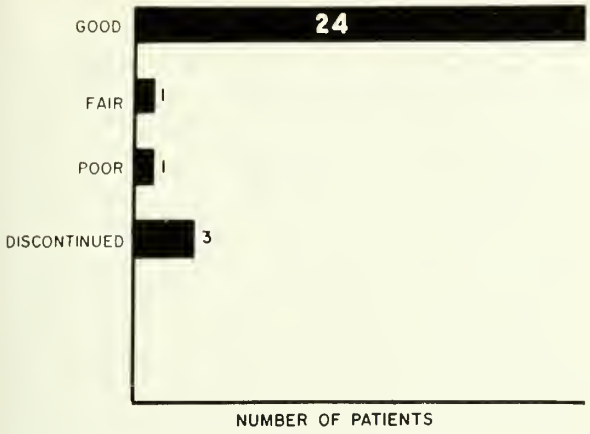

Fig. 1. Response of 29 patients to isosorbide dinitrate therapy.

the relationship between the headaehe and the aetivity of the drug is explained. Vaseular headaehes are definitely not psychosomatic, and it is ineoneeivable that suggestion could play any role in their origin.

All patients responding favorably to isosorbide dinitrate had a dramatic decrease—over 50 per eent in all cases—in the incidence and extremity of angina pectoris and reported an inereased sense of well-being and a notable increase in aetivity toleranee. These results refleeted improvement over and above that obtained with previous combined therapy.

The total number of attaeks of 23 of the 24 patients averaged 123 before administration of the nitrate and 28 at the end of the study period—a decrease of 77.2 per cent. One patient,

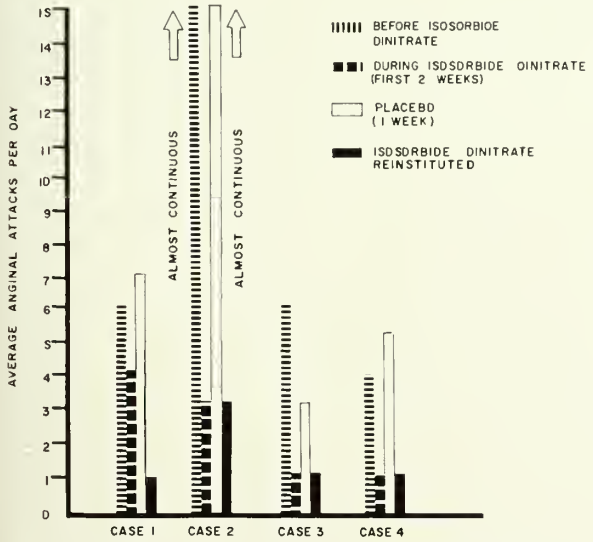

Fig. 2. Response of 4 patients to isosorbide dinitrate and placebo therapies.

a 71-year-old woman, was in status anginosus before institution of isosorbide dinitrate therapy and had extreme bronchial asthma. After institution of therapy, frequency of attacks averaged 3 per day. When a placebo was substituted during the fourth week of the investigation, the original symptoms returned during the first day. In 3 other patients who had reported remarkable relief with isosorbide dinitrate, substitution of the placebo caused a rapid reversion of the original symptoms (figure 2), which again disappeared when isosorbide dinitrate therapy was reinstituted.

Although only 4 patients of this series experieneed eomplete relief from anginal symptoms during the study, the accumulated data in fig-

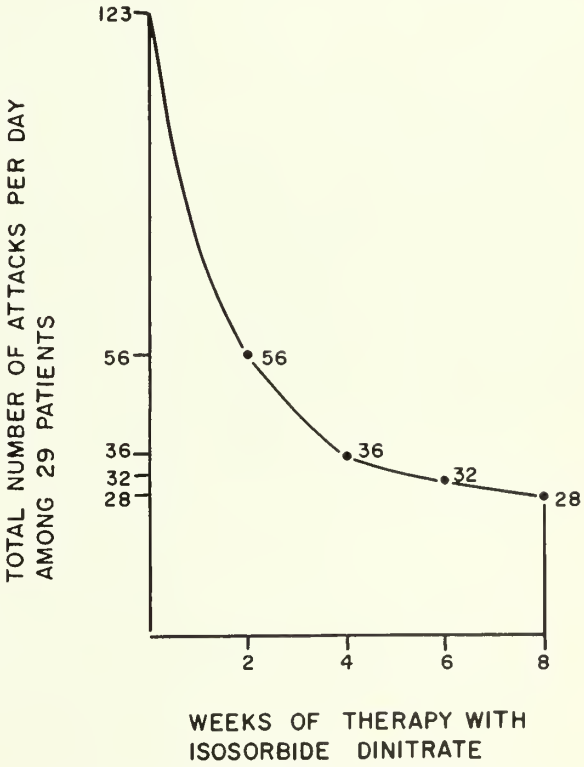

Fig. 3. Total number of attacks of angina pectoris per day in 29 patients (showing increasing response to isosorbide dinitrate with continued use).

ure 3 would indieate that improvement was progressive over the first eight weeks of therapy. This may be related to gradual disruption of the psyehie elements and eonditioned reflexes, whieh are known to be important faetors in the genesis of angina pectoris.[6,7]

Headaehes oeeurred in 5 of the study group. As indieated earlier, 3 diseontinued therapy because of this distressing side effeet. One of the

patients was able to tolerate a dose of 5 mg. four times a day with good response. Subsequent experience has indicated that headaches subside with continued therapy. The annoyance of the headache almost always is made bearable by proper education, and, at this date, this side effect is not regarded as a significant drawback to the drug.

Since the initial evaluation, an additional number of patients have been treated with isosorbide dinitrate in this clinic, and the results have continued excellent. The drug appears to exert a more consistent and profound effect than any drug previously employed for the prophylaxis of angina pectoris.

DISCUSSION AND SUMMARY

Anginal attacks usually are precipitated by effort or some form of emotional excitement which causes an increase in the work load of the heart. If the oxygen supply to the myocardium does not meet the accelerated demands, metabolites accumulate and trigger the pain mechanism. The acute attack is relieved by complete rest and administration of nitroglycerin or amyl nitrite. The prevention of angina pectoris depends upon restriction of activity within limits imposed by inadequate circulation, reduction of emotional factors, rational diet, and prophylactic use of long-acting coronary vasodilators.

Isosorbide dinitrate, a newly developed member of the homologous series of nitrated sugars, appears to exert a more consistent and more profound vasodilation of coronary vessels than do other coronary vasodilators, with the exception of nitroglycerin. Rapid onset of action and prolonged effect are additional clinical advantages.

In this clinical evaluation of isosorbide dinitrate in patients with arteriosclerosis of the coronary arteries, good response was obtained in 24 of 29 patients. Of the remaining 5 patients, extreme vascular headache necessitated interruption of therapy in 3, improvement was fair in 1, and response was poor in 1. Benefits from therapy with isosorbide dinitrate seemed to be more marked with continued use.

Isosorbide dinitrate (Isordil) used in this study was supplied by Ives-Cameron Co., New York 16.

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The average life span of patients with primary hypertension is not lengthened by antihypertensive drugs.

For seven years, 29 patients with primary hypertension of at least five years' duration received antihypertensive drugs. Standing blood pressure was kept at or below 160 104 mm. Hg. The same number of matched controls were treated symptomatically. Both groups were given sedatives, analgesics, digitalis, and diuretics. During the observation period, 16 patients in each group died. Average survival time was forty-two months for the test group and forty-five months for the control group. Most deaths resulted from atherosclerotic complications.

Limitations on the findings of the study were (1) blood pressure probably was not held at 160 104 mm. Hg or less around the clock; (2) the series was small and the index cases were selected; and (3) only patients with longstanding hypertension and signs of myocardial damage were studied.

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The Platform Bipolar Myocardial Electrode for Prolonged Treatment of Total Heart Block

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TOTAL HEART BLOCK is a most treacherous disease for the patient and exasperating for the doctor. According to Zoll and Linenthal,[1] the major problem in this disease is prevention of recurrent seizures. Despite available pharmacologic measures, Stokes-Adams attacks recur and may be fatal. For assured prevention of seizures, whether caused by ventricular standstill or fibrillation, the unreliable intrinsic ventricular pacemaker must be replaced by a reliable electric mechanism to drive the ventricle continuously and indefinitely.

CATEGORIES OF TOTAL HEART BLOCK

There are three major categories of total heart block. The first is congenital. This type requires no therapy whatsoever, but does require a diagnostic search to determine the presence or absence of associated intracardiac defects. If such a defect is found, surgery may be advisable. The second category is that which develops during open heart surgery. Needless to say, the best treatment is to remove the offending stitch, but this is not possible in all cases. For surgical heart block, Weirich and Lillehei have described a myocardial electrode of the unipolar nature with a neutral electrode implanted subcutaneously.[2] This method has been used successfully for as long as eight to ten weeks, which is usually more than sufficient for the return of normal cardiac conduction. Beyond eight to ten weeks, the unipolar system with the implanted single wire is not successful.

The third type of heart block develops after an ischemic process, infectious or vascular, in or around the bundle of His. The combination of acute septal infarction plus total heart block is nearly always fatal. However, there are survivors from this treacherous combination and others in whom the total heart block develops more insidiously. The patient with this type of heart block leads a most difficult existence. The intrinsic ventricular pacemaker is totally unreliable, so that the patient is constantly threatened by a Stokes-Adams attack. Some persons suffer as many as 30 to 40 such attacks each year. It is for such patients that the bipolar myocardial electrode was devised.

The electrode platform, which measures 2.5 by 1.5 cm., is made of highly purified silicone rubber. The electrodes, made of high grade stainless steel, are 1.5 cm. long and are spaced 1.5 cm. apart (figure 1). The original electrodes were .75 cm. in length, but it was found that the left ventricle was more satisfactory for implantation of the electrode and that the longer electrode needle made possible stimulation of the heart at the endocardial surface. There are now ample data to suggest that a lesser amperage will stimulate the ventricular musculature if the point of excitation is just subendocardial. This is logical, since the conducting system of the heart is largely subendocardial.

The electrodes are electric-welded to stainless steel wires which are insulated with a thin layer of teflon and covered with an extrusion of the silastic rubber from the platform, thereby producing a waterproof system. The system is powered by a conventional Medtronic pacemaker which is capable of delivering 20 to 30 milliamperes across 600 to 1,000 ohms resistance at rates appropriate for driving the blocked heart. We have found 70 per minute the most advantageous rate.

METHOD OF IMPLANTING ELECTRODES

I have implanted the pacemaker in 3 patients in St. Paul, Minnesota, with all three surviving and active to this date. The first implantation was performed on April 4, 1959, and the patient, who is living at the time of this writing,[3] is the longest survivor of those utilizing an artificial pacemaker. The details of the surgical procedure are as follows:

1. As soon as the cardiologist and surgeon

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Fig. 1. The platform bipolar silastic silicone myocardial electrode.

have agreed that artificial stimulation is necessary, the patient is prepared by scrubbing the chest front and back with pHisohex for ten minutes on four separate occasions, for a total of forty minutes. This step is essential when a permanently implanted foreign body is to be used.

2. An intravenous drip of 5 per cent glucose containing 4 μg. of isuprel per cubic centimeter (4 mg. per 1,000 cc.) is started before moving the patient to the operating room. Zoll and Linenthal have shown that intravenous isuprel is the most reliable pharmacologic method of maintaining the intrinsic cardiac pacemaker.[4] The intravenous drip is maintained preoperatively, through induction of anesthesia, and throughout surgery, until the electrode is fast in place.

3. The patient is moved quietly to the operating room. A minimum of preoperative sedation is used in conjunction with adequate atropine.

4. An external pacemaker is taped on the chest at sites V-1 and V-6 during induction and left in place until the preparation of the chest is begun.

5. The patient is placed in the right lateral position (left side up), the chest is prepared and draped, and incision is made in the fifth interspace. General anesthesia with tracheal intubation is used.

6. The pericardium is opened; a bare spot of the left ventricle is chosen and the electrode thrust against the epicardium. The lead wires are attached to temporary cables and the cables in turn are attached to the terminals of the Medtronic pacemaker. As soon as this is accomplished and the pacemaker turned to rate 70, the blocked heart will increase in rate from its idioventricular rhythm of 30 per minute or thereabout to 70 per minute. For some inexplicable reason, the milliamperage requirement may be considerable, up to 20 milliamperes. In two or three minutes, however, the driving current reduces to 4 or 5 milliamperes or even less.

7. The silastic platform is next stitched in place with six 3-0 silk stitches—one in each corner and one in each midside (figure 2). The corner stitches are best mounted in the silastic before approximation to the epicardium. One must avoid occlusion of any branch of the coronary system.

8. The pacemaker must be disconnected for a few seconds while the wire is brought through the chest wall. The most acceptable point of emergence is the third or fourth interspace just lateral to the sternum. Care must be taken to avoid the costal cartilages which are less resistant to infection. A loop of wire is left inside the chest cavity to prevent acute angulation and fatiguing of the lead wire.

9. One million units of penicillin and 1 gram of streptomycin are left in the chest cavity. The pericardium is closed loosely and the chest is closed in the conventional manner, leaving a tube within the thorax for re-expansion and removal of fluid. A minimum of 4 to 5 million units of penicillin is given daily for seven days

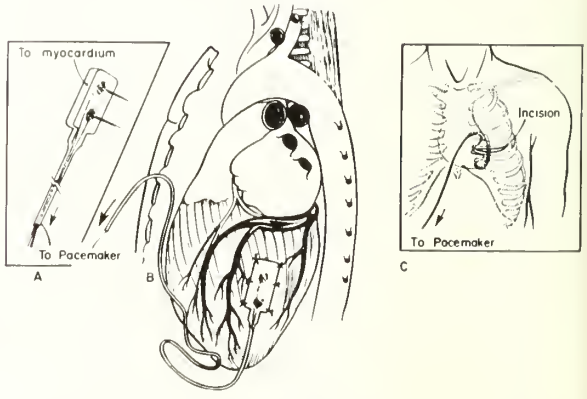

Fig. 2. Surgical details for implanting the bipolar platform electrode on the left ventricular myocardium. Note loop of lead wire left within the chest cavity.

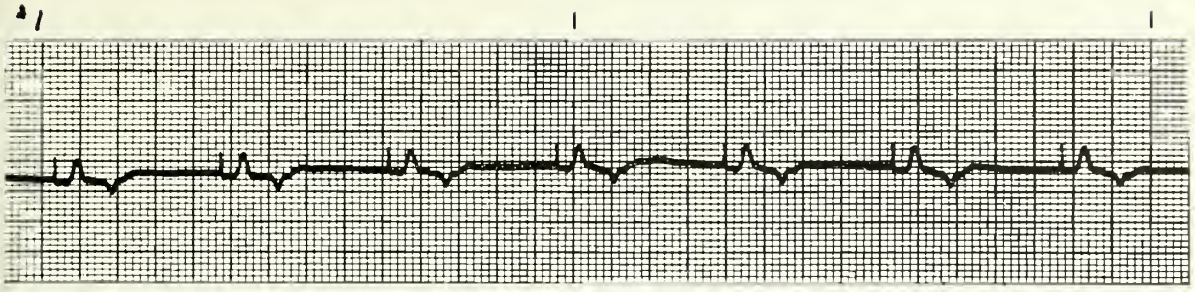

Fig. 3. Electrocardiogram showing complete control by the electric pacemaker. The stimuli are spaced 0.89 seconds apart and are followed not only by a QRS complex but also by an inverted P wave indicating retrograde activation of the atria.

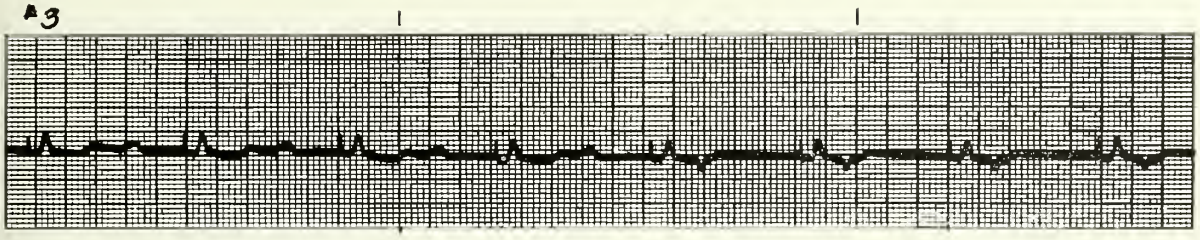

Fig. 4. Electrocardiogram showing effect of increasing the artificial rate.

along with 1 gram of streptomycin daily. In addition, an antibiotic ointment is used at the venting site of the skin.

10. The postoperative course in the hospital averages seven to ten days.

An electric cardiograph taken in June 1960 demonstrates again complete control of the patient's myocardial action by the pacemaker (figure 3). Figure 4 shows the effect of gradually increasing the rate of stimulation until the artificial rate is faster than the sino-auricular rate (figure 4). As the rate increases, the sinus P waves disappear and the retrograde P waves again occur regularly (figure 4).

SUMMARY

Three patients with total heart block were treated with bipolar myocardial electrodes, and all three are now living. The first case has been satisfactorily so treated for over twenty-two months.

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MEDICAL GRAND ROUNDS
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Pheochromocytoma and the Catecholamines

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Apheochromocytoma, literally a tumor of gray cells, is a functionally active chromaffin tumor which may be located in the adrenal medulla or wherever sympathetic ganglia or chromaffin tissue exist. Chromaffin tissue is so named because of the characteristic brown staining of tissue sections upon exposure to chromates.

Biologically active amines have been studied experimentally for years, but overproliferation of amine-producing tissue in man has provided the great stimulus to investigation. Some patients with urticaria pigmentosa produce excesses of histamine. Carcinoid tumors may produce excesses of 5-hydroxytryptamine (serotonin), and pheochromocytomas produce large amounts of catecholamines—dopamine, epinephrine, and norepinephrine.[1]

Frankel, in 1886, reported the first patient with pheochromocytoma and associated hypertension. Manasse reported a case in 1893 and demonstrated the chromaffin reaction of the tumor cells in another patient in 1896. Pick suggested naming the tumor for the predominant cell type, the pheochromocyte, in 1912. In 1929, Pincoffs made the first correct preoperative diagnosis and Shipley successfully removed the tumor. Rabin, in 1929, demonstrated that the tumor contained epinephrine or a related pressor agent in amounts greater than the normal adrenal medulla and suggested that this was the cause of the associated symptoms. Beer and associates, in 1937, found a pressor agent in the blood of a patient with a pheochromocytoma during a hypertensive crisis. Engel and von Euler, in 1950, demonstrated large amounts of norepinephrine in the urine of 2 patients with proved tumors. These are but a few of the large number of investigators who have contributed to our knowledge of this tumor and its manifestations.[2]

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EMBRYOLOGY AND ANATOMY OF CHROMAFFIN TISSUE

Neural crest cells of ectodermal origin migrate ventrally to form sympathetic ganglion cells in the embryo. Certain of these cells are transformed into peculiar endocrine glands rather than into neurons. These chromaffin cells clump together to form chromaffin bodies. The largest group forms the medullae of the adrenal glands by migrating into the center of the mass of adrenocortical cells derived from mesoderm. Some chromaffin bodies become partially embedded in the dorsal surfaces of the sympathetic ganglia and are appropriately called paraganglia. Other groups are found on the sympathetic plexus; the largest pair, at the root of the inferior mesenteric artery, is called the organs of Zuckerkandl. The carotid body is a mesodermal condensation on the wall of the internal carotid artery. It is classified in the chromaffin category but apparently lacks true chromaffin cells.[3] After birth, the chromaffin bodies decline but do not disappear.

PHYSIOLOGY AND BIOCHEMISTRY OF THE CATECHOLAMINES

Formation. The main stages of formation of epinephrine as known today are shown in figure 1.[2,4]

The enzyme, L-dopa carboxylase, requires a coenzyme, pyridoxal-5-phosphate, to convert L-dopa to L-dopamine. Dopa carboxylase is found in the adrenal medulla of all animal species investigated. The highest activity, however, is found in peripheral sympathetic ganglia, in postganglionic adrenergic neurons, and in the sympathetic trunk. Smaller amounts are present in the brain and spinal cord. In the adrenal medulla, biosynthesis proceeds via norepinephrine to the methylated end product, epinephrine. In nervous tissue, biosynthesis stops at the norepi-

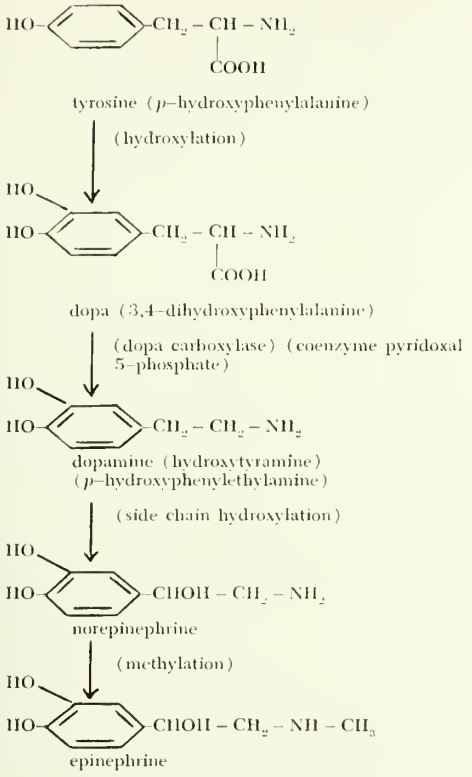

Fig. 1

nephrine level, and dopamine is the precursor and, possibly, an effector substance. Dopamine is the end product in lungs, intestine, and liver, where its action is unknown.[5]

Carbonyl trapping agents inhibit dopa carboxylase by inactivating the coenzyme. This is a general phenomenon for most carboxylases and transaminases requiring pyridoxal-5-phosphate. Some compounds causing inhibition by this mechanism include nicotinic acid, isonicotinic acid hydrazide (isoniazid), monamine oxidase inhibitors such as iproniazid (Marsilid), and Apresoline.[6]

The carboxylase catalyzing the formation of serotonin from 5-hydroxytryptophan (5-HTP) is also pyridoxine-dependent and is thought by some investigators, including Holtz,[5] the discoverer of L-dopa carboxylase, to be identical with dopa carboxylase (figure 2).

Dr. H. Langemann[4] reported that human enterochromaffinoma decarboxylates dopa as well as 5-HTP. Similarly, extracts of mouse mast cell tumors which contain serotonin but no catecholamines act not only on 5-HTP but also on dopa. Dr. Holtz and his associates[5] found that all organs which decarboxylate dopa also decarboxylate 5-HTP, although they may not contain serotonin. Carcinoid tumors containing large amounts of serotonin also decarboxylate dopa. Therefore, catecholamines and serotonin would not only share amine oxidase as a catalyst in their inactivation but also an enzyme that participates in their formation.[4]

Storage and release. Epinephrine, norepinephrine, and dopamine are present in mammalian tissue, primarily in the sympathetic nervous system cells, chromaffin tissue, and central nervous system. Catecholamines also have been reported in the spleen, lungs, heart, and blood vessels but are probably within sympathetic nervous tissue in these organs. Weil-Malherbe and Bone[7] have found small amounts of norepinephrine in platelets by use of their ethylenediamine method. Platelets also contain serotonin. Much controversy exists concerning the presence of separate epinephrine- and norepinephrine-storing cells in the adrenal medulla. The evidence rests principally on differential staining with Giemsa's stain or differential fluorescence of various areas in thin sections. Definite proof is not yet available.

Catecholamines in the adrenal medulla are stored with adenosine triphosphate (ATP) and protein within circular chromaffin granules varying between 50 and 90 mμ. in diameter. By centrifugation, the dense chromaffin granules settle to the bottom. The larger, less dense granules, which are mitochondria, remain near the top. By electron microscopy, the chromaffin granules are more numerous than mitochondria and seem to occupy spaces in the endoplasmic reticulum of the cell. The granules have a finely stippled internal structure and a thinner, less conspicuous outer membrane than do the mitochondria. The granules are stable in isotonic solutions but release their amines, ATP, and about 77 per cent of their protein when placed in hypotonic solutions. Certain detergents and changes in the *p*H of the suspending solution also cause the granules to release their amines.

Norepinephrine of sympathetic nerves is also within granules that have sedimentation charac-

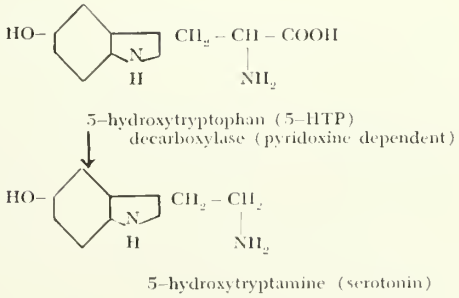

Fig. 2

teristics similar to those in the adrenal medulla. However, the dopamine is primarily in the nonparticulate cytoplasm and thus differs from dopamine in the adrenal medulla, which is largely intragranular.

The adrenal medulla contains more ATP than any other mammalian tissue. It is almost entirely within the chromaffin granules, where the molar ratio of amines to ATP is about 1 to 4. The 4 negative charges of one molecule of ATP balance the 1 positive charge of a molecule of catecholamine. At present, whether the chromaffin granules are solely storage granules or whether some of the reactions involved in biosynthesis also occur there is not known.[8]

The presence of a very active adenosine triphosphatase in the adrenal medulla suggests that hydrolysis of ATP with an accompanying change in the electrical charge is responsible for mobilization of the amine and its eventual appearance in extracellular fluid. A parallel loss of ATP and amine occurs after insulin administration to sheep, cats, and rats.[9,10]

Action. Goldenberg[11] contrasted the actions of epinephrine and norepinephrine by infusing these drugs into man (see table). Although both drugs increase systolic and mean blood pressures, they do so differently. Epinephrine hypertension is the result of a significant increase in cardiac output in spite of a decrease of total peripheral resistance. Norepinephrine hypertension is due to an increase of total peripheral resistance with no significant change, or even a fall, in cardiac output.

TABLE 1

EFFECTS OF EPINEPHRINE AND NOREPINEPHRINE ON MAN

	Epinephrine (0.1–0.3 mg/kg/min.)	*Norepinephrine (0.1–0.4 mg/kg/min.)*
Pulse rate	+	−
Cardiac output	+++	−
Systolic blood pressure	+++	+++
Diastolic blood pressure	+	++
Total peripheral resistance	+	+++
Oxygen consumption	++	+
Blood sugar	+++	+
Central nervous system action	+	0
Eosinopenic response	+	0

− to +++ = degree of response
0 = insignificant response
+ = slight or insignificant response
− = decreased or insignificant response
Modified from Goldenberg[11]

The increased oxygen consumption after epinephrine administration is well known but little understood.[11] Epinephrine increases the rate of glycogenolysis both in liver and in striated muscle, causing an immediate increase in blood sugar. The end product of glycogenolysis in the liver is glucose but in muscle is lactic acid, because muscle lacks the phosphatase enzyme. After the action of epinephrine is over, liver glycogen may actually be increased because of glycogen synthesis from lactic acid. The hyperglycemic effect of epinephrine is a physiologic counterpoise to the action of insulin. When the blood sugar is low, epinephrine secretion is stimulated and hastens the return of blood sugar to normal.[12] The glycogenolytic action of epinephrine probably is due to an accumulation of 3′,5′-adenosinemonophosphate, which converts phosphorylase from an inactive to an active form.[12]

Central nervous system action is indicated by restlessness, apprehension, and a feeling of anxiety.[11] Epinephrine increases adrenocortical secretion but probably is not the primary cause of ACTH production in the body.[11,14]

Patients with a pheochromocytoma produce essentially normal amounts of adrenocortical glucocorticoids despite the theoretic possibility that adrenal compression may occur with bilateral tumors. Only an occasional case is associated with Addison's disease. For some unknown reason, adrenal androgen secretion is reduced in some cases.[2]

Metabolism. Only 1.4 per cent of intravenous epinephrine or norepinephrine is excreted unchanged in the urine and does not necessarily reflect endogenous metabolism (figure 3). The principal mode of degradation is by the action of catechol o-methyl transferase, an enzyme widely distributed in all organ tissue, including the autonomic and central nervous systems (figure 3). The methoxy product is either conjugated and excreted in the urine or converted to 3-methoxy 4-hydroxy mandelic acid (VMA) under the influence of monamine oxidase.[1,15] Iproniazid, which blocks monamine oxidase, increases the output of 3-methoxy epinephrine at the expense of VMA.[16] A small amount of epinephrine and norepinephrine is converted to 3,4 dihydroxy mandelic acid by means of monamine oxidase and then to VMA by catechol o-methyl transferase.[1,15]

Recent concepts of autonomic nervous system. The autonomic nervous system regulates the activities of structures not under voluntary con-

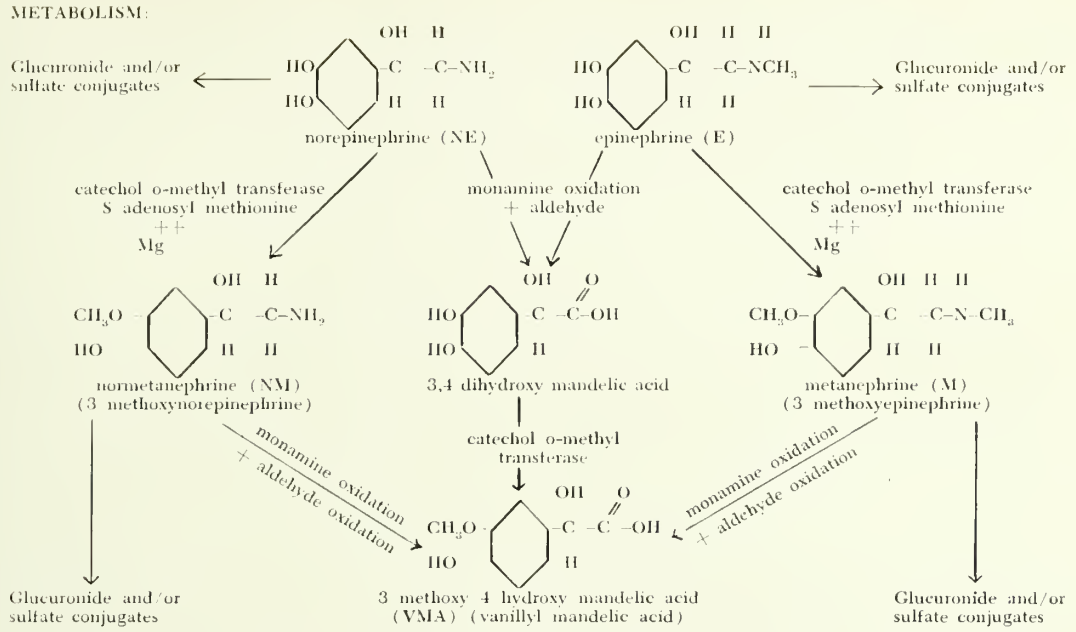

Fig. 3

trol and, as a rule, controls functions below the level of consciousness, for example, respiration, circulation, digestion, sweating, and so forth. The two anatomic divisions are the sympathetic, or thoracolumbar, and parasympathetic, or craniosacral. Preganglionic sympathetic fibers ramify to a greater extent than and may synapse with as many as 20 postganglionic fibers. Thus, a diffuse discharge can be obtained and is reinforced by epinephrine from the adrenal medulla. Stimulation of the parasympathetic system causes a more discrete discharge, because preganglionic fibers synapse with not more than one or two postganglionic fibers in terminal ganglia very near to the innervated organs.

Autonomic nerves may now also be classified chemically as cholinergic or adrenergic. Cholinergic nerves release acetylcholine at their terminals and include all autonomic preganglionic nerves, all postganglionic parasympathetic nerves, somatic motor nerves to skeletal muscle, preganglionic nerves to the adrenal medulla, and anatomic sympathetic fibers to sweat glands and certain blood vessels. The action is stopped locally by acetylcholine esterase or other choline esterases.[14,17] The adrenergic fibers include all other postganglionic sympathetic fibers. Adrenergic nerves release norepinephrine principally, if not entirely. Dopamine also is found in the sympathetic nerves, but its role has not yet been investigated.[8]

In 1931, Cannon and Bacq postulated that stimulation of adrenergic nerves produced sympathin, which circulates in the blood. Since injected epinephrine did not quite match the actions of sympathin, Cannon and Rosenblueth postulated that nervous stimulation produces two sympathins that act locally on the effector cell and then circulate. Epinephrine plus E at the receptor site produces sympathin E, an excitatory form. Epinephrine plus I at the receptor site produces sympathin I, an inhibitory form. Adrenergic impulses are known to be excitatory, as in acceleration of heart rate, or inhibitory, as in decreased intestinal motility. The more modern theory is that epinephrine is the primary mediator of inhibitory actions and that norepinephrine is the primary mediator of excitatory actions, but the problem is not yet completely solved. Perhaps the mediator is always the same but the receptor site in the effector cell determines whether the action will be excitatory or inhibitory.

Autonomic blocking agents do not interfere with release of the chemical mediator but selectively inhibit the response of effector cells to stimulation of the nerve, the chemical mediator, and related amines. The terms sympatholytic, which means a blockade of the responses to adrenergic nerve impulses, and adrenolytic, which means a blockade of responses to epinephrine, have now been replaced by the all-inclusive and preferable term, adrenergic blocking agent. All known autonomic blocking agents are

more effective in antagonizing circulating sympathomimetic agents than in blocking responses to autonomic nerve activity.[14,17]

MEASUREMENT

The technics for estimation of catecholamine fall into 3 general categories: (1) bioassay, which, in its latest abbreviated form, measures only norepinephrine, since all pheochromocytomas secrete an excess of norepinephrine;[18] (2) formation of fluorescent trihydroxyindole derivatives of the catecholamines and determination of the concentration fluorometrically;[19] and (3) formation of fluorescent derivatives of the catecholamines by condensation with ethylenediamine.[6] Concentrations estimated by the trihydroxyindole method are close to those determined biologically but are much less than those estimated by the ethylenediamine method, probably because of the lack of specificity of the latter technic for biologically active catecholamines. The trihydroxyindole method can be used for either urine or blood, whereas the ethylenediamine technic is more useful for blood than for urine.

Healthy patients will have < 6 μg. of epinephrine plus norepinephrine per liter of plasma. Patients with tumors have from 10 to 100 μg. of epinephrine and norepinephrine per liter of plasma. Daily epinephrine–norepinephrine excretion in the urine is < 100 μg. for healthy patients and 300 to 3,000 μg. for patients with tumors.[20]

Since about one-third of radioactively labeled epinephrine given intravenously is recovered as VMA in the urine, attempts have been made to measure the VMA. Armstrong[1] first measured VMA by paper chromatography and found that VMA excretion returned to normal after the pheochromocytoma was removed. Kraupp and associates[1] assayed twenty-four hour urine from a patient with pheochromocytoma and found the catecholamine excretion parallel with the VMA in crises. In remission, the VMA remained high, while the catecholamines decreased to normal. The most recent method for VMA determination[15] employs the colorimeter and can be done in any routine clinical laboratory. If this screening test is positive, the more time-consuming and cumbersome chromatography must be used for confirmation.

No cases of persistent hypertension and only one case of paroxysmal hypertension in which urinary catecholamines were not elevated, even during the period immediately after an attack, have been verified.[21] In healthy people, the urinary catecholamines are higher during the day, while standing, during muscular work, during severe surgical and traumatic stress, and after the injection of insulin. Values almost as high as those seen in patients with pheochromocytoma may be seen only with myocardial infarction or severe muscular exercise.[2]

Blood catecholamines will establish the diagnosis in patients with persistent hypertension or after a spontaneous or histamine-produced crisis in patients with paroxysmal hypertension. With the ethylenediamine method, blood levels may be falsely elevated in some patients with azotemia, jaundice, increased intracranial pressure, and lymphoma or after the use of catecholamines or related products, tetracycline, or chlorpromazine.[2,22,23]

Pheochromocytomas contain high levels of norepinephrine and lesser, more variable amounts of epinephrine and 3-methoxy analogues, but cases have been described in which dopamine or even dopa predominates. Clinical observation of such tumors is badly needed.[1] Most tumors contain 500 to 10,000 μg. of total catecholamines per gram of tumor, with the norepinephrine–epinephrine ratio similar to that in the urine.[20]

PHEOCHROMOCYTOMA

Incidence. Roth and associates[23] reported the discovery and successful removal of 76 pheochromocytomas from 66 patients at the Mayo Clinic as of July 1959. Incidence of tumors in 12,713 patients screened with pharmacologic and chemical tests was 0.51 per cent. Barbeau,[24] in 1957, reviewed the world literature up to January 1, 1957, and found 626 cases of pheochromocytoma. Minno and associates[25] found 15 pheochromocytomas in 15,984 autopsies from 1928 to 1951 at the Mayo Clinic; 3 of the patients had benign pheochromocytomas without symptoms. In 1950, Smithwick and associates[26] found 8 unsuspected pheochromocytomas in the course of 1,700 splanchnicectomies performed for hypertension, an incidence of 0.47 per cent. In 3 additional cases, the diagnosis was made preoperatively.

Most reported pheochromocytomas have appeared between the ages of 20 and 50 years, with a range from 5 months to 82 years. There is no special sex differential. Pheochromocytomas appear in women in 54 per cent of adult cases and in boys in 63 per cent of cases in children.[2]

Symptoms and signs. A pheochromocytoma should be suspected if hypertension is associated with: (1) any sort of attack; (2) diabetes mellitus or an elevated fasting blood sugar, especially in patients between 20 and 50 years of age and if the basal metabolic rate is elevated; (3)

hypermetabolism without other signs of hyperthyroidism, that is, an elevated basal metabolic rate with normal thyroid function studies and serum cholesterol; (4) postural hypotension, vasomotor phenomena, and elevated temperature or excessive sweating; (5) weight loss or failure of a thin person to gain weight; (6) extreme hypertension during induction of anesthesia; (7) unexplained hypotension after minor injury or operation; (8) a paradoxical reaction to ganglionic blocking agents; (9) neurofibromatosis; (10) a familial history of pheochromocytoma; (11) a previously removed pheochromocytoma; (12) a positive reaction to the Regitine test; (13) absence of renal disease or coaretation of the aorta in children; and (14) pregnancy, especially with persistent headaches, vomiting, and perspiration in the last trimester; hypertension in the first trimester; or a hypertensive episode or shock during delivery or in the postpartum period.[2,22]

The hypertension is paroxysmal or persistent. The reported incidence of paroxysmal hypertension is 25 to 50 per cent in adults and only 8 per cent in children. Symptoms may occur with typical paroxysms or attacks and consist of severe headache, palpitation, nausea and vomiting, epigastric or substernal pain, profuse sweating, dyspnea, vertigo, pallor, apprehension or fear of impending death, and visual difficulties, in that order. Symptoms in children are somewhat different, with sweating and visual aberrations being the most common.

The attacks may last a few moments to many hours and may occur several times a day or only once every year or two. Precipitating factors include emotional upsets, changes in posture, intercourse, physical effort, trauma, sneezing, eating, and urination. The attack often is accompanied by a rise in blood sugar, body temperature, and blood and urinary catecholamines. The attacks may occur for several years and then disappear altogether for several years, only to return again. The first sign may be sudden death, or symptoms may persist for thirty-two years or more. Patients who have paroxysmal attacks at first may develop sustained hypertension or continue to have paroxysmal attacks.[2] Duration of the symptoms seems to have no bearing on the secondary vascular damage that the intermittent attacks produce. One woman with excruciating headaches for ten years had normal ocular fundi and a normal vascular system. On the other hand, a 38-year-old man with symptoms for only eight months had both a coronary occlusion and thrombosis of the basilar artery before the diagnosis could be made.[22]

Continuous hypertension cannot be distinguished clinically from essential or malignant hypertension, but some patients will have attacks similar to those experienced by patients with paroxysmal hypertension. During the attack, the blood pressure rises to even higher levels. The usual symptoms are increasingly severe headaches, excessive perspiration, nervousness, palpitation, and loss of weight. If the condition is unrecognized, the chief symptom may be due to secondary vascular damage, for example, loss of vision, coronary occlusion, cerebral vascular thrombosis, and congestive heart failure.[22]

The clinical picture does not indicate the type of catecholamine secreted by the tumor, since large amounts of epinephrine will cause vasoconstriction, whereas large amounts of norepinephrine cause metabolic changes. All tumors secrete large amounts of norepinephrine, but only a few secrete large amounts of epinephrine in addition. The presence of metabolic changes probably depends on the rate and constancy of secretion of norepinephrine.

Children who have persistent hypertension and thus large secretions of norepinephrine have an elevated basal metabolic rate in 83 per cent of cases and an elevated fasting blood sugar in 40 per cent of cases.[2,11] The basal metabolic rate is increased in about 3 times as many adults with sustained hypertension as with paroxysmal hypertension. However, the number with elevated fasting blood sugar is about the same.[22] Surprisingly, patients with tumors containing large quantities of epinephrine may have a picture of essential hypertension with a normal heart rate, absence of hyperglycemia, and a normal basal metabolic rate.[11]

The majority of patients, particularly those with sustained hypertension, tend to be thin. However, 3 reported patients with paroxysmal hypertension weighed 192, 200, and 210 lb., respectively. The latter patient had been hypertensive for fifteen years. The heaviest patient with persistent sustained hypertension weighed 169 lb.[2]

At least 37 reported cases have occurred during pregnancy. Nine instances of familial occurrence comprising 22 patients have also been reported.[2] The incidence of associated neurofibromatosis is about 4 per cent. Cerebellar hemangiomas and Lindau-von Hippel disease also may be associated with a pheochromocytoma.[27]

Localization of tumor. The tumor is palpable in 14 per cent of cases.[28] The tumor can sometimes be located by tomography or by the production of a hypertensive attack by massage in

a particular area.[2] Intravenous pyelograms have shown the tumor distorting the renal pelvis or displacing the kidney in 56 per cent of unselected adult cases[28] and 31 per cent of the cases in children.[2]

Presacral air injection and aortography are dangerous procedures and may give completely misleading results. When localization is particularly desired, for example, after negative abdominal exploration, a catheter is inserted into the vena cava to obtain samples of blood at different levels for catecholamine determination.[29,30] Localization, however, is not essential, because the entire abdomen should be explored through a transverse upper abdominal incision.

Pathology. Tumors of the adrenal medulla are named according to the cell of origin (figure 4). Sympathicogoniomas and sympathicoblastomas are often grouped together as neuroblastoma. Both are malignant and usually occur in young children. Ganglioneuromas occur from infancy to old age and usually are benign. Pheochromoblasts and pheochromocytes are called pheochromocytoma. Approximately 8 per cent are malignant. The malignant form is sometimes called pheochromoblastoma. The malignant lesion cannot be distinguished from the benign histologically except for demonstration of capsule invasion. Blood vessel invasion is not a criterion for malignancy. Metastases which are often functioning may occur to lung, liver, bone, and other areas.[2,31]

The tumors are usually small, ranging from 1 to 10 cm. in diameter, but may be as large as 3,600 gm.[32] Small tumors are poorly defined, but those up to 10 cm. or more appear to be encapsulated. The color varies from a pale gray or pink to a dusky brown. Foci of yellow necrosis, hemorrhage, and calcification may be present.

The vast majority of tumors are located in the adrenal glands, the right more often than the left, and 9 per cent are bilateral. Bilateral tumors are more common in children than in adults.[2,31] Graham[28] found that 10 per cent of abdominal pheochromocytomas in 207 patients were extraadrenal and an additional 1 per cent were thoracic. Tumors have been reported in the brain, neck, urinary bladder, and elsewhere.[2,31]

Microscopically, pleomorphism may be conspicuous, even in benign tumors. The cells are polygonal, fusiform, spherical, or elliptical. The cytoplasm is abundant, eosinophilic, and slightly granular. The nucleus is somewhat vesicular, with a fine chromatin network. The diagnosis is not positive unless the chromaffin reaction is positive. Chrome salt fixatives are desirable, but formalin-fixed material may be treated for twenty-four hours with 3.5 per cent potassium dichromate in 10 per cent formalin. The positive cells stain brown. The stain is in the cytoplasm between granules rather than in the granules themselves. Some cells are nonreactive. Giemsa's or azocarmine stains also give characteristic color reactions.[31]

Diagnostic tests. Many drug tests have been suggested as diagnostic aids to differentiate between essential hypertension and pheochromocytoma. In general, the drugs effect a release of catecholamines from the tumor if the patient has paroxysmal hypertension or depress the action of catecholamines if the patient has sustained hypertension. No single test is always completely reliable. The tests are not without danger, for fatal results have occurred. However, the chemical tests for pressor amines present pitfalls just as do the pharmacologic tests. The Mayo Clinic now uses only the cold pressor, histamine, and Regitine tests.

Cold pressor test. This test is done after the basal blood pressure is determined unless the diastolic blood pressure is more than 150 mm. Hg. One of the patient's hands is immersed well above the wrist in water at 4° C., in a pail 8 in. high, for one minute. The blood pressure is measured in the opposite arm at fifteen, thirty, and sixty seconds during the immersion. The highest blood pressure reading indicates the lability. The average increase in the blood pressure in proved cases is 40/29, with a range from 12 to 68 mm. Hg systolic and from 10 to 78 mm. Hg diastolic; in other words, the blood pressure is not very labile. This test never produces an attack in a patient with pheochromocytoma because there is a sudden rise in the blood pressure instead of the sudden fall that stimulates secretion by the tumor.

Histamine test followed by Regitine test for paroxysmal hypertension. If the basal blood pressure is less than 170/110, 0.05 mg. of histamine base in 0.5 cc. of normal saline solution is injected intravenously with a tuberculin syringe. The needle is left in the vein, and a solution containing 5 mg. of Regitine is attached for

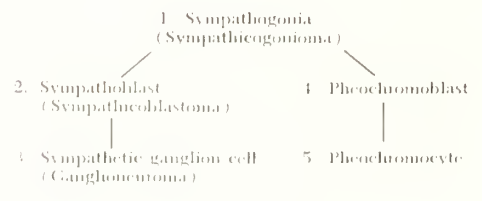

Fig. 4

immediate administration in case the blood pressure becomes alarmingly high.

Blood pressure is determined every thirty seconds for the next two minutes. It always decreases thirty seconds after the injection, unless the histamine has not entered the vein. Immediately thereafter, the blood pressure increases rapidly and usually is maximum in two minutes. If the patient has a pheochromocytoma, the characteristic clinical signs and symptoms of a severe attack appear, with an increase in blood pressure to well above the cold pressor level. Regitine is injected two minutes after the histamine, sooner if necessary. Within one minute, signs and symptoms disappear and blood pressure decreases. If the tumor is large, blood pressure elevation and symptoms may reoccur and more Regitine may be needed.

Regitine test for sustained hypertension. If the basal blood pressure is more than 170/110, 5 mg. of Regitine is given intravenously. If a pheochromocytoma is present, the blood pressure should decrease at least 35/25 in the first four or five minutes after injection and then return to the previous basal level in ten to fifteen minutes. A decrease in the blood pressure of some apprehensive patients may occur in the first one or two minutes in the absence of a tumor, but the blood pressure returns toward the basal level in the next minute.

Mecholyl test. Mecholyl, like histamine, stimulates the release of catecholamines from the tumor. The dose is 10 to 25 mg. administered subcutaneously. It offers no advantage over the histamine test and is more dangerous.[33]

Benzodioxane test. Over a period of two to three minutes, during which the blood pressure is recorded at thirty-second intervals for three minutes and then sixty-second intervals for fifteen minutes, 15 to 20 mg. of benzodioxane is given intravenously at doses of 0.25 to 0.50 mg. per kilogram of body weight. A fall of 30/20 within four minutes after the start of injection is positive proof of a tumor. False negative reactions are more common than with Regitine. Dangerous pressor responses sometimes occur with or without a pheochromocytoma.[2,34]

Dibenamine test. Dibenamine, 400 mg. in 500 cc. of 5 per cent dextrose and water, is injected intravenously over a one- to two-hour period and produces a slowly developing but prolonged lowering of blood pressure. The test is nonspecific and unreliable.[2,35]

Tetraethylammonium test. This drug causes a release of catecholamines from the tumor and blocks regulating mechanisms of the secretion but seldom is used.[2,36]

Reasons for false results. A reliable basal blood pressure is a prime requisite for accurate interpretations of the tests. The blood pressure must also be followed very closely, as the timing is very precise. The blood pressure should be measured routinely in both arms; if any disparity is found, determinations are made in both arms during pharmacologic tests.

False positive results may occur if sedatives or narcotics are taken within forty-eight hours of the test. Sedatives inhibit blood pressure rise during the cold pressor test. The increase of blood pressure during the histamine test may be greater than during the cold pressor test, thus falsely suggesting the presence of a tumor. Sedatives and tranquilizers in patients with sustained hypertension may cause a fall of blood pressure typical of that produced by pheochromocytoma after intravenous Regitine. Vasoconstrictive drugs used for nasal stuffiness may produce a profound fall in blood pressure for as long as forty minutes after intravenous Regitine. Uremia may cause a false positive Regitine test.

False negative results may be produced by various antihypertensive drugs. These drugs should be withheld for at least ten and preferably sixteen days.[23] False negatives also may be due to secondary vascular changes, which produce sustained hypertension even when the pheochromocytoma is removed.[2]

TREATMENT

Treatment consists of abdominal exploration and complete surgical removal of all tumor tissue through a transverse upper abdominal incision. The blood pressure should be reduced and the general condition improved preoperatively in children and some adults. Regitine is probably the best substance now available for this purpose and may be given every two hours several days before operation. Thorazine may also be utilized. An intravenous injection of 5 mg. of Regitine should be given just before anesthesia. Pentothal induction with nitrous oxide and oxygen anesthesia supplemented with Demerol and succinylcholine is probably the best form of anesthesia. Regitine is used in 5 mg. increments intravenously as frequently as necessary to control the blood pressure. Pressure rises are most common when the tumor is handled. Profound hypotension may suddenly occur after excision of the tumor.[2] If blood pressure does not fall after removal of a tumor, confirmation of another tumor may be obtained by administration of Regitine, which will cause a definite decrease in blood pressure.[22] Hypotension is counteracted by the administration of an intravenous

infusion of norepinephrine in 5 per cent dextrose and water. Usually, the drug can be decreased and discontinued within the first twenty-four hours. The blood pressure usually returns to normal after surgery but remains elevated if it is fixed due to secondary vascular changes. If the tumor is bilateral, adrenocortical insufficiency may develop, and hydrocortisone should be given intravenously.

Since cardiac arrest is not uncommon, the left chest should be prepared and draped so that cardiac massage can be performed under sterile conditions.[2,11]

After removal of a pheochromocytoma, the patient should be examined frequently to be sure that no recurrence has developed or metastases occurred. If either is the case, further operative or roentgenologic treatment may prolong life.[22]

SUMMARY

A pheochromocytoma is a functioning benign or malignant tumor of chromaffin cells which produces large amounts of catecholamines. Norepinephrin is always produced. Epinephrine, dopamine, or both may also be formed. Present knowledge of the catecholamines has been summarized.

Pheochromocytomas produce sustained or intermittent blood pressure elevation with or without associated hypermetabolism. Removal of the tumor will result in return of the blood pressure to normal if functioning metastases are absent or secondary vascular changes causing a fixed blood pressure elevation have not developed.

Diagnosis of a pheochromocytoma is established by symptoms and signs and pharmacologic testing.

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The Fat of the Land

The following article is reprinted by permission from TIME, *The Weekly Newsmagazine; copyright Time, Inc. 1961. Since Dr. Ancel Keys has been a contributor and a member of the Board of Editors of* THE JOURNAL-LANCET *for many years, the Editors have asked Dr. Keys to comment on the* TIME *article. His comments,* Time Marches On, *follow this reprint.*

THE READING PUBLIC, the theatergoing public, the skindiving public, the horse-playing public—all these and others fill substantial roles in U.S. life, but none is so varied, vast and vigilant as the eating public. The Department of Agriculture averaged out U.S. food consumption last year at 1,488 lbs. per person, which, allowing for the 17 million Americans that John Kennedy said go to bed hungry every night, means that certain gluttons on the upper end must somehow down 8 lbs. or more a day. That mother hen of the weight-height tables, the Metropolitan Life Insurance Co., clucks that 48 million Americans are overweight.

Through previous centuries, eating changed by nearly imperceptible degrees, and mostly toward just getting enough. Now big forces buffet food. For the first time in history, the U.S. has produced a society in which less than one-tenth of the people turn out so much food that the Government's most embarrassing problem is how to dispose inconspicuously of 100 million tons of surplus farm produce. In this same society, the plain citizen can with an average of only one-fifth his income buy more calories than he can consume. Refrigeration, automated processing and packaging conspire to defy season and banish spoilage. And in the wake of the new affluence and the new techniques of processing comes a new American interest in how what people eat affects their health. To eat is human, the nation is learning to think, to survive divine.

Fads, Facts . . . Not all the concern for health is well directed. From the fusty panaceas of spinach, eggs and prunes, the U.S. has progressed to curds, concentrates and capsules. Each year, reports the American Medical Association, ten million Americans spend $900 million on vitamins, tonics and other food supplements. At juice bars in Los Angeles' 35 "health" stores, a new sensation is a pink, high-protein cocktail, concocted of dried eggs, powdered milk and cherry-flavored No-Cal, which sells for 59 cents per 8-oz. glass. Grocery stores sell dozens of foods that boast of having almost no food value at all.

But a big part of the public wants to know facts about diet and health, and a big group of U.S. scientists wants to supply them. The man most firmly at grips with the problem is the University of Minnesota's Physiologist Ancel Keys, 57, inventor of the wartime K (for Keys) ration and author of last year's bestselling *Eat Well and Stay Well.* From his birch-paneled office in the Laboratory of Physiological Hygiene, under the university's football stadium in Minneapolis ("We get a rumble on every touchdown"), blocky, grey-haired Dr. Keys directs an ambitious, $200,000-a-year experiment on diet, which spans three continents and seven nations and is still growing. Pursuing it, he has logged 500,000 miles, suffered indescribable digestive indignities, and meticulously collected physiological data on the health and eating habits of 10,000 individuals, from Bantu tribesmen to Italian *contadini.* He has measured the skinfolds (the fleshy areas under the shoulder blades) of Neapolitan firemen, studied the metabolism of Finnish woodcutters, analyzed the "mealie-meal" eaten by Capetown coloreds, and experimented on Minneapolis businessmen.

. . . *And Fats.* Keys's findings, though far from complete, are likely to smash many an eating cliché. Vitamins, eggs and milk begin to look like foods to hold down on (though mothers' milk is still the ticket). Readings of the number of milligrams of cholesterol in the blood, which seem to have value in predicting heart attacks, are becoming as routine as the electrocardiogram, which can show that the heart has suffered a symptomatic attack. Already many an American knows his count, and rejoices or worries depending on whether it is nearer 180 (safe) or 250 (dangerous).

Out of cholesterol come Keys's main messages so far:

• Americans eat too much. The typical U.S. daily menu, says Dr. Keys, contains 3,000 calo-

ries, should contain 2,300. And extra weight increases the risk of cancer, diabetes, artery disease and heart attack.

• Americans eat too much fat. With meat, milk, butter and ice cream, the calorie-heavy U.S. diet is 40 per cent fat, and most of that is saturated fat—the insidious kind, says Dr. Keys, that increases blood cholesterol, damages arteries, and leads to coronary disease.

Obesity: A Malnutrition. Throughout much of the world, food is still so scarce that half of the earth's population has trouble getting the 1,600 calories a day necessary to sustain life. The deficiency diseases—scurvy, tropical sprue, pellagra—run rampant. In West Africa, for example, where meat is a luxury and babies must be weaned early to make room at the breast for later arrivals, a childhood menace is *kwashiorkor*, or "red Johnny," a growth-stunting protein deficiency (signs: reddish hair, bloated belly) that kills more than half its victims, leaves the rest prey for parasites and lingering tropical disease.

In the well-fed U.S., deficiency diseases have virtually vanished in the past 20 years. Today, as Harrison's *Principles of Internal Medicine*, a standard internist's text, puts it, "The most common form of malnutrition is caloric excess or obesity."

Puritan New England regarded obesity as a flagrant symbol of intemperance, and thus a sin. Says Keys: "Maybe if the idea got around again that obesity is immoral, the fat man would start to think." Morals aside, the fat man has plenty to worry about—over and above the fact that no one any longer loves him. The simple mechanical strain of overweight, says New York's Dr. Norman Jolliffe, can overburden and damage the heart "for much the same reason that a Chevrolet engine in a Cadillac body would wear out sooner than if it were in a body for which it was built." The fat man has trouble buying life insurance or has to pay higher premiums. He has—for unclear reasons—a 25 per cent higher death rate from cancer. He is particularly vulnerable to diabetes. He may find even moderate physical exertion uncomfortable, because excess body fat hampers his breathing and restricts his muscular movement.

Physiologically, people overeat because what Dr. Jolliffe calls the "appestat" is set too high. The appestat, which adjusts the appetite to keep weight constant, is located, says Jolliffe, in the hypothalamus—near the body's temperature, sleep and water-balance controls. Physical exercise raises the appestat. So does cold weather. In moderate doses, alcohol narcotizes the appestat and enhances appetite (the original reason for the cocktail); but because liquor has a high caloric value—100 calories per ounce—the heavy drinker is seldom hungry. In rare cases, diseases such as encephalitis or a pituitary tumor may damage the appestat permanently, destroying nearly all sense of satiety.

Food for Frustration. Far more frequently, overeating is the result of a psychological compulsion. It may be fostered by frustration, depression, insecurity—or, in children, simply by the desire to stop an anxious mother's nagging. Some families place undue emphasis on food: conversations center on it, and rich delicacies are offered as rewards, withheld as punishment. The result, says Jolliffe: "The child gains the feeling that food is the purpose of life." Food may act as a sedative, giving temporary emotional solace, just as, for some people, alcohol does. Reports Dr. Keys: "A fairly common experience for us is the wife who finds her husband staying out more and more. He may be interested in another woman, or just like being with the boys. So she fishes around in the cupboard and hauls out a chocolate cake. It's a matter of boredom, and the subconscious feeling that she is entitled to something, because she's being deprived of something else."

For the army of compulsive eaters—from the nibblers and the gobblers to the downright gluttons—reducing is a war with the will that is rarely won. Physiologist Keys flatly dismisses such appetite depressants as the amphetamines (Benzedrine, Dexedrine) as dangerous "crutches for a weak will."

Keys has no such objections to Metrecal, Quaker Oats's Quota and other 900-calorie milk formulas that are currently winning favor from dieters. "Metrecal is a pretty complete food," he says. "It contains large amounts of protein, vitamins and minerals. In the quantity of 900 calories a day, anyone will lose weight on it—20, 30 or 40 lbs." But Keys worries that the Metrecal drinker will never make either the psychological or physiological adjustment to the idea of eating smaller portions of food.

That Remarkable Cholesterol. Despite his personal distaste for obesity ("disgusting"), Dr. Keys has only an incidental interest in how much Americans eat. What concerns him much more is the relationship of diet to the nation's No. 1 killer: coronary artery disease, which accounts for more than half of all heart fatalities which kill 500,000 Americans a year—twice the toll from

all varieties of cancer, five times the deaths from automobile accidents.

Cholesterol, the cornerstone of Dr. Keys's theory, is a mysterious yellowish, waxy substance, chemically a crystalline alcohol. Scientists assume that cholesterol (from the Greek *chole*, meaning bile, and *stereos*, meaning solid) is somehow necessary for the formation of brain cells, since it accounts for about 2 per cent of the brain's total solid weight. They know it is the chief ingredient in gallstones. They suspect it plays a role in the production of adrenal hormones, and they believe it is essential to the transport of fats throughout the circulatory system. But they cannot fully explain the process of its manufacture by the human liver. Although the fatty protein molecules, carried in the blood and partly composed of cholesterol, are water soluble, cholesterol itself is insoluble, and cannot be destroyed by the body. "A remarkable substance," says Dr. Keys, "quite apart from its tendency to be deposited in the walls of arteries."

When thus deposited, Keys says that cholesterol is mainly responsible for the arterial blockages that culminate in heart attacks. Explains Keys: As the fatty protein molecules travel in the bloodstream, they are deposited in the intima, or inner wall of a coronary artery. The proteins and fats are burned off, and the cholesterol is left behind. As cholesterol piles up, it narrows, irritates and damages the artery, encouraging formation of calcium deposits and slowing circulation. Eventually, says Keys, one of two things happens. A clot forms at the site, seals off the flow of blood to the heart and provokes a heart attack. Or (more commonly, thinks Keys) the deposits themselves get so big that they choke off the artery's flow to the point that an infarct occurs: the heart muscle is suffocated, cells supplied by the artery die, and the heart is permanently, perhaps fatally injured.

Fats & Coronaries. Ordinarily, the human liver synthesizes only enough cholesterol to satisfy the body's needs—for transportation of fats and for production of bile. Even eggs and other cholesterol-rich foods, eaten in normal amounts, says Dr. Keys, do not materially affect the amount of cholesterol in the blood. But fatty foods do.

During World War II, doctors in The Netherlands and Scandinavia noted a curious fact: despite the stresses of Nazi occupation, the death rate from coronary artery disease was slowly dropping. Not until long after the war—1950, in fact—did they get a hint of the reason. That year, Sweden's Haqvin Malmros showed that the sinking death rate neatly coincided with increasingly severe restrictions on fatty foods. That same year the University of California's Dr. Laurance Kinsell, timing oxidation rates of blood fats, stumbled onto the discovery that many vegetable fats cause blood cholesterol levels to drop radically, while animal fats cause them to rise. Here Keys and others, such as Dr. E. H. Ahrens of the Rockefeller Institute, took over to demonstrate the chemical difference between vegetable and animal fats—and even between different varieties of each.

All natural food fats fall into one of three categories—saturated, mono-unsaturated and poly-unsaturated. The degree of saturation depends on the number of hydrogen atoms on the fat molecule. Saturated fats can accommodate no more hydrogens. Mono-unsaturated fats have room for two more hydrogens on each molecule, and the poly-unsaturated fat molecule has room for at least four hydrogens.

The three fats have similar caloric values (about 265 calories per ounce), but each exerts a radically different influence on blood cholesterol. Saturated fats in meat and dairy products promote production of cholesterol in quantities too large for the body to excrete. Mono-unsaturated fats (predominant in olive oil, most margarines) have no apparent effect at all on blood cholesterol levels. Poly-unsaturated fats, such as those in corn, cottonseed or fish oils, on the other hand, actually lower cholesterol by increasing the excretion of bile acids.

Marbled Meat. Thus, says Physiologist Keys, the big cut in reducing U.S. fat intake should come in the popular saturated fats which, although more expensive, have become a bigger and bigger part of the American diet. Restaurants take pride in heavily marbled meat. Most margarine manufacturers convert liquid fats into partly saturated solids by "hydrogenating" them —that is, by forcing hydrogen atoms onto the liquid fat molecules. Dairy farmers are paid more for milk with high butterfat content. Keys is a milk drinker himself—but only of modified skim milk that contains a maximum of 2 per cent butterfat.

Proof in Tests. Neither Keys nor anyone else claims to know the whole complex chemical-mechanical story of cholesterol deposition, but he regards the cause-and-effect relationship between cholesterol and heart disease as proved. In 1946, long before Keys suspected that this relationship existed, he and Dr. Henry Taylor persuaded 286 Minneapolis-St. Paul businessmen, then aged 45 to 54, to submit to painstaking, yearly physical examinations. The idea: to

see if the onset of ailments in general could be accurately forecast by physiological measurements, *i.e.*, weight, blood pressure, electrocardiogram, cholesterol count. So far, among other diseases, 27 of the businessmen have suffered heart attacks, 16 of them fatal. The common element in 18 of the cases was high (240-360) cholesterol levels. Moreover, it was the only significant common element. The electrocardiograph, says Keys, "doesn't hurt anybody and looks impressive in a doctor's office," but it is a poor predictor of coronary disease.

Later, Keys studied the eating habits and coronary death rates of middle-aged Japanese — in Japan, Hawaii and California. The native Japanese, he reports, get only 13 per cent of their calories from fats. They eat a high-carbohydrate diet of rice, fish and vegetables, have an average cholesterol count of 160. The Hawaiian Japanese, on the other hand, also eat fish, along with meat, eggs and dairy products; they get 32 per cent of their calories from fats, have an average cholesterol count of 223. The Los Angeles Nisei's diet is typically American; they get 45 per cent of their calories from fatty foods, and their average cholesterol count is 248. For every one heart attack in Japan, Keys notes, the Hawaiian Japanese have four, the Los Angeles Nisei ten.

"I've Got 5,000 Cases." Though Keys's theory gained sanction from the American Heart Association last month (TIME, Dec. 26), it is still questioned by some other researchers with conflicting ideas of what causes coronary disease. The main difference is that they variously blame hypertension, stress, smoking and physical inactivity, while Keys gives these causes only minor roles. But the army of Keys supporters is growing. Some of them are converted skeptics, like Heart Specialist Irvine Page (TIME cover, Oct. 31, 1955), who, with Harvard Nutritionist Frederick Stare and others, drafted the A.H.A.'s position paper. Keys's chief weapon has been the sheer weight of solid statistics. Says one Philadelphia physician: "Every time you question this man Keys, he says, 'I've got 5,000 cases. How many do you have?' "

Keys gets his cases all over the world. A doggedly inquisitive scientist, he is as familiar a figure in the vineyards of Crete, the mountains of Dalmatia and the forests of Finland as he is on the University of Minnesota campus. Money to support his wide-ranging studies comes from the U.S. Public Health Service ($100,000 a year), the American Heart Association ($17,000), the International Society of Cardiology, six foreign governments and about a dozen other no-strings sources. One of his chief fund raisers is Dr. Paul Dudley White, President Eisenhower's heart specialist, who, together with Mrs. White and Mrs. Keys, has traveled widely with Keys on foreign research missions. Keys used to get money also from the National Dairy Council and American Meat Institute. Shrugs Keys: "They didn't like my findings."

Three Breakfasts a Day. A man whose interest in food is sybaritical as well as clinical, Ancel Keys tends to regard his own life as one long experience of culinary concern. As a child in Berkeley, Calif., he satisfied his early (and still strong) yen for fresh fruits by stealing apples, apricots and cherries from neighborhood orchards. Meals at home were varied and imaginative—"Mother was reputed to be a great cook"—but Ancel was not home much. Bright but unbridled, he disliked school, at ten spent three days camping with two young friends on the slopes of nearby Grizzly Peak. "We didn't see a solitary soul," says Keys. "Just hiked and ate. Three breakfasts a day—Aunt Jemima pancakes, dried prunes and bacon. Not too bad a diet. You can eat anything for a few days."

Already his present height (5 ft. 7½ in.) at 13, Ancel "sort of stopped growing." But he did not stop eating. "I was always ready to eat," he says. "Chinatown was wonderful: an egg roll and two bowls of chow fan for 40 cents. A little concentrated on the calories, perhaps." Precociously peripatetic at 15, Ancel spent the summer in a lumber camp, left school midway through the year to shovel bat manure in an Oatman, Ariz. cave. "Great fun," says Keys. "I slept out in the desert with the other desert rats. I'd hate to think what we ate. Stews and sourdough bread, I guess."

From a short hitch as assistant powder monkey in a Colorado gold mine, Keys came home with a new straw hat and $75—and finally stayed long enough to finish high school. A budding chemist in his freshman year at the University of California at Berkeley, he loaded up with brain-crushing courses (chemistry, physics, calculus, German, Chinese, English), worked 30 hours a week in the university library, took his classmates for "$20 or $30 a month" playing bridge, and kept a big bag of dried apricots beside his dormitory bed. That spring, embittered by his failure to capture the chemistry department's sole scholarship, Keys signed on as an oiler aboard the *President Wilson*, bound for China, and quickly dispensed with nutritional niceties. "The diet was mainly alcohol," he says. "I don't remember eating anything." Back again at Cal,

Keys switched to economics, graduated in two years, went to work for Woolworth, quit in boredom after eight months and returned to the university. Although he had never before taken a college biology course, [he] entered the school of zoology, completed a major in six months.

Up, Down & Around. Three years and a Ph.D. later, Keys headed for Europe on a National Research Fellowship and began a seven-year odyssey that took him to Copenhagen to study under Nobel Prize-winning Biochemist August Krogh, to Cambridge University for another degree, to Harvard for human-fatigue experiments, and to an 18,000-ft. peak in the Chilean Andes for high-altitude studies of miners. Then he landed at the Mayo Clinic, where he found himself "in a real medical environment" for the first time. Dr. Keys also found his wife-to-be, Margaret Haney, when he interviewed—and hired—her for a medical technologist's job at Mayo. By 1940 Keys had moved to the University of Minnesota to open and head its Laboratory of Physiological Hygiene. His broad franchise: "To try to find out why people got sick before they got sick."

An early riser (6:45 in winter, 5:30 in summer), Dr. Keys eats a leisurely breakfast—half a grapefruit, dry cereal with skim milk, unbuttered toast, jam and coffee. Then, brown paper lunch bag on the seat beside him, he drives to work in a two-toned Karmann-Ghia. Although lunch is slim—a sardine sandwich, an olive, a cooky and a glass of skim milk—Keys eats with deliberate slowness. "I don't like to insult food," he says. Lunch done, he sits back, closes his eyes, and goes to sleep for exactly ten minutes in his office chair.

In the Keyses' French provincial home on the shore of Lake Owasso in the St. Paul suburb of Shoreview, dinner is a neatly scripted ritual, played to soft Brahms and candlelight, that often lasts for two hours. At first, recalls Keys, Margaret was not much of a cook: "She fed me—but she was pretty inexperienced." She learned; the walls of kitchen and den are lined with 254 cookbooks, not counting copies of *Eat Well and Stay Well,* for which Mrs. Keys supplied 200 tasty recipes.

The Keyses do not eat "carving meat"—steaks, chops, roasts—more than three times a week, and a single entré normally is not repeated more than once every three weeks. For cocktails they have martinis or negronis (¼ gin, ¼ Campari bitters, ¼ sweet or dry vermouth, ¼ soda water, over ice in an old-fashioned glass). The typical Keys dinner contains 1,000 calories, only 20 per cent of which come from fats of any kind, 5 per cent from saturated fats. A sample menu: *pasta al brodo* (turkey broth with noodles), veal *scallopine a la Marsala,* fresh green beans, homemade Italian bread (no margarine or butter), cookies, a tossed salad (dressed with tarragon vinegar and corn oil), espresso coffee and fruit.

No-Cal & Nonsense. One of the paradoxes of this era of affluence is that such civilized dining ceremony is not everybody's lot. Prosperity and faddism, suggests the A.M.A.'s Dr. Philip White, go hand in hand. "People are able and willing to seek the easy way out. Today they have the money and leisure time to indulge themselves, and they have been conditioned by the dramatic progress of medicine in the past few decades to believe that almost any pill, capsule or tonic is a miracle drug. People are disease conscious, and their fears about disease set them up for exploitation by the pseudo-scientific huckster."

Most fads are short-lived and harmless. Even the worst usually harms only a relatively few susceptible people. But fads encourage distrust of doctors and self-diagnosis. In such an atmosphere of skepticism, it is difficult for a physician to convince a patient who feels fine that he must give up something he likes, to preserve his health. Yet, says Dr. Keys, that is exactly what many Americans should do. The average blood cholesterol count among middle-aged (40-60) U.S. men, says Keys, is an uncomfortable 240. "People should know the facts," he says. "Then if they want to eat themselves to death, let them."

Drugs? There is no effortless way to control cholesterol, warns Dr. Keys. Some drugstores peddle bottles of artificially flavored safflower seed oil emulsion (poly-unsaturated fat), suggest drinking it by the spoonful to offset the effects of saturated fat in the diet. Says Keys: "Nonsense. All this does is to increase the total fat intake and breed obesity." Although poly-unsaturated fats are a healthful substitute for saturated fats, they make an ineffective antidote. It takes more than 2 oz. of poly-unsaturated fat, says Keys, to reduce blood cholesterol by the same amount that 1 oz. of saturated fat increases it.

Widely touted preparations such as triparanol and nicotinic acid (one of the B vitamins, also called niacin) do lower blood cholesterol, but they have undesirable side effects. Triparanol interferes with the liver's formation of cholesterol, forces it instead to produce a suspicious substance called desmosterol that is chemically related to cholesterol—and may even have the same

damaging effect on arteries. Nicotinic acid, to be effective, must be administered in massive doses. The result: flushing, itching, nausea, headaches, changes in the blood.

The only sure way to control blood cholesterol effectively, says Keys, is to reduce fat calories in the average U.S. diet by more than one-third (from 40 per cent to 15 per cent of total calories), and take an even sterner cut (from 17 per cent to 4 per cent of total calories) in saturated fats. He also warns against confusing the blood cholesterol level with cholesterol actually deposited in the arteries. No known diet will remove deposited cholesterol, and the object of all diets is only to keep deposits from growing to the point that they cut off the heart's blood supply.

His diet recommendations are fairly simple: "Eat less fat meat, fewer eggs and dairy products. Spend more time on fish, chicken, calves' liver, Canadian bacon, Italian food, Chinese food, supplemented by fresh fruits, vegetables and casseroles." Adds Keys: "Nobody wants to live on mush. But reasonably low-fat diets can provide infinite variety and esthetic satisfaction for the most fastidious—if not the most gluttonous—among us." On such fare, Gourmet Keys keeps his own weight at a moderate 155, his cholesterol count at a comfortable 209.

Time Marches On

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Approbation in the public press, even a cover story in *Time*, does not mean that everyone now agrees about the role of the diet in the etiology of coronary heart disease. But recollection of the skeptical indifference afforded the epidemiologic argument as I presented it ten years ago and comparison with the mounting enthusiasm of today shows that time, indeed, marches on. Acceptance by the medical and general public of the book *Eat Well and Stay Well* (Doubleday & Co.) is further evidence.

The general idea began before World War I with the Russians and Germans, who saw atheromata develop in rabbits fed carnivorous diets. But interest faded in the face of apparently fatal defects in the theory; discrepancies in reality stemming from confusion about rabbits versus people and about atherogenesis versus clinical status; failure to understand individual variability and statistical theory; and, above all, the persistence of the idea, carried over from infectious diseases, that a disease must have only a single cause.

Now multifactorial etiology is fashionable, and the argument is about how much blame to put on diet fats, the role of exercise lack, the relative importance of blood pressure and heredity, and what, if anything, to conclude about "stress." Insurance companies point to the mortality of their overweight policy holders, and the American Cancer Society notes that coronary heart disease mortality is excessive among cigaret smokers.

Fatty diets and the elevated blood cholesterol levels they induce are not the whole story, but there is much reason to believe that the majority of heart attacks in middle age in the United States may be attributable to this factor. We now know a great deal about the influence of the human diet on the serum cholesterol level and predictions from controlled experiments in the laboratory are borne out in the diets and cholesterol levels of populations. A clear picture emerges when the frequency of coronary heart disease in populations is compared with the average serum cholesterol levels of those populations. By and large, an average difference of 50 mg. of cholesterol per 100 cc. of serum between populations is associated with a four- to tenfold difference in the frequency of the disease in middle age.

The importance of serum cholesterol is consistently shown in 5 follow-up studies covering 10,000 middle-aged men in the United States. Business and professional men in the Twin Cities are typical. When these men are divided into upper and lower halves of cholesterol distribution and measured in terms of clinical health, the follow-up shows a thirteen-year incidence of coronary heart disease of 154 per 1,000 men in the upper half and only 49 in the lower half. Men with serum cholesterol values over about 230 mg. per 100 cc. had 3.1 times the risk of men of the same age and occupation with lower cholesterol values.

All these follow-up studies show no important

penalty for overweight except in the 5 or 10 per cent of men at the extreme end of the overweight scale. Blood pressure, too, was less important for prognosis than cholesterol and was significant only in definite hypertension—for example, diastolic blood pressure consistently above 95 mm.

Some epidemiologists hold that the vast mountain of evidence from all sources counts as nothing in the absence of the definitive controlled experiment on massive numbers of people showing that dietary alteration alone will greatly change the attack and mortality rates. The almost inconceivable difficulty and expense of such an ideal experiment means, of course, that final judgment must be indefinitely delayed while the mortality roll increases by many millions.

No one can guarantee that a lowered cholesterol level resulting from dietary control will safeguard the man whose arteries already bear the marks of many years of hypercholesteremia. But it should be realized that most decisions in medical and public health practice have been made on far less evidence than that offered for the importance of the diet in the development of coronary heart disease.

Not all of these points are brought out in the *Time* cover story, which, incidentally, I did not write or even see before publication. The story is reasonably accurate as far as it goes. The cholesterol figures cited for the Japanese are those of the beta lipoprotein cholesterol. The Los Angeles Nisei diet should read 40, *not* 45, per cent of total calories from fats. And my own weight (nude) and serum cholesterol values for the past several years average 150 lb. and 179 mg. per 100 cc., *not* 155 and 209, respectively.

My main regret with the *Time* story is the concentration on one person. I should like to see recognition of the contributions of Drs. J. Stamler (Chicago); J. Groen and M. Toor (Israel); I. Vartiainen (Helsinki); A. Strøm (Oslo); J. Higginson, A. R. P. Walker, and A. Antonis (Johannesburg); G. Schettler (Stuttgart); T. R. Dawber (Boston); J. T. Doyle (Albany, N. Y.); I. H. Page (Cleveland); F. H. Epstein (Ann Arbor); N. Scrimshaw (Guatemala City); M. Oliver (Edinburgh); F. Stare's group at Harvard; and many others, including Dr. J. N. Morris of London, with whom I debate amiably. And real credit belongs to my own collaborators here and abroad: Drs. H. L. Taylor, J. T. Anderson, H. B. Blackburn, Francisco Grande, and E. Simonson (Minneapolis); J. Brozek (now at Lehigh, Pa.); O. Mickelsen (now at Bethesda, Md.); B. Bronte-Stewart (now at Cape Town); F. Fidanza, V. Puddu, A. del Vecchio, M. Mancini, A. Poppi, and G. Bergami (Italy); N. Kimura, M. Yoshitomi, A. Kusukawa, and H. Mori (Japan); A. S. Dontas, C. Aravanis, C. Chlouverakis, and D. Lekos (Greece); R. Buzina, B. Tiefenbach, E. Ferber, I. Mohacek, and A. Hahn (Yugoslavia); M. J. Karvonen, P. Soisalo, E. Orma, S. Punsar, and P. Rautaharju (Finland); G. Biörck and G. Blomquist (Sweden); F. Vivanco and C. Jimenez Diaz (Spain); F. S. P. van Buchem and L. Daldorp (The Netherlands); N. P. Larsen (Hawaii); and P. From Hansen (Denmark).

A host of workers assure progress while *Time Marches On.*

Operation should not ordinarily be done for ulcerative colitis until vigorous medical treatment, including full doses of corticosteroids, has been tried. If improvement does not ensue, the patient's condition should not be allowed to deteriorate by delaying surgery. If medical treatment is beneficial, later surgical treatment is made safer.

Among 131 patients with ulcerative colitis treated by one-state subtotal colectomy and ileostomy, mortality was 40 times greater for the 18 most extremely ill than for the 73 less ill patients. Mortality, morbidity, length of hospitalization, and risk of surgical perforation of the bowel were slightly greater among the 52 patients receiving steroids sometime during the year before operation. Some of the differences probably were due to the higher proportion of extreme cases of colitis in the steroid-treated group. No correlation was noted between the dose or duration of treatment and the surgical result. Undue reliance on steroids probably led to delay in operation for 3 of 15 patients becoming worse during treatment; 2 died. Delay and deterioration, with 1 fatality, also occurred in 2 patients not receiving steroids.

W. B. Ewart and J. E. Lennard-Jones: Corticosteroids in preoperative medical management of ulcerative colitis. Lancet 2:60-64, 1960.

Report of a Case

Acquired Hemolytic Anemia

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Though improved since the introduction of adrenal steroids, the management of acquired hemolytic anemia may still be difficult. The following case illustrates such a problem in which three possible means of therapy were used.

REPORT OF CASE

A 68-year-old man reported to the Mayo Clinic in November 1956 for his annual examination. He had been feeling well during the previous year; however, he thought that he might have been slightly jaundiced on occasion and that at these times his urine was darker than usual. Past history included two transurethral prostatic resections, a myocardial infarction, recurrent angina pectoris, and a stroke without apparent residual.

Physical examination showed a pale-appearing, obese man in no acute distress. Vital signs were within normal limits. The scleras were slightly icteric and the tip of the spleen was palpated just below the left costal margin. Other physical findings were essentially normal.

Laboratory observations included: hemoglobin 8.6 gm. per 100 ml. of blood; erythrocytes 2,120,000 per cubic millimeter; reticulocytes 41.4 per cent; leukocytes 9,400 per cubic millimeter; and differential count: 30 per cent lymphocytes, 6 per cent monocytes, 60.5 per cent neutrophils, 1.5 per cent eosinophils, 1.0 per cent basophils, 0.5 per cent myelocytes, and 0.5 per cent promyelocytes. Smears of the peripheral blood showed microspherocytosis, polychromasia, basophilic stippling, and a rare normoblast. Hypercellularity, normoblastic hyperplasia, and large numbers of hemosiderin-laden phagocytes were found in the bone marrow. The sedimentation rate was 42 mm. in one hour (Westergren method). Urinalysis was not remarkable. The direct reaction for serum bilirubin was negative and the indirect reaction gave a value of 3.14 mg. per 100 cc. The prothrombin time was eighteen seconds (normal seventeen to nineteen). The Coombs' test gave a positive result. A ninety-six-hour stool specimen contained 3,472 mg. (868 mg. per twenty-four hours) of fecal urobilinogen. Red-cell fragility in hypotonic saline solution was normal. No underlying explanation for the patient's hemolysis was found and a working diagnosis of idiopathic acquired hemolytic anemia was made.

In view of the patient's past history of coronary and cerebrovascular disease and his antipathy to surgical treatment, a trial of adrenal steroid therapy was undertaken initially. Satisfactory remission was induced by 10 or more mg. of methylprednisolone, as shown in the figure, and sustained during the next eight months. Then the patient complained of a severe low back pain and was admitted to the hospital. X-ray examination on admission revealed a compression fracture of the eighth thoracic vertebra. He was fitted with a back-supporting garment and dismissed with instruction to take a lessened dose of adrenal steroids.

Two months later, the patient was readmitted to the hospital, now with angina and dyspnea on trivial exertion. Increased hemolysis, a hemoglobin value of 6.5 gm., and a reticulocyte count of 24 per cent had accompanied the attempt to lower the dose of adrenal steroids. The patient was given 650 roentgen units to the spleen in 6 divided doses, on the off chance that the hemolytic process was secondary to a lymphoma. There was no apparent benefit from the radiation, so adrenal steroid therapy was resumed. After this he was asymptomatic except for some mild low back pain. However, four months later (fourteen months after the beginning of steroid therapy) the patient was again admitted to the hospital complaining of severe low back pain. X-ray examination on this admission showed the old compression fracture of the eighth thoracic vertebra and recent compression fractures of the sixth thoracic and the second lumbar vertebra. The radiologist also reported severe osteoporosis of other vertebrae.

Thirteen days later he suffered a compression fracture of the first lumbar vertebra, his fourth compression fracture. At this time the patient, although at rest in bed, coughed and fractured his sternum. The dosage of adrenal steroid hormone was again decreased and uncompensated hemolysis with severe anemia (hemoglobin value, 8.0 gm.) promptly followed. Splenectomy became obligatory and the patient acceded to this recommendation. He received his last steroid treatment in preparation for surgery. The operation was surprisingly well tolerated and all adrenal steroid treatment was discontinued by the sixth postoperative day. In the ensuing thirty-one months, the patient's concentration of hemoglobin and his reticulocyte count have remained normal, as shown in the figure.

DISCUSSION

Although it is not clear how adrenal steroid hormones bring about benefit in the treatment of acquired hemolytic anemia, Dacie believes that splenectomy should be reserved for patients who fail to respond adequately to treatment with steroid hormones or who need such large doses of the hormones for control of their hemolysis that the metabolic side effects are serious.[1] Moreover, splenectomy is not always effective.[1,2] In

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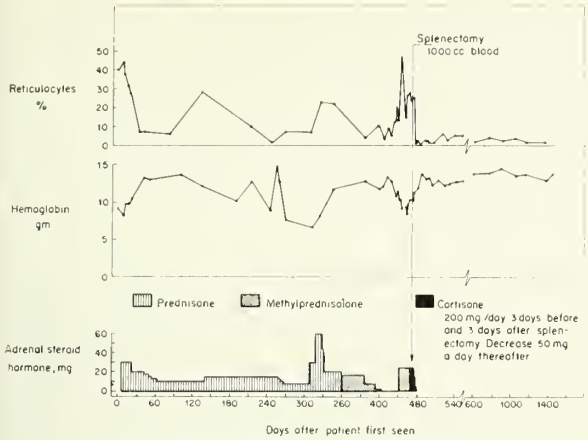

Blood findings during and after treatment.

only about half the patients are the results "good" or "fair,"[1] and often the patients in whom hemolysis is most active seem to derive the least benefit.

Young and co-workers administered adrenal steroids to 35 of 44 patients who had idiopathic acquired hemolytic anemias.[3] Two-thirds were completely relieved of anemia and one-fourth were improved, while 5 to 10 per cent were refractory. Eighteen of the original 44 patients were ultimately splenectomized. One-half to two-thirds of nonsplenectomized patients had exacerbations of hemolysis, whereas only about one-third of the splenectomized patients had recurrences of hemolysis. Ferris and co-workers subjected 71 patients with idiopathic acquired hemolytic anemia to splenectomy; of 59 patients followed up, 47, or 80 per cent, received excellent results.[2] In the group of 71, 2 hospital deaths occurred.

As seen in this case, the side effects of steroid therapy can be disabling and can rival the disease itself in its ill effects. Withdrawal of steroids under such circumstances is mandatory. Roentgen therapy to the spleen was of equivocal benefit. Splenectomy was definitive. No further pathologic fractures occurred thereafter and the patient has been active to date, more than two years postoperatively.

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A GLUTEN-FREE diet generally cures childhood celiac disease and adult idiopathic steatorrhea if strictly adhered to for six or more months. Hematologic recovery is speeded with hematinics and iron therapy, but vitamin B_{12} and folic acid are unnecessary; macrocytic anemia usually disappears when the gluten-free diet restores normal gastrointestinal tract function.

Failures may result from ingestion of foods often thought to be nonglutenous, such as sausages; baking powder; gravies and sauces; soups; mayonnaise; fish, beans, and tomatoes canned in sauces; meat extracts; malted drinks; and peanut butter. If a food is not certainly known to be free of gluten, the manufacturer should be asked. Treatment failures also may be due to bacterial enteritis. Sex, age, duration of symptoms, and occurrence of celiac disease in childhood have no effect on results of treatment in adults.

The behavior of adult idiopathic steatorrhea, or nontropical sprue, is the same as that of celiac disease. A more proper name for the former would be adult celiac disease.

J. M. French, C. F. Hawkins, and W. T. Cooke: Clinical experience with the gluten-free diet in idiopathic steatorrhea. Gastroenterology 38:592-595, 1960.

Malt Soup Extract in Treatment of Potassium Deficiency

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MILD POTASSIUM DEFICIENCY, characterized by weakness and numbness of extremities, is commonly seen when the thiazide drugs are used. Since these drugs have so many uses in medical practice—in treatment of all edema states, hypertension, toxemia of pregnancy, premenstrual tension, and so on—all physicians will see this syndrome. The more extreme manifestations of potassium deficiency—muscle flaccidity, decreased to absent reflexes, severe apathy, drowsiness, anorexia, nausea, paralytic ileus, hypotension, shallow respiration, and death—are seldom seen, but even mild deficiency may increase the toxicity of digitalis, which often is used with the thiazide group of drugs. Mild deficiency also may be serious in patients with ischemic heart disease, with which irregular rhythms are commonly seen, increasing the frequency and severity of these irregularities.

Intravenous or oral administration of potassium as a salt has certain hazards, particularly if the patient is receiving digitalis. Measurement of potassium content in the blood does not give an accurate indication of the amount of potassium needed, since most of the potassium is retained in the cells. Since potassium exerts a depressant action on the heart muscle which is more marked when the patient is digitalized, the heart may stop beating.

In my experience, most of the patients receiving long-term thiazide drugs have essential hypertension and most of them are overweight. These patients have difficulty staying within a 1,000-calorie diet, because most foods containing sufficient amounts of potassium are also relatively high in calories. For example, 1 cup of unsweetened orange juice contains 110 calories and 200 mg. of potassium. Thus, in order to obtain 1,000 mg. of potassium, a person would consume 550 calories, over one-half of the 1,000-calorie diet. Because of this problem, a food substance high in potassium and low in calories is needed. Malt soup extract, as liquid or powder, supplies 510 mg. of potassium per 2 tbs., or 1 fluidounce. Each tablespoon contains 64 calories.

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MATERIAL AND METHODS

Malt soup extract was given to 22 patients for the weakness that occurred after administration of chlorothiazide, hydrochlorothiazide, flumethiazide, or benzydroflumethiazide. The thiazide drugs originally were given in treatment of essential hypertension, with and without obvious myocardial failure; coronary artery disease with myocardial failure; advanced cervical carcinoma with local edema of one leg. This group consisted of 15 women and 7 men, ranging in age from 49 to 76 years. Analysis of these patients revealed the following facts:

1. In comparing their actual and ideal weights according to sex and height, 4 were within normal weight range, 4 were 10 per cent overweight, and the balance were 40 per cent overweight.

2. The time interval between initiation of the thiazide drugs and onset of symptoms of potassium deficiency varied from five days to eight months, with over half of the patients having symptoms within the first seven days.

3. Average weight loss during the first week was 5 lb., but some persons had no weight loss at all, so a diuresis evidently is not necessary to produce weakness.

4. Average fall in systolic blood pressure was 35 mm. Hg between first administration of the thiazide drug and onset of profound weakness; diastolic fall was 20 mm. Hg, but 2 patients had no fall in blood pressure.

5. Digitalis was administered in association with the thiazide drug to 6 patients; definite evidence of digitalis intoxication developed in 2, one with coupled beats and the other with a completely irregular rhythm, which became regular when digitalis dosage was decreased and the potassium deficiency corrected.

In all 22 patients, potassium deficiency was presumed to be present because response to the administration of 2 tbs. of malt soup extract in ½ cup of hot water twice a day occurred within twenty-four hours. All patients expressed amaze-

ment that so much improvement could take place in so short a time. Because this syndrome occurs so commonly with initiation of thiazide drugs, I do not insist that obese patients go on a restricted diet until after the first full week of treatment, and the patients are urged to eat foods which are high in potassium.

CASE REPORTS

Case 1. A 57-year-old woman, weighing 165 lb., was 28 per cent overweight and had a blood pressure of 210/120 when chlorothiazide and reserpine, 1,000 and 2.5 mg. a day, respectively, were started. Seven days later, her weight was 158¼ lb. and blood pressure was 165/95. Extreme weakness and leg cramps were noted, and the patient believed that she was having serious complications of hypertension. She took 2 tbs. of malt soup extract three times, with immediate alleviation of symptoms. She has continued taking 1,000 mg. of chlorothiazide for the last year, gradually reducing to 148 lb., without recurrence of the weakness and fatigue.

Case 2. This 49-year-old woman was 70 per cent overweight. Her blood pressure was 230/110 when 1,000 mg. of chlorothiazide with 2.5 mg. of reserpine per day was started. During the first six months, her weight dropped from 246 to 216 lb., and blood pressure fell to 130/80; suddenly, overwhelming fatigue with marked generalized weakness developed. Chlorothiazide was cut to 500 mg. daily, and the patient was given malt soup extract, 2 tbs. twice, with marked improvement within twenty-four hours. One year later, she injured her right leg and knee. Her weight was 228 lb., and blood pressure was 145/85. During the next nine days, leg swelling abated, weight dropped to 218 lb. with no change in blood pressure, and profound weakness and fatigue again developed. As before, 4 tbs. of malt soup extract relieved the weakness and fatigue.

DISCUSSION

Chlorothiazide, hydrochlorothiazide, and flumethiazide were reported by Moyer[1] to have caused potassium deficit characterized by weakness, numbness of extremities, flaccidity of muscles, hypoactive reflexes, and so forth. I have observed that benzydroflumethiazide (Naturetin) will also produce this same syndrome.

Wilkins[2] and Bartels and associates[3] state that, in using chlorothiazide for the treatment of hypertension, 40 per cent of patients had a fall in potassium, with one half of them falling below 3.5 mEq. per liter, and that the potassium deficit eventually was replaced without assistance. They were also concerned about the harmful effect of this deficit on those patients with ischemic heart disease with arrhythmias and those receiving digitalis. According to Schwartz and associates,[4] this weakness occurs most commonly within the first week or two of therapy with hydrochlorothiazide, as was also observed in the majority of my patients, but it may occur later.

The weight loss of my patients during the first weeks of thiazide treatment was similar to that shown in toxemia of pregnancy by Assali and associates.[5,6]

Freis[7] advised use of a potassium supplement with the thiazide drugs and also mentioned the gastric irritating effects of potassium salts and the danger of overdosage. Malt soup extract is an excellent source of potassium and results in immediate improvement, without waiting for the body to make a gradual adjustment over a four- to six-week period, during which time the patient would have weakness and fatigue in varying degrees.

No obvious factor that will indicate whether or not the potassium deficiency syndrome will occur after initial administration of the thiazide drugs appears to exist. However, the syndrome seems to occur most commonly in obese patients who lose large amounts of fluid within a period of a few hours to a few days. When used as the first oral liquid after the patient regains consciousness, malt soup is also of value in treating the potassium deficiency that occurs after diabetic coma.

Around the country, malts probably vary from 65 to 85 mg. of potassium per tablespoon of malt extract, whereas Borcherdt's malt soup extract contains approximately 255 mg. of potassium per tablespoon of liquid malt soup extract, according to repeated assays done by the Wisconsin Alumni Research Foundation.

CONCLUSIONS

Malt soup extract, with its controlled high potassium content, is a very satisfactory treatment for potassium deficiency syndrome as long as the patient is able to eat or drink.

It offers the potassium as food without markedly increasing the calories, which is of great importance to the obese patient on a low calorie diet or the diabetic person recovering from coma.

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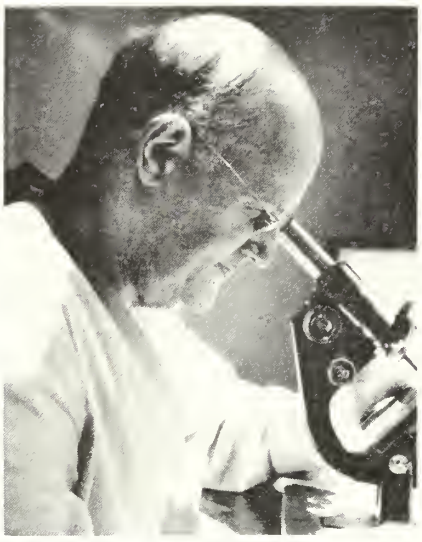

Henry W. Morris

Pioneer in Medical Photography

J. ARTHUR MYERS, M.D.

Minneapolis

MANY PERSONS who have spent their professional lives on the University of Minnesota campus have done work in a particular field which has contributed significantly to the greatness of the University. Such a figure is Henry W. Morris, whose first appearance on the campus was in 1906, when he was still a high school student. Until July 1958, when he reached retirement age, he was head of the medical photography department of the University. He took the first color photomicrograph in Minnesota to be used in medical research, and many other firsts in photography as applied to medicine and research have been his brain children. In 1906 the boy who was then a junior at East High School little knew that, with his arrival on the campus, he was to begin a career that was to cover more than a half-century of service and result in his becoming known as one of the most outstanding biological photographers of all time.

Henry Morris is a native of Minnesota, born in 1890 to Henry C. and Carrie Morris. Even before starting his long career at the University of Minnesota, Henry had selected for his life motto: "Do something that you like to do and always keep trying to do a better job." While in high school Henry worked after class hours for a druggist whose store was near the University. One day the druggist, who had admired the boy as an enthusiastic and capable worker, said to him, "Henry, I heard there is an opening for someone like yourself over in the laboratory in the pathology building. Why don't you find out about it?" Dr. Frank F. Wesbrook, who had come to the University in 1896 as a professor and who was dean in 1906, was the man Henry contacted. He was interviewed and hired.

A favorite professor at East High School, who taught classes in physics and biochemistry, had already interested Henry in these subjects. The new job proved anything but monotonous. Henry attended classes in the mornings and by 1:30 P.M. was ready to dash for the campus. "I did all of the odd jobs, did planting of cultures, and made media." His school was on Central Avenue, and, en route to the laboratory, he stopped at the post office, where he picked up the daily medical school mail. His work, on reaching the campus, included sorting and distribution of the mail.

An anecdote told at the University about Henry at the time of his graduation from high school gives an insight into his perseverance, which stood him in such good stead in his later work. With diploma in hand, Henry marched up to his favorite professor on graduation day. He said, "I have my diploma now, so I'm going to ask you something I've wanted to for a long time. I want to know why you have always pronounced the word humidity incorrectly as 'humididity?'" The astonished professor burst into laughter and said, "Henry, for eight years I have done that purposely, hoping some student would catch me. You are the only one who ever has."

When he first came to work at the University, Henry was in the original medical science building, now Wesbrook Hall, which housed the medical school, the dental school, the pathology and bacteriology departments, and a branch of the State Board of Health.

In 1907, Dean Wesbrook summoned him and said, "The time has come when we need a photographer to serve in medical and research work, and

we would like you to leave the campus for a year of study and come back a full-fledged photographer." He also told him that the photography department would be set up in a new building, soon to be erected. Dr. Wesbrook continued, "We have arranged for you to go to Rochester, New York, and study at the headquarters of the Eastman Kodak Company. Your expenses will be paid and you will have a salary of $90.50 per month." Henry accepted the opportunity. His future at the University of Minnesota was now firmly established.

The young man was not aware when he left for Rochester that it was the first such course in basic photography ever to be offered by the Eastman Kodak Company. Henry was 1 of 4 chosen students who learned basic photography by "doing" under the instruction of the Eastman experts. Another of the 4 students was Walt Disney, from Pittsburgh, whose later success is already history. After they finished their course, Henry did not meet his classmate, Walt Disney, again until 1946 at the annual national meeting of the Biological Photographic Association in Los Angeles. Henry Morris is a charter member of the organization and was a member of the Board at that time. Because of the friendship between the two, the entire delegation was invited to visit and be royally entertained at Disneyland.

When Henry finished at Rochester, he asked permission to do additional studying at Rockefeller Center in New York at the invitation of a classmate, Louis Schmidt, who had received previous training in Germany. Dean Wesbrook answered his request with the reply, "Stay as long as necessary, but come back a photographer."

While in the East, Henry made arrangements for the equipment of the new photography department, which was to be quartered in the new Institute of Pathology and State Board of Health Building. In 1907, the State Legislature had passed a bill for an appropriation of $310,000 for the new building, which was completed in 1908. The photography department occupied the third floor of the building and had a darkroom for the finishing work and a skylight for taking pictures. At that time, the allotment of $5,000 for complete equipment served ably.

Henry likes to recall that during this period the University was in a heyday of progress. By 1912, 3 new medical buildings had been completed—the Elliott Memorial Hospital in 1911, the anatomy building in 1911, and Millard Hall, named for the first dean, Perry Millard, in 1912. The Morris' son, Phillip, who is now employed by the University, was the first person to be born in Elliott Memorial Hospital.

Henry Morris is an authority on University history, as well as photography. He tells that the first faculty of medicine was appointed at the University in 1883 and that its function was to determine whether young doctors had sufficient knowledge to practice medicine. Now this job is done by special examining boards, first appointed in 1887. At that time, there were 14 medical students; by 1893, there were 82.

The first teaching faculty in medicine at the University was appointed in 1888. That year, the faculties of the Minnesota Hospital College and the St. Paul Medical College appeared before the Board of Regents with the offer to surrender their charters and tender their properties for the temporary use of the state. Soon thereafter, the Minnesota College of Homeopathic Medicine made a similar offer. In February 1908, Hamline University presented a plan whereby its department of medicine would be taken over by the University of Minnesota. Since 1908, there has been only one school of medicine in Minnesota.

From the time he returned from the East until 1909, Henry Morris pursued his duties as a medical photographer. The skills he had learned during the year of study were put into practice, and soon he was much sought after by faculty physicians, professors, and instructors. He took countless pictures of patients, both children and adults, with disease, deformities, and fractures, and of those whose cases the physician wanted to record for medical history. Many stages of research surveys were photographed and used to illustrate articles and books. Such photographs taken from x-ray films were particularly helpful in illustrating lectures. The young photographer became closely allied with the medical profession. He audited many classes in anatomy and pathology in order to become familiar with the different medical terms for the convenience of the physicians and himself in the work of medical photography.

One morning in the fall of 1909, Dr. Charles W. Mayo sent for Henry and asked, "Can you take a picture of that patient?" The satisfactory result of the photograph brought about a change in Henry's routine. He spent two weeks of each month at the Mayo Clinic and two weeks at the University of Minnesota.

In 1911, Dr. Charles W. Mayo went to Paris to accept a gold medal and a cash award in recognition of his surgery. He was allowed to bring back the medal but not the cash. While in Paris, he heard of a new color plate being used in photography called autochrome. He investigated the usefulness of the product, and $500 of the award money went into the purchase of the plate, which he brought to Henry. Dr. Mayo wanted this first commercial plate adapted for use in the field of medical photography. In 1912, Henry Morris made the first

color photomicrograph for medical history record. A short time later, he took color photographs of lesions of poliomyelitis for Dr. H. E. Robertson. These first photomicrographs were costly, as they had to be imported, but later they were commercially developed in this country. Soon the work at the University became so heavy that Henry had to give up his trips to Rochester.

As early as 1912, the success of this native Minnesotan became known, and he received the blue ribbon and certificate of achievement presented by the Royal Photographic Society. His work was exhibited in a collection sent from this country to England that year.

With the entry of the United States into World War I, Henry Morris went into service with Base Hospital No. 26, which was organized at the University of Minnesota and the Mayo Clinic. He went overseas, and his work in medical photography continued at the station behind the lines at Château-Thierry and other fronts. He was kept overseas with the medical unit until 1920. On one interesting assignment, he was sent to Oxford, England, where he took photographs of Sir William Osler in his academic robes and as a British general. These pictures may now be seen in the Army Medical Museum in Washington, D. C.

During the war, Henry's photography equipment was stored in the basement of the Institute of Anatomy building. On his return, the department had to be set up in considerably reduced space, so that films and plates were filed in a room available in the subbasement. In 1922, he and the University faculty were saddened by a great loss to medical history. Two floors of the building were inundated, including the subbasement, with the result that more than 350,000 film prints of medical photographs which he had taken were destroyed. Fortunately, however, a large number of the photographs taken were used, and thus preserved, as illustrations in the *Textbook of Pathology*, written by Dr. E. T. Bell.

In 1946, Henry Morris received a fellowship from the Biological Photographic Association, of which he was a charter member. This is the highest honor conferred by that organization and only 3 men were selected from the entire country to receive the award that year.

In 1956, Henry was honored by the Eastman Kodak Company on his fiftieth anniversary as a photographer. He was invited to Rochester, New York, and at an anniversary dinner was presented with $50 in gold pieces.

Over the long period of his career, Henry Morris has witnessed rapid progress in medicine and research, and his contributions to these advances have been numerous. He has been closely associated with many of the eminent physicians who have figured in making medical history. He has made photographic records of research projects that were first done experimentally with animals and later with human beings. He has taken copious photographs of the works of faculty members in black-and-white and in color. The most modern photographic equipment has been installed under his direction and, in recent years, high speed electronic flashes have been developed, which operate at one ten-thousandth of a second. This method permits accurate photographic recordings during operations without interruption of any of the proceedings. Even before color photography, Henry took many series of black-and-white photographs which have been used in classroom lectures and to illustrate surveys and research projects of faculty physicians.

He has known all the University presidents from Dr. William Watts Folwell, who was president emeritus when he came to the campus. He surprises people with long-forgotten facts about the University, such as that the first college of medicine was housed in a building on Seven Corners and Washington Avenue, which still stands. He also takes pride in having known several generations of University faculty, such as the Ritchie family, with 4 generations in the medical field.

The photographic headquarters was moved to the new Mayo Memorial Medical Center in 1957, and the department functions under plans recommended by Henry Morris.

I have been closely associated with Henry Morris for forty-six years, during which time he has contributed significantly to my lectures and publications. For most of that time, Miss Jean Hirsh directed the medical art shop, producing illustrations of the highest quality. When her illustrations were completed, they were often passed on to Henry, to be made into glossy photographic prints, lantern slides, and so forth. The work of these two experts was superb, and the finished products for my activities alone number in the thousands. Their work was indispensable to much of the research done at the University of Minnesota School of Medicine.

Henry Morris' suggestions to physicians as to how to get the most out of an illustration, together with his exquisite work, caused him to be recognized as a close ally of the medical profession. His professional career was a specialty, and Henry W. Morris is a very special man. Not the least important of of forty-six years of association with him has been his true and abiding friendship.

The author wishes to thank Miss Dorothy Riley for her assistance in the preparation of this manuscript.

Book Reviews . . .

Communicable and Infectious Diseases

FRANKLIN H. TOP, M.D., *1960. St. Louis: C. V. Mosby Company. 768 pages. Illustrated. $20.00.*

This is a thorough and completely up-to-date textbook of communicable and infectious diseases, with contributions from 21 specialists. The book is well bound and printed. There are 15 color plates and 122 black-and-white pictures and other figures.

The 63 chapters in the volume include not only the common contagious diseases but such conditions as leprosy, malaria, leptospirosis, granuloma inguinale, trachoma, chancroid, lymphogranuloma inguinale, and others. A unique feature of the volume is the section on infection and immunity, epidemiology, regulations governing control of communicable diseases, specific prevention of particular communicable diseases, serum and serum reactions, communicable diseases in the hospital, and chemotherapeutic and antibiotic agents. These chapters are basic and are especially pertinent at a time when resistant staphylococcal infections are emerging in hospitals, making attention to isolation technic and other preeautions of paramount importance. The chapter on chemotherapeutic and antibiotic agents should be of particular interest and value to the practicing physician.

Top has divided the book into 2 sections. Section 1 has already been referred to and is titled, "General Considerations Applicable to Communicable Diseases." Section 2 is headed, "Communicable and Infectious Diseases Classified by Common Portal of Entry." Diseases entering by way of the respiratory tract, the gastrointestinal tract, and the mucous membranes or skin are considered in this section. Top has attempted to classify diseases which may enter the body by more than one portal according to the more common or more important portal of entry. Thus, although it is established that poliomyelitis, in its early stages, may also be spread by way of the respiratory tract, it is listed under diseases entering by way of the gastrointestinal tract.

The chapter on poliomyelitis is worth special mention, as it goes beyond the usual textbook description of the disease and is illustrative of the completeness of the entire book. In addition to the customary outline and discussion of history, symptomatology, prevention, and treatment, Top also includes a lucid explanation of the Kenny concept of the disease, together with critical comments. There is also a detailed description of hot packing technic, physiotherapy, and the use of bed and foot boards and explicit information concerning the use of the respirator, which usually is difficult to find.

This volume is recommended as a valuable addition to the library of every general practitioner, pediatrician, and internist, as a reference and for study and review.

L. G. PRAY, M.D.
Fargo, North Daktoa

Clinical Use of Aldosterone Antagonists

FREDERIC C. BARTTER, M.D., *editor, 1960. Springfield, Ill.: Charles C Thomas. 208 pages. Illustrated. $5.00.*

This symposium pools the preliminary results of studies by 23 investigators on the clinical and metabolic effects of aldosterone antagonists in man. The mechanisms of action of these agents, spirolactones, are explained. Data demonstrate that sodium excretion is promoted through the mechanism of aldosterone antagonism. Considerable metabolic data of exceptionally good quality show the effect of these agents in normal and abnormal patients. Results are presented of the use of aldosterone antagonists in patients with cirrhosis and ascites, cardiac failure and edema, hypertension, nephrosis, and unexplained edema. Limitations and contraindications are also defined.

The book is well assembled, with excellent reproductions of metabolic charts. It is easy to read, and the discussions are helpful. The book is of value for physicians or students interested in problems of renal and electrolyte metabolism and for clinical investigators in these and related fields.

B. J. KENNEDY, M.D.
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Cardiac Auscultation

J. S. BUTTERWORTH, M.D., MAURICE R. CHASSIN, M.D., ROBERT MCGRATH, M.D., *and* EDMUND H. REPPERT, M.D., *1960. New York: Grune & Stratton, 98 pages. Illustrated. $6.25.*

The chief value of this primer on heart sounds lies in the illustrations. Every clinical situation discussed is illustrated by a phonoeardiogram or a drawing, usually on the same page as the discussion. The result is that the points of the authors are most forcefully presented with the double impact of the word and the picture. The subject of cardiac auscultation certainly is adequately, even admirably, covered.

One criticism of a volume of limited scope such as this is the tendency to overemphasize the importance of the modality under discussion. For instance, in discussing the Austin Flint murmur, the book mentions "helpful points in the differentiation . . . from mitral stenosis are the absence of an opening snap of the mitral valve and of an accentuated pulmonic component of the second sound." Perhaps this suffices for a thesis on auscultation, but it is a narrow-minded clinician indeed who depends only or even primarily upon auscultation for this differentiation. The left ventricular type of electrocardiogram in aortic insufficiency and the characteristic shape of the heart in various projections with the barium-filled esophagus are most important differential points.

I question the differentiation of insufficiency versus incompetence arbitrarily set up by the authors. Incompetence of a valve, they maintain, occurs with a normal valve subjected to external forces, such as a dilated valve ring. Insufficiency is reserved for the deformed valve. This is stretching the meaning of words beyond their power to differentiate, since no one can doubt that an incompetent valve is insufficient, and vice versa.

The format of the book is to present the sounds heard in various diseases. It would have been helpful to present, also, the physical findings as the clinician sees them, that is, to start with the physical finding and explore the possibilities from there.

These somewhat carping criticisms should not ob-

secure the fact that this is an excellent treatise recommended for anyone interested in a review of this most artful skill of the physician.

REUBEN BERMAN, M.D.
Minneapolis

Electroencephalography in Anesthesiology

ALBERT FAULCONER, JR., M.D., *and* REGINALD G. BICKFORD, M.D., *1960. Springfield, Ill.: Charles C Thomas. 90 pages. Illustrated. $4.75.*

During administration of general anesthesia, recognition of the depth of anesthesia usually is important. Use of the electroencephalogram about ten years ago demonstrated that depth of anesthesia could be recognized; servo anesthetizers were tried and made to work. As new agents were introduced, more and more were studied.

This book is worthwhile reading for members of the surgical team. The authors are to be commended for preparing *Electroencephalography in Anesthesiology* so that this particular phase of surgery may be firmly and permanently established.

JOHN S. LUNDY, M.D.
Chicago

Cancer in Families

DOUGLAS P. MURPHY, M.D., *and* HELEN ABBEY, M.D., *1959. Cambridge, Mass.: Harvard University Press. 76 pages. $2.50.*

In this comprehensive and detailed study of 200 living women with breast cancer and approximately 6,000 relatives of 2 generations, no evidence of unusual frequency of cancer of the breast or of other sites was found. The control group of 198 living women and an approximately equal number of relatives as the cancer group was investigated in the same thorough manner. These findings are of considerable interest, because they differ from several previous reports that have all seemed to agree that breast cancer occurs with unusual frequency in relatives of patients with this disease. The previously published disagreement has been whether or not cancer in general appears to be increased among relatives of breast cancer patients.

The study is based on data collected after the events have occurred. The initial study population of cancer and control groups was investigated over a thirty-eight-month period, beginning in February 1949. The resurvey, undertaken to also include male relatives not listed initially, began December 1952 and continued for thirty-seven months. Four field workers conducted both surveys. The second survey uncovered additional female relatives, in approximately equal numbers in both control and cancer groups, but no significant alteration of incidence of cancer.

The authors have presented their methods and findings in detail, as evidenced in 35 tables covering as many conceivable categorical analyses as possible. They have also compared their findings with several previous surveys in an attempt to find reasons for their differences.

It is somewhat disturbing in this study to note that more cancer than expected has been found in some control groups when compared with the cancer groups. This was particularly true in 2 families. On the basis of their statistic analyses, however, the authors conclude that their study was not large enough to detect a real familial tendency to develop cancer, if such did exist. Also, they found, in certain instances, that the relationships of increase in the number of relatives with cancer to the index persons interviewed was a relatively remote one.

The impression remains, however, that there may be a higher incidence of cancer in certain families. It was not within the scope of this study to attempt to reveal factors, such as intermarriage, which might account for this impression. The book is well worth reading, nevertheless, for those interested in as thorough an investigation of this type as possible. The authors have emphasized the limitations, with the more obvious pitfalls inevitable, which they encountered in field surveys encompassing control and cancer groups. A larger study population might well reveal more indisputable answers regarding frequency of cancer in familial groups. The increased time and personnel needed could be estimated on the basis of this study.

VIRGINIA DOWNING, M.D.
Denver

Atlas of Anatomy and Surgical Approaches on Orthopaedic Surgery—Upper Extremity

RUDOLFO CONSENTINO, M.D., *1960. Springfield, Ill.: Charles C Thomas. 192 pages. Illustrated. $10.50.*

The present volume is the first of 3 to be published by Rodolfo Consentino, research associate in orthopedic surgery at the University of Iowa and originally assistant professor in orthopedic surgery at the University of LaPlata, Argentina. This volume is confined to the upper extremity; the second will be on the lower extremity, and the final one on the neck and back.

The author's intention is to demonstrate with vivid accuracy the anatomic structures of the upper extremity as encountered by the surgeon, layer by layer, from skin to bone or joint or muscle. This is not a compendium of orthopedic procedures after one reaches the bedrock problem but rather a pristine book on the anatomy and the surgical approaches to the articular and bony structures of the upper extremity.

Schematic drawings are conspicuous by their absence. To show the relationship of the skin incision to the underlying skeletal structures about the shoulder, elbow, and wrist, 12 radiographics have been included. Most of the 134 plates are excellent black-and-white photographs of the anatomic structures, beautifully laid out by an orthopedic surgeon. The labels on the plates are sharp and clear, and the legends accompanying each plate are succinct, factual, and informative.

This is a graphic recording of fundamental anatomy by a clinician. The simple approaches to easily accessible structures are omitted. In the reviewer's opinion, the unforgivable tragedy is to have this great work by a dedicated student documented in black and white in an age of high speed color presses. Even if the eventual 3 volumes were more expensive, color would enhance their beauty and usefulness.

The book is a *must* purchase for anatomists, orthopedic surgeons, traumatologists, and all general surgeons doing any but the simplest of surgical procedures on the bones and joints of the upper extremity. The book is sturdily bound in cloth; the plates and legends are clearly printed on good quality gloss paper, and the cost is vastly outweighed by the contents.

TAGUE C. CHISHOLM, M.D.
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The Journal Lancet

SERVING THE MEDICAL PROFESSION OF MINNESOTA, NORTH DAKOTA, SOUTH DAKOTA, AND MONTANA

The Time Is Now

Tuberculosis is still very much with us, as evidenced by the various articles in the current issue of *The Journal-Lancet*. The decline of tuberculosis could be accelerated if the recommendations of the Arden House Conference, sponsored by the National Tuberculosis Association and the U.S. Public Health Service, and held in December 1959, are vigorously put into operation. You will recall that last year I mentioned this conference which stressed the importance of ascertaining that every patient with tuberculosis complete his necessary treatment with the effective drugs now available.

At a press conference last spring with regard to the Arden House Conference, Dr. Rene Dubos, the famous bacteriologist of the Rockefeller Institute of New York City, stressed that "the time is now." His sense of urgency was based upon his fear of further development of resistance to the drugs on the part of tubercle bacillus. Some felt that the evidence for such misapprehensions was not too strong, but, since that time, there has been a definite increase in the frequency of encountering drug-resistant tubercle bacilli in the sputum of newly recognized tuberculosis patients who have never previously received drug treatment.

Most communities throughout the country have studied the Arden House recommendations with care and have begun to take steps to see that the recommendations are implemented. This is true of North Dakota, South Dakota, Iowa, and other areas in the midwest, but particularly in Minnesota. Taking the lead in the follow-up on the Arden House Conference, the Minnesota Thoracic Society held a two-day conference at the Lowell Inn in Stillwater, drawing up clear-cut recommendations for Minnesota. In addition to recommending additional staff in the Minnesota State Department of Health to assist in this program, specific ways were formulated for carrying out the other Arden House recommendations, including: (1) better case reporting, backed by a Tuberculosis Mortality Committee of the State Medical Association and laws to require reporting on positive specimens from pathologists and bacteriologists; (2) a state-wide case register; (3) tuberculin testing—in doctors' offices, on all school personnel, on children in certain school grades, and on admission to college or trade school; (4) chest films on all positive reactors and high incidence groups in the population; (5) free laboratory service for testing susceptibility of tubercle bacilli to drugs; (6) continued stringent surveillance of bovine tuberculosis; (7) abolition of the means test and legislation to require financial support by counties and the state of hospital treatment; (8) an infectious disease committee of the hospital association to prepare a standard technic for isolation of patients with active tuberculosis; and (9) a program for protection of hospital personnel with BCG, to be used only wherever a nonreactor to tuberculin might be exposed to infection.

The report from this conference resulted in a joint statement by the Minnesota State Medical Association (Pulmonary Committee), Minnesota Thoracic Society, the Minnesota Tuberculosis and Health Association, and the Minnesota Chapter of the College of Chest Physicians. In addition, the Hennepin County Medical Society has approved a detailed statement of recommendations for the control of tuberculosis within that county. A steering committee is now working at publicizing the recommendations and setting up priorities, responsibilities, and methods for carrying them out.

On the national front, the U.S. Public Health Service, in cooperation with the National Tuberculosis Association, has tackled the assignments given it by the Arden House conferees. One of the most difficult assignments, the formulation of goals and standards for the country as a whole, was carried out by a competent committee of tuberculosis workers representing such groups and agencies as the U.S. Public Health Service, the National Tuberculosis Association, state health department commissioners, city health departments, state tuberculosis associations, tuberculosis sanatoriums, physicians in private practice, and others. These goals, published in the November 1960 issue of the *NTA Bulletin*, provide for two intermediate objectives, a new active case rate by 1970 of not more than 10 per 100,000 population and for each community to control the spread of infection to the point where not more than 1 per cent of the 14-year-olds react to tuberculin.

The performance standards call for a satisfactory report to the Health Department on at least 75 per cent of the referred tuberculosis suspects within six months after the end of the initial screening operation; chest x-ray examination of at least 90 per cent of the tuberculin reactors within two months of the end of a tuberculin survey; examination of 90 per cent of the close contacts of newly discovered active cases, either by tuberculin test followed by a chest film for reactors, or by x-ray initially; a conversion of at least 75 per cent of the newly reported active cases with positive findings to a negative bacteriologic status within six months of the date of the new case report; at any given time, at least 90 per cent of all the known active cases in the hospital or under drug treatment elsewhere; and finally, at any given time, at least 80 per cent of all cases at home with active disease at last report to have had a bacteriologic examination within the preceding six months.

Comparable committees are at work formulating guides for the evaluation of case detection programs and for the reporting of cases of tuberculosis.

On the international front, the Thirteenth World Health Assembly, held in Geneva in May 1960, supported the recommendation of the International Union Against Tuberculosis that the World Health Organization "now accept as another target to receive top priority and emphasis, the elimination of tuberculosis as a public health problem throughout the world" and decided "to intensify the tuberculosis control program and to bring about the eventual disappearance of tuberculosis as a public health problem." The Assembly also requested the director-general of WHO to prepare a concrete plan for the intensification of the control of tuberculosis for submission to the fourteenth World Health Assembly, held in New Delhi, India, in February 1961. The scientific theme for this World Health Assembly was the control of tuberculosis. Representatives from over 100 countries attended this Assembly and the discussions should assist in accelerating the elimination of tuberculosis as a public health problem throughout the entire world.

James E. Perkins, M.D.
Managing Director
National Tuberculosis Association

Tuberculosis Control in Manitoba

E. L. ROSS, M.D.

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THE CURRENT DRIVE to reduce tuberculosis to a minor cause of illness and death comes at a time of great opportunity. There is an urgency, for the advantages of today may not last for long. The momentum of ten years of remarkable progress must be more than sustained. The "big push" must not only be big, but planning should be for a long-term, continuous program. The application of our knowledge to this end should be basically the same throughout the continent but will vary according to practical considerations, the extent of the problem, and progress and organization to date.

The purpose of this paper is to demonstrate what progress can be made by applying the knowledge we have energetically and continuously through official and voluntary agencies and with the support and cooperation of the public and the medical profession. Many states in the United States can report similar progress to Manitoba, but in our province the problem may have been somewhat greater because of geographic factors and the prevalence of tuberculosis among our native Indians and half-breeds.

Manitoba, bounded on the south by Minnesota and North Dakota and extending 800 miles to the Northwest Territories, has a population of 900,000, half being in the Winnipeg metropolitan area. The vast northland is sparsely settled and devoted mainly to mining, lumbering, fishing, and trapping; the south is devoted to agriculture and industry.

NEW ACTIVE CASES

An indication of the effectiveness of tuberculosis control is the annual number of new cases. Identifying, isolating, and treating sources of infection control the spread of tuberculosis, and benefits of a comprehensive case-finding program are compounded year by year and generation by generation. Between 1955 and 1958, there was virtually no reduction in the number of new cases. In 1959, figures were much more encouraging, showing a total decrease from 331 to 258, or 22 per cent. For non-Indians, the reduction from 1958 was 18 per cent; for Indians, it was 32.6 per cent. Although the 1959 reduction is gratifying and a stimulation to more intensive effort, too much reliance should not be placed on the figures for any one year. For the previous three years, there was almost no decrease in the number of new cases, and again in 1960, there are no fewer cases.

In spite of educational efforts and tuberculin and x-ray surveys, 21 per cent of the newly reported cases are of far advanced disease. This means a less hopeful prognosis and, often, the spreading of infection to countless others. The recovery rate is good for persons between the ages of 20 and 40. In this age group were 36 per cent of the new cases but only 6 per cent of the deaths.

The distribution of new cases has a bearing on the intensity and location of preventive activities. Manitoba has 142 municipalities, of which 87, or 61 per cent, had no new active cases in 1959. Only 1 case was reported in 27 other municipalities. Winnipeg, which comprises 29 per cent of the population in Manitoba, accounted for 42 per cent of the new active cases. New Canadians who had emigrated from Central Europe since 1950 account for 12 per cent of the new cases. This is a relatively high incidence. The case rate, active and inactive, is 41 per 100,000 population. Considering only the active cases, the rate is 30 per 100,000.

Besides the new active cases, there are the known inactive cases which have become active. This is characteristic of tuberculosis and is significant because recurrence of activity usually also means recurrence of infectivity. During 1959, active disease appeared in 106 patients at home, whose disease had been classified as inactive. Since this constitutes 29 per cent of all active cases, it is evident that inactive disease requires close follow-up for a number of years. One-third were originally found by routine roentgenograms and considered not to need treatment, 25 per cent of the reactivated cases have had sanatorium treatment since 1955, and 6 per cent, pulmonary resectional surgery. Case-find-

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ng is concentrated upon high incidence groups, of which the highest are elderly people, those with a low economic status, those who are known to have had contact with a tuberculous person, and those known to have had a lesion at one time.

TUBERCULOSIS DEATHS

The decline in deaths from tuberculosis during the last fifteen years has been remarkable (table 1). Nevertheless, it should still be a matter of concern that 39 people died from this one disease in 1960, because many could have been saved if treatment had been started earlier.

In 1959, 17 of the 32 non-Indians who died from tuberculosis were 70 years of age or older. Only 3 deaths occurred in persons under the age of 40 years and none in children under 10. The preponderance of elderly non-Indian men dying of tuberculosis is the same all across Canada.

Of the total of 41 deaths, 34 were from pulmonary disease and 4 from nonpulmonary diseases (kidney and spine); 2 Indian children died of meningitis and another, of generalized tuberculosis.

Of the deaths, 29 occurred in sanatoria, 10 in general hospitals, 1 in a mental hospital, and only 1 at home. No Indians died at home—a rather marked contrast compared to twenty years ago, when most of the 166 Indian deaths occurred in crowded, unhygienic homes on the reserve.

Perhaps one wonders why 10 people died of tuberculosis in general hospitals. The reason is that, except for 3 Indians with acute and terminal meningeal or cerebral tuberculosis, all were elderly people and most had pneumonic illnesses of short duration which were not proved tuberculous until after death.

TUBERCULOSIS PREVENTION

Why are fewer people developing tuberculosis? Why are only about half as many needing sanatorium treatment as did ten years ago? Why is infection as shown by the tuberculin test becoming less and less common? The answer is that the spread of the tubercle bacillus is being controlled. There is less opportunity for infection. Early discovery means prompt treatment and saving others from infection. Antituberculosis drugs soon make the patient noninfectious and deaden the germ's power of reproduction. The year-in, year-out combing of the province by x-ray and tuberculin surveys may seem tedious—indeed, with diminishing returns, costly—but in the long run, it is paying off in health, life, and dollars saved.

Last year, Manitoba Sanatorium and the Sanatorium Board marked a half century of service to the people of Manitoba in lessening the menace of a deadly and tragic disease. Fifty years ago, tuberculosis was a scourge from which few families escaped. Infection was everywhere. At that time, emphasis was placed on building up body resistance, but, before many years, as beds for isolation and treatment increased, it became evident that people could be spared infection and subsequent illness. It was finally realized that, to control the spread of tuberculosis, we must reach out beyond the sanatorium walls. Tuberculosis has to be sought, not waited for. So, in 1926, the traveling clinics began, followed, 20 years later, by the mass x-ray surveys, which now incorporate tuberculin testing. Interest is being focused on infection, the prerequisite to disease.

Chest x-ray surveys. For many years, most of the province was covered by biennial x-ray sur-

TABLE 1
TUBERCULOSIS DEATHS FROM 1935 TO 1960

	Whites and Indians		*Whites*		*Indians*	
Year	*Rate per 100,000*	*Total deaths*	*Rate per 100,000*	*Total deaths*	*Rate per 100,000*	*Total deaths*
1935	60.8	432	38.6	269	1,258	163
1940	50.3	369	27.7	203	1,140	166
1945	12.7	344	25.1	185	793	129
1950	22.8	181	12.8	102	438	79
1955	8.5	72	6.8	56	80	16
1956	7.2	61	1.9	41	100	20
1957	7.5	65	5.1	46	90.4	19
1958	4.8	42	3.9	34	38.1	8
1959	4.6	41	3.7	32	39	9
1960	4.4	39	3.8	33	25	6

veys. But when the finding of active tuberculosis diminished to 1 case in 6,000 studied by x-ray, we began to concentrate on areas with a higher prevalence of disease. In 1959 and 1960, half the number of residents were studied by x-ray as compared with 1958. This decrease was compensated for by tuberculin testing.

All new cases for the past three years were charted by municipalities. This chart serves as a guide in determining where traveling clinics and surveys are most needed. It is surprising, and certainly gratifying, to observe what can be accomplished by intensive effort. Five years ago, 2 small districts with a predominantly half-breed population were our worst areas of infection, with as many as 10 cases appearing in a year. Since then, we have held 2 or 3 clinics there annually, including the vaccination of a number of residents with BCG. This past year there were no new cases.

Out of 63,184 non-Indians in the x-ray surveys, only 15 were found with active disease—about 1 in 4,200. When the 26 with inactive lesions are included, the catch is 1 in 1,500. Of 14,983 Indians studied by x-ray, only 3 had new active disease. The Indian population is 24,000, with over half of them scattered throughout the North and accessible only by plane. Twenty years ago, their death rate was over 1,200 per 100,000; ten years ago, 438; and now, 25. By surveying 15,000 of them yearly and treating in hospital all active cases, progress has been remarkable.

Tuberculin testing. Most people infected with the tubercle bacillus do not develop manifest disease. Because the tuberculin test, as far as infection goes, distinguishes the "haves" from the "have nots," the latter are screened out and only the former need chest films. All people over 40 are given x-ray examinations, however, because of the higher prevalence of nontuberculous conditions.

The tuberculin test is not new; it has been in use for over sixty years. What is new is its application on a mass scale. When infection rates are low, the test is of increased importance in the differential diagnosis of respiratory diseases. Applied to large population groups, its value is also epidemiologic, as it is the most accurate measurement of the infection rate.

During 1959, the total population tuberculin-tested on surveys was 81,749. A total of 7,679, or 9.3 per cent, did not return for a reading of their test. In 1960, 110,000 were tuberculin-tested by the Sterneedle method, but at the time of writing, an analysis has not been completed.

TABLE 2

INCIDENCE OF TUBERCULOSIS IN 24 MUNICIPALITIES ACCORDING TO HEAF TEST

Age group	*Number negative*	*Number positive*	*Per cent positive*
0- 1	528		
1- 4	6,102	17	.27
5- 9	11,149	95	.85
10-14	9,883	361	3.54
15-19	4,934	329	6.25
20-24	1,894	325	14.6
25-29	2,317	635	21.5
30-34	2,496	1,144	31.4
35-39	2,468	1,636	39.8
40-44	1,969	1,750	44.0
45-49	1,515	1,623	51.7
50-54	915	1,442	61.1
55-59	622	1,182	65.5
60-64	450	874	66.4
65-69	384	831	68.3
70 and over	633	918	59.1
Totals	48,259	13,162	21.4

Heaf test. The largest group surveyed in 1959 consisted of 24 municipalities, in which 61,421 tests were read. It will be noted in table 2 that few children today under the age of 10 are infected—only a fraction of 1 per cent have a positive test. From 15 to 19 years of age, the percentage is 6.25; from 20 to 24, 14.6. Up to the age of 50, there is a steady rise to about 50 per cent. From 65 to 69, the tuberculin-positive rate is 68.3 per cent, but this can be expected, as most of these people in their younger years had a greater chance of becoming infected. It is of interest that the rate decreases slightly for persons over 70. This may indicate a loss of sensitivity to tuberculin and may have a bearing on the increased incidence of disease among the elderly. Infection rates are a little higher in Winnipeg than in the rural or suburban municipalities.

The over-all average of positive tests for the 61,421 tested is 21.4 per cent. Most of the tuberculosis in the next twenty-five years will come from this percentage, so they will require closer following. A tuberculin registry is kept on these reactors.

I mentioned before that tuberculin testing is not new. In 1939, 3,000 rural and suburban school children were tuberculin-tested, and a comparison of the infection rate then and now is interesting. In 1939, 18 per cent of the students had a positive test, compared with 3 per cent in 1959. Although last year's group included more children in the 5- to 19-age group, the

figures do show that today, up to the age of 19, 97 per cent of the young people in this rural area have never encountered the tuberculosis germ.

For fifty years, we have concentrated on the early discovery and treatment of the disease, and this accounts for the progress attained. But now we are finally getting down to the root of the problem—infection before disease develops.

General hospital x-ray program. A program to have all patients admitted to general hospitals given chest roentgenograms was initiated ten years ago, because this large segment of our population was known to have a much higher prevalence of active tuberculosis. In 1956, five times as much tuberculosis was found in general hospitals as in community surveys. This ratio has decreased until, in 1959, there was only twice as much tuberculosis in general hospitals (1960 figures not yet available). Of the 127,081 patients admitted to general hospitals in 1959, 53,356, or 42 per cent, had chest films (table 3). In

TABLE 3
NUMBER OF PERSONS* IN 71 GENERAL HOSPITALS HAVING CHEST FILMS IN 1958 AND 1959

	1958	*1959*
Admissions	67,984	53,356
Outpatients	10,559	9,770
Hospital staff	8,171	7,229
Totals	86,714	70,355

*Admissions, outpatients, and hospital staff.

1957, chest films were taken of 68 per cent and in 1958, of 51 per cent. There are several reasons for this decrease: (1) due to the low infection rate, paucity of positive findings, and avoidance of radiation, children under 15 are excluded; (2) many persons coming into general hospitals are readmissions, and chest films are not repeated within the year; and (3) with free treatment for all in effect in general hospitals, more standard-size chest films are being ordered by physicians.

It is understood that these x-ray films are a method of screening out abnormalities which have to be assessed by further investigation. The value of this program, and, indeed, of all our surveys, is not confined to discovering tuberculosis. Many other abnormalities are drawn to attention and referred to the private physician. This is evident by the fact that, among 53,356 patients given x-ray examination on admission, 3,510 (1 in 15) had nontuberculous chest conditions, and 3,252 (1 in 16) had suggested cardiac abnormalities (table 4).

TABLE 4
RESULTS OF 1959 HOSPITAL X-RAY PROGRAM

Admissions having chest films	53,356
Apparently active	26
Inactive	459
Doubtful	67
Suspect	213
Total	765
Nontuberculous chest conditions	3,510
Cardiac abnormalities	3,252
Outpatients having chest films	9,770
Apparently active	9
Hospital staff having chest films	7,229
Apparently active	1

All case-finding methods need to be kept under constant review, and I consider that the general hospital admission films contribute to the control of tuberculosis. The program creates and maintains the interest of physicians and hospitals in tuberculosis and provides a liaison with the official tuberculosis control body. This is important because, with falling infection rates, fewer people needing treatment, and fewer people dying of the disease, professional and public concern is tending to wane.

Table 5 shows the limited extent of our BCG vaccination program. This is much the same as in previous years except for a marked reduction in vaccinations by Indian Health Services because of a change in policy. It is considered that

TABLE 5
BCG VACCINATIONS ADMINISTERED

Group	*Number*
Tuberculosis contacts	194
Medical students	3
Student nurses*	338
Student nurses†	23
Student nurses‡	78
Nurses' assistants	42
Sanatorium staff	50
Laboratory technicians	21
Others	68
Total	817
By Indian and Northern Health Services	508
Grand total	1,325

*General hospitals. †Mental hospitals. ‡Practical.

BCG provides some degree of protection if a previously uninfected person is infected with the tubercle bacillus. A mass vaccination program would not be warranted with our low infection rate. We therefore confine vaccination to those who may not be able to avoid infection. The fact that the tuberculin test is of increasing diagnostic and epidemiologic significance is a deterrent to a more comprehensive BCG program, as the vaccine artificially produces a reaction to tuberculin.

CENTRAL TUBERCULOSIS REGISTRY

The Central Tuberculosis Registry is the medical accountancy department. It records and analyzes medical and social data pertaining to all phases of tuberculosis control. The entire system is practical and economical and is essential for appraisal and direction of the tuberculosis control program, even day by day.

Records on all sanatoria patients and their contacts, as well as data on all known cases, regardless of whether or not they have had treatment, are readily available. Details are also recorded about x-ray and tuberculin surveys, new cases, and deaths. The Registry follows up all medical recommendations. Current general recommendations regarding control of tuberculosis are:

1. Tuberculin-test everyone—all ages.

2. Take chest films only of those with a positive tuberculin reaction—any age.

3. Tuberculin-test or at least take chest films of the household contacts of children with a positive tuberculin test.

4. Those with a negative tuberculin test should be retested every two years, if possible.

5. Those between 15 and 24 with a positive tuberculin test and a negative chest film should have a chest film every year. Those of other ages with a positive tuberculin test should have chest films periodically, that is, every three to five years, unless more frequent chest films are advised.

6. Those with a 4+ tuberculin reaction should have chest films again in three months and then at yearly intervals.

7. A known recent tuberculin converter or a child under the age of 3 years with a positive tuberculin test should be considered for home treatment with INH.

8. Anyone with a positive tuberculin test and any abnormal parenchymal pulmonary lesion showing in the x-ray film should have a large film and advice regarding further follow-up.

9. Anyone with a known inactive tuberculous lesion should have a chest film yearly.

10. More people in the older age groups are breaking down with tuberculosis, which emphasizes the need for awareness of this possibility. Chest x-ray and sputum examination for tubercle bacilli are still the most important diagnostic procedures.

TREATMENT

There is no doubt whatever that rest is effective against tuberculosis, and not so many years ago, strict bed rest for even slight and asymptomatic pulmonary lesions was routine treatment. However, even before the advent of chemotherapy, there was a tendency to place a little less emphasis on rest alone; indeed, the question now with chemotherapy is just how intense and for how long rest is really necessary.

Rest unquestionably is indicated in the absence of effective chemotherapy, and all chemotherapy certainly is not effective. Indeed, a recent study of 600 hospital admissions and readmissions in Ontario has shown tubercle bacilli in 28 per cent to be resistant to streptomycin, 14 per cent resistant to Isoniazid, and 6 per cent to PAS. Another sound reason for hospital rest is the opportunity afforded the patient for indoctrination and education, which is not only of immediate benefit but will contribute to maintenance of health in the future. Tuberculosis is still a chronic disease subject to periods of reactivation, and relapses, although now less frequent, still occur too often. This is evident by the fact that over 20 per cent of the active cases reported have had lesions previously considered to be inactive, although many of these had no previous treatment.

Intensive rest is secondary in importance to chemotherapy, and we no longer think of hospitalization in terms of years but rather of months. An initial period of three to six months in a tuberculosis hospital is advisable, but, apart from the first few weeks, when there may be symptoms and toxemia, rest does not need to be intensive. Another feature, of course, is that the patient is likely to be infective during this period and, if at home, would constitute a danger to the family. Hospitalization at the beginning of treatment also affords the opportunity for sensitivity studies, laboratory examinations, gastric cultures, observation for intolerance or sensitivity to drugs, and special planigraph x-ray studies, which often have a bearing on future management, especially surgery. If disease originally is bilateral and advanced, the hospitalization period will be longer.

Recent advances in our knowledge of tuberculosis and the increased effectiveness of treatment by adequate chemotherapy and resectional surgery have greatly improved the prognosis for the average patient with new disease. The patient can usually expect to return to work within the year. There are about 500 patients in Manitoba having hospital treatment now, compared

to twice this number five years ago. The number of new cases is less, but the lowered occupancy in sanatoria is mainly accounted for by shorter hospitalization periods.

Over one-third of those hospitalized for tuberculosis in Manitoba are Indians. They require full periods of treatment in sanatoria because they will not take drugs at home, home conditions are not good, and close follow-up is not possible. For these same reasons, indication for resection of residual lesions is greater among Indians.

Since the advent of effective chemotherapy as well as other measures, surgical removal of tuberculous tissue has proved to be highly effective and relatively safe. If a residual focus, especially a filled-in or open cavity, persists after three to six months of chemotherapy, resection should be considered. A disadvantage of late resection is the greater possibility of resistance to antituberculosis drugs, in which case resectional surgery carries a much higher complication rate. There is still, however, a place for such older surgical measures as limited thoracoplasty and extraperiosteal plombage.

Although treatment is much more effective than in the past, it is more complex and has created some new problems. Even the best chemotherapy does not restore damaged or destroyed tissue. Over 20 per cent of patients admitted have far-advanced disease; many have gross involvement and marked cavitation and would have died within a few months in the pre-chemotherapy era. Now, their lives are usually saved, but they are often respiratory cripples without sputum or with positive sputum resistant to drugs. Limited surgical collapse may salvage about one-third of these but, at the best, requires prolonged treatment and a great deal of courage and patience from the patient and surgeon.

Breakdown with tuberculosis is occurring much later in life than twenty years ago, especially among men. One-third of those being treated are over 50, and new cases over 70 or 80 are common. These people often have other respiratory, vascular, or metabolic conditions which complicate the management of their tuberculosis.

The private physician has always had a vital role in tuberculosis control, especially in the field of diagnosis. Recent trends are bound to bring him into closer touch with treatment because of shorter hospitalization periods and the continuation of chemotherapy at home. However, as stated earlier, there are many sound reasons why almost all patients with pulmonary tuberculosis should have initial treatment in a tuberculosis hospital.

At least two years' drug therapy should be given patients with active pulmonary tuberculosis, no matter how slight. Of 193 patients receiving streptomycin, para-aminosalicylic acid, and isoniazid in various combinations for at least nine months, 75 of whom also received surgical treatment, 23 patients, including 8 who had received drugs twenty-one months or more, relapsed during treatment or up to four years after drug therapy was stopped. Extension of disease with cavitation was the most frequent type of relapse. Organisms from 7 to 10 patients with positive sputum during relapse were fully sensitive to all 3 drugs.

J. Batten, M. Turner-Warwick, C. Hoyle, and H. Nicholson: Prolonged drug treatment for pulmonary tuberculosis. Lancet 1:409-412, 1960.

Tuberculosis in Persons Over 45 in Indiana

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With so much emphasis being placed on people in the older age groups socially and economically, as well as medically, it seems appropriate to review the situation from the standpoint of tuberculosis in a midwestern state.

POPULATION

The population of Indiana is 4,633,395, which is almost double what it was fifty years ago. An interesting part of this growth is the percentage of people aged 45 years and older. In 1900, they comprised 19.7 per cent of the population, while in 1958, this group was estimated to be 29.1 per cent. The number of persons aged 65 and over, however, doubled in the same interval, and they are now considered to comprise 9.18 per cent of the total population.

The population changes are typical of what has taken place in the United States as a whole. A table showing percentages of population by various age groups in Indiana could be superimposed on a similar one of the United States, and the percentage would vary 1 per cent or less in the different age groups. The only exception is the group aged 65 and over, which, in Indiana, is greater by about 2 per cent or more than the United States average.

NEWLY REPORTED CASES

Along with the steady increase in total population, there has been a decrease in the number of newly reported cases of tuberculosis for all ages in this state, particularly during the last fourteen years. In 1959, the number of cases reported was a little more than half of those reported in 1945 (figure 1). However, when this decrease was considered from the standpoint of age group, it was found that tuberculosis in persons aged 45 and over had increased, particularly in the last eight years. In fact, since 1956, this age group has comprised 50 per cent or more of the newly reported cases. This is shown graphically in figure 2. This chart also shows that the percentage of new cases in women has remained constant, even though the total number of living women in this age group is greater than that of men. On the other hand, there has been a steady increase in the last eight years among the men who were newly reported as having tuberculosis.

Today, the newly reported cases serve as our best guide to the effectiveness of tuberculosis work in the state. This is due in part to better diagnosis of the disease and in part to better education of the laity regarding tuberculosis.

Strangely enough, even though there has been a decrease in the number of newly reported cases over the years, the percentage classified as having advanced tuberculous disease has changed very little. However, the degree of advancement is not as great nor are there as many complications as formerly. Laryngeal tuberculosis, for instance, occurred in 8 to 10 per cent of patients twenty and thirty years ago and intestinal tuberculosis in 50 to 90 per cent of advanced cases. Today, these complications are seldom encountered.

Indiana has a nonwhite population of between 4 and 6 per cent—mostly Negroes. In spite of this percentage in the population, the newly reported cases of tuberculosis in the nonwhites have varied between 15 and 18 per cent. One-fourth to one-third of these were 45 years of age or older. This brings out the fact that tuberculosis is found earlier in life among nonwhites than among whites.

ECONOMIC STATUS

In this state during the past few years, 14 to 21 per cent of the newly reported cases of tuberculosis have been in persons aged 65 and over. Their disease, when coupled with a low income, becomes a dual and difficult problem.

The incomes of men and women 65 and over are low, as shown by a recent report[1] that gives the following figures: of every 100 men and women, 15 have an income of $2,000 or more per year; 11, between $1,000 and $2,000; 36, less

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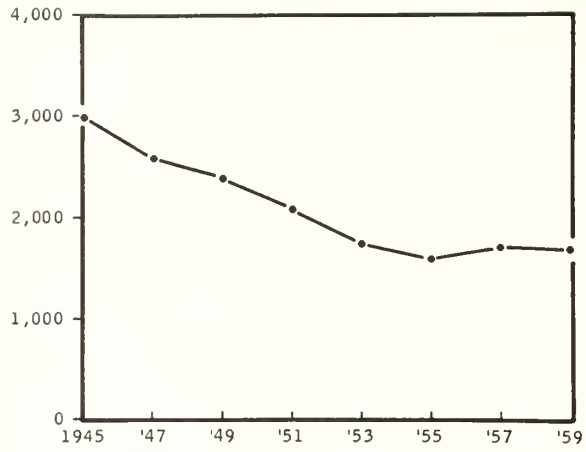

Fig. 1. New cases of tuberculosis in Indiana, 1945 to 1959.

than $1,000; and 38, no income at all. Of the 15 in the $2,000 bracket, only 4 have an income of $5,000 or more.

Ordinarily, many persons of 65 have to live with their children. However, if tuberculosis is found in this age group, it is the duty of their physicians to see that these older people are sent to a tuberculosis hospital and kept there until their disease has been stabilized for several months.

REGISTERED CASES

The number of cases listed on the state tuberculosis register has remained fairly constant, particularly during the last eight years, when it has varied between 8,000 and 9,000 for each year. Cases to be so registered were classified as active at the time of registration or two years before. For instance, in 1959, which was a rather typical year, there were 8,624 cases so registered. These were subdivided as follows: 1,202 were hospitalized, 894 were in penal or mental institutions, and 6,528, or 75 per cent, were in homes. Treatment of active tuberculosis in the home is possible *if* home conditions are satisfactory, but certainly the majority of homes do not so conform.

In late 1959, the Indiana Tuberculosis Council became concerned with these nonhospitalized patients and studied a large sample. It was found that more than half of the formerly hospitalized patients had left their hospitals without medical approval, and of this half, 216 were 45 years of age or over. These people in need of treatment constitute one of our problems.

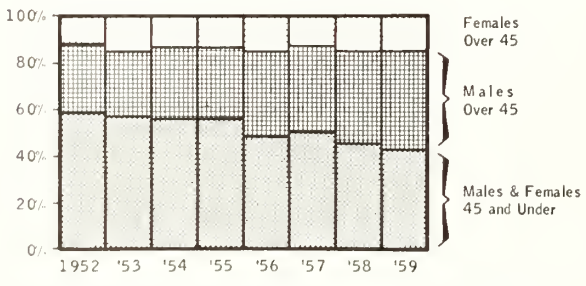

Fig. 2. Percentage of new cases of tuberculosis in Indiana, by sex and age, 1952 to 1959.

DEATHS

Deaths from tuberculosis have steadily declined over the past fifty-eight years in this state. In 1900, 4,819 persons died—a rate of 191.4 per 100,000 persons. In 1958, 278 persons died of tuberculosis, or a rate of 6.2. This fact is impressive and gratifying. When consideration is given to age groups, it will be noted that, in persons 45 and over, the drop over the last eight years particularly has been less precipitous than in persons 15 through 44 (figure 3).

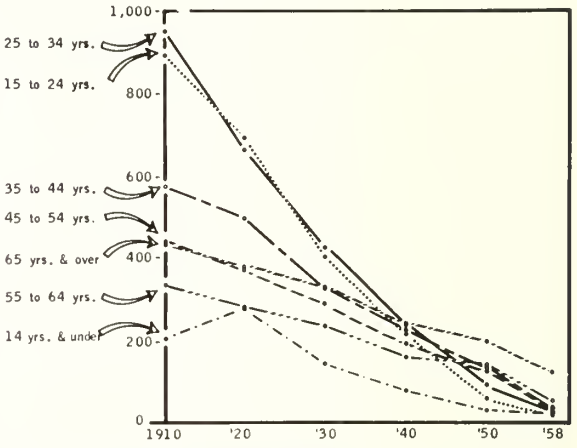

Fig. 3. Total number of deaths from tuberculosis in Indiana by age groups, 1910 to 1958.

A factor not readily explained is brought out in figure 4, where it will be seen that in the last twenty years there has been a steady decline in the deaths from tuberculosis in all ages in this state. However, when these facts are considered from the standpoint of sex in those persons 45 and over, it is found that the percentage of deaths among women has not declined as might be expected but instead has remained rather constant over a twenty-year span. But there has been a steady increase in the number of deaths among men, which, in 1958, was almost 3 times as great as the number of deaths among women.

Tuberculosis has always been a factor in deaths among older people. Formerly, there was

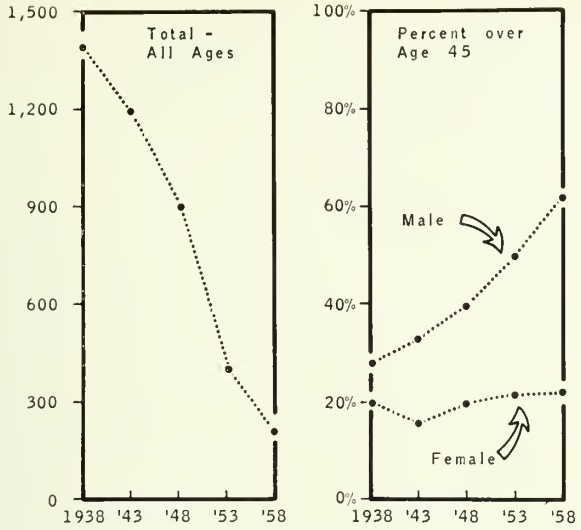

Fig. 4. Deaths from tuberculosis in Indiana by age and sex, 1938 to 1958.

such a large percentage among the younger age group that it overshadowed its occurrence in older people. For instance, in 1910, there were more than 2 deaths in the younger group to 1 in the older group. Even today, if an older person with chest symptoms enters the office of a recent graduate of medicine, the doctor is apt to think of several other lung diseases before he considers tuberculosis.

The records of 1958 show a different trend from those of 1910. Instead of 2 deaths in the younger age group to 1 in the older age group, the ratio is 3 deaths in the older group to 1 in the younger group. Many of these older people are encountering tuberculosis for the first time. The following case is illustrative of many:

N.W., a factory worker who had always considered himself to be in good health, entered the hospital for the first time at the age of 72. He first experienced symptoms related to his lungs six months before admission. His history revealed that, at the age of 69, he had a chest film taken which was considered negative for tuberculosis. On admission to the hospital, however, he was found to have advanced, bilateral tuberculosis (figure 5).

How do older people acquire tuberculosis? I believe that N.W. was infected by an older brother who was hospitalized with far advanced tuberculosis. I also believe that a large number of older citizens is infected late in life. This idea is in contrast to former theories which held that, if an older person acquired tuberculosis, it was the result of a childhood infection which had lain dormant for years and that the stresses of life had caused the primary lesions to break down and release tubercle bacilli.

The majority of these nodules, which result from infection in early life and which for the most part have fibrous walls with necrotic centers, are sterile. Canetti,[2] working in France, found 74 per cent of these nodules to be sterile, while Auerbach and associates,[3] working in this country, found that 80 per cent were sterile. Today, therefore, while we cannot definitely rule out endogenous infection in the older age group, we can say with certainty that exogenous infection does occur.

Tuberculosis of the respiratory system is so common that we are apt to lose track of the fact

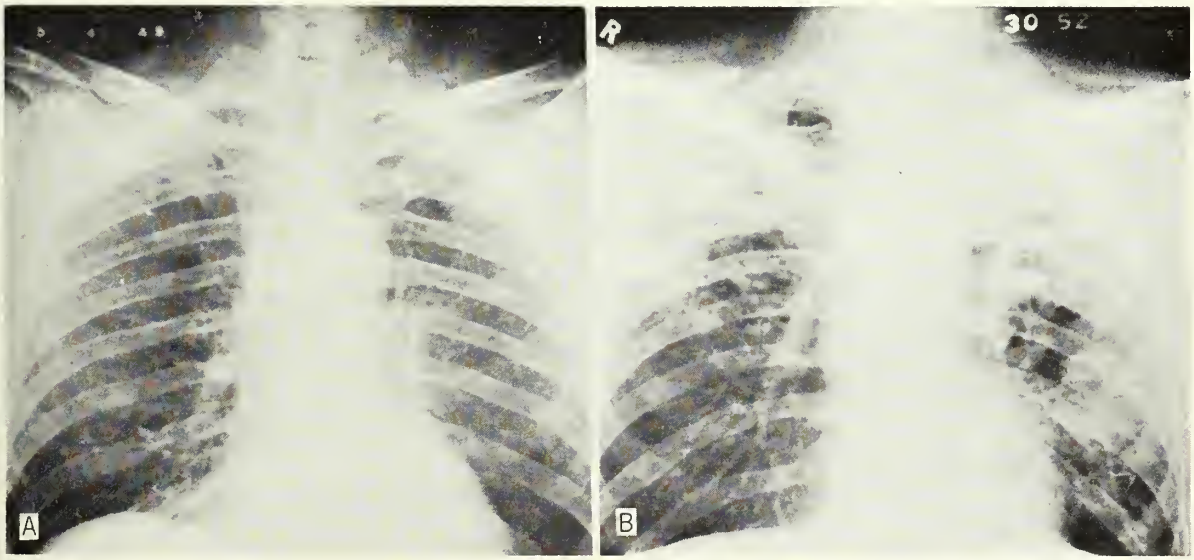

Fig. 5. (A) Chest film taken in 1949 showing no tuberculosis. (B) Chest film taken on hospital admission in 1952 showing bilateral tubercuiosis.

that tuberculosis of other organs may be fatal. During the past twenty years, roughly 10 per cent of the tuberculosis deaths in this state have been due to disease in other organs, and about one half of those have been among persons aged 45 and over.

DISCUSSIONS AND CONCLUSIONS

Indiana's situation has been unique in the sex ratio of mortality from tuberculosis. From 1890 to 1930, the deaths of women exceeded those of men, while in other localities, particularly in Massachusetts and Rhode Island, where records have been kept for many years, the reverse was true. In these states, deaths of men have been greater since 1890.[4]

From 1930 to 1935, the ratios in Indiana varied, but since 1935, deaths of men have been greater. However, when we consider the age group of 45 and over, we find that the number of men dying from tuberculosis has exceeded that of women since 1921, at least.[5]

The 2 best indexes that we have for evaluating the tuberculosis problem—namely, newly reported cases and deaths due to tuberculosis—have both shown downward trends, as noted in the figures. In order to continue these downward trends, we cannot relax our present efforts.

In fact, additional efforts should be put forth in (1) supervision of the nonhospitalized infectious patient, because of his menace to others; (2) discovery and treatment of tuberculosis among the nonwhite population, because the incidence of tuberculosis is out of proportion to their numbers in the population; and (3) discovery and treatment of tuberculosis in men 45 and over, because of the increased incidence in this group.

I am indebted to Mrs. Galloway and Dr. Calhoun of the Indiana State Board of Health and Mr. Wineriter and Mr. Asher of the Indiana Tuberculosis Association for many of the basic data presented here.

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Malignant gastric lesions difficult to diagnose by roentgenography may have a more favorable prognosis. The five-year survival rate of patients with false-negative or delayed diagnoses is approximately double that of all patients with gastric carcinoma. Delayed diagnosis is potentially more serious than false-negative or false-positive diagnosis, however, since a lesion with an initially good prognosis may become uncontrollable over a long period of time.

In 861 cases of carcinoma of the stomach, 7.8 per cent false-positive and 8.4 per cent false-negative diagnoses were made. Only 7 of the 67 patients in the false-positive group had completely normal stomachs, and only 5 of the 72 persons in the false-negative group were considered entirely negative. In the remainder, the diagnosis was considered most likely or equivocal. The five-year survival rate of the false-negative group was 16 per cent, as compared with 7.8 per cent for the entire group.

In 52 patients, gastric carcinoma was diagnosed as long as three years after the initial x-ray examination. Review of the roentgen films suggested that the lesions may have been present but unrecognized in 29 patients. The five-year survival rate of this group was 17 per cent.

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Tuberculin Testing — An Educational Tool

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THE TUBERCULIN TEST is an excellent tool for building an educational wall against tuberculosis. Long known for its specific ability to detect the presence of tubercle bacilli, it has more recently been recognized as a device for imparting knowledge. Every time that a person is skin-tested, he can, and should, be informed why the test was done and what it is hoped will be learned. Positive reactors should be taught that there are now ways of preventing a latent infection from ever becoming active; the negatives, or nonreactors, may be congratulated on having successfully eluded infection.

The Arden House recommendation that treatment be used as the tool for eradication of tuberculosis has been misunderstood by some to indicate that public health education no longer is necessary. This is, of course, inaccurate, because education is, as it always has been, the classic means by which tuberculosis control has been promoted. Education is essential to the success of the Arden House proposals, but it must be an on-going process—not stopped with a single, set procedure. The tuberculin test is a suitable device for beginning this education and should be the start of promoting public knowledge. It is not an end in itself and must always be an integral portion of a full-scale tuberculosis program. To be sure, not all those who administer the tuberculin test are primarily interested in education, but the impact of the test can be an excellent stimulant to acquisition of facts.

It needs to be emphasized that the tuberculin test is a specific means for learning whether active, viable tubercle bacilli are within the body of the person tested. Whether these organisms are causing serious damage is a matter for subsequent determination. A positive test means that such microorganisms exist in the body of the person so tested; this is a fact, whether the test be the well-known Mantoux, or intracutaneous, method, the Vollmer patch test, or the Heaf test. With a few exceptions, a negative test means that such germs are not present.

The test is not dangerous. Properly performed, there is little probability that any latent tuberculous process will thereby be activated. The several techniques are easy to learn, and no great amount of skill is needed. While some authorities may wish to measure the degrees of positivity by determining the exact geometric outlines of the area of indurated skin, most observers are satisfied to establish arbitrary limits for themselves and to interpret a test as positive or negative. Until a direct relationship between the size of a positive test and the amount of disease has been proved, it will suffice for our purpose to determine merely that a person is positive or negative.

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SCHOOL CERTIFICATION

Education at all levels must be a continual process. In the primary grades and high schools, the school certification program is ideal. This means that a certain percentage of students, faculty, and personnel will be skin-tested in order to achieve certification.

It is essential to have a good working relationship with the voluntary tuberculosis association on the one hand and, on the other hand, with the official health agency. Before tuberculin tests are administered to students, there must be a thorough briefing of faculty and students—and, preferably, of parent-teacher organizations—on the test, what it means, and what the testing hopes to accomplish. It is not sufficient merely to administer the tests, without adequate preparation.

A considerable degree of confusion has arisen because of lack of understanding of the basic motives for this program. While case detection is still possible, it is not the sole purpose of this effort. Enthusiasm for school certification has waned in some places because people still think of the tuberculin test as a means of detecting tuberculosis among students themselves and are discouraged because so few cases should be found among school children. The point is precisely that fewer and fewer cases should be found among the school children as our methods of curbing tuberculosis become efficient.

In addition to acquiring tremendously valuable epidemiologic data, school certification activities help to point to the unexpected focus of tuberculosis in the community. Whenever a

given class shows a marked increase in the percentage of positive reactors, someone in close contact with that group is excreting viable, infection-producing tubercle bacilli. Finding this unexpected focus is the job of the official health agency, an excellent reason for insisting that, before any school certification program is undertaken, the agency agree to participate.

But even more important than the public health and epidemiologic considerations are those of education. Students need to know more and more about their health. One of the significant and unique contributions of this country to public health in general has been the emergence of the voluntary health association. Certainly, voluntary health organizations will be helped by forming a reservoir of well-informed students, whose interest in community health is stimulated by their interest in their own health.

After administration of the tests, there is a follow-up job for the official health organization. The local health officer is essential to the program.

Those students who fail to react to the tuberculin administered (the negatives) may be congratulated, while the positives must be carefully taught the implications of this test. It is unfortunate that, all too often, students are frightened by the test and do not obtain a proper interpretation. At this stage, education will be most successful and student and parent alike are most impressionable and ready to learn. For this reason, a short time spent explaining the basic facts of tuberculosis will be most rewarding. Those who are positive may need, and those who were previously negative but have only recently become positive will unquestionably need, therapy with the antimicrobials specific for the Mycobacterium tuberculosis. Whenever tuberculosis has been discovered, all those in family or household contact should be tuberculin tested. Those who react positively may need antimicrobials, but whether or not therapy is indicated, long-term observation is essential. The contact must be told the significance of the positive test and must be educated in the necessity for periodic reevaluation over many years. There is as yet no established time limit after breaking contact beyond which tuberculosis cannot develop.

Another educational opportunity exists at the time of performance of college entrance physical examinations. It is appalling to note how many students appear for examination before entering college completely unaware of the results of their previous health examinations. Many of them do not recall specifically the results of tuberculin testing. Many schools specifically require that the tuberculin test be performed as part of the examination.

RECORDING THE TUBERCULIN TEST

Physicians concerned with tuberculin tests are chiefly pediatricians, internists, and general practitioners. Their responsibility is to inform the patient or parent of the results of tests and of the need for further evaluative studies or subsequent observation. It is rather discouraging to note the development of tuberculosis in a previous tuberculosis contact, one who had not been taught the necessity for annual reexamination.

Perhaps it would be a good idea to encourage all patients to record the results of medical examinations in a booklet such as *Your Family Health Record*, which is prepared as an American Medical Association public service and distributed through state medical societies without charge. The current edition makes no provision for entry of the results of tuberculin testing. This deficiency should be corrected and a copy given by the pediatrician to the parent at the time of initial immunization series.

CONCLUSIONS

1. The tuberculin test is an excellent method for imparting knowledge of tuberculosis to a maximum number of persons with a minimum expenditure of time, effort, and money.

2. The school certification program provides a means whereby students may learn not simply whether they are positive or negative but, more importantly, the basic factors pertaining to tuberculosis eradication in the community and treatment of the disease in the individual.

3. The school certification program is an integral portion of the community campaign to eradicate tuberculosis and should not be regarded as an end in itself. For this reason, those sponsoring such an effort need to enlist the support of the voluntary tuberculosis association and of the official health agency.

4. Adequate preparation of those to be tested by preliminary health education and suitable follow-up by the local health officer and his staff will make such a program worthwhile.

5. Whether the tuberculin testing is done as part of a school program or on an individual basis in a physician's office, the results of the testing must be made known to the person tested or his parent. Each individual so tested should have his own record, preferably with the results of other tests and immunizations.

Surgical Treatment of Tuberculosis in the Diabetic Patient

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THE PROBLEM OF the management of tuberculosis in the diabetic patient is a recurring one, of considerable interest and importance. Before the introduction of insulin, the combination of diabetes and tuberculosis presented a major problem, for the dietary restriction necessary for the adequate control of the diabetes was diametrically opposite the program then thought to be essential for the treatment of pulmonary tuberculosis. With the advent of insulin, this conflict was largely eliminated, rendering the problem somewhat simpler. When surgical operations became necessary, the problems were again multiplied, particularly in those individuals in whom nausea, vomiting, or inability to take food persisted for a period longer than a few hours. Careful regulations of food intake and insulin dosage were necessary.

Since the introduction of specific drug therapy for tuberculosis, the toxic manifestations of the disease and its effect upon food intake and insulin utilization have been rapidly reduced, allowing the diabetic program to become stabilized at a much earlier date. Subsequently when surgery becomes necessary, it may be done upon a patient in better general condition, with the diabetic control on a stable basis.

INCIDENCE

The incidence of diabetes in tuberculous individuals is, of course, a variable one. The combination is consistently present in tuberculosis sanatoria. At Glen Lake Sanatorium from January 1955 through December 1959, there were 49 individuals, or 2.3 per cent, who had both tuberculosis and diabetes. At the North Dakota State Sanatorium from July 1, 1956, to June 30, 1960, 36 of 555 patients discharged, or 6.5 per cent, were diabetic. From July 1, 1958, to June 30, 1960, however, there were 24 diabetics among the 220 tuberculous patients in residence, that is, 10.9 per cent. There were 3 diabetics, or 5 per cent, among 59 patients in residence at the Minnesota State Sanatorium during November 1960. However, 5 additional diabetic patients had been discharged in the previous six months. The combination of the two diseases, then, occurs with sufficient frequency so that it always must be borne in mind when patients with either condition are under observation.

Certainly, from these figures, all diabetic patients, particularly those who have a positive tuberculin test, must be screened periodically by roentgenogram so that any developing disease may be discovered at the earliest possible date. Unfortunately, the tuberculosis found in the diabetic patient, while it may be much the same as seen in the nondiabetic person, is all too frequently extensive and often bizarre in character. Diabetic patients, then, comprise another group, in addition to those who have had extensive gastric resections and those receiving cortisone therapy, in whom repeated screening must be done to discover developing tuberculosis before it becomes extensive.

CASE REPORT

The interest of one of us (T.J.K.) in the problem of the surgical treatment of the tuberculous diabetic patient goes back to 1929.

At this time, we were confronted with the problem of operating upon a 26-year-old woman, 6 feet tall, weighing 167 lb., who presented far advanced pulmonary tuberculosis that involved the entire right lung, with extensive cavitation and secondary tuberculous enteritis. When bed rest alone did not control the disease and pneumothorax had been tried unsuccessfully, a permanent phrenic nerve interruption was done in May 1928. The patient's diabetes was controlled by diet, with 30

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units of insulin daily. The problem, if multiple stage extrapleural thoracoplasty were tried, would be to avoid nausea and vomiting so that the patient could continue her regular diet throughout the postoperative period.

On February 15, 1929, the patient was given her normal breakfast and, later, a light lunch. At 4:30 P.M., with a very light nitrous oxide narcosis with infiltration anesthesia superficially and infiltration block of the intercostal spaces, the 5 upper right posterior ribs were removed without difficulty. After the surgery, there was no nausea or vomiting and the patient was able to take and retain her evening meal. The insulin was increased to 45 units for three or four days, then dropped back to 30 units again.

One month later, the next 6 right posterior ribs were excised during infiltration anesthesia, with only a little nitrous oxide and oxygen for a few minutes at the beginning of surgery. This surgery also was accomplished without difficulty. The insulin again was increased to 45 units for three or four days postoperatively. The patient again took food by mouth the same evening and on subsequent days without difficulty.

Since then, hundreds of multiple stage thoracoplasty operations have been carried out under local infiltration anesthesia alone, using the same general technic. This patient was discharged from the sanatorium on April 26, 1930, and has remained in good health and is working full time up to the present. She had a positive sputum in June 1929, after her thoracoplasty, and has been negative ever since, including negative gastric cultures. No drug therapy was used on this patient, as this was long before any specific drugs were available.

MATERIAL AND METHODS

This report covers a series of 49 patients, 22 men and 27 women, all of whom had both diabetes and pulmonary tuberculosis and received surgical therapy for control of the pulmonary disease. Of this group, 32 presented far advanced pulmonary tuberculosis, while 17 were originally admitted with moderately advanced lesions; 35 were of the white race, while 14—13 women and 1 man—were American Indians. Their ages ranged from 26 to 73, with the largest number falling in the third and fourth decades. However, there were 6 patients between the ages of 25 and 30, 10 between 50 and 60, 8 between 60 and 69, and 1 at the age of 73 years. The known duration of the diabetic condition ranged from two months to thirty-three years. Thirty-two patients were known to have had diabetes before the development of tuberculosis, 7 were discovered to be diabetic upon admission to the sanatorium, and 8 had tuberculosis before diabetes. The average duration of diabetes before operative intervention was 11.7 years.

All patients received adequate sanatorium treatment at the Minnesota State, North Dakota State, or Glen Lake Sanatorium before surgical intervention with control of the acute tuberculous process. Two-thirds of the patients had their operation performed at St. Mary's Hospital, Minneapolis, and one-third at Glen Lake Sanatorium. All patients except the 7 who had thoracoplasty operations alone before the development of antituberculosis drugs received adequate preoperative drug therapy with 2 or 3 of the specific drugs—isoniazid, streptomycin, para-aminosalicylic acid, or combinations thereof—and improved to or approaching "target point" before surgery was undertaken.

The indications for surgical treatment in this group are much the same as for the nondiabetic tuberculous patient. Our general policy, however, was somewhat more aggressive, preferring to resect lesions, especially cavitary disease, a little earlier in order to avoid the development of resistant organisms. Likewise, we have felt that, after adequate chemotherapy, residual nodular disease should be resected, thus not permitting any caseous areas to persist and possibly cause reactivation at a later date.

As a matter of principle, it was felt that surgery should be undertaken before significant drug resistance developed, for it is a well-recognized fact that the incidence of postoperative complications—bronchial fistulas, wound infections, empyema, and so on—increases sharply in patients harboring resistant organisms. It is especially important to avoid such complications in the diabetic patient. If there was even a suspicion of development of resistant organisms, additional antituberculosis drugs—viomycin, cycloserine, or Pyrazinamide—were added to the regimen before and for some period after surgery. Penicillin and sulfadiazine or Declomycin were given thirty-six hours preoperatively and for five or six days postoperatively to all patients in order to avoid any wound complications if possible. Perhaps it is coincidence, but primary healing of all wounds occurred without suppuration, and only 2 patients had wound drainage.

Postoperatively, after periods ranging from five to fourteen days, all patients were returned to their original sanatoria for continuation of treatment for both tuberculosis and diabetes. This period varied according to the amount of disease present, the response to treatment, and various factors in each individual case.

It is interesting to note that, in our present series of patients, the diabetes was classified from mild to moderate. None of the patients was appreciably underweight at the time of surgery. The insulin dosage was variable, but most of the patients were on combination-type insulin therapy. Only 2 patients in this series were receiving an oral hypoglycemic agent, tolbutamide; 7 patients were controlled by diet alone. It was the

policy of the sanatorium to be sure that the diabetes was adequately controlled before referring the patients for surgical treatment.

TREATMENT

Management of the diabetes through the immediate surgical period was as follows:

The morning of surgery, our general policy was to give approximately one-half of the patient's usual dose of long-acting insulin before surgery. Preoperative blood sugars were normally obtained, and, if higher than we felt was desirable, some additional regular insulin was given subcutaneously. This was correlated with the patient's normal dosage of insulin.

Routinely, an intravenous solution of 5 per cent glucose in distilled water was started during surgery. This was covered with varying amounts of insulin, depending upon the severity of the diabetes. We felt that our smoothest control was obtained by giving the regular insulin during surgery subcutaneously just before the institution of the intravenous glucose infusion.

Hourly urine specimens were obtained through an indwelling catheter and were tested by Clinitest or Testape. Again depending upon the severity of the diabetes, insulin was given as necessary. Blood sugars were usually obtained at the conclusion of surgery before the patient left the operating room. These were found to be a further aid in accurate management of the patient's diabetes.

Intravenous fluids were rarely given postoperatively, and it is the feeling of the internist that diabetic control was made much simpler and much easier because the patient was promptly encouraged to eat and adequate nutrition was restored. In the few instances when the long-acting insulins were not used preoperatively, the diabetic control was considerably more erratic postoperatively, especially on the day after surgery and for two or three days thereafter. In this particular series of patients, there were no deaths or serious complications from the diabetes. Only 2 patients had acetonuria after surgery, and these were patients who had not been given the aforementioned long-acting insulin before surgery.

We have preferred to allow patients with diabetes to spill a moderate amount of sugar postoperatively rather than risk the tight control necessary to produce aglycosuria, with the concomitant danger of insulin reactions during surgery itself or in the immediate postoperative period. Subsequent follow-up evaluations at the sanatoria often showed some drop in the amount of insulin necessary for diabetic control after the diseased area was removed.

Surgical procedures carried out in this group of patients include 3 total pneumonectomies, 2 pneumonectomies with additional thoracoplasty, 16 lobectomies or lobectomy plus additional segments, 4 lobectomies with concomitant thoracoplasty, 29 partial lobectomies, and 4 concomitant decortications. Seven patients had thoracoplasty alone performed in 21 separate stages. Seven patients had a preliminary thoracoplasty carried out before the resectional treatment, and 10 had thoracoplasty concomitant with resection. In all, 38 stages of thoracoplasty were involved. Thirty-one patients had operations on the right side, 23 on the left, including 5 who had bilateral surgical procedures. Altogether, 83 separate operations, not counting concomitant procedures, were carried out on 49 individuals.

The anesthesia for patients in whom thoracoplasty alone was carried out was accomplished by local infiltration with half of 1 per cent procaine without general anesthesia except for the first case previously mentioned. The patients in whom resection was carried out with or without thoracoplasty were anesthetized with intravenous pentobarbital with Flaxedil or curare with nitrous oxide and oxygen. A physician anesthesiologist gave all general anesthetics. Under his skillful management, the anesthesia was so regulated that the patients were awake and responsive before leaving the operating table. Intratracheal intubation was used routinely to insure an adequate airway and to permit aspiration of all secretions as rapidly as they accumulated.

Blood loss was estimated by the weighed sponge technic and adequate replacement was made as the operation progressed. Only one single unit transfusion was given. A total of 52 units of blood was given to 12 patients, or 25 per cent of the whole series.

DISCUSSION

The surgical technic employed differed in no essential from that used in nontuberculous resections. For lobectomy or pneumonectomy, individual double ligation of all vessels, with continuous suture of the bronchus, was carried out, using chromic catgut throughout. More limited resections were usually done by clamp or wedge excision instead of a strip-out segmental technic, suturing behind the forceps with a Heidenhain suture of chromic catgut. Prompt and complete obliteration of space was considered essential, so closure was always made, leaving 2 or 3 suction catheters strategically

placed to remove all air and fluid. If, at the time of closure, it appeared likely that the remaining lung would not completely fill the pleural cavity, a tailoring thoracoplasty was carried out at once. Closure throughout, except for the skin, was made with catgut.

The only hospital death in the series was that of a 40-year-old woman with advanced pulmonary disease, eighteen years a diabetic, upon whom a preliminary upper thoracoplasty had been carried out on May 4, 1951, with a second stage delayed to November 17, 1951. She was known to have very poor respiratory reserve, hence the delay between the upper and lower stages of thoracoplasty. One year later, as a desperation measure, because of continued activity of her trouble, a right total pneumonectomy was carried out under the thoracoplasty on November 22, 1952. She died of respiratory insufficiency ten days later.

SUMMARY

A review of the medical-surgical management of tuberculous pulmonary disease covering 83 operations upon 49 diabetic patients is presented. The combination of diabetes and pulmonary tuberculosis, while not desirable, may be adequately managed by the cooperative effort of phthisiologist, internist, anesthesiologist, and surgeon. These patients, under proper medical control, may be successfully treated by resections or other surgical means with no greater risk than the nondiabetic patient and with equally good results.

Skin reactions to 1 mg. of old tuberculin (OT) or to second-strength purified protein derivative (PPD), or 0.005 mg., are not the result of chemical irritation but are true allergic reactions. Lack of reaction to such doses in reasonably healthy persons practically eliminates the possibility of infection with acid-fast organisms or tubercle bacilli.

Persons reacting strongly to intermediate-strength PPD, or 0.0001 mg., or failing to react to second-strength PPD are less resistant to development of overt tuberculosis than are healthy persons reacting only to second strength. The low-grade sensitivity assures relative immunity, whether induced by atypical acid-fast organisms, other unknown organisms, or true tubercle bacilli.

Of 120 patients with known tuberculosis, 30 per cent reacted to skin tests with OT in a 1:10,000 dilution. With 1:1,000 OT, the percentage of reactors rose to 69 per cent, and 85 per cent reacted to 1:100 OT. In tests with first-strength PPD, 84 per cent of 81 patients reacted; 5 per cent reacted to second-strength, and 10 per cent to intermediate.

W. W. Johnson, H. A. Saltzman, J. H. Burkin, and D. T. Smith: The tuberculin test and the diagnosis of clinical tuberculosis, Am. Rev. Resp. Dis. 81:189-195, 1960.

Effectiveness of demethylchlortetracycline in low doses is accompanied by few side reactions. Results in 170 patients hospitalized with pneumococcal pneumonia, scarlet fever, or other infections generally were comparable to those obtained with other tetracyclines. Among 127 patients given 125 or 150 mg. of the antibiotic every six hours, only 2 had temporary diarrhea.

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Program of the Texas Tuberculosis Association

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Organized tuberculosis control in Texas began with the appointment in January 1907 of a state health officer whose concept of public health was considerably ahead of his era. Moreover, in the performance of his duty, he never lacked the courage to "damn the torpedoes" and move straight toward his objective. He was Dr. William M. Brumby who died in Houston on November 29, 1959, at the age of 93. He was one of the founders and the first president of the Texas Tuberculosis Association, and an honorary vice-president at the time of his death.

The problems Dr. Brumby faced when he assumed his responsibilities in a state of some 3,000,000 persons scattered over 263,513 square miles were not for the fainthearted.

Four years before his appointment, the name of the department he would administer had been changed from the State Department of Quarantine to that of the State Department of Public Health and Vital Statistics. Unfortunately, the legislature neglected to appropriate funds for recording and tabulating the statistics. Dr. Brumby's solution to that problem was characteristic. In a paper he wrote,"The So-Called Texas Quarantine Against Tuberculosis," he stated:

> My funds and my duties were supposed to relate to Quarantine on the Coast and Border. However, upon finding in my office a freight car load of reports on vital statistics from various counties, I attempted to tabulate same. No yellow fever in sight, I called two Quarantine Inspectors from unimportant stations to assist me.

The data indicated that Texas had more to fear from tuberculosis than from yellow fever.

The 1906 death rate from tuberculosis in the U. S. Registration Area—which, incidentally, did not include Texas until 1933—was 175.8 per 100,000 population. Dr. Brumby found that San Antonio's rate was 632.9 and that "85% of the pauper consumptive patients in San Antonio were non-residents." (Some of O. Henry's most poignant stories reflect the plight of these people who came West believing the climate would cure their disease.)

A similar situation existed in El Paso, where the city health officer reported:

> . . . 90% of the pauper consumptive patients were non-residents, with the tide of immigration increasing year by year. In 100 recorded deaths, 54 of the deceased had resided in El Paso less than a year; 14 showed a residence of five years; 5 showed a residence of less than one day; 3 died in the trains in the railroad yards without medical aid; 42 were embalmed and shipped back to various states; 18 were buried as paupers.

In his paper, Dr. Brumby relates the results of a press conference on the facts revealed by this first "survey" of the tuberculosis problem in Texas. "The other states," he commented, "would blush with shame to think of sending healthy paupers to Texas simply to avoid giving them food and shelter, but they unblushingly ship many indigent consumptives to Texas."

Asked how he proposed to stop this practice, Dr. Brumby reminded the reporters that, *as state health officer, he was authorized to bar any contagious disease from the state!*

> The main object I wished to get before the people was overlooked by a reporter from the Associated Press. Uppermost in his mind was a sensational news item—quarantine; in mine was local responsibility—every state and county to assume care of their indigent consumptives. In consequence, headlines in the press from Maine to California proclaimed QUARANTINE BY TEXAS AGAINST CONSUMPTIVES. . . . Widespread censure and criticism was hurled at my head for my "inhumanity to man."

Personal letters to the editors of the nation's most influential newspapers later resulted in very considerate editorials advocating local responsibility for the care of the tuberculous patient and urging necessary appropriations to provide it.

EDITOR'S NOTE: *In August 1960,* DR. J. EDWARD JOHNSON, *president of the Texas Tuberculosis Association, accepted an invitation to sum up the tuberculosis work in Texas, although he had written that he had developed cancer of the pancreas. He was hopeful that the new pancreatic enzyme, Cotazym, which had markedly reduced symptoms, would tide him over for this accomplishment. He prepared the outline and immediately went to work on this paper. When he died on December 17,* MISS PANSY NICHOLS, *the association's executive director, and* DR. ROBERT B. MORRISON, *long-time board member, kindly completed the manuscript.*

That fracas over, the state health officer was distressed to learn from the National Tuberculosis Association that it feared that Texas would not be adequately represented at the International Congress on Tuberculosis to be held in Washington in September 1908. A personal appeal to the Governor for cooperation brought these instructions: "Take necessary steps to secure for Texas a proper and fitting representation in the Congress."

The steps Dr. Brumby took resulted in 1,600 Texans being appointed official delegates to the Congress, 100 of whom actually got there. They traveled to Washington in special railroad coaches. En route, they organized the Texas Anti-Tuberculosis Association, elected Dr. Brumby president, and made charter members all 1,600 of the appointed delegates.

They stopped in St. Louis to meet with delegations from Kansas and Missouri, with whom they adopted joint resolutions to present to the Congress and made other plans calculated "to stem the tide of immigration of advanced and hopeless cases of tuberculosis from the Eastern States that were swamping the charities of the Southwest." The Texas Anti-Tuberculosis Association had launched its first educational campaign!

We later saw many states forge far ahead of us in providing tax-supported facilities for the detection and treatment of tuberculosis. Thus it became our turn "to blush for shame" when migratory agricultural workers from Texas broke down with tuberculosis in northern beet fields and other communities—to be hospitalized or given public care not available to them at home. Fortunately, insofar as state hospitals are concerned, Texas now provides adequate care of its own. Clinics and certain other tuberculosis control facilities in local communities are in short supply, but certain coordinated efforts to meet the needs are promising.

In its fifty-three-year history, our organization has made its share of mistakes—not the least of which, in the opinion of this writer, occurred in 1914, when our name was changed to that of the Texas Public Health Association. Following this, our program was expanded to include a number of activities which, whatever they may have contributed to health and welfare in general, had little bearing on the control and prevention of tuberculosis. In 1931, our state charter was again amended to give us our present name, the Texas Tuberculosis Association (TTA)—which, it may be, we shall bear to the end of our usefulness as an organization.

Chief among the concepts to which we have always subscribed is that the state association has the responsibility to inform the people of the tuberculosis problem in the territory it serves, to promote the assumption by tax-supported agencies of tuberculosis activities appropriate for them, and to assist and encourage acceptable performance of such activities by those agencies.

Since 1912, when its earliest efforts resulted in the establishment of our first state sanatorium with a capacity of 57 beds, the TTA, supported by its local groups, which provide the essential grass roots influence, has spearheaded nearly every measure introduced in the legislature for the provision of hospital and other facilities for tuberculous persons. In these efforts, we have had the active cooperation of the Texas Medical Association and its Committee on Tuberculosis.

As the result of a campaign to expand our facilities for tuberculosis control, the number of state tuberculosis hospitals was increased, between 1946 and 1954 from 2 to 5 and the number of beds from 1,000 to 3,125. Hospital construction was given a tremendous boost in 1950, when the legislature, in a special session, provided for a long-range building program for our entire system of state hospitals and special schools by instituting a 1-cent cigaret tax covering a period of seven years.

The TTA has since worked vigorously, and with considerable success, for legislation to provide qualified personnel and other facilities necessary to insure adequate patient care in these institutions.

STRUCTURE

The present structure of the TTA makes it actually a federation of local tuberculosis associations, currently numbering 92. Annually, as each local group meets requirements making it eligible for a Christmas Seal contract, it has the privilege of naming its own representative to serve on the TTA board for the ensuing year.

The board meets three times a year, with an average attendance of 65. Our bylaws provide that local representatives shall outnumber, by a considerable majority, the 30 directors-at-large. Thus our local affiliates are always assured of an active voice in determining the policy and program of the TTA. Usually, even our directors-at-large are also directors of their respective local associations. Board members participate actively in the affairs of the Association or they are dropped from membership.

At each meeting of our board, the Texas Conference of Tuberculosis Workers is represented

by its president. Recommendations from the professional workers in our local associations can thus be presented directly to the TTA's policy-making body. This is true also of the Texas Trudeau Society, which is the medical section of the TTA.

FIELD SERVICE

The TTA serves as the connecting link between its local associations and the National Tuberculosis Association. In this connection, and in consultant services rendered by its staff directly to local communities, its program parallels that of many other state tuberculosis associations.

Our staff is presently attempting to concentrate its field service chiefly in areas where statistics indicate the incidence of tuberculosis to be greatest. These areas embrace, mainly, counties near the Mexican border, where tuberculosis takes a high toll among our Latin-American citizens. However, they also include counties in south and east Texas, with large Negro populations.

A local project in which the TTA is cooperating will serve as an example of the kind of field service we believe is effective. It began last May, when an offer of funds by a philanthropic foundation to a county on the Mexican border sparked an all-out tuberculosis case detection, follow-up, hospitalization, and bilingual educational program. Participating, in addition to the Butt Foundation, were the state health department and the TTA, the local medical society, health department, tuberculosis association, and school system, all public information media, and various other community groups.

Our first field consultant assisted in the setting up of special record forms and in the tuberculin-testing and x-raying phase of the program. The second consultant is assisting the local tuberculosis association in a gratifying educational program.

Designed originally to promote acceptance of hospitalization by those found to have tuberculosis and to encourage examination of their family contacts, this program is being expanded to promote community interest in rehabilitation and job placement of breadwinning patients returning from the hospital; in education of returning patients who are homemakers; and in education that will encourage patients and family contacts to remain under medical supervision.

This county has a population of 65,141. Between June 4 and November 30, 1960, there were 129 new cases of tuberculosis diagnosed, and 78 of these patients entered a state hospital. The tuberculosis problem in many other Texas counties is comparable.

COORDINATED EFFORTS IN TUBERCULOSIS CONTROL

Overlapping occurs in the implementation of all the functions of the TTA but especially in connection with coordinating local association programs with the TTA's and those of other state agencies. This is particularly true where tax-supported agencies are concerned.

Many of our functions are manifest in a grass roots study of tuberculosis made from 1954 through 1956. Called "Searchlight on TB," the study involved 15 state agencies, all local tuberculosis associations, and other local agencies and community leaders in 240 of our 254 counties. It culminated in the presentation of a report, with 22 specific recommendations for tuberculosis control, at a meeting of 500 persons from all sections of the state, called by the Governor in May 1956. While some of the recommendations have already been met, others are yet to be achieved. Official state agencies have been especially vigilant in their continued reference to the Searchlight report and their efforts to follow through on recommendations.

One Searchlight recommendation, which was met in 1959, was that of recodification of all state tuberculosis laws. Actually, this was one of the long-range objectives of the TTA adopted by our board after a small-scale study of its own in 1946, but for a long time we lacked the funds to implement it. In 1957, the TTA budgeted $5,000 for the legal services needed for this undertaking, and the Texas Medical Association agreed to provide services in kind to equal our cash appropriation. The actual preparation of the Texas Tuberculosis Code was delegated to the legal counsel of the medical association.

Among other things we wished especially to have included were clearly defined legal provisions for the compulsory isolation of recalcitrant, infectious tuberculous patients and for case reporting. The Texas Tuberculosis Code was passed by the legislature in the spring of 1959.

Last August, the legal counsel of the Texas Medical Association published a brief article in the *Texas State Journal of Medicine* highlighting the provisions for compulsory isolation and for reporting of tuberculosis cases. Conviction for failure to observe the requirements for reporting tuberculosis entails punishment of a fine of not less than $50 nor more than $500 or imprisonment up to thirty days. Later, a letter was writ-

ten to each of the 8,400 members of the Texas Medical Association calling attention to the provisions for compulsory isolation and for case reporting. A reprint of the article that had appeared in the medical journal was enclosed.

The state tuberculosis hospitals have been surveyed annually since 1949 by our Committee on Hospitals, comprised of 8 physicians of our board, whose specialties enable them, in one or two days at each hospital, to determine, in conferences with staff and patients, both the needs and progress of these institutions.

One of the Searchlight recommendations was that a State Coordinating Council on Tuberculosis be organized. This was accomplished in the fall of 1956, with membership composed of 2 representatives each from the TTA; the Texas Medical Association; and the state health department, welfare department, hospital board, and education agency's Division of Vocational Rehabilitation.

In the spring of 1960, the Governor appointed 1 representative each from these agencies to membership on a State Coordinating Committee on Tuberculosis. The old voluntary council, therefore, disbanded to become more or less an official committee, invited by the Governor to "develop a frontal attack on tuberculosis" and to forward to him "quarterly progress reports from the Committee and any recommendations it may choose to make for eventual consideration by the Governor and the Legislature."

RESEARCH AND MEDICAL TRAINING

Routinely, the TTA budgets approximately 1 per cent of its income for promising medical research projects within the state and $1,200 annually for medical training fellowships. Through our Committee on Research and Medical Training, local associations are alerted to promising projects. Through the TTA, funds voluntarily contributed by local groups for these purposes are pooled and disbursed. In addition, certain large local associations finance research and medical training in their respective communities. In the fiscal year ended March 1960, funds disbursed by the TTA and its local affiliates for medical research within the state equaled 3.3 per cent of Texas' gross returns from the Christmas Seal campaign.

PUBLIC EDUCATION

As in the rest of the country, tuberculosis case-finding procedures in Texas have recently undergone some radical changes—not all of which have satisfied a public that had become accustomed to (and had liked!) mass x-ray surveys among apparently healthy people. The transition to more selective and productive case detection is not proving easy to accomplish or to "sell," but progress is being made.

We should do more to encourage all physicians to do routine tuberculin tests on their patients of all ages and, with the family's help, to attempt to locate the source of infection of all positive reactors. A project to that end, sponsored by the tuberculosis and public health committees of the local medical society and conducted and financed by the local tuberculosis association in one Texas community, has effectively demonstrated the interest of the general practitioner in tuberculosis case detection and follow-up, from his own office.

The TTA publishes a monthly bulletin entitled *Here and There*, edited by its director of public information, which has a circulation of 1,900. Through this medium, local executives and presidents, as well as local board members who request it, are informed of what goes on in the tuberculosis movement in the state and, briefly, on national and international levels.

Within the past two years, we have published 2 pamphlets requested by local associations. One, "Planning To Get Well," in English and Spanish editions, is designed to promote acceptance of hospitalization by tuberculous patients. The other, "Finding Tuberculosis Through Contact Investigation, or Tuberculosis in Children," by Dr. Katharine H. K. Hsu has run into 3 editions and has been widely used by agencies throughout the country.

In addition to the publication of pamphlets, we maintain a loan service of motion picture films, film strips, and certain transcriptions.

Public apathy regarding tuberculosis control, resulting from over-optimism about miracle drugs and spectacular decreases in the death rate, makes it more essential than ever that we keep constantly before the people of Texas the true facts about tuberculosis in our state. To this end are resources of our public information division directed. We receive generous cooperation from newspapers, radio, and television.

PROBLEMS REMAIN

The problems faced by our founders were more staggering but no less complex than those we face today. We are encouraged by the progress that has been made. We are confident that further advances will come. But with the unresolved problems that remain, we cannot yet be "proud and loud" concerning tuberculosis control in Texas.

Safety Precautions for Tuberculosis Laboratories

WILLIAM H. FELDMAN, D.V.M.

Washington, D. C.

All who work regularly or even occasionally in a laboratory or some other environment in which virulent tubercle bacilli exist should be constantly aware that the tubercle bacillus is the cause of tuberculosis. Tuberculosis is a serious, infectious disease. It is capable of producing prolonged and expensive incapacitation, and it may have a fatal termination. Also important to remember is the fact that tubercle bacilli are not necessarily host-specific; man is susceptible to both human and bovine forms of the tubercle bacillus.

Tuberculosis infections are highly contagious, and tubercle bacilli–laden aerosols are especially hazardous to laboratory workers and others who may be repeatedly exposed to such infectious material. To reiterate, we must never forget that tuberculosis is a serious, potentially lethal, infectious, communicable disease.

GENERAL ASPECTS

Workers in bacteriologic laboratories engaged in tuberculosis research, including the processing of unfixed tuberculosis materials and the handling of cultures of tubercle bacilli, occupy positions that are particularly hazardous. It is therefore essential that all who work in such laboratories or in infected environments be fully informed of the danger to themselves and to others. Furthermore, all such persons should be thoroughly indoctrinated in the use of proper technics, so as to reduce to a minimum the possibility of becoming accidentally or inadvertently infected while engaged in routine laboratory procedures.

Needless to say, safety precautions are more effectively carried out if laboratories are properly designed and adequately equipped. Outdated and outworn apparatus or lack of certain essential items of equipment may contribute to making laboratories unsafe for laboratory workers and hazardous for others who visit such premises.

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Quite apart from laboratory design and equipment in the achievement of maximal protection is the human equation. In the following basic principles for diagnostic and research laboratories concerned with Mycobacterium tuberculosis and other pathogens, the human equation is indeed the most important factor.

1. There must be constant alertness and adherence to strict but common-sense rules and procedures. This is imperative in the prevention of accidental laboratory infections.

2. Personal, rather than delegated, supervision of the laboratory must be accepted by those officially responsible.

3. Maximal safety in an area of potential infection depends on the acceptance by every member of the laboratory staff, professional and nonprofessional, of individual responsibility and a consideration for the welfare of others. Failure to accept this responsibility could make one guilty of negligence should harm come to others as a result of his dereliction.

With this perfunctory introduction, I shall comment briefly on the more significant items which, collectively, constitute guidelines for the safe operation of a laboratory service primarily concerned with the handling of infectious materials potentially hazardous to human beings.

PERSONNEL

Before they are employed, technicians or other workers in a tuberculosis laboratory should have a complete physical examination, including a roentgenogram of the thorax. After such workers are employed, roentgenograms of the thorax should be made every six months. If the possibility of exposure to tubercle bacilli is excessive, roentgenograms of the thorax should be made at intervals of three months. In addition, all personnel in such laboratories should be tested with tuberculin. Subsequent testing of persons whose tests initially gave negative results should be done every three to six months.

No professional worker should be permitted to work in a laboratory concerned with the processing of virulent and infectious materials unless he has had previous training in the handling of pathogenic microorganisms. Furthermore, secretaries and others whose duties are normally be-

yond the area of contamination should not be permitted to enter areas in which laboratory procedures are carried out.

Last, it is important that all illnesses and accidents, particularly accidents which occur on the laboratory premises, be reported to the director immediately. A written account of all such instances should be filed for future reference. Wounds, scratches, abrasions, or cuts of the skin must be protected by proper coverings.

It should be emphasized that it is the responsibility of the laboratory director to indoctrinate all laboratory personnel in the principles of health maintenance and in the use of safety measures. All workers should receive thorough instruction in aseptic technic; methods of handling specimens, cultures, and animals; methods of avoiding contamination of self and surroundings; and methods of effective decontamination of self and surroundings.

PRECAUTIONS APPLICABLE TO THE LABORATORY AREA

It must be assumed that workrooms in which tuberculosis materials are processed are likely to be contaminated. Such rooms should be separated from areas used for general laboratory purposes. The room in which the infective materials are processed should be large enough to accommodate an incubator, a safety hood, a specimen shaker, and other essential equipment. It is important that the room be kept meticulously clean and be air-conditioned and properly ventilated, so that doors and windows can be kept closed at all times.

GENERAL RULES

Those who work in contaminated areas must be provided with proper laboratory garments. When it is necessary to be in areas such as the necropsy room, suitable covering for the shoes and head should be worn. There should be *absolute prohibition of the consumption of food, soft drinks, or coffee in the laboratory.* Furthermore, such items must not be stored in refrigerators which serve infectious areas or which are used to store infectious materials. Smoking should be permitted only in offices or other areas in which there are no contaminated materials.

All grinding or emulsifying of animal tissue and all in vitro procedures must be performed under a bacteriologic hood that provides a slight but adequate negative pressure. The importance of operating the exhaust mechanism while the bacteriologic hood is in use cannot be overemphasized. Failure of the exhaust mechanism to operate properly will cause air to rise from the work area directly to the face of the person who is using the apparatus. Obviously, improper use of the hood in this manner is likely to be more hazardous than if the same work were done in the open.

Homogenization by mechanical agitation is an essential feature in processing specimens of sputum preliminary to culturing for tubercle bacilli, and cognizance should be taken of the potential hazard of this procedure to laboratory personnel. Loosening or removing stoppers of bottles containing sputum after vigorous agitation never should be done in the general laboratory area, where possible dispersal of aerosols potentially dangerous to human beings may occur. Instead, the removal of caps or stoppers from bottles or tubes containing, or thought to contain, tubercle bacilli always should be accomplished in a suitably designed and properly installed bacteriologic safety cabinet.

Pipetting of cultures or other fluids must not be done by mouth. Instead, a sterile, Pasteur-type, dispensable glass pipet should be used, the blunt end of which contains a cotton stopper. Attached to the pipet is a rubber bulb, with which fluid can be drawn into or discharged from the pipet. It is assumed that all plumbing will meet the requirements of a modern plumbing code.

All glassware used for live cultures, before being washed, must be autoclaved at a minimal pressure of 15 lb. for at least thirty minutes. Discarded bacterial cultures must also be autoclaved before the glassware is washed. The efficiency of sterilization by the autoclave should be determined at intervals by a suitable test. The sterilization of all contaminated materials used in the animal necropsy room must be accomplished with equipment permanently installed either within the room in which necropsy is done or within an area contiguous to and entered from the necropsy room.

Virulent bacteriologic cultures and cultures of pathogenic fungi always should be kept under lock and key during week ends and holidays. The key should be assigned to one member of the laboratory staff designated by the director.

Frequent washing of the hands should be an unfailing routine. It is especially important that the hands be washed thoroughly before the worker leaves the laboratory. A final rinse in 70 per cent alcohol is desirable.

ANIMAL QUARTERS AND NECROPSY

Unused or stock animals should be maintained in an area separate and distinct from that in which animals are kept under experimental ob-

servation. If the same person is assigned to care for both types of animals, proper supervision and means must be provided to prevent the possibility of dissemination of infections of any kind from infected animals to those considered normal. Apropos of this, convenient shower facilities, with adequate locker space, must be made available for animal caretakers. Too often, this has not been done.

Essential precautions include the following:

1. Animal cages, food containers, and the like should be decontaminated with live steam or with boiling water containing lye before these articles are reused.

2. Necropsy should not be conducted in the workspace occupied by the animal colony.

3. Necropsy should not be done until after the blood of the animal is coagulated.

4. The prosector and his assistants must wear laboratory garments and suitable foot coverings before they enter the area in which infected animals are maintained or in which necropsy is performed. The prosector should wear a plastic face shield and rubber gloves.

5. Contaminated clothing, rubber gloves, and footwear must be so handled as to facilitate subsequent decontamination. After necropsy has been completed, the animal carcasses should be enclosed in waterproof bags or waterproof paper cartons and placed immediately in the incinerator.

It must be emphasized that necropsy of experimental animals is the responsibility of a qualified member of the professional staff. Necropsy must not be entrusted to technicians, as, unfortunately, is so frequently done. All employees who have access to the animal quarters must be medically certified as free from active tuberculosis. After hours and during week ends and holidays, rooms containing animals inoculated with infective materials must be kept locked. Unauthorized persons never should be permitted to enter rooms in which animals inoculated with pathogenic materials are maintained. Appropriate signs to this effect should be displayed prominently on doors leading to rooms in which infected animals are housed.

MEDICOLEGAL FACTORS

There remains one additional aspect of the many problems common to any laboratory concerned with infectious diseases communicable to human beings. This is the medicolegal situation created when an employee of the laboratory becomes a victim of an infection that may have been contracted during the performance of his regularly required duties.

Potentially hazardous procedures include the culturing, subculturing, and other manipulations of Mycobacterium tuberculosis, certain fungal agents, species of the genus Brucella, bacillus of anthrax, and certain species of the genus Pasteurella. These infectious agents are pathogenic for man and must always be handled with circumspection if the possibility of accidental human infection is to be reduced to a minimum.

Most states have workmen's compensation laws which provide benefits to persons who suffer injury or illness in the course of performance of duties in areas potentially hazardous to human health. In the case of federal employees, similar provisions are contained in the United States Employee Compensation Act.*

Responsibility for safety measures commensurate with the magnitude of the hazards which exist in laboratories concerned with diseases communicable to man must be accepted by the employer. He can best discharge this responsibility by (1) providing adequate and well-designed equipment; (2) selecting intelligent, dependable, and conscientious employees; and (3) insisting on generally acceptable standards of technical performance.

Laboratories operating with inadequate or obsolete equipment and laboratories which employ improperly trained technicians are dangerous to all personnel. I have been advised by competent legal counsel that the director of such a laboratory could properly be held accountable for damages for incapacitating illness stemming from unwise and undisciplined practices.

SAFETY OF PERSONNEL AND AVOIDANCE OF CROSS-INFECTION

Finally, I would reiterate that safety measures in laboratories concerned with infectious diseases must be strictly maintained if two major objectives are to be realized. The first of these objectives concerns the welfare and safety of personnel whose duties at times require intimate and repeated exposure to virulent bacteria, many of which are capable of producing serious, disabling disease that may have lethal consequences. The second objective is to preclude the possibility of cross-infection from one animal to another. Should this occur—and it has occurred—the results may not only be confusing and inaccurate but may well create a situation that could require much time, energy, and expense to correct. Confidence in the reliability and accuracy of results in research or service laboratories cannot be established or maintained if there exist attitudes of complacency or indif-

*According to Wedum, "under the Federal Employees' Compensation Act, occupational death of the head of a family, consisting of a wife age 35 and three children average age 4, may result in payments based on the minimum salaries for the respective positions of $84,000 for a GS-7 technician, and $167,000 for a GS-13 supervisor."

ference or if carelessness or negligence is tolerated.

COMMENT

Strict observance of reasonable rules or regulations contribntes to an atmosphere of confidence on the part of those who work in areas of this kind. There is no place in tuberculosis service or research laboratories for those who persist in an attitude of indifference to the rules of safety. Likewise, *persona non grata* is the occasional hardy, indestructible person who is certain of his own invulnerability to infection by tubercle bacilli or other pathogens. He cannot be bothered by observance of safety procedures, and he considers them foolish and unnecessary impediments to his freedom of action.

Rules of procedure must apply to all; they should be of a common-sense character, and their reasonableness should be accepted by the laboratory personnel as minimal requirements designed not to harass them but to assure the personal safety and protection of every person whose duties require him to be present in an area of potential infection.

SUMMARY

The potential hazard of human and bovine tubercle bacilli to human beings has been reiterated, and the tuberculosis laboratory as a source of tuberculosis infection is emphasized. The most basic factor in avoidance of accidental laboratory infections with tubercle bacilli is the human equation. Every member of the laboratory staff must accept his or her responsibility for strict adherence to rules which, by common consent, are essential for the protection of one's self as well as others. Knowledge of the disease-producing potential of tubercle bacilli, the intuitive practice of personal hygiene, and a compelling sense of responsibility for the welfare of others are indispensable personal ingredients without which safety rules, regulations, directives, entreaties, and commands are futile.

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Significant differences in dissolution rates for different brands of plain aspirin tablets probably account for conflicting reports on the relative advantages of plain and buffered tablets. Dissolution half-times varying from eight and three-fourths to thirteen and three-fourths minutes for 6 brands of plain tablets have been reported. Half-time for the buffered form is about five minutes. Incidence of irritation and the absorption rate of the drug are functions of the dissolution rate. Therefore, if differences in dissolution characteristics of 2 products are not pronounced, no differences between them may be notable clinically. The converse also is true.

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Tuberculosis Control in Saskatchewan—Past and Future

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THE YEAR 1961 marks the fiftieth anniversary of the Saskatchewan Anti-Tuberculosis League. However, not until 1917 was the first sanatorium completed and ready for occupancy.

The changes that have occurred in the field of tuberculosis control during the past fifty years is a tribute to the soundness of the program that was developed by the early workers in the fight against tuberculosis. That the fight has been successful to date can be amply demonstrated by most tuberculosis associations, including the one in Saskatchewan.

During the early years, progress appeared to be slow, beds were at a premium, and a large number of active cases remained in the community to propagate their infection. Infection was universal, so that, by the time an individual reached adulthood, he had already been infected with the tubercle bacillus. If he did not develop tuberculosis with the first infection, he was considered to have acquired immunity to subsequent infections. A positive tuberculin reaction was considered to be a good thing—and so it was, considering the fact that infection was high in the community.

EARLY EFFORTS

The effort to control tuberculosis was directed at lowering the amount of infection in the community. The first requirement to be met was adequate bed facilities to segregate active cases of tuberculosis. The next step was to promote every possible aid to early diagnosis and to remove the financial burden from patients requiring treatment. Free treatment, which became available to residents of Saskatchewan in 1929, was a big step forward in the control of tuberculosis in this province. Patients could now stay in the sanatorium until their disease was controlled and did not have to leave prematurely because of inability to pay. In addition, patients were admitted to sanatoriums earlier and with less advanced disease, and therefore treatment became more successful.

In 1941, the first mass x-ray survey was held in Saskatchewan, and such surveys have been held each summer since that time, bringing about the earlier diagnosis of new active cases among the healthy population. At first, for every 700 persons x-rayed, 1 new case of tuberculosis was discovered. However, it was not long until this rate began to drop. Today we are in the process of covering the population for the fifth time, and the rate is in the neighborhood of 1 case for every 6,000 persons examined. In addition to the active cases that are discovered, the mass surveys have been useful in detecting persons who have had tuberculosis but who have never received treatment—that is, the tuberculosis-inactive group. Through the mass surveys, we have been able to obtain an extensive case registry of persons with inactive tuberculosis. Also, many nontuberculous chest conditions, such as cancer, heart conditions, and so forth, have been reported to the family physician.

In 1948, the hospital admission x-ray program was instituted. This program has been more productive of new cases than the mass x-ray program. The current case rate of this program is approximately 1 case for every 2,000 x-rayed, compared to 1 for 700 at the beginning.

The net result has been the early diagnosis of tuberculosis, which in turn has resulted in lowering the infection in the community. That the amount of infection has been lowered is beyond argument—this is shown by the results of our mass tuberculin surveys.

We have been conducting mass tuberculin surveys in Saskatchewan since 1954, and at this writing, we have completed all areas except the adult populations of the 4 larger cities in the province—Regina, Saskatoon, Moose Jaw, and Prince Albert. Year after year, the results of our tuberculin surveys show that approximately 80 per cent of the population have never been ex-

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posed to tuberculosis. This percentage varies with the age group—from a high of 99.7 per cent with a negative test in children under the age of 5 to a low of 37.47 per cent with a negative test in the 60 to 64 age group.

CHANGES IN THE TUBERCULOSIS PICTURE

The reduction in the amount of infection in the community has produced several changes in the tuberculosis picture.

Fewer new active cases discovered. Nearly every tuberculosis association today is able to cite figures showing the reduction in the number of new active cases that are being discovered each year. For the province of Saskatchewan, the reduction in the number of new active cases is given in table 1.

Fewer new active cases from contacts. The manner in which the number of new active cases has been reduced suggests that, in the past, the vast majority of new cases arose from individuals recently infected. The examination of contacts has always been a good source of new active cases. Most preventive campaigns include contact examinations in their case-finding programs. However, since more emphasis has been placed on earlier diagnosis, the results from contact examinations have shown a decline. During the 1940 decade in Saskatchewan, the rate of new active cases from contact examinations varied from 2 to 3.6 per 100 examinations. Since 1958, the rate has been in the neighborhood of 1.2 per 100 examinations—that is, it has been reduced from one half to one third of its former value. In the early 1930s, the rate at times went as high as 6 per 100 examinations.

Shift in age incidence of tuberculosis. Since infection in the community is being eliminated, and since the recently infected individual is no longer the major source of new cases, what, then, is the source of new active cases of tuberculosis? A walk through the wards in any sanatorium will provide the answer. The most startling discovery is the age of the patients that we see on the wards. At one time, tuberculosis was considered a disease of the young adult—most patients were in their 20s or 30s—the most productive age groups in our society. However, today an ever-increasing number of patients are over 60, and a goodly proportion of these are in their 70s and 80s.

Table 1 shows the percentage of new active cases in persons over 60. The percentage has increased from 3.6 per cent in 1936 to 30.7 per cent in 1958. Today, the age group over 60 constitutes the largest single group in the sanatorium population and is the group in the community that has the highest percentage of positive tuberculin reactors. This group lived in the community when tuberculous infection was at its height, which would seem to indicate that this group is developing tuberculosis as a result of infection received fifty years ago. It would not seem logical to assume that this group is being exposed to new infection any more than other age groups, especially when we know that the amount of infection in the community has been drastically reduced.

Since the previously infected, or tuberculin-positive, section of the population is becoming the major source of new cases, it would seem logical to conduct special x-ray surveys among this group. During the summers of 1958 and 1959, the Saskatchewan Anti-Tuberculosis League carried out a special x-ray survey among the previously known positive tuberculin reactors. Altogether, 33,229 persons with a known positive tuberculin reaction were x-rayed and 10 new active cases of tuberculosis were discovered. This is equivalent to a rate of 1 new active case per 3,323 x-rayed, which is almost double the rate for the general population. The tuberculin-positive group, therefore, would seem to be worthy of special consideration. However, we have decided not to pursue this type of survey further. It was our opinion that, with the same effort, a larger number of people could be studied by x-ray, and we would therefore discover more active cases. We cannot afford to neglect new cases of tuberculosis that develop among the large section of the tuberculin-negative population as the result of recent infection. In addition to this, we found, on closer study of the 10 cases discovered by this special survey, that 8 would have or should have been discovered by one of the other programs in our preventive campaign.

TABLE 1
NEW ACTIVE CASES OF TUBERCULOSIS

Year	*Number of new active cases*	*Rate per 100,000*	*Per cent over age 60*
1931	624	67.7	— — —
1936	513	54.7	3.62
1941	523	58.4	3.28
1946	588	70.6	7.14
1950	415	49.8	10.36
1955	314	35.7	15.29
1956	227	25.8	21.14
1957	212	24.1	22.64
1958	225	25.4	30.67
1959	192	21.3	27.6
1960	208	22.9	21.6

STUDY

However, the tuberculin-positive section of the population still should be considered as a reservoir for the tubercle bacillus in the community. In Saskatchewan, this group is made up of approximately 200,000 individuals. This is actually too large a group to keep under constant surveillance, but if we could determine whether there was a subgroup which was more responsible for our new active cases, it might be possible to evolve a preventive program of early detection. In order to discover whether there was a subgroup among the tuberculin-positive population, we decided to make a case study of the new active cases admitted to the Fort Qu'Appelle Sanatorium during 1958 and 1959. The Fort Qu'Appelle Sanatorium zone covers approximately 50 per cent of the population of the province. During 1958 and 1959, 143 new active cases were admitted to the sanatorium, of which 29 were discarded because of a change in the diagnosis (inactive tuberculosis, nontuberculous conditions, and so on) and 23 were nonpulmonary forms of tuberculosis. The remaining 91 cases of pulmonary tuberculosis were divided into the following 3 main categories: (1) tuberculin converters, 28, or 30.8 per cent; (2) previous negative x-rays, 12, or 13.2 per cent; and (3) previous inactive lesions, 51, or 56 per cent.

In the group classified as tuberculin converters, we had records—from mass tuberculin surveys, clinics, and so on—of a previous negative tuberculin test (to 0.1 mg.) followed by a positive tuberculin test. The interval between the two tests varied, but in no case was it greater than five years.

In general, the group with previous negative films did not have a record of a previous tuberculin test; 4 had a previous positive tuberculin test. All cases had previous films which on review were considered as showing no evidence of tuberculosis. In all probability, the majority of this group should be considered as recent converters.

The last group had previous chest films which showed such evidence of healed tuberculosis as calcification or fibrosis. Many of these patients had been on regular follow-up for years, with numerous negative sputum examinations before their breakdown.

The total number in this study is small, and we intend to continue with the study for several years. However, the distribution of the 3 main categories is interesting, and it would seem to confirm our suspicions that there is a special group within the tuberculin-positive population that is worthy of special attention. This group consists of those individuals who show x-ray evidence of previous infection with the tubercle bacillus. At the same time, it is still very important to discover new cases that arise as a result of recent infection, as this group still accounts for approximately one third of our new active cases.

The age distribution of the 3 categories is of interest and is shown in table 2.

The majority of the converters are in the age groups up to the age of 19; the previously inactive group accounts for most of the cases beyond this age and for all those in persons over the age of 60.

HAZARDS OF OPEN TUBERCULOSIS

It has been mentioned that infection was universal fifty years ago and that exposure to the tubercle bacillus usually occurred early in life. If a person did not develop tuberculosis after his first infection, he was considered to have acquired more resistance to subsequent exposure. That is, the general level of resistance in a community should have been higher in the days of universal infection than it is today, when 80 per cent of the population has never been exposed to tuberculosis. Since the level of acquired resistance of the general population is lower today, the presence of an open case of tuberculosis presents a much greater hazard to the community than it did fifty years ago. Although tuberculosis has usually been considered an endemic disease rather than an epidemic one,

TABLE 2
AGE DISTRIBUTION OF 91 TUBERCULOUS PATIENTS

	<1	*1-4*	*5-9*	*10-14*	*15-19*	*20-24*	*25-29*	*30-34*	*35-39*	*40-44*	*45-49*	*50-54*	*55-59*	*Over 60*	*Total*
Tuberculin converters	1	6	7	4	2	1	2	1	1	0	2	0	1	0	28
Previously negative chest films	0	1	0	1	1	3	0	1	1	2	1	1	0	0	12
Previously inactive lesions	0	0	0	0	2	2	4	4	4	4	3	3	4	21	51
Totals	1	7	7	5	5	6	6	6	6	6	6	4	5	21	91

because of these altered circumstances, local epidemics should be expected.

As an example of what can happen in a community, I should like to cite the following case.

Mrs. K., a mother of 5 children, attended a mass tuberculin and x-ray survey in May 1958. Her tuberculin test was 4+ positive, and the miniature (70 mm.) film revealed minimal calcification at both hila. The 5 children had negative tuberculin tests, and the x-ray film of her husband was clear. In September 1959, Mrs. K. had a respiratory illness. She was treated as an outpatient, but no chest film was taken. She improved on treatment, although she still had some respiratory symptoms, such as cough.

During the Christmas holidays in 1959, she visited several members of her family at scattered points throughout the province, attending several Christmas parties and other affairs. In February 1960, she had an x-ray film of the chest taken because of persistence of respiratory symptoms.

As a result of this x-ray film, she was admitted to the sanatorium with the diagnosis of far advanced bacillary tuberculosis. Her family was examined, and the 5 children and her husband were admitted to the sanatorium with active pulmonary tuberculosis. During the period from February to September 1960, 121 contacts were examined, with the result that a total of 25 new cases were diagnosed. Only 1 of the 25 is considered a tuberculous infection—that is, no demonstrable x-ray lesion but evidence of recent tuberculin conversion; all the other cases have x-ray evidence of pulmonary tuberculosis. Many of the 25 cases have records of a negative tuberculin test during the summer of 1959.

CONCLUSION

A great deal of progress has been made in the past fifty years toward the control and eradication of tuberculosis. Much of this progress has been the result of a decrease in the amount of tuberculous infection that is in the community because of early diagnosis and segregation.

This progress has been rewarding, but it has also left us with many problems which will be just as difficult to overcome in the future as those that have been solved in the past.

We have living in our communities today a large section of the population who have never been exposed to tuberculosis. Side by side with this group, we have a smaller section of the population acting as a reservoir for the tubercle bacillus. Thus, it is the responsibility of the medical profession, the tuberculosis associations, and the departments of health, working together, to carry out a campaign of prevention and control so that this situation does not get out of hand.

PAROXYSMAL ATRIAL tachycardia (PAT) with atrioventricular block is an increasingly common manifestation of digitalis intoxication. The arrhythmia may ensue during constant maintenance therapy with digitalis if cardiac compensation deteriorates or potassium stores are depleted. Diuresis, hemodialysis, or vomiting may induce negative potassium balance, although serum values usually are normal. Misdiagnosis of PAT with block as a variant of atrial flutter may cause additional administration of digitalis, further endangering the patient. Normal cardiac rhythm is restored by therapy with potassium or procaine amide, singly or combined, and omission of digitalis and diuretics. Electrocardiographic features of PAT with block are (1) atrial rate of 200 or less, (2) changes in contour of P waves, (3) isoelectric baseline between atrial complexes, and (4) variable degrees of atrioventricular block. Occasionally, only response to potassium administration permits differentiation between flutter and PAT with block.

B. LOWN, N. F. WYATT, and H. D. LEVINE: Paroxysmal atrial tachycardia with block. Circulation 21:129-142, 1960.

Small Tuberculosis Outbreaks

J. ARTHUR MYERS, M.D.

Minneapolis

In January 1961, there was great concern manifested about a tuberculosis outbreak in Superior, Wisconsin. Attention was called to this situation on radio and television news and in newspaper items. All of this created an intense interest among people of a large geographic area which could not have been accomplished in any other way. Those striving to eradicate tuberculosis are everlastingly grateful to the management and news departments of these organizations.

The Superior incident is not a new experience among tuberculosis workers. Such happenings were so commonplace a few decades ago that, in some cities, 70 per cent of the children had been infected with the tuberculosis germs by the age of 14 and 90 per cent or more by 18 years. However, the organized tuberculosis eradication campaign that apparently began at Willmar, Minnesota, in 1890, was placed on a state scale in Pennsylvania in 1892 and on a national basis in 1904. For many years, there have been more than 2,500 tuberculosis associations which have been so well supported by the sale of Christmas seals as to enable them to disseminate much-needed information about tuberculosis. This information led to providing sanatoriums and numerous other procedures designed to reduce spread of tubercle bacilli among people and animals. The veterinary profession has so reduced tuberculosis among cattle that it has become rare for a child to acquire infection by direct contact with or from products of animals.

The antituberculosis work in this country has been so effective that the great majority of children through high school age do not harbor tubercle bacilli. Outbreaks like that in Superior, which were so trite in the past, now occur only here and there. They will continue to appear as long as children and school personnel are allowed to harbor unrecognized tubercle bacilli. Several occur in this country each year, such as the one in Superior and the one reported in the January issue of *Horizons*, official publication of the Ohio Tuberculosis and Health Association, under the title "TB Pocket in Henry County Boosts Infection Rate Skyhigh." That outbreak also started with a senior high school student.

Such outbreaks denote one of the death struggles of tuberculosis. Foci of tubercle bacilli now existing in bodies of children and school personnel may be likened to machine gun nests and land or sea mines in potential destructiveness. Whenever and wherever an outbreak occurs, whether it be in children or in other segments of the population, it should be promptly controlled by the procedures Dr. Shaffer employed in the management of the Superior outbreak, which he describes in this issue of The Journal-Lancet. If left unmolested, tuberculosis pyramids and soon regains its former destructiveness. When persons harboring tubercle bacilli are identified, diagnostic procedures are available which will detect evolving clinical lesions while they are minimal, before they become contagious, and when they can be successfully treated.

It was recognition of these facts which led the Committee on Tuberculosis of the American School Health Association (A. O. DeWeese, M.D., executive secretary, Kent, Ohio), in close cooperation with tuberculosis associations and health departments, to develop and promote a plan for certifying schools on the basis of tuberculosis control work in progress.

In setting up the qualifications for certification of schools nearly twenty years ago, the A.S.H.A. committee and the state tuberculosis associations recognized dangerous loopholes created if only children in certain grades were tested with tuberculin and if testing of school personnel were on a voluntary basis. Therefore, provision was made whereby at least 95 per cent of all children and 100 per cent of personnel members could be tested, with appropriate follow-up procedures for a school to qualify for a certificate. Moreover, the goal established by those who set up qualifications for certification was, and continues to be, eradication of tubercle bacilli. To condone discontinuing the tuberculosis eradication program when only 1 per cent of school children in any area react to tuberculin was, and is, considered poor economy. Even if less than 1 per cent of school children are left harboring tubercle bacilli, the disease could, in

a relatively short time, regain its former stronghold among people and animals.

The first schools were certified in 1945. Now certificates are displayed in thousands of schools in a sizable group of states in this country. The certification of schools project, when properly conducted, spells the doom of a tuberculosis outbreak before it is created by the tubercuIous teacher or other personnel member, or even the occasional high school student. In several places, the certification of schools project is on a statewide basis, where the goal is a certificate in every school.

While outbreaks should become fewer as the number of infected children and staff members decreases, they will not vanish until tubercle bacilli are eradicated. With well-nigh one-third of the population of the United States in schools, our opportunities and our responsibilities are obvious.

Tuberculosis Outbreak in a School

S. A. SHAFFER, M.D.

Hawthorne, Wisconsin

In August 1960, a young woman of 18 years was admitted to the Middle River Sanatorium with far-advanced, exudative pulmonary tuberculosis and positive sputum. She had been graduated in June 1960 from East High School in Superior, Wisconsin. The case was duly reported to Dr. E. G. Stack, Jr., health officer, who attempted to get the class together during the summer for tuberculin testing, with incomplete success. However, in those whom he tested, apparently no other reactor was found.

Toward the end of 1960, another girl of 18, who had recently left East High School, was found to have pleural effusion and to have recently converted to a strongly positive tuberculin reactor. Bacteriologic studies revealed tubercle bacilli in gastric washings. She was also admitted to Middle River Sanatorium and is being treated with antituberculosis drugs. This occasioned the following investigation.

In late December 1960, a tuberculin skin-testing program was carried out throughout East High School; 380 students and some adults were tested. In the 380 students, 18 positive reactors were found, and 4 positive reactors were found among the adults. Among the 18 students, 2 more cases, presumably active, were disclosed, one of which had a pneumonic patch in the left lower lung field and the other, an early infiltrate in the right upper lung field. They were classified, therefore, as moderately advanced and minimal cases of tuberculosis.

No other evidence of definite infiltration was found on the x-ray films of the remainder of the children. However, a series of bacteriologic studies is being made on all the tuberculin reactors, and they are being encouraged to take a course of isoniazid therapy for precautionary measures even though, in some cases, their conversion looks roentgenologically as if it may not have been recent. It is noteworthy that none of these children had a history of positive tuberculin reaction previously. The four, of course, who have active disease are being retained at the sanatorium.

Repeat tuberculin-testing was carried out on 130 children who missed the first round, and 9 more were found to be reactors, as well as one more member of the staff. Roentgenograms are being made of the chests of these tuberculin reactors, and they will be handled as were the previous group.

Dr. Stack recently surveyed Central High School in Superior and found that there were 14 positive reactors among 1,235 students tested and 6 positive reactors in 31 of the school staff tested. The difference in the percentage of positive reactors in the two schools appears to be significant.

Cathedral High School in Superior was surveyed on January 31, 1960, and, of 368 students tested, there were 3 positive reactors; of the 13 staff members tested, none was a positive reactor.

S. A. SHAFFER *is superintendent and medical director of the Middle River Sanatorium, Hawthorne.*

William Hugh Feldman

D.V.M., M.Sc., D.Sc. (Hon.)

J. ARTHUR MYERS, M.D.

Minneapolis

MINNESOTANS are likely to forget that Dr. William H. Feldman is not a native son of the state. He now lives in Washington, D. C., where he is chief of laboratory research in pulmonary diseases in the Department of Medicine and Surgery of the central office of the United States Veterans Administration. He left Minnesota in the fall of 1957, before his retirement from the staff of the Mayo Clinic on January 1, 1958. Since 1944, he had been professor of comparative pathology at the Mayo Foundation Graduate School, University of Minnesota.

After graduation from Colorado State College* in 1917, he was occupied for several years in teaching and research at his alma mater. Dr. Feldman started his long career in Minnesota in 1927. His pioneer work in experimental tuberculosis has brought him recognition throughout the world.

PREPARATION

William Feldman was born in Glasgow, Scotland, in 1892 and was brought by his mother to the United States in 1894. They settled in the town of Paonia, which was then still the frontier country of western Colorado. Of his childhood days, he recalls, "There I attended the public schools with perhaps the usual indifference that seems to be the native characteristic of many, if not most, of the present generation."

Paonia had experienced an influx of Easterners who were attracted by the salubrious climate and natural resources of the area. Many of these newcomers were college graduates. By the time Bill Feldman had completed his high school course, a University Club had been established in Paonia, with a membership of 50. This was a rarity in so small a community, the population then being around 1,200.

At this time, the national average of high school graduates entering college was around 4 per cent, but in Paonia more than 50 per cent of the graduates went to college. Dr. Feldman has always paid tribute to the college graduates from the east for their influence on the subsequent careers of the high school students of Paonia.

After graduation, more than half of William Feldman's class of 16 entered various colleges and universities; he enrolled in the fall of 1913 at Colorado State College at Fort Collins. He was not prepared financially, but this did not affect his decision in the least. He went to college because many of his high school friends were going and with, as he put it, "a very limited conception regarding what it was all about."

In 1913, the total enrollment of Colorado State College was 600. It was not difficult for a student to meet all or part of college expenses by working in Fort Collins, then a thriving town of 10,000. "If one could obtain a room paid for by cash or service, board could be had for $12 to $15 per month." William procured a job as night clerk at the local Y.M.C.A., which provided him with a room. During his early school years, he had learned to play the cornet and now he became a member, and eventually director, of the college band, in this way adding to his always depleted cash resources. Through much personal sacrifice, his parents supplemented his earnings sufficiently to spare him any actual hardship.

William went to Fort Collins a few weeks before the fall term opened with no particular concept of the course he was to take. His decision in this matter was aided when a junior in the veterinary school

*Now known as Colorado State University.

told him the course required no higher mathematics. This sounded fine, so he promptly enrolled.

World War I came along in April 1917, the year of his graduation. All members of his class who were without dependents immediately sought commissions in the Veterinary Corps and in a short time, all received orders for duty except William. It came out in his application that he was a "foreigner," having arrived in this country at the age of 2. This was a blow to him, as he had always considered himself an American and had voted in 1916 for Woodrow Wilson. Finally, this situation was straightened out, and he became a naturalized citizen in 1922.

His failure to be accepted for service in the Veterinary Corps of the United States Army, William felt, had a great influence on his subsequent career. He attempted to join up with the British after his rejection, but a severe attack of influenza in November 1918 prevented his doing so. Hostilities ceased with the Armistice on November 11.

William Feldman became a member of the faculty of Colorado State College in 1917, shortly after graduation. He attributed his invitation to join the teaching staff as an assistant professor to the teaching shortage and the fact that he was available. During the next decade, he taught laboratory classes in pathology and bacteriology, did meat inspections for the city of Fort Collins, and taught classes in meat inspection and pharmacology. This was a hard schedule but an experience which proved invaluable to his future work. He augmented his beginning salary of $1,600 per year by directing the college band and by playing trumpet in a dance orchestra.

At the end of the war, the veterinary division of the college was reorganized, and Dr. Feldman had the opportunity to devote more time to pathology and bacteriology. He still had too little time to apply to research, which was also expected of him. In 1920, he went to the University of Michigan for work in pathology under Dr. A. S. Warthin. It was this course that inspired him to remain in pathology permanently.

EARLY EARLIER

Dr. Feldman writes of his works, ". . . in the list of my publications, most of my earlier papers, like those of many others of that era, were concerned with reports of cases. Actually, at that time the field of animal neoplasia offered a rich and, to the novice, a very exciting field for microscopic exploration."

While still at Colorado State College, Bill became acquainted with the newly appointed professor of pathology at the Medical School of the University of Colorado, Dr. Ralph G. Mills. Later, after Mills joined the staff of the Mayo Clinic, he heard of an opening for a veterinary research pathologist at the Institute of Experimental Medicine of the Mayo Clinic. Upon his recommendation, Dr. Feldman became associate in the Institute in June 1927. Following his arrival in Rochester, he had an opportunity to expand the material for which he had received the degree of Master of Science at Colorado State College in 1926. This was published as a book, *Neoplastic Diseases of Domesticated Animals*, in 1932.

His initiation into the realm of tuberculosis was a case report, which the late Frank B. Mallory accepted for publication in the *American Journal of Pathology* in 1927. It concerned a lesion on the tongue of a 36-year-old man, who had had pulmonary tuberculosis for fourteen years. From examination of a frozen section, Feldman concluded that the lesion was a tuberculous granuloma. Ater appropriately stained paraffin sections were prepared, he found acid–alcohol-fast bacilli within the substance of the lesion. He said, "My interest aroused, I reviewed the literature and found that all who previously had studied the condition considered tuberculosis of the tongue to be of infrequent occurrence." Accordingly, he prepared photographs to illustrate the article and submitted it for publication.

From that time, most of his work has been devoted to tuberculosis. When asked why he became so deeply interested in this disease, he goes back to his boyhood days in Paonia, when the invigorating climate of western Colorado was considered beneficial to persons suffering from tuberculosis. Some of those who flocked there recovered and became citizens of the area, others returned east, and still others died. Dr. Feldman recalls that his mother had great sympathy for those afflicted with the disease and on occasion had furnished the seriously ill with a bed on her front porch. He remembers one person who died there.

WORK WITH TUBERCULOSIS

In 1917, when Dr. Feldman was graduated in veterinary medicine, the United States Bureau of Animal Industry instituted a nationwide campaign for the eradication of tuberculosis among cattle. Beginning in 1892, when Dr. Leonard Pearson and his student, Charles E. Cotton, University of Pennsylvania, demonstrated the efficacy of the tuberculin test in diagnosis of tuberculosis in cattle, such a tremendous amount of confirmatory postmortem work was done that a sound method of ultimate eradication was sought and eventually evolved. This consisted of using the county as the unit and officially certifying those which met established qualifications. Before this national eradication program began, the loss to cattle owners in the United States from tuberculosis was $300 million each decade. At the points of federal inspection in slaughter houses in 1916, the carcasses of 40,000 cattle were condemned because of tuberculosis.

Dr. Feldman was aware not only of the tremendous economic situation but also of the serious public health problem, inasmuch as bovine tuberculosis may cause in people a serious deforming and incapacitating disease, with lethal potentialities. Throughout the years, he has been a potent force in this program, not only by supporting it to the nth

degree but also by producing new fundamental information in his laboratory.

The program was so sueeessful that, by 1940, all states had qualified for the modified accredited tubereulosis-free rating. However, total eradication had not been achieved, as the modified, accredited tubereulosis-free rating was awarded when eounties had redueed the pereentage of tubereulin-reactor eattle to 0.5 or less. Dr. Feldman, with others, recognized that periodie testing of all cattle must eontinue until none reaets. In Minnesota and some other states, the goal is being approached, sinee only 1 tubereulin reactor is found in eaeh 5,000 cattle tested. Testing among the 97 million cattle in the United States in 1960 revealed 0.15 per cent reaetors.

Dr. Feldman has always recognized that tubereulosis eannot be eradieated exeept by the elimination of all types of pathogenie tubercle bacilli. Therefore, there must be elose eooperation betwcen the veterinary profession and those working on the disease in human beings. To this end, he has provided mueh information as to disease produeed by the different types of organisms in various animal speeies, including man. An exeellent example of this endeavor was the publieation of a monograph, *Avian Tuberculous Infections*, in 1938. This 483-page book is an outstanding contribution, and it was the first time that all pertinent information on avian tubereulosis had been brought together in a single volume.

When the Committee on Tuberculosis of the Minnesota State Medieal Association, whieh had existed as a subeommittee sinee 1924, was advaneed to regular seientifie eommittee status in 1940, the chairman promptly recommended Dr. Feldman as ex-offieio member. For many years, he served in this capaeity, pratieally never missing a monthly meeting. As he was a leader in a profession whieh was forty years in advanee of the medieal profession in its tubereulosis eradication movement, Bill Feldman proved a most important member in developing for the medieal assoeiation a state-wide human tubereulosis eradieation program superior to that in any other area.

When Dr. Thomas G. Hull wanted a well-qualified person in this eountry to write a chapter for the 1947 edition of his book, *Diseases Transmitted from Animals to Man*, he ehose Dr. Feldman, who produeed a most eomplete and authoritative manuseript on tubereulosis. Later, for the fourth edition, he prepared, at Dr. Hull's request, a ehapter on pseudotubereulosis.

CHEMOTHERAPY

In the early part of this eentury, hope of produeing an effeetive drug for the treatment of tubereulosis had almost vanished. However, when Ehrlieh diseovered the effeet of arsphenamine on Treponema pallidum, interest in finding an effective drug against the tuberele baeillus was revived. All effort was unavailing, but hope again revived in 1935, when Domagk proved the effectiveness of Prontosil in dealing with hemolytic streptococeal infeetions in mice. This was followed promptly by the synthesis of a large number of related eompounds, some of which were effective in treating serious and often fatal infectious. Everywhere there was wonderment as to what effect these compounds might have on tuberele bacilli.

During the years, Dr. Feldman had developed ideal laboratory facilities for work in experimental tuberculosis. Therefore, everything was in readiness to put the various sulfonamide derivatives and other substances to the most rigid and exacting tests of their effieaey in eontrolling tubereulosis in animals, espeeially guinea pigs.

Dr. Feldman also emphasizes his good fortune in having had as a partner Dr. H. Corwin Hinshaw, formerly of the staff of the Mayo Clinie, when the investigation of chemotherapy of tubereulosis was started. Dr. Hinshaw was well prepared in experimental methods and was also an astute student of clinical tubereulosis. The mutual respeet and admiration these two researehers had for one another made them the perfeet team for the task before them.

Their primary interest was in two items: (1) tolerance of a host for a drug in adequate doses and (2) ability of the drug to bring about unequivoeal repressive effects on a previously progressive tuberculous proeess.

They began testing sulfonamides, starting with sulfapyridine and following with sulfathiazole, sulfadiazine, and sulfamerazine. In addition, they tested many other sulfonamide eompounds, using hundreds of laboratory animals.

While there were some encouraging clues in the results of this large series of studies, no drug of the many tested was able to arrest completely the progress of experimental tubereulosis. Nothing was found to justify the use of these drugs in the treatment of tuberculous people. Soon after the studies on sulfapyridine were completed, another group of ehemicals, known as sulfones, was made available by Dr. E. A. Sharp of the Parke, Davis Company. Promin is the trade name of the first one studied. A preliminary report of the first in vivo experiment with Promin was published in the *Proceedings of the Staff Meeting of the Mayo Clinic,* Oetober 30, 1940. The results of this first experiment appeared so promising that investigations were extended not only with Promin but with several other related synthetie organie eompounds, ineluding Promizole.

In 1941, Dr. Feldman was invited to present the annual John W. Bell Memorial Tuberculosis Leeture, sponsored by the Hennepin County Tubereulosis Assoeiation, the County Medieal Soeiety, and the Minneapolis Department of Health. His title was "Chemotherapy in Experimental Tubereulosis." He said,

> There has been no more fascinating or epochal phase of modern medicine than the development and clinical ap-

plication of new drugs that have conquered infections due to streptococci, meningococci, gonococci, and pneumococci. This is only a partial list of the infectious agents that have been shorn of their disease-producing, and perhaps life-taking, propensities by the relatively new sulfonamide-containing drugs. New compounds are constantly being prepared, and the possibilities for future development that may eclipse even the spectacular achievements already witnessed are limited only by the imagination of the research chemist.

Although he had recently observed encouraging results from the use of Promin, he warned that, "until facts have been firmly established by repetition of the original experiment and confirmed by independent workers, it is wise to maintain a conservative attitude concerning chemical substances said to have therapeutic value in tuberculosis."

Concerning the studies on sulfones, particularly Promin, Dr. Feldman later said,

> That we had been able to demonstrate the vulnerability of the pathogenesis of tuberculosis to the action of a specific chemical substance was gratifying and of significance in sustaining our enthusiasm and persistence in the search for more effective agents. We had in a sense "got our foot in the door," a door which previously had seemed an impassable obstacle.

Early in 1942, Drs. Feldman and Hinshaw were invited to present the results of their studies on Promin in experimental tuberculosis before the thirty-eighth annual meeting of the National Tuberculosis Association held in Philadelphia. Despite the fact that they clearly illustrated to the audience the striking effect of Promin on experimental tuberculosis in guinea pigs, which was something never before demonstrated in the world, they received no encouragement from the audience, and, in fact, the report was received with cynicism. For this attitude of the audience, there were probably several reasons: (1) many physicians and others had long been of the opinion that no drug would ever be found that was effective in controlling tuberculosis in animals or people and therefore would not believe what had been so clearly demonstrated to them; (2) at that time, few people knew of the meticulousness with which Drs. Feldman and Hinshaw were conducting their work in experimental tuberculosis and, therefore, many did not believe what was said or what they actually saw illustrated; and (3) few in the audience had little, if any, understanding of experimental tuberculosis and therefore were in no position to evaluate the results of such a study.

Nevertheless, this attitude on the part of the audience did not have the slightest discouraging influence on Drs. Feldman and Hinshaw. There was no question in their minds that they had demonstrated something that proved beyond all doubt that lesions produced by tubercule bacilli are susceptible to drug treatment. Dr. Feldman said, "However, the shortcomings of Promin in clinical trials indicated that our triumph was incomplete and that the search for drugs more effective than this sulfone was just beginning."

Since Promin was the first antimicrobial substance proved unequivocally effective in suppressing experimental tuberculous infection induced by human tubercle bacilli, the use of the drug in the treatment of leprosy soon followed at the leprosarium at Carville, Louisiana. Subsequently, the extensive use of Promin and other related sulfones in the treatment of leprosy throughout the world has had a tremendous impact on the social and medical aspects of this disease.

In a paper published in J.A.M.A., May 28, 1960, James A. Doull, Medical Director, Leonard Wood Memorial (American Leprosy Foundation), wrote:

> In 1937, Tillotson and colleagues, starting with DDS, prepared a soluble and less toxic compound, glucosulfone (Promin) sodium. During the next two years, the effect of glucosulfone was studied in several infections, but the results were not spectacular. It was toxic when given orally, even in small doses, irritating when injected subcutaneously, but well tolerated when given intravenously.
>
> The discovery of glucosulfone led to the use of sulfones in leprosy. The intervening and significant event was the publication on Oct. 30, 1940, by Feldman, Hinshaw, and Moses at the Mayo Foundation, of favorable results with the drug in experimental tuberculosis in the guinea pig. This report came to the attention of Dr. G. H. Faget of the National Leprosarium who obtained a supply of the drug. In March 1941, the first patients were treated in a study which eventually revolutionized the treatment of leprosy.

In 1944, Drs. Feldman and Hinshaw decided to try, in their studies on experimental tuberculosis, any likely antibiotic that was not unduly toxic. Through the literature and meetings, they knew of the work of Dr. Selman A. Waksman of Rutgers University, New Brunswick, New Jersey, and his extensive studies on soil organisms.

In July 1943, Dr. Feldman wrote Dr. Waksman to inquire about a highly potent antibiotic he and his associates had discovered and whether it might be available for experimental studies in tuberculosis. Dr. Waksman replied that this substance (clavicin) was so toxic that it had proved disappointing. He invited Dr. Feldman to visit him and his laboratory at any convenient time. This invitation was accepted in November 1943. Dr. Waksman was gratified by Drs. Feldman and Hinshaw's willingness to do experiments on animals with any substance that he might produce and believe worthy of such a study.

STREPTOMYCIN

In January 1944, Schatz, Bugie, and Waksman announced the discovery of streptomycin, which had been produced from a mold known as Actinomyces griseus. Dr. Feldman promptly requested a supply of streptomycin which he estimated would be sufficient to test its antituberculosis activity in a small number of infected animals. This material arrived, and on April 27, 1944, the first experiment, consisting of only 4 guinea pigs, was started. The supply of streptomycin was exhausted after fifty-four days and the animals were killed. Examination

showed that streptomycin was well tolerated in a dose sufficient to exert a marked suppressive effect on otherwise irreversible tuberculous infection in guinea pigs. However, streptomycin had not destroyed all the tubercle bacilli in the tissues of these animals. Therefore, the drug apparently had bacteriostatic, rather than bacteriocidal, power. The results of this experiment were communicated to Dr. Waksman, and all were desirous of conducting further experimental studies. The problem was the production of streptomycin in sufficient quantity. The prospects seemed so good that Drs. Feldman and Hinshaw went to New Brunswick to confer with Dr. Waksman early in July 1944. It was learned that it would be impossible for Dr. Waksman's laboratory to produce the amount necessary for a more complete study. However, he had arranged a meeting with representatives of Merck & Co., Inc., Rahway, New Jersey. This company agreed to produce an adequate amount of streptomycin, and Drs. Feldman and Hinshaw decided to put it to the same long-term study that had been used in the studies on sulfones. After animals were infected with tubercle bacilli, the experimenters waited for six or seven weeks before administering the drug. To thoroughly document their studies, just before beginning the administration of the drug, the liver of each animal in the study, including the controls as well as those to be treated, was subjected to biopsy. Thus, the doctors established unequivocal evidence of the existence of tuberculous lesions before treatment was started, so they were able to compare the situation revealed at biopsy with that present after treatment.

Trial experiments had actually begun on June 29, 1944, when animals were inoculated with virulent tubercle bacilli. Forty-eight days later, biopsies of the liver were done by Dr. F. C. Mann, then director of the Institute of Experimental Medicine, Mayo Foundation. One day after these biopsies, treatment with streptomycin was begun and continued for one hundred sixty-six consecutive days, ending on January 29, 1945. The results of this long-term experiment demonstrated the "unquestionable ability of streptomycin to reverse the potentially lethal course of well-established inoculation tuberculosis in guinea pigs, and the relatively low toxicity and corresponding safety of purified streptomycin." Subsequently, other experiments were carried out and other facts established concerning the effect of streptomycin on tuberculosis. One such fact was that the drug is effective against bovine, as well as human, tubercle bacilli. The experimenters also found that it was not necessary to administer the drug every few hours to obtain satisfactory results. They also demonstrated that streptomycin is not effective in suppressing tuberculosis in animals due to streptomycin-resistant tubercle bacilli. When put to the most rigid test, namely, administration to animals which had been inoculated with large numbers of tubercle bacilli intravenously, the drug modified favorably and often dramatically the course of the disease.

The results of the long-term study, ending on January 29, 1945, were so favorable in every respect that Drs. Feldman and Hinshaw believed streptomycin was worthy of a trial in tuberculosis among people. In December 1944, the supply of the drug was sufficient to start such a study. Therefore, in collaboration with Dr. Karl H. Pfuetze, medical superintendent of the Mineral Springs Sanatorium, Cannon Falls, Minnesota, and several associates at the Mayo Clinic, such studies were begun. By June 1946, 75 persons had been treated. In the earlier studies, it had been observed that the drug had a toxic effect on the eighth cranial nerve, as evidenced by disturbance of equilibrium and decrease in the sense of hearing. This was later overcome, for the most part, by modifying the dosage of the drug and lengthening intervals between administration.

Throughout the earlier observations on tuberculous people, it was pointed out that the drug did not exert fast curative effects but did change the course of the disease in a favorable manner and did definitely suppress previously progressive types of tuberculosis. It was again pointed out that, in people as well as in experimental animals, the action of the drug was largely bacteriostatic and that its usefulness in people was dependent upon continuation of the suppressive action for an indefinitely long time.

There is no finer example in the history of medicine than the care these workers practiced in issuing reports to prevent the public, as well as the medical profession, from becoming overoptimistic about the results of their studies on Promin and streptomycin. They were aware of the great harm that had been done so many times in the past by unjustified claims that had been made for the success of various methods of treatment of tuberculosis. These had often reached the public through large newspaper headlines, giving the millions of tuberculosis sufferers and their families hope that was soon shattered.

Drs. Feldman, Hinshaw, and their associates were so determined that no announcement be made that might be misleading that they exacted an agreement with newspaper reporters to the effect that nothing was to be published except what they, themselves, wrote for that purpose or which they carefully edited before it was printed. Not infrequently, they brought such script to the members of the Committee on Tuberculosis of the Minnesota State Medical Association for approval before it was released. The newspapers were most cooperative, and, therefore, no large headline suggesting that the problem of treatment of tuberculosis had been solved or that its solution was near appeared in the state's papers. The physicians were equally cautious in the various articles published in medical journals to avoid overoptimistic statements that might mislead the medical profession and its allies or that might be misconstrued by writers of newspaper and magazine articles. They continuously pointed out that extensive and prolonged clinical investigation would be required to determine the place of streptomycin in the treatment of tuberculosis among people. In 1954, Dr.

Feldman said, "Now eight years later, many phases of the problem still require additional elucidation."

On June 14, 1945, a conference was called by the Committee on Medical Research of the Office of Scientific Research and Development, which exercised authority in the distribution and use of medicinals in short supply, in Washington. This committee arranged for the attendance of those who had been investigating streptomycin as an antibacterial agent. The drug had become available in sufficient amounts to permit its limited distribution for investigative purposes and to several individuals and groups. One week later, June 20, Merck & Co., Inc., arranged a conference at Rahway, New Jersey. Of course, Drs. Feldman and Hinshaw, having pioneered this work, were invited to both these conferences, where they presented the results of their studies on the use of streptomycin in controlling experimental tuberculosis. The results were so favorable that the management of Merck & Co., Inc., soon thereafter authorized construction of a new plant for the production of streptomycin at Elkton, Virginia.

Drs. Feldman and Hinshaw were invited to present a summary of their observations on streptomycin at the forty-second annual meeting of the National Tuberculosis Association, held in Buffalo, New York, in June 1946. When their presentation was completed, the atmosphere was in sharp contrast to that when they had reported on Promin four years before. In fact, they were completely surprised and highly gratified when during the discussion, Drs. Walsh McDermott and Carl Muschenheim announced that they and their associates at Cornell University Medical College had confirmed the observations of Feldman and Hinshaw. This insured the prompt acceptance of streptomycin as a potentially useful drug in the treatment of tuberculosis.

In 1946, Lehmann (Sweden) presented para-aminosalicylic acid, commonly known as PAS, which he had found had a suppressive effect on tubercle bacilli. In 1951, a chemical now commonly known as isoniazid was introduced and was proved to have a suppressive effect on tubercle bacilli, both in animals and man. Since that time, there have been the 3 major drugs, namely, streptomycin, PAS, and isoniazid, in general use in treating tuberculosis. A number of other drugs, including viomycin and cycloserine, are effective, but not to the same degree as the 3 major drugs. Nevertheless, they are used, especially in individuals whose tubercle bacilli have become resistant to, or whose tissues have become sensitized to, the major drugs.

The United States Veterans Administration and the Armed Forces, with the cooperation of the National Tuberculosis Association, have developed regular conferences on the chemotherapy of tuberculosis. The nineteenth such conference on drug treatment of tuberculosis was held in Cincinnati, Ohio, February 8 to 11, 1960. At these conferences have been presented the reports of the most intensive studies on treatment of tuberculosis in the history of the world. The amount of excellent and well-controlled research work done is almost unbelievable.

Dr. Feldman has been in close touch with all of the work throughout the years, concerning which he wrote in 1954.

> Although modern chemotherapy of tuberculosis has contributed much in combating this disease, it is well to be reminded that the final conquest of tuberculosis is not yet in sight. Furthermore, there exist valid doubts whether the disease can ever be banished by the use of specific chemotherapeutic substances alone, even by drugs far more potent than any presently foreseeable. We should, nevertheless, experience a sense of gratification that the advent of practical and effective medicinals has become a source of reassurance to the tuberculous patient. Furthermore, it has armed the phthisiologist with new weapons with which he can prescribe with confidence an effective therapeutic regimen for the recovery of the patient and his restoration to a useful and productive life.

He has also made the following excellent statement:

> The word "cure" should be used with reservation in regard to the chemotherapy of tuberculosis, since it is extremely difficult to establish with certainty that a "cure" has been accomplished. It is, however, less difficult to recognize whether or not the disease has been influenced favorably or its course arrested as a consequence of a therapeutic procedure.

HONORS

The pioneer work in drug treatment of experimental tuberculosis was so clearly demonstrated and illustrated that an exhibit presented in 1944 by Feldman, Hinshaw, and Mann received the Gold Medal Award of the American Medical Association.

In 1946, Dr. Feldman was invited to London, to deliver the Harben lectures, sponsored by the Royal Institute of Public Health and Hygiene.* These 3 lectures were given under the title, "The Chemotherapy of Tuberculosis—Including the Use of Streptomycin."

That same summer, he delivered lectures on invitation in 7 other cities in Europe and was awarded the Pasteur Medal by the Pasteur Institute in Paris. In the fall of 1946, he received the Alvarenga Prize of the College of Physicians of Philadelphia for laboratory studies on the chemotherapy of tuberculosis.

In 1951, he went to Dublin, at the invitation of the Medical Research Council of Ireland, to participate in a colloquium on the chemotherapy of tuberculosis.

In 1951, the Mississippi Valley Conference on Tuberculosis awarded its Dearholt Medal to Dr. Feldman.

In 1953, he received the Trudeau Medal of the

*The Harben lectures were established in 1894 by Sir Henry Harben, at that time Master of the Worshipful Company of Carpenters. The lectures are given annually and pertain to "some subject embodying the results of original research in conjunction with the science of public health." Others from the United States who have been Harben lecturers are: Simon Flexner, 1912; William H. Park, 1930; and Philip Drinker, 1956.

National Tuberculosis Association for "early careful studies of the action of drugs on tuberculosis which contributed immeasurably to the successful use of chemotherapy in this disease." Nothing could have been more fitting than for a fellow pathologist, and particularly one also of world-wide eminence for his contributions in the field of tuberculosis, Edgar M. Medlar, to present the medal. Dr. Medlar said,

It has always been the hope of those who care for the sick to find a pill to cure an ill. As specific causes of illness become known, there comes the urge to find specific pills for specific ills. This has long been the case with regard to tuberculosis. Although numerous chemical substances had been used from time to time in the treatment of tuberculosis patients, it was not until 1938 that it began to appear that a survivor in this field was possible. One of the first conclusive demonstrations that experimentally produced tuberculosis could be favorably influenced by a chemotherapeutic agent was produced by the man whom we honor today.

This demonstration was not by accident. It is necessary for an investigator to be prepared for the day when an opportunity may arise and then to have the foresight, determination, and courage to pursue relentlessly the opportunity at hand.

In his response, Dr. Feldman said,

We who are recipients of this award must maintain our hope for a more nearly complete solution of the problems of tuberculosis. We must welcome new concepts with optimism and submit them to fair and critical appraisal. Whether a new proposal proves valuable or worthless, never should we view a succeeding proposal with cynicism—a pernicious, debilitating attitude and a killer of dreams. We must be ever ready and willing to serve where our experience and abilities can best be employed.

We must assume at least indirect responsibility for the conduct of proper public relations on the part of investigators. Unwittingly, investigators may assist in premature and inept announcements which appear to be newsworthy, but which are not in the best interests of the public. All of us have witnessed cruel disappointments following the sensational announcement of new and so-called miraculous substances that were hailed as the long-awaited means of salvation of the tuberculosis patient.

Concerning recipients of the Trudeau Medal, he said,

It requires that the recipient have appreciation and understanding of what has been accomplished by others. For whatever we of today may have achieved, each of us is, in Tennyson's words, "the heir of all the ages," indebted to those who, with courage, imagination, hope and selflessness, made the first deposits in the account of our scientific legacy. So-called discoveries, with few exceptions, are the development to fruition of earlier, and sometimes of very old concepts.

In May 1957, the Minnesota State Medical Association cited Dr. Feldman for distinguished service to medicine; the citation read in part, "for his contributions to the fundamental research which led to several great modern advances in chemotherapy and, especially, for his work in the development of basic medical knowledge of the antibiotics such as streptomycin and related compounds for use in the treatment of human tuberculosis." The same year, the American College of Chest Physicians bestowed upon Dr. Feldman its Distinguished Service Medal. Here again, it was most appropriate that his closest associate for so many years, H. Corwin Hinshaw, made the presentation.

Dr. Feldman's alma mater, Colorado State University, has honored him on two occasions. In 1945, he received the degree of D. Sc. (Hon.) and, in 1950, the Alumni Honor Achievement Award.

The twelfth International Veterinary Congress Prize of the American Veterinary Medical Association was awarded Dr. Feldman in August 1959.

Dr. Cecil Jackson, University of East Africa, who is internationally famous as a veterinary pathologist, wrote to Dr. Feldman:

I remember so well the mixed feelings I experienced years ago on hearing that you were to devote yourself to T.B. instead of to neoplasms. Later, when in this second special field you had again become a leading international authority, I realized that conscientious devotion to any tough problem makes one a better man, able to attack other problems with greater balance and judgment.

Concerning this letter, Dr. Alfred G. Karlson, who was long intimately associated with Dr. Feldman, said,

The words above express my own feeling that Bill Feldman has become an international authority in two fields. This reflects his ability, diligence, and keen perspective. I have a great love and admiration for Bill Feldman and have gained a great deal through our association from his fine philosophy, his tolerance, and his curiosity. He is always so interested in matters of the moment that he does not indulge in reminiscenee, nor does he often speak of his own accomplishments or honors. He does, however, recognize the good in others and does not fail to acknowledge the worth of his fellows. The work of a well-adjusted human being is to be objective about one's personal attributes, and Bill Feldman bears this mark.

PERSONAL EXPERIENCE

The announcement late in 1948 that Dr. Feldman had pulmonary tuberculosis came as no great surprise to his many friends. As a small boy and as a young man, he was in contact with people who had this disease. After his first report in 1927 of the pathologic and bacteriologic diagnoses of tissue removed from a tuberculous person, he devoted a great deal of time to the study of tubercle bacilli and the lesions they produced. This was followed by intensive and almost constant contact with thousands of animals he rendered tuberculous. He treated some and did postmortem examinations of all, including controls, beginning in 1938.

Dr. Feldman had had routine x-ray film inspections of his chest annually, with no abnormal finding until December 1948. On that examination, a definite shadow-casting lesion appeared in one of his lungs. Previous annual films were reexamined in great detail, but no abnormality was found. Thus, since the last annual examination, the area of dis-

ease had attained size and density sufficient to cast an x-ray shadow.

Dr. Feldman was strongly of the opinion that he had contracted the infection in his laboratory, where he had worked with tubercle bacilli of the 3 pathogenic types, namely, human, bovine, and avian, for more than twenty years. He was immediately placed on strict bed care at the Methodist Hospital in Rochester, Minnesota, under the care of his associate, Dr. H. Corwin Hinshaw, and others of the Mayo Clinic Staff. However, at the end of a month, it seemed advisable for him to transfer to some distant place where there were not so many intimate friends as visitors and which would allow for more conservation of energy. In early January of 1949, he transferred to Presbyterian Hospital, Albuquerque, New Mexico, where he received medical care from staff members of the Lovelace Clinic. Mrs. Feldman and their son, Bill, set up temporary living quarters in Albuquerque. At the end of May, Dr. Feldman transferred to the Nopeming Sanatorium, located near Duluth, Minnesota, where the summer months are generally cool. There, he was under the medical care of his good friend, the late Dr. G. A. Hedberg.

Dr. Feldman was discharged to his home in Rochester just before Christmas in 1949. He did not undertake any routine duties throughout most of 1950. However, he managed to accomplish many things unofficially. The period away from work was by no means lost, as it provided for retrospection as well as prospection, which has since been so valuable to him. On resuming his work in 1950, he continued to make one fine contribution after another.

ROLE OF PHOTOGRAPHY

Dr. Feldman has always believed in the importance of technically good photographic illustrations to supplement the text of technical reports. This is particularly important in pathology. He also believes that only the pathologist knows what he wants emphasized by photographs. To obtain the results desired and to know who is at fault when an illustration is not successful, the pathologist should develop the knowledge and skills necessary to make technically good pictures of both gross and microscopic materials.

In his research work, photography has occupied a most important position, largely because of the enthusiasm Dr. Feldman has for this means of recording structural changes but also because of the fun he has in making pictures. In a real sense, the photography that he has done in relation to the recording of observations in the laboratory has been fun and relaxation and has developed into a delightful hobby. Through the years, Dr. Feldman has made what is considered a valuable collection of camera portraits of men, most of whom have had distinguished careers in science, medicine, or music. He has always felt that it is somewhat of an impertinence to ask a busy man—perhaps any man, busy or not—to permit scrutinization and optical dissection of his face in search for that elusive and frequently completely hidden something that is the key to his personality. He says there is more to this than just pointing the camera and releasing the shutter. "When I succeed in obtaining a likeness of a man which is acceptable to his wife, my triumph is complete."

CONCLUSION

How fortunate that Dr. Feldman has so carefully recorded and printed the results of his work, now so important to people in every part of the world. He has published 300 articles, chapters in books, and 2 books of his own. Approximately half of his publications have been on tuberculosis, which remains the world's most life-taking and incapacitating communicable disease but which is now being conquered, both in animals and people, far more rapidly than ever before—in no small part as a result of Dr. Feldman's contributions to knowledge of this disease.

As he approached the age for retirement at the Mayo Clinic on January 1, 1957, various organizations were hopeful of inducing Dr. Feldman to join them and to participate in their work during his so-called retirement years.

The United States Veterans Administration offered him the position of chief of laboratory research in pulmonary diseases in its Department of Medicine and Surgery in the central office in Washington, D.C. He was well qualified for this work and, since the fall of 1957, has continued to investigate and direct others in their studies of various tuberculosis projects with an aim to hastening the still far-off day when eradication of tuberculosis will be declared. His complete dedication to his profession and the results of his scientific investigations bear witness to his integrity. The slogan he has followed so long reads, "It does not matter who is right; the only important question is 'What is true?'" (Bensley).

William Feldman continues to be active in organizations in his own and in closely allied fields, including leprosy. He has been a member of the Medical Advisory Board of the Leonard Wood Memorial for the control of leprosy since 1947 and is now chairman.

Other organizations in which Dr. Feldman has been active during most of his professional life include: Scientific Advisory Board of the Armed Forces Institute of Pathology, member since 1947; American College of Veterinary Pathologists (president, 1949); Conference of Research Workers in Animal Diseases (secretary and treasurer, 1936 to 1948; president, 1952); American Association of Pathologists and Bacteriologists (president, 1952-53); Committee on Institutional Grants of the American Cancer Society, a member since 1958; Sociedad Peruana de Tisiologia, honorary member; and Società Italiana delle Scienze Veterinarie, honorary member.

Doctor Feldman's sense of gratitude to his associates was reflected on the occasion of the presentation of the Trudeau Medal in 1954. He said, "Anyone who has engaged in laboratory research for any length of time soon becomes conscious of the debt of gratitude due his professional and nonprofessional associates. To acknowledge this obligation and express appreciation to those who through the years contributed so unselfishly to the advancement of my numerous investigational projects is indeed a genuine pleasure. Throughout my years in research I have been fortunate in having professional associates who were exceptionally capable. They had enthusiastic persistence, the insight and the capacity to think adventurously, and were not averse to work. Most importantly, they were able to function effectively as members of a team. Those to whom I am particularly indebted and for whose collaboration I express warm appreciation are my good friends, Dr. H. Corwin Hinshaw, whom I have already mentioned, Dr. Karl H. Pfuetze, and Dr. Alfred G. Karlson. Appreciation is also due the Mayo Foundation and the Mayo Clinic for providing generously, over many years, facilities for the conduct of our investigations. I want particularly to thank Dr. F. C. Mann, former director of the Institute of Experimental Medicine, Mayo Foundation, for his understanding, his wise counsel, and his disposition to allow us complete freedom in the conduct of our investigations. Lastly, a tribute is due our loyal and dependable technicians, without whose assistance our work could not have been accomplished."

Study of calcium and phosphorus metabolism in patients being treated for peptic ulcer may lead to detection of associated hyperparathyroidism before kidney damage and renal insufficiency occur. Simple serum calcium and phosphorus determinations should be done for all peptic ulcer patients, with more complicated tests used if results suggest abnormal parathyroid function. Interpretation difficulties associated with diet and antacid therapy can be overcome. When calcium and phosphorus studies of 300 peptic ulcer patients were done, parathyroid adenomas were diagnosed in 1.3 per cent.

B. Frame and W. S. Haubrich: Peptic ulcer and hyperparathyroidism. Arch. Int. Med. 105:536-541, 1960.

Administration of anticoagulants does not affect survival rate after acute nonembolic, nonhemorrhagic cerebrovascular accident.

Of the strokes that anticoagulants may benefit, only a few are distinguishable early, when treatment should be started. If a patient is observed for a time, the opportunity for effective therapy may be lost. On the other hand, immediate use of anticoagulants carries the risk of aggravating undiagnosed cerebral hemorrhage.

Of 26 patients with acute nonembolic, nonhemorrhagic cerebrovascular lesions given anticoagulants, 20 lived at least six weeks. Of 25 controls, 22 survived the same period. After six months, 18 patients in each group were alive. Cerebral ischemic recurrences numbered 3 and 2 among the treatment and control groups, respectively.

J. Marshall and D. A. Shaw: Anticoagulant therapy in acute cerebrovascular accidents. Lancet 1:995-998, 1960.

Book Reviews . . .

Functional Anatomy of the Limbs and Back

W. HENRY HOLLINSHEAD, *Ph.D., 1960. Philadelphia: W. B. Saunders Co. 424 pages. Illustrated. $10.00.*

Professor Hollinshead has contributed another fine textbook of anatomy in this second edition of his well known *Functional Anatomy of the Limbs and Back*. The author intends this book for use, as he states, as "a text for students of physical therapy and others interested in the locomotor apparatus." This will include many physicians who wish a concise description of the anatomy of these regions without consulting reference works.

Although written in a more simplified manner than the standard textbook, Dr. Hollinshead has thoroughly covered the basic anatomic features of the locomotor system clearly and succinctly. The anatomic nomenclature used throughout the book is consistent and does not require the memorization of synonyms. The author emphasizes, in his introduction and throughout the book, a common-sense approach to the study of anatomy, which should be particularly helpful to the student with little prior acquaintance with the subject. The use of numerous diagrammatic illustrations placed adjacent to the corresponding text is further evidence of this approach. These diagrams are clear and concise. The descriptions of the functions of various muscle groups and the mechanics of joint movements are outstanding.

The author is on less secure ground when discussing certain clinical aspects of the anatomy of the locomotor system. For example, achondroplasia is not the result of lack of pituitary growth hormone, and narrowing of an intervertebral interspace is not necessarily evidence of a herniated disk. A description of the terms varus and valgus would have been helpful in a volume such as this.

These are minor criticisms and should detract in no way from the over-all excellence of the book. The publisher has presented the volume in an attractive manner. This book should be in the library of anyone interested in the basic anatomy of the organs of movement.

WILLIAM D. ARNOLD, M.D.
New York City

Back Pain

JOHN MENNELL, M.D., *1960. Boston: Little, Brown & Co. 218 pages. Illustrated. $9.50.*

Back pain is a symptom, subjective and incapable of measurement. It must have a cause, and present medical philosophy is based on the premise that eradication of the cause will result in disappearance of the pain. However, a considerable number of patients with back pain have no clearly demonstrable cause for their symptoms. Dissatisfied, many such patients seek charlatans, who always have flourished when science has been inadequate.

Manipulation has long been a popular tool in the armamentarium of quacks, and every doctor of experience knows of occasional dramatic "cures" following such irregular treatment. Mennell is not a quack but a reputable member of the medical profession. He, and his father before him, have championed manipulation for a generation. Their explanation for otherwise unexplainable back pain is based on a concept of "dysfunction" of involuntary joint motion, which is relieved by stretching the joint.

Those who seek in this book the usual exposition of the results of a method of treatment by case histories, statistics, and follow-up studies will be disappointed. None is there, nor does the author recognize the enormous amount of thought, study, and analysis that other minds have applied to this problem. In 218 pages, there are only 2 references to the literature.

One wonders how a method of treatment based on the stretching of ligaments can be reported as successful at the same time that a method based on a completely opposite concept, the contracture of ligaments by the injection of sclerosing solutions, is enthusiastically described (HACKETT, G. S.: Joint Ligament Relaxation Treated by Fibro Osseus Proliferation. Springfield, Ill.: Charles C Thomas, 1958).

It is to be hoped that some day the place of manipulation in the treatment of back abnormalities producing pain, if it has a place, will be defined according to the criteria demanded by medicine since Hippocrates.

T. B. QUIGLEY, M.D.
Boston

Basic Office Dermatology

STUART MADDEN, M.D., JULIUS L. DANTO, M.D., *and* WILLIAM D. STEWART, M.D., *1960. Springfield, Ill.: Charles C Thomas. 296 pages. Illustrated. $11.75.*

This book contains brief and terse discussions of the 70 most common dermatoses, organized to give a practicing physician maximum information with minimum time and effort.

Section I classifies 26 groups of diseases. A good innovation in format is the first statement under "Office Management: Primary Objective." Such a clear statement of what treatment is designed to do would be a good addition to other textbooks. Section II contains 10 pages of color plates. Section III is on "Regional Diagnosis and Therapy," discussing, for example, what is good or bad practice in treating lesions of the buttocks and groin. Section IV has clear diagraming—that is, line drawings—and instructions on how to carry out diagnostic measures, including biopsy, mycologic examination, and patch testing. Section V covers therapy in similar detailed, diagramed fashion; specific proprietary compounds are recommended throughout. Exact dosage, quantity prescribed, and detailed instructions for administration are always given. Section VI is a similarly detailed discussion of "Therapy for Internal Diseases with Skin Manifestations." Section VII is on "Dermatologic Allergy." Section VIII is entitled "Dermatological Counselling Based on Physiology." This is another excellent innovation that future text writers could copy. It discusses *normal* care of *normal* skin, scalp, and hair; the effects of diet, cosmetics, and climate; and psychosomatic factors.

Diagraming is adequate and graphic. Line sketch diagrams are more commonly used than photographs. Most of the time, photographs are not so well chosen nor reproduced so as to be diagnostic without seeing the printed caption.

(Continued on page 24A)

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(Continued from page 182)

Most prescriptions call for proprietary compounds. While this procedure may be debatable, at least the prescribing physician knows that the patient is likely to get a reasonable approximation of that which he prescribes. It is probably equally possible to prescribe the same thing by the judicious use of compounds included in the *United States Pharmacopeia, New and Nonofficial Remedies*, and *National Formulary* at a much lower cost to the patient.

There are a few points on which I disagree with the author, such as his statement that "hair is continually being shed, each hair lasting several months, and taking several months to regrow." Truth of this would, of course, mean that the maximum length of hair achieved would be about half an inch. Bibliography is limited to "selected readings," but these are, in general, well-selected, authoritative reviews of the subjects discussed.

For the practitioner who wishes a quick reference work with which to brush up on diagnosis, treatment, or both quickly and with a minimum of verbiage, this book would be recommended.

MURRAY C. ZIMMERMAN, M.D.
Whittier, California

Medieval and Renaissance Medicine

BENJAMIN L. GORDON, M.D., *1959. New York: Philosophical Library, Inc. 821 pages. Illustrated. $10.00.*

This book is a rather pedestrian recounting of the main facts and highlights of the period it covers. The style is somewhat cumbersome, so that the drama and romance are not apparent. While the period was not one of great discoveries, the light of medicine was kept alive by the Arabians and the Jews. The history here offered is dependable, and the book may well serve as a reference in spite of the difficulty in reading it.

MORRIS FISHBEIN, M.D.
Chicago

Human Apocrine Sweat Gland in Health and Disease

HARRY J. HURLEY, M.D., *and* WALTER B. SHELLEY, M.D., *1960. Springfield, Ill.: Charles C Thomas. 129 pages. Illustrated. $6.50.*

This book is a thorough treatise on the physiology and pathology of the apocrine glands of man. Both authors are well qualified and noted for their research studies in the physiology, pharmacology, biochemistry, anatomy, and pathology of these sweat glands.

Chapters deal with the anatomy; physiology and pharmacology; and physical, chemical, and bacteriologic characteristics of the apocrine sweat gland, starting with the embryology, morphology, histology, and histochemistry. Blood, lymph, and nerve supplies also are covered. Experimental research that leads to the various conclusions is described in brief, concise, and easily understandable language. Interesting experimental studies in the production and control of body odors are presented. Osmidrosis, bromhidrosis, localized chromhidrosis, apocrine sweat retention as in Fox-Fordyce disease, and hidradenitis suppurativa are described in detail.

This book presents an excellent and thorough coverage of a very important but previously neglected part of the human glandular system, however, it probably will not appeal as greatly to the general practitioner as to the practitioner of dermatology. It can serve as an excellent reference for the anatomist, physiologist, and biochemist who delves into this field.

HAROLD G. RAVITS, M.D.
St. Paul

Handbook of Poisoning: Diagnosis and Treatment

ROBERT H. DREISBACH, M.D., *1959. Los Altos, Calif.: Lange Medical Publications. 474 pages. $3.50.*

Dr. Dreisbach's second edition of *Handbook of Poisoning: Diagnosis and Treatment* is most comprehensive and deals with the diagnosis and therapy of all poisons that a physician would have to cope with, including the most uncommon ones. Dr. Dreisbach, who is a professor of pharmacology at Stanford University School of Medicine, has placed this information in a book that could easily fit into the pocket, a physician's bag, or the glove compartment of an automobile.

The first 70 pages deal with general considerations of poisons, and Dr. Dreisbach gives detailed information on topics such as emergency and supportive management of poisoning. He also stresses symptoms and signs that would alert a physician to consider poisoning in his differential diagnosis.

Poisons have been divided into pesticides, industrial hazards, household chemicals, medicinal poisons, and plant and animal hazards. Chemical formulas of poisons have been reproduced throughout the book. The role of action of the poison has been elucidated and the method of treatment clearly indicated. Writing is clear and to the point, and there is no superfluous information.

The last section of the book concerns poisonous fish and plants and was of particular interest to this reviewer. Though some trade names of possible poisons are present in the index, the majority are not, so there will be occasions when the ingredients of a particular poison under a trade name will be unknown. This information will have to be obtained from a poison control center or the manufacturer.

This book could well be considered an essential addition to the bag of any general practitioner, pediatrician, or internist. Dr. Dreisbach deserves credit for being able to put so much useful information into such a small package.

C. N. CHRISTU, M.D.
Fargo, North Dakota

Medical Science and Space Travel

WILLIAM A. KINNEY, *1959. New York: Franklin Watts, Inc. 147 pages. Illustrated. $3.95.*

With the advent of the Sputniks, the Explorers, and other artificial satellites and with the major advances in the development of rocket engines, space travel is appearing on the horizon. It is inevitable that man will want to be part of any space, lunar, and planetary exploration program. Consequently, demands will be made on our scientists and, more so, on medical and allied scientific researchers to provide the knowledge for protecting and sustaining man in space, an acknowledged hostile environment. These investigators form a new group, often referred to as human factors and life support scientists.

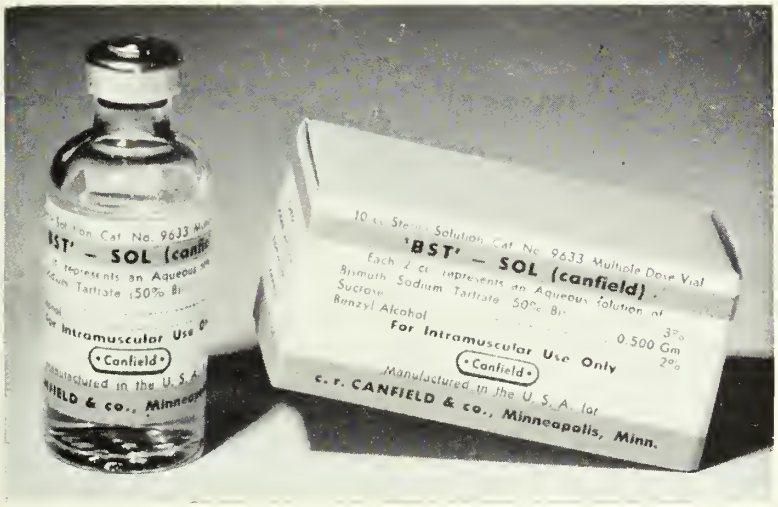
Fortunately, the gaps in our knowledge relative to man's tolerance of the physical forces to which he will

(Continued on page 26A)

A RESEARCH MILESTONE . . . *NOW CLINICALLY PROVEN!* The new therapeutic chemical formulation . . . developed by Canfield to meet the major requirements of *POSITIVE VIRUS THERAPY* in medical practice today.

'BST'-SOL* (Canfield)

Synergistically strengthened, multi-spectrum therapy



Adds certainty to anti-virus therapy, offering a new maximum in therapeutic effectiveness, in protection against the emergence of resistance, and in freedom from side effects.

'BST'-SOL (Canfield) is a basic, water-soluble compound, containing 50% of bismuth. This aqueous solution is buffered with 0.50 Gm. of sucrose per 2 cc., and 2% (v/v) of benzyl alcohol is added for its local anesthetic and preservative effect. The solution is available in two strengths, containing 1.5% and 3% of Bismuth Sodium Tartrate.

INDICATIONS

- **Acute Infectious Hepatitis**
- **Virus Pneumonia**
- **Acute Infectious Mononucleosis**
- **Herpes Zoster**
- **Acute Poliomyelitis**
- **"Chronic Store Throat"**
- **Mumps**

ACTION AND USES

'BST'-SOL is employed as a means of obtaining the systemic effects of bismuth. In view of its aqueous character, 'BST'-SOL is compatible with tissue fluids, and therefore promptly and dependably absorbed. It is theorized that the virus activity is inhibited or neutralized rather rapidly because of the penetration through the hemato-encephalic barrier of Bismuth ions in the 'BST'-SOL solutions intramuscularly injected. This penetration seems to occur rather quickly. It is indicated in all forms and any stage of syphilis, and may be employed either alone or in preparing the cerebrospinal luetic patient for extensive antibiotic therapy.

Other clinical applications are in the treatment of Virus Pneumonia, Acute Infectious Hepatitis, Acute Infectious Mononucleosis, Chicken Pox (Severe form), Measles (Severe form) and Mumps. Gratifying clinical results also have been obtained in the treatment of Herpes Zoster, Herpes Simplex and Verrucae.

Bibliography and Reprint Available on Request

Dosage and Administration

TWO DOSE PATTERNS – *Acute Case:* 2 cc. daily for three days.

Sub-Acute and Chronic States: Employed by intramuscular injection, preferably placed deeply within the gluteal muscle, optimum bismuth effect may be obtained by the administration of 1½% 'BST'-SOL three times a week, or by the use of 2 cc. of the 3% solution two to three times a week. The 3% concentration is designed primarily for institutional and outpatient clinic use.

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No. 9633:
10-cc. Multiple Dose Vial
'BST'-SOL 1½%

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(Continued from page 24A)

be exposed in going forth and returning from space are not large, since the United States Air Force has been pursuing extensive programs in support of high speed and high altitude aircraft. In addition, a space medicine program was initiated at the School of Aviation Medicine at Randolph Air Force Base, Texas, as early as 1952. Related activities were to be found at the Aero Medical Laboratory, Wright-Patterson Air Force Base, Ohio. Comforting as it is to know that considerable achievements have been attained, much more effort and accumulation of knowledge is required before man can be sent safely on his way for prolonged journeys into space. It is safe to say, however, that man is now ready for brief, "look-see" trips.

William C. Kinney, experienced journalist who writes for the publication, *Air Force Airman*, has taken upon himself the arduous task of not only publicizing what has been and is being accomplished in preparation for space travel but also of striving to give his readers a broad but complete picture of what is encompassed in the work areas of aviation and space medicine. Relying on his extensive journalism experience, Kinney has included in his book plentiful numbers of photographs of actual research activities at various aviation medicine facilities of the United States Air Force. Moreover, he does not overwhelm the reader with technical details, which makes for quick and easy reading and is ideal for the professional scientist who is already behind in reading his more technical literature.

Although not intended for textbook use, *Medical Science and Space Travel* would be excellent for reference material and for the library of those who have an avid interest in space travel and exploration.

GEORGE KITZES, PH.D.
Dayton, Ohio

Emergencies in Medical Practice

C. ALLAN BIRCH, M.D., *Editor, 1960. Baltimore: Williams & Wilkins Co. 721 pages. Illustrated. $8.50.*

The sixth edition of this British book is simple and readable. The illustrations are uncomplicated and memorable, and the coauthors have well tabulated and simplified their special problems.

The book contains tidbits of therapy and little tags to memory. For example, in his chapter on gas asphyxiation, Dr. Birch refers to those persons most susceptible as the 4 D's of carbon monoxide poisoning: the decrepit, the diseased, the drugged, and the drunk. He describes the child who has eaten poison berries of the belladonna group as being "hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hen." He suggests a saccharine circulation time to determine quickly whether a wheezing patient has cardiac failure or bronchial asthma. The cardiac patient's circulation time will be prolonged.

This book takes cognizance of emergencies in particular circumstances. There are chapters on (1) crises in air travel, with specific notes on tolerable pressures and altitudes for various diseases; (2) shipwreck (immersion foot), seasickness, submersion (caisson disease),

(Continued on page 28A)

(Continued from page 26A)

and resuscitation while in a lifeboat; (3) tropical diseases, with brief, specific paragraphs ranging from geographical distribution through the more serious complications; and (4) practical procedures, ranging from a simple explanation of milliequivilents to a simple technic for embalming while abroad ship.

Perhaps the greatest value of this book is its specificity. Symptoms, medication, dosages, and referral sources for emergency, appliances, aid, or information are described in detail. Unfortunately for the American reader, such information is in British terms of reference. Appended references to American medical and appliance agencies, specialists in snake bite venoms, or centers for the treatment of hemophilia would be extremely useful.

This book is recommended to all physicians as a handbook, to be read for interest against and as quick reference during the hour of emergency. Emergency room physicians, ship doctors, industrial physicians, and all doctors who make house calls will find it particularly useful.

FRANK ANKER, M.D.
Oakland, California

Science and Medicine of Exercise and Sports

WARREN R. JOHNSON, *Editor, 1960. New York: Harper Brothers. 725 pages. Illustrated. $12.00.*

Written by a group of distingnished investigators, this book is divided into 6 different aspects of sports and exercise: (1) structural and mechanical, (2) physiologic, (3) psychologic, (4) cultural and historical, (5) maturing and aging, and (6) therapeutic aspects of exercise. Each section is written by a person who has a particular interest in that subject. The book does not have many illustrations but contains graphs that aid in understanding the authors' views.

I believe this book will mainly interest those who wish to conduct experiments on some of the scientific medical problems encountered in sports. For those looking for help in solving some of the clinical problems in the various sports as played today, it may be rather disappointing.

In reading this book, I had a hard time maintaining an interest in all of its chapters and felt that it would have been more interesting and useful had more of the practical aspects of exercise and conditioning been brought in.

EDWARD N. NELSON, M.D.
Minneapolis

NEW BOOKS RECEIVED

Books and publications received will be listed here periodically and must be regarded as sufficient return for the courtesy of the sender. Those of special interest to our readers will be reviewed as space permits. Additional information to all listed books will be furnished on request.

Biological Organisation: Cellular and Sub-Cellular. C. H. WADDINGTON, Editor, 1959. New York: Pergamon Press. 317 pages. Illustrated. $12.50.

BOOK REVIEWS

Carcinogenesis: Mechanisms of Action. G. E. W. WOLSTENHOLME and MAEVE O'CONNER, Editors, 1959. Boston: Little, Brown & Co. 336 pages. Illustrated. $9.50.

Care of the Patient With a Stroke. GENEVIEVE WAPLES SMITH, R.N., M.A., 1959. New York: Springer Publishing Co. 148 pages. $2.75.

Cellular Aspects of Immunity. G. E. W. WOLSTENHOLME and CECILIA M. O'CONNER, Editors, 1960. Boston: Little, Brown & Co. 477 pages. Illustrated. $10.50.

Current Concepts in Leukemia. Report of the 34th Ross Conference on Pediatric Research. Columbus, Ohio: Ross Laboratories. 126 pages. Illustrated.

Digest of Official Actions, 1846-1958. F. J. L. BLASINGAME, M.D., 1959. Chicago: American Medical Association. 758 pages.

Endemic Goitre. CLEMENTS, DE MOERLOOSE, DE SMET, HOLMAN, et al., 1960. Geneva, Switzerland: World Health Organization. 462 pages. Illustrated. $8.00.

Handbook of Medical Treatment. MILTON J. CHATTON, M.D., SHELDON MARGEN, M.D., and HENRY BRAINERD, M.D., 1960. Los Altos, Calif.: Lange Medical Publications. 546 pages. Illustrated. $3.50.

Merck Index of Chemicals and Drugs, seventh edition. PAUL G. STECHER, Editor, 1960. Rahway, New Jersey: Merck & Co., Inc. 1,600 pages. $12.00.

Metabolism of Cardiac Glycosides. S. E. WRIGHT, Ph.D., 1960. Springfield, Ill.: Charles C Thomas. 74 pages. Illustrated. $4.75.

On the Shoulders of Giants. ELEANOR CHAPPELL, 1960. Philadelphia: Chilton Co. 105 pages. $2.75.

Peripheral Vascular Diseases: An Objective Approach. TRAVIS WINSOR, M.D., 1959. Springfield, Ill.: Charles C Thomas. $16.50.

Radioisotope Studies of Fatty Acid Metabolism. JAMES F. MEAD and DAVID R. HOWTON, 1960. New York: Pergamon Press. 142 pages. $7.50.

Recent Studies in Epidemiology. J. PEMBERTON, M.D., and H. WILLARD, M.D., Editors, 1958. Springfield, Ill.: Charles C Thomas. 203 pages. $5.75.

Review of Medical Microbiology. ERNEST JAWETZ, JOSEPH L. MELNICK, and EDWARD A. ADELBERG, 1960. Los Altos, Calif.: Lange Medical Publications. 370 pages. $5.00.

Significant Trends in Medical Research. G. E. W. WOLSTENHOLME, CECILIA M. O'CONNOR, and MAEVE O'CONNER, Editors, 1959. Boston: Little, Brown & Co. 335 pages. Illustrated. $9.50.

X-Ray and Radium in Dermatology. BERNARD A. WANSKER, M.D., 1959. Springfield, Ill.: Charles C Thomas. 114 pages. $5.00.

Year Book of General Surgery, 1958-1959 series. MICHAEL E. DE BAKEY, M.D., Editor, 1958. Chicago: Year Book Publishers. 588 pages. $7.50.

The Journal Lancet

SERVING THE MEDICAL PROFESSION OF MINNESOTA, NORTH DAKOTA, SOUTH DAKOTA, AND MONTANA

The papers which follow were presented at the recent MEDICLINICS *of Minnesota, Fort Lauderdale, Florida, March 5 to 15, 1961, and have been selected for publication in* THE JOURNAL-LANCET.

Intracranial Hemorrhage

HAROLD F. BUCHSTEIN, M.D.

Minneapolis

BLEEDING within the head is usually dramatic, always serious, and frequently catastrophic. A high percentage of persons with massive intracranial hemorrhages die within a matter of hours. Those who survive their initial episode display a tendency toward recurrent bleeding, eventually with a fatal result. Thus, in these persons, it is essential that the cause of the hemorrhage be determined as accurately as possible in order that treatment may be instituted to prevent recurrent bleeding.

CAUSES

The most frequent cause of intracranial bleeding undoubtedly is trauma. Any blow to the head of more than a minor nature will produce some bruising of the surface of the brain, with laceration of small vessels. In most instances, however, the resulting hemorrhage is but one aspect of the whole injury to the skull and its contents, and a relatively minor one at that. In a few instances, such as when the middle meningeal artery is torn, the bleeding may be of such volume that the brain is compressed, and death will result unless the clot is recognized and removed.

HAROLD F. BUCHSTEIN *is a clinical associate professor, Division of Neurosurgery, University of Minnesota.*

In a typical case, the patient will have sustained a blow to the side of the head which renders him unconscious for a time, after which he may appear to improve and at times may seem entirely well. Within a matter of minutes or hours, however, deterioration of the patient's condition is obvious, with drowsiness progressing to coma and the development of a dilated pupil on the side of the lesion, together with weakness of the opposite extremities. Roentgenograms of the skull usually will demonstrate a fracture line crossing the groove in which lies the middle meningeal artery. Typical examples of these extradural hematomas are easily recognized. Unfortunately, only about one-half of cases exhibit the classic clinical course.

The possibility of an expanding clot should be borne in mind in connection with any head-injured patient whose condition worsens and who exhibits focal findings or a fracture as described. These patients should be investigated further either by carotid angiography or by direct exploration in the temporal region. The removal of such a clot usually will produce dramatic improvement in the patient's condition. However, if the clot is allowed to grow too large before it is recognized and removed, irreparable damage may be done to the patient's brain by compres-

sion. This type of clot constitutes one of the few actual neurosurgical emergencies.

TYPES

Nontraumatic intracranial bleeding, the chief concern of this discussion, usually occurs rather suddenly and presents the clinical picture of spontaneous subarachnoid hemorrhage or of stroke, depending upon the source, amount, and location of the hemorrhage. A history of preceding hypertension is common in the stroke group, but many normotensive individuals bleed intracranially as well. Inquiry should always be made regarding episodes which might represent previous and unrecognized bleeding.

Spontaneous subarachnoid hemorrhage. The clinical picture of spontaneous subarachnoid hemorrhage is well known. The patient is seized with a sudden, severe headache that is usually suboccipital or occipital in location, no matter what the site of the bleeding. Nausea, vomiting, and vertigo soon follow and may become so severe as to obscure the presence of the headache as the presenting symptom. Stiffness of the neck (meningism) develops fairly rapidly in most instances. The patient frequently is unconscious for a brief period and may remain drowsy. If coma persists or deepens, the presence of intracerebral as well as subarachnoid bleeding may be suspected.

Subarachnoid hemorrhages may be precipitated by strenuous activity, such as coughing, straining, lifting, and so forth, but many attacks occur while the patient is sedentary. Frequently, the patient has had previous bouts of severe headache, which presumably represent milder and unrecognized episodes of subarachnoid bleeding.

The actual volume of blood loosed into the subarachnoid pathways in the average nonfatal case is not great. In these instances, it is a matter of leakage rather than of actual rupture of a vessel or aneurysm. The blood in the subarachnoid space does not compress the brain and, if the patient survives, will be absorbed in the course of time and without particular treatment. The use of repeated spinal punctures for the removal of the blood is irrational and unnecessary.

When a patient with subarachnoid bleeding remains unconscious for a prolonged time, it does not necessarily follow that this is the result of massive hemorrhage, although such may be the case. One of the frequent and, in fact, anticipated results of leakage of blood from a vascular lesion such as an aneurysm is the development of rather marked vasospasm in the intracranial arteries in the vicinity of the leakage. In some individuals, this vasospasm may be severe and may involve large areas of the intracranial arterial system. In such patients, postmortem examination may disclose a grossly softened brain and only a relatively small and seemingly innocuous subarachnoid clot. The degree of vasospasm in such patients has been so great as to produce actual anoxia of the brain. It has become well recognized that patients who exhibit these more extensive and prolonged areas of vasospasm are very poor subjects for any type of intracranial surgery and in general have a poor prognosis.

Strokes. When intracranial bleeding is principally into or within the substance of the brain, a different clinical picture will be seen. These patients, for the most part, will fall into the category of strokes in that they will have a sudden onset of unilateral weakness, often associated with disturbance of consciousness. If the bleeding extends into a ventricle, a serious state of affairs develops rapidly as the ventricular system fills with blood. The patient becomes profoundly unconscious, may retch and vomit, and frequently has dilated pupils and signs of decerebrate posture. Death usually follows in a few minutes or hours.

If the bleeding is less in amount and remains confined within the substance of the brain, the patient may simply develop headache and signs of increased intracranial pressure with or without focal findings, depending upon the location of the clot. Such a patient presents essentially the findings of a rapidly growing brain tumor rather than of apoplexy. If the clot forms principally in a frontal lobe, the resultant symptoms may be largely psychic in character and the patient may be suspected of having an acute schizophrenic attack.

DIAGNOSIS

The diagnostic work-up of patients with intracranial hemorrhage usually begins with a lumbar puncture. The spinal fluid will contain blood in varying amounts corresponding roughly with the severity of the bleeding and the seriousness of the situation. Most individuals with intracerebral bleeding will also have some leakage of blood into the ventricular system or subarachnoid space so that it will be detected by spinal puncture. If the patient, after subarachnoid hemorrhage, exhibits signs of severe meningism with actual opisthotonos, it is probably just as well to omit the spinal puncture. In most instances, it is well to centrifuge the fluid obtained so as to observe the color of the supernatant fluid. If the hemorrhage has been present for more than a day or so, there will be definite xanthochromia, which

establishes the presence of previous bleeding and resolves any question as to whether the findings may be simply the result of a traumatic or bloody tap.

Further investigation of the situation will revolve largely around the use of carotid and vertebral angiography. Plain x-ray films of the skull only rarely will reveal a potential source of bleeding, such as a calcified aneurysm or vascular anomaly. If a displacement of the calcified pineal gland from its normal midline position is noted, the presence of a mass lesion of significant size on the affected side may be assumed and further investigation may be directed there first. The electroencephalogram rarely will contribute significantly to the management of a case of intracranial bleeding. A focal area of slow waves will suggest an underlying tumor that may, of course, be an intracerebral clot.

The present tendency is to carry out angiographic studies relatively soon after a bleeding episode, unless the patient remains deeply comatose. If the patient has regained consciousness or is at least less comatose than upon admission, there is no good reason for delaying angiographic studies and, in fact, every reason not to do so. The greatest danger of recurrent bleeding in the patient with an intracranial aneurysm is within the two-week period after his initial hemorrhage. If angiography is delayed too long, the patient may find himself in new and more serious difficulties before any definitive treatment can be instituted.

The danger of causing additional hemorrhage by angiography apparently is very slight, since the normal pressure imparted to the blood stream by the heart's action is fully as high as that created by the angiographer with his syringe.

When a group of patients with subarachnoid hemorrhages is subjected to angiography, a little over one-half will have one or more intracranial aneurysms. Since aneurysms are multiple in some 10 to 15 per cent of cases, it is always essential that angiography be carried out bilaterally. In another, smaller group of patients, the source of the bleeding will be some sort of arterial or arteriovenous malformation within the head (angioma). Occasionally, the source of hemorrhage will be an intracranial tumor. This, however, is a much less common finding than is frequently thought.

In about 30 to 40 per cent of persons with subarachnoid hemorrhage, no cause or source of the hemorrhage is demonstrated. This state of affairs is disappointing to the physician who is seeking a definite and specific answer to his problem but is fortunate for the patient. Several studies of fairly large groups of patients with subarachnoid hemorrhage have established the fact that prognosis is quite good in those instances in which no aneurysm or other bleeding source can be demonstrated, whereas, if a definite lesion is visualized, the prospect for recurrent bleeding is indeed considerable. Of course, if only carotid angiography is performed, the possibility exists that the patient may have an aneurysm in the vertebral-basilar artery system. These, however, are relatively rare as compared with aneurysms in the carotid arterial tree.

In those patients with intracranial hemorrhage presenting the clinical picture of stroke, the angiogram frequently will disclose the presence and location of an intracerebral blood clot, which appears in the angiogram simply as a relatively avascular area that is displacing blood vessels. The absence of any tumor stain or other characteristic vascularity will distinguish the lesion from a neoplasm. In most instances, no source of the bleeding that has produced the intracerebral clot will be noted. Many of these lesions apparently result from the rupture of small vessels which become clotted and thus are not visualized. When some aneurysms leak, the blood not only may escape into the subarachnoid space but also may be directed into the brain. The brain is so soft that a tiny stream of blood can easily cut an extensive tract in the brain and fill it with a clot of blood.

TREATMENT

The treatment of intracranial hemorrhage falls into two phases. The first is supportive in character and extends through the acute phase of the patient's illness and until diagnostic studies have been completed. Some acutely ill patients can be carried through the acute stage of their trouble with the aid of prolonged hypothermia.

If an intracranial aneurysm or vascular malformation is found, definitive surgical treatment should be undertaken in most cases. The actual procedure will vary with many factors, including the size and location of the lesion, the age of the patient, the presence or absence of serious paralyses, and the general competence of the patient's intracranial circulation. In recent years, there has been an increasing tendency to attack the lesion directly with a view toward removing it or excluding it from the circulation. The development of reliable methods of shrinking the brain (intravenous urea) and lowering the blood pressure to any desired level by means of trimethaphan camphorsulfonate (Arfonad) have made intracranial surgery in these cases much

easier and safer. The use of hypothermia adds considerably to the technical complexity of the procedure but does permit interruption of portions of the cerebral circulation for brief periods without the usual risk of irreparable brain damage.

An intracranial hematoma should be surgically removed. Usually, this can be accomplished with minimal difficulty and with definite benefit to the patient. Mental blunting and paralyses which may be due to compression of the brain by the expanding intracerebral clot will be relieved. Usually, when the blood is removed, no source of the bleeding is demonstrated. An aneurysm that has been revealed by preoperative angiography usually will be found at one end of the clot, and removal of the clot then considerably enhances the exposure of the aneurysm.

CONCLUSION

Recent years have seen the adoption of a much more agressive attitude toward the treatment of intracranial bleeding, whether it be within the brain or around it. All such patients who survive their initial acute bleeding episode should be thoroughly investigated with a view to establishing, if possible, a definite etiologic and localizing diagnosis. This will permit definitive surgical measures which, in most instances, will relieve present symptoms and prevent future disaster.

CANDY BARS can be used in a simple tolerance test to detect diabetes. The use of candy bars is preferable to the usual two- or three-hour dextrose tolerance test for diabetes because (1) the dextrose test creates stresses not duplicated in ordinary eating and is objectionable to patients, sometimes causing vomiting; (2) dextrose often is not available in the doctor's office; (3) preparation of the solution is time-consuming; and (4) the test is relatively expensive. Since sucrose is as satisfactory as dextrose for detecting diabetes, candy is a cheap, readily available substitute.

The test is included with diagnostic studies if the patient is over 40 years old, has relatives with diabetes, or is obese. The patient eats 2 candy bars containing approximately 100 gm. of sucrose and drinks 180 cc. of water. Tests of urine and blood sugar are made after ninety minutes.

If blood sugar is under 130 mg., the patient does not have diabetes. When blood sugar is 160 mg. or over and is accompanied by glycosuria, treatment for early diabetes is started. Dietary regulation without insulin or oral hypoglycemic agents may prevent progression or retard the disease. When blood sugar is between 130 and 160 mg., further observation and, possibly, a three-hour dextrose test are required.

Blood sugar of the first 200 patients tested varied from 45 to 218 mg. true glucose, with a median of 94. Blood sugar was abnormally high in 8, borderline in 20, and normal in 172 patients.

F. N. ALLAN and L. W. GEORGESON: A candy tolerance test in the detection of early diabetes, M. Clin. North America 44:429-432, 1960.

The Ileum and the Urinary Tract

C. D. CREEVY, M.D.

Minneapolis

THE IDEA of using a segment of ileum to replace or supplement a defective portion of the urinary tract is not new. In 1898, Mikulicz[1] used an ileac segment to increase the capacity of a contracted human bladder, a technic modified and more extensively used by Scheele (1922).[2] In 1908, Shoemaker[3] diverted the urine from a solitary kidney through an isolated segment of ileum opening onto the abdomen. Eighteen months later, the inflamed bladder having healed, he successfully anastomosed the ileum to it. Thus he was apparently the first to divert the urine through a segment of ileum, as well as to use such a segment to replace a part of the ureter. Finally, about 1950, Couvelaire[4] replaced an entire bladder with ileum. About this same time, the reports of Bricker,[5] Cibert,[6] Pyrah,[7] and others led to a rather wide application of these methods.

ADVANTAGES AND DISADVANTAGES

The ileum has two characteristics which favor its use in the urinary tract: its mobility and persistence of normal peristalsis after isolation. It also has some objectionable features: its peristalsis differs from that of the ureter in that it stops, churns, and reverses, then continues downward and repeats itself. While this makes for effective digestion and absorption, it does not propel urine as efficiently as does normal ureteral peristalsis.

The ileum's capacity to absorb electrolytes is probably fairly well balanced by its tendency to secrete them into its lumen,[7] but is disadvantageous with seriously impaired renal function, since damaged kidneys cannot cope with the resulting overload, statements to the contrary in the literature notwithstanding.

The ileum continues to form mucus after connection to the urinary tract. While this is usually of no importance, the mucus may clog a segment used to enlarge the bladder, and its expulsion from a substitute ureter may cause renal pain. It may also serve as the nucleus for a stone, particularly in the presence of urea-splitting bacteria.

It is possible to eliminate both the absorptive capacity and the formation of mucus by removing the ileac mucosa and lining the ileum with urinary epithelium, either with actual patch grafts[8] or by outgrowth from urinary organs connected with it. This procedure is not yet altogether practical in the human being.

Other disadvantages include the magnitude of the necessary operations and difficulties with the collecting apparatus when an external stoma must be used. The urinary tract cannot be kept sterile with such an external opening.

INDICATIONS FOR USE OF THE ILEUM

It must be emphasized that the ileum is not used if simpler methods fulfill the patient's needs. The most frequent indication for attaching an isolated segment of ileum to the urinary tract is a locally inoperable neoplasm of the bladder which is still amenable to cystectomy. In such a case, the ureters are anastomosed to the segment, one end of which is closed while the other opens upon the abdomen (figure 1).

The same operation is occasionally useful

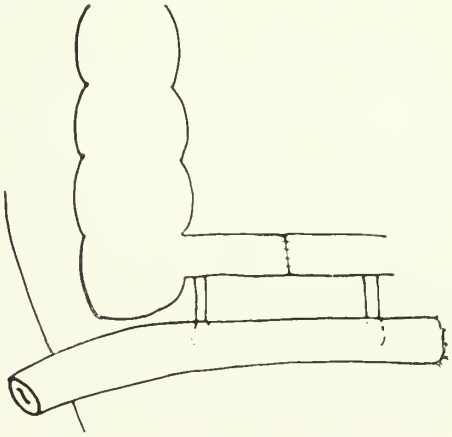


Fig. 1. Ileac diversion of urine, or Bricker's operation.

C. D. CREEVY *is professor and director of the Division of Urology, Department of Surgery, University of Minnesota.*

when the bladder cannot be made to serve as a reservoir. In this category is otherwise irreparable urinary incontinence, such as occurs with meningomyelocele, exstrophy, severe epispadias, and damaged urethral sphincters.

Similarly, the operation may be used in instances of uncorrectible urinary retention or in those cases in which correction of the retention fails to arrest progressive dilation of the upper urinary tract, such as with congenital obstruction of the vesical neck, atonic bladders secondary to meningomyelocele, traumatic paraplegia, and certain cases of congenital ureterectasis.

Malfunctioning ureterosigmoidostomy with recurrent infection and hyperchloremic acidosis may be converted to an ileac diversion, with relief of symptoms and arrest of renal damage. The durability of such a result is still to be determined.

Intolerable contracture of the bladder due to primary interstitial cystitis (Hunner's ulcer) or to the secondary variety, which sometimes follows severe pyogenic or postirradiation cystitis, occasionally can be corrected by attaching a segment of ileum to the bladder so as to increase its capacity (figure 2).

The ileum is also useful in certain disorders of the ureter, part or all of which may be replaced by it: ureteral fistulae with ureters not suitable for anastomosis or reimplantation; megaloureters with good renal reserve despite progressive dilation; ureteral neoplasm with a solitary kidney; and ureteral reflux not amenable to simpler methods (figure 3).

CONTRAINDICATIONS

First of these is a very poor surgical risk. Of equal importance is lack of intelligence and ability to cooperate, either on the part of the patient or the parents, if a collecting device has to be used. Less clear-cut but of great importance are aperistaltic ureters; if the ureters cannot transport the urine effectively, anastomosing them to the ileum will only compound the patient's difficulties. The condition is best recognized by cinefluorography. I thought at first that removal of the normal resistance of the intramural ureters in these cases would result in arrest of the dilation of the kidneys, or even in improvement, but this has not been the case.

Similarly, if the kidneys are badly damaged by hydronephrosis due to inadequate ureters, use of the ileum will lead to hyperchloremic acidosis and other disturbances of electrolytes as the kidneys continue to deteriorate. This happens whether the ureters are anastomosed to an isolated segment or replaced by a loop of ileum

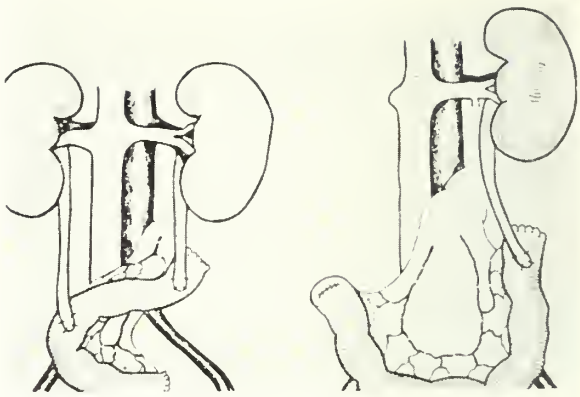


Fig. 3. Replacement of distal ureter (courtesy of J. S. Arconti[10]).

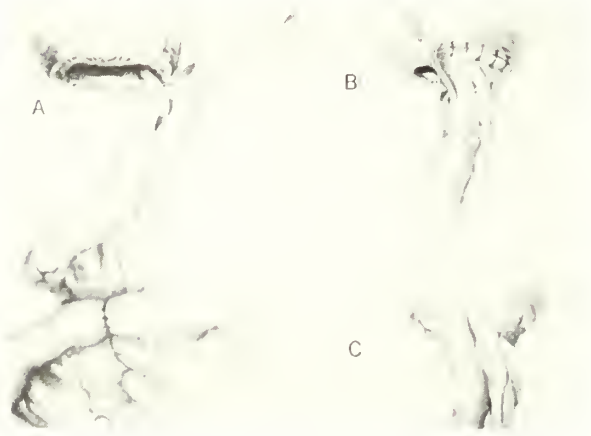


Fig. 2. Enlargement of bladder with segment of ileum (courtesy of H. G. Hanley[9]).

TABLE I

ILEAC DIVERSION FOR NON-NEOPLASTIC DISEASES

Congenital ureterectasis	8
Exstrophy	6
(Primary operation 5; secondary 1)	
Posttraumatic paraplegia	5
Meningomyelocele	4
Congenital obstruction vesical neck	4
Urethral stricture	3
(Congenital 2; acquired 1)	
Malfunctioning ureterosigmoidostomy	2
Posttuberculous reflux	2
Absence abdominal muscles	1
Postirradiation cystitis	1
Postirradiation fistulae	1
Phimosis	1
Total	38

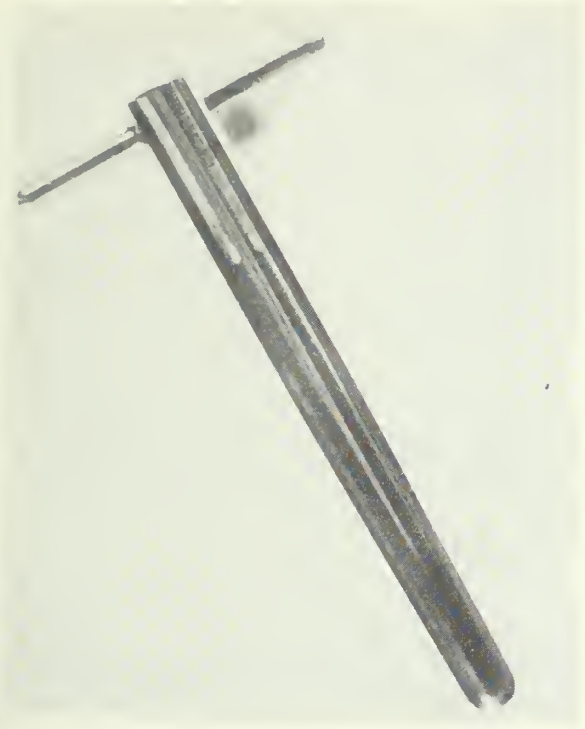


Fig. 4. Dilator for ileac stoma—size 34F.

connected at one end to the renal pelvis and at the other to the bladder; the renal pelvis must also be capable of effective peristalsis.

It has been found, however, that hydronephrosis due to relatively recent mechanical obstruction of previously normal ureters is likely to improve with ileac diversion or ureteral replacement.

We have enlarged the bladder once, replaced damaged ureters 7 times, and diverted the urine via an isolated loop 38 times in patients with nonneoplastic disorders (table 1). There have been 3 surgical deaths, or 6.5 per cent. All but 1 patient of the first 2 groups who survived operation are living and doing well up to eighty-four months later. Of the third group, 8 died between nine and eighty-four months after operation. All of these had relatively atonic ureters with progressive hydronephrosis before operation. Ileac diversion apparently failed to arrest the progress of the underlying disease and may have shortened survival by increasing the burden of the kidneys through absorption via the mucosa of the bowel.

Other late complications have included urinary lithiasis, which occurred 3 times in the kidneys and twice in the ileum, and 12 strictures of the stoma, which affected one-third of the survivors of the operation. The stones in the loop had formed on nonabsorbable sutures unwisely used therein; this procedure has been discontinued. The stones in the kidneys probably resulted from infection by urea-splitting organisms entering through the open stoma.

Stricture of the stoma has been a serious problem. It has occurred irrespective of the type of construction employed and is actually a ring of scar in the abdominal wall around the ileum. While all patients receive dilators (figure 4) with careful instructions, it is amazing how often they will stop using them. A tight stricture will, of course, aggravate an existing hydronephrosis and may cause acute pyelonephritis. It is readily correctible by a simple plastic operation.

CASE REPORTS

The following case histories illustrate some of the problems encountered.

Case 1. An 18-year-old Indian boy had a large, infected, congenital solitary left hydronephrosis and hydroureter. Nephrostomy provided adequate drainage, but he did not take care of the tube, going swimming and failing to have it changed before it had time to plug. This behavior led to repeated attacks of pyelonephritis.

The ureter was replaced with ileum. While the anastomoses remained patent (figure 5), chills and fever followed every attempt to clamp the nephrostomy tube

Fig. 5. Replacement of ureter in patient with congenital ureterectasis was unsuccessful despite patent anastomoses because of rigid renal pelvis and impaired renal function.

because the renal pelvis was aperistaltic. The patient died of renal failure after eighteen months.

Case 2. A 5-year-old girl had had 2 transurethral resections and a cystostomy for obstruction at the vesical neck. Her bladder had contracted so that she was in continuous pain and she was mildly hypertensive. A segment of ileum was attached to the bladder, and the tube was removed (figure 6). The child has been perfectly comfortable and normotensive for thirty-three months.

Case 3. A 9-year-old boy had had attacks of chills, fever, and pain in the left loin. Studies disclosed a normal right kidney and a nonfunctioning left hydronephrosis, with fairly thick parenchyma and a hugely dilated ureter, which was replaced with ileum. The patient has remained asymptomatic, with sterile urine and pronounced improvement in the left kidney (figure 7).

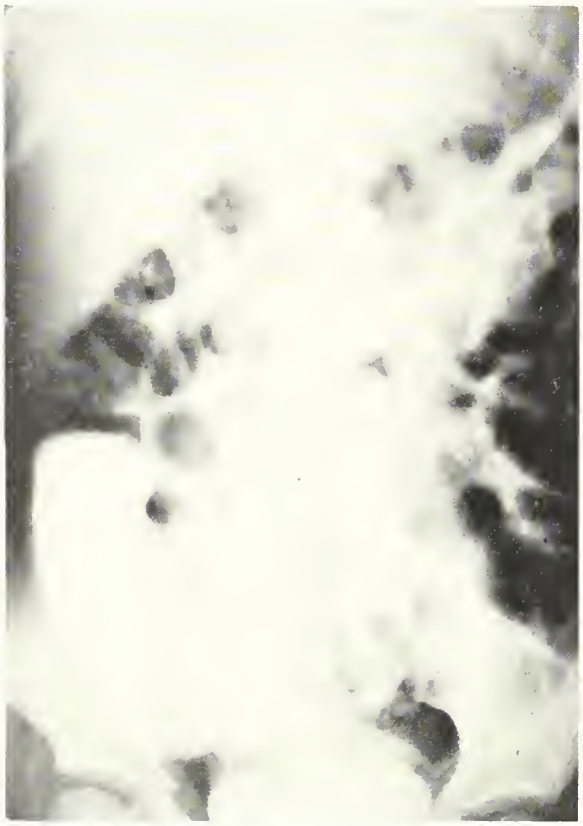
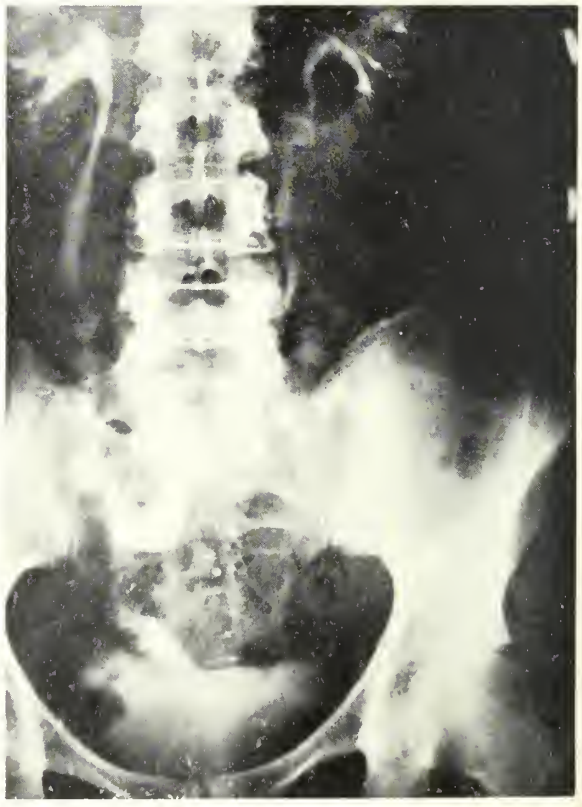


Fig. 6. Successful enlargement of capacity of contracted bladder with segment of ileum one year after operation.

Case 4. Bilateral ureterovaginal fistulae developed in a 39-year-old married woman after irradiation and radical hysterectomy for cervical cancer. Left nephrostomy was necessary for acute pyelonephritis. Both pelvic ureters were later replaced by a single segment of ileum (figure 3). One year later, the patient was asymptomatic and had a normal upper urinary tract, with sterile urine (figure 8).

Fig. 8. Successful replacement of both lower ureters with a single segment of ileum in patient with ureterovaginal fistulae; one year after operation.

Fig. 7. Successful replacement of aperistaltic ureter with ileum one year after operation. Sterile urine.



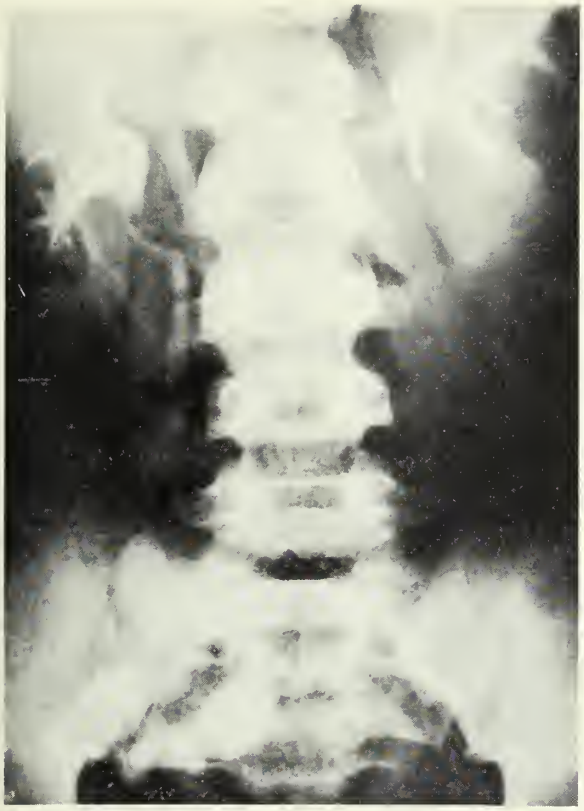


Fig. 9. Ileac diversion of urine in patient with exstrophy of the bladder five years after operation.

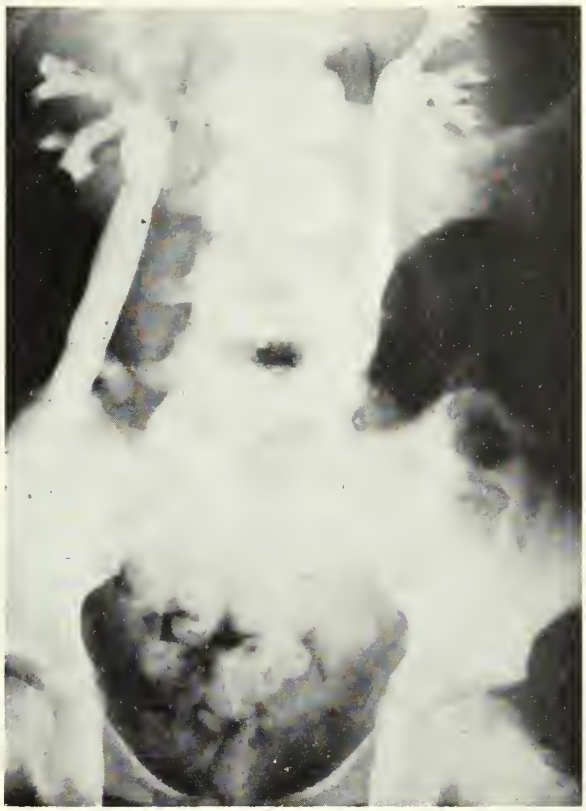


Fig. 10. Ileac diversion for enormously dilated pelvic ureters, which were excised, two years after operation.

Case 5. A 1-year-old boy had an ileac diversion for exstrophy of the bladder. It was planned later to close the bladder and urethra and to join the ileac segment to it, but this proved impractical. Figure 9 shows his upper urinary tract five years later.

Case 6. A 5-year-old boy was sent in after studies made because of recurrent urinary infections showed enormously dilated lower ureters, with fair preservation of the kidneys. The dilated lower ureters were excised, and ileac diversion was done. A urogram made two years later suggested that progress of the dilation had been arrested, as the size of the renal pelves had been substantially reduced, but too little time has elapsed to permit any final conclusion (figure 10).

SUMMARY AND CONCLUSIONS

The ileum has been used at the University of Minnesota Hospitals to enlarge a contracted bladder once, to replace a damaged ureter 7 times, and to divert the urine because of otherwise irreparable incontinence or for progressive dilation of the upper urinary tract 38 times.

The most common late complications have been stenosis of the external stoma, progressive renal failure, and lithiasis.

The procedure is exceedingly useful in carefully selected cases if there is a reasonably good renal reserve, with potentially effective peristalsis in the renal pelves and, if diversion is used, in the ureters.

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Diffuse Connective Tissue Diseases in Childhood

With a Special Comment on Connective Tissue Diseases in Patients with Agammaglobulinemia

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DIFFUSE CONNECTIVE TISSUE DISEASE presents the physician with one of the most challenging diagnostic problems, therapeutic dilemmas, and distressing scientific puzzles that exist in medicine today. Since most diseases in this group are uncommon, no single practitioner has a wealth of experience with these cases. When such patients are encountered, therefore, the family doctor frequently raises questions of differential diagnosis, diagnostic approach, therapeutic management, and prognostic significance.

It is the purpose of this paper to present very briefly some of the experiences we have had in studying disorders of the diffuse connective tissue in the Children's Rheumatism Clinic at the University of Minnesota Hospitals during the past several years. The diseases studied have included the following: (1) lupus erythematosus—especially disseminated lupus erythematosus, (2) acute rheumatic fever, (3) rheumatoid arthritis, (4) anaphylactoid purpura, (5) periarteritis nodosa, (6) scleroderma, (7) dermatomyositis, (8) plasma-cell or "lupoid" hepatitis, (9) scleredema of Buschke, and (10) familiohereditary dysmetabolisms of the connective tissues.

LUPUS ERYTHEMATOSUS

Perhaps the disease most often considered to be the prototype of this group is systemic lupus erythematosus. Although lupus erythematosus is relatively uncommon among children, we have had an opportunity to study 18 cases during the last eight years. The following patient is a typical example.

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Case report. This 13-year-old girl was first seen in September 1958, when she presented with a one-year history of epistaxis and a tendency to bruise. Nine months prior to admission, swelling of the interphalangeal joints had developed. This subsided in several days but recurred several times. Four months prior to admisison, her ankles and feet became swollen and painful. She later became lethargic, lost 10 pounds, and received 2 transfusions for anemia. Two months prior to admission, she was exposed to an insecticide.

Her past history was not remarkable, but her family history revealed 14 siblings, 1 of whom had had a brain tumor. On admission, she was described as having a premorbid personality. She had red hair, moderate lymphadenopathy, and hepatosplenomegaly. She also had a grade 2 systolic apical murmur. Her erythrocyte sedimentation rate was 109, hemoglobin 11.2 gm., and white blood count 3,900 with normal differential. Total serum protein was 7.8 gm. per cent with 5.2 gm. per cent globulin. Several lupus erythematosus tests were positive. About one month after admission, a typical facial rash appeared. Renal biopsy revealed some glomerular proliferation. She was begun on 300 mg./M²/day of cortisone. Attempts to reduce the dosage to less than 150 mg. per day were not successful because of a rise in sedimentation rate below this level. She was discharged in December 1958 on 150 mg. per day of cortisone with potassium chloride and Maalox. She was followed in the Children's Rheumatism Clinic and did well until March 1959, when she was admitted with a fever and cough. Hyperpyrexia developed, but she responded to antibiotics and was discharged on maintenance cortisone ten days later.

She became a severe behavior problem and was readmitted one month later. She was continued on 100 mg. of cortisone per day and seemed to improve psychologically. Cortisone was increased again to 150 mg. daily, and she did only fairly well for three months. At this time—August 1959—she was readmitted because it was apparent that she was not receiving medication. Steroid therapy was changed to methylprednisolone (Medrol). She responded and was much improved on discharge in November 1959. Her Addis counts were noted to be abnormal during this admission. Her maintenance dose was 15 mg. of methylprednisolone per day.

During the next ten months, she did very well. She attended school and had no joint or abdominal symptoms. In October 1960, a skin infection of her hands

appeared from which β-hemolytic streptococci and coagulase-positive staphylococci were isolated. Addis counts were also abnormal during this hospitalization, and methylprednisolone was increased to 42 mg. per day. She was discharged on this dosage in November 1960 and again did reasonably well until February 1961, when skin infections necessitated readmission.

Of the 18 children with systemic lupus erythematosus we have seen, 16 have been female, and all have had evidence of renal disease. Characteristic manifestations of the children in this group, as in those of Wedgwood and Janeway,[1] have included: (1) fever, often of low-grade intensity; (2) joint symptoms, including pain, swelling, stiffness, and soreness; (3) skin rash, which is sometimes in a butterfly distribution; (4) hematologic abnormalities, including hemolytic anemia, leukopenia, thrombocytopenia, and lupus erythematosus cells; (5) hypertension and cardiac enlargement; (6) pulmonary infiltrations; and (7) central nervous system manifestations.

Of great importance is the striking tendency for this disease to be familial in nature.[2–4] In our series, 4 patients had a family history of lupus erythematosus. Siblings of 3 patients had died of the disease; in the other, mother and daughter were affected. In addition, data are accumulating which indicate that members of families of patients with lupus erythematosus are prone to have hypergammaglobulinemia, rheumatoid arthritis,[5] frequent positive lupus erythematosus tests,[6,7] and rheumatoid factor in their circulation.[8] It is noteworthy that one patient had a younger brother with rheumatic fever and severe carditis and a parent with rheumatoid arthritis.

Accumulating evidence of the familial nature of this disease and associated disturbances suggests that precipitating environmental factors may be superimposed on the genetic propensity to develop this illness.

Immunologic abnormalities in lupus. Although the lupus erythematosus cell is not always found in lupus erythematosus, it was found almost uniformly in the bone marrow and blood clots of the children in our series. Since Hargraves and associates[9,10] originally identified this morphologic concomitant of systemic lupus, the diagnosis of this disease has been more certain. Abundant evidence establishes the immunologic nature of the lupus erythematosus cell.[8] This element results when gamma globulin, apparently antinuclear antibody, combines with nuclei of dead or injured cells. This nuclear material is then engulfed by viable leukocytes, usually of the polymorphonuclear series. Formation of lupus erythematosus cells is strictly an in vitro autoimmune phenomenon. Recent studies by Miescher and Fauconnet,[11] Seligman,[12] Holman and associates,[13] and Friou[14] have established that patients with systemic lupus are further characterized by the presence in their serum of antibodies against a variety of nuclear and cytoplasmic constituents. In addition, apparent autoantibodies against red cells, white cells, and even platelets are often found in their circulation. This evidence has led many to conclude that lupus erythematosus is basically a genetic fault, permitting the development of autoimmune phenomena with resultant destruction of the host.

Prognosis for systemic lupus is generally bad and, in untreated patients, death is often the outcome. A particularly bad prognosis, however, attends the development of renal manifestations in young women.[15]

In children, disseminated lupus is a highly malignant disease. Before 1955, when we began treatment in our clinic with truly massive doses of cortisone, all children with lupus had renal disease, and all had died within one year after apparent clinical onset of the disease. Since 1955, we have been using a treatment regimen derived from the philosophy that we should administer as much cortisone or its newer analogues as the patient will possibly tolerate. In children with disseminated lupus, we generally initiate therapy with cortisone acetate in a dosage of 300 mg./M^2/day. This dosage is maintained until severe evidence of Cushing's syndrome or untoward side reactions appear. The initial period of treatment often lasts three to six months. The dosage is then lowered to 150 to 200 mg./M^2/day and is again maintained as long as possible or until distinct improvement in the Addis count occurs. Finally, a maintenance dosage of 50 to 150 mg. per cent may be maintained for several years or as long as the disease appears to be active.

Death within a year of onset was the natural history of the disease when a more relaxed or low-dosage approach to adrenal steroid therapy was employed in our clinic. In contrast, none of our patients treated with the larger dosage regimen in this manner has died. Since 1955, we have treated 10 patients with massive-dose adrenal therapy. Eight are still alive and two are dead. Both of the patients who have died could not be treated by the massive-dose regimen. Of these cases, 1 was an adolescent child who tired of the distortion produced on her body by the large doses of cortisone; she began surreptitiously to discard her cortisone and, within two months, she died from fulminating lupus erythematosus. The second death occurred in a child whose fulminating renal hypertension precluded use of

what we considered to be adequate steroid dosage. Consequently, adrenal steroid therapy was discontinued, and an effort was made to control the disease with 6-mercaptopurine (6MP), according to the regimen of Dameshek and Schwartz.[16] Following a mild toxic reaction to the 6MP and exposure to the sun, fulminating lupus developed and the patient died.

Drug-induced lupus. Among the most interesting patients with lupus erythematosus whom we have studied recently is a group with lupus induced by medication. Of the group, symptoms appeared in 3 patients being treated with one of the hydantoin anticonvulsant compounds together with one of the dione derivations. These patients had skin rash, fever, hepatosplenomegaly, lymphadenopathy, pulmonary infiltration, renal disease, and, in 1 instance, pericardial effusion, pleural effusion, and ascites. Lupus erythematosus cells were found in abundance in their bone marrow, lupus erythematosus clot tests were positive, and renal biopsies showed changes characteristic of lupus erythematosus by both light and electron microscopy.[17] Lupus secondary to prolonged treatment with sulfamethoxypyridazine (Kynex) developed in a 5-year-old child.[18] In every respect, the disease observed in these children was characteristic of lupus but, in each instance, the outcome was different from the usual course of lupus. After discovering the drug or drugs associated with appearance of the disease, discontinuing their use, and avoiding reinstitution of treatment with these agents, the patients recovered completely.

Similar cases of lupus developing in children treated with hydantoin and trimethadione (Tridione) for idiopathic epilepsy, which have been reported to us, have not fared so favorably.[19,20] Death ensued in 2 patients with pathologic findings compatible with systemic lupus erythematosus, and 1 has had persistent manifestations of lupus erythematosus over a prolonged period.

We interpret this experience to indicate (1) that lupus erythematosus possibly can be induced by certain exogenous chemicals and (2) that, in this form, the entire disease is reversible if the precipitating agent can be identified and avoided completely.

ACUTE RHEUMATIC FEVER

Much has been written in recent years about the nature, diagnosis, and management of rheumatic fever, so it is not considered within the scope of this paper to extensively review this problem.[21,22]

Several points deserve emphasis when the connective tissue diseases are being considered by the family physician: the incidence of this disease today, diagnostic criteria, association with streptococci, and treatment. The question is frequently asked, "Isn't rheumatic fever disappearing?" or "Is rheumatic fever still an important medical problem?" Using cause of death reported on death certificates as a basis for his curve, Paul[23] presented evidence indicating that rheumatic heart disease, and presumably rheumatic fever, has been declining in frequency since the turn of the century. However, we think that the apparent decrease in incidence of rheumatic fever in recent years, as reflected by its infrequency in the large diagnostic centers, is more an apparent decrease than a real one.

To answer this question in Minnesota, 2 surveys, 1 in 1955 and 1 in 1958, were carried out by the State Department of Health under sponsorship of the State Medical Association and the Minnesota Heart Association.[24–26] These surveys indicated that (1) rheumatic fever continues to be a significant health problem in Minnesota, since from 3,000 to 4,000 new cases occurred in each of these years, (2) rheumatic fever is being well diagnosed in Minnesota, as based on the physicians' adherence to the modified Jones criteria for diagnosis, and (3) many patients, for one reason or another, are not being given prophylactic chemotherapy or antibiotic therapy to prevent recurrence.

The following case illustrates the manifestations of this disease in the young child.

Case report. This 3½-year-old boy had pneumonia in May 1960. Although the pneumonia responded to antibiotics, he subsequently had dyspnea and pedal edema. Diuretics and sodium restriction were not beneficial, and he was admitted to the University of Minnesota Hospitals in August 1960, where erythema marginatum was noted. Past history disclosed no known allergies nor previous serious illnesses. Review of the systems revealed no previous joint involvement. Family history disclosed an older sister with disseminated lupus erythematosus and another with a brain tumor. Physical examination on admission revealed no arthritis; however, edema, hepatomegaly, and cardiac enlargement with mitral stenosis and insufficiency were noted. Laboratory examinations at that time showed an antistreptolysin O titer of 250 Todd units, erythrocyte sedimentation rate of 3 mm. per 60 minutes, and negative blood and throat cultures. The initial urinalysis revealed 1+ protein, but this abnormality was not evident again. The erythrocyte sedimentation rate rose to 55 mm. per 60 minutes as failure subsided and dropped to 28 mm. per 60 minutes by the time of his discharge from the hospital. The antistreptolysin O titer fell throughout the hospital course, as did the anti-DNAse-B. Repeated lupus erythematosus clot tests were negative. The total serum proteins were 6.2 gm. per cent with 3 gm per cent albumin and 3.2 gm. per cent globulin. Gamma globulin was 1 gm. per cent. An electrocardiogram revealed a right bundle-branch block. Therapy with cortisone for two weeks, digitalis, diuretics, and antibiotics produced good

response. He was discharged in October 1960 on digoxin, benzathine penicillin G (Bicillin) prophylaxis intramuscularly, and vitamins. He was followed in the outpatient department at frequent intervals. He had an episode of pneumonia in November 1960 and was treated with chloramphenicol.

He did well until January 1961, when the mother noted onset of dyspnea and fever associated with diffuse abdominal pain. He was admitted to the University of Minnesota Hospitals three days after onset. On physical examination, he had grade 2 apical systolic and aortic diastolic murmurs, tachycardia, bilateral basilar rales, marked hepatomegaly, moderate splenomegaly, and minimal pitting ankle edema. His urine was normal. His hemoglobin was 8.6 gm. per cent and white blood count was 11,200 with a moderate left shift. The erythrocyte sedimentation rate was 40 mm. per 60 minutes and serum electrolytes were normal. The C-reactive protein was 4+ and antistreptolysin O titer was 125 Todd units. The Addis count revealed 1 million white blood cells but no red blood cells. The quantitative protein was negative. His therapy initially consisted of antibiotics, diuretics, and steroids. His response was slow, but progressive improvement occurred.

To be emphasized in this case is the onset of clinical disease with pneumonitis, presumably rheumatic pneumonitis, severe carditis with heart failure, lack of overt joint disease, and low sedimentation velocity accompanying heart failure.

Since neither a true diagnostic test nor an absolutely certain pathognomonic sign of this disease exists, diagnosis of rheumatic fever continues to be based on the constellations of manifestations which fit the criteria of Jones. By the modified criteria, the major manifestations include (1) carditis, (2) polyarthritis, (3) chorea, (4) subcutaneous nodules, and (5) erythema marginatum. Minor manifestations include (1) fever, (2) arthralgia, (3) prolonged P-R interval in the electrocardiogram, (4) increased erythrocyte sedimentation rate and white blood count, or appearance of C-reactive protein, (5) preceding β-hemolytic streptococcal infection, and (6) previous rheumatic fever or inactive rheumatic heart disease.

When 2 major manifestations occur together with at least 1 minor manifestation, rheumatic fever can be diagnosed with reasonable security. Also, 1 major manifestation occurring together with at least 2 minor manifestations permits a reasonably certain diagnosis.

It is of great importance to realize that abundant evidence links rheumatic fever with streptococcal infection.[27,28] Once rheumatic fever is diagnosed and treatment, by whatever means, is begun, the physician assumes the obligation of ensuring as far as possible the child's freedom from further recurrences. This can be accomplished by continuous treatment with prophylactic doses of sulfadiazine (0.5 gm. once a day for children less than 60 pounds and twice daily for children heavier than 60 pounds), 400,000 to 500,000 units per day of oral penicillin, or 1,200,000 units of benzathine penicillin given intramuscularly once each month.

During the past six years, we have seen approximately 100 children with first attacks of rheumatic fever. The great majority of these have been associated with streptococcal infection. Although no controlled studies have been employed, approximately one third of the patients have been treated with large-dose steroid therapy, one third have been given small- or moderate-dose steroid therapy, and one third have been treated with salicylates and bed rest or just bed rest. The figures slightly favor use of large-dose steroid treatment from the standpoint of subsidence of manifestations and laboratory abnormalities and the disappearance of murmurs. However, this minor advantage is not gained without a real cost in serious life-threatening reactions to the hormones. These have occurred in approximately 10 per cent of our patients and 1 patient died from a bleeding duodenal ulcer.

RHEUMATOID ARTHRITIS

Innumerable papers, monographs, and books have been written about rheumatoid arthritis, but rheumatoid arthritis in childhood is only beginning to receive the comprehensive treatment it warrants. Although juvenile rheumatoid disease accounts for only 5 to 7 per cent of the total incidence of rheumatoid arthritis, we believe this form of arthritis may be far more significant than the frequency indicates. In childhood, rheumatoid arthritis is often expressed as an acute systemic disease with sudden onset. Therefore, etiologic and pathogenic mechanisms may be potentially easier to delineate among children than adults, for whom onset and precipitating factors are clouded in a long and indefinite history of increasingly severe joint disease. Secondly, juvenile rheumatoid arthritis may appear at a very early age when certain immunologic mechanisms, which might otherwise be implicated in the etiology or pathogenesis of this disease, are grossly deficient. During childhood, exposure to trauma, intoxication, and even infection are more readily assessed because they are relatively limited.

However, incisive consideration and consequent analysis of rheumatoid arthritis in childhood have been limited by the inadequacy of the descriptions of this disease available in the medical literature, which are derived from studies carried out by specialists concerned with adult arthritis clinics, orthopedic clinics, or

clinics for physical rehabilitation. Textbooks, pediatric and medical literature, and most published reports give inadequate descriptions of arthritis in children and are concerned primarily with children having advanced joint disease. Relatively little attention has been paid to the general systemic manifestations and protean nature of rheumatoid disease as it occurs in children. The recent reports by Johnson and Dodd[29] and Gauchat and May[30] partially correct this deficiency, but reports of large groups of patients, comprehensively investigated by modern clinical and laboratory technics, are still lacking.

Because of the inadequacy of available descriptions, the early and fulminating forms of rheumatoid disease present great diagnostic difficulty to most pediatric specialists, rheumatologists, internists, and general practitioners. It is common experience in consultative pediatric practice to see patients with obvious early or fulminant forms of juvenile rheumatoid arthritis who have been extensively studied by several pediatricians and internists using virtually every known laboratory test. In spite of these efforts, the child's disease remains undiagnosed until someone familiar with the clinical manifestations of juvenile rheumatoid disease sees the child. Alternatively, diagnosis may be arrived at by exclusion when the actual "weight of the evidence" (by this, I mean the chart size) suggests juvenile rheumatoid arthritis. Delay may continue until time provides an assist, permitting appearance of inflammatory and deforming processes in numerous joints of the body.

Sir George Still[31] originally recognized that arthritis occurring in children might be manifest in several relatively distinct forms. For example, in 1897, he wrote of the adult type of rheumatoid arthritis occurring in children. He distinguished this from a form of arthritis especially involving the knees, wrists, spine, and fingers, which is characterized by an elastic fusiform swelling of the proximal interphalangeal joints and associated with lymphatic and splenic enlargement. He was further impressed with the fact that pericarditis was a prominent manifestation in 5 of his 12 cases.

Since Still's publication, violent forms of rheumatoid arthritis associated with evidence of systemic disease have been recognized and delineated by the term, Still's disease. Indeed, much debate has centered about whether Still's disease, the other forms of rheumatoid arthritis in childhood, and adult rheumatoid arthritis are the same disease or fundamentally different processes. Although no critical evidence has been supplied, the present consensus is that Still's disease is but a variant of rheumatoid disease in childhood, conditioned somewhat by the age of the patient. Certainly, perfectly typical Still's disease can be observed on occasion among adults with rheumatoid arthritis. Children whose disease begins with the classic picture of Still's disease can settle down to become indistinguishable from the adult type of rheumatoid arthritis of childhood.

To facilitate discussion, we have somewhat arbitrarily divided our patients into 3 groups: (1) Still's type of rheumatoid arthritis, manifested by variable prodromal periods of spiking septic temperature, typical skin rash, generalized adenopathy, and splenomegaly associated initially or at a later date with the development of joint disease; (2) intermediate type, in which arthritis is associated with septic temperature curve, typical skin rash, or lymphatic involvement but not both; and (3) adult type, manifested by insidious onset of arthritis with or without overt fever and by lack of typical skin rash, lymphadenopathy, or visceral involvement.

In our series of 150 consecutive cases, approximately 50 per cent were classified as the adult type of rheumatoid arthritis, 30 per cent as the classic Still's type, and 20 per cent as the intermediate form.

Age of onset. In this group of children, rheumatoid disease began at all ages. In the youngest patient, the disease apparently began with septic temperature shortly after birth. The disease was characterized by typical skin rash, lymphadenopathy, and splenomegaly by the time the child was four months old and by typical deforming joint manifestations by eight months of age. The pediatric age range in our clinic naturally limited the age of patients—the oldest was 15. The ages of highest incidence were the second and third years. However, approximately 50 per cent of cases began in children between 7 and 16 years of age and 50 per cent in children younger than 7. In children with the adult type of rheumatoid disease, the majority of patients were older than 7 at onset, whereas the majority of those with Still's type were less than 7. In patients of the intermediate type, approximately half began prior to the seventh year and half began later. Thus, although all 3 forms of rheumatoid arthritis may occur at any time in childhood, Still's type with violent onset, spiking temperature, skin rash, hepatosplenomegaly, and lymphadenopathy tends to occur more frequently in very young children, and the adult type of disease occurs more frequently in older children.

Historical data. The historical data recorded on the charts of these patients are interesting,

Approximately 30 per cent gave a family history of arthritis occurring among siblings, parents, or grandparents. A family history of rheumatic fever was noted in 20 per cent and a family history of allergy in 35 per cent. More than 40 per cent had had an infection, often an ill-defined respiratory infection, which preceded the onset of rheumatoid disease. For 10 per cent of patients, significant trauma, often to a joint, had occurred within one month of the onset of arthritis or rheumatoid disease.

Without suitable control data from a similar population of sick and healthy children, relatively little significance can be attached to these records. For example, infections are very frequent among children of all ages. An average of 7 separate respiratory infections occurred each year in children 5 to 7 years old in the group studied in Cleveland, and as many as 9 or 10 infections were not unusual at this age. Similar observations were made on a group of allergic children under study in our clinic.[32] Such a normally high frequency of respiratory infections leaves little opportunity for any except the youngest child to have been free of infection for a reasonable period prior to onset of rheumatoid disease. Expressed in this way, the familial incidence of rheumatoid arthritis and other rheumatic diseases is also of indefinite significance, since rheumatoid disease in one form or another is of relatively high frequency—2 to 10 per cent—in the general population. Current evidence, however, suggests that rheumatoid arthritis tends to occur with high frequency in certain families,[33] and this experience was certainly not contradicted by our observations.

Symptoms and signs. Certainly, at least in part because it is the basis for the current definition of the disease, the most frequent manifestation observed was arthritis. In all except 1 of 150 children in this series, frank, objective evidence of arthritis existed. Usually, arthritis was manifest as an indolent process with redness, swelling, pain, and tenderness, involving multiple joints, which persisted for prolonged periods. In a number of patients, however, the initial joint involvement was migratory although the arthritis ultimately became indolent. Joints most frequently involved were the knees, ankles, fingers, wrists, and elbows. Involvement of the lumbar spine occurred in 21 per cent of patients and of the cervical spine in 26 per cent. Other involved joints were hips, mandibular-temporal joint, and joints of shoulders, feet, and toes. In most patients, multiple joint involvement was a presenting symptom. In almost 20 per cent, the presenting joint disease was monarticular in nature, but it was persistently monarticular in only 4 per cent.

As previously mentioned, rheumatoid disease was diagnosed in 1 patient without objective joint involvement. This last case deserves special mention. The patient was included as a case of juvenile rheumatoid arthritis because he had the typical fever curve, diagnostic skin rash, generalized lymphadenopathy, splenomegaly, and arthralgia involving many joints, even though objective joint disease has not yet appeared. We felt this to be justified because numerous other cases, manifested in exactly the same way, have regularly turned out to be juvenile rheumatoid arthritis.

We believe that all children of this series suffered from some degree of arthralgia. As is often true of children with joint disease, these patients did not complain of joint pain. Children are naturally stoics. This latter point has, we believe, been overlooked by a number of investigators who have erroneously concluded that rheumatoid arthritis in childhood differs from adult disease in being less painful. We contend that this conclusion is incorrect. When old enough to express themselves and to understand, the children admitted the presence of joint pain with great regularity.

In younger children, arthralgia and joint tenderness were inferred from several observations. In the first place, extreme fussiness and irritability accompanied the approach of parents or physicians to the bed and were accentuated by manipulation of the joints. Even more revealing was the observation that children with rheumatoid disease did not move their extremities as do normal children. Instead, sometimes for long periods prior to onset of objective joint disease, these children would assume a position of minimal motion and maximal support to the joints. In younger children, the position often assumed was one of maximal flexion and stability. The knees and hips were flexed, the feet flat on the bed or folded about one another, the elbows flexed, and the hands supported behind the head or held folded together over the chest. This position would often be maintained for prolonged periods, even for several hours at a time, permitting only minimal motion. Attempts by parents, medical staff, or nurses to alter this position would be resisted with crying, whining, and fussing but not with muscular resistance.

Fever. More than 90 per cent of the 150 patients observed by us had significant fever at one time or other during the course of the disease. Indeed, 60 per cent had fever when actually observed in our clinics or hospitals. The

fever curve which seemed characteristic of juvenile rheumatoid arthritis, and was often helpful in its early diagnosis, was a septic temperature curve with daily spikes and troughs. In many children, the temperature would spike to 104 to 106° F. and fall to levels of 97 to 99°. Usually, the highest temperature came in the late afternoon or evening, but patients having peak fever at other times during the day or night were also observed. This spiking temperature course would often persist for months.

The septic phase was usually associated with severe joint disease. However, in many cases, the septic temperature, associated with lymphadenopathy, splenomegaly, and typical skin rash, preceded the onset of objective joint disease by periods exceeding six months. One notable feature of this septic phase was that the children often had a general appearance of well-being in spite of extreme temperature elevations.

Muscle pain and tenderness were occasionally observed, and 13 children had subcutaneous nodules. These nodules occurred primarily on the extensor surfaces, especially on the ulnar surface of the forearm and about the elbows. The nodules usually were small and similar to those observed in children with rheumatic fever.

Unlike adult rheumatoid arthritis, in which stiffness, especially in the mornings, is a prominent complaint, the disease in children was not often associated with joint stiffness. This manifestation was sufficiently significant to warrant inclusion on the hospital or clinic record in only 24 patients of this series. In many more children, especially those with the adult type of disease, minimal stiffness occurred but was not a prominent feature.

Skin rash. Children often have a skin rash typical of the disease. This skin rash has recently been well illustrated by Gauchat and May[30] and Isdale and Bywaters.[31] This characteristic rash is very helpful in diagnosis. Indeed, it has been our experience that, when observed, this rash is as characteristic of rheumatoid arthritis as the rashes of measles and chickenpox are of their respective diseases. The rash is a salmon pink, erythematous, macular or slightly maculopapular eruption which is evanescent in character and usually appears on the trunk, neck, and proximal portion of the extremities at the height of fever. The rash may appear and disappear in a matter of hours. In some early cases, the rash, like the septic fever, may exist for months prior to onset of articular disease. In a number of cases in our series, the skin rash permitted a reasonably certain diagnosis of rheumatoid disease long before joint disease was evident.

The diagnostic skin rash was observed in 38 per cent of our cases. The history in well-established cases, however, suggested that rash had been prominent with the early disease in a somewhat larger percentage of patients, as suggested in the paper by Gauchat and May.[30] However, the 80 per cent figure given by these authors seems somewhat high in light of our observations. In addition to the characteristic skin rash, some patients had other rashes, including erythema multiforme, purpura, and erythematous, nondescript, macular rashes.

Cardiac manifestations. Unlike rheumatic fever, cardiac manifestations were not common. However, 7 patients had pericarditis, 1 had myocarditis and went into heart failure, and approximately one fifth of patients had significant electrocardiographic abnormalities at some time during the acute disease. Murmurs were frequently heard and recorded. These were usually systolic murmurs which disappeared upon recovery or persisted only as functional murmurs without clear evidence of valvular heart disease. Unlike the situation existing in acute rheumatic fever, none of the children studied has developed clear evidence of residual valvular heart disease.

Pulmonary involvement. Pulmonary infiltrations developed in a number of patients, especially during the acute phase of the disease, and it was not uncommon to observe pleural effusion or peritoneal irritation reflected by abdominal pain and tenderness. Indeed, in several cases, peritoneal involvement was sufficiently severe to prompt consideration of abdominal exploration.

Although several patients were confused, no evidence of chorea or encephalitis was recorded. Unlike the Scandinavian experience, iritis and iridocyclitis, although looked for, were diagnosed in only 3 patients. Amyloid disease appeared in none of our 150 cases.

Laboratory manifestations. Laboratory features, when abnormal, reflected the systemic disturbance characteristic of the active phase of this disease. Thus far, no specific diagnostic laboratory test has been developed. The sedimentation rate was regularly elevated. In most acute cases, the erythrocyte sedimentation rate was markedly elevated, being recorded at values greater than 100 mm. per hour by the Westergren method. Another frequent finding was reversal of the albumin-globulin ratio, which on electrophoretic analysis was shown to be due to a slight decrease in albumin, a marked increase in alpha-2 globulin, and a significant increase in the gamma globulin. Leukocytosis was frequently observed, with approximately 50 per cent of patients having significant elevations

of the total white count. The differential count, especially in patients with markedly elevated leukocyte counts, regularly revealed polymorphonuclear preponderance. Hematologic studies in these patients often revealed a shift to the left with numerous so-called toxic neutrophils in the peripheral blood. In 15 patients, a total white count greater than 25,000 was recorded and, in 1, a count of 90,000 with 95 per cent polymorphonuclear leukocytes was noted.

Anemia existed in slightly more than 25 per cent of patients. This was almost always a microcytic hypochromic anemia, presumably due to inadequate utilization of dietary iron, since it did not respond well to treatment with supplemental dietary or parenteral iron salts. Studies of the bone marrow were made in approximately one third of patients. Prominent features were proliferation of the neutrophils, plasmacytosis, and slight normoblastopenia.

In many patients, slight albuminuria was observed during the febrile phase of the disease; however, urine was otherwise completely negative and no evidence of renal involvement was obtained.

Bacteriology. Blood cultures were repeatedly drawn in most patients and, except for obvious occasional contamination, were regularly negative. Cultures of the joint fluid performed on a number of occasions were likewise negative. Throat cultures were usually negative for pathogens but, in approximately 25 per cent of patients, β-hemolytic streptococci were cultured and the throat cultures were considered positive.

Unlike the regular elevations observed in children with rheumatic fever, the majority of children with rheumatoid arthritis had antistreptolysin O titers within the normal range. However, in more than 20 per cent of cases studied with this serologic method, elevations in the titer were observed, suggesting the recent occurrence of streptococcal disease.

The best interpretation of these data together with the bacteriologic observations would be that, in contrast to rheumatic fever, rheumatoid arthritis in childhood usually occurs in the absence of recent hemolytic streptococcal infection. It is still possible, but not proved, that some cases of juvenile rheumatoid arthritis may be initiated by streptococcal infection.

Acute phase reactants. Serologic reactions were often, but not always, positive during the acute phase of active juvenile rheumatoid arthritis. For example, C-reactive protein was usually noted in serum of children with the most active disease and especially in those with systemic involvement. When the disease was of low-grade activity or was inactive, the C-reactive protein was negative. Similarly, most children with active disease showed increased amounts of mucoprotein in the serum. In patients with acute, severe systemic disease, the mucoprotein values tended to be very high. Indeed, among more than 10,000 determinations of mucoprotein concentration in our laboratories, some of the highest values were observed in children during the septic phase of juvenile rheumatoid arthritis.

Lupus erythematosus phenomenon in juvenile rheumatoid arthritis. Since it has been observed that adults with rheumatoid arthritis have positive reactions for lupus erythematosus in from 5 to 20 per cent of cases, it was of interest to study this reaction in children with rheumatoid disease. The testing technics used in these analyses included several modifications of the Gonyea clot test, incubated bone marrow preparations, the Weiss-Barnes test, and the Haserick modification of the Hargraves test. Although the so-called tart cell[9] and erythrophagocytosis were occasionally observed in these studies, no clearly positive lupus erythematosus tests were observed in any of 175 tests on 56 patients. This was true despite intensive systemic disease and extensive involvement of the lymphoid tissue and skin, as well as the joints, in the patients tested. It seems safe to conclude that false-positive lupus erythematosus tests either do not occur at all or are extremely rare in juvenile rheumatoid disease.

Liver function studies. Studies of liver function were carried out in approximately 25 per cent of children. In spite of frequent hepatomegaly in these patients, all tests were normal except for abnormal increases in cephalin cholesterol and thymol turbidity and a slight increase in Bromsulphalein retention in a few patients. No child evidenced retention or regurgitation of bilirubin.

Toxoplasmosis tests. One laboratory finding deserves brief comment. In searching for a diagnostic clue, toxoplasmosis neutralization tests were carried out in 7 patients and strongly positive Sabin neutralization tests were observed in 4. However, when dye tests and complement–fixation tests were carried out on some of these same sera as well as on additional sera, negative results were regularly obtained.

The best interpretation of this observation is that sera of children with juvenile rheumatoid arthritis often contain a substance capable of interfering with the infectiousness of toxoplasmosis organisms for rabbit skin; this substance almost certainly is not specific antibody against toxoplasma. This observation, which led to

erroneous diagnosis of acquired toxoplasmosis in 1 child, deserves further study.

Other laboratory studies. Because of frequent difficulty in diagnosis of early or fulminating cases, numerous other laboratory studies were performed on patients with juvenile rheumatoid arthritis. These tests, including heterophil antibody titer, blood cultures, brucellosis agglutinations, typhoid-paratyphoid agglutinations, study of urinary sediment, serologic tests for syphilis, tuberculin tests, and special cultures of the blood and joint fluid for pleuropneumonia-like organisms, were regularly negative.

Sex incidence. Although prevalence of females among patients with rheumatoid arthritis has been much discussed, no satisfying explanation of this relationship has been forthcoming.

Among Still's 12 cases with juvenile rheumatoid arthritis,[31] males and females were almost equally distributed. However, in several other series, females have appeared to predominate just as they do among adults with rheumatoid arthritis. Thus, in our material, we were somewhat surprised to find that, of 150 children with rheumatoid arthritis, the number of males and females was almost equal.

Single or multiple diseases. Much argument has appeared concerning whether or not adult rheumatoid arthritis and juvenile rheumatoid arthritis of the Still's type are basically different diseases. General agreement exists that rheumatoid disease indistinguishable from the adult disease in mode of onset and expression can occur at any age during childhood. However, one-third to one-half of cases ultimately diagnosed as juvenile rheumatoid arthritis in our large pediatric clinic differ strikingly from the standard textbook description of the disease. The greatest difference between these patients and those with the adult form of the disease seems to reside in the extensiveness of systemic involvement, the prolonged septic prodrome, the skin rash, and the protean nature of the manifestations in some patients. However, upon serial study, one sees cases with the most extreme form of systemic disease and no recognizable joint involvement become cases with deforming, crippling arthritis no longer characterized by extensive symptomatic disease. It is not difficult to conclude that the two processes may be intimately related. In a series such as this, one observes all shades of variation from the adult type of disease with insidious involvement primarily of the joints to the extreme case of Still's disease with little or no joint involvement. One concludes that even the two extremes are merely different phases of the same disease process.

Course of the disease. Just as the disease varies in its initial expression, so does the course it follows. For example, we have observed that, in some patients, rheumatoid disease (1) developed as a generalized systemic process, (2) was sustained through several complete and incomplete spontaneous remissions, (3) settled down to an indolent, painful arthritis with striking joint involvement lasting for several years, and (4) without explanation, had spontaneous remission with complete recovery except for slight residual joint damage. In others, initial stiffness and swelling of a single joint without fever or leukocytosis developed after apparent trauma to the joint; swelling, pain, tenderness, and heat persisted in the joint and, after several months, the disease appeared in other joints. Thus developed, the joint disease might persist for months or years and then disappear without explanation or residual damage. Other patients, having either a septic or insidious onset, might have early extensive, severe joint disease with marked destruction and tendency to ankylosis and contracture formation that progresses to severe joint destruction. Indeed, the method of onset, course of disease, and ultimate outcome expressed almost as many variations as there were patients. This fact makes it extremely difficult to offer a meaningful prognosis to parents of a child with juvenile rheumatoid arthritis.

One point seems clear, however. These children do not die of their disease, even though it is a most trying experience for the child and his family and requires that the pediatrician have almost infinite patience, skill in counseling, and, often, the ability to do nothing rather than something new or drastic. Of our 150 cases, 2 have died and, in both instances, death resulted from medical treatment. A transfusion reaction was fatal in 1, and the other died of thrombopenic purpura secondary to salicylate treatment in large dosage. Even though many patients suffered from severe disease that often lasted five to eight years, none has amyloidosis. This has made us wonder whether the high incidence of amyloidosis referred to in textbooks and older descriptions of juvenile rheumatoid arthritis does not reflect recurrent and indolent bacterial disease, which was the lot of debilitated children prior to the antibiotic era.

Differential diagnosis. Diagnosis has been simple and uncomplicated in many patients at onset of primary joint disease. Even from the earliest phase, patients have fit the criteria of Ropes and associates[35] and have not been diagnostic problems. However, approximately 50 per cent of children with juvenile rheumatoid ar-

thritis have presented distinct problems in differential diagnosis to the referring physician and consultant. In addition, a number of diseases distinct from juvenile rheumatoid arthritis have repeatedly been misdiagnosed as rheumatoid disease. Thus, a word about differential diagnosis might be helpful.

In our experience, illnesses most frequently diagnosed erroneously as juvenile rheumatoid arthritis include malignant diseases, leukemia, Hodgkin's disease or other lymphoma, neuroblastoma, other forms of sarcoma including osteogenic sarcoma and Ewing's tumor, other fibrinoid or collagen diseases, Henoch's nonthrombopenic purpura, hemophilia with periarticular and intraarticular hemorrhage, dermatomyositis, periarteritis nodosa, lupus erythematosus, rheumatic fever, and traumatic or posttraumatic joint effusion. In 1 patient, septicemia due to chronic meningococcemia was thought to be rheumatoid posttraumatic arthritis until a blood culture established diagnosis.

On the other hand, physicians frequently seem to be unfamiliar with the septic and protean nature of juvenile rheumatoid arthritis. When faced with such a case, they tend to consider diagnoses ranging from the general term, malignant disease, through every conceivable septic or infectious process to rheumatic fever and the other so-called collagen diseases, particularly subacute or acute septicemia.

The differences between rheumatoid arthritis of childhood and acute rheumatic fever have always seemed to us to be more striking than their similarities. In spite of the lack of specific diagnostic tests for either disease or any single pathognomonic sign, recognition of these differences usually permits a clear distinction early in the disease course.

Arthritis is seldom migratory in juvenile rheumatoid arthritis. Except during the inception of disease in a few cases, arthritis tends to select certain joints and remain in them as an indolent, refractory process. On the contrary, the arthritis of rheumatic fever is evanescent and regularly migratory, skipping from one joint to another in a matter of just a few hours or at most several days. In both diseases, the larger joints, such as the knees and ankles, are most frequently involved. However, there is a much greater tendency for juvenile rheumatoid disease to involve the smaller joints, such as the proximal interphalangeal joints of the hands and feet, temporomandibular joints, joints of the cervical and lumbar spine, and small joints of the hands and feet. Given sufficient time, the indolence and destructive characteristic of the joint disease in rheumatoid arthritis often sets the disease clearly apart from the evanescent, benign joint disease of rheumatic fever. Although cardiac manifestations may occur in both diseases, those with juvenile rheumatoid arthritis are transient and do not appear to damage the heart valves, whereas the carditis of rheumatic fever may be life-threatening and often leaves residual valvular damage.

In our patients with juvenile rheumatoid arthritis, the septic temperature course with spiking fever up to 105° and 106° daily was not uncommon. This septic temperature curve, particularly persisting over several weeks, did not occur among children with rheumatic fever. Splenomegaly and marked generalized lymphadenopathy were prominent features in many patients with juvenile rheumatoid arthritis but were extremely rare in patients with rheumatic fever. Similarly, juvenile rheumatoid arthritis could virtually be diagnosed by the skin rash, which was not seen in patients with acute rheumatic fever. Rheumatic fever patients often had skin rashes of varying types, but we have yet to see the salmon pink, blotchy, evanescent, erythematous rash with the small, pale centers so frequently noted during the septic phase of juvenile rheumatoid arthritis. Another point deserving emphasis is that the septic temperature occurring in some patients with juvenile rheumatoid arthritis was not abolished or even appreciably affected by treatment with large doses of salicylates.

Treatment of rheumatoid arthritis in childhood, as in adults, rests primarily on symptomatic relief, gentle physical therapy, local intraarticular steroid therapy, and, when necessary, on splinting of inflamed joints. At first, steroid hormones offered real promise for this disease. Unquestionably, large doses of steroid hormones can produce dramatic, apparently beneficial effects on the disease. However, the serious side reactions to steroids[36,37] and the long-term therapy required to maintain beneficial effects make it seem desirable to avoid use of the steroid hormones whenever possible and to keep the dosage to an absolute minimum. Our constant practice is to try to eliminate treatment with steroids, even in children with such severe disease that initial therapy with adrenal steroids seems advisable.

DERMATOMYOSITIS

Dermatomyositis, a generalized disease involving the skin and striated muscle, occurs occasionally among children. The most common manifestations include:[38–41] (1) swollen eyelids—peri-

orbital edema, (2) heliotrope rash in butterfly distribution, (3) muscular weakness, (4) muscular soreness, (5) fever, and (6) induration of muscles. Universal calcinosis, generalized edema, respiratory difficulty, and difficulty in swallowing occur occasionally. Respiratory and swallowing difficulties are prominent features, primarily in the most severe cases.

Since 1954, we have studied 9 cases of dermatomyositis in the Children's Rheumatism Clinic, comprising 6 females and 3 males. Age at onset ranged from six months to thirteen years. Family histories were negative for dermatomyositis, scleroderma, rheumatoid arthritis, or lupus erythematosus.

In almost every instance, onset of the disease was insidious. Within weeks, however, the entire spectrum of the disease became apparent. Particularly notable were the butterfly heliotrope rash and trophic changes over the knees, fingers, and elbows, along with the striking weakness, pain, and tenderness of the muscles characteristic of this disease. No evident association with infection, especially streptococcal infection, could be demonstrated. Electrophoretic studies of the serum proteins revealed elevation of alpha-2 and gamma globulin in all cases. Studies of bone marrow and Gonyea clot test were negative in every instance, providing a nice differential point from lupus erythematosus. Urine has been normal. By light microscopy, skin and muscle biopsies have revealed nonspecific inflammatory changes and edema.

Treatment of dermatomyositis has been very unsatisfactory. In 5 instances, we observed improvement in the presenting manifestations while patients were receiving large doses of ACTH, cortisone, or a cortisone analogue. However, these meager gains have been offset by severe side reactions to adrenal hormone therapy. Patients with dermatomyositis have more than the usual incidence of gastric or duodenal ulceration while taking steroid hormones, and this propensity is an extreme risk when these patients must be so treated. Testosterone has been of little benefit. Our current opinion is that these children should not be treated with adrenal hormones unless the disease is progressing rapidly and a brief trial with hormone is considered essential to save the child's life.

RHEUMATOID ARTHRITIS AND AGAMMAGLOBULINEMIA[42-45]

Since evidence that antibodies and gamma globulins participate in the pathogenesis of rheumatoid arthritis and collagen disease seems commanding, it is particularly important to recognize evidence which suggests a different relationship. Recent experience with patients simultaneously having agammaglobulinemia and one of the collagen diseases is considered very significant.

COLLAGEN DISEASES ASSOCIATED WITH AGAMMAGLOBULINEMIA

Patients with agammaglobulinemia	32
Number with collagen disease	10
Number with classic rheumatoid arthritis	6
Number with probable rheumatoid arthritis	3
Number with other collagen disease	1

During the past several years, we have studied 32 patients with agammaglobulinemia in the Children's Rheumatism Clinic. These patients represent both the acquired and congenital sex-linked recessive forms of agammaglobulinemia. Among these 32 patients, collagen diseases have occurred with inordinate frequency (see table). Manifestations of rheumatoid disease in these patients have included morning stiffness, pain or tenderness of joints during motion, swelling of one or more joints, symmetric joint swelling, subcutaneous nodules, and, in 3 instances, subcutaneous nodule formation. In 1 patient, the disease began with the appearance of Still's disease, but infection with a gram-negative organism developed and the patient died with a diffuse fibrinoid vascular disease and bilateral renal cortical necrosis. Among patients with acquired agammaglobulinemia who have concomitant arthritis, there is a striking family history of crippling, classic rheumatoid arthritis and arthritic manifestations. Other authors have observed dermatomyositis, scleroderma, and even diseases suggestive of lupus erythematosus to be associated with agammaglobulinemia. From this experience, the most important points are:

1. It is now clear that rheumatoid arthritis, or variants of rheumatoid arthritis, and other representatives of the so-called collagen group of diseases occur with inordinate frequency in agammaglobulinemia. Among our patients, approximately 30 per cent of agammaglobulinemic patients have had rheumatoid disease.

2. Acquired agammaglobulinemia with rheumatoid arthritis occurs among families in which rheumatoid disease is extremely common.

Janeway and associates[42] have observed this same high frequency of association of agammaglobulinemia and rheumatoid disease. Further, joint disease and other evidence of collagen disease have been frequent observations among the reported individual cases of agammaglobulinemia.[43-45]

These observations have important implica-

tions. They establish that these patients lack abnormally high serum levels of gamma globulin and antigen-antibody reactions which depend upon excessive formation of antibody and rheumatoid factors. Therefore, these elements cannot be essential to the development and perpetuation of rheumatoid arthritis and certain other collagen diseases. They do not, however, completely rule out the operation of immunologic mechanisms, since agammaglobulinemic patients retain specific immunologic capacities of certain types. For example, they can develop delayed allergic and specific drug reactions. It is also pertinent that Dixon and associates[46] have found that, among rabbits repeatedly stimulated with antigen, chronic glomerular vascular lesions develop in mediocre and poor antibody producers, not in those most vigorous in antibody production.

SUMMARY

Clearly, children with diffuse connective tissue diseases present many unsolved problems. We hope that, in our studies of various forms of diffuse collagen disease from a multifaceted approach, answers to these problems will be forthcoming.

It has been impossible to cover in detail the entire problem of diffuse vascular connective tissue diseases which we are studying in the Children's Rheumatism Clinic at the University of Minnesota. However, we have presented an over-all view of our experience with several of these, including lupus erythematosus, rheumatic fever, rheumatoid arthritis, and dermatomyositis. Special emphasis has been given to the concomitant occurrence of rheumatoid arthritis and other collagen diseases with agammaglobulinemia.

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Echothiophate (Phospholine Iodide), an anticholinesterase agent with prolonged action, lowers intraocular pressure in glaucomatous eyes and prevents progressive field loss. More stable than other anticholinesterase phosphate esters, the preparation can be administered in an aqueous rather than an oil solution. Nevertheless, refrigeration of the aqueous solution is recommended, since about a fourth of the activity is lost in two months at room temperature.

Daily instillation of 0.125 per cent echothiophate kept intraocular pressure at less than 22 mm. Hg in 7 eyes treated satisfactorily with other drugs and in 6 of 7 eyes previously untreated. For more advanced glaucoma, 0.25 per cent strength was sometimes necessary, with epinephrine or acetazoleamide (Diamox) or both also used in many cases. Such therapy controlled intraocular pressure in 27 of 38 eyes in which other treatment had failed. Side effects, such as pain and blurring, were common but usually disappeared within a week.

R. C. Lawlor and P. Lee: Use of echothiophate (Phospholine Iodide) in the treatment of glaucoma. Am. J. Ophth. 49:808-813, 1960.

Red cell life in patients with chronic liver disease is often shortened, due to increased rate of aging and random destruction of cells. Accelerated erythropoiesis generally compensates for increased cell loss, however, and subnormal red cell volume is uncommon.

Volume and survival of erythrocytes were determined with radiochromium for patients with chronic liver conditions, mainly cirrhosis, and rate of red cell production was calculated. All had relatively stable disease and had received an adequate diet for at least two weeks.

Red cell life span was normal in only 6 of 21 patients and shortened in the remainder, with random red cell destruction evident for all but 1 of the 21. Only 1 of 20 patients, all with normal or increased red cell production, failed to maintain a normal red cell volume. Total and effective erythropoiesis, measured with radioiron, in 5 patients was normal or increased.

Macrocytosis and shortened cell life were not found to be closely related, nor were splenomegaly or alcoholism and random red cell destruction.

C. A. Hall: Erythrocyte dynamics in liver disease. Am. J. Med. 28:541-549, 1960.

Hypnosis in General Medical Practice

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Hypnosis has a long and colorful history which is beyond the scope of this presentation. For those with a special interest in the topic, the several references will supply data on history, technic, and theoretical considerations. The purpose of this article is to acquaint general physicians with the highlights of its medical applications.

The recent past has seen a reawakening of medical interest in hypnosis. Several years ago, hypnosis was formally acknowledged as a medical procedure by the American Medical Association. Before discussing the medical uses of hypnosis, a few general remarks are in order.

The question as to what constitutes the phenomenon known as hypnosis has been speculated for hundreds of years. The majority of these speculations, however, are of historical interest only. General agreement today is that hypnosis represents an interpersonal relationship in which the degree of suggestibility is high on the part of the person being hypnotized. The degree of suggestibility, on which hypnosis depends, relates to numerous factors such as status of therapist, motivation of patient, attitude toward hypnosis, and so forth. Hence, the ability to be hypnotized shows a wide individual difference and varies in the same person at different times. Probably any person can be hypnotized to some degree if he cooperates; probably no person can be hypnotized if he is aware that it is being attempted and decides not to cooperate.

Hypnosis cannot be compared to natural sleep as often has been the case. The hypnotized patient is not unconscious and, as a matter of fact, may be wide awake. He hears, sees, follows instructions. None of this can be duplicated in natural sleep. Hypnosis is a heightened state of suggestibility, not sleep.

The medical uses of hypnosis fall into three categories:

1. A method of anesthesia.

2. A method for the removal of symptoms, mainly hysterical in nature.

3. A means to "uncover" old memories which are lost to consciousness, that is, an aid to psychotherapy.

Anesthesia. Much of the recent medical interest in hypnosis has lain in the area of anesthesia. Dentists particularly have become interested, and some have made fairly extensive use of hypnosis for minor dental work. Obstetricians and surgeons have shown great interest, and numerous articles have appeared recently.

Hypnosis used as anesthesia has an appeal from a physiologic standpoint. If one could eliminate chemical anesthetics, particularly in disease processes for which their use increases the risk, the patient could be greatly benefited. However, it is by no means known that hypnosis can replace chemical agents for all (or many) patients. Certainly the individual difference in ability to be hypnotized must be taken into consideration, and the anesthesiologist undoubtedly would need to be present to give chemical agents in the event of failure of hypnosis. I do not know of any situation wherein surgical anesthesia cannot be produced by one or another of the anesthetic agents. I suspect that many times the desired level of surgical anesthesia could not be produced by hypnosis. Furthermore, it is difficult to see how hypnosis would save professional time. It would be a choice between having an anesthesiologist or a hypnotist, or both, attending in the operating room, unless the procedure is so minor that the physician could do his own hypnosis such as a dentist might.

Surgical anesthesia by hypnosis should probably be reserved for those situations in which the condition of the patient presents undue risks with chemical agents. It may become a useful method in normal delivery.

The effect of a person's motivation to be hypnotized is nowhere more apparent than when hypnosis is used in anesthesia. A gravely ill patient who cannot be given chemical anesthetics understandably will have a high motivation to be hypnotized as will the average woman undergoing normal delivery. The motivation of pain avoidance is a potent factor which aids the hypnotist in effecting anesthesia.

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Symptom removal. This area was the chief medical use of hypnosis in past years and was employed extensively in treating gross hysterical symptoms such as hysterical monoplegia, hemiparesis, blindness, deafness, and so forth. One hears very little now about this application of hypnosis, probably for two reasons: (1) gross hysterical symptoms which apparently were common fifty years ago are seldom evident today and (2) most psychiatrists seem to feel that, while hypnosis may well remove a hysterical symptom, it does nothing to help the person with the emotional conflicts that provoked the symptom. It is usually assumed that, if treatment goes no further than the removal of symptoms, the old conflicts will establish a new set of symptoms (or the old) and no therapeutic value will have been gained. I have not seen in the literature a controlled study performed on whether or not adequate follow-up studies show that symptoms return. Probably this must be regarded as an opinion and not an established fact.

Nor, to my knowledge, can anything factual be said about the use of hypnosis to help a person stop smoking, eating excessively, taking drugs, and so forth. Here again I am not aware of good studies having been undertaken in the area of treating "habits" of this kind. Hypnotic effects on both alleviation of hysterical symptoms and change of habit patterns require additional investigation before any realistic statements can be made.

Hypnosis and psychotherapy. This represents a specialized medical use of hypnosis and requires postgraduate psychiatric training. Hence, it falls outside the scope of this presentation. In brief, properly controlled studies of sufficient size to warrant meaningful conclusions have not yet been done in this area, and again, one is largely in a position of expressing opinions, not necessarily facts. It is possible that the well motivated patient might be able to approach "forgotten" (repressed) material more quickly via hypnosis than by more conventional psychotherapeutic methods. Some experts object to this use of hypnosis on the grounds that the patient may not recall what he has remembered (unless specifically instructed to do so), and, therefore, the uncovered material is not available for conscious inspection and action in relation to it. It is also believed by some that the hypnotic "trance" puts the patient in a needlessly dependent emotional position and may foster neurotic dependency rather than help the patient stand on his own two emotional feet. Others point out that some patients may interpret the procedure as a type of seductive act, an interpretation which may take a long time to combat, that is, may prolong rather than shorten the course of psychotherapy. We meet, herein, a therapeutic area about which there is no generally held opinion on the part of psychiatrists, and one again has to point to the need for well planned research.

SUMMARY

In general medical practice, hypnosis probably has its only utility as a method of anesthesia. For any major surgical procedure, its indication probably is restricted to those conditions wherein chemical anesthesia presents too grave a risk. As a routine method of anesthesia, hypnosis may well turn out to be the method of choice in uncomplicated deliveries. It may develop to have extensive use in minor procedures such as dentistry, wherein no great harm is done if hypnotic anesthesia is not effective.

Use of hypnosis to remove hysterical symptoms and to uncover repressed memories must be considered as part of specialized psychotherapy and hence would not be so employed by the practitioner without postgraduate psychiatric training.

Hypnosis is an interesting procedure which long has been neglected in medicine. Much investigation needs to be done before meaningful statements can be made about extending its medical applications.

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Unconsciousness with Diabetes

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Although we readily recognize that diabetic persons are subject to all the forms of unconsciousness which may occur in nondiabetic individuals, this discussion is confined to the causes and treatment of the unconsciousness that results as a consequence of diabetes and its complications.

CAUSES

Three main causes of unconsciousness in diabetics are (1) insulin shock, (2) diabetic acidosis and coma, and (3) peripheral vascular shock. If available, the history is of prime importance, but unfortunately, many diabetic persons are found unconscious, and consequently no history can be obtained from them. In addition, relatives frequently are not available to give an adequate history.

If a history is at hand, it is necessary to know if the unconsciousness was gradual or sudden in its onset. Diabetic coma comes on slowly; the individual does not suddenly become unconscious in diabetic acidosis or coma but rather becomes ill over a period of days with accompanying nausea and vomiting. There may have been infection, dietary irregularity, or discontinuance of insulin. Insulin shock, however, usually is rapid in onset. For example, a patient may be under reasonable diabetic control but, because he skips a meal, vomits his food, or develops diarrhea, may have an inadequate supply of carbohydrates and thus develop hypoglycemia, suddenly becoming unconscious. The only other possibility which can occur in insulin shock is that sometimes, with long-acting insulin such as protamine zinc insulin (PZI), it is possible for this unconsciousness to come on rather gradually rather than with a sudden onset as usually occurs with regular or rapid-acting insulin.

SYMPTOMS

Symptoms, other than unconsciousness, are varied, depending upon the condition involved. Breathing, however, is an important symptom, for with diabetic acidosis and coma, a unique type of respiration, known as Kussmaul respiration, occurs. Breathing is deep, regular, and slow. There is a definite odor of acetone on the breath, the eyeballs are soft to the touch, and the patient may or may not appear to be dehydrated.

On the other hand, with insulin shock, the ocular tension is normal and the breathing is not Kussmaul in type and may be irregular. Convulsions may be present. The individual usually has not been vomiting, as in the case of those in diabetic acidosis. In those individuals who are in peripheral vascular shock—and this occurs fairly frequently with diabetic acidosis and coma—the blood pressure will be extremely low.

TREATMENT OF INSULIN SHOCK

What do we do for the individual who is unconscious because of his diabetes and for whom no history is available? If his blood pressure is normal, two possibilities are involved: this individual is either in insulin shock or in a diabetic coma. The obvious first step should be to draw blood immediately to determine the blood sugar level and the carbon dioxide combining power. It sometimes is impossible to obtain the blood test results for some time, and in the interim, some other form of treatment must be instituted.

Because hyperglycemia cannot injure the individual, the proper approach is to treat him as if he had hypoglycemia—that is, as if he were in insulin shock. If he can be aroused at all under these conditions, he could be given glucose orally; otherwise 25 to 50 cc. of 50 per cent glucose may be given intravenously. At times, 0.5 cc. of adrenalin will mobilize sufficient glycogen from the liver to raise the blood sugar sufficiently to bring the individual out of insulin shock. Raising the blood sugar in this fashion will cause no difficulty, and, if his hypoglycemic level has been raised to a normal level in this way, the patient should recover consciousness. A word of caution—individuals who have had fairly long hypoglycemic reactions after PZI administration frequently do not recover as rapidly after the introduction of glucose as do those who have not been in this prolonged shock status, and

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the physician can be lulled temporarily into believing that the individual may not be in a hypoglycemic state. We must watch for a while and even at times repeat the dose if the individual seems to be improving.

Nearly all hypoglycemia can be correctly treated in this manner, and the individual will be brought out of his hypoglycemic state. He may or may not go back into this state, depending upon the amount and type of insulin he has taken previously and whether he is able to eat when he arouses. If he has been on large doses of PZI and does not take sufficient glucose orally, he may return to a hypoglycemic state and unconsciousness.

Beyond this point, further treatment of hypoglycemia depends upon the usual treatment of diabetes with proper diet and regulation of the insulin supply. If the individual does not respond to intravenous glucose after one or, at the most, two doses of the amounts given, then the condition probably is diabetic acidosis. Treatment of this condition is much more prolonged and has several important phases.

TREATMENT OF DIABETIC ACIDOSIS AND COMA

In my opinion, there are 5 basic problems involved in the treatment of diabetic acidosis and coma: (1) cessation of the production of new acetone bodies, (2) alleviation of the present acidotic state, (3) elimination of acetone bodies already present in the body, (4) avoidance of peripheral vascular shock, and (5) control of the potassium level. Each will be discussed separately.

Cessation of acetone production. While much has been written on the large amounts of insulin required in the treatment of diabetic coma, my experience reveals that such is not the case. After all, the primary function of insulin in the treatment of diabetic acidosis and coma is to prevent the formation of new acetone bodies—in other words, to burn glucose correctly so that acetone, diacetic acid, and other products will not be formed in the improper burning of glucose. It does not require 300 to 500 units of insulin per day to achieve this. In reality, a total diabetic patient, were he in perfect shape, probably could do well if he burned 100 gm. of glucose a day, and this would require approximately 50 units of insulin. Even if the individual were in an abnormal situation and needed more insulin to burn the glucose required, he still would not need such extremely large doses. I see no particular advantage in the bonfire theory, which supposedly burns acetone bodies, for I cannot believe that this is the case.

Our practice has been to give the ordinary diabetic in coma 40 units of insulin subcutaneously or intravenously immediately and then to give 20 units of insulin subcutaneously every two hours as long as the urinary sugar obtained by catheter remains 4+. As soon as the urinary sugar drops to a value of 3+, we reduce the insulin dosage to 15 units every two hours, and as soon as it is 2+ or less, we discontinue the use of insulin until the amount of urinary sugar rises. I agree that this will not give absolutely perfect blood sugar levels, but I do not believe that this is of prime importance. The important fact is that sufficient amounts of glucose to prevent the formation of new acetone bodies are burned. I see no value in attempting to burn large amounts of glucose in order to burn up previously produced acetone bodies.

Obviously, sufficient amounts of sugar must be on hand in order to burn sugar correctly. With ordinary diabetic acidosis and coma, the blood sugar is high enough so that sufficient blood sugar will be on hand to continue to use insulin in the suggested manner without the use of intravenous glucose. As soon as the individual has been brought back to a state in which he can again begin to eat and not have any vomiting, he should be placed on a basic diabetic diet. His urine should then be checked four times a day—once before each meal and at bedtime—and his urinary sugar again treated according to the previous rule for a few days. Finally, the patient should be given a mixture of longer-acting and regular insulin in the morning to control his hyperglycemia.

Alleviation of acidosis. A serious situation exists when individuals already have marked acidosis, together with nausea and vomiting. It is important that we eliminate, or at least alleviate, the acidosis as much as possible in order to overcome the accompanying nausea and vomiting.

Several methods may be used. I would personally rather use sodium bicarbonate than sodium lactate, but on the other hand, those who use the lactate solution have also been satisfied. The ordinary-sized individual in diabetic coma would be given approximately 25 gm. of sodium bicarbonate intravenously, the exact dose depending upon the carbon combining power. I have seen a miraculous response to this medication and can recall unconscious individuals with nausea and vomiting who, within twenty minutes after administration of sodium bicarbonate, sat up, asked for food, ate and were mentally alert. This method will quickly and dramatically relieve the acidotic state.

After alleviating the previously present acidosis and having again supplied enough alkali to the blood stream to carry the carbon dioxide from the tissues to the lung, the patient is out of the acidosis and, as long as no new acetone bodies are formed, the status of the individual can be maintained. It is not generally necessary to give sodium bicarbonate more than once to a patient if the insulin and glucose burning has been carried out as herein described.

Elimination of acetone bodies. After the production of new acetone bodies has been stopped and the individual has been supplied with sufficient amounts of alkali to bring his carbon dioxide combining power to normal, the problem remains of eliminating those acetone bodies still in the individual. Some of these are eliminated through respiration and perspiration, but the major elimination is through the urine outflow. Consequently, a substantial diuresis must be developed to wash out the acetone bodies in the blood stream and tissues. This requires that fluids be forced into the individual. In my experience, the forcing of fluids by mouth in the comatose or near-comatose patient is ineffective. The person may drink 1, 2, or 3 liters of fluid, only to vomit it all two or three hours later. Therefore, intravenous or subcutaneous fluids must be used, and, at the present time, intravenous fluids seem to be more readily available. I think the patient should receive a minimum of 3,000 cc. of normal saline intravenously during the first twenty-four hours, and this should produce a large volume of urine, assuming that reflex anuria has not developed as a result of insulin shock. The large amount of diuresis will carry acetone bodies with it and they will, therefore, be eliminated. As soon as the individual is over his acidosis, he no longer has nausea and vomiting and he can then take fluid orally, eliminate urine, and get rid of the remainder of the acetone bodies via oral fluid.

Avoidance of peripheral vascular shock. Peripheral vascular shock occurs because the patient (1) is a diabetic and has not been taking sufficient fluids and (2) has nausea and vomiting. The lack of fluid, plus the toxic effect of the acidosis itself, tends to produce peripheral vascular shock with a drop in blood pressure. This can produce unconsciousness, as previously discussed, but, worse than that, it tends to produce a reflex anuria that can be fatal. Avoidance of shock can be brought about by use of the intravenous fluids already instituted in order to eliminate acetone bodies. If a good intake of intravenous fluids is continued, we will rarely be faced with peripheral vascular shock in the case of diabetic acidosis or coma. Under extreme circumstances, it might be necessary either to transfuse these individuals or to give them plasma intravenously, but this would be extremely rare as long as intravenous fluids were continued. I cannot recall when either transfusion or plasma was necessary in order to control peripheral vascular shock.

Control of potassium level. Control of the potassium level is not primarily a problem in the beginning of the treatment of acidosis but frequently becomes a major problem as soon as diuresis begins. Such individuals will eliminate large amounts of potassium. Also, with diabetes, a definite potassium deficiency may occur. This condition produces lassitude, changes in the electrocardiogram, and, occasionally, alkalosis. Under these circumstances, if the individual has had a severe coma or has had severe acidosis for any period of time, it is routine to use potassium intravenously—say 40 mEq. in every liter of intravenous fluid—when diuresis begins. It is not always possible to obtain a potassium level in such individuals, but I doubt if any of them would be injured by raising the potassium level above the normal limits. Reducing potassium to a low level may cause definite difficulties, however. Under these circumstances, there is no harm in adding 40 mEq. of potassium chloride to each liter of normal saline given intravenously. As soon as the patient is able to take food and fluid by mouth, oral administration of potassium chloride in the form of tablets will control this situation. Much postacidotic weakness and lassitude can be controlled by potassium, for it is the lack of this which apparently causes these symptoms.

I agree that the treatment cited is didactic and simplified. However, I can say that I have never lost a diabetic coma patient in thirty years when this treatment has been followed.

SUMMARY

This discussion has outlined the causes of unconsciousness which are due to diabetes. The more common of these — namely, hypoglycemia and diabetic coma—have been thoroughly described, and a rational, practical therapeutic approach to them has been outlined.

Management of Breech Presentation

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Breech presentation and management has been under distinct critical analysis from many points of view during recent years. This is understandable for a number of reasons:

1. There is an admittedly high fetal mortality associated with the delivery of breech presentations as compared to vertex presentations.

Hall and Kohl[1] reviewed 1,456 breeches occuring in 7 teaching hospitals during the years 1950-1954. They found a gross mortality of 14.4 per cent, with a perinatal mortality of 32.5 per cent for prematures (about 30 per cent of the cases), and 6.5 per cent mortality for mature infants. By correcting these figures to estimate the loss caused by breech presentation alone, they arrived at 9.2 per cent for premature and 2.6 per cent for mature breeches. This compares with their estimate of 1 per cent loss in term vertex presentations.

Other large series, such as those of Potter, Heaton, and Douglas[2] and those of Dieckman and Harrod[3] arrive at somewhat similar figures.

2. Attention has been focused upon the breech because of the high fetal morbidity associated with breech delivery. Gold and his associates[4] have shown that the *recognized* birth injury rate for breech delivery was 14 per 1,000 live births, compared to 1.3 per 1,000 for low forceps delivery. These figures do not include cases of mild or unrecognized cerebral injury resulting in palsy, mental retardation, and epilepsy. For example, Churchill,[5] in a series of epileptics, found that 19.6 per cent were delivered by the breech.

3. Breech is one of the few vaginal deliveries still responsible for high maternal morbidity resulting from extensive lacerations, hemorrhage, and infection.

4. The increasing safety of abdominal delivery with widening of the indications for cesarean section has naturally placed breech, an abnormal position, into prominence as an indication for cesarean section.

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Thus, we think it timely to review some of the changing concepts regarding breech presentation and management and to re-evaluate our personal philosophies on the subject as influenced by past experience and thoughtful interest in changes and trends in this area of obstetrical teaching and practice.

The old masters in obstetrics of one and two generations ago—the men who taught many of us—had a great deal of respect for the breech. Each of them had special technics and pet maneuvers that worked well in his particular hands. Each warned against certain dangers and pitfalls that should be anticipated, carefully searched for, and then properly handled, sometimes in rigid mechanical sequence. Many of these dedicated teachers had slogans and bits of advice that clearly expressed their concern. Dr. Williams often said that he could tell a really good obstetrician by the manner in which he conducted a breech delivery. Our old teacher, Dr. J. C. Litzenberg, liked to say that "any physician who said that he wasn't afraid of a breech or never had trouble with a breech was either someone who didn't do any work in obstetrics or was an 'outright' liar, and he could choose his own category!" Another exhorted the medical student to always be friendly with his competitor across the street, "because you may need him to help you with a breech some time!" They were acutely aware of the dangers inherent in breech delivery. They had to be. They had to depend upon their hands and a keen mechanical sense which experience developed into a type of intuitive perception and manipulation that DeLee liked to call the "art of obstetrics." They couldn't readily resort to cesarean section once delivery from below was chosen. They didn't have blood banks, antibiotics, and highly trained anesthesiologists.

No doubt our old teachers are turning in their graves as they contemplate upon the number of cesarean sections we are doing for breech today. We can only hope that St. Peter has tried to explain why things have changed. That might help a little but I'm sure that it wouldn't completely satisfy that fine group of "Old-Timers."

ETIOLOGY

What causes a breech to present? There are certainly a multiplicity of etiological factors, not excluding pure chance. We were taught, and do teach, that as term approaches, a natural mechanical accommodation occurs between the normal fetal ovoid and the peculiar concavity of the distended muscular uterus with its "false bottom," the pelvic inlet. The average fetal head just fits into the pelvic inlet like a loose piston in a cylinder. The baby in its typical fetal attitude is "comfortable" that way. Anything that disturbs this natural accommodation tends to create an abnormal position such as breech, brow, or transverse lie. Disturbing factors may include a small or borderline pelvis, a large baby, placenta previa, tumor of the cervic or lower segment, relaxed uterine and abdominal walls, multiple pregnancy, hydramnios, hydrocephalus, prematurity, abnormality of the uterus such as a septate uterus, and so forth. Stevenson[6] has found a cornual implantation of the placenta in a high percentage of frank breech presentations. Others have verified this at cesarean section. Hay[7] believes that breech presentation is often related to a partial septate uterus which results in bilateral pocketing of the uterine cornua. He demonstrated this in 36 of 37 patients. Vartan[8] is of the opinion that a large percentage of breech presentations are caused by the combination of oligohydramnios and extended legs. He theorizes that the breech with the extended legs gets into the pelvis several weeks before term when breech presentation is frequent. As term approaches, the extended legs splint the breech and the back is straight and stiff; these conditions, in addition to scanty fluid, hinder the fetus from turning readily.

A thorough knowledge of the etiology of breech presentation has important clinical significance. When we diagnose a breech in the latter weeks of pregnancy, we should systematically eliminate the various etiological factors that could cause trouble. Having completed that discipline to our satisfaction, we are properly prepared to formulate plans for management. We find this system to be very satisfying and productive. We become alert. We discern things which could easily be overlooked. By anticipating danger, we are in a good position to avoid it.

EXTERNAL VERSION

What is the place for external version of the breech discovered during the latter weeks of pregnancy?

Thompson[9] has shown that fetal mortality for the premature breech may be two times that for the premature vertex, and that the mortality for the term breech may be three times that of the term vertex. It would seem clear, therefore, that all breeches should be turned. Theoretically, this is logical but from a practical standpoint, it is not that simple. The most common breech, the frank variety which composes about 60 to 70 per cent of breeches, is the most difficult to turn. In addition, in the primigravida, where we are most anxious to do the external version, we meet great difficulty because of the resistant abdominal wall and generally poor patient cooperation. The "worthwhileness" of the maneuver has been seriously questioned by many astute observers. For example, Alexis Brosset[10] of Stockholm conducted a clinical experiment in which he followed two series of breeches. One series of 73 cases he left to nature. In the other series of 74 cases he attempted external version, sometimes repeatedly. In the latter series, he discovered that he was successful in 24 of the 74 cases, and that spontaneous version occurred in 35 of the remaining 50 cases. So he was left with 15 breeches. In the first series which were not touched, 57 of 73 turned themselves at various intervals during the last six weeks of pregnancy. Here, he was left with 16 breeches. He naturally concluded that he gained little by external version.

Many insist that with experience the breech can be safely turned in a large percentage of cases so that the incidence of breech in their practice is materially reduced. Greenhill summarizes an article by Ikle,[11] who cut his breech incidence to 0.64 per cent, or 4 breeches in 620 patients. He repeated attempts at successive prenatal visits but did not use anesthesia. David Johnson, who favors external version, mentions an incidence of only 1.45 per cent breech presentations in 12,425 deliveries, but there was nothing in the article that tried to prove that this low incidence was anything but pure coincidence.

On the other hand, the majority of our professors with large teaching services are of the opinion that the incidence of breech cannot be effectively altered by external version. Also, they frankly state, they must have breeches for teaching purposes.

There are a few writers (notably British) who will resort to external version under anesthesia in the primigravida with a borderline pelvis, where a vertex presentation would probably mold through while an aftercoming head would probably be damaged. The "leave alone" proponents speak of a fetal mortality of 1 to 3 per cent where external version is routinely prac-

ticed. This figure seems to us to be absurdly high, except if cases where anesthesia has been used are included. The use of anesthesia is fraught with a number of real and potential dangers:

1. The anesthesia must be ether or chloroform and must be deep to effect the external version. We then have the dangers of maternal aspiration and fetal asphyxia to contend with.

2. When the patient is asleep, it is amazing how much force the operator inadvertently uses. We have witnessed sizeable hematomata under the skin of the abdominal wall following such attempts at external version.

3. It is not surprising, therefore, that cases of spontaneous abruption have occurred, as well as bleeding from a low placenta.

In our own practice, we make gentle but sincere efforts at external version unless there are definite contraindications (cesarean section scar, possible low-lying placenta, maternal hypertension or toxemia, partially dilated cervix). Ordinarily, we do not attempt the procedure before the thirty-fourth or thirty-fifth week. Usually, we make an effort to turn the fetus so that the occiput leads in order to better preserve flexion. But failing this, we simply turn it in whichever direction it most readily goes.

TECHNIC OF EXTERNAL VERSION

We try to lift the breech out of the pelvis by a lever-like action of the fingers pressing into the pelvic inlet and pushing the presenting breech upward and then laterally. At times, we resort to vaginal or rectal examination to help dislodge the breech. Here the Trendelenburg position is a distinct aid. While the lower abdominal hand is working the breech toward one or the other iliac fossa, the higher hand is directing the rounded head downward along the opposite flank toward the pelvic inlet. When the uterus becomes irritable, we stop and try to hold what we have gained. When the uterus relaxes again, we gain a little more. During this time, we use the head stethoscope frequently; if there is an appreciable variation in the fetal heart rate, we desist in our efforts or even push the fetus around to its original breech presentation. We do not hesitate to make repeated efforts at external version at weekly intervals. We have for years asked the occasional patient who has a "stubborn" breech to do the knee-chest exercise two or three times daily during the interval between office visits. It is surprising to observe how many of these babies turn themselves or can be turned with ease at the next visit. But, as our "leave alone" friends always remark, "these babies probably would have turned themselves anyway!" Under this type of office management, we haven't encountered a single complication.

X-RAY PELVIMETRY

Failing in external version, we review from time to time the possible etiologic factors that may be operating in any particular breech presentation. This includes clinical reassessment of the pelvis and estimation of the probable size of the baby. We agree that in the breech the determination of disproportion between the size of the head and the maternal pelvis is to some degree "at best an educated guess." But we also think that we can educate ourselves to "guess" better as the years go by.

Our experience parallels studies such as those of Moore and Steptoe,[12] which clearly show that fetal mortality and morbidity in term breeches rise rapidly as we go from minor to borderline degrees of pelvic contraction. We have a strict rule that roentgenographic studies of the pelvis including pelvimetry be done on all primigravida and on a selected group of multipara, especially those who do not have a "well-documented" history of excellent past obstetrical performance. Where a roentgenographic study is indicated, we usually order it before the thirty-eighth week, late enough to make it unlikely for the fetus to turn and, yet, at a reasonable time before the expected onset of labor. Realizing that there is no place for trial of labor as such in breech presentation, we must muster all possible information before the onset of labor. Furthermore, if we delay the roentgenographic studies until the patient is in the hospital in labor, we may find ourselves caught in the middle of a busy night with overworked and possibly second-rate technical assistants hurrying pelvimetry studies on a frightened uncooperative patient advanced in labor.

THE FIRST STAGE OF LABOR

When it is decided that the breech can be safely managed from below, the patient is warned to go to the hospital immediately with any of the triad of signs and symptoms of labor. The importance of this admonition is obvious when we recall that bleeding may be indicative of placenta previa which occurs to some degree in about 10 per cent of breech presentations. And, if the membranes should rupture, the patient should be examined as soon as possible inasmuch as prolapse of the cord is manifest in about 5 per cent of breech presentations.

Some of the principles concerned in the management of the first stage of labor include the following:

1. It is desirable that an even, gradual and complete dilation of the cervix develops in order to avoid the disaster of the "trapped head."

A. The integrity of the membranes should be preserved as long as possible.

B. This may be facilitated by urging the patient *not* to bear down in the first stage.

C. It may be advisable to have the patient rest on the side. When she is on her back, there is often a natural tendency to bear down. In so doing, the membranes may rupture prematurely, and, if the membranes are already ruptured, the relatively small and soft presenting breech would be forced through the incompletely dilated cervix.

D. Internal examinations should not be done any more frequently than necessary, and then as gently as is possible and still get the desired information.

2. We should be watchful for prolapse of the cord which, as mentioned before, may be expected to occur in about 5 per cent of breeches (as compared to 0.5 per cent in vertex presentations). In frank breech, this complication is only slightly more frequent than in head presentations. But in the complete and incomplete varieties, prolapse of the cord may occur in 10 per cent or more of the cases.

Prolapse of the cord is suspected by variations in the fetal heart rate which must frequently be checked and recorded. It is confirmed by vaginal examination which must be done whenever significant changes in fetal heart rate are noted, and also when the membranes rupture at any time during the first stage of labor.

3. During the first stage, we should be constantly aware of the type of labor with which we are dealing. Is this a desultory, dystotic labor characterized by a poor or irregular labor pattern, or both, by a slow, almost imperceptible cervical dilation, by a lack of descent of the presenting breech? How long has the labor continued without any real progress? How long have the membranes been ruptured? What is the mother's general condition as represented by signs of exhaustion, abdominal distention, pulse elevation, and elevation of temperature? These questions demand a favorable answer. Otherwise we are dealing with an unpropitious labor, and the patient and her baby may best be served by an abdominal delivery.

THE SECOND STAGE

The second stage may be terminated in one of three ways, (1) spontaneously, (2) by partial breech extraction, and (3) by total breech extraction.

In partial breech extraction, the breech is permitted to deliver spontaneously as far as the umbilicus and the remainder is gently extracted. All things considered, this method seems to be the safest and the most logical course to pursue. Without entering into the mechanics of breech delivery, there are a few general principles and precautions that must be rigidly kept in mind:

1. As the second stage draws near, have everything in readiness for delivery and for all possible emergencies associated with an operative delivery.

2. Check the fetal heart after each contraction.

3. Empty the bladder per catheter.

4. Do a thorough vaginal examination:

A. Make sure that the *cervix is completely dilated.*

B. Check on possible cord prolapse.

5. If an extremity is prolapsed, leave it alone.

6. If you are positive that the cervix is completely dilated, the patient may be encouraged to bear down with contractions.

7. A light gas-oxygen mixture may be given with contractions.

8. We do a pudendal block at early crowning.

9. A generous episiotomy is advisable:

A. This is best delayed until the buttocks are almost completely delivered.

B. If the second stage is unduly prolonged, the episiotomy may be done earlier and the breech is allowed to push into it.

10. Don't get too concerned about a prolonged second stage (up to two hours plus), provided there is no other cause for alarm.

11. The breech is allowed to progress spontaneously until the umbilicus is born.

12. Do not use undue traction in delivery of the trunk. This will often result in extended arms and an extended head.

13. It is best not to have anyone but the most experienced assistant exert any follow-up or "so-called" gentle fundal pressure. This can push the head down through the arms, and may cause lethal damage to the brain and spinal cord.

14. Technics of shoulder and head delivery should be well known and well understood by anyone who accepts responsibility for breech delivery.

15. The Piper forceps (or any long-shanked forceps) should be used more frequently in delivery of the head.

16. The head should not be permitted to "pop out." Intracranial hemorrhage may result.

From our remarks throughout this discussion, it is apparent that cesarean section is assuming a progressively more prominent role in the management of breech presentations. We have endeavored, as we have developed our theme, to bring out the background of reasoning that has prompted this change. Everyone admits that abdominal delivery is safer for the infant than a possibly complicated vaginal delivery, and is certainly to be preferred to a complicated and difficult breech extraction. Most of the statistics that report representative series of breech deliveries critically analyze the infant deaths attributable to vaginal delivery. Invariably they conclude that further improvement could have been accomplished by the more "liberal use of cesarean section." But they also add that the major feature of these deaths is not one of hasty injudicious delivery, but of "failure to appreciate the importance of moderate degrees of disproportion," or failure to "recognize the incompletely dilated cervix," or failure to "discover prolapsus of the cord" before it was too late, or failure to interfere timely in the "unpropitious labor"—features which could largely be eliminated by good prenatal care and by meticulous observation of the patient in labor.

Yet, there are a few obstetricians, notably Wright,[13] who have become so concerned with the problem of fetal mortality and morbidity associated with breech delivery that they advocate routine cesarean section on "any patient of over thirty-five weeks' gestation who enters labor with a living baby in breech presentation providing there is no maternal disease that contraindicates abdominal delivery." In their fanaticism, they forget that abdominal delivery by no means guarantees a baby that will survive the neonatal period; that cesarean section is still a major operation carrying with it a definite though admitted small maternal mortality, and a not so inconsequential maternal morbidity; that of every 300 women who happen to carry a "breech in labor at thirty-five weeks" or more and are sectioned, about 275 may have had an unnecessary operation; and that the woman who has been sectioned is in a sense an "obstetrical cripple" carrying a scar that has 1 to 2 per cent chance of rupturing in some subsequent pregnancy, thus endangering her life and almost certainly sacrificing the life of the fetus. Eastman[14] in the Obstetric and Gynecology Survey and Greenhill[15] in the 1960-1961 Year Book of Obstetrics and Gynecology have soundly refuted this fad, and we heartily agree with most of their arguments.

In conclusion, we will list a number of indications for cesarean section in breech that would probably be acceptable to the majority of our obstetricians of today:

1. The elderly primigravida. The age is commonly expressed as 35 years and older. With no offense to the woman concerned, we often drop this age limit to 30 years and even less if the condition of the cervix and maternal soft parts portend trouble.

2. Women who have had a longstanding infertility problem. (Most of these are included in point 1.)

3. Any degree of pelvic contraction deserves most serious consideration.

4. Large baby.

5. The hyperextended breech.

6. Certain maternal complications, such as diabetes, severe toxemia, and so forth.

7. Previous stillbirths ("bad obstetrical history").

8. Labor that does not progress propitiously (see management of First Stage).

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Athletic Injuries

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Despite marked increased participation in organized athletics since World War II, the incidence and severity of athletic injuries has steadily decreased. This has been due primarily to better equipment, greater knowledge of training methods, and better understanding of athletic injuries by the general physician.

A head injury in the heavy contact sports of football and hockey is rare today, and most of the credit should be given to the redesigning of helmets and headgear. Similarly, injuries to the cervical spine occur relatively infrequently. A number of other injuries, however, are contracted more often.

STRETCH INJURIES OF A NERVE PLEXUS

Most common in football linemen, stretch injuries of a nerve plexus are caused by a direct blow to the lateral portion of the shoulder when the head and neck are twisted in the opposite direction. A player usually complains of weakness in the arm, inability to abduct the arm, and generalized tingling in the entire arm area. The muddling of sensation and the motor power will return within a matter of minutes or, at most, after one or two hours. It is easily possible, however, for this injury to recur. We have never seen the condition progress to a point which necessitates treatment, and we have never observed permanent disability. If a player has been so injured more than three times, however, we have advised him not to participate further in football. We have never allowed a player to continue to a degree where permanent injury might be possible.

SHOULDER AREA

The two most common athletic injuries of the shoulder area are anterior dislocation of the humeral head and acromioclavicular separation. Any dislocation of the shoulder requires at least three full weeks of cross-chest type immobilization and a minimum of one month away from all practice or participation in contact athletics. Shortening this period of immobilization markedly increases the incidence of recurrent dislocation. Any patient with a recurrent dislocation is almost always limited in his athletic competition. The treatment of choice of an acromioclavicular injury depends entirely on the degree of separation. In a first degree separation, the damage is only to the acromioclavicular ligaments and to the joint itself. From a clinical standpoint, arm traction type roentgenograms made from comparative views of the opposite shoulder show less than a 50 per cent upward displacement of the lateral tip of the clavicle in relation to the acromion. Abduction and rotation of the shoulder usually causes subjective pain. There is local tenderness over the acromioclavicular area, but no tenderness is manifest over the coracoclavicular area, and gross instability of the lateral segment of the clavicle does not occur. This injury can be adequately treated with a Velpeau or high sling immobilization for two weeks and limited activity for the third week. Athletic participation is not possible for a minimum of three or four weeks. A second degree separation is one with damage both to the acromioclavicular and coracoclavicular ligaments, complete upward displacement of the lateral tip of the clavicle, and gross instability of the lateral segments of the clavicle. This injury requires an open surgical repair of not only the acromioclavicular joint, but of the coracoclavicular ligaments. Immobilization after surgical repair is necessary for six weeks and no athletic participation is possible for at least two months. We have found that the various methods employing weighted hanging casts, multiple type strapping, or blind wire fixation of the acromioclavicular joint without internal repair cause multiple complications and rather unpredictable results.

PARTIAL AVULSION OF MUSCULAR ATTACHMENTS

One injury which is caused only by participation in football is a partial avulsion of all the muscular attachments along the anterior iliac

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crest. It masquerades under a variety of training room names, "hip pinch," "pointer," or "cresty." The injury is caused when a player wears hip pads which are too small or when he wears them too low and he receives a direct blow over the iliac crest. The hip pad actually cuts the muscular attachments along the iliac crest. The abdominals pull medially and upward, and the entire gluteal attachments pull inferiorly. The injury is very painful. The player cannot cough or laugh without contracting the painful abdominals and is unable to run for a period of at least two weeks. When the injury occurs, immediate application of an ice cap will prevent some local swelling. Pain must be controlled with medication for two or three days. All physical therapy must be rather carefully selected and administered; excessive heat and massage tends to irritate the iliac area and prolong disability. Usually the player has to be treated symptomatically with complete limitation of activity for a week, gradual increase of painless motion and running during the second week, and a gradual return to contact during the third week. Fortunately, the injury almost never recurs and may be completely prevented by the proper selection and proper use of hip pads.

KNEE INJURIES

The most common and, unfortunately, the most severe injuries in football usually involve the knees. The best evaluation of damage can be made immediately after the injury, and the doctor who sees the player on the sidelines during the game has a definite advantage. It is particularly valuable to have an immediate history of injury since the mechanism of the injury often provides a tip-off to the probable diagnosis. When a player is hit from the side, the damage occurs almost invariably to the opposite side of the knee. A player who is struck directly from the front or the back has a good chance of sustaining damage to the cruciate ligaments, and a player who is "piled on" is prone to have hyperflexion or hyperextension type injuries of the joint capsule. Examination before swelling occurs should give a good idea of the location of tenderness, stability, and ability to fully extend the knee. If a patient has lateral or medial tenderness with medial or lateral instability, a major tear of a collateral ligament is almost always manifest. If a patient has medial or lateral anterior compartment tenderness and has a loss of active and passive extension, a complete tear of a meniscus should be considered. Anteroposterior stability is almost impossible to test accurately in well conditioned athletes, but a better impression can be obtained immediately after the injury has occurred than later when spasm of the quadriceps group has developed. If a patient is not seen until swelling of the knee has developed with its associated muscle spasm, it is best, before examination, to give sufficient pain medication to decrease the pain and reduce the spasm. The knee should then be cleaned and, under aseptic conditions, aspirated completely dry. The character of the joint fluid obtained is of help in outlining treatment and in determining prognosis. After the fluid has been removed and maximum extension has been obtained, an x-ray should be taken. A radiograph at this time will demonstrate a fracture of the spines of the tibia, an avulsion fracture of an attachment of a collateral ligament or osseous free bodies in the knee joint associated with injury. If there is a gross decrease in lateral stability, a surgical repair may be considered. At present, the indications for open surgical repair of ligamentous injuries have not been clearly established. In ligamentous injuries where the point of maximum tenderness is at the proximal or distal attachment of the ligament, the prognosis for a successful surgical repair is quite good. If the roentgenogram indicates an avulsion of even a flake of bone at the attachment of a collateral ligament, a repair is indicated because it is usually possible to fairly well reattach the ligament surgically. In cases of decreased stability with point tenderness directly over the joint level, the ligament often is shredded to such a degree that a surgical repair is difficult and the result rather questionable. In instances of gross medial instability with obvious rupture of the medial collateral ligament, about 35 per cent of the cases will have an additional injury to the medial meniscus and about 12 per cent will show an additional injury to the anterior cruciate ligament. If a patient has only minimal or moderate instability, but has a loss of extension suggestive of a meniscus tear, it is worthwhile to attempt to reduce the locking and replace the meniscus by traction. This is best done by below-the-knee skin traction for twenty-four hours. During this time, the patient is given general sedation, and care is taken to assure that no one attempts to make him more comfortable by placing a pillow under his knee. An arthrotomy is indicated if at the end of twenty-four hours the locking has not been reduced. If the knee does straighten and the meniscus returns to its former position, it is best to try to let it heal without surgical intervention. A favorable prognosis for the meniscus injury is indicated if at the time of aspiration the joint

fluid is bloody. Generally, blood in the knee joint suggests that the tear is in a vascular rim area position and that it is possible to obtain healing. In these cases, a stovepipe walking plaster is applied with the knee in neutral and left in place for three weeks. During the period of immobilization, quadriceps exercises are constantly maintained and, after removal of the cast, regular rehabilitation is instituted.

When extension is not obtained after traction, the player should never be allowed to walk with the knee locked, but should be kept on crutches until arthrotomy can be carried out.

It is important that the knee be carefully watched after a minimal injury. Sometimes slight internal bleeding will produce a secondary joint effusion which is not severe, but which is sufficient to prevent full extension. In this instance, the player will feel that the knee is strong enough to allow him to continue in athletics, and he will make an effort to run and scrimmage with the knee slightly flexed. Any time a player attempts to continue in athletics with increased joint effusion, he not only plays poorly, but is extremely liable to have a second knee injury which may be severe. In our experience, 42 per cent of players receiving anterior cruciate tears give a history of having had a minimal knee injury within the preceding six weeks.

After a knee has been treated either surgically or nonsurgically, a complete program of rehabilitation is necessary before the player returns to athletics. This program requires close cooperation between the player, trainer, coach, and responsible doctor. The basis of rehabilitation is essentially the restoration of quadriceps strength; strength and coordination of other muscle groups will return quite easily without special effort. All Ace bandage wraps and circumferential dressings should be discontinued as soon as possible because their prolonged use slows quadriceps rehabilitation. A program of progressive weight resistance exercises is most beneficial. In patients with an associated chondromalacia of the patella, it is important that these exercises be performed in such a manner that increased joint irritation and secondary joint effusion do not develop. A player with the undesirable combinations of meniscus injury, ligamentous injury, and anterior cruciate injury can stabilize his knee by adequate quadriceps built up to a point which allows him to return to football and other contact athletics. During the period of rehabilitation, swelling is a good index of overactivity of the knee. Joint effusion is caused by irritation and usually is associated with a too intense or too early return to activity. It is particularly important that repeated aspirations of a knee are not carried out; they do not give permanent benefit and represent a definite risk. On occasion the removal of fluid with the installation of a small amount of hydrocortison (Hydrocortone) into the joint may be beneficial. A player requiring this treatment certainly is in no condition to consider contact athletics at the time. The use of any type of knee brace for athletics is also to be condemned. It is worth while to have the knee adequately taped for scrimmage, but if stability is not sufficient to allow the player to get along without a brace, a return to football should not be considered.

INJURIES TO MUSCLE AREAS

In general, sufficient attention is not given to bruises and injuries to muscle areas. Any bruise which is accompanied by hemorrhagic discoloration will benefit from immediate application of ice to prevent further hemorrhage. If heat is applied too soon or physical therapy instituted too early, hemorrhage may be restarted or prolonged and the period of disability lengthened. Areas of persistent tenderness with associated firm but irregular swelling should be considered to be deep hemorrhages. Many of these deep hemorrhages are actually associated with an elevation of periosteum. Unless they are surgically drained, the disability period is extensive and the chance of myositis ossificans is great. Hemorrhages, particularly over the lateral aspect of the elbow, deep in the mid thigh and over the posterior lateral knee area, usually require surgical drainage. If a deep hemorrhage is not drained and progresses to a degree where calcification is present on roentgenograms, it is best to delay any surgical drainage until a stable point of calcification or ossification has been reached.

MEDICATIONS

Many types of medication for use in the treatment of injuries have been advocated during the past few years. Few of these have ever been evaluated with the accompanying use of a blind control, and, thus, their value is rather uncertain. We have formed an impression, however, that the enzyme products designed to decrease or prevent swelling may have some limited value. We have found little difference between the products requiring local injection and those used as buccal medication. We do feel that the large group of medications advertised as muscle relaxants and antispasmodics have demonstrated no particular value.

Therapy of Hodgkin's Disease and Other Malignant Lymphomas

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As soon as diagnosis is established, Hodgkin's diseases and other malignant lymphomas require aggressive, definitive treatment to afford the patient the best possible prognosis.

Ample evidence supports this approach, and it is time to abandon the philosophy of treating only the symptomatic patient. After diagnosis of Hodgkin's disease, loss of time while awaiting appearance of symptoms may very well represent the loss of the best opportunity to provide the patient with a long term remission from disease.

Malignant lymphomas include a group of diseases arising in lymphoid tissue, such as Hodgkin's disease, giant follicular lymphoma, lymphosarcoma of lymphocytic or lymphoblastic cell type, reticulum cell sarcoma, Brill-Symmers disease, and a number of other pathologic diagnoses which are variants of terminology (Gellhorn and associates[1]). One group of pathologists takes the view that these diseases are a single neoplastic entity, having a number of variants. We have, in fact, seen patients who have had multiple biopsies during the course of disease, and, as his disease progressed, most of these pathologic diagnoses have been made on the same patient at different times. Transition from the less to the more malignant forms of disease has been the usual pattern described (Custer and Bernhard[2]).

DIAGNOSIS

Many patients have enlargement of peripheral groups of lymph nodes as their first sign of disease. Node enlargement in cervical, supraclavicular, axillary, and inguinal areas accounts for a large proportion of initial involvement. If the physician, therefore, views node enlargements with suspicion, he often can make an earlier diagnosis.

Healy, Amory, and Friedman state that the first manifestation of disease in 74 per cent of their patients was an enlarged node in the neck. They suggest the following indications for biopsy:

A. Enlarged low cervical node.

B. Persistent enlargement for more than three weeks.

C. Absence of regional inflammatory process as cause for enlargement.

The same general criteria may be applied to node enlargements elsewhere in the body. Peters has suggested the desirability of observing a node for brief periods of two to four weeks to gain insight into the rapidity of progress of the patient's disease; this information can be quite helpful in future management of the disease process.

Excision biopsy of the node is desirable. Node groups other than those in the groin are preferable for diagnosis, if one has a choice. The pathologic diagnosis of "reactive hyperplasia" or "lymphadenitis" should not dull one's suspicion of trouble ahead for the patient, and follow-up examinations at intervals of two or three months should be arranged. The use of antibiotic therapy for enlarged lymph nodes is not desirable, for a temporary decrease in size of enlarged nodes may delay diagnosis.

In some patients, the onset of the disease will occur in the thorax and abdomen. Chest radiography will reveal most thoracic lesions. Intravenous urography will often reveal retroperitoneal node involvement by displacement of the kidneys or ureters. Back pain without demonstrable bony lesions, including radiating pain into the buttocks and lower extremities, should arouse suspicion of a retroperitoneal process. Occasionally, a patient will complain of pain or accentuation of pain in the thorax or abdomen after ingestion of modest amounts of alcoholic beverages; this should immediately arouse suspicion of the presence of one of the lymphomatous diseases. In addition, general symptoms of weight loss, malaise, fever, and anorexia should arouse one's suspicions.

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Peters[3,4] has stimulated interest in clinical staging of Hodgkin's disease in particular and has outlined these stages:

Stage I. Involvement of a single group of nodes.

Stage II. Involvement of two or three adjacent groups of nodes.
A. Without generalized symptoms
B. With generalized symptoms

Stage III. Involvement of two or more separated groups of nodes with or without generalized symptoms.

Healy and associates[5] have also used this system of staging. Clinical staging is helpful in determining the course of therapy. As will be seen, there is prognostic significance in clinical staging.

TREATMENT

Radiotherapy and chemotherapy are the principal methods of therapy for these diseases, and many patients will be treated by both methods at some time during the course of disease. Radiotherapy is usually administered by external beams of x-rays or gamma rays; the use of internally administered radioactive isotopes has not been particularly effective or desirable. Chemotherapy has included use of nitrogen mustard and similar compounds and steroid hormones.

Surgery for lesions in the gastrointestinal tract is usually necessary to establish diagnosis and to deal with existing or potential obstructions or perforations. There is no sound evidence on which to base a primary surgical approach to these diseases elsewhere in the body. Surgical operation for lymphomatous diseases should practically always be followed with radiotherapy; one succeeds or fails on basis of radiation effect, and every effort should be made to avoid interference with radiation benefits by unduly extensive operation.

Stage I lesions are treated primarily by radiotherapy. It is important that an adequate dose of radiation be delivered to the node areas involved. The dose may vary from 2,500 to 4,000 roentgens in two to four weeks, depending on the patient, his disease response, and the radiotherapist treating him. It is important to give an adequate dose; the dose should never be just sufficient to shrink the nodes, for it is possible in unusually sensitive lesions to eradicate nodes temporarily with small inadequate doses, only to see recurrence in the same area in a short time. Peters' work suggests the desirability of treating the next adjacent node group even though it is apparently uninvolved.

Stage II A lesions are to be managed in the same manner. Stage II B lesions need to be considered on an individual basis. Some may require initial radiotherapy, others initial chemotherapy. This decision is best made by the physician, either radiotherapist or chemotherapist, experienced in managing these diseases.

Stage III lesions usually are best treated initially by chemotherapy.

Many patients can be benefited by judicious use of radiotherapy or chemotherapy as further manifestations of disease become evident. For example, a patient with Stage III disease may have a good response to chemotherapy initially; later, one expects regrowth of peripheral node groups, and these may be treated subsequently with radiotherapy.

In general, the duration of response of local node groups to radiation is longer in duration than to chemotherapeutic agents. Both radiation and chemicals damage the bone marrow and, therefore, each complicates further therapy by any method.

Careful posttreatment follow-up of patients is an important aspect of management of these diseases. Follow-up examination should include determination of patient's physical status, physical examination, blood studies, and chest radiography. Clinical signs or symptoms may suggest the necessity of other laboratory or radiographic studies.

If further disease progress is noted on follow-up examination, appropriate definitive therapy is indicated. Blood transfusions may be required, as well as other supportive measures, such as antibiotic therapy for intercurrent inflammatory diseases.

Prognoses given by physicians to patients having these diseases have often been unduly pessimistic and often provide an unfair, occasionally unnecessarily dim, perspective of the future. Progressively more evidence is available for long-term survivors with proper therapy. The older approach of therapy for symptoms only may have justified a pessimistic view, but this is no longer true if the patient is treated aggressively.

Peters,[3,4] Healy and associates, Curti and Maurer,[6] Nice and Stenström,[7] and Cook and associates[8] have excellent reports of long-term survivors in Hodgkin's disease. There are also long-term remissions of the other diseases, although the prognosis in some is better than others; these variations will not be dealt with here.

Table I best expresses the outlook in Hodgkin's disease.

TABLE 1

SURVIVALS IN PATIENTS WITH HODGKIN'S DISEASE

	Stage I *Per cent*	*Stage II* *Per cent*	*Stage III* *Per cent*
Peters:			
5 yr.	71	56	15
10 yr.	58	35	2
15 yr.	50	21	0
20 yr.	33	37	0
Healy et al.:			
5 yr.	50	43	32
10 yr.	12	9	4
Nice and Stenström:			
5 yr.	85	90	10
10 yr.	77	35	2

Perusal of the individual articles will give the reader more specific details. The long-term groups are small in number, which will explain apparent discrepancies in results; the variations are to be expected statistically.

SUMMARY AND CONCLUSIONS

1. Aggressive active therapy should be instituted upon diagnosis of Hodgkin's disease and other lymphomas.

2. Radiotherapy and chemotherapy are the preferred treatment methods.

3. Close cooperation of the radiotherapist and the chemotherapist gives the patient the best possible prognosis.

4. Careful follow-up examination at intervals of three months is necessary for the management of these diseases.

5. Long term survivors are sufficiently common to justify a hopeful prognosis to patients with localized disease.

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The mongoloid child generally has a better chance to become a happy, somewhat productive, and easily cared for person if he can be kept at home during the first years of life without undue disturbance of the family. However, the abilities of children with mongolism vary, and some will be extremely retarded despite the best possible care.

Comparison of 32 mongoloids who had been placed in foster homes or institutions after birth with 32 who had been kept at home until age 2½ or older revealed that those in the first group were extremely retarded while those in the second were moderately retarded. Thus, the second group was largely trainable, but the first was not.

Compared with those placed away from home, the children kept at home had better nutrition and growth and walked much earlier.

At about 7 years of age, the average intelligence quotient of the group placed away from home was 16, while that of the other group was 23. Respective average social quotients at the same age were 24 and 32.

S. A. Centerwall and W. R. Centerwall: A study of children with mongolism reared in the home compared to those reared away from the home. Pediatrics 25:678-685, 1960.

The Pathogenesis of Atherosclerosis as of March 1961

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It is almost presumptuous to discuss the broad problems of the pathogenesis of atherosclerosis. It is presumptuous because there is the lurking suspicion that you might think you know the cause of atherosclerosis. We don't, but we do know some of the important aspects of this multifaceted disease.

In a sense, the difficulty of a discussion such as this is aggravated by the persistent demand on the part of the public to have the cause and cure of heart attacks announced at each annual meeting of the American Heart Association. When occasionally a statement is actually made, a great uproar ensues and statements appear in profusion from experts who have been under rocks for years. As one disappointed editorial writer put it, "back to the laboratories, men."

But we have learned some important things and the problem is being clearly defined. For a discipline which has been under serious investigation for only about twenty years, I think we are doing better than we had a right to expect.

THE FILTRATION THEORY OF ATHEROGENESIS

In any rapidly growing field, it is desirable to have a framework on which to build. It keeps thought in orderly channels. I have found the filtration theory of atherogenesis the most generally useful for such purposes.[1] According to this theory, the blood pressure constantly forces plasma through the blood vessel walls into intracellular spaces to be picked up in lymph and poured back into the blood stream. This is a slow, but continuous, filtration process with the blood vessels acting as the filter bed. There is now substantial evidence in favor of this concept.

If lipid constituents of the blood become entrapped in the filter bed, the action of tissue enzymes causes the constituents to break down to form substances which act as foreign bodies. In lipids, the large, relatively unstable lipoproteins break down and free, insoluble fatty acids act as irritants. That fatty acids stimulate giant cell and other evidences of inflammatory reactions has been known for a number of years.

It is evident that the results of analysis would vary depending upon the age of the lesions. Tuna, Reckers, and Frantz[2] found no qualitative and gross quantitative differences between the total fatty acids of normal plasma and atheromatous plaques when studied by a variety of modern technics. Much the same result was obtained by Bottcher and associates.[3] They stress the possible importance of some differences in lipid composition of coronary arteries and the aorta. Both these beautiful studies firmly support earlier attempts to show that the lipids in atheroma are about the same as those found in the plasma. To date, no one has found anything singular about the plasma lipids of persons who have atherosclerosis. In many cases there is just too much of them.

Another aspect of the problem is whether changes in the filter bed precede deposition of lipids. These changes may range from being normally anatomical to being grossly pathological. Dock[4] has pointed out, for example, that the intima of male babies is thicker than that of females. The male starts out with a strike against him. In addition, the internal elastic membrane also shows some remarkable changes, as recently emphasized by Gillman[5] in South Africa. The search for subtle changes in intima, elastic membranes, and ground substances is important because of ability of these changes to alter the capacity of the filter bed to entrap and react to lipids. Clearly, there is nothing antithetical in the propositions that both lipids and mucopolysaccharides are concerned with atherogenesis. It is the either-or type of thinking I object to.

Some still doubt that plasma constituents actually traverse the vessel wall from the inside outward. But much evidence has accumulated in support of this theory. One of the most interesting and convincing recent works is that of Dun-

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can and Buck[6] in which they show that there is close similarity in both the gradients and relative magnitudes of the rates of passage of albumin and labeled cholesterol into the aortic wall of normal dogs. Studies on aortic transplants of lyophilized grafts or of plastic grafts also show deposition of lipid which could have originated only from the blood stream.

There are many other aspects of the filtration theory of atherogenesis. I hope, however, I have told you enough of it so that it will be a usable hypothesis on which to hang some of the many facts that are now so rapidly being uncovered. Fat, it will be remembered, is the only insoluble nutrient the body faces. The body combines fat with protein to make it soluble; this solubilized fat is carried in slightly permeable blood vessels under pressure. These tubes are living; hence, their anatomy and metabolism are hereditarily conditioned. This is the essence of the problem.

THE CORONARY PROFILE

To date, we have found no singular change in the blood to which atherosclerosis can be attributed. On the other hand, there is substantial evidence that directly relates the amount of lipid in the blood and the rate of atherogenesis. There is evidence of lesser cogency that the ratio of phospholipid to cholesterol or alpha-lipoprotein to beta-lipoprotein may also participate in determining rate. It is important to remember that the rate of atherogenesis is not governed by one factor alone; the outcome is determined by the interrelationship of many factors.

Can we then begin to outline the characteristics of a patient which indicate high risk, or high susceptibility, to atherosclerosis? This characterization is currently far from satisfactory, but, at least, the problem has been defined and progress to its solution is being made (Page and Lewis[7]).

Maleness is one of the first characteristics in this profile. In conjunction, one finds a short squat, muscular mesomorphic body build. This man has poor resistance as regards vascular disease. He is often obese and has been so for a number of years. He may be sedentary; one gets the impression that he has forgotten his legs are to be walked on, not to be looked at. He enjoys only spectator sports. He often overdoes many things—eating, smoking, drinking, and talking. Friedman and Rosenman[8] believe they can spot him by his reaction to taped recordings, one calculated to arouse and the other to soothe his emotions. I am told that someone in England has measured the stub length of cigarettes and related this to the kind of person. The coronary profile man is inclined to go the limit while his opposite stops at the limit of 16 mm. The latter are known as "doofers," which, I believe, means that it will do for another time.

The coronary profile includes slight elevation of plasma lipids, or more especially, cholesterol. There has been much discussion and, strangely, much propaganda concerning this problem. This has taken the form of special pleading for a particular fraction of the lipids as being more atherogenic than others. All we can say as a certainty is that elevation in cholesterol hastens atherogenesis. The triglyceride or chylomicron fraction may also be involved. Whether the separated fractions are measured or whether they are measured in their combinations as lipoproteins has not been proved to make much difference as far as offering a better measurement of rate of atherogenesis.

Finally, a correlation may be made with elevated blood pressure. It follows from the tenets of the filtration theory that any increase in the pressure filtering off the plasma lipids through the blood vessel walls would increase the rate of that filtration and, therefore, increase the amount of lipid which traverses the wall. It has been known for some time that patients with essential hypertension have a higher incidence of atherosclerosis than normal subjects,[9] and recent studies at Framingham[10] have shown the association with very slight elevation in a normal population.

Development in the past few years of coronary angiography by Sones and others has added one more potential way of characterizing the high risk coronary subject. Autopsies during the Korean war showed the high incidence of coronary disease in young men. Angiography allows some of these plaques and anatomic abnormalities of the coronary vessels to be seen. This method, of course, is not a mass screening procedure, but for some persons with questionable angina, among others, it is one of great usefulness. With further refinements, I feel certain that angiography will be one of the widely used methods in the future.

You can now form an image of the individual who belongs to the high risk group. For good reason, this person may be more than usually interested in participating in experiments designed to reduce the rate of atherogenesis.

DIET

There is no longer need to review the problem of the participation of diet in relationship to plasma cholesterol levels and atherogenesis. A

popular magazine simply is behind the times if it hasn't already done so. I suppose there has never been a time when there were so many homegrown experts raising such a cloud of dust and then complaining they couldn't see.

The problem is divided into two parts: (1) the effects of excess calories, no matter what their source, and (2) the effects of the amount of total fat and of the specific kind, whether saturated and polyunsaturated. The evidence is good that there is an association between the level of blood cholesterol and the total amount of calories consumed. It is also good in associating the level of blood cholesterol and the total amount of fat in the diet as Keys' work has shown. Since the early work of Kinsell, it has become clear that the amount of polyunsaturated fat has an important bearing as well. Without doubt, other factors are important, such as the amount and kind of carbohydrates, the bulk, and so forth; so far, however, none has been clearly defined as being the dominant factor in controlling blood lipid levels.

The recent committee report to the American Heart Association clearly demonstrated a unanimity of opinion on these two points. The report did not say there was a proved causal relationship between these diet factors and atherogenesis, but it did say that the association was sufficiently strong to justify broad scale clinical trial. Such a clinical trial is now in the planning stage. Hopefully, a mass feeding experiment will determine whether change in the American food pattern reduces the incidence of heart attacks. As far as I can determine, this is the only way to find out, first, whether such changes in diet are practical, and second, if they are, will these changes be beneficial?

I realize the difficulties of executing such a broad scale experiment are staggering to those of us raised, as most of us were, in a science of penury. But times have changed, and the costs are trivial in terms of the possible benefits. For those who are chicken hearted, I recommend comparison of the few millions this might cost with the billions that are spent to get a few men into outer space. There is no doubt need for that, but I suggest that before such travel becomes successful most of us who would be customers will long since have been dead of a heart attack.

THROMBOSIS

Thrombosis can be disastrous, and, in the majority of cases, it seems to be in some way related to the underlying atherosclerosis. The point is that thrombosis need not inevitably occur just because of the presence of atherosclerosis. The relationship between the two is highly complex.

For a number of years, we have used the term coronary thrombosis, or myocardial infarction, synonymously with heart attack. We have assumed that a clot was always, or almost always, present to produce the infarction. As time passes, we are less and less sure of this. The figures of competent pathologists vary in showing that about one-fourth to two-thirds of patients have demonstrated clots. Spain and Bradess[11] have recently suggested that the number depends on how quickly the patient dies after the attack: if within a few minutes, no clot may be found, but if in hours or days, a clot may be present. More and more, it seems to me that clotting may not be the primary cause of death of the myocardium in anything like the number of patients we had formerly thought.

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Factitial Proctitis

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FACTITIAL PROCTITIS is a condition often seen following treatment of pelvic viscera with radium or roentgen rays. It is characterized by all degrees of severity, ranging from mild inflammation of the anterior rectal wall to complete destruction of the rectovaginal septum with resulting rectovaginal fistula or to development of a stricture with subsequent intestinal obstruction.

There is a definite calculable risk to patients undergoing irradiation therapy. Patients and physicians must recognize that factitial proctitis will develop in a certain percentage of patients even when the operator is highly skilled in irradiation therapy.

The term "factitial proctitis" was first used in 1930 by Buie and Malmgren[1] and embodied the concept that changes within the rectum are produced unintentionally or by artificial means.

Obviously, this lesion or condition is important to all physicians dealing with patients who receive irradiation therapy, but it is of particular concern to the radiologist, gynecologist, and proctologist. It is essential to establish a prompt and accurate diagnosis in all patients with bowel symptoms occurring any time after irradiation therapy. This is important because an erroneous diagnosis of primary rectal malignancy or recurrence of the pelvic tumor with extension to the rectum may be disastrous if it is made simply because the physician is not aware of the true nature of this lesion, which is benign and responds to conservative treatment. In our opinion, occurrence of this lesion does not connote poor technic. Rather, the possibility of proctitis should not prohibit the proper use of irradiation, which is intended to destroy the malignant process. In other words, proctitis may be termed a justifiable lesion. The literature includes many cases of pelvic malignancies treated by irradiation with permanent damage to the rectum, most commonly noted in the form of strictures.

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HISTORY

Combined use of roentgen rays and radium first became popular in about 1918. The first report of rectal symptoms after irradiation therapy appeared in 1915, when Futh and Ebeler[2] reported 5 patients in whom rectal symptoms developed after treatment solely by radium for extrarectal pelvic lesions. In two of these patients, stricture developed; in one, a rectovaginal fistula occurred.

In 1930 Buie and Malmgren[1] reported on a series of 65 cases seen at the Mayo Clinic during a nine-year period and described for the first time the proctoscopic picture and clinical findings. They called attention to the ever-present telangiectases which occurred even in healed cases, noting that such lesions are self-limiting and ultimately heal with or without treatment in from twelve to twenty-four months.

In 1937, in a report on 39 patients with factitial proctitis, Bacon[3] stated that radium was the causative factor since he had never observed a case after use of roentgen rays alone. He also noted that, although bleeding was the most common symptom, profuse hemorrhage occurred infrequently.

Based on symptomatology, Wigby[4] classified intestinal reaction from irradiation into 3 groups. Diarrhea alone he called a first degree reaction; blood and frequent loose stools were said to be a second degree reaction; and strictures necessitating colostomy he classified as third degree.

INCIDENCE

There is wide variation in incidence depending on dosage and technic. Todd[5] reported an incidence of 5 per cent from several clinics.

In 1942, Aldrich[6] reported that some degree of intestinal injury developed in approximately 17 per cent of his patients, but he felt that most previous reports had included only patients with the most serious injuries whose symptoms required active treatment or surgical intervention.

Sherman[7] and Kaplin[8] reported that proctitis developed in one fifth of University of Minnesota patients who received irradiation for uterine

cancer. According to Kaplin,[8] bowel damage or factitial proctitis developed in nearly 15 per cent of a series of patients treated at the University of Minnesota from October 1953 through December 1954.

A review of the literature reveals that the onset of factitial proctitis may vary from two or three months to as long as five years after irradiation.

PATHOGENESIS

Irradiation produces an obliterative endarteritis of the vessels of the bowel wall. This results in necrosis, ulceration, subsequent fibrosis, and stricturing, which is chiefly submucosal fibrosis. As stated, radium is probably the principal cause, although roentgen ray and cobalt radiation are capable of producing the lesion. Among Buie and Mahngren's cases,[1] the smallest amount of radium known to produce factitial proctitis was 800 milligram hours, whereas many larger doses did not result in damage. Obviously, individual tolerance to radiation varies. Reirradiation after inadequate primary dosage frequently causes the lesion. Also, we must realize that, in recent years, increased dosages of radiation are producing higher cure rates for uterine cancer. Consequently, a higher incidence of factitial proctitis must be anticipated.

Proctoscopic appearance. The proctoscopic picture of factitial proctitis is characteristic, with the most important single finding being telangiectasis. This is the presence of exposed surface vessels which bleed easily and may exist in the earliest cases as well as in long-standing cases that are considered healed. This condition may persist for years and result in prolonged rectal bleeding. It is usually seen on the anterior wall anywhere from the dentate line to the rectosigmoid junction but is most marked along the mid-anterior wall closest to the cervix or opposite the placement of the radium.

The more severe the proctitis, the more marked is the erythema and edema of the mucosa. As proctitis progresses in severity, the mucosa loses its normal smooth appearance and becomes granular, bleeding easily when rubbed with a cotton swab. The surface of the bowel, anterior wall, and midportion of the rectum become involved with a pale yellowish membrane surrounded by areas of inflammation of varying distances. Eventually, the pale area becomes eroded and then ulcerative with a characteristic appearance. The ulcer is usually covered with a thick, tenacious, dirty gray slough, and the mucosal edges surrounding the ulcer are often markedly inflamed and bleed readily.

If healing starts, the base of the ulcer begins to assume a less depressed appearance, and the ulcer gradually becomes smaller because of the inward growth of the mucosal edges. When healing is complete, a pale, stellate scar remains, surrounded by telangiectasis that has supplanted the ulcer.

If such healing does not occur after this stage of ulceration, varying degrees of proctitis develop involving all layers of the rectum. Proctitis gives the wall a thickened appearance, and stenosis of the lumen results with possible progression to a marked stricture formation.

Occasionally, an ulcer will continue to penetrate the anterior rectal wall until eventually it perforates through its center into the vagina. The result is a rectovaginal fistula. The fistula edge may be large enough to allow passage of a standard ⅝-in. proctoscope into the vagina. Edges of the fistula usually appear rolled and are pale and firm. It may be difficult to tell whether one is dealing with infiltrating carcinoma or inflammatory tisue. In such instances, multiple biopsies of the fistulous edge should be taken.

Classification. Most attempts at classifying the stages of factitial proctitis have been based on pathologic changes. However, in 1954, Sherman[7] offered the new classification based entirely on proctoscopic appearance. These classifications are as follows:

Grade 1. A. A localized erythema and telangiectasis. Friable mucosa that bleeds easily. No ulceration or stricture. B. Diffuse erythema with accompanying paraproctitis.

Grade 2. Ulceration with a grayish, tenacious slough, usually involving the anterior rectal wall.

Grade 3. Stricture plus proctitis and ulceration, with either of the latter coexisting in varying degrees.

Grade 4. Proctitis, ulceration, rectovaginal fistula, or stricture or bowel perforation.

Symptoms. Symptoms of proctitis depend on the type of lesion. Kaplin[8] and Sherman[7] have reported these symptoms in order of frequency: bleeding, diarrhea, pain, constipation, abdominal cramping, rectal tenesmus, and excessive mucoid discharge. Kaplin's study revealed that objective changes could be present in the rectum without any evidence of subjective symptoms.

Differential diagnosis. Conditions to be considered in making differential diagnosis of factitial proctitis are primary carcinoma of the rectum, secondary or metastatic carcinoma with involvement of the rectum, ulcerative type of lymphogranuloma, nonspecific rectal ulceration, and enema tip abrasions.

TREATMENT

Unless complications requiring surgical correction occur, most forms of treatment are conservative. Among them are rectal douches, use of warm cod liver oil, and instillation of olive oil and astringent agents to control bleeding, such as tannic acid or ferric chloride solution. None of these methods has been very effective. Recently, topical use of 2½ per cent hydrocortisone cream has offered some encouraging results. Also, hydrocortisone topically applied by suppository has been used. This seems to be the treatment of choice for lesions responsive to conservative management. Recommended prophylactic measures include (1) protecting the rectum by adequate packing of the vagina with gauze during radium therapy, and (2) frequent change of position by the patient to keep loops of bowel out of the pelvis and away from the radium source.

Surgical measures are recommended for repair of grade 3 lesions with obstruction and grade 4 lesions. Diversionary colostomies have been advocated for temporary relief of symptoms of abdominal cramping, rectal tenesmus, and bleeding. However, resection is recommended for incapacitating rectal strictures and rectovaginal fistulas. If the primary tumor is under control, Sherman[7] and Brintnall[9] have recently advocated "pull-through" procedures with preservation of the anal sphincter as the operation of choice for grade 3 and grade 4 lesions. This is recommended because local repair and anterior resections will be unsuccessful because of the excessive tissue damage from irradiation and injury to the blood supply in this area.

SUMMARY AND CONCLUSIONS

Bowel complications after irradiation for pelvic malignancies are reviewed. Emphasis is on the rectal complication known as factitial proctitis, which occurs after irradiation therapy in about 5 to 15 per cent of cases.

Pathologic changes in the bowel wall are probably in the nature of obliterative endarteritis with resulting necrosis and ulceration. The principal etiologic factor in the production of factitial proctitis is probably radium. However, this does not result from improper technics but from the definite and calculable risk involved whenever irradiation therapy is undertaken.

When bowel symptoms develop after irradiation therapy, the diagnosis should be suspected and proctoscopic examination should be done. The condition must be clearly and promptly differentiated from malignancy. Factitial lesions are self-limiting in their course and, if the primary condition is controlled, will heal in from twelve to twenty-four months.

Topical hydrocortisone acetate by rectum has proved efficacious in treating inflammatory and ulcerative cases. However, such treatment is not used for those cases of grades 3 and 4 proctitis in which surgical intervention is indicated.

In our opinion, there has been a growing trend toward a surgical approach to pelvic malignancies, and a consequent reduction of irradiation therapy. For example, I believe that more hysterectomies for early in situ carcinomas of the cervix are being done now than in previous years. The acceleration of this trend, if it is one, means that some of the problems discussed here will not be as pronounced in the future as in the past.

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Splenectomy: Indications and Limitations

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THE SPLEEN, its physiological functions and surgical problems, has long been surrounded by a mantle of mystery which has been lifted only within the past few decades, at least in part.

Whereas history records that marathon contestants, in the time before Christ, were splenectomized in order to improve their athletic performance (presumably to rid them of the "caked" malarial enlargement of this organ), precise evidence in favor of this provocative concept for the athletically inclined is lacking. In fact, until the mid nineteenth century, reports of successful splenectomy in man are virtually absent from the literature. This is quite understandable because of the sepsis potential after all operations at that time. Furthermore, suitable anesthetic agents were lacking, and no means were available for replacing a blood volume depleted by ooze from this organ. Nevertheless, this challenge must have loomed clearly before surgeons learning their professions, although during that era the profession was probably more of a craft, while serving with armies marching to and fro the continents of Europe, Asia, and Africa. They surely must have noted the lethal effects of tearing the tender capsule of this organ by blow or penetrating weapons.

At approximately the same time, Adelman and Simon in Germany reported a small series of successful cases of splenic removal after injury or for other reasons. It remained, however, for Spencer Wells, the ovariotamist, worthy opponent of Lister, and extraordinary technician of his day, to develop (and somewhat exploit) the operation of splenectomy. One suspects that he viewed these cases of splenomegaly with much the same glint in his eye that a bounty collector examines a marauding coyote or wolf nicely aligned with the bead on his rifle.

Even today, the indications for splenectomy, at least for certain conditions, are obscure. Yet, there are other circumstances in which the need for surgical removal of this gland is clear-cut. If we are to tabulate these in their approximate order of merit, the results might be somewhat as follows:

Indications for Splenectomy

1. Rupture of the spleen
2. Congenital (hereditary) hemolytic (spherocytic) anemia.
3. Hypersplenism:
   - A. Primary splenic neutropenia
   - B. Idiopathic thrombocytopenic purpura
   - C. Pancytopenic anemia
4. Splenectomy to expedite other surgical procedures or permit a more complete removal of contiguous involvement of the esophagus, stomach, or pancreas by neoplasm.
5. As a preliminary to the establishment of a spleno-renal anastomosis.
6. Rarely in the treatment of localized Hodgkin's or other lymphomatous processes including primary neoplasms of the spleen (and usually because of a secondary hypersplenism).
7. As a prophylactic measure against the hazard of rupture in a spleen massively enlarged due to: malaria, metabolic disorders of the reticuloendothelial system, granulomatous infections, or parasitic infestations.

Contraindications to Splenectomy

1. When the spleen is the site of secondary myeloid metaplasia in the presence of aplastic or hypoplastic bone marrow.
2. Acquired thrombocytopenic purpura secondary to some chemical toxin in the environment.
3. Idiopathic purpura with megakaryocytic hypoplasia.

DIAGNOSTIC CONSIDERATIONS

Ruptured spleen. Under most circumstances, the diagnosis is readily made upon the patient's clinical history: dullness (increasing) in the left upper quadrant; roentgenogram revealing a fractured twelfth or eleventh rib and an irregular space-occupying mass; a falling or erratic blood pressure requiring repeated transfusions for stabilization; loss of the normal splenic config-

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uration on a plain upright film of the abdomen, an item which can be reinforced by giving the patient barium by mouth and noting the altered impression on the contour of the stomach; a white count in excess of 15,000 shortly after an injury to the splenic region, and the late appearance of a pleural effusion on this side as a harbinger of delayed bleeding from the spleen. Technical aspects of splenectomy will not be considered in detail. Suffice it to say that the procedure today has been made safe by surgeons skilled in the management of problems related to removal of this organ. For the largest spleens, a thoraco-abdominal approach is to be recommended. In children, however, a short lateral incision will usually be sufficient. Under almost no circumstances is damage to the pancreas or stomach to be condoned or accepted as an inevitable byproduct of splenic operations.

Congenital hemolytic anemia. At the present time, congenital hemolytic icterus often can be readily recognized upon the patient's clinical history, knowledge of familial tendency, the globular appearance of the red cell in smear preparations, and increased red cell fragility to hypotonic concentrations of saline. The results after operations are excellent as regards the elimination of recurrent anemia tendencies and more severe acute hemolytic episodes. Spherocytosis persists, however. It is pertinent to indicate that 25-30 per cent of patients suffering from this condition, including some children, have evidence of gall stones. Although obstructive (regurgitation) jaundice may be associated with the latter condition, under such circumstances, the basic problem is not cholelithiasis. Particularly in young persons, the lithiasis should be suspected as being the byproduct rather than the basic problem. It is worthy to recall that splenectomy does not change the genetic problem producing spherocytosis, but that it does relieve the patient of the crippling tendency toward increased packing of spherocytes into this enlarged organ with the ultimate establishment, thereby, of an increased rate of destruction of red cell elements.

Hypersplenism

A. Primary and acquired splenic neutropenia may be difficult to separate in a particular case. The clinical syndrome described by Felty and virtually the identical complex later reported as the Wiseman-Doan syndrome (neutropenia, at times cyclic, arthritis, splenomegaly, recurrent infections, febrile episodes) is a somewhat ill defined entity from which cases, however, can be selected that will benefit materially by splenectomy.

B. Idiopathic thrombocytopenic purpura (Werlhof's disease) remains, in a large measure, an enigma with regard to causation and the reasons for therapeutic failures. However, as a clinical entity it is sharply to be differentiated from the acquired thrombocytopenic purpuras secondary to toxic inhalations or injestions, as well as certain responses to drugs. Werlhof's disease occurs most commonly in children or young females and may have an explosive onset characterized by purpuric manifestations and spontaneous bleeding from various orifices, together with internal bleeding, an event quite likely to be most serious when it occurs intracranially. The spectrum of cases in any substantial series, however, can shade off to those with an insidious onset in which there is little more to identify the presence of this disease than the patient's tendency to bruise easily. Under certain circumstances, it appears that there is almost irrefutable evidence that idiopathic thrombocytic purpura is an immunologic mechanism. And, in the case of some patients, there is reason to believe that idiopathic thrombocytopenic purpura may be but a phase in the picture of disseminated lupus erythematosus. A variation of this complex, also to be distinguished from "true," idiopathic thrombocytopenic purpura is thrombotic thrombocytopenic purpura. In the latter, intravascular agglutination of platelets occurs and for best management requires the establishment of an anticoagulation regimen despite the altered bleeding time. Treatment also consists of blood or platelet transfusions.

Steroid therapy has proved of considerable value as a means of reducing the hazard from capillary bleeding in the presence of profoundly lowered thrombocyte counts in idiopathic thrombocytopenic purpura. Indeed, steroid therapy will benefit a number of these patients and preclude the need for surgical operation. Administration of steroids to other patients will better prepare them for the operation which can then be carried out with less risk. A failure of platelets response over a matter of a few weeks, however, usually augurs in favor of splenectomy if the patient has suffered from a moderately severe acute episode; a longer time can safely be devoted to testing the patient's response to steroid management (or the cyclic nature of the disease) when the episode has been a milder one. After splenectomy for this disease, in the majority of cases (approximately two-thirds), the patients have a permanent remission of signs and

symptoms; for the remaining one-third of the patients, the interval of relief may last from a few weeks to a few years. This, of course, is contingent upon not overlooking any accessory splenic tissue.

C. Pancytopenic anemia: Various combinations of red cells, lymphocytes, and platelets may be involved in the increased rates of splenic destruction. Identification of this condition is usually possible upon evidence of increased destruction of red blood cells in addition to the occurrence of splenomegaly when other contributing causes for such signs and symptoms have been disproved.

Splenectomy. Indications for removal of the spleen are generally self-evident and require no additional discussion. It is sufficient to say that the search for an accessory spleen which may lie anywhere from the diaphragm to the pelvis, and on *either* side, should be a responsibility of the surgeon lest he through such an oversight jeopardize, or even preclude, the benefits possible from splenic removal. On the other hand, when an accessory spleen is thought to offer an explanation for persistence or recurrence of symptoms following splenectomy, this organ can be searched for by radioactive technics with considerable confidence that any appreciably sized gland will thereby be made identifiable.

SPLENECTOMY: CONTRAINDICATIONS

Whenever the spleen serves as a site of limited but contributing bone marrow formation, its removal, despite the occurrence of some splenomegaly, should be viewed with considerable reluctance unless there is evidence that by such an excision net over-all benefit (reduction of the total rate of cellular elemental destruction) is thereby achieved. To attempt to help the patient with acquired thrombocytopenic purpura by splenectomy when rather the cause is bone marrow suppression, which must be evidenced by clinical history as well as direct bone marrow examination, is to deny that patient the best chance of recovery. Moreover, splenectomy prejudices the functional capacity of the reticuloendothelial system by excising that substantial fraction present in the spleen. And, indeed, where there is no megakaryocytic response to the thrombocytopenic events associated with "idiopathic" purpura, there is considerable justification for questioning the advantage to the patient of removal of the spleen. Finally, current evidence indicates that the case for treating patients with acquired hemolytic anemia by splenectomy appears to be based on failure of the patient to respond to medical management by steroid therapy and other supportive measures; no more than half are likely, even temporarily, to be benefited from splenectomy.

ADMINISTRATION OF glucagon may be useful in the diagnosis of hyperinsulinism and in differential diagnosis of the hypoglycemic syndrome.

When healthy persons were given 1 mg. of glucagon by intramuscular injection six to eight hours after eating, the blood sugar level rose rapidly by about 50 to 100 mg. per 100 cc., reaching a peak within one half to three quarters of an hour and gradually returning to normal within two hours.

The same amount of glucagon was given under similar conditions to 4 patients with organic hypoglycemia due to hyperinsulinism. In each instance, the blood sugar level rose rapidly after injection, reaching a peak by thirty minutes and falling to or below normal by ninety minutes.

After two hours, extreme hypoglycemic symptoms necessitated administration of glucose in 2 patients. Hypoglycemic symptoms appeared after two to two and one-half hours in the other 2 but were not extreme; the hypoglycemic nature of the symptoms was confirmed by improvement after glucose administration.

V. MARKS: Response to glucagon by subjects with hyperinsulinism from islet-cell tumours. Brit. M. J. 5185:1539-1540, 1960.

Book Reviews . . .

The Gentle Legions

RICHARD CARTER, *1961. New York: Doubleday & Co. 335 pages. $4.50.*

The first book-length appraisal of the big, voluntary health organizations gives penetrating insight into the background and operations of these charities. The author devotes a chapter to each of the following health agencies:

The Red Cross. "The prototype of voluntary health organizations is the American Red Cross, which antedates the disease-type agencies by many years but has never been remote from health . . ." The author states that few Americans have the foggiest knowledge of what the Red Cross is! An interview with General Alfred M. Gunther, its president, revealed some of the criticism directed at the Red Cross. The author explodes these myths and tells of the many and efficient services which it gives the public.

The Seal of Good Health. Following a brief history of the organized tuberculosis movement, the author points out that the National Tuberculosis Association concentrated on education of the public, hoping to stimulate pressure for state establishment of proper health departments, firm sanitary codes, and good tuberculosis hospitals. This was decided after it was found economically impractical to pay for patient care and treatment.

The National Tuberculosis Association launched a modern health crusade in the schools so, by 1920, numerous children were being taught good health measures.

The means to raise money for these activities was the Christmas Seal—"the brightly colored stamp that has become so cherished a part of the Christmas tradition for so many Americans that it stands unrivaled among fund-raising devices."

Despite the tremendous reduction in tuberculosis mortality since the last century and the unceasing efforts of the National Tuberculosis Association, the disease continues to exceed all other infective and parasitic illness as a killer of Americans. The death rate is at least 7 per 100,000.

The author sums up the problem, "Most of the 12,000 Americans who will die of TB this year will die because they did not get the right medical attention soon enough. The 150,000 other Americans who are known to have active cases must, therefore, be encouraged by all available means to get proper care. Meanwhile, 80,000 new cases of active TB can be counted on to arise each year among the 30 to 40 million of us who are already infected. If these hair-raising facts are unfamiliar, it is because we have been reading too many headlines . . . that TB is practically extinct."

The Polio Triumph. The announcement of the Salk vaccine on April 12, 1955, made the National Foundation for Infantile Paralysis "the most successful voluntary health organization on earth." Having dropped "for infantile paralysis" from its name, the group is now working against arthritis and congenital defects while still pursuing polio research along broader lines.

The Cancer Crusade. Nearly every person knows "the seven danger signals of cancer" because of the tremendous job the American Cancer Society has done. Until 1943, the society was mainly interested in promoting education via leaflets, lectures, and posters. The press and radio were wary about using the word cancer, considering it an indelicate term reserved for medical circles.

An outstanding example of the society's educational program was the promotion of Dr. George N. Papanicolau's vaginal-smear technic for detecting cervical cancer in its early stages. Although he made the discovery in 1926, it wasn't accepted among physicians until the society "sold the technic to them and created a public demand for the service."

The Heart Fund. Although the Heart Association was formed in 1924, it was not known much before its reorganization in 1948. In 1947, the association was opened to membership of laymen and an educational job was done to make the public aware of the group.

"The association is proud it allots a higher percentage of revenue to research than does any other large voluntary health agency ($9 million for 1960-61)."

Other Agencies. In one chapter, the author presents a brief description of more than 20 smaller health agencies.

United Fund. The final chapter is devoted to the United Fund. He says, "Those who condemn multiplicity as a chaotic, wasteful nuisance are usually strong supporters of United Funds, in which the individual community merges the campaigns of local and national health, welfare, and recreation agencies for one big community drive. Campaign goals are set and the giver's money is parceled out by committees of civic leaders, according to their view of the agency's relative need."

He concludes: "If Big Brother can be prevailed upon to leave the national health movement alone, voluntary work and voluntary giving will continue to flourish in that field, offering the public and its governments the kind of creative leadership and vital services that have distinguished health voluntaryism for almost seventy years."

DONNIE CRONIN CARR
Minneapolis

An Approach to Old Age

MARGARET NEVILLE HILL, C.B.E., *1961, Edinburgh, Great Britain: Oliver & Boyd. 132 pages. Illustrated. 15s. Net.*

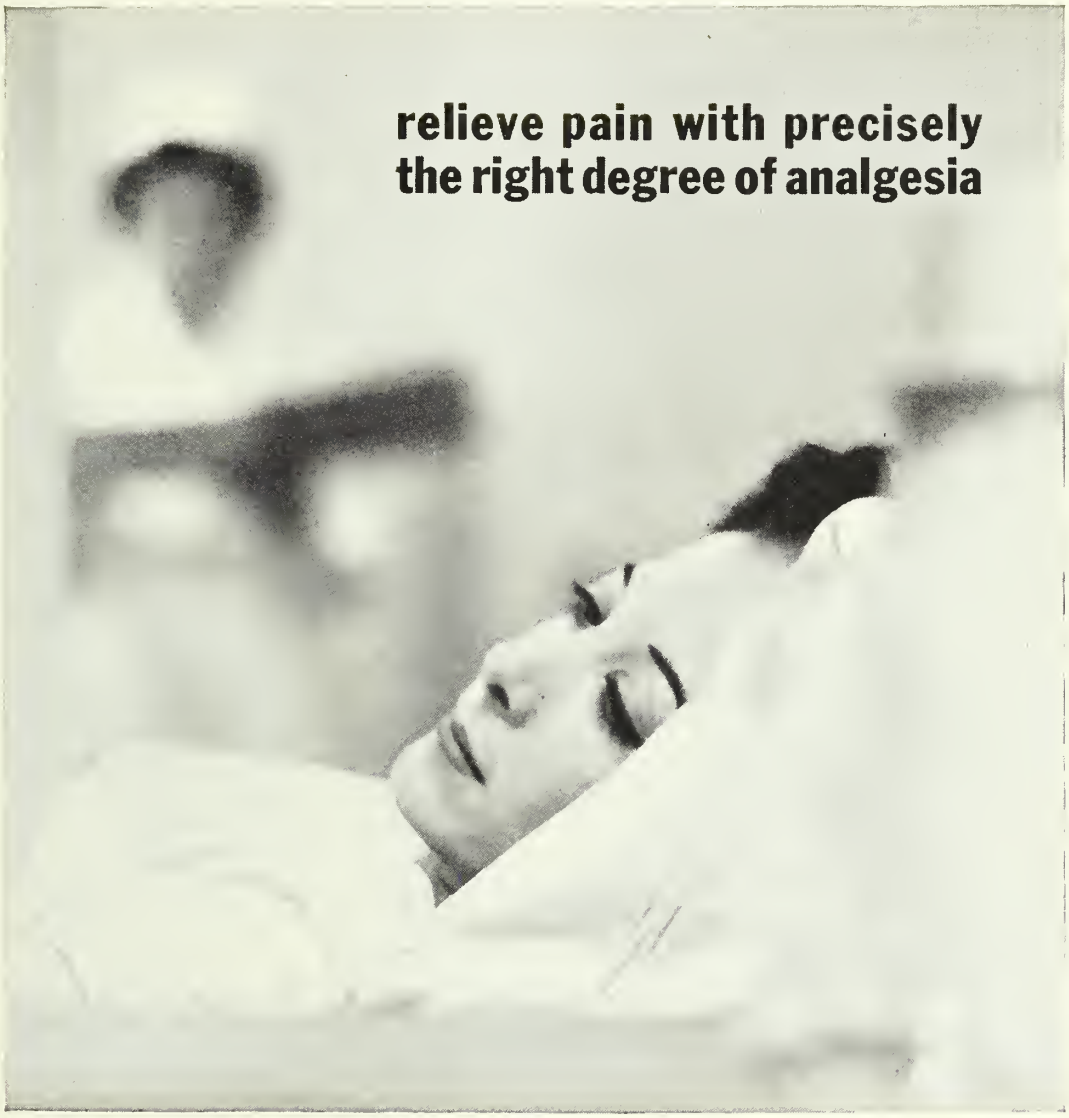
In the September 1960 issue of *Geriatrics*, Dr. Reuben F. Erickson gave an interesting history of Hill Homes in London. Dr. Erickson well described the homelike atmosphere in the 7 old residences in the High-Gate district of North London, where Mrs. Hill maintains a remarkable program of good care for older people.

Dr. Erickson says: More impressive than any one physical feature about the Hill Homes is the happy attitude of the residents, which is so different from the sour, complaining atmosphere often found in such homes.

The Hill residences are neat, clean, and happy but without the undue fussiness and overemphasis on a hospital type of spotlessness, which really is unnecessary in a place of this sort.

Now Mrs. Margaret Hill, the wife of Professor A. V. Hill, Nobel prize winner in physiology, has written an account of her experiences in providing effective care for old people. She has prepared an informative and stimu-

(Continued on page 18A)



control moderate to severe pain 'Empirin' Compound and 'Empirin' Compound with Codeine Phosphate products provide pinpoint control, anywhere along the pain scale, for all intensities up to that which requires morphine—without narcotic excess. For effective analgesic, antipyretic and antitussive action, prescribe the 'Empirin' Compound that suits your purpose best.

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*Subject to Federal Narcotic Regulations.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

(Continued from page 230)

lating little book entitled *An Approach to Old Age and Its Problems*. This work is the result of Mrs. Hill's wide personal experience and the large experience she has gathered through her years of close contact with old people and with the district nurses, social workers, and physicians who have cared for them.

The book deals with the history of the care for the aged, with charitable trusts, with plans for the care of the aged, with wartime experience with old people, with sickness in old age, with homes for mentally aging, and with residential homes such as Mrs. Hill herself has so well maintained. Sir Henry Willink, former Minister of Health, writes a forward paying tribute to Mrs. Hill's understanding, kindness, and resourcefulness in her pioneering work.

Hill Homes in London were founded in 1940. The 7 houses now accommodate about 230 old people, 80 of whom are more than 85 years old. These people are housed in a series of beautiful old private homes in High-Gate, with attached gardens, and are operated by a full-time staff of 75. Hill Homes proves that the attractiveness of actual home surroundings can be preserved in units of 20 to 40 people in a private house, with a cook, nurse, and housekeeper for each unit.

Mrs. Hill's book will help all those who have the problem of caring for old people, particularly in regard to understanding their needs and difficulties. It will be helpful to students of sociology, physicians, nurses, and assistants in homes for old people.

The practical experience which Mrs. Hill has had in the care of older people is well summarized in this attractive book.

CHAUNCEY D. LEAKE
Columbus, Ohio

The Mother-Child Interaction in Psychosomatic Disorders

ANN M. GARNER *and* CHARLES WENAR, *1959. Urbana, Ill.: University of Illinois Press. 284 pages. $6.00.*

This book is the report of an excellently conceived and designed, well-executed, and fully presented research study on the differential patterns of mother-child interaction, especially in the child's first year of life. It significantly distinguishes between equated groups of neurotic, psychosomatic, and nonpsychosomatic chronically ill children and their mothers. Reading it will be well worth the reader's time, both as to the results obtained and as an engrossing adventure in research.

Statistic data are presented in 34 main tables and profuse minor ones. The book is attractive in appearance, well bound and printed, and highly recommended.

LEONARD S. ABRAMSON, PH.D.
Fort Meade, South Dakota

A Guide to Antibiotic Therapy

HENRY WELCH, PH.D., *1959. New York: Medical Encyclopedia. 69 pages. $3.00.*

This comprehensive, succinct handbook on antibiotics provides the busy practitioner and the researcher with current concepts, as of 1959, regarding general indications, side effects, major dosage forms, average daily dose, and anticipated blood and urine concentrations of antibiotics and in vitro susceptibility of each group of important pathogenic microorganisms to the antibiotic. The material is arranged so that the reader can obtain the information desired without first wading through a morass of qualifications.

Of the 31 antibiotics described, 28 are currently available for general use in the United States. Leucomycin, Spiramycin, and Colimycin are as yet available in this country only on an investigational basis but are included in this brief text.

The awe-inspiring era of antibiotics, of which we apparently are in only the dawn of creation, is moving so rapidly that a drawing together of the facts as we know them at this time, accumulated from published scientific literature and personal experiences, is a necessity for the evaluation of our current position in this field. This has been ably accomplished by Dr. Welch in this volume.

Generic and trade names are given in the introduction; however, only generic names are used in the text. It might have saved the reader time had the trade names been listed in the text either under the generic name or with adequate reference made to them. No index is included, but none is actually needed, as the drugs are listed alphabetically.

In his introduction, Dr. Welch wisely warns that "when interpreting the data in this text, the reader should keep in mind that there is a general relationship between the blood concentration obtainable with a given dose of the antibiotic, the degree of susceptibility of the organism, and the expected therapeutic effect. An antibiotic can, nevertheless, give poor results in vitro and still be in vivo success." Clinical success, then, depends on many factors, but the antibiotic of choice, in the dose of general choice, against common or even rare pathogens, is fairly well delineated for us in this book.

There are no illustrations. The scope of this book precludes any lengthy discussions of either organism or antibiotic. The book is arranged so as to facilitate the frequent revisions that will become necessary as we sort through our annual 3 million odd pounds of antibiotics. This book is well written and well worth the $3.00. It is recommended for all physicians working with antibiotics, which includes most of us.

ROBERT E. MITCHELL, JR., M.D.
Richmond, Virginia

Nerve Endings in Normal and Pathologic Skin

R. K. WINKELMANN, M.D., PH.D., *1960. Springfield, Ill.: Charles C Thomas. 195 pages. Illustrated. $7.50.*

The preparation of this book began in 1950 for the Atomic Energy Commission. The work was continued under the United States Public Health Service and was finished at the Mayo Clinic.

This book is well indexed and contains 404 references. It is printed on good paper and is easy to read. It provides an appendix with descriptions of special staining methods. Photomicrographs are advantageously utilized.

Both sensory and autonomic nerves and nerve endings are well described and pictured. This book naturally is essential to dermatologists, but the balance of the medical profession is bound to be interested in the innervation of the skin, since the skin envelops the entire body.

An illustration of a section of special interest is the chapter on the glomus body, which gives a simple explanation of an anatomic entity that is generally a mystery to most physicians.

This book is a significant contribution to the practice of medicine.

JOHN S. LUNDY, M.D.
Chicago

The Journal Lancet

SERVING THE MEDICAL PROFESSION OF MINNESOTA, NORTH DAKOTA, SOUTH DAKOTA, AND MONTANA

Cardiac Aspects of Chest Pain

BEN SOMMERS, M.D., and ALAN RUSTERHOLZ, M.D.

St. Paul

CHEST PAIN is a very common problem in differential diagnosis and we should like to discuss this subject with reference to angina pectoris, myocardial infarction, acute pericarditis, and dissecting aneurysm of the aorta.

ANGINA PECTORIS

Although technically meaning merely pain in the chest, angina pectoris has come to denote a certain type of chest pain which is related to temporary coronary insufficiency and is thought to be due either to muscle anoxia or, perhaps, to accumulation of metabolites in the heart itself. Diagnosis is made primarily on the basis of the history, as physical examinations and laboratory procedures are often confusing or of no help.

Symptoms. Anginal pain has a typical location, a typical radiation, is produced by typical factors, and its duration and relief are also typical. Anginal distress is commonly retrosternal and is rarely precordial. It almost never occurs at the apex, in the left mammary region, or in the inframammary region. Radiation of pain to the left shoulder and down the left arm is rather common; however, radiation down both arms also occurs. Radiation to the teeth or jaw or to the epigastrium is also not uncommon. Radiation to the back is unusual.

Angina pectoris is classically a squeezing or constricting feeling, perhaps giving the sensation of a weight on the chest. It may also be mild and described as merely a peculiar sensation rather than a pain. Sharp, stabbing pain is not usually angina.

Anginal pain is not influenced by deep respiration or by the Valsalva maneuver but is characteristically produced by walking, especially uphill, after a meal, or in cold weather. Chilling of even part of the body, as by ice cubes in the hands, will decrease the exercise tolerance. Walking to lunch may not produce pain, but walking from lunch may. The pain may often be associated in the patient's mind with gas, and belching may produce a certain degree of relief.

The pain is usually of short duration and rarely lasts more than five minutes. It occurs at the time of exertion or of severe emotional stress and usually recedes within one minute after cessation of the inciting incident or after the sublingual ingestion of a potent nitroglycerin tablet. Chest discomfort that occurs some time after exertion or emotional stress is not angina.

A valid diagnostic procedure consists of observing the effect of sublingual nitroglycerin upon the pain. This test is not infallible, however, as the pain of gallbladder disease, peptic ulcer, or hiatus hernia occasionally will subside after nitroglycerin administration. It is important to interrogate the patient carefully regarding the rapidity with which nitroglycerin produces relief, since nitroglycerin acts within one

BEN SOMMERS *and* ALAN RUSTERHOLZ *are specialists in internal medicine, practicing in St. Paul, Minnesota.*

minute. Unless the physician is very clear about this matter, he may be misled, since patients frequently will respond in the affirmative when asked whether or not the little tablets under the tongue have relieved their chest discomfort. However, further questioning may reveal that the discomfort did not disappear until half an hour to an hour after the tablet was put under the tongue.

A simple test for angina pectoris popularized by Dr. Samuel Levine of Boston[1] consists of the use of carotid sinus pressure during an attack of pain. Dr. Levine massages the carotid sinus and asks the patient whether the pain has become worse. Anginal pain is apt to cease during carotid sinus stimulation, particularly if the heart is slowed. However, if the pain does not relent, one is not justified in excluding angina. It is important that the physician should not lead the patient or put words into his mouth. This is the reason why Dr. Levine advocates asking whether the pain has become worse, rather than if it has become better.

Any pain with the above-mentioned characteristics—that is, typical location, typical radiation, typical means of production, and typical method of relief—is almost certainly angina and, in a great majority of cases, is due to disease of the coronary arteries, although angina may rarely occur in the absence of coronary narrowing. Examples of this are syphilitic aortitis, in which the coronaries themselves may be normal but their ostia may be occluded by the syphilitic process at the root of the aorta; a severe anemic state in which the oxygen-carrying capacity of the circulating hemoglobin is reduced; and perhaps severe protracted tachycardias, in which coronary filling which normally occurs in diastole may be deficient because of the shortening of diastole. It should be borne in mind that a patient has angina or he doesn't have it! There is little reason to use the term "mild angina," because the severity of the sensation perceived tells little about the severity of the arteriosclerotic process and does not influence the prognosis.

Differential diagnosis. For years it has been known that hiatus hernia; peptic ulcer; gallbladder disease; and diseases of the cervical spine, including ligamentous disease, cervical disk, and cervical arthritis, can produce chest pain simulating angina pectoris.

A recent article by Mainzer[2] stresses the coexistence of some of these conditions with angina pectoris and the modification ("concatenation") of the anginal syndrome. Whenever, in coronary disease, the trigger mechanism producing the anginal attack, its duration, or the site of radiation of the pain are atypical, or nitroglycerin fails to produce relief, coexisting involvement of other organs as a modifying factor should be suspected. For example, should a patient with proved angina have pain on bending or stooping as well as walking up hill, and should nitroglycerin produce no, incomplete, or inconsistent relief, cervical spondylitis might be suspected. Treatment of the spondylitis with physical therapy might then cause amelioration of the angina, which would again respond to nitroglycerin.

A 69-year-old man was seen in the early 1940s with a duodenal ulcer, cervical arthritis, and angina. At times nitroglycerin gave relief and at other times it did not. In 1943, pyloric obstruction developed and was treated by gastroenterostomy, after which the patient noted symptomatic relief not only from his ulcer but also from the discomforts of the arthritis and the coronary disease. He is still alive and occasionally has exertional chest discomfort.

Extremely common types of left chest pain are left inframammary pain, which may be on the basis of an intercostal neuritis or myositis and costochondral junction pain (Tietze's syndrome). In the latter entity, pressure over the costochondral junctions or over the xiphoid process may produce the patient's symptomatology. Local infiltration with procaine or systemic cortisone may help determine whether the patient has anginal or costochondral pain.

Another entity which may simulate angina is the splenic flexure syndrome, in which there is distention of a segment of the splenic flexure of the colon associated, as a rule, with left upper quadrant pain. The pain, however, may be perceived in the lower retrosternal area. The story of relief upon passing flatus and, occasionally, the production of the discomfort by inflating the splenic flexure with air under fluoroscopic observation aid in clarifying the diagnosis.

The resting electrocardiogram may be completely normal in the case of true angina pectoris caused by coronary disease. Although various tests, usually employing the electrocardiogram before and after stress of one sort or another, have been devised, there is no completely satisfactory laboratory or electrocardiographic test for use in the diagnosis of this entity.

MYOCARDIAL INFARCTION

Pain may be entirely absent in myocardial infarction or may be so severe as to be agonizing. Substernal pain lasting twenty minutes or longer should be considered that of myocardial infarction until ruled out. Occasionally, the pain of myocardial infarction is limited to the abdomen

and may simulate acute gallbladder disease, acute pancreatitis, or perforating peptic ulcer. If pulmonary embolism occurs on the left, the pain may closely simulate that of myocardial infarction until cough and hemoptysis develop. Occasionally the electrocardiogram in pulmonary embolism resembles inferior infarction, thus adding to the difficulty of differential diagnosis. A positive Homans' sign, atrial fibrillation, or a history of recent trauma to the extremities favor a diagnosis of pulmonary embolism.

Impending myocardial infarction. There is an entity standing between angina pectoris on the one hand and myocardial infarction on the other. In practice, one frequently sees patients whose anginal pain has become of greater duration, has perhaps been relieved incompletely by nitroglycerin, and in whom myocardial infarction cannot immediately be excluded. Another group comprises those patients whose first symptoms develop suddenly and without adequate cause, as shown in the following history.

A 31-year-old man suffered substernal discomfort one afternoon while walking up a slight incline to his home. The pain recurred after supper and again the next morning. Clinical investigation failed to demonstrate infarction, and the pain, always of short duration, gradually disappeared. Anticoagulants were administered for six weeks, then discontinued. Eight weeks later, without warning, this patient had an acute anterior infarction.

We feel that these patients are in the state of impending myocardial infarction. With the advent of anticoagulants, it is important to recognize these cases promptly, since, in a certain number, one can avert serious muscle damage, as shown in the following history.

A 50-year-old man sustained a myocardial infarction followed by complete recovery without development of angina. In his occupation, running a small grocery store, he was able to tolerate heavy lifting. Eight years later, while watching television, he experienced severe pain in both arms radiating to the chest, lasting twenty to thirty minutes. Repeated electrocardiograms, sedimentation rates, and blood enzyme studies failed to show infarction. He was placed on anticoagulants, the acute situation dissipated itself, and he is asymptomatic except that he now has angina on moderate exertion, with good relief from nitroglycerin.

Anticoagulants will not always prevent infarction in these cases, however, as illustrated in the following history.

A 68-year-old retired engineer was hospitalized with an impending infarction one year after his original posterior infarction and received anticoagulants. T-wave changes suggested ischemia, and laboratory studies were normal. On the tenth hospital day, when the prothrombin time was thirty-two seconds, the electrocardiographic pattern of severe anterior infarction appeared.

Perhaps 50 per cent of patients with acute myocardial infarction give a history of pain, often quite mild, beginning from three weeks to a few hours before the severe attack.

ACUTE IDIOPATHIC PERICARDITIS

This not uncommon disease presents symptoms easily mistaken for myocardial infarction. A correct diagnosis is most important, since the use of anticoagulants is contraindicated in this disease. There have been reported several cases of fatal cardiac tamponade following anticoagulant therapy in pericarditis mistakenly diagnosed as myocardial infarction. Yet there are clear-cut differences in the clinical picture of each of these two diseases: (1) the pain of acute pericarditis is more stabbing and knifelike and rarely radiates to the arms; (2) the pain in pericarditis is much aggravated by lying down, is relieved by sitting up, and is usually aggravated by a positive Valsalva maneuver; and (3) aspirin and cold packs to the chest and neck often control the pain of pericarditis. The diagnosis should be suspected early from the clinical picture, and anticoagulants should be withheld, for the electrocardiographic pattern of ST elevations may be mistaken for early infarction until serial studies are obtained.

DISSECTING ANEURYSM OF THE AORTA

This term is a misnomer as there is no aneurysm present. It should more accurately be called acute dissection of the aorta. Here again myocardial infarction may be mimicked, and here also anticoagulants are contraindicated. Classically, back pain is present as well as chest pain, but it is important to realize that the clinical manifestations of this entity vary tremendously from case to case, and so-called classical features all too often are lacking. Extreme shock may be present. The pain depends upon the site and extent of the dissection. Involvement of one or both carotid arteries may produce vertigo and syncope. Hematuria and anuria may occur if the renal arteries are blocked. If the physician always palpates the carotid, radial, and femoral arteries, he will minimize the possibility of misdiagnosing a dissection of the aorta. A previously absent pulse may reappear during the course of this disease. This may be caused by further dissection or perhaps by dissection back into the original aortic lumen with formation of a double channel. This situation is occasionally compatible with relatively good survival time. In dissecting aneurysm, the electrocardiogram may be normal or may merely show ST-T depressions of ischemia.

There are many other entities which can pro-

duce chest pain which has, in the past at least, occasionally been confused with the pain of coronary disease. Certainly herpes zoster in the pre-eruptive stage can be confusing. Some confusion has arisen when chest pain turns out to be due to Bornholm disease, a viral infection characterized by a severe, unremitting type of chest pain popularly called the devil's grip.

SUMMARY

The physician should make every effort to diagnose or exclude angina pectoris on the basis of the history because he will get little real help from the physical examination or the electrocardiogram. Correct identification of angina pectoris is important, as a great deal of harm can be done by diagnosing this entity indiscriminately. On the other hand, persons with coronary disease must be advised to live within their coronary reserve and to avoid the production of angina whenever possible. We hope that this discussion will re-emphasize the diagnostic and differential diagnostic aspects of angina pectoris caused by coronary insufficiency and will in some small degree contribute to the better handling of patients with chest discomfort or pain of many types.

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Death usually is due to heart disease in persons who survive their first myocardial infarction, then die in the next decade.

The most significant single index of good prognosis in patients having myocardial infarction for the first time is the ability to return to normal activities. Men and young persons have a comparatively favorable outlook. Inauspicious prognostic factors are preexisting angina pectoris, hypertension, and congestive failure. Whether the patient's occupation is sedentary or nonsedentary seems to make little difference.

Of 224 patients who survived their first diagnosed myocardial infarction by at least one month, 68.8 per cent were alive at the end of three years; five- and ten-year survival rates were 55.4 and 29.2 per cent, respectively.

At postmortem examination of 82 patients, 3 had no healed infarcts. Among the other 79, the infarct was located on the anterior wall in 52 per cent, posterior wall in 42 per cent, lateral wall in 5 per cent, and ventricular septum in 1 per cent. Infarcts were subendocardial in 54 per cent and transmural in 46 per cent.

Of the 79 patients with validated infarcts, 82 per cent died of heart disease. Death was due to recurrent acute myocardial infarction in 34 per cent, myocardial failure in 24 per cent, and other cardiac causes in 27 per cent.

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Convulsive Disorders

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A CONVULSIVE DISORDER is one of the most common neurologic disorders encountered in the practice of medicine. An estimated 2,000,000 people are afflicted in the United States alone, thus giving an incidence of almost 2 per cent of the population.

A convulsive disorder is a state produced by abnormal, excessive neuronal discharges within the brain. A seizure is, therefore, a *symptom* rather than a disease. Clinically, a seizure consists of a brief stereotyped reaction, the manifestation of which will depend upon the part of the brain involved. The clinical manifestations of convulsions can, therefore, be as variable as the function of the human brain, and the only real characterizing feature is its paroxysmal and often inappropriate occurrence. It must be kept in mind that seizures may be caused by a wide variety of conditions, such as toxins, infections, high fever, alcohol, and systemic diseases such as uremia, nephritis, and so forth. Since, in the above conditions, the seizures disappear when the patient recovers from the primary illness, this type of seizure manifestation is not classified as a true convulsive disorder. The latter term is reserved for chronic intermittent recurring seizures which, although introduced by a variety of etiologies, persist even after the original precipitating mechanism has been removed. They are nearly always associated with abnormal electrical discharges and some alteration of consciousness.

CLASSIFICATION

The following classification has proved most useful in an understanding of the convulsive disorders. This classification is based on a division of seizures into 2 large groups, namely, those that originate subcortically with spread to all cortical areas (centrencephalic) and those seizures that are focal in nature, being limited, at least at onset, to a specific cortical area.

I. Centrencephalic seizures (idiopathic, generalized)
   - A. Myoclonic epilepsy
   - B. Petit mal
   - C. Grand mal

II. Focal cerebral seizures
   - A. Neocortical seizures
     1. Motor seizures: jacksonian, adversive, tonic-postural
     2. Sensory seizures: somatic, visual, and auditory manifestations
   - B. Limbic system seizures
     1. Sensory: vertiginous, circulatory, gustatory
     2. Autonomic: vasomotor, epigastric, miscellaneous
     3. Psychic: forced thinking, dreamy states, hallucinations, emotional changes
     4. Automatism

III. Mixed type
   - A. Multifocal
   - B. Centrencephalic and focal

ETIOLOGY

Any condition that injures the brain and produces focal areas of functional disturbances can result in seizures. Seizures, therefore, can be caused by a wide variety of conditions, such as toxins, infections, injuries, tumors, or metabolic disturbances.

Toxins. Generally, seizures produced by toxins are transient in nature and do not result in a true convulsive disorder. Seizures are frequently seen in uremia, eclampsia, acute alcoholism, and intoxication by various alkaloids. As the intoxi-

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cation subsides, the convulsions disappear, leaving no continuing seizure problem.

Congenital defects. Maldevelopments and anomalies of the brain can well result in a convulsant disorder. The seizures usually develop early in life and are often accompanied by abnormalities in the neurologic examination.

Brain injury. Brain injury at or shortly after birth is a very common cause of seizures. Often the onset of the seizures is delayed until late infancy or childhood. In the adult, the development of seizures after head injury depends upon the severity of the injury and its site.

Infections. Any infectious process, if extreme enough to produce focal brain damage, can result in seizures. It is possible that the infectious diseases of childhood may well be the cause of many of the seizures encountered later in childhood and adolescence. Frequently, because of the mildness of the infectious process, it is overlooked as an etiologic possibility. Infections later in life are less likely to produce convulsions.

Tumors. Brain tumors must always be considered as a possible cause of seizures. This is particularly true of tumors situated near the surface of the brain. Any patient in whom the seizures appear for the first time in adult life must be considered a tumor suspect and a careful work-up should be done before drug therapy is instituted.

Arteriosclerosis. This is a possible cause of seizures in the older age group only. Actually, cerebral softening due to arterial disease is a relatively uncommon cause of convulsions and the diagnosis, therefore, should be made with caution. Much too often, the presence of seizures in an elderly individual is an indication of the associated presence of a space-occupying lesion.

Degenerative lesions. Degenerative processes rarely produce seizures and should not be considered readily in their presence. In multiple sclerosis, for example, it is estimated that seizures occur in less than 1 per cent of cases.

CLINICAL MANIFESTATIONS

Generalized (centrencephalic seizures)

These seizures originate subcortically or deep within the brain and spread to involve all cortical areas bilaterally. Therefore, they have certain characterizing features, such as bilateral synchronous motor movements and bilateral and often total sensory occlusion resulting in loss of consciousness. Two types of seizures are included in this group: typical petit mal and grand mal seizures.

Petit mal seizures occur most commonly in children. The classic attack consists of a momentary lapse of consciousness, rarely lasting more than a few seconds and accompanied by a staring or rotating of the eyes upward, blinking, or fine twitching of the hands or mouth. They occur most frequently in the early hours of the morning and may be very frequent, with as many as fifty or more attacks a day.

Some attacks are characterized by sudden, brief bilateral synchronous jerks, implicating chiefly the eyelids and forearms. This condition is known as *myoclonic epilepsy.* Occasionally, these seizures may present with a sudden loss of muscle tone, resulting in a falling to the ground. These have been termed *akinetic seizures* and are often mistaken for an awkwardness or stumbling on the part of the patient rather than a seizure phenomenon.

The drugs of choice for this type of seizure are Tridione, Paradione, and Milontin.

Grand mal, or major epilepsy is the best known and most striking form of seizure. The onset is sudden, with a loss of consciousness and a generalized tonic spasm, during which time the limbs are extended. The patient falls to the ground and may seriously injure himself. Sometimes the onset is accompanied by a shrill cry due to the sudden expulsion of air as the convulsion begins. The tonic phase generally lasts for a few seconds but may be prolonged to half a minute. During this period, the body is rigid, the limbs extended, the jaws tightly closed, and the pupils often dilated and immobile. Respiration ceases and the face becomes blue and livid. Incontinence of urine or even evacuation of bowels may occur in this stage.

This phase of the seizure is followed by the clonic stage, which is ushered in by a sudden deep respiration followed promptly by disappearance of the cyanosis and complete relaxation of the musculature. There is now a jerking of the head and limbs, noisy stertorous breathing, rapid feeble pulse, and a churning of the jaw resulting in drooling of saliva, often bloody or blood-tinged. This phase lasts from one to five minutes and is followed by complete relaxation, with the patient remaining unresponsive. Deep, prolonged sleep may follow the attack, and, in some cases, confused automatic behavior or, less commonly, even furor with violence may precede the return to consciousness. Upon recovery, the patient may note exhaustion, muscle pain, or persistent headache.

Grand mal seizures may occur at any time but frequently are nocturnal in nature. It is important to differentiate between the typical grand

mal seizure and the generalized seizure that may follow any form of focal discharge. In the latter case, there is usually an initial aura or some lateralizing signs, but these may be so brief as to be overlooked. The typical grand mal seizure occurs without such aura or lateralizing signs.

The most effective drugs for the treatment of typical grand mal attacks are Dilantin, phenobarbital, Mebaral, Mesantoin, Mysoline, and Peganone.

FOCAL CORTICAL SEIZURES

These include those cases in which the abnormally epileptogenic tissue is limited to more or less circumscribed areas of the cerebral cortex. In most cases, there is some evidence of injury to the cortex.

Motor seizures. The type of motor manifestation will depend upon the region of the cortex involved. In lesions of the motor cortex, the seizure starts with convulsive twitching of one portion of the body, usually the distal part of an extremity, and spreads to involve the entire limb, the other homolateral extremity, and even the face on the same side. This is termed a *jacksonian seizure.* Consciousness is retained unless the seizure becomes generalized. The attack may be followed by a postictal weakness of the extremity most involved.

Lesions of the frontal cortex may produce a strong deviation of the head and eyes to one side with or without an associated loss of consciousness. This is referred to as an *adversive seizure.* Contralateral head turning may also arise from the occipital region but in such cases is usually preceded by an aura of flashing or colored lights.

Tonic-postural movements, such as slow elevation of the arms over the head, with the eyes and body turning as if to "look at" the uplifted arms, are characteristic of a seizure arising from irritation of the vertex and mesial surface of the hemisphere.

Sensory manifestations. Lesions of the sensory areas of the cortex may also result in seizure manifestations. These are often less dramatic than the motor seizures and are overlooked in many of the milder cases. The nature of the seizure pattern obviously will depend upon the type of sensory cortex involved. Three fairly well-defined types have been recognized: somatic, visual, and auditory. Vertiginous and olfactory sensations may also occur, but these are classified under temporal lobe or limbic seizures.

Somatic disturbances of paresthesia or numbness in a limb indicates an irritation of the contralateral postcentral gyrus. Such seizures may remain localized to one area or may show a "march" similar to the jacksonian motor seizure. Postictal numbness of an extremity may follow.

Visual sensations of flashing lights or spots may arise from lesions of the occipital cortex. Lesions more anterior in the posterior temporal region produce formed images, such as figures of animals or man, often with alterations in size (macropsia and micropsia).

Lesions of the superior temporal gyrus occasionally produce simple auditory disturbances, chiefly in the form of sudden hearing impairment. More complex auditory disturbances result from lesions of the limbic system.

The drugs of choice for motor and sensory seizures are Mesantoin, phenobarbital, Dilantin, Mebaral, Gemonil, and Mysoline.

Limbic (temporal lobe) seizures. The limbic system includes the orbital frontal gyri, anterior and medial portions of the temporal lobes, amygdala and hippocampal formation, and cingulate gyrus. Seizures arising in this system present widely varying manifestations which are often complex and bizarre. These seizures may occur at any age and are characterized by sudden alterations in awareness or consciousness often associated with complex disturbances in sensation, autonomic function, thinking, and behavior.

The *sensory* alterations involve chiefly the vestibular and olfactory systems and consist of episodes of dizziness or unsteadiness or of hallucinations of disagreeable smells usually described as a "burning of rubber." These disturbances are often associated with disturbances in consciousness, often described as a "dreamy state."

Autonomic disturbances may implicate many systems. The most common is the epigastric phenomenon, beginning with an aura of nausea and progressing to belching, abdominal discomfort, or acute abdominal pain. This type of seizure manifestation is almost invariably associated with chewing movements and excessive salivation. Vasomotor symptoms, such as palpitation, blanching, cyanosis, flushing, or even transient elevated blood pressure, may be prominent. Rarely, some patients may manifest such diverse symptoms as urinary frequency, hyperventilation, or respiratory arrest. Since these manifestations closely resemble visceral disturbances, they often are overlooked as seizures and the diagnosis is not made. The characterizing feature is their paroxysmal occurrence, which should alert the physician as to their possible cerebral origin.

One of the characteristic features of temporal lobe seizures is the *psychic manifestations* which may occur alone or in association with sensory or autonomic disturbances. These consist of illu-

sions, hallucinations, forced thinking, dreamy states, or mood changes. The hallucinations may be simple sensations of light, smell, taste, or sound or more complex hallucinations of vision or hearing, such as scenes, visions, acts, or organized sound. In forced thinking, the patient experiences recurring compelling thoughts. The dreamy states also involve both visual and auditory perceptions, with a feeling of familiarity *(déjà vu)*, a feeling of strangeness, distortion of the environment, and so on.

Automatism comprises one of the most striking features of these seizures. The individual behaves as though he were only partially conscious. He may fumble with his clothes, walk as though in a trance, carry out semipurposeful movements, or even manifest unexplained attacks of rage with destructive behavior.

A single temporal lobe seizure may last from minutes to hours. Consciousness is altered but not lost, so that these patients rarely injure themselves. There is usually complete amnesia for the episode. Postictal behavior disorders such as temper tantrums and rages are common and difficult to control.

The drugs of choice for these seizures are Mysoline, Dilantin, phenobarbital, Mebaral, Mesantoin, and Phenurone, although none of these is completely satisfactory.

EVALUATION OF A SEIZURE PROBLEM

Because of the many possible causes of seizures and the wide variety of treatment methods now available for this condition, it is important that seizure diagnosis be accurate. It is imperative that the physician decide whether the symptoms represent a seizure mechanism and, if so, that he determine its cause and method of treatment.

Obviously, a careful history and examination are of utmost importance as the first steps in evaluation. Such procedures may well reveal evidence of an expanding lesion such as a neoplasm or of a birth injury with secondary atrophy of one side of the body. In patients who have had seizures for many years and who have no abnormal findings on neurologic examination, no further studies may be necessary, and treatment based upon a careful evaluation of the seizure type can be instituted.

Certain seizure patients always warrant more detailed evaluation and careful study. Such a detailed seizure work-up is advisable in the following patients:

1. Any patient whose seizures first appear after the age of 20 years
2. Any seizure patient who shows abnormalities on neurologic examination
3. Any patient whose seizures cannot be adequately controlled by carefully planned therapy
4. Any patient who manifests furor states during a seizure episode.

A proper seizure work-up should include the following specialized procedures: (1) spinal fluid studies, (2) skull roentgenogram, (3) blood sugar evaluation, (4) electroencephalography, and (5) pneumoencephalography in selected cases. The electroencephalogram is the single most useful test in the evaluation of a convulsive disorder. Properly carried out, it will be positive in 90 per cent of all seizure cases. The electroencephalogram is not only of value in determining the presence of an abnormality but also is most helpful in assessing the value of medication.

TREATMENT

Although drug therapy comprises the most satisfactory method of treating the convulsive disorders, therapy, to be successful, must consist of more than drugs and must encompass all those factors that might reduce the irritability of the brain. Each patient must be watched and guided by the physician until good control is obtained. Under proper guidance, over 85 per cent of seizure patients can be controlled or improved. Each of the following procedures should be considered and instituted in each case: (1) removal of the cause if indicated, such as in cases of a tumor or a large cyst; (2) avoidance of exposure to toxins that might increase cerebral irritability; (3) adequate rest; (4) establishment of emotional stability by proper environmental adjustment (social, marital, occupational, and familial); and (5) institution of proper drug therapy.

Avoidance of toxins

Many exogenous toxins will produce increased irritability of the brain and may accentuate seizures. The most common of these is alcohol. It is, therefore, wise to caution all seizure patients to limit or discontinue the use of alcohol. Industrial toxins such as carbon monoxide should also be eliminated if possible. Even some drugs, such as Thorazine, which has a tendency to accentuate cerebral irritability, may be harmful to these patients and should be avoided.

Adequate rest

It is well known that lack of sufficient sleep will cause an individual to be more restless and irritable. This may be harmless to a normal individual but often is not well tolerated by patients with seizures. It is, therefore, advisable to caution patients with convulsive disorders to

obtain adequate rest. These patients should not get inadequate sleep on any series of consecutive days because of the danger of accentuating their seizure pattern.

Emotional adjustment

Aside from drug therapy, this is probably the most important aspect of seizure therapy. An emotionally disturbed patient is often very difficult to control adequately even with large doses of anticonvulsant drugs. It is, therefore, imperative that the physician take time to discuss environmental adjustment with the patient and at least make some attempt to determine whether there might be some emotional disturbances that might interfere with adequate seizure control. It is important to keep in mind that the presence of the seizures themselves frequently create many problems for the patient that can be quite distressing. Because of his position in a community, the physician can help the patient greatly in handling and adjusting to many of these problems. It might be well to list a few of the problems that should be considered in every patient with seizures.

In children:

1. Rejection by the family because of the imagined stigma resulting from having a member of the family with seizures

2. Rejection by neighbors who through ignorance will not allow their children to play with the patient

3. Poor understanding of the problem by teachers, who frequently will refuse to work with the patient or demand that the patient be removed from school.

In young adults:

1. Fear of being stigmatized by having a spell while with friends

2. Limitation of certain activities, such as driving a car, swimming in an unsupervised area, climbing in a high area, and participating in such traumatic sports as football and boxing

3. Partial restriction of social activities, such as frequent late parties, drinking, and so forth

4. Fear of disrupting a dear friendship or a potential marriage by revealing the presence of the illness.

In adults:

1. Anxiety of a mother concerning possible injury to an infant during a seizure

2. Difficulty of a wage earner to obtain or maintain a job because of seizures or even a history of seizures. It must be remembered that many industries will not engage patients with seizures, even if fairly well controlled, because of insurance regulations or often because of bias.

In addition to the above factors, there are many problems unrelated to the presence of seizures, such as financial problems, marital maladjustments, health problems, and so on, which can produce emotional tensions. All of these should be investigated, particularly if the patient proves resistant to drug therapy or shows increased seizures after a period of good control.

DRUG THERAPY

Phenobarbital is available in tablets of ¼, ½, and 1½ gr. The daily anticonvulsant dose for an adult ranges from 1 to 7 gr. This drug is indicated chiefly for patients with grand mal or focal neocortical seizures. The chief limitations to its use are the drowsiness and loss of mental alacrity resulting from larger doses of the drug. A liquid form is available in an elixir than can be used with children.

Mebaral is a barbiturate that is available in white tablets of ½, ¾, and 1½ gr. Like phenobarbital, it is most useful in grand mal and focal neocortical seizures. Its chief value is that it does not produce the lethargy that is often found with the use of phenobarbital and therefore is better tolerated by patients even in large doses. The average adult dose is 4.5 to 7.5 gr. daily. Occasionally, this drug will produce a diffuse rash that will necessitate discontinuing it.

Gemonil is a barbiturate that is very similar to Mebaral. Available in tablets of 1½ gr., it is used chiefly in focal neocortical and limbic seizures. The average adult dose is 4.5 to 7.5 gr. daily.

Dilantin is a hydantoin dispensed in capsules of ½ and 1½ gr.; in infatabs containing ¾ gr.; as a delayed action capsule; as a Dilantin suspension, a pleasantly flavored liquid containing 1½ gr. per 4 cc.; and in an intravenous preparation containing 3¾ gr. per vial. The dose for adults is generally 4½ to 9 gr. daily. This drug is most efficacious in controlling grand mal, focal neocortical, and limbic seizures. Toxic manifestations may appear in the skin, mucous membranes, or central nervous system. The skin lesions consist of a morbilliform rash, hypertrichosis of the face and extremities, and, rarely, severe bullae. Hypertrophy of the gums occurs in 10 per cent of patients. Neurologic complications vary from moderate nystagmus and/or ataxia to an acute picture resembling acute cerebellar disease. When toxicity appears, the drug must be reduced to safe levels and therapy sup-

plemented by other anticonvulsant drugs efficacious in this type of seizure.

Mebroin is an orange tablet that contains 1½ gr. of Mebaral and 1 gr. of Dilantin and is very useful in the treatment of grand mal and focal neocortical seizures. Each of the ingredients seems to supplement the other in its action. The toxic symptoms from overdosage are the same as for each of its ingredients.

Mesantoin is closely allied to Dilantin and is available in purple tablets of 1½ gr. Its use is identical to that of Dilantin, but it is considerably more toxic. Mesantoin therapy sometimes causes acute hematologic manifestations, such as anemia, leukopenia, agranulocytosis, and fluctuating pyrexia. Because of its toxicity, this drug is usually used in doses of 1½ to 3 gr. as supplementary therapy to Dilantin or Mebaral. During its use, complete blood counts at least once a month are advisable.

Peganone is one of the newest hydantoinates and is available in tablets of 4½ and 9 gr. Peganone is most useful as an adjuvant drug in combination with other anticonvulsants in grand mal, focal neocortical, and limbic seizures. Peganone may produce a mild rash, gastrointestinal symptoms, ataxia, and fluctuations in the blood leukocyte count. When toxic symptoms occur, the drug should be reduced or discontinued.

Tridione is the best drug for the treatment of petit mal and myoclonic seizures. It is obtainable in a large white capsule of 3 gr. and in an aqueous solution of 150 mg. per fluidram. The average adult dose is from 15 to 25 gr. daily. Tridione, although very effective in petit mal seizures, may precipitate major seizures and therefore is always used concomitantly with Dilantin or Mebaral. The complications of Tridione are blood dyscrasias, meralopia, or rash. The blood dyscrasias consist of aplastic anemia, agranulocytosis, or both. Every patient placed on this drug must have complete blood counts monthly. The meralopia is usually transient and consists of a peculiar blurring of vision in bright light. Rash is uncommon.

Paradione is a homologue of Tridione. The dosage, indications, and contraindications are the same as for Tridione. It is somewhat less toxic but also not as effective as Tridione.

Milontin is a very nontoxic product that is most useful in petit mal seizures. It is supplied in a 0.5-gm., light orange capsule with an orange band or as an anis-pineapple flavored suspension of 250 mg. per 4 cc. The average daily dose is 2 gm. Toxic symptoms are few and consist of a transitory rash and, occasionally, drowsiness.

Celontin is a succinimide used chiefly in the treatment of petit mal and, perhaps, limbic seizures. It is available in a 0.3-gm. yellow capsule with an orange band. The dose varies from 0.3 to 1.2 gm. Toxic symptoms are fairly common and consist of a rash, anorexia, ataxia, confusional states, leukopenia, and drowsiness. The toxic manifestations often negate Celontin's usefulness as a good therapeutic agent.

Phenurone is a highly toxic product that is often very helpful in limbic (temporal lobe) seizures. It is produced as a large white tablet of 0.5 gm., and the daily dose ranges from 1.5 to 4 gm. Acute psychotic manifestations develop in about 20 per cent of patients. In addition, the drug may produce severe liver damage or agranulocytosis. Because of its toxicity, this drug must be used with great caution and with constant evaluation of the liver and blood status.

In addition to the above, a number of drugs have been advocated in special circumstances. *Ammonium chloride* and *Diamox* have been used in women whose seizures are related to periods of water retention at the menses and in some refractory cases of petit mal seizures. *Benzedrine sulfate* has been suggested as being helpful in cases of purely nocturnal seizures, as well as in petit mal seizures unaffected by other medications.

The goal of medical therapy is the control of seizures without toxic effect of the medication. Once this state has been achieved, it is important not to reduce or to discontinue the medication too rapidly. Generally, medication, once successful, should be continued for at least twenty-four months before reduction is contemplated. The rate of reducing the medication must be very slow, and the dosage should promptly be returned to a safe level if there is any indication of recurrent difficulty.

Status epilepticus. This term applies to a state of successively recurring seizures in which the patient does not regain consciousness between episodes. This is a very grave condition that, if not corrected, will result in death of the patient. Sudden withdrawal or discontinuation of anticonvulsant medication is an important cause of status epilepticus. Intravenous or intramuscular administration of medication is necessary both to save time and because of the patient's clinical conditions, which make oral administration impossible. A number of drugs can be used in the treatment of status: (1) phenobarbital, 1 to 5 gr. intramuscularly; (2) Amytal sodium, 7½ gr. intravenously or until seizures stop; (3) paraldehyde, 5 to 15 cc. intravenously or rectally; (4) ether; and (5) Avertin, rectally.

MEDICAL GRAND ROUNDS
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Diabetes Mellitus and the Adrenal Gland

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DIABETES MELLITUS is a derangement of carbohydrate metabolism characterized by glycosuria and hyperglycemia. A disturbance of the normal insulin mechanism is closely associated with this disease. When the carbohydrate metabolism becomes seriously upset, there are accompanying, readily demonstrable abnormalities in the metabolic states of fat and protein. These derangements can give rise to ketosis, acidosis, coma, and death.

The disturbance in the insulin mechanism is believed to be due to reduced elaboration of insulin by the pancreas in some cases and, in others, to an increased insulin requirement by the tissues. The capacity to metabolize carbohydrate is a fundamental process in almost all tissue cells. What part primary disturbances of the intrinsic enzyme systems concerned with these oxidative processes may play in diabetes is obscure. It is known, however, that certain endocrine glands and their hormones profoundly influence the metabolism of carbohydrate, fat, and protein.[1] The relation of these glands to the origin of diabetes has to be considered.[2]

I will discuss the role of the adrenal gland in carbohydrate metabolism and the relation of the adrenal hormones to the diabetic state.

ADRENAL MEDULLA

Histology. The cells of the adrenal medulla are ectodermal in origin, having arisen from the neural crest. The parent cell is the sympathogone, which matures to either the ganglion or the chromaffin cell. These cell types are found in the adrenal medulla and wherever there is sympathetic nervous tissue.[3]

Hormones. Epinephrine was the first hormone to be isolated. In 1946, norepinephrine was isolated from the adrenal and adrenergic nerve fibers by von Euler. These two hormones are catacholamines and differ only in a methyl group possessed by norepinephrine.[4]

In the adrenal medulla, there are 2 to 4 mg. of these hormones per gram, of which 10 to 30 per cent is norepinephrine. The plasma concentration is 3 μg. per liter, with norepinephrine making up 80 per cent. Urine contains 15 to 45 μg. of catacholamine, with norepinephrine making up 85 per cent.[4] The increased amount of norepinephrine probably represents additional release from adrenergic nerve endings.

In contrast to the normal medulla, in which the predominant hormone is epinephrine, norepinephrine is often contained in large amounts in a pheochromocytoma. The pharmacology with regard to the cardiovascular actions of these hormones is well established. Epinephrine, however, also has a prominent metabolic effect, which is possessed to only a limited extent by norepinephrine.

Epinephrine causes increased oxygen consumption, with rises in body temperature and basal metabolic rate; accelerates hepatic glycogenolysis, with a consequent rise in fasting blood sugar levels; can produce a diabetic glucose tolerance curve; accelerates muscle glycogen breakdown to lactic acid; and decreases glucose utilization by the muscles.[5] Blum, in 1901, was the first to report glycosuria with the injection of adrenal extracts and termed the condition "adrenalin diabetes." The action of epinephrine is explained with reference to figure 1.[5]

Glucose-1-phosphate is both the precursor of glycogen formation and the product of glycogenolysis. This interconversion is catalyzed by phosphorylase.[6] Since enzyme activity facilitates the attainment of a given equilibrium, the observation that epinephrine always induces glycogenolysis presented a paradox and suggested

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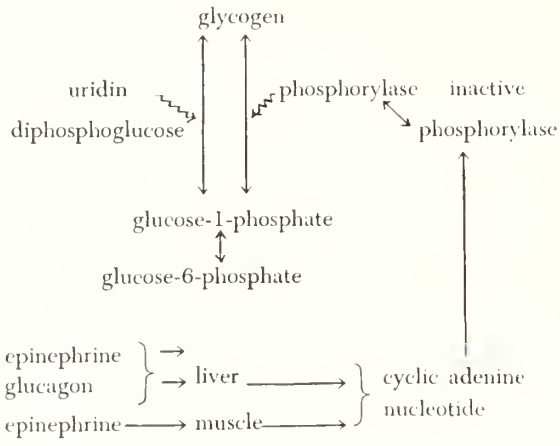

Fig.1.

that phosphorylase primarily catalyzes glycogen breakdown. Leloir and Cardini[7] demonstrated that glycogen synthesis may occur by a pathway not involving phosphorylase. This pathway requires uridine diphosphoglucose.

Epinephrine exerts its effect by conversion of inactive phosphorylase into the active form. This activation in liver and in muscle involves the synthesis of a cyclic adenine nucleotide. Therefore, the sequence of events is as follows: Epinephrine reacts with tissue components to accelerate the formation of adenine nucleotide, which in turn accelerates the formation of active phosphorylase; this in turn alters the steady state of uridine diphosphoglucose and phosphorylase systems in favor of glycogenolysis. Glucagon apparently has the same mode of action, but only in the liver.[5]

The accumulation of phosphorylated intermediates, specifically glucose-6-phosphate, inhibits the conversion of glucose to glucose-6-phosphate. Thus, there are two reasons for the diabetes-like state induced by epinephrine—increased hepatic glycogenolysis and blockage of phosphorylation of free glucose by the presence of excess phosphorylated intermediates.[5]

Epinephrine has a similar effect on lipid synthesis, facilitating lipid breakdown and release of fatty acids and glycerol into the circulation. This is seen clinically in patients with pheochromocytoma associated with loss of body fat. Epinephrine may also be indirectly diabetogenic by acting on the anterior pituitary gland, thus causing an increased secretion of corticotrophin.[8]

Clinical observations: pheochromocytoma. As might be suspected, the incidence of glycosuria and hyperglycemia in patients with pheochromocytoma varies widely, presumably depending on the relative excess of epinephrine secretion. As noted previously, depletion of adipose reserves in such patients should be anticipated, since both epinephrine and norepinephrine are lipolytic. A study of blood ketone bodies or unesterized fatty acids might prove helpful in investigating a suspected pheochromocytoma. Obesity in conjunction with hypertension would make the diagnosis unlikely.[5,9]

Pheochromocytoma has become widely known and the syndrome frequently diagnosed, with over 600 cases now published. In 207 cases of pheochromocytoma, Graham[10] found 10 per cent with frank diabetes and 9 per cent with abnormal glucose tolerance curves. This incidence greatly exceeds chance association. The reverse circumstance—that is, the incidence of pheochromocytoma associated with diabetes—is 0.3 per cent, as noted in a study of 1,100 diabetic patients by Freedman and associates.[9] A review of the charts at the Minneapolis Veterans Administration Hospital for the last ten years reveals 3 cases of pheochromocytoma coded, of which 2 were associated with abnormal glucose metabolism but not with frank diabetes mellitus.

Most pheochromocytomas cause hypertension of some degree, but those which mainly secrete epinephrine usually produce metabolic disturbances, diabetes, and anxiety in addition. On the other hand, norepinephrine-secreting tumors, which are in the majority, cause symptoms consequent to the rise in blood pressure.

The diabetic state in medullary tumors will vary with the fluctuation of circulating levels of epinephrine. Surgical removal of the tumors results in unpredictable changes in the diabetic state, ranging from complete amelioration to no notable change.

Instances of adrenal medullary insufficiency have not been recognized clinically, so hypoepinephrine states do not play a role in relation to diabetes.

ADRENAL CORTEX

Approximately 30 steroid compounds have been isolated from the adrenal cortex. Six of these which are capable of maintaining life have been identified and studied: (1) hydrocortisone (compound F), (2) cortisone (E), (3) corticosterone (D), (4) dehydrocorticosterone (A), (5) desoxycorticosterone (DOC), and (6) aldosterone. These are termed corticoids and have an α-ketol side chain ($CO\text{-}CH_2\text{-}OH$) at carbon 17 of the steroid nucleus. Hydrocortisone and cortisone have oxygen at the 11,17 positions and are called 11,17-oxygenated corticoids. The others are 11-oxygenated corticoids.[2]

The functions of the adrenal gland are many and include regulation of electrolytes and water; androgen secretion regulation of hematopoiesis and tissue reactivity; control of pigmentation; and regulation of metabolism of protein, fat, and carbohydrate. This discussion will concern itself mainly with the latter function, realizing that the metabolism of carbohydrate cannot be separated from other metabolic processes.

The discussion also will be restricted to hydrocortisone and cortisone, since they are the most important and influential of the several biologically active steroids. Furthermore, experimental evidence is lacking regarding the effect of adrenal androgens on carbohydrate metabolism, and the effects of corticosterone and aldosterone are qualitatively similar to that of hydrocortisone.

Glucocorticoid effect on carbohydrate metabolism. Most of the enzymatic reactions of glycolysis in hepatic tissue are well known and appear to be freely reversible. There are three steps, however, that provide separate reactions upward and downward, which would seem to be particularly suitable sites for the exertion of a directional control of metabolic flow.[5,11] These steps are illustrated in figure 2.

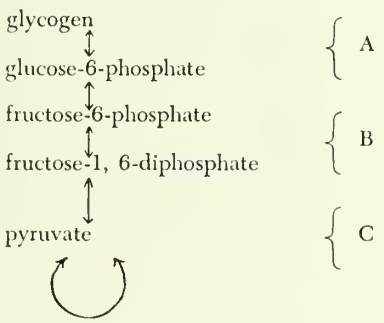

Fig. 2

Glucose phosphorylation is catalyzed by hexokinase, while its dephosphorylation is catalyzed by glucose-6-phosphatase (figure 2A). Fructose-6-phosphate is further phosphorylated to fructose 1,6-diphosphate in the presence of phosphofructokinase, while fructose 1,6-diphosphatase catalyzes the reverse reaction (figure 2B). Although phosphoenolpyruvic acid is freely metabolized to pyruvate, pyruvate encounters energetic difficulties in being converted to phosphoenolpyruvic acid directly and does so by way of malate, with incorporation of carbon dioxide (CO_2) and subsequent decarboxylation to phosphoenolpyruvic acid (figure 2C).

When hydrocortisone is given to experimental animals, it results in increased glucose-6-phosphatase activity, increased fructose diphosphatase activity, and increased incorporation of CO_2 into hepatic glycogen and glucose.[11] Thus, adrenocortical extract is effective in increasing total synthesis of carbohydrate. In rats treated with large doses of cortisone, the rate of incorporation of labeled pyruvate and CO_2 into blood glucose or liver glycogen was increased between ten- and a hundredfold.[5]

To summarize, glucocorticoids apparently have a firmly established metabolic effect upon hepatic glucose production. It is possible to point out the individual steps which are able to direct the metabolic flow in a specific direction.

Glucocorticoid effect on protein metabolism. It has been generally accepted that glucocorticoids increase protein catabolism and decrease protein anabolism.[12] This has been corroborated by the fact that glucocorticoid administration results in increased amino acid release by extrahepatic tissue and the entrapping of these amino acids by the liver.[5] Hydrocortisone also results in the increased rate of transamination and increased activity of transaminases in hepatic tissue. These observations are compatible with the concept of increased mobilization of protein by way of amino acids to the liver, with presumably their eventual conversion to glucose.[5]

Despite excellent evidence for increased gluconeogenesis and for protein catabolism as a result of glucocorticoid action, the increased glycosuria produced by adrenal extract administration cannot be accounted for entirely by increased protein catabolism as reflected by urinary excretion of nitrogen. It is felt that the effects on carbohydrate account for some of the discrepancy, and it also has been postulated that the steroids interfere with glucose utilization. Other explanations for the discrepancy are accelerated resynthesis from three carbon fragments, the use of glycerol from the mobilization of fatty acids, and the glucose-sparing action of increased lipid oxidation.[5]

Glucocorticoid effect on lipid metabolism. There is no doubt that glucocorticoids exert an important effect on over-all lipid metabolism as seen in altered fat distribution in hypersteroid states. Administration of glucocorticoids will increase ketone production, as well as blood and urinary glucose levels, in the diabetic state.[13] However, in vitro experiments have failed to show a direct effect of glucocorticoids on adipose tissue as measured by fatty acid synthesis.

Role of ACTH. ACTH exerts an effect on adrenal glycogen similar to that which occurs with epinephrine in liver and muscle and glucagon in liver.[14] This glycogenolytic activity of

ACTH appears to proceed along the same pathway as illustrated in figure 1. In some manner not yet clearly defined, this metabolic pathway exerts an influence on steroid synthesis.

Observations in man. Glucocorticoid effects on glucose balance in human beings agree with the information available in intact animals and isolated tissues. Patients with Addison's disease exhibit fasting hypoglycemia and subnormal urinary nitrogen excretion, while glucocorticoid administration increases fasting blood glucose levels and urinary excretion of nitrogen. It also has been observed that elevated blood values of lactate and pyruvate are a characteristic feature of spontaneous or induced hyperadrenocorticism, which might be interpreted as a decreased ability to metabolize pyruvate.[15]

From the clinical standpoint, it has been recognized that several important features of hyperadrenocorticism directly suggest the importance of the adrenal cortex to protein catabolism and anabolism. This is evident in Cushing's syndrome, which has as one of its characteristics marked and widespread protein depletion in muscle and supporting structures, such as skin, blood vessels, and bone. Evidence of protein derangement may be present in these patients before the occurrence of grossly deranged carbohydrate metabolism.[5]

As previously noted, there is also no doubt that the glucocorticoids exert an important effect on over-all lipid metabolism. Patients with Cushing's syndrome exhibit a loss of peripheral adipose tissue with an increase in centrally located fat, particularly in the abdominal and interscapular regions. This clinical observation not only suggests an effect of glucocorticoids on adipose tissue but also suggests that adipose tissue in different areas of the body may respond differently to increased glucocorticoid activity.

Cushing's syndrome. Excessive secretion of cortical steroids by hyperplastic and hypertrophic adrenal glands or by an adrenocortical tumor eventually leads to full-blown manifestations of Cushing's syndrome, of which loss of carbohydrate tolerance is one of the most frequent and consistent.[2] A diabetic reaction to the glucose tolerance test was reported in 31 of 33 patients with Cushing's syndrome. Frank diabetes occurred in 5 cases.[16] Of 44 patients with Cushing's disease reported by Thorn and associates,[5] 33 had abnormal glucose tolerance tests, 15 had glycosuria, 13 had fasting hyperglycemia, and 11 had overt diabetes mellitus. Of 4 cases diagnosed as spontaneous Cushing's syndrome in ten years at Minneapolis Veterans Administration Hospital, evidence of carbohydrate derangement existed in 3 patients, the other not having been completely worked up from this point of view (table 1).

TABLE 1
EVIDENCE OF CARBOHYDRATE DERANGEMENT IN CUSHING'S SYNDROME

Total cases	4
Number investigated for carbohydrate derangement	3
Abnormal glucose tolerance	2
Glycosuria	2
Fasting hyperglycemia	1
Overt diabetes	1

Since this diabetic state is associated with increased hydrocortisone secretion, the term steroid diabetes has been applied to it.[17] Several features distinguish this type of diabetes from true pancreatic diabetes:

1. Great elevation of the fasting level of blood glucose is unusual.

2. Relative insensitivity to exogenous insulin is the rule, while ketosis is rare.

3. In the early stage of Cushing's syndrome, negative nitrogen balance exists even when glycosuria is minimal or absent.

4. Urinary excretion of 17-hydroxycorticoids is elevated.

5. Levels of blood lactate and pyruvate are greatly elevated. It has been suggested that the increase in blood levels of pyruvic acid may be due to interference with the normal mechanism for its metabolism.[17]

6. Steroid diabetes is reversible and disappears after surgical removal of the adrenal lesion.

Exogenous Cushing's syndrome. The characteristics of steroid diabetes observed in spontaneous Cushing's syndrome is reproducible in healthy subjects by administration of large doses of ACTH, cortisone, or hydrocortisone. When these steroids are administered to diabetic patients, hyperglycemia and glycosuria usually increase in intensity, but the degree of change with a given dose varies from patient to patient. Thus, the development of decreased carbohydrate tolerance depends on: (1) the dose of ACTH or steroid employed; (2) the duration of administration; (3) whether the index is the fasting blood sugar level or the glucose tolerance test, which is more sensitive; and (4) the individual.

The appearance of a diabetic state in the early period of administration of adrenal steroid may

be due to insufficient augmentation of insulin secretion to compensate for the extrapancreatic diabetogenic action of glucocorticoids. However, depression of insulin production is another possible explanation.[18] As time goes on, the magnitude of the beta cell response to the diabetogenic action of adrenal steroids may determine the degree of eventual loss of carbohydrate tolerance. The large functional reserve of insulin-producing cells usually is sufficient to compensate for the diabetogenic action of cortisone and to prevent clinically significant impairment of carbohydrate tolerance.[5,17]

In the initial stages of cortisone administration, this adaptive response may not be great enough to prevent mild reduction of carbohydrate tolerance. With prolonged administration, the tolerance may return to normal. This adaptation does not occur in patients who have had diabetes before the administration of steroids.

From a clinical point of view, the presence of diabetes mellitus does not contraindicate administration of adrenal steroids. The intensification of hyperglycemia and glycosuria usually can be controlled by increased doses of insulin.

The adrenal steroids elicit a temporary diabetic state much more commonly in relatives of diabetic patients than in individuals without a family history of diabetes.[19] In an attempt to unmask the potential diabetic person who manifests normal carbohydrate tolerance by present testing methods, a cortisone-modified glucose tolerance test was employed to bring to the surface a subclinical defect in the metabolism of carbohydrate. It was found that 24 per cent of presently nondiabetic relatives of diabetic patients responded to this test positively, while this same response was observed in only 3 per cent of people without a known family history of diabetes. When applied to patients with diabetes, this test was positive in 94 per cent of cases.[17,19]

Hypofunction of the adrenal cortex. The various forms of adrenal insufficiency may be classified as acute or chronic. Adrenal hemorrhage and surgical removal of adrenal tissue make up the first group, while Addison's disease, hypopituitary conditions, and exogenous steroid depression of the adrenal glands comprise the second group. Addison's disease is the most frequent clinical condition and also the most important with regard to carbohydrate metabolism.

Addison's disease. With regard to carbohydrate metabolism, patients with Addison's disease manifest the following changes:[17,19–21] (1) inability to fast or to take low carbohydrate diets without profound hypoglycemia, (2) greatly increased sensitivity to exogenous insulin, (3) abnormally intense secondary hypoglycemia after oral or intravenous administration of glucose, (4) high fasting respiratory quotients, (5) symptoms of hypoglycemia at somewhat higher levels of blood sugar than when corticoids are present, and (6) low urinary excretion of nitrogen in the fasting state.

Administration of cortisone or hydrocortisone in physiologic amounts reverses these effects of adrenal insufficiency and results in: (1) maintenance of blood sugar on prolonged fasting, (2) increase in blood sugar levels during glucose tolerance tests, (3) decreased sensitivity to hypoglycemic symptoms at borderline levels of blood sugar, (4) a fall in respiratory quotient, (5) decreased sensitivity to exogenous insulin, and (6) increased urinary nitrogen during fasting.

The coexistence of Addison's disease and diabetes mellitus is rare but represents an excellent opportunity to assess the influence of adrenocorticoids on carbohydrate metabolism in man. This is illustrated in the following case history.

E.S., a 36-year-old man, was first seen at the VA Hospital in 1954 because of upper respiratory infection and visual hallucinations. He had had alopecia, progressive weakness, fatigue, muscle aches, anorexia, and headaches. Physical examination revealed a blood pressure of 90/60, generalized increased pigmentation, buccal pigmentation, alopecia areata, infected pharynx, palpable spleen and liver, and bilateral Babinski's sign. Laboratory findings included a mild anemia of 12 gm. per cent; leukocytosis; fasting blood sugar, 93 to 117; sodium, 131; chloride, 94; carbon dioxide, 19; and potassium, 5.4. Addison's disease was suspected. The water loading test was positive, but, after further observation, the patient was believed not to have Addison's disease.

E.S. was readmitted October 1959 with frank diabetes mellitus. Fasting blood sugar was 160 to 300 without ketonuria. The patient now had polyuria and polydipsia, as well as weakness and fatigue. He gave a family history of diabetes mellitus. Physical examination again revealed skin and mucosal pigmentation, alopecia, decreased body hair, palpable spleen and liver, and bilateral Babinski's sign. Blood pressure was again 90/60. Laboratory findings at this time were an anemia of 11.5 gm. per cent; sodium, 124; chloride, 88; carbon dioxide, 20.6; and potassium, 5.9. No abdominal calcification could be seen on the roentgenogram. Protein-bound iodine was 7.3 gamma, radioactive iodine uptake was 9 per cent, and calcium phosphorus was normal.

Investigation of adrenal status revealed urine excretion of 17-hydroxycorticoids, 1.1 mg. per twenty-four hours; of corticoids, 0.41 mg. for six hours, with 0.27 mg. after ACTH stimulation; and of plasma corticoids, 5.5 mg. before and after ACTH. There was no activity of the pituitary-adrenal axis.

Treatment with 0.1 mg. of 9 α-fluorocortisone, 4 mg. of long-acting methyl prednisolone, and 20 to 35 units of insulin resulted in general improvement and reduction of pigmentation.

The present problem is regulation of diabetes. Also of interest is the development of Addison's disease in a nephew of this patient.

The total number of such cases in the literature has reached 66.[20–22] Until 1949, a review of the literature revealed only 24 cases.[19] The increased number reported during the past ten-year period probably represents more frequent clinical recognition and the diabetogenic influence of administered steroids.

The coexistence of these two diseases can be evaluated by grouping the cases as to the time of onset of the Addison's disease and the diabetic state.[22] A review of the 66 reported cases shows the following distribution: (1) 23 patients with an initial diagnosis of Addison's disease in whom diabetes mellitus subsequently developed, (2) 38 patients in whom diabetes mellitus preceded the onset of Addison's disease, and (3) 5 patients in whom the onset of both conditions apparently was simultaneous.

Only 7 of the 66 patients from the literature are reported as never having had hypoglycemic symptoms. The amount of insulin required ranged from none to a high of 75 units. About 30 per cent of cases required 20 to 40 units of insulin daily. When diabetes preceded Addison's disease, there was an almost universal drop in the insulin requirement. The timing between the recognition of the two diseases ranged from simultaneous diagnosis to a twenty-two-year difference.[22]

A review of the charts at the VA Hospital for the past ten years reveals a total of 13 cases of spontaneously occurring Addison's disease, of which 4 had concomitantly occurring diabetes mellitus (table 2)—a startlingly large number compared to the literature. In 2 of the cases, Addison's disease preceded diabetes, with the reverse in 1 case. Simultaneous occurrence appeared in 1 case. All but one of the patients had hypoglycemic episodes, with one patient's death being attributed to such an occurrence. One patient needed 80 units of insulin to maintain diabetic balance. Of the cases reported in the literature, only one had a similar high dosage requirement—75 units.

There has been only one death in this group of 4 patients. At autopsy, adrenal cortex and islet cell atrophy was noted. Further information with regard to these patients is available in table 2.

Adrenocortical insufficiency should be suspected when a diabetic patient manifests a sharp decrease in total insulin requirement together with great instability of the blood sugar level and extreme hypoglycemic episodes. Despite amelioration of the diabetic state, the patient shows the progressive deterioration characteristic of untreated Addison's disease. Administration of physiologic amounts of glucocorticoids results in restoring the previous intensity of the diabetes. However, the patient will derive important benefits from such steroid therapy. These steroids not only alleviate the symptoms of adrenocortical insufficiency but also make the diabetes easier to control with insulin. Although more insulin is required, susceptibility to hypoglycemic episodes is sharply diminished. This principle has been used in the management of persons with brittle diabetes in an effort to establish some element of stability. There is no good evidence, however, that decreased endogenous production of hydrocortisone is the cause of brittleness in clinical diabetes.[17,21]

As has been mentioned, unexplained amelioration of the diabetic state should cause suspicion

TABLE 2

ADDISON'S DISEASE AND DIABETES MELLITUS*

(4 cases)

Case	*Year of last contact*	*Age at last contact*	*Respective onset of 2 diseases*	*Insulin dosage*	*Hypoglycemic episodes*	*Family history*	*Etiology of Addison's disease*	*Steroid*
G.A. 104,076	1950 Dead	25	Addison's disease six years before diabetes	Regular insulin, 5-10 U.	Yes	None	Primary adrenal atrophy at autopsy	DOCA. Adrenal extract
W.N. 103,156	1959 Alive	38	Diabetes four years before Addison's disease	80 U. N.P.H. in divided doses	Yes	No diabetes; excessive pigmentation	?	9 alpha fluoro. Prednisone
R.S. 69,415	1960 Alive	35	Addison's disease fourteen years before diabetes	22 N.P.H.	No	Diabetes	?	DOCA, switched to 9 alpha fluoro. Hydrocortisone
E.S. 94,085	1960 Alive	36	?Simultaneous	35 P.Z.I.	Yes	Diabetes and Addison's disease (not in same people)	?	9 alpha fluoro. Methyl prednisolone

*These 4 cases will be published in detail in the near future.

of coexisting adrenal insufficiency. However, such a condition occurs in other states, both endocrine and nonendocrine. Thus, hypothyroidism and hypopituitarism will alleviate the severity of the diabetes, while hyperthyroidism and acromegaly will aggravate it.

In contrast to the improvement in carbohydrate metabolism that occurs when adrenal insufficiency develops in a diabetic patient, the appearance of diabetes in a patient with previously well-controlled Addison's disease is characterized by an apparent exacerbation of the adrenal insufficiency. In such cases, there is a return of anorexia, lassitude, loss of weight, and low blood pressure. The physician is tempted to increase the amount of steroid replacement therapy, but it is the osmotic diuresis caused by glycosuria which is causing secondary renal loss of salt and water. Increasing the dosage of glucocorticoids does not correct the situation and may magnify it by augmenting the glycosuria. Large doses of salt-retaining steroids are likewise relatively ineffective in preventing further losses of salt and water. However, when the diabetes is recognized and appropriate treatment with insulin and diet instituted, control of the Addison's disease is readily achieved with replacement therapy similar to that required before onset of the diabetes.[17]

Aldosteronism and diabetes mellitus. Primary aldosteronism is now a well-recognized clinical entity. This syndrome is characterized by periodic muscular weakness, intermittent tetanus, paresthesia, polyuria, polydipsia, and hypertension with hypokalemia, hypernatremia, and alkalosis.[23,24] Approximately 40 such cases have now been reported in the literature.

Conn and Fajans[17] state that 30 per cent of patients with primary aldosteronism exhibit decreased tolerance for carbohydrate. In the one case of primary hyperaldosteronism diagnosed at the VA Hospital, the patient had a fasting blood sugar of 106 mg. per cent and a two-hour postprandial sugar of 162 mg. per cent but did not require insulin. After operation, which revealed diffuse adrenal hyperplasia, the fasting blood sugar ranged from 95 to 99 mg. per cent.

Aldosterone is almost 40 times as effective in maintaining proper electrolyte balance as is hydrocortisone but only two-thirds as effective in influencing carbohydrate metabolism. Only 0.2 mg. of aldosterone is produced daily, as compared to 30 mg. of hydrocortisone.[24,25]

The incidence of secondary aldosteronism—congestive heart failure, cirrhosis, nephrosis, and so forth—associated with diabetes mellitus has not been calculated. In most cases, the level of the hormone is not high enough to account for clinical diabetes. There certainly is a high incidence of diabetes accompanying cirrhosis and congestive heart failure, but the common denominator is probably age and not aldosterone.

Adrenogenital syndrome. In this syndrome, there is increased secretion of androgens by the adrenal cortex. This group of steroids has little if any direct effect on carbohydrate metabolism. Since the syndrome is often accompanied by a state like Addison's disease, it is not surprising to find no significant reference to diabetes mellitus associated with the syndrome.[2]

ADRENOCORTICAL FUNCTION IN DIABETES MELLITUS

The adrenocortical hormones have been said to play an important role in the etiology of the chronic vascular complications occurring in diabetes mellitus. There are claims stating that the severity of the vascular changes is due to the level of secreted adrenal steroids. However, there are counter-claims denying this theory.[1,5,26,27]

The evidence in favor of this view is largely indirect and circumstantial. The following points have been cited:[17]

1. Pregnancy is known to be associated with increased adrenocortical function. During pregnancy, diabetic retinopathy may appear or progress, subsiding after termination of pregnancy.

2. Diabetic retinopathy has occurred in patients receiving intravenous ACTH.

3. Diabetic patients with retinopathy have a greater urinary excretion of corticosteroids than do diabetic patients without retinopathy.

4. Patients with diabetic retinopathy have a greater adrenal response to ACTH than do patients without this complication.

5. Patients with the Kimmelstiel-Wilson syndrome have heavier adrenal glands post mortem.

6. Patients with Kimmelstiel-Wilson syndrome have more lipid vacuolation of the zona fasciculata and demonstrate a greater incidence of adrenocortical adenomas than do patients without this syndrome.

7. Administration of cortisone and ACTH to alloxan rabbits produces diabetic retinopathy and Kimmelstiel-Wilson syndrome.

Despite the circumstantial character of this evidence, experimental adrenalectomy and hypophysectomy have been performed in persons with diabetes associated with rapidly developing or far-advanced retinopathy, nephropathy, and other vascular disorders[17,28] with at least a sug-

gestion of either improvement or slowing of progression. After adrenalectomy, of course, the patient needs steroid replacement. The procedure leaves much to be desired and has not received adequate trial or follow-up.[30]

SUMMARY

1. Diabetes mellitus and carbohydrate metabolism are influenced by other endocrine states. The pituitary, thyroid, and adrenal glands play important roles.

2. Epinephrine will produce a diabetes-like condition by its influence on hepatic and muscle glycogenolysis. Pheochromocytomas frequently are associated with such adrenalin diabetes. Three cases seen at this hospital are noted.

3. The glucocorticoids exert a profound influence on carbohydrate, protein, and fat metabolism. Ther steroids act in a diabetogenic manner.

4. In Cushing's syndrome, the diabetogenic effect of the adrenal cortex is manifest. Over 75 per cent of patients with Cushing's syndrome have demonstrable abnormalities of carbohydrate metabolism. Four such cases were seen at this hospital.

5. Diabetes mellitus associated with Addison's disease is a rare condition, with only 66 such patients reported in the literature. One case from this hospital is reported. A total of 4 cases of Addison's disease plus diabetes mellitus has been seen at this hospital during the past ten years and has been reviewed.

6. Aldosterone has a relatively weak effect on carbohydrate metabolism. The one case of aldosteronism at this hospital had latent diabetes.

7. Adrenocortical hormones may play a role in the severity of diabetes and its complications. Adrenalectomy and hypophysectomy have not been overly successful in ameliorating diabetic complications.

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Treatment of Constipation in the Postpartum Patient

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Constipation is a frequent problem in the postpartum patient. The majority of patients require some form of therapy by the second day after childbirth. Such treatment usually consists of the highly unpopular second-day enema or one of a lengthy and venerable list of cathartic preparations.

Despite their long service to medicine, it must be remembered that these cathartic preparations have come down to us from a less sophisticated era and do not meet the requirements of modern obstetrical practice. Beil and Brevetti[1] pointed out that irritant purgatives may be excreted in the milk and should be avoided in nursing mothers, bulk laxatives cause fullness and bloating, and saline cathartics are exhausting to the patient and are more inclined to produce cathartic habituation than to re-establish normal bowel habits.

In 1955, Wilson and Dickinson[2] introduced the use of dioctyl sodium sulfosuccinate for the treatment of fecal impaction and lesser degrees of constipation. Two years later, Middleton[3] used dioctyl sodium sulfosuccinate successfully for the treatment of postpartum constipation. This compound emulsifies fats and allows greater penetration of the feces by water. The softened feces is then more easily propelled by weakened or uncoordinated peristaltic movements.

While fecal softening agents have the advantage of being nonirritant and nonhabit-forming, they do not work well in cases of atonic constipation. For this reason, a mild peristaltic stimulant, 1,8-dihydroxyanthraquinone (Danthron), was added.

The preparation used in this study (Doxidan*) differs from that described in that it contains dioctyl calcium sulfosuccinate as the fecal softener and Danthron as a peristaltic stimulant. This calcium salt of dioctyl sulfosuccinate has approximately three times the surface tension lowering ability of the sodium salt and so should be a superior fecal softener.

MATERIALS AND METHODS

At the end of their second day post partum, 234 consecutive patients were questioned concerning their need for a laxative. Of these, 36 had spontaneous bowel movements within the first forty-eight hours and exhibited no further need for this type of therapy. The remaining 198 patients were given 1 capsule of Doxidan and instructed to inform the nurses of the effectiveness of the laxative throughout the third postpartum day. This included the number of bowel movements, consistency of the stool, and any side effects such as cramping or diarrhea. If no results were noted, 1 or 2 capsules were given on the evening of the third postpartum day. If there were still no bowel movements at the end of the fourth day, an enema was given.

RESULTS

Of the 234 patients, 198, or 84.6 per cent, required laxative therapy. In most of these, 1 capsule was sufficient to re-establish normal bowel habits. Forty-eight patients required an additional one or two capsules the following day. It was necessary to resort to enemas in only two patients.

Side effects occurred in only 9.9 per cent of the patients. These consisted of gas and cramps in 6.5 per cent and diarrhea in 3.4 per cent.

Patient acceptance was excellent and the ease of administration and the reduced nursing care required added to the value of this new therapy.

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Occurrence of Relapse on an Antidepressant

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THERE HAVE ALWAYS been risks in assuming responsibility for the treatment of depression. One risk of increasing importance occurs in the treatment of patients who apparently respond to medication, only to relapse while receiving the drug. The literature did not reveal a description of relapse during imipramine hydrochloride (Tofranil) therapy.

Since Kuhn[1] published his results with this antidepressant drug, there have been numerous articles expounding its clinical effectiveness. Reports vary all the way from 82 per cent good or moderate response of endogenous depression[2] to less than 20 per cent favorable response of endogenous depression.[3]

We have used imipramine extensively because of our confidence that the drug is helpful in many cases. Imipramine does not, unlike many of the new antidepressive drugs, have any monamine oxidase inhibitory effect but rather is chemicaly related to the phenothiazine drugs. It does not appear to have any direct stimulating effect on the central nervous system and is classified as a central nervous system suppressant by Schiele and Benson.[4]

CASE REPORTS

The following three patients were admitted to the University of Minnesota Hospitals. All experienced a relapse while receiving imipramine therapy (see table).

I.O., a 36-year-old woman, was admitted on August 1, 1960, with guilt feelings and overconcern about religion, morality, and personal worth. She was sad and had insomnia, weight loss, anorexia, and loss of interest in her previous activities. These symptoms began about two months before admission. History revealed that the patient had had 2 attacks similar to her present illness eighteen and ten years before admission. Both of these attacks had required hospitalization and had been treated with electroshock therapy. Physical condition was essentially normal. Mental status examination indicated depression and paranoid delusions.

During her hospitalization, the patient was first treated with a course of ataractic medication and monamine oxidase inhibitors, without response. She was then started on a three-week course of imipramine, 100 mg. daily, with apparently excellent results. After four weeks of hospitalization, the patient was judged ready for discharge. However, on the day of discharge, a sudden relapse occurred, with the return of a full-blown psychotic depressive picture. Decision was made to give the patient electroshock therapy, and she received a total of 12 treatments. She was discharged, much improved, on October 6, 1960. Discharge diagnosis was manic-depressive psychosis, depressed type.

G.R., a 67-year-old woman, was admitted during her seventeenth episode of manic-depressive disease, depressed type. Symptoms of depressed mood, motor retardation, anorexia, and insomnia began two months before her admission on June 27, 1960. She was given imipramine, starting with 150 mg. daily. After three weeks, this was increased to 200 mg. daily. Two weeks after institution of imipramine therapy, she was also placed on thioridazine, up to 200 mg. daily. Very little change in her depression was noted for approximately four weeks, after which her mood began to improve. She seemed much less depressed but at times somewhat euphoric. For this reason, the imipramine dosage was reduced to 75 mg. daily and was continued until the time of her discharge on August 26, 1960. It was felt that she was greatly improved with respect to her depression. She was sent home on imipramine, 50 mg. daily. She was readmitted on September 7, 1960, approximately ten days after discharge, as profoundly depressed as on her previous admission. At this time, all medication was discontinued, and the patient was given a course of 10 electroshock treatments over twenty-one days. With this treatment, the patient improved remarkably, and she was discharged on October 28, 1960.

O.G., a 58-year-old man, was first admitted on June 23, 1960, with severe agitated depression characterized by insomnia, anorexia, and many somatic complaints. There was evidence of bizarre mentation and visual hallucinations. The patient was greatly concerned about an alcoholic brother, with whom he lived. Physical examination and routine laboratory work were within normal limits. The patient was treated with chlorpromazine, 400 mg. daily, and imipramine, up to 150 mg. daily. Twenty days later, his depression started to clear, as did his psychotic mentation, and he was discharged on

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August 17, 1960, on imipramine, 50 mg. daily. Discharge diagnosis was psychotic depressive reaction.

One week later, the patient was readmitted with depression as profound as on the previous admission. He related that his alcoholic brother had left home for three days shortly after his return. On readmission to the hospital, this patient was again treated with imipramine, dosage being increased to 100 mg. daily, and 20 mg. of proclorperazine daily. Variations of drug therapy were tried with imipramine. The proclorperazine was continued until September 16, 1960, at which time the patient was placed on chlorpromazine, 100 mg. daily. The chlorpromazine and the imipramine were continued at 100 mg. each daily through September 23, 1960, when the dosage was reduced to 50 mg. each daily. On October 18, 1960, both drugs were discontinued. The patient was given a series of 7 electroshock treatments, starting on September 30, 1960, and ending on October 14, 1960. On this regimen, his depression cleared, and on discharge on November 26, 1960, the patient was considerably improved.

DISCUSSION

Depression is one of the more common psychiatric syndromes and is frequently described as being one of the worst kinds of suffering. It is difficult not only for the patient but for his family and the surrounding community. Through advances in the medical and pharmacologic sciences, physicians now have better tools to give relief to patients who suffer from depression and to prevent what could be serious tragedy.

As with other new therapies, complications peculiar to the new treatment are likely to occur. One of these is the problem of the patient who apparently responds to treatment, only to return to the previous morbid state. We found, in the cases reported here, that relapses appeared to be rather sudden and severe, as if the "props" had been rapidly pulled from the patient. A sudden return to illness after having some relief from the throes of depression is exceedingly discouraging and may add to the danger of suicide.

There are several possibilities to consider when analyzing the etiology of relapse; for instance, failure to consider environmental stresses can make the difference in dealing with depression. If it is felt that the environmental stress remains severe even after the patient shows definite relief of symptomatology, extreme caution must be used as the patient is being reintroduced to this environment. To correctly assess the environment of the patient, it is wise to enlist the aid of a responsible member of the family.

Another most important consideration we have noted in our work with antidepressants is that frequently people get over a depression not primarily because of the drug but because they are in a helpful relationship and they feel that someone is taking an interest in helping them with their particular problems. In instances of this nature, any drug instituted could have good results. However, if the physician becomes satisfied too quickly that the drug has caused relief of depression and withdraws his full interest from the patient during patient-doctor contacts, the supportive effects of the relationship will be reduced, and relapse may occur.

Whether the drug or the relationship is most important, it is safer to continue medication in

COMPARISON OF RELAPSE OF 3 PATIENTS DURING IMIPRAMINE TREATMENT

Sex and age	*J.O. female (36)*	*G.R. female (67)*	*O.G. male (58)*
Diagnosis	M-D* disease, depressed type	M-D disease, depressed type	psychotic depressed reaction
Maximum dose	100 mg.	200 mg.	150 mg.
Period of imipramine therapy before improvement	5 days	25 days	20 days
Dose at relapse	100 mg.	50 mg.	50 mg.
Period of imipramine therapy before relapse	21 days	60 days	60 days
Ataractics used in addition	Perphenazine	thioridazine hydrochloride	chlorpromazine and proclorperazine dimaleate
Period from discharge to relapse	0 days	12 days	7 days
Treatment of relapse	electroshock therapy	electroshock therapy	electroshock therapy
Results of treatment of relapse	good	good	good

*M–D-manic–depressive

good dosage for a longer period. Many patients will refuse to see their doctors unless they are getting some form of "medical" treatment acceptable to them, such as pills, shots, or other physical treatment.

We suggest the following guide as being helpful in using antidepressant medications:

1. Do not forget the suicidal risk in each case and protect the patient from this complication.

2. In instances of depression other than the very mild, continue medication for at least three months.

3. Maintain interest in the patient, as the doctor-patient relationship may be the key to success. See the patient at least once a week at first and later twice a month. Making scheduled appointments is a good technic to demonstrate interest in the patient.

4. Do not assume responsibility for a depressed patient without the knowledge of a responsible member of the family.

5. Be alert to the significance of signs of relapse.

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Emotional disturbance appears to be a prominent cause of irritability, depression, and headache before menstruation. Meprobamate in doses of 400 mg. three times a day often will provide total or pronounced relief. If the tranquilizer is not effective, ½ gr. of chlorothiazide twice daily, a progesterone derivative, or a combination of drugs should be tried.

Hormone imbalance and water retention may be the most important etiologic conditions in some cases. Premenstrual swelling of the breasts and abdomen and a weight gain of 3 lb. or more is noted in one third of women. However, water retention may occur without premenstrual tension. Perhaps somatic changes produce discomfort in some women only when aggravated by psychologic disturbances. Therefore, even when fluid retention is apparent, a tranquilizer may be more effective than chlorothiazide.

Efficacy of meprobamate, chlorothiazide, 2 oral progesterone products, and a placebo for 32 women with premenstrual tension was compared. Symptoms included irritability in 24, depression in 23, headache in 15, listlessness in 5, vertigo in 3, and nausea in 1.

The drug was taken nine days before the expected date of menstruation and continued until menstruation commenced. Each woman used each therapeutic agent for three months. One half of patients had complete or pronounced relief of symptoms with meprobamate, one third with chlorothiazide, and one fifth with progesterone.

B. P. Appleby: A study of premenstrual tension in general practice. Brit. M. J. 5170:391-393, 1960.

Treatment of Salicylate Intoxication Using Extracorporeal Hemodialysis

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The derivatives of salicylic acid are used in larger amounts by the laity and by the medical profession than is any other medication.[1] As a result of the widespread use of the salicylates, accidental poisoning and suicide attempts involving these medications are frequent. The most common salicylate derivatives resulting in intoxication are methyl salicylate (wintergreen oil) and acetylsalicylic acid (aspirin). Done and Otterness[2] refer to data from the U. S. Bureau of Census describing 526 reported instances of fatal salicylate poisoning from 1933 to 1943.

There is wide individual variation in the amount of salicylate required to produce toxic symptoms. As little as 6 cc. of methyl salicylate has been fatal for children, but doses larger than 20 gm. have been ingested by adults without fatal results. Acetylsalicylic acid is rapidly absorbed by the gastrointestinal tract, and peak plasma levels occur in two to four hours. However, the excretion and breakdown are much slower and require twenty-four to thirty hours. As a result, a cumulative effect occurs with multiple doses. Approximately 80 per cent of the absorbed salicylate is excreted in the urine, partly as free salicylate but more readily as salicyluric acid and salicyl glucuronide. In the treatment of rheumatic fever, a plasma salicylate level of 25 to 30 mg. per 100 cc. is generally felt to be the most effective; toxic symptoms are usually apparent with a plasma salicylate level over 30 mg. per 100 cc.[3] and are the same regardless of the type of salicylate taken. They consist of tinnitus, nausea, vomiting, hyperventilation, and, often, mental changes of excitement and restlessness.

Treatment of salicylate intoxication is aimed primarily at correction of the changes in acid-base balance and speeding of renal excretion of salicylates. Abel and associates[4] first demonstrated removal of salicylate from the blood by dialysis in animal experiments in 1913. The first successful application of hemodialysis in man was reported by Schreiner and associates[5] in 1955. The only measures available for removal of salicylate at a rate greater than endogenous breakdown and excretion are hemodialysis and exchange transfusion. Exchange transfusion has been used with success in children but is felt to be less effective in salicylate removal than is hemodialysis.[6]

The importance of rapid effective removal of salicylates was emphasized by Doolan and associates[7] when they reported pathologic findings in the brain stem of a fatal case of aspirin poisoning suggesting irreversible brain damage. Eyschen and associates[8] reported degeneration and necrosis of the medulla and upper cervical cord after salicylate intoxication and severe acidosis in a 2-year-old child in spite of adequate dialysis with removal of the salicylate and correction of the acidosis. It would then seem as though severe salicylate intoxication can produce irreversible neurologic damage.

Early and effective treatment of salicylate poisoning utilizing extracorporeal hemodialysis appears to be an efficient method of abruptly lowering the plasma salicylate level and, if used early, should prevent neurologic damage. The following case demonstrates the effectiveness of hemodialysis with the Kolff twin-coil disposable artificial kidney in the treatment of salicylate intoxication.

CASE REPORT

A 45-year-old housewife was transferred to St. John's Hospital in Fargo, North Dakota, on December 14, 1960, in coma. The patient had been well until 11 A.M. the day before admission, when she took 100 5-gr. aspirin tablets in a suicide attempt. Following ingestion of the aspirin, she had vomited an unmeasured amount and, approximately six hours after ingestion, was admitted to another hospital, where gastric lavage was done. At this time, her temperature was 101.2° F.; pulse, 96; respirations, 22 and deep; and blood pressure, 110/70. The patient was semicomatose and responded to pain. Lab-

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oratory work on admission showed a leukocyte count of 16,000 and a trace of sugar in the urine. The next morning, twenty-one hours after ingestion of the aspirin, the patient was comatose. Her temperature was 104° F. and respirations, 28 and labored. Her laboratory examination demonstrated a blood salicylate level of 98.6 mg. per cent, fasting blood sugar of 109 mg. per cent, carbon dioxide combining power of 13.0 mEq., prothrombin time of 20.5 seconds (control 12.5 seconds), and a trace of albumin and sugar in the urine. The patient was then transferred to St. John's Hospital for extracorporeal dialysis. At the time of transfer, she had received 2,000 cc. of 5 per cent dextrose in distilled water, 1,000 cc. of 1/6 molar sodium lactate, and a small amount of sodium bicarbonate intravenously.

On admission, the patient was completely comatose and did not respond to pain. Blood pressure was 90/70; pulse, 120; temperature, 105° F.; and respirations, 30 per minute and very deep. Her eyes were fixed, and no corneal reflex was obtained. Deep tendon reflexes were minimal but present. Laboratory examination on admission showed a hemoglobin of 14.9 gm., leukocyte count of 25,950, hematocrit of 45, carbon dioxide combining power of 15.3 mEq., chloride of 100 mEq., potassium of 3.3 mEq., and sodium of 143 mEq. per liter. Shortly after admission, blood pressure fell to 70/50, and norepinephrine was added to an intravenous infusion of 5 per cent dextrose in distilled water to keep the systolic blood pressure between 100 and 110.

Extracorporeal dialysis was begun approximately one and one-half hours after admission, twenty-seven hours after the ingestion of aspirin. After one and one-half hours of dialysis, the patient began to move her arms and legs and her respirations had slowed to 22 per minute. After six hours of dialysis, the patient responded to verbal stimuli and could speak and drink fluids and her temperature had fallen to 100° F. She was returned to her room in good condition, and the intravenous vasopressor was slowly reduced and discontinued, with her blood pressure remaining at 110 systolic. Analysis of the bath solution showed a concentration of 3.2 mg. per cent of salicylate at the end of the first two hours. Laboratory examination after dialysis showed a blood salicylate level of 33 mg. per cent and a carbon dioxide combining power of 21.3 mEq. The patient's postdialysis course was uneventful, and she was discharged under psychiatric care on the fifth hospital day.

DISCUSSION

The dramatic reversal of the clinical signs of severe salicylate intoxication in this patient demonstrates the effectiveness of hemodialysis. Although Hoffman[3] reports recovery with a plasma salicylate level of 85 mg. per 100 cc., salicylate levels of over 70 mg. per 100 cc. ordinarily are fatal. In this patient, who demonstrated hyperpyrexia, coma, and peripheral vascular collapse, a fatal outcome would have been expected without hemodialysis. The hyperpyrexia and peripheral vascular collapse were felt to be manifestations of involvement of the brain stem.

The removal of salicylate was calculated by measuring the amount of salicylate in the circulating bath solution at the end of two hours of dialysis. The concentration of salicylate at this time in the bath was 3.2 mg. per 100 cc., or a total of 3.2 gm. of salicylate in two hours. With the flow through the twin-coil kidney at 250 cc. per minute and a pressure of 130 mm. Hg, this represented removal of 26.6 mg. of salicylate per minute. Because of declining plasma concentrations of salicylate resulting from this removal, the rate of removal would gradually decrease. As the usual renal excretion of salicylate is only 75 to 150 mg. per hour, this represents a manifold increase in salicylate clearance.

CONCLUSIONS

Extracorporeal hemodialysis has been demonstrated to be a safe and effective method of removing salicylates from the body. Dialysis also accomplishes correction of the changes in acid-base balance which usually accompany salicylate poisoning. Because of stimulation of the respiratory center with hyperventilation and resultant loss of CO_2, the acid-base balance shifts toward respiratory alkalosis. However, the excretion of base with the salicylate in the kidney tends to produce a metabolic acidosis. Thus, in salicylate poisoning, two opposite disturbances in acid-base balance occur, and plasma *p*H levels may be necessary to follow accurately the patient's course. Use of the artificial kidney greatly simplifies the chemical management of these patients and permits prompt and accurate restoration of the chemical equilibrium. Since hemodialysis accomplishes removal of salicylates from the body and correction of the changes in acid-base balance promptly and safely, it is an important part of the treatment of the patient with salicylate intoxication. Early dialysis in patients with severe poisoning could well be important in the prevention of irreversible neurologic damage.

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Healing Rib Fracture Simulating Solitary Circumscribed Chest Shadow

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THE PRESENCE of a solitary, well-demarcated, circumscribed shadow in the chest film immediately suggests the presence of a neoplasm. Frequently, however, these shadows are inflammatory rather than neoplastic. Differential diagnosis of these rounded shadows is usually very difficult, and exploratory surgery is often the only means of obtaining a definitive diagnosis.

Recently, 4 cases have come to our attention which were described as having a solitary circumscribed nodule in the lung. These were subsequently proved to be healing rib fractures. In 2 cases, a definitive diagnosis was not made and, because of the possibility of a neoplasm, surgery was performed. In each of these cases, a healing, nonpathologic fractured rib was demonstrated. In the other 2 cases, although the circumscribed lesion appeared to have no contiguity to the rib, planigrams clearly demonstrated the healing rib fracture with the secondary callus sharply circumscribed, explaining the routine chest film findings (figures 1 to 5).

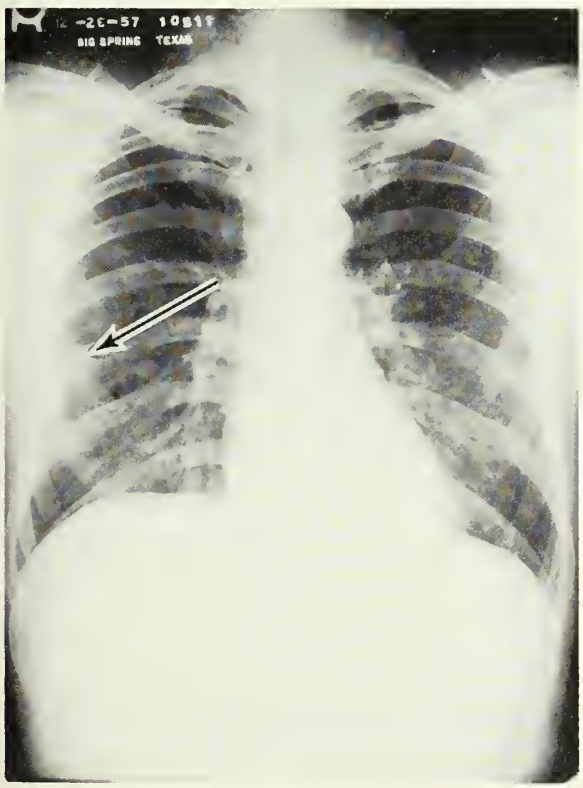

Fig. 1. Circumscribed chest lesion requiring surgery for diagnosis.

The preceding cases show that a healing fractured rib can simulate a pulmonary nodule. In

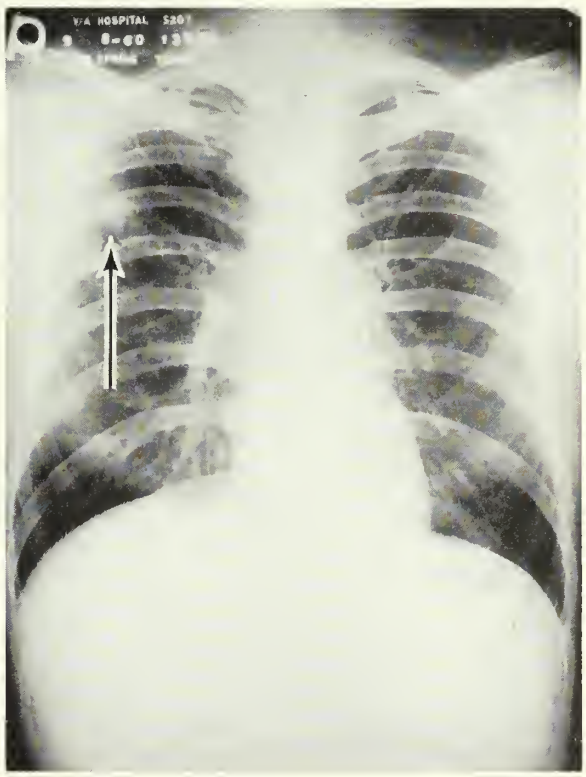

Fig. 2. Circumscribed chest lesion.

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Fig. 3. Planigram of lesion in figure 2 showing a healing fractured rib.

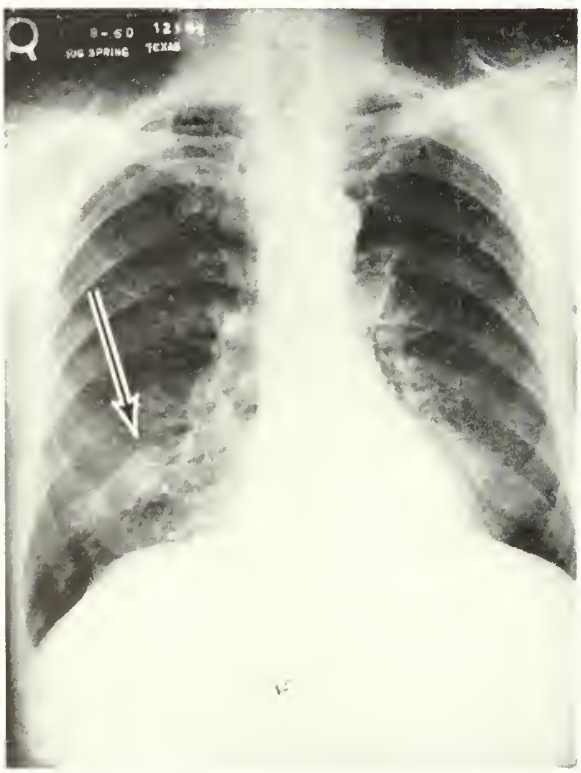

Fig. 4. Circumscribed chest lesion.

each case, there was no history that would lead one to suspect a fractured rib. In view of this, we strongly recommend planigraphic examination of each pulmonary nodule and consideration of a healing fractured rib in the differential diagnosis of solitary circumscribed shadows in the chest.

A review of the major roentgenology textbooks and a search of the literature[1–7] did not reveal any reference to the above findings.

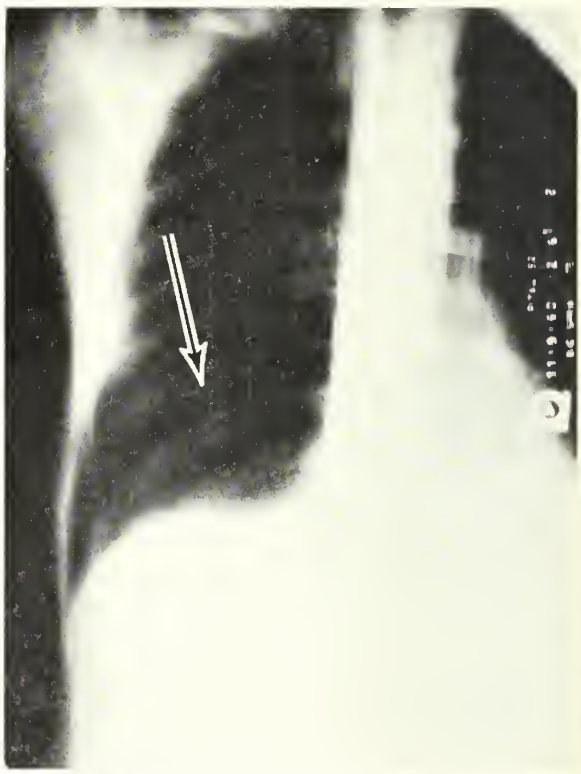

Fig. 5. Planigram of lesion in figure 4 showing a healing fractured rib.

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Glomus Jugulare Tumor with Multiple Distant Metastases

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THE GLOMUS JUGULARE TUMOR is rarely encountered in general practice and rather infrequently in otologic practice. Nevertheless, it is significant, as is evidenced by the increasing number of reports concerning this tumor appearing in the literature. As with any tumor infrequently encountered, much disagreement exists in the reported case records and analyses concerning etiology, nomenclature, treatment, and malignant potential. We will briefly review the literature available to us and present a report of a case with proved malignancy and distant metastases.

REVIEW OF LITERATURE

Guild,[1] in 1941, first described small, glomus like structures of the adventitia of the jugular bulb. In 1945, Rosenwasser[2] described a tumor that he felt was a carotid-body tumor of the middle ear and mastoid, and he described it histologically as a glomus jugulare tumor. These were the first case reports. The term "carotid-body–like tumor" was suggested by Rosenwasser[2] because of the strikingly identical morphology with known carotid-body tumors in the neck. In 1948, Winship and associates[3] suggested the term "glomus jugulare tumor." The next year, the term "nonchromaffin paraganglioma" was suggested by Lattes and Waltner[4] although there was no evidence to indicate that these structures possessed a paraganglionic or any other function —to recognize the fact that the tumors were nonchromaffin-staining. In 1949, Lundgren[5] applied the term "tympanic body tumors." The name "chemodectoma" was suggested in 1950 by Mulligan,[6] because he felt it was a descriptive term for any neoplasm arising from paraganglionic tissue. Zettergren and Lindström[7] labeled these tumors "glomerulocytomas." Gaffney,[8] in 1953, stated that he felt these structures were neither glomus nor paraganglionic; if they had any function, it was probably that of a chemoreceptor organ. Thus, he labeled these neoplasms "receptomas."

Considerably more unanimity exists in the discussion of the pathology of this neoplasm. In 1953, Guild[9] elaborated on his earlier paper[1] and indicated that the glomus jugulare tumor might arise in places other than the jugular bulb area. This idea was commented upon further by Taylor,[10] who pointed out that nonchromaffin paragangliomas vary according to their particular point of origin, such as the tympanic plexus or the adventitia of the jugular bulb. These present either a slow-growing tumor or a more rapidly invasive type of tumor. Rosenwasser,[11] in an excellent article in 1948 in which he reports on a small series of metastatic tumors, emphasizes that the majority of clinically reported cases point up the slowly growing, locally destructive nature of the tumor and that, most often, these cells do not contain mitotic figures and have thus been regarded as benign tumors.

Pathologic[10] and microscopic patterns may vary from that which is very similar to a paraganglionic structure to the potentially hemorrhagic angiomatous type with a rich vascular network and a thin endothelial lining. There is a variation[9] between nonchromaffin paragangliomas with abundant epithelioid cells and the other type of tumor with a rich vascular network. The latter type frequently presents with hemorrhagic tendencies. The tumor is more likely to be invasive when its site of origin is the adventitia of the dome of the jugular bulb than when it is confined to the middle ear, as on the promontory or invading locally into the eustachian tube or ossicular chain and, occasionally, the labyrinth. Riemenschneider and associates[12] and Capps[13] have suggested that these tumors be

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classified into 2 categories: (1) those which are confined to the middle ear and cause deafness and tinnitus but no destruction of the tympanic membrane and (2) those which arise from glomus structures in the jugular bulb and involve the middle ear, the petrous pyramid, and the intracranial cavity. This latter group has been termed malignant because of its invasiveness, although the tumors do not show mitotic figures.

The subject of histologic and/or clinical malignancy has been the point of heated discussion and disagreement throughout the literature regarding this tumor. Generally, the tumor is conceded to be histologically benign but clinically malignant due to the erosion of bone by pressure necrosis rather than actual invasion.[11] It is felt by some[15] that the tumor is invasive in its own right but that the long life of the tumor in most cases indicates that invasiveness is usually moderate.

Case reports supporting the hypothesis of actual metastatic spread are those of Winship and associates,[3] reporting a case of spread to regional lymph nodes; Lattes and Waltner,[4] to the liver; Tamari and associates,[16] to the liver and lungs; Henson and associates,[17] to the liver, lungs, and spleen; Rosenwasser;[11] and Hoople and associates.[18] For the negative side regarding the question of metastases, we have the reports of Gaffney,[5] who stated that these tumors were not metastasizing, though locally very invasive; Figi and Weisman,[19] who felt that instances of reported metastases were probably coincidental occurrences of chemodectoma and carotid-body tumors; and Williams and associates,[20] who regarded with some doubt the earlier report of Lattes and Waltner[4] and further stated that it was the consensus of most observers at that time that these tumors were malignant only because of their encroachment on intracranial structures, that they did not metastasize and, that, therefore, they should be classified as benign neoplasms.

A typical clinical picture involves the following findings: deafness, tinnitus, vertigo, ataxia, otalgia, otorrhea, aural polyp, and pulsation. These symptoms are found most often in the 30- to 60-year age group, more often in women, and are usually of long duration, often having been present from six to ten years.[15] When the tumor is confined to the middle ear, the symptoms are otologic[21] and include loss of hearing, tinnitus, discharge, and vertigo. When a middle ear growth expands while the tympanic membrane is still intact, a reddish or bluish discoloration[10] may show evidence of pressure on the membrane.

Probably the least disagreement arises over the proper treatment for this tumor. Taylor[10] states that the vast majority of these tumors, when confined to the tympanic cavity, can be removed surgically with dissection, using high-power loops. On the other hand, a tumor that originates in the dome of the jugular bulb is more prone to invade bone and grow along the vascular network to the petrous tip, causing clinical vascular phenomena of major proportions. It may present neurologic symptoms affecting the facial nerve as well as any of the other cranial nerves from the fifth to the twelfth, depending upon the direction of expansion. The ideal treatment is considered to be complete surgical removal of the tumor, with irradiation used as an adjunct only. In the so-called nonsurgical cases, such as petrous erosion, recurrent tumors, and cases of incomplete surgery, irradiation also would be indicated.

Rosenwasser[11] states that therapy in a case caught early should be elevation of the drum and complete ablation before the hearing is seriously impaired and before local invasion of adjacent important structures takes place. If erosion of the tympanic membrane and mastoid bone and infection has taken place, the case is then one of middle ear suppuration, and a radical mastoidectomy is indicated. If the entire tumor is resectable, irradiation is withheld; if in doubt, radiation, preferably of a cobalt type, is added after resection. Lastly, if the patient is seen late in the course of the disease, with obvious intracranial involvement, irradiation is the only type of treatment recommended.

CASE REPORT

The following is a case report of our only experience with this tumor, which demonstrated proved metastases to both lungs, the right seventh rib, and the right temporal lobe of the brain.

Mrs. F.K., a 63-year-old housewife, was first seen at this clinic on April 21, 1956, with right earache of one month's duration. The ear had been draining for the preceding two weeks. The patient had been examined elsewhere and given oral penicillin. She had had bilateral mastoiditis in childhood. Initial examination disclosed that the right ear canal was swollen shut and contained much pus and blood. The patient also had a total right facial paralysis of one year's duration.

Laboratory work was essentially within normal limits. Roentgenograms of both mastoids were obtained and demonstrated bilateral chronic mastoiditis, with considerable destruction on the right. Several million units of penicillin was given preoperatively, and the patient was then admitted to Jamestown Hospital, where, on April 26, 1956, a right radical mastoidectomy was done by the endaural approach. External, dural, and sinus

plates were completely eroded and the cavity was filled with granulation tissue. The malleus, incus, and drum were removed, the dura cleaned, and the edges of bone rounded with a burr. An iodoform pack was inserted. The specimen obtained was submitted to the University of North Dakota, whence slides of the specimen were submitted to the Mayo Clinic at Rochester, Minnesota, where a diagnosis of chemodectoma, or nonchromaffin paraganglioma, arising from the glomus jugulare was made.

A hospital chest film showed all pulmonary fields to be clear, and colon and upper gastrointestinal series were essentially normal, with the exception of a few small traction diverticula of the distal esophagus. After the patient's dismissal from the hospital, postoperative x-ray therapy was carried out at this clinic. Daily treatments, utilizing a single portal to the right mastoid region and instituted as deep therapy with a half-value layer of 2.45 curies, were given over a two-week period. The field size was 6.6 cm. in diameter, and the skin dose was 3,240 r. The estimated tumor dose was 2,365 r. The patient was seen for dressings and changes of packs for about the next two months, and by November 5, 1956, the cavity was dry. There appeared to be no recurrence of the tumor, and the right facial paralysis remained complete.

At this point, it should be mentioned that this patient was a member of a religious group which did not rely on medicine or physicians for solutions to its health problem. Consequently, it was most difficult to keep track of her, as she steadfastly refused to continue consulting with us despite the necessity for her to do so.

The patient next went to the University of Minnesota hospitals, where the diagnosis was again confirmed and where roentgenograms showed further bone destruction. It was felt that no further surgical attack could be attempted, and the patient was given an additional course of x-ray therapy consisting of a calculated tumor dose at 7 to 8 cm. depth of 6,600 r over forty-three days. Although the tumor regressed fairly well, it was felt that the treatment was only palliative.

The patient was next seen here in October 1957, when she was admitted to the hospital in a state of coma, appearing to have had a cerebrovascular accident. After oxygen therapy for twenty-four to forty-eight hours, she exhibited a spontaneous and complete recovery and was discharged in good condition five days after admission.

In August 1958, while visiting in Illinois, she experienced a bilateral spontaneous pneumothorax. Her report states: "Following a period of bilateral closed drainage, bronchoscopy was done but was not productive, either therapeutically or diagnostically. Serial chest films demonstrated unusual round cystic-appearing lesions in both lungs, with larger ones in the left lower lobe. Since her left lung would not remain expanded, the patient was advised to have a left thorocotomy. . . . At thorocotomy, there were two cystic areas opened and found to contain small bronchial fistulae; one of these was in the left upper lobe and one in the left lower lobe. These were closed, and no further points of leakage were found. There was a hemorrhagic area in the left lower lobe which was partially cystic, but the main portion of this area was quite firm and resembled nothing more than recent infiltrate. Because of an area of necrosis of this portion of the lung, it was excised, and the subsequent tissue examination confirmed the fact that these were metastases from the original primary in the right ear."[22] The patient was discharged from the hospital nine days after surgery and returned to Jamestown.

On December 1, 1958, the patient was admitted to Jamestown Hospital and died suddenly. Autopsy revealed a tumor mass protruding from the right auditory canal, extending around the right petrous bone and measuring approximately 3×2×1.5 cm.; metastases to the right temporal lobe of the brain; metastasis to the right seventh rib; and multiple metastases to the lungs. Numerous round, well-circumscribed tumors, the largest being 3 cm. in greatest diameter, were palpable in both lungs. These findings were subsequently confirmed histologically.

DISCUSSION AND SUMMARY

Although there is considerable lack of unanimity regarding the nomenclature, pathology, and malignancy of this interesting tumor, we feel that greater study and increased reporting of its occurrences will, in time, resolve these differences. We cannot agree with those who maintain that this tumor does not metastasize as any other malignancy does, since our only experience with it demonstrated its metastatic character.

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Cardiac Work Evaluation Unit

A Continuing Approach to Cardiac Therapy

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Minneapolis

PERCEPTIVE PHYSICIANS are aware of the size of the heart disease problem, particularly that of coronary artery disease. However, it is wise to remind ourselves that every year in the United States three-quarters of a million individuals—a group larger than the population of North Dakota—recover from the acute phase of a coronary occlusion, and that of this number about 75 per cent can go back to work, either to their previous occupation or to a new one. The size of the problem makes it imperative that medicine reevaluate its approach to these persons, especially in relationship to their eventual employment status.

As physicians, we bear a heavy responsibility toward all our patients, but the cardiac patient, because of his numbers, his complex emotional and vocational needs, and his rehabilitation possibilities, may call more upon our professional skills and energies. These people turn to us, and perhaps our group should now reassess its role in the care of the cardiac patient.

EARLY OBJECTIVES

Medical teaching, under its scientific influence, directed its energies toward making accurate diagnoses and providing effective treatment. Many of us can recall when coronary thrombosis was unknown and remember the struggle to get it recognized. The pressures of making the diagnosis and, in a sense, justifying it and finally evolving the proper therapy consumed our energies, and the patient's recovery became the objective. We wanted to find out what was wrong with the patient and how to correct it as expeditiously as possible. These are laudable aims and form the bedrock of acceptable medical practice everywhere.

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WORK EVALUATION UNITS

Today let us look at the other side of the coin. After diagnosing and treating the cardiac patient, we should evaluate the assets left and measure liabilities. The question might be posed: What residual capacities are left? The cardiac patient cannot be disposed of with only physical restoration; this should be used as the foundation for other equally important work.

The work-unit approach began in Bellevue Hospital in New York City, when a cardiac unit was established to demonstrate that cardiac patients could work. By accumulating data, it was found that 7 of 10 postcoronary patients did go back to work. This was an auspicious start indeed and proved that the cardiac patient could work. Following Bellevue's example, other units sprang up; there are now about 52.

Of these units, the Cleveland Unit, supported by the Cleveland Heart Association, became the most publicized. This unit discovered that medicine needed the help of other specialized fields, such as social work, vocational counseling, psychology, and others. The physician was the team captain and brought the various disciplines to bear upon the problem of the cardiac patient.

These units are oriented to getting the individual back on the job, if at all possible. One of the major facts emerging from these units involves workmen's compensation. Not one unit has reported a single case of workmen's compensation arising from a properly certified, properly employed worker. This does not say that some individuals did not die during that period, but it means that, if the cardiac's work ability is adequately evaluated and if he is placed in accordance with this certification, workmen's compensation cases do not occur.

THE MINNESOTA UNIT

Minnesota's work evaluation unit is slightly more than 18 months old and is located at the Kenny

Institute in Minneapolis. We have processed 185 clients, all of whom have been referred by private physicians, which are the only referrals we accept. However, a fair number have been referred indirectly by the Old Age and Survivors Insurance section of the Division of Social Security.

Teamwork. Our procedure is much like that of other units. The individual appears at the unit at a scheduled time. He is interviewed by the unit secretary, the social worker, and the vocational counselor. He is then seen and tested by the medical team. Although most physicians are unaware of the valuable contributions possible from the social worker and the counselor, they are extremely helpful to the medical members of the team.

The social worker interviews the individual concerning his problems and work habits and attempts to find out the person's degree of motivation. It is our opinion that motivation is the most important single factor influencing the cardiac patient's return to employment. The vocational counselor, too, attempts to plumb this aspect, as well as to assess the kind of work available within this person's ability. The object is to place the client in a position in which he will not harm himself, his colleagues, or his employer.

During our team discussion, we attempt to ascertain whether the client has any motivation, and if not, to find the reasons impeding positive motivation for rehabilitation.

Assessment. The examination given by the physicians of the unit is a vitally important aspect of the work evaluation unit. This may be done by one physician but usually is conducted by several. An examination is made to establish a diagnosis. A small number of persons referred do not have heart disease. Their chest and arm pains and other cardiac symptoms have been erroneously interpreted as angina pectoris or even coronary insufficiency.

Once the diagnosis is made, the team tries to determine the individual's work capacity. Some excellent information can be obtained by routine questioning about the individual's ordinary activities. He is asked if he can dress himself, shave himself, take a bath, walk down the street, and climb a set of stairs. These questions are important in determining his individual work capacity. However, we have other technics, too, that measure work capacity.

The double Master's 2-step test, standardized for our purposes as 40 trips over the 2-step apparatus in a period of three minutes, involves an average caloric output of approximately 8.5 calories per minute. This test is tried on all patients if deemed reasonable or possible. If an individual can actually do 8.5 calories per minute without chest pain, shortness of breath, or change in the postexercise electrocardiogram, he appears to have good work capacity. If he has any of these symptoms, he fails this test, having less than an 8.5-calorie-per-minute capacity, and must be tested at a lower level.

We also have the help of the Department of Physical Medicine and Rehabilitation at the University of Minnesota, through its director, Dr. F. J. Kottke. This department offers highly specialized, technical procedures and equipment which enable exact and continuous measurements to be made of persons working at various energy levels and at different tasks.

We are also working with the Minneapolis Rehabilitation Center, so patients can be tested for jobs ranging from stuffing envelopes to shoveling sand for two to three hours at a time. During this period, they will be monitored by the electrocardiogram, which is connected by an underground conduit to the Kenny Institute, about 150 ft. away. As soon as the details of this plan are worked out, we will be able to state that an individual can perform certain tasks at a specific energy level for a definite period of time.

After evaluating the work ability of a person, all team members—the social worker, the vocational counselor, the 3 staff physicians, and 1 to 3 outside internists, who attend the unit on a rotating basis—gather for a conference. (Physicians are always welcome to attend the unit, which meets each Wednesday afternoon.) As a result of this conference, a final prescription is written covering the work capacity of the individual.

MOTIVATION

One of the major problems our unit faces is motivation to work. We can cite example after example of clients who are perfectly able to work but who, because of attitude, will not accept our recommendations.

Reasons for lack of motivation are unclear but may fall into several categories. The first, and probably most important, is iatrogenic. We have had cardiac patients who have been told by their physicians that they cannot work again, that if they do they will create difficulty for themselves, and that if they do do anything against the doctor's recommendation, the doctor will assume no liability because the patients are

doing this on their own. We have seen many individuals with high work capacity who will not return to work because of fear created by their own physicians. If we could overcome this tendency of many physicians to unwittingly handicap their patients' motivation, we could move more rapidly toward rehabilitation.

A second reason for lack of motivation is disability insurance payments. If a patient's wife has a job, his life is not too unpleasant.

We have found that the element of motivation makes a considerable difference in the testing of the individual. Highly motivated persons who wish to work and who want a job will therefore try hard in the test, will not complain, and will accomplish more things. Individuals without motivation have difficulty with the testing, deny being able to do anything, and refuse to acknowledge that they can do many things far more difficult than the job for which they have been recommended.

A clarification of the caloric values required in different activities will illustrate my point that many cardiac patients are doing "work" even though it does not fall into the category of a "job." Lying in bed involves an output of approximately 1 calorie per minute in the ordinary individual; sitting up, approximately 1.5 calories per minute; washing the face, pulling on pants, or shaving, approximately 3.5 calories per minute; taking a lukewarm shower, about 3.5 to 4 calories per minute; climbing into a bathtub, over 5 calories per minute; making a bed, 7 calories per minute; and having sexual intercourse, about 7 calories per minute.

Contrast these energy values with those in industry. A survey was made of the entire Cleveland industrial area, where most of the work is of the light industrial machine shop type. The average caloric output was 3.5 calories per minute, with peak loads of not over 4.5 calories per minute. It is apparent that an individual who can handle his own toilet, who can take his own tub bath, and who can continue to have sexual intercourse can also continue to work at a level of 3.5 calories per minute. To be sure, various types of work have a much higher caloric output —sawing wood is 8 and 9 calories per minute— but most machine shop, office, and farm jobs— tractor riding, for example—will be under the 3.5 calorie per minute level.

This means that the individual who can do 8.5 calories per minute on our double Master's test without difficulty and who can take care of most of his needs at home can be certified to go back to work at a level of 3.5 calories per minute or even somewhat higher. We never certify a postthrombotic patient to do more than 5.5 calories per minute at peak loads or 5 calories per minute at regular loads. We do not certify our cardiac patients to drive heavy equipment, such as semitrailers, buses, or trucks, on the road. This last restriction is not because of the effort involved but because of the fear of recrimination should one of these persons have an episode while driving and precipitate an accident.

A number of individuals surveyed are unemployable because of the severity of their disability, and we have stated this; many are employable to some degree, and some can work at full capacity. We find that about 75 per cent of all who come to our unit can do some kind of work, although not all of these 75 per cent have found employment. At least a majority, however, are now working.

CONCLUSION

The rationale for this paper is not necessarily to present the scientific aspects of the work evaluation unit but to enunciate a point of view—a philosophy, if you will—about the physician's responsibility to establish the proper constructive attitude in his cardiac patients and to recognize that the work evaluation unit is a valuable resource in his efforts to handle the employment aspects of his patients. If physicians inculcated a more positive attitude among their cardiac patients, rehabilitation processes could be used more wisely and more persons could be restored to productive employment.

Notes from a Medical Journey

Haarlem, The Netherlands
4 October 1960

Dear Jay:

Here in Holland, the lovely fall weather of Sunday faded yesterday, and now a soft drizzle portends the onset of the long season when leaden skies are the rule in the region around the North Sea. I hope for Indian summer when I get home tomorrow -- days when autumnal colors blaze red and gold in the sunshine and nights spectacular with Northern lights. Then, too soon, a morning will come when all the gardens have been blackened by a killing freeze. So with a sigh I look out at the neat flower beds here and say goodbye to summer.

I am staying at the home of Dr. F. S. P. van Buchem, who recently resigned his chair of medicine at Gröningen for more leisurely scholarship. He is the leader of the Dutch team in the international collaborative program of heart research I try to coordinate. Between technical conferences at the Hague and Leiden and visits to great collections of paintings, we have gone over preliminary findings in the recently completed survey at Zutphen. Twenty cases of myocardial infarction among about 800 men aged 40 to 59 -- 85 per cent of all men in the total population roster -- give the lie to the idea that Holland is singularly spared from the coronary epidemic prevailing in countries that subsist on diets high in saturated fats.

Of course diet is not the whole story, but from our own direct observations, we now have 4 coronary-prone populations to contrast with 8 others more fortunate, and the parallel between saturated fats in the diets and cholesterol concentration in the blood still holds.

We are not sure of a continuous linear correlation between coronaries and blood cholesterol, but it is easy to make a demarcation between two categories. Populations in which middle-aged men average less than about 200 mg. of cholesterol per 100 cc. of serum are in one class. In another class, with much higher prevalence of the disease, are the

populations with higher average cholesterol values. Kimura's Japanese farmers and fishermen average only 140 to 160 mg. per 100 cc., while the rural men of Crete, southern Italy, and Dalmatia average 180 to 200. In all of these groups, the prevalence of coronary heart disease is really low, but we have not proved that the Japanese are much better off than the Greeks and the others. In the other class, too, we find it hard to prove that populations in which the middle-aged men average 235 mg. are much better off than in those with averages of 265 mg. Other factors at work? Or is it simply that our numbers are too small? Besides better methods, we probably need samples 5 times as big as those now being studied.

Since my last letter from Bucharest, the International Colloquium on Arteriosclerosis and the European Congress of Cardiology, both at Rome, have come and gone, and I have had a good visit with our team working on the island of Grete. The team on Crete -- doctors from Sweden, Italy, and England, as well as the very competent Greeks from Athens -- has put a fine-toothed comb to the villages, but coronaries are just as scarce as we found in our first survey there three years ago. In desperation, the team rounded up 100 men over 70 -- the "papoos" with great white mustaches and voluminous baggy pants, who abound there. Many of them were creaky and deaf and half blind, but the electrocardiograms were good.

From Greece, I hurried back to Rome to join a U. S. group made up of Paul White, E. Cowles Andrus, Luther Terry, and John Turner, a protégé of Paul's, in a meeting with the Russian delegation -- Myasnikov, Speransky, Vassilenko, and Khibshidsky -- to discuss cooperation in cardiovascular research. We got along fine personally, but too much time was given to talk about criteria based on recollections from clinical experience. This may be fun, but it is a poor substitute for actually working together or the analysis of objective data put into uniform classification systems. However, we agreed on some plans for more prolonged contacts, and we have increased hopes for real cooperation in the future.

After the conference, several of us went to a small restaurant I know across the Tiber and dined at 9 P.M. on mussels, "ossobuco," fruit, and the golden Frascati wine made in the nearby Alban Hills. Later, we drove up to the Campodoglio, the official heart of Rome, stopping on the way to toss coins into the Trevi Fountain to assure another visit. From the parapet behind the Campodoglio, we looked down over the vast, floodlit Roman Forum and pondered the march of two thousand years of history since those white marble columns were new. Then the bells tolled midnight, the lights went out, and we went back to the hotel through deserted streets. I noted that it was just thirteen hours since Dr. Kimura and I had boarded the plane to Athens, and now he should have arrived at Boston, where he would be telling Ina White that Paul will be home shortly.

Then I was flying northeast, watching the clouds thicken as we left Italy and finally coming down through the mist to Zagreb, where auto traffic and parking are not yet a problem in the center of a city of 600,000. But Zagreb is not cut off from the West, and the Palace Hotel was full of chatter in Italian and German -- as well as of pictures of Tito in every room.

A few of us may meet again in Yugoslavia in the spring. Belgrade wants to embark on work parallel to that which we started in Dalmatia and Slavonia two years ago, and an outsider like myself may help cooperation between Zagreb (the Croats) and Belgrade (the Serbs). Anyway, while tempers flare in the U. N., it is increasingly possible to get on with the job of international cooperation in medical research. We may not yet know how to prevent coronary heart disease, but infarcts are just as unpopular in Moscow and Belgrade as they are in Minneapolis and Helsinki.

Now, in a couple of hours, I shall be standing around at the airport, waiting for plane departure, buying newspapers, drinking coffee, looking at counters full of stuff I don't want, and pondering my impression that Congresses are scientifically disappointing and emotionally (or only physically?) exhausting. In other words, this promises to be a typical ending of a fairly hard trip.

With best wishes to all in Minnesota,

As ever,

Ancel Keys

AK:ml

Jerome T. Syverton, M.D.

An Appreciation

WILLIAM F. SCHERER, M.D.

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JEROME T. SYVERTON began his outstanding career in microbiology as an instructor in bacteriology at the University of North Dakota in 1928. Born in Courtenay, North Dakota, on March 29, 1907, he entered the university of that state in 1923, obtaining an A.B. degree in 1927 and a B.S. degree in 1928. He was graduated from Harvard University School of Medicine in 1931, and, after an internship and assistant residency in medicine at Duke University Hospital in 1931-32, he became an assistant in pathology and bacteriology at the Rockefeller Institute for Medical Research. There he acquired his basic knowledge in virology under Dr. P. K. Olitsky and in 1932 joined the faculty of the University of Rochester School of Medicine and Dentistry.

It was during his years in the University of Rochester Department of Bacteriology from 1934 to 1947 that he developed his skill as a teacher and student advisor, and accomplished his pioneer work on tumor viruses and multiple viral infections of single animal cells. For his outstanding research in virology, he received the Lilly Award in Bacteriology and Immunology in 1938. From 1944 to 1946 he was on active duty in the United States Navy as a visiting investigator at the Rockefeller Institute and as a member of Naval Medical Research Unit 2 in the Pacific theater. In 1947, he became professor and head of the Department of Microbiology at Louisiana State University School of Medicine and, from 1948 until his death on January 28, 1961, he was professor and head of the Department of Bacteriology at the University of Minnesota.

His enthusiastic approach to professional life with simultaneous devotion to his family and friends set an extraordinary example for students and associates. His graduate and postdoctoral students during twelve years at the University of Minnesota numbered over 65. As Dr. Richard E. Shope of the Rockefeller Institute said, "One of the very nicest things that I know about Dr. Syverton was the generosity with which he shared his scientific ideas, and their exploitation, with others, usually graduate students or younger assistants in his Department. He published almost none of his most significant observations alone, and, where he shared in the publication with others, his name was almost never in the senior author position."*

Dr. Syverton's productivity as an investigator was remarkable; in 1957-58 he received the Commonwealth Fund Award for Creative Work. Eighty-seven articles describing his own work and 119 in conjunction with his students and associates were published between 1933 and 1960. In the words of Dr. Shope, "Dr. Syverton was a prolific worker in the field of virology and his interests ranged widely. He worked first at the Rockefeller Institute on the viruses of vesicular stomatitis and equine encephalomyelitis, sharing in pioneer work with these agents. Later, at Rochester, he initiated work with the rabbit papilloma, and his continuing studies of the papilloma-to-carcinoma sequence in this virus-induced tumor contributed materially to our understanding of the progression through which a benign tumor cell acquires malignant properties. It was also at

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*From introductory comments of a lecture entitled, "The Case of a Lurking Virus and Its Exposé," presented by Dr. Shope to medical students at the University of Minnesota on February 14, 1961.

Rochester that, with Barry, he did his fundamental work dealing with multiple viral infections of single host cells, showing that the cells of virus-induced tumors could be superinfected with other non-neoplastic viruses.

"From time to time throughout his career, Dr. Syverton contributed significantly to our understanding of the possible mechanisms by which viruses prevail and are perpetuated in nature. In this connection, he studied the host range of Western equine encephalomyelitis virus in various wild animal species and showed the hereditary transmission of this virus in the wood tick. In a similar vein, he demonstrated the potentiality of the Trichina worm to serve as a transmitting agent for the virus of lymphocytic choriomeningitis. Later, he extensively exploited the use of stable strains of mammalian cells in the cultivation and study of viruses—a pioneering effort of great importance to virology. Recently, with Brand, he developed a hemagglutination test for the species determination of cultivated mammalian cells.

"What was probably Dr. Syverton's most significant contribution was made very recently when he discovered with McLaren and Holland that the ribonucleic acid of poliovirus could infect nonprimate cells that were ordinarily refractory to infection with complete poliovirus. The importance of this discovery is very great and its significance to virus work in general and tumor virus work in particular will undoubtedly be far-reaching."

Dr. Syverton's stature in science and academic medicine was evidenced by his membership in 22 professional societies and 11 scientific advisory committees, and his enthusiastic support of science at international and national levels was widely recognized and appreciated. The world's scientific community has lost a creative and productive investigator; the educational community, an enthusiastic teacher; his circle of colleagues and associates, a true friend; and his family, an affectionate and lovable father.

As Dr. Shope said to the medical students of the University at his passing, "Dr. Syverton was a fine scientist, a gentleman, and a grand person to have as a personal friend. I think that you were fortunate indeed to have had him as one of your professors for as long as you did."

Although the prognosis is grave, survival is possible after surgical intervention for perforation of obstructed colon in patients with large bowel carcinoma. Outcome is best after exteriorization or resection of the perforated bowel.

Among 24 of 34 patients with perforation, results were no better after colostomy or cecostomy and drainage and little better after simple drainage of the peritoneal cavity than without treatment. The only survivor was 1 patient treated with simple drainage who had only slight fecal contamination of the peritoneum. Exteriorization was done for 5 patients and resection for 5, with 2 and 3 patients, respectively, surviving. Continued infection of the peritoneum from bowel extensively damaged by distention and ischemia probably accounted for the lack of success with colostomy and drainage.

The arguments that fatal retroperitoneal cellulitis will result from mobilization of the intestine when gross fecal contamination exists and that such patients are too sick to undergo an extensive operation were not substantiated by results. Neoplasms in 29 of the 34 patients were clearly resectable, as noted generally by postmortem examination, with spread only to adjacent lymph nodes in 2 instances.

I. Russell and N. Johnson: Perforation of the colon in large bowel obstruction due to carcinoma. Australia & New Zealand J. Surg. 29:332-339, 1960.

Book Reviews . . .

Fundamentals of Gynecology

SAMUEL J. BEHRMAN, F.A.C.S., *and* JOHN R. G. GOSLING, M.D., *1959. New York: Oxford University Press. 407 pages. $9.50.*

This new book presents the basic information on gynecology in a lucid, systematic fashion that should be welcome to the general practitioner and, particularly, to the medical student. The first chapter on gynecologic history, physical examination, and simple laboratory studies contains a clear discussion of the special problems of the adolescent and the geriatric patient. After this excellent beginning, the volume is divided logically into sections on anatomic problems, menstrual and endocrine disorders, inflammations, tumors, and conditions related to conception. The final chapters provide a good discussion of lower abdominal and pelvic pain and a brief outline of the principles of radiation therapy. The last portion of the book before the index contains a partial list of commercially available endocrine products that should prove quite useful in this day of confusion over the tangle of brand names.

The material is presented with appropriate illustrations. The use of photomicrographs, together with so-called histologic maps, aids in understanding the normal histology as well as the pathologic appearance. The index is well done, and the bibliography is adequate.

Although this book is not intended to be a text on gynecologic surgery, the minor procedures, particularly those related to infertility, are described very satisfactorily. Office procedures are outlined in detail.

There has been an apparent effort on the part of the authors to avoid controversy over methods of therapy. However, failure to mention alternate procedures may be unfair to the student who is becoming acquainted with the various surgical approaches for the first time. For example, in the discussion of therapy of uterine prolapse, no mention is made of the Spalding-Richardson composite operation or the Watkins transposition operation. Admittedly, these operations are uncommon in some areas of the country; nevertheless, the medical student needs to learn of their existence from his textbook of gynecology. This lack of information in small areas, however, should not prevent us from recognizing this book as a good, readable text.

All in all, this volume is well written, is of convenient size, and is well arranged for ready reference. It should be of value to the practitioner who does medical and minor surgical gynecology. The text should also appeal to the student who wishes to absorb the basic principles of gynecologic diagnosis and treatment without becoming involved with the minute details of surgical technic.

FRED S. GACHET, JR., M.D.
Lakeland, Florida

Histoplasmosis

HENRY C. SWEANY, M.D., *1960. Springfield, Ill.: Charles C Thomas. 519 pages. Illustrated. $14.50.*

This volume represents the collective efforts of 24 authors to bring together current and cumulative knowledge of the biology of *Histoplasma capsulatum* and the laboratory and clinical aspects of the spectrum of disease that it produces.

Among the contributors are to be found most of the names associated with the rapid evolution of histoplasmosis as a disease entity which has occurred in the past two decades: namely, Emmons, Palmer, Furcolow, Ajello, Procknow, Tenenberg, Sweany, Salvin, and others. As all of the pioneers in elucidating this disease are not represented as authors, very appealing photographs of Amos Christie, Katherine Dodd, and others are included in the section on the history of the disease. A personal note on S. T. Darling by Meleny emphasizes the wide talents of the discoverer of this disease.

All phases of the disease and the organism are covered. In all parts of the book, and summarized nicely by Furcolow, emphasis is given to the wide spectrum of clinical disease that this organism produces in human beings. Where methodology is currently useful, it is given in detail. For example, Mowry and Frenkel described the several staining technics most useful for demonstrating the organism in the isolated pulmonary nodule ("coin" lesion). Larsh presents cultural technics and methods of animal research. Ecology of the organism and pathology of the disease are thoroughly treated, including both basic and clinical aspects.

Most contributions are well organized and clearly written, and the volume is beautifully illustrated. The weakest sections are those devoted to the clinical aspects of the disease. Perhaps this is more a reflection of inadequate knowledge of the clinical aspects of diagnosis and, until recently, unsatisfactory management available, than to the way in which existing information is presented. All current clinical diagnostic and management problems, including surgical therapy, are covered. The volume should be useful to the medical practitioner as well as the pathologist, radiologist, microbiologist, epidemiologist, and researcher.

RICHARD T. SMITH, M.D.
Gainesville, Florida

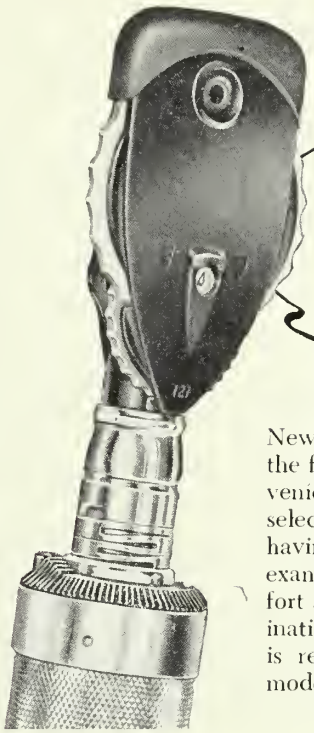
Fellowship of Surgeons: A History of the American College of Surgeons

LOYAL DAVIS, M.D., *1960. Springfield, Ill.: Charles C Thomas. 507 pages. $10.50.*

The twenty-two years which followed the organization of the American College of Surgeons from the earlier and more informal Clinical Congress of Surgeons of North America saw the College become an influence of far greater significance than that of any other organized segment of American medicine. Nor was the program solely concerned with surgery and surgeons; it ranged from the ambitious project of hospital standardization through various programs in cancer—clinics in hospitals, bone sarcoma registry, archives of "cured" cases, detection centers, and end result reporting—graduate training in surgery, care of fractures, industrial medical standards, professional relations and medical services, and economics.

The primary founder and driving force behind the

(Continued on page 26A)



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(Continued from page 26B)

College, as well as the originator of *Surgery, Gynecology and Obstetrics*, was Dr. Franklin Martin. At his death, the Fellowship of the College numbered over 12,000, *Surg., Gynec., and Obst.* had become the top surgical journal in the English language, and the American Medical Association had publicly reviled the College and its Board of Regents for its advocacy of prepaid health insurance.

The second era is the story of the College under an administrative board that functioned in lieu of a "top banana" for fifteen years, until the appointment of General Paul R. Hawley in 1950. It is the story of a continuing struggle to maintain and improve the ethics of surgical practice against the evil influences of fee splitting, ghost surgery, itinerant surgeons, unnecessary operations, excessive fees, and the advocates of laissez-faire. Progress was often made in a faltering style, becoming more assured after Hawley's appointment. The vigorous attack upon these evils later brought the wrath of the A.M.A., the American Academy of General Practice, and even of Fellows of the College. Publicized in the newspapers and seized upon by feature writers for magazines, the College went through some of its roughest times on this score.

Through the background of this expertly woven fabric of history are the figures of the great men of American surgery, though not without each one's particular form of clay foot becoming apparent in some instances.

The author maintains a pace and a sense of proportion that prevent overemphasis, much less dullness. He employs the device of frequent short inserts of contemporary national and world affairs, providing the reader with better orientation in time.

The book is attractive in format and easy to handle, and the type is extraordinarily easy to read. This book should edify and entertain any surgeon and, remarkably enough, we must say the same of it for almost any literate citizen who still prefers reading to television.

IAN MACDONALD, M.D.
Los Angeles

Synopsis of Ear, Nose, and Throat Diseases

ROBERT F. RYAN, M.D., WILLIAM C. THORNELL, M.D., *and* HANS VON LEDEN, M.D., *1959. St. Louis: C. V. Mosby Co. 383 pages. Illustrated. $6.75.*

This slim volume, designed as a synopsis, offers fundamental information in the field of otorhinolaryngology to nonspecialists, interns, medical students, and such allied professionals as speech or voice pathologists and nurses. Ear, nose, and throat disorders constitute a large part of the daily practice of medicine, and this book has been written to satisfy the needs and requirements of those who deal with these ailments. The material is organized in such a way as to review initially clinical anatomy and physiology as they pertain to the ear, the nose and paranasal sinuses, the pharynx, and the larynx. Thus oriented, the reader is then quickly acquainted with the less involved technics and tests necessary for routine examination of the ear, nose, and throat structures.

Common otorhinolaryngologic diseases are discussed in relation to the classic divisions so familiar to all physicians and medical undergraduate students: etiology, pathology, symptomatology, prognosis, and treatment. Comments on surgical procedures are limited to those areas that would appeal to nonspecialists. For purposes of rapid summation, the symptoms and treatment of the more common diseases are outlined at the end of each chapter. Among the more interesting chapters are those dealing with hoarseness and voice rehabilitation, headache that is often confused with sinusitis, pharyngeal manifestations of systemic diseases, dizziness, and deafness. In the reviewer's opinion, the abbreviated chapter on the physiology of the nose is sufficiently important to warrant expansion in a future edition.

The binding and printing are satisfactory, and the illustrations are informative, although uneven in pictorial presentation. As a handy, concise reference of generally accepted methods of diagnosis and treatment in the field of otorhinolaryngology, this volume will prove most useful to those to whom it is directed.

NOAH D. FABRICANT, M.D.
Chicago

Therapeutic Radiology

WILLIAM T. MOSS, M.D., *1959. St. Louis: C. V. Mosby Co. 403 pages. Illustrated. $12.50.*

This work on therapeutic radiology should be called to the attention of anyone practicing medicine who is concerned with malignant disease problems. It is of interest not only to the radiologist and the radiology resident but also to the surgeon who is interested in what radiation therapy has to offer his patients with malignant disease, either in conjunction with or in lieu of surgery.

The various systems of the body are well covered. There are good sections on radiation effects on normal tissues, good illustrations of various disease problems, and thoughtful discussions of many of the problems of medical management.

This book can be recommended enthusiastically to anyone interested in the treatment of malignant disease.

DONN G. MOSSER, M.D.
Minneapolis

Electrohysterography

SAUL D. LARK, M.S., PH.D., *1960. Springfield, Ill.: Charles C Thomas. 120 pages. Illustrated. $5.75.*

This monograph is a compendium of Lark's prodigious studies on electrical activity of the human uterus during pregnancy. Dr. Lark is a biophysicist at the University of California at Los Angeles, working in a department of obstetrics and gynecology. He has tried to apply the technics of electroencephalography to the study of normal and abnormal uterine contractions during pregnancy. He reviews in his introductory pages muscular electrical activity as observed by Galvani in 1791. Even Galvani's work was preceded by others with the same thought. Lark's thesis is that there is a single dominant pacemaker in the myometrium as in the myocardium. His studies indicate multiple pacemakers in the myometrium during inertia labor. Oxytocin appears to aid in the attainment of normal pacemaker dominance with concurrent correction of uterine inertia in this abnormal function of the uterus.

Lark's monograph is an excellent discourse on the subject of electrohysterography and is accompanied by all the pertinent bibliography of the subject. Clinicians should not read this book in terms of solving questions such as: (1) What causes normal labor? (2) What causes premature labor? or (3) What causes primary uterine inertia? Rather, one should read this book for the knowledge it unfolds in electrical activity of the human pregnant uterus in normal and abnormal labor. Such observations add to an understanding of biology through physics and provide links in our information that may even-

(Continued on page 28A)

(Continued from page 26A)

tually help solve the questions asked above. It is refreshing to see someone like Dr. Lark working in a fundamental science, making observations on human subjects.

E. STEWART TAYLOR, M.D.
Denver

Radiological Examination of the Small Intestine

ROSS GOLDEN, M.D., *1959. Springfield, Ill.: Charles C Thomas. 533 pages. Illustrated. $28.50.*

This is a very extensive treatment of a long neglected subject. It deals with a part of the intestinal tract vital for proper nutrition and well-being and with indications for study of this organ and methods by which it can be accomplished. Embryology and developmental abnormalities, as well as anatomy, physiology, pharmacology, and pathology, of the small bowel are considered at length. The material used takes into consideration the observations of the author as well as the contributions to the literature.

The book covers diseases that affect the mesentery and the small bowel directly, as well as those generalized diseases which involve them systemically, as allergy, nutrition, purpura, or amyloidosis. Each chapter has a bibliography at its conclusion, so that, if the reader feels that the treatment of the topic has not been sufficient, he may find an available reference.

The book is of great interest to all physicians but is more valuable to the radiologist and internist. The necessary therapeutic procedures and how they are best effected are discussed and include the use of a Miller-Abbott tube, small bowel enema, and conventional small bowel study.

The material is presented clearly and points of variance are noted. There are 176 figures in the book, including roentgenograms, photomicrographs, drawings, and diagrams. The figures of x-rays dealing with clinical cases include a comment on case history, surgical findings, and response to medication. The book can be very practically employed by student and practitioner and is a most enlightening treatment of a very fascinating subject.

OSCAR LIPSCHULTZ, M.D.
Minneapolis

Pharmacology of Anesthetic Drugs

JOHN ADRIANI, M.D., *1960. Springfield, Ill.: Charles C Thomas. 204 pages. Illustrated. $11.00.*

The fourth edition of this fine book essentially adds data on new drugs and brings up-to-date data on anesthetic drugs that have been used for a long time. The clinical use of drugs is the dominant theme, and a fine list of references has been included. This book will be very useful to one who desires to be as well informed as possible. It is books like this that make it possible for anesthesiologists to keep abreast of their field. The illustrations save a great deal of reading and are helpful for quick reference.

JOHN S. LUNDY, M.D.
Chicago

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PSYCHIATRY

Introduction to a series of articles on psychiatry for the nonpsychiatric physician

THE PAST DECADE has seen the beginning of a new era in psychiatry, with advances on several fronts. Most notable is the advent of the tranquilizing and antidepressive drugs. The major tranquilizers have had an important impact on mentally disturbed patients and on mental hospitals. They have already contributed to the improvement of vast numbers of patients, resulting in the virtual elimination of disturbed wards and, for the first time in history, a general reduction in the need for psychiatric beds. These compounds, along with the psychotomimetic agents, have stimulated an unprecedented surge of research in psychiatric and related fields.

With all the attention given the ataractic agents and other physiologic therapies, we must not lose sight of the real progress which has been made in other areas as well. There have been steady developments in psychotherapy and family therapy. Psychotherapy, utilizing dynamic concepts, is beginning to replace traditional psychoanalysis. Many psychotherapeutic procedures can be carried out by all physicians.

Most remarkable has been the slow, steady evolution of a better social attitude toward psychiatric patients, particularly the sicker ones in hospitals. The latter are being treated with more respect and given more responsibility; less restraint and coercion are used. Hospitals are successfully unlocking their doors, and hospital personnel are finding their work more rewarding and satisfactory.

One of the most encouraging notes of the past decade is the emergence of an eclectic point of view which favors the utilization of any indicated treatment modality for a given patient.

It is the intent of this series of articles to summarize and review these advances in the field of psychiatry.

BURTRUM C. SCHIELE, M.D.

Psychiatric Syndromes Due to Acute Reversible Brain Disorders

IAN GREGORY, M.D., D.Psych.

Minneapolis

ORGANIC MENTAL DISORDERS, or brain syndromes, are disorders of thinking, emotion, or behavior resulting from a variety of biochemical and/or structural changes in the brain. Two major groups of organic brain disorders are usually distinguished as to whether the disordered brain and mental functions are temporary and reversible or permanent and irreversible.

In both acute (reversible) and chronic (irreversible) brain disorders, there are *primary symptoms of organic mental dysfunction:* (1) impairment of orientation (most marked for time, then place and person); (2) impairment of memory (most marked for recent rather than remote events); (3) impairment of all intellectual functions (comprehension, calculation, knowledge, learning, and so on), ideation tending to be impoverished and concrete, associated with stereotyped repetition (perseveration) and compensatory fabrications (confabulation); (4) impairment of judgment, conscience, and ability to plan for the future; and (5) lability and/or shallowness of affect (emotional response).

In addition to these symptoms of organic intellectual impairment, which are present to some degree in all disorders caused by or associated with impairment of brain tissue function, there are certain other symptoms which are more characteristic of either acute reversible disorders (delirium or stupor) or chronic irreversible disorders (dementia). The main differences between symptoms, pathogenesis, and outcome of these 2 groups of organic brain disorders are summarized in table 1.

It may be noted that all the same traumatic, toxic, infective, metabolic or other disorders that commonly cause acute reversible brain disorders may also lead to chronic irreversible brain disorders if damage to brain cell function is sufficiently severe. However, chronic irreversible disorders commonly arise from local intracranial lesions or degenerative processes with insidious onset (sometimes hereditary) which are never characterized by complete reversibility and resolution. In view of such differences in causation, symptoms, course, and management, the reversible and irreversible brain disorders are being considered in separate sections and the remainder of the present paper will be devoted only to acute reversible brain disorders commonly associated with clinical syndromes of either delirium or stupor.

The following is a brief classification of the main types of disorders known to cause acute reversible impairment of brain function:

1. Infections
   - (a) primarily affecting the central nervous system (meningitis, encephalitis)
   - (b) systemic infections sometimes producing mental symptoms
2. Intoxications
   - (a) exogenous (medications, poisons, alcohol)
   - (b) endogenous
3. Trauma (head injuries)
4. Cerebrovascular disease (disorders of heart, blood vessels, or blood)
5. Convulsive disorders (primary or secondary)
6. Metabolic disorders (anoxia, dehydration, vitamin deficiencies, and disorders of mineral, carbohydrate, protein, or fat metabolism)
7. Intracranial tumors
8. Reversible disorders of unknown etiology

IAN GREGORY *is assistant professor of psychiatry, University of Minnesota Medical School.*

TABLE 1
CHARACTERISTICS OF BRAIN DISORDERS

Acute Reversible Brain Disorders	*Chronic Irreversible Brain Disorders*
Usual clinical syndrome delirium (sometimes stupor or coma).	Usual clinical syndrome dementia.
Primary impairment of orientation, memory, all intellectual functions, judgment, and affective response.	Primary impairment of orientation, memory, all intellectual functions, judgment and affective response.
Usually associated with disordered perception (especially visual illusions and hallucinations), consciousness (e.g., stupor) and psychomotor activity (excitement or retardation)	May be prominent secondary "functional" manifestations due to release or accentuation of latent personality characteristics—psychotic, neurotic or behavioral (e.g., depressed, paranoid, anxious, or antisocial behavior).
Due to temporary, reversible changes in brain cell function, or "biochemical lesion."	Due to permanent, irreversible damage to brain structure or "morphological lesion."
Frequently "symptomatic" of generalized toxic, infective, or metabolic disorder, also affecting other parts of the body.	May result from all the same pathogenic agents as acute (reversible) disorders; but also from insidious, localized intracranial lesion or degenerative process (sometimes hereditary).
Commonly encountered on general medical and surgical, pediatric or obstetric wards of general hospitals.	Commonly encountered on neurological services of general hospitals or in mental hospitals.
Course brief, and may terminate in (1) death, (2) complete remission, (3) chronic (irreversible) brain disorders.	Course may be (1) chronic or (2) progressive (with fatal termination).

FREQUENCY AND DISTRIBUTION

By definition, these disorders are of brief duration and are usually associated with severe physical illness, intoxications involving other parts of the body, or both. These factors result in a relatively high proportion being treated in general hospitals (by physicians other than psychiatrists) rather than in mental hospitals. The brief duration also results in a relatively low *prevalence* at a given point in time as compared with a relatively high *incidence* of new cases within a given period.

There are no adequate statistics on the frequency with which acute reversible brain disorders complicate the illnesses of all patients treated in a given general hospital, but the relatively few studies undertaken by psychiatrists and psychologists suggest a considerably higher frequency than is generally recognized by the physicians and surgeons responsible for the patient's care. Among patients admitted to mental hospitals, the proportion of patients with acute brain syndromes will depend upon such factors as the frequency of their various disorders in the general population, the geographic proximity of the mental hospital to centers of population, the attitude of the public and general physicians toward the mental hospital, and the admitting policy of the mental hospital administration with respect to acute alcoholic psychoses and other acute brain syndromes. Among first admissions to all Canadian mental hospitals in recent years, the proportion of patients having alchoholic psychoses has been about 2 per cent (nearly 4 per cent of the males as compared with less than 1 per cent of the females) and of patients with other acute brain syndromes, about 4 per cent.

With respect to age distribution, there is probably an increased frequency of acute brain syndromes at both extremes of life—in childhood because of the lability of homeostatic mechanisms and susceptibility to numerous minor infections to which the child responds with a very high fever, and in old age due to the presence of degenerative changes (arteriosclerotic or senile cortical atrophy), associated with poor nutrition and other metabolic defects, so that any additional insult readily provokes decompensation. At these extremes of life, the sex distribution does not appear to differ greatly, but during the intermediate period of adult life, each sex is more vulnerable to certain hazards than the other. There is, for example, a much higher frequency of alcoholic psychoses and of psychoses resulting from industrial poison among men; whereas women have a relatively higher frequency of brain disorders associated with hypothyroidism (myxedema), and with the complications of pregnancy and childbirth. In former years, there was a tendency to classify all *postpartum (puerperal) psychoses* as cases of delirium or acute

reversible brain disorders. However, it has been increasingly recognized that all varieties of mental disorder may have their onset during pregnancy or the postpartum period (depressions and acute schizophrenic reaction being particularly frequent) and that only a certain proportion of them should be classified as acute brain syndromes—for example, those clearly associated with toxemia or eclampsia or those immediately following sudden and severe postpartum hemorrhage with shock.

As might be anticipated, there is considerable variation in the frequency of illnesses and intoxications responsible for acute brain syndromes from one geographic area to another, depending on such factors as the development of industry, sanitation and other public health programs, the general level of nutrition, and the nature of parasitic infections in the area. Acute and chronic brain syndromes associated with malnutrition, malaria, and trypanosomiasis are still prevalent in certain underdeveloped countries, whereas those associated with alcholoism and industrial poison are more characteristic of those that are technologically developed. Within the latter countries, there appears to be an inverse relationship between the frequency of these disorders and socioeconomic status which may be related to 2 groups of factors: (1) low socioeconomic status involves increased rates of exposure, morbidity, and mortality from a variety of physical illnesses and (2) low socioeconomic status tends to be associated with limited intellectual resources and the same degree of intoxication or disordered metabolism may be more likely to result in intellectual and behavioral decompensation than in those with a higher native intellectual endowment.

It may be appreciated that no reliable estimates are available of *lifetime expectancy* of any or all of these disorders, but that it may amount to a considerable proportion of the total population. However, not every acute brain syndrome represents these first such attacks in a given patient. It is reasonable to suppose that a certain small proportion of the population may be relatively more vulnerable to repeated attacks, either through hereditary predisposition; limited intellectual endowment; repeated exposure to the same agent, such as alcohol; or to a variety of toxic or biologic stresses.

FAMILY HISTORY

Some clinicians have the impression that there is some nonspecific vulnerability to acute confusional psychoses among the members of certain families, but this impression still requires statistical confirmation. If true, it would suggest a nonspecific hereditary predisposition on a polygenic basis, probably related to genetic determinants of intellectual capacity, immune responses to infection, and resistance to nutritional deficiencies and other biologic stress. However, it should also be recognized that membership in a given family may imply similar habits of nutrition (which may also be related to the development of immunity to infection) and exposure to similar types of pathogenic agents (physical, chemical, or biologic).

PERSONAL HISTORY

There is no consistent history of prenatal stress or deprivation, birth injury, or delayed or deviant early postnatal maturation and development. The interpersonal relationships of early childhood (with parents, siblings, and, later, peers) tend to be compatible with the norms for other people from similar socioeconomic and cultural backgrounds. However, in patients whose acute brain syndrome is related to a long-standing personality disorder such as alcoholism, retrospective information obtained at the time of their admission to the hospital (or from the patient after remission of his confusional symptoms) tends to indicate a lifelong history of unsatisfactory human relationships.

School performance, education completed, occupational adjustment, residential and socioeconomic status, attitudes toward authority (parental, school, military, police, and so on), and the patient's sexual and marital adjustment show wide variations and also tend to conform with what might be expected among others of the same age, sex, and sociocultural background as the patient—again with exceptions among patients showing certain deviations in personality and behavior. Dewan and Spaulding remark that "A history relatively free of emotional instability in spite of considerable psychological and social stress through the years should immediately suggest the possibility of an organic factor operating in the production of the psychosis. On the other hand, a long history of emotional upsets does not automatically rule out the need to consider a physical element in the present breakdown."

By definition, the acute reversible brain disorders cannot have a slow, insidious onset over a period of many years, but there may still be considerable variation in the nature of onset. Thus, the onset may be extremely abrupt, such as that following trauma, from one or more epileptiform seizures; a cerebrovascular accident; systemic hemorrhage and shock; and cardiac arrest or severe anoxia during surgery. On the

other hand, the onset of many acute reversible brain disorders may be more gradual, over a period of hours, days, weeks or even a few months, as in the case of some intoxication or of a slowly growing benign intracranial neoplasm such as a meningioma. However, it should be recognized that the more severe in degree and the more prolonged the symptoms of organic intellectual dysfunction, the greater the probability of some degree of permanent residual intellectual impairment after remission of the acute symptoms.

At the time the patient comes to medical attention, specific inquiries should of course be made concerning all previous physical illnesses and currently associated symptoms, particularly those involving the nervous system, such as headache, vomiting, defective vision, epileptiform seizures, paresthesias, paralysis, and defects in balancing or other evidence of incoordination.

MENTAL EXAMINATION

In some cases, the appearance, attitude, and behavior of the patient with an acute organic confusional state may be quite characteristic even before an attempt at verbal communication is undertaken. The usual clinical syndromes are those of either delirium (with illusions, hallucinations, and increased psychomotor activity) or stupor (with apathy and retardation). In either case, the patient is apt to appear physically sick and may be lying in bed unshaved and unkempt in appearance with haggard or expressionless facies and often sweating profusely. Patients with active visual illusions or hallucinations may pick at imaginary objects in the air or on the bedding and may have a worried or fearful expression. Patients with alcoholic delirium tremens have a coarse tremor of the extremities ("the shakes"), and those with increased psychomotor activity tend to be excited and sometimes aggressive, but usually their activity appears purposeless and confused.

The patient in stupor offers little or no spontaneous conversation, limited replies to direct questioning, and sometimes may be completely uncommunicative. The state of retardation and lethargy may proceed to somnolence or coma from which the patient cannot be aroused. However, when he is awake and accessible for conversation, replies to questions reveal the characteristic organic intellectual deficit that is also present in states of delirium and excitement.

There is impairment of all intellectual functions (comprehension, calculation, knowledge, learning, and so forth) associated with concrete thinking and reduction of new concepts, with a tendency toward stereotyped repetition of a few thoughts or answers. When the patient keeps answering the same word or phrase to a number of different questions asked him, this is known as perseveration.

There may be impairment of orientation in all 3 spheres, but the most vulnerable is the sense of time (which is the first to be impaired and the last to be restored after an acute insult to the brain—as may be observed following spontaneous or electrically induced epileptiform seizures). Orientation as to place also tends to be more vulnerable than as to persons that have long been known to the patient, although the latter may also be lost in severe confusion.

There is impairment of memory, especially for events of the immediate past rather than for remote events, and, in some cases, there is a tendency to compensate for this deficit by fabricating answers to questions asked.

The emotional tone tends to be one of apathy, but alternatively, there may be a predominant mood of depression, fear, or even anger. The emotional response tends to be either shallow or labile.

Hallucinations and illusions may involve any of the five senses, but, most typically, involves vision, including moving animals and reptiles which may be quite frightening. However, hallucinations of touch, hearing, smell, or taste are not infrequent. Delusions frequently relate to the content of the preceding disturbances in perception and tend to consist of poorly systematized delusions of persecution.

There may be considerable fluctuation in the mental state within quite short periods. During lucid intervals, judgment and insight may be fairly well preserved, but they are grossly impaired during episodes of confusion.

PSYCHOLOGIC EVALUATION

During the acute phases of delirium or stupor, the patient is frequently not accessible for psychologic testing; but when the gross behavioral manifestations are quiescent, testing is apt to reveal the typical picture of organic intellectual and memory impairment.

While it may be estimated from past educational and occupational performance that the patient's intellectual capacity was within normal limits, during an acute organic brain syndrome the over-all intellectual function will often fall in the mentally defective range, with an IQ below 70. Certain intellectual functions tend to be preserved better than others, which is reflected in the subtest scores of the Wechsler Intelligence

Scale. Thus, vocabulary, to a lesser extent, information and comprehension, and, sometimes, picture completion and object assembling tend to be well preserved. Verbal subtests are generally higher than performance. Preservation of vocabulary in the presence of impaired abstract thinking is the basis for the Shipley-Hartford test, from which a numerical Conceptual Quotient may be derived.

Impairment of various aspects of memory forms the basis of the Wechsler Memory Scale, from which a numerical Memory Quotient may be derived. A variety of other tests is available for evaluating organic impairment of intellectual functions, such as the Goldstein-Scheerer tests, but there may be great difficulty in distinguishing between mental deficiency, which is intellectual subnormality from birth, and intellectual impairment on the basis of either an organic brain syndrome or advanced schizophrenia.

The Minnesota Multiphasic Personality Inventory does not usually differentiate patients with organic brain syndromes, although the 29 profile (combined elevations on depressive and manic scales) has been found more frequently among patients with organic reactions than other groups. The Rorschach Test may reveal a number of findings suggestive of organicity— for example, an impoverished record containing relatively few responses which are poorly elaborated and of poor form level—but projective tests as a whole do not offer nearly as much information about organic brain disorders as tests of various intellectual functions such as those mentioned above.

PHYSICAL INVESTIGATIONS

Because of the extremely wide variety of bodily diseases and intoxications that may result in impairment of brain cell function, it is impossible to itemize here all the possible findings on physical examination or laboratory investigation. For detailed elaboration of the possible findings and their interpretation, the reader is referred to textbooks of physical diagnosis, internal medicine, and neurology.

Careful physical examination may lead to discovery of pathology in almost any system of the body. However, since brain cell function is affected in every organic psychosis, local neurologic signs are often present and may be found by systematic examination of fundi, cranial nerves, reflexes, spontaneous movements and muscle fasciculation, motor power and tone, coordination, and sensory examination.

Further evidence of pathology may be revealed by routine laboratory investigations such as hemoglobin, white cell count and blood smear, a serologic test for syphilis, chest roentgenograms, and examination of the urine for specific gavity, albumin, sugar, ketones, bile, urobile, porphyrins, and abnormal microscopic particles.

Other laboratory procedures that may result in positive diagnosis in certain cases include a wide variety of blood tests, such as blood sugar and glucose tolerance; nonprotein or blood urea nitrogen; electrolytes, blood pyruvates, and exogenous toxins such as alcohol, bromides, barbiturates, thiocyanates, lead, and sulfonamides; urine tests, such as those for renal function, vitamin B complex excretion, and elimination of exogenous toxins; tests of cerebrospinal fluid; radiologic examinations, including ventriculography and angiography; electroencephalograms, and tests of endocrine function.

TREATMENT

Treatment of the wide variety of bodily diseases and intoxications that cause acute brain syndromes is also too detailed for comprehensive discussion here but may be found in textbooks of internal medicine, medical therapeutics, and nursing. Such treatment may be considered as either *specific*—directed toward the established causative agent—or *supportive*—symptomatic or general measure for use in various forms of delirium or stupor.

Among the specific treatments that may be indicated are chemotherapy for the elimination of infecting organisms of parasites; termination of exposure to exogenous poisons; drugs designed to help the body eliminate toxic materials present in excess, such as sodium chloride for bromide intoxication; neurosurgery—for example, for evacuation for intracranial clot, elevation of a depressed fracture, or removal of a tumor; drugs or procedures intended to increase the blood supply to brain; administration of anticonvulsant medication; or specific measures designed to correct metabolic disorders, such as administration of fluids, electrolytes, minerals, vitamins, or hormones.

Supportive therapy, symptomatic or general, includes a variety of measures designed to minimize such manifestations as confusion, agitation, fever, dehydration, and malnutrition. It has often been recommended that, if possible, the patient be treated in a quiet, cool room, with a constant subdued lighting, neither too bright nor total darkness, and that nursing attendants be at a minimum number, thus diminishing confusion and facilitating isolation precaution in the case of infectious diseases. The patient requires suffi-

cient supervision to protect him from self-injury and may also require restraint to prevent excessive agitation and aggression against others. Today the latter is usually accomplished by means of sedatives and tranquilizing drugs. Phenothiazines are particularly effective, and one of the earliest and simplest of these, promazine, is still satisfactory because it can be given intramuscularly without causing irritation and can also be given intravenously for rapid action. Other supportive meaures that should receive consideration in all cases include means of reducing excessive fever; maintaining hydration and electrolyte balance; administration of supplementary vitamins, particularly thiamine, niacin, and vitamin B_{12}; and attending to bowel and bladder function and care of the skin in bed patients.

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Atopic allergic conditions, especially hay fever and asthma associated with positive skin reactions, may divert attention from and mask underlying cystic fibrosis in young adults. Later, pulmonary complications related to increasingly serious infections may lead to diagnosis.

A pathogenetic relationship may exist between asthma and cystic fibrosis, with the thick mucus characteristic of cystic fibrosis obstructing the small bronchi throughout the lungs, contributing to the progressive nature of the condition. In addition, atopic rhinitis and asthma may aggravate or trigger some of the pulmonary infections, thereby increasing tissue reaction and damage.

Treatment must be adjusted to the individual patient. Substances and measures most often useful include (1) bronchodilators; (2) pancreatic enzymes; (3) all the fat-soluble vitamins; (4) whatever antibiotics are indicated by a study of the sputum during an acute infection; and (5) desensitization and avoidance of significant antigens, if allergic rhinitis and atopic asthma occur. Corticosteroids may be of value for patients with asthma.

Diagnosis of cystic fibrosis of the pancreas is being made more often in young adults. Of 14 patients with the condition who were more than 11 years of age, 8 had allergic manifestations such as asthma, rhinitis, nasal polyps, and hay fever.

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Current Status of Emulsion Therapy in the Treatment of Allergy

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Conventional allergy desensitization therapy employing multiple injections of aqueous extracts in increasing strengths has been in use since 1911, with little modification from the procedure first advocated by Freeman and Noon.[1]

In 1923, the first attempt to utilize emulsion therapy was made by Sutton,[2] who used a crude emulsion of olive oil. Since then, other vegetable oil emulsions of various types have been employed with little success. It remained for Loveless[3] to first utilize pollen in a mineral oil emulsion as a repository injection. In 1947, after several years of investigation, she published her initial report, based on the work of Freund and McDermott[4] who showed that antibody production could be enhanced and prolonged after the injection of antigenic substances emulsified in mineral oil. Vegetable oils did not possess these properties.

Beginning in 1957, Dr. Ethan Allan Brown[5–9] has been the leading exponent of repository therapy. Largely through his efforts, this form of treatment has gained widespread interest among allergists. The advantages cited by Brown are (1) enhancement of clinical results, (2) ease of treatment by reducing the number of office visits, and (3) increased safety. If these advantages can be corroborated, repository therapy in allergy will become the method of choice.

EMULSION THERAPY

The principle of emulsion therapy is the administration of a large amount of antigen, often as a single injection, given as a depot or repository. The slow, constant absorption from the depot is apparently a factor leading to a greater immunity response. It is a water-in-oil emulsion, the allergen being dispersed in the water phase. At present, the mineral oil used is the highly refined Drakeol 6-VR. The emulsifying agent is mannide mono-oleate (Arlacel-A). At this time, these emulsion antigen preparations are not available for general use.

Technics relating to the time, number of injections, interval between injections, optimum dosage, and safety are in the process of evolvement. At present, six to ten weeks before a pollinating season appears to be the optimum time for injection of the repository depot, if the 1-injection program is given. Many allergists prefer to give 1 or 2 smaller primer doses.

Originally, Loveless[10] and Brown[11] devised technics utilizing conjunctival as well as skin tests as a guide to optimum and safe dosage. Conjunctival tests have been discarded, to a great extent, because later studies have not substantiated them as true indicators of clinical sensitivity. In addition, they are technically difficult to perform and, frequently, the conjunctiva is nonreactive in patients with hay fever and bronchial asthma. Although there is certainly no perfect correlation between skin tests, dosage, and clinical sensitivity, Brown[11] still advocates skin tests as the best guide for optimum dosage. Many allergists also advocate the use of one to several preliminary feeler aqueous injections as a guide to the patient's tolerance for repository dosage.

CLINICAL STUDIES

Several thousand patients have already been treated by the repository method during the past three years. This method has been limited primarily to patients with seasonal hay fever and bronchial asthma. These patients were sensitive to tree, grass, or ragweed pollen. The use of emulsions has been extended to include patients with perennial symptoms who are sensitive to molds, dust, and animal dander antigens. Critical analysis thus far has been limited to pollen therapy.

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During the 1960 ragweed season, the Committee on Specific Therapy of the American Academy of Allergy[12] conducted a collaborative study of repository ragweed therapy. This study included 1,777 patients in over 30 cities with varying pollen counts throughout the United States. Included was a double-blind study in which 200 patients received repository placebos. Of those patients who had repository treatment, 75 per cent noted moderate to marked relief, although the percentage in the double-blind study was somewhat less—70 per cent. These results correspond rather closely with the observations that have been made throughout the years with conventional aqueous desensitization treatment. It would appear at this time that repository therapy in pollinosis is equally as effective as previous desensitization methods.

The American Academy of Allergy is extending its study on the efficacy of repository therapy. We are now in the process of selecting previously untreated ragweed hay fever patients for a study evaluating repository ragweed treatment. Because of the relatively high ragweed pollen counts in Minneapolis, the results should be highly significant.

Injection of pollen antigen, whether by the conventional method or in repository form, is not without hazards. The danger of constitutional, or systemic reactions from overdosage in the form of urticaria, sneezing, or asthma is always present. Systemic reactions in Loveless'[10] series were somewhat in excess of 5 per cent. A reaction rate of 6.5 per cent was noted in the collaborative study of the American Academy of Allergy. Eisenberg[13] reported that systemic reactions were as high as 20 per cent when extremely high dosages were used but were reduced to 10 per cent, 6 per cent, and finally to 0 per cent as the dosages were progressively decreased. In Brown's series,[11] the reaction rate was considerably less than 1 per cent. It would seem that constitutional or systemic reactions decrease with the experience of the investigator, which is paralleled in the use of conventional aqueous extracts.

TECHNIC

Care must be taken to insure a properly emulsified antigen for injection. A proper emulsion should not contain more than 2 per cent of immediately releasable active antigen. As previously mentioned, technics are now being evolved to minimize overdosage and subsequent reactions. Many allergists protect their patients by giving orally a combined preparation of an antihistaminic and a sympathomimetic drug, such as Hyadrine, Copyronil, Algic, or Pyribenzamine with Ephedrine, several hours before and after the subcutaneous injection of the emulsified antigen. Constitutional reactions occur two to four hours after the injection—somewhat later than with conventional therapy. These reactions may last twenty-four to forty-eight hours.

At the site of injection, nodules and, occasionally, sterile abscesses have been noted. However, as more experience has been gained as to dosage and type of antigen employed and with improvement in the preparation of the emulsion itself, they are becoming infrequent. Among the 1,777 patients receiving repository injections in the American Academy of Allergy study, 6 sterile abscesses were noted, of which 5 occurred in children; some of these were in Negroes. This corroborates the studies of Davenport and Berlin,[12] who reported that abscess formation was more frequent in children, particularly in Negroes, injected with emulsified influenza vaccine. On the other hand, Berman[14] has given approximately 2,000 emulsion injections to over 300 patients during the past three years, with the occurence of only 1 sterile abscess.

The present ingredients used in the preparation of pollen emulsions were developed by Salk.[15] Salk,[15,16] in his investigative studies with influenza vaccine, used emulsified vaccines extensively. He confirmed the earlier reports of increased and prolonged antibody response. With improved emulsified vaccines, he confirmed its safety with his studies on monkeys and subsequently with human beings. We are now using emulsified pollen antigens in similar animal studies. We are also attempting to ascertain the eventual fate of the mineral oil. Studies thus far appear to indicate that the oil is taken up by the lymphatic system.[17] There are some studies indicating that it may be partially metabolized[18,19] which are extremely important when the possible cumulative effects of repeated emulsion injections over a period of many years are considered.

One observation needs further clarification. Feinberg and associates[20,21] noted the production of delayed hypersensitivity in nonallergic subjects. They exhibited delayed positive skin reactions to intradermal tests with the pollen which previously had been given in repository form. This observation suggests that, unless a true clinical sensitivity to an allergen has been definitely established, it may be hazardous to give such treatment with that allergen to a patient.

SUMMARY

At this time, we can conclude that repository, or emulsion, therapy in the treatment of respira-

tory allergy, primarily in pollinosis, is most promising. Studies thus far in pollinosis reveal that it is equally as effective as, if not somewhat superior to, conventional treatment. However, before this method is universally substituted for conventional therapy—utilizing rapidly absorbing aqueous extracts—more time and observation are needed to develop the technics of administration and to corroborate its effectiveness and safety.

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Recurring focal seizures and progressive neurologic deficiency in children and young adults may be manifestations of an otherwise latent encephalitis.

Patients with the condition often have had febrile illness associated with convulsions in early life, with subsequent seizures and symptoms such as increasing hemiparesis and intellectual deterioration. By periodic radiographic examination, progressive cerebral atrophy may be seen, and electroencephalographic tracings may indicate extension of damage. The pronounced degree of intellectual deterioration suggests a diffuse process. By psychologic testing, well-established skills and acquired knowledge are found to be essentially normal, but attention, concentration, and new learning are impaired.

Probable viral etiology of the condition cannot be proved by present methods, and the chronic inflammatory process apparently is not extensive enough to produce detectable cerebrospinal fluid changes. Brain tissue findings, typical of those with chronic encephalitis of proved viral origin, include widespread perivascular cuffing, microglial activity, chronic leptomeningeal inflammation, vascular changes, gliosis, neuronal depopulation, and, in rare instances, intranuclear inclusion bodies.

When the disease process has become relatively quiescent and the epileptogenic area defined, surgical treatment may arrest or reduce seizures but will not prevent further brain damage.

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Value of the Sex-Chromatin Test

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Soon after the delivery of a baby, anxious parents and relatives await the doctor's reply to their first question, "Is it a boy or a girl?" Occasionally, the external genitalia are ambiguous, and a sex is assigned that seems most apparent at the time. It is most important that any errors made initially be corrected as early as possible to minimize the psychologic problems of the child and parent. Any simple laboratory test to support the clinical diagnosis of the sex of a newborn infant would be valuable and might avoid future reassignment of sex.

A case of an anomaly of the reproductive system is presented here to illustrate the way in which recent discoveries in developmental biology and cytogenetics can aid the clinician in the diagnosis and understanding of such problems.

SEX-CHROMATIN TEST

In 1953, Barr[1] discovered a test to identify the chromosomal or genetic sex of an individual as determined at the time of fertilization. This stimulated an entirely new science of cytogenetics. The test is based on the presence of a chromatin mass in the nuclei of somatic cells of the normal female and the absence of the chromatin mass in the normal male. In normal persons, the presence of sex chromatin is related to the XX chromosome complex, or female sex chromosome, and the absence of the sex chromatin to the XY chromosome complex, or male sex chromosome.

This chromatin pattern can be studied in buccal smear preparations, skin biopsy specimens, or neutrophils of the peripheral blood. The buccal smear is preferred because of its simplicity. A more recent contribution that uses tissue culture technics, not yet available in clinical laboratories, makes it possible to analyze the entire chromosome complement of a cell, which now is known to number 46 in human beings. Thus, many genetic errors can be identified at the visible chromosome level as distinct from the effects of submicroscopic genes.

We now know that Barr's sex-chromatin test may give incomplete information in certain sex anomalies due to the presence of unusual sex chromosome complexes.[2,3] Yet the sex-chromatin test is still a valuable diagnostic aid, and, when used with other laboratory and statistical data available, most of these problems can be managed.

While the chromosome usually controls the differentiation of the fetal gonad into an ovary or testicle in accordance with genetic sex, its influence is only temporary; further sex differentiation, which takes place later in fetal life, is under the control of the fetal gonad and not the chromosome. Jost[4] has shown that the differentiation of the genital ducts and external genitalia is not influenced by the chromosomal sex but rather by the gonad. In his fetal castration experiments, he showed that a fetal testis is necessary to develop male genital ducts and external genitalia. In the absence of any gonad, the fetus always develops in the female direction. Exogenous hormones given mothers during the early stages of pregnancy are now recognized as having an effect on the genital development of the infant.[5]

In the rare case of sex reversal, gonads develop which are opposite the chromosomal sex.[6] In human beings, the cause of this failure of the gonads to develop in accordance with the chromosomal sex is not known. In amphibians, experimental alteration of the hormonal environment of the fertilized eggs has produced offspring having gonads opposite the chromosomal sex. There is no evidence of chromosome influence on the development of the child beyond gonad differentiation.

CASE REPORT

A 4-week-old infant was seen in consultation at the request of the family physician, who had noted a genital anomaly at the time of delivery. The first impression was

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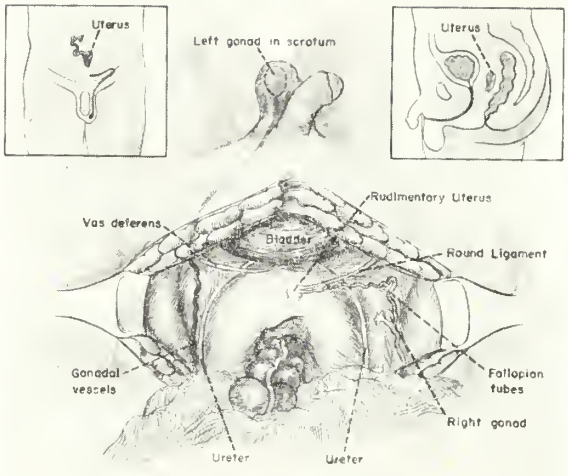

Fig. 1. Appearance of internal genitalia at laparotomy. Note development of male genital ducts on side of testes and female genital structures on side of undifferentiated right gonad.

that this was a boy with a severe hypospadias deformity. The baby was full term, weighing 6½ pounds at birth. No hormones had been given the mother during the prenatal period. Examination revealed a vigorous, healthy infant, who was completely normal except for the external genitalia. The phallus was of generous size for an infant of 4 weeks but was bound down by a chordee. The urethral meatus was in the middle of a bifid scrotum. A testicle, which seemed to be of normal size and consistency, was palpable in the left scrotum. The right scrotum was empty.

A buccal smear to determine the chromosomal sex indicated that this child was chromatin-positive and, therefore, a genetic female. The parents were told that final assignment of a sex would have to be based on further studies.

At the age of 7 months, cystoscopy revealed a female posterior urethra, with no evidence of a prostate gland.

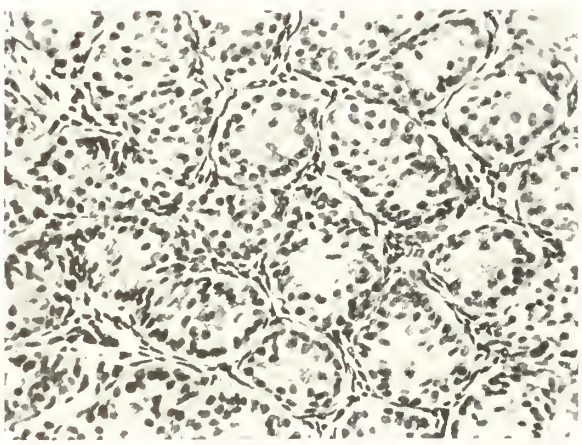

Fig. 2. Microscopic appearance of biopsy specimen from left gonad. Tubules appear to be normal infant testes.

There was no sign of a vagina or a diverticulum of the posterior urethra. The 17-ketosteroid excretion of 0.36 mg. in twenty-four hours was considered normal for the age and ruled out adrenal hyperplasia with excess adrenal androgen secretion as the etiology for the deformed external genitalia.

Laparotomy was performed to identify the gonadal sex and internal genitalia (figure 1). On the left side of the pelvis, the vas deferens was identified, and, as the left gonad was pulled up from its scrotal position, there appeared to be a normal testis with an epididymis measuring 1.5 × 1 × 1 cm. A generous biopsy specimen was taken, and the testicle was replaced in the scrotum (figure 2). On the right side, a unicorn uterus, fallopian tube, and a gonad were found. The gonad was in the usual position of an ovary. The gonadal structure and appearance of the external genitalia heavily favored male development, so the chromosomes were disregarded when the first stage of converting the infant to a boy was begun. The contradictory ovary and uterus were excised, and the chordee was corrected (figure 3). Later, a urethroplasty will extend the urethral meatus to the normal location, and the child will direct his stream as does any normal boy.

Histologic studies of the removed tissue confirmed the presence of the uterus and fallopian tube. There were no germinal cells in the right gonad, and it had to be classified as an undifferentiated gonad (figure 4).

Fig. 3. Appearance of external genitalia after correction of chordee. Testicle is in left scrotal compartment. Right scrotum is empty. Urethral meatus is in center of bifid scrotum.

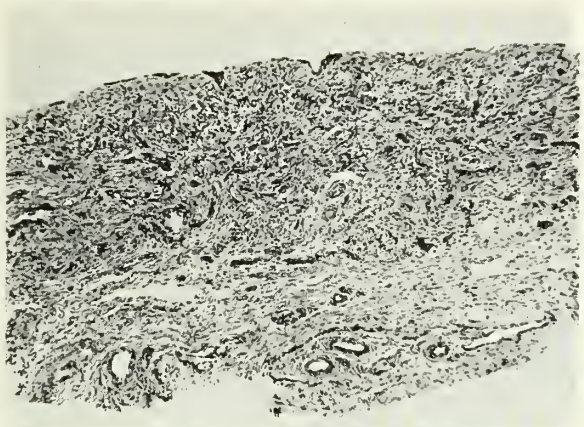

Fig. 4. Low-power photomicrograph of right gonad. Serial sections revealed no ovarian follicles, although stroma was ovarian. This is classified as an undifferentiated gonad.

DISCUSSION

This child is an example of unilateral sex reversal, since the left gonad is completely reversed from the chromosomal sex. The anatomic findings of male genital ducts on the left side and female genital ducts on the right support the experimental embryologists' theory that genital duct differentiation is determined by the inductors from the fetal gonad rather than by the genetic effect. If hormones can influence genital development in the fetus, a careful history of medication given the mother during pregnancy is vital to the evaluation of sex anomalies. The buccal smear was the key to the solution of a complicated problem that might have gone unrecognized until later, when the male presented himself for operation on his undescended testes or for infertility. It appears to the authors that more frequent use of the chromatin test as a screening examination in patients with hypospadias deformity, cryptorchism, or fertility problems would find some unsuspected or hidden anomalies.

SUMMARY

A case of partial sex reversal, which demonstrates some of the present theories on the etiology and pathogenesis of sex anomalies, is presented. A simple chromatin test was the key to the diagnosis. More frequent use of this test, especially in newborn infants with ambiguous external genitalia, will lead to an early diagnosis and better management of sex anomalies.

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Apparently, infection with group A streptococci almost always is associated with acute glomerulonephritis. Evidence of an antecedent streptococcal infection was found for each of 51 patients with acute glomerulonephritis. Antistreptolysin O titers of more than 160 units were found for 47, and beta hemolytic streptococci were isolated from throat cultures for 31 patients. Early diagnosis and adequate treatment of pharyngitis due to beta hemolytic streptococci are needed to prevent ensuing renal disease. Patients with acute glomerulonephritis should be given an adequate course of penicillin therapy.

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Pancoast Tumor

Diagnosis and Treatment

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A SINISTER SYMPTOM COMPLEX was described by H. K. Pancoast in 1932,[1] and the disease entity now bears his name. Pancoast expressed the opinion that this superior sulcus tumor was of embryonal origin, arising from the embryologic transplants of branchial arch tissues. Later studies, however, have proved this concept to be in error, and it is now acknowledged to be a primary bronchogenic carcinoma arising from peripherally located bronchi in the lung apexes. The intimate association of the primary tumor with adjacent structures—parietal pleura and successive layers of chest wall tissue, brachial plexus, and sympathetic ganglia—often obscures the primary origin of the neoplasm. The direction of malignant spread shuns the usual routes of drainage toward the pulmonary hilus.

Although bronchogenic carcinoma is unquestionably the most frequent cause of the syndrome, the rare primary branchial cleft tumors, sympathicoblastomas of the cervical ganglia, osteogenic sarcomas, and metastatic tumors can be responsible, as can nonmalignant conditions such as infiltrating tuberculosis, aneurysms of the innominate and subclavian vessels, and organizing hematomas. The bronchogenic carcinomas most often responsible for the syndrome are of the well-differentiated squamous cell type—the type most prone to invade the wall of the thorax by direct extension.

Benign or malignant tumors occurring in the region of the pulmonary apex may produce the symptoms and findings described by Pancoast solely because of their anatomic location and not because of a particular pathologic structure. Nevertheless, the occurrence of the syndrome should at all times be considered due to a malignant process unless contradicted by tissue confirmation of a benign disease. The malignant process occurs principally in men and frequently within an age range which is substantially lower than that usually recorded in primary bronchogenic carcinoma otherwise located in the lung.

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SYMPTOMS

The initial symptoms are caused by local invasion of adjacent tissues. The dominant symptom is pain. The location of the pain varies; however, the apex of the chest, as well as the shoulder and arm, is usually involved. Paresthesia, weakness, and atrophy of the affected extremity may occur. Because of the close proximity of the tumor to the sympathetic ganglia, the latter are frequently reluctantly engaged during the period of tumor expansion and are revealed clinically by the development of a Horner's syndrome.

Although these symptoms appear discouragingly late, they express the body's earliest cry of alarm. The usual respiratory symptoms resulting from bronchogenic carcinoma are extremely late manifestations and often are absent during the entire course of the patient's illness. Like the killer submarine, this tumor lies submerged, quietly spreading its devastation, and surfaces only to acclaim victory.

Any one or a combination of these symptoms should focus attention on the pulmonary apex. A comparison of both apexes is often helpful in defining early abnormalities. Diagnostic access by x-ray examination is frequently impeded or denied by the bony structures sheltering the pulmonary apex. Additional roentgenographic refinements, such as lordotic views, Bucky exposures, and laminagrams, may unveil early abnormalities not evident on conventional roentgenograms. Initial radiographic studies may reveal no abnormality or may show only a thickening of the apical pleura of the involved side. More frequently, however, a diffuse, homogenous density is evident in the pulmonary apex with or without a sharp inferior margin. The osteolytic involvement of the ribs and vertebrae

may be obscured by the superimposed density of the tumor. Additional findings of destruction involving the ribs, vertebral bodies, and transverse processes confirm the diagnosis and unfavorably tip the balance of the prognostic scale. Bronchoscopy, which is second only to roentgenography as a diagnostic tool of pulmonary disease, renders little aid because of the peripheral location of the lesion.

The extreme variation of early and late detection may hardly be perceptible by plain roentgenograms. Radiographs of 2 of the author's 8 cases are shown for purposes of illustration (figures 1-4). The astute roentgenologist is credited with pronouncing as a questionable lesion the pleural thickening at the left apex. This apical "eyebrow" was revealed to be a definite lesion by lordotic views and later was confirmed by surgical resection. This patient exhibited no symptoms referable to the chest or shoulder girdle.

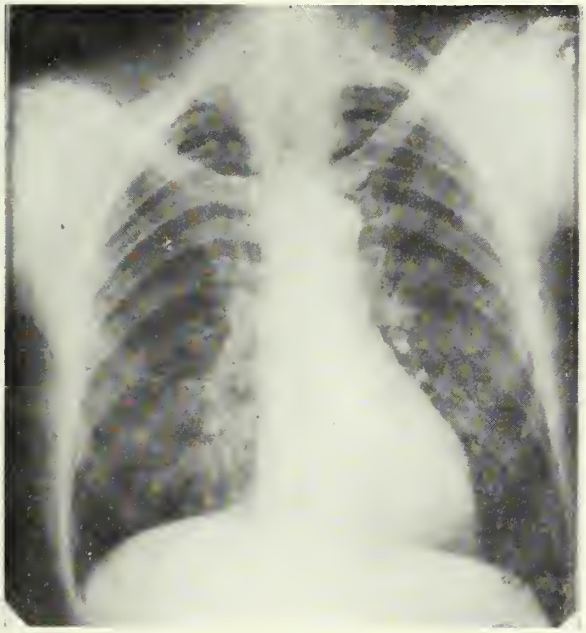

Fig. 1. *Case 1.* This patient was without pulmonary or shoulder symptoms. Pleural thickening is evident and suggestive of underlying disease at left apex.

Fig. 2. *Case 1.* Underlying disease is well demonstrated (see markers) on this lordotic view.

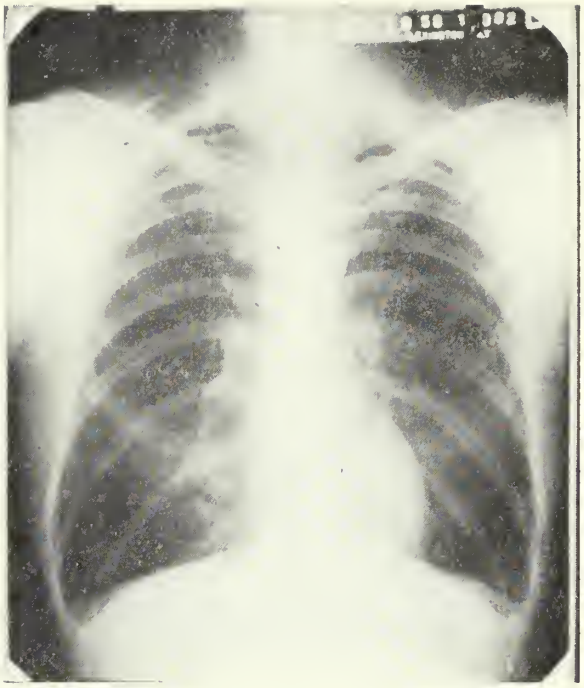

Fig. 3. *Case 2.* This roentgenogram reveals a haziness at left apex blending with first rib and clavicle. A chest film one month earlier was reported as showing no evidence of disease.

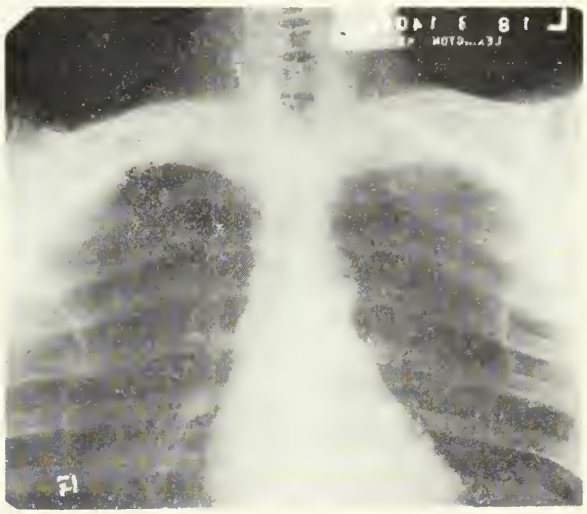

Fig. 4. *Case 2.* The soft, round lesion is evident on this lordotic view, and destruction of portions of the first and second ribs has occurred.

The destruction as evidenced in the next case was not readily apparent by plain film, and the patient had been receiving treatment for shoulder pain for several weeks on the basis of a normal chest roentgenogram. The lordotic film revealed the far-advanced disease.

TREATMENT

The management of the superior sulcus tumor may be divided into surgery, irradiation, or a combination thereof. Preoperative and postoperative x-ray therapy has been advanced, and the proponents of each have survival rates attesting to the proficiency of their respective modes of treatement. Surgical resection, even when it is only palliative, is beneficial as a decompressing measure to alleviate the distressing and often unrelenting pain which is invariably associated with this tumor.

Irradiation therapy yields temporary but significant relief of pain caused by spinal and bony metastases. Additional avenues of approach to the relief of pain consist of chemotherapy and neurosurgical procedures. The latter must be weighed carefully because, to exercise greatest benefit, one should expect a survival time exceeding four to six months.

CONCLUSION

The most obvious means of countering the adverse survival rate is by earlier detection of the lesion. This fierce competitor precludes parking on observatory hill. An awareness coupled with prompt diagnostic armaments establishes the front line of defense. The x-ray is the indispensable ally both in diagnosis and treatment.

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Changes in steroid or ACTH therapy may cause arteritis and neuropathy in rheumatoid disease. Once neuropathy, which seems to be secondary to arteritis, occurs, the prognosis is poor. No treatment seems to be effective.

Of 18 arthritic patients having neuropathy, 15 were or had been receiving steroids or ACTH at the time of onset. In 10, initiation, interruption, or reduction of therapy appeared directly related to the start of systemic symptoms. The 3 patients never given steroids had only slight symptoms. Within one year after neuropathy appeared, 5 patients died.

Lower limbs were affected in 12 patients, both upper and lower in 5, and a single upper limb in 1. Sensory symptoms, observed in all 18, preceded the motor changes and affected only the lower limbs. Symptoms included: (1) tingling, burning, and numbness of the limbs; (2) muscle pains and tenderness of the calves; (3) negative or impaired response to pinprick, temperature, and light touch; (4) loss of position sensation, usually confined to the toes; (5) loss of vibration sense; and (6) unilateral or bilateral foot drop.

Associated features of neuropathy were (1) digital arteritis; (2) lung changes; (3) lupus erythematosus cells; and (4) fever, splenomegaly, and albuminuria.

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Diseases of the Extrapyramidal Motor System

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THE EXTRAPYRAMIDAL MOTOR SYSTEM is composed of the caudate nucleus, putamen, globus pallidus, thalamus, hypothalamus, subthalamic nucleus, red nucleus, substantia nigra, and reticular formation plus portions of the cerebral cortex which have connections with the basal ganglia. Involvement of these structures generally results in the appearance of abnormal motor movements called dyskinesias. These abnormal motor phenomena vary widely in type, and often one or more will predominate in a specific illness of the extrapyramidal system. In order properly to understand the clinical diseases involving this region of the nervous system, one must have some knowledge of the different types of abnormal movements.

TYPES OF ABNORMAL MOVEMENTS

Tremors. These consist of involuntary, rhythmic, oscillatory movements which result from alternate contraction of opposing muscle groups. They most often involve the distal part of the limbs but may also implicate the lips, face, or head. Rate of the tremor varies from 10 to 20 oscillations per second (fast) to 4 to 7 oscillations per second (slow). Tremor may be present at rest or only during use of limbs (kinetic tremor). Emotional stress, fatigue, or anxiety increases the tremor.

Tremor is the characteristic feature in a number of diseases, such as parkinsonism, Wilson's disease, hereditary tremor, and toxic states, such as manganese or carbon monoxide poisoning.

Rigidity. This consists of increased muscle tone in both flexors and extensors that results in resistance of the limb to both passive and active motion. Rigidity produces a slowing of muscle activity, a loss of automatic movements such as swinging of the arms in walking and crossing of the legs while sitting, and a loss of facial expression. Often there is marked difficulty in initiating muscle movement in the involved parts.

Diseases characterized by rigidity are parkinsonism, Wilson's disease, and Jakob-Creutzfeldt disease.

Chorea. This refers to quick, jerky, purposeless, nonrhythmic, unsustained, involuntary movements that jump from one muscle group to another. Each individual movement is discrete but varies in type and location, thus forming an irregular pattern of constantly changing movement. Choreatic movements may involve all parts of the body but are most often confined to the distal portions of the upper extremities, the face, and the head. Facial involvement results in facial grimacing, and limb involvements impair voluntary function because of an inability to maintain muscle contraction.

Two diseases are characterized by choreatic movements—Sydenham's infectious chorea and Huntington's chronic hereditary chorea.

Athetosis. This consists of a slow, sinuous, twisting, writhing movement that chiefly implicates the head and distal parts of the limbs and is usually associated with increased muscle tone. This type of abnormal movement is seen in a group of uncommon neurologic disorders such as double athetosis (status marmoratus), Hallervorden-Spatz syndrome, and Pelizaeus-Merzbacher disease.

Dystonia. Dystonia is a slow, sinuous, twisting or turning movement that involves the larger portions of the body, such as an entire limb, half the body, or the entire body. It implicates chiefly the proximal part of the limbs, such as the hip and shoulder girdle, and is usually accompanied by some increase in muscle tone.

Dystonia is encountered most commonly in spasmodic torticollis and in dystonia musculorum deformans. It may also occur in infectious diseases of the nervous system.

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Ballism. This is a wild, flinging movement of the limbs which may be confined to one limb (monoballism) or one side (hemiballism). It is usually caused by a lesion of the corpus luysi, resulting from vascular disease.

Myoclonus. This consists of a rapid, involuntary muscular contraction which may be limited to a small number of muscle fibers or to an entire muscle. It occurs in paroxysms at irregular intervals and can be activated by emotional stimuli. It occurs most often in the muscles of the extremities but may affect the muscles of the jaw, tongue, pharynx, or larynx.

Myoclonus may accompany some infections or degenerative diseases of the nervous system. It may appear as a prominent part of such diseases as myoclonus epilepsy or essential myoclonus (Friedreich's disease).

PARKINSONISM

Etiologically, two forms of paralysis agitans have been described—a postencephalitic form and an arteriosclerotic form. The former is the result of the large influenza epidemic of 1918 through 1925. This epidemic apparently resulted in specific damage to the extrapyramidal system, with the subsequent appearance of symptoms years after the initial infection. The arteriosclerotic form is seen chiefly in elderly individuals but differs very little clinically from the postencephalitic type. Actually, there is considerable question as to whether these two types of the disease are basically different.

Clinical features

The two chief clinical features of this disease are rigidity and tremor. Either may predominate or may occur alone. Probably, muscle rigidity is the most consistent manifestation and plays the most prominent role in determining the course and prognosis of this disease. When the rigidity predominates, onset of the illness may be so subtle as to be overlooked for years by both the patient and the family. Early in the course of the disease, the patient develops pain in the shoulder girdle musculature after a full day's work. He often finds that he is unable to complete his work in spite of increased effort. At this point, examination may not readily detect the cause for either the pain or the decreased work efficiency. Also early, these patients show a reduction in automatic movements. The arms do not swing during walking, the legs are not crossed during sitting, and the facial musculature becomes immobile.

As the illness progresses, the arms become more rigid, interfering with finer movements such as sewing, buttoning, or writing. In the latter case, the written words gradually decrease in size until they become illegible. Walking also becomes impaired, due to difficulty in automatically lifting the feet. The patient tends to shuffle and to take small steps. As the rigidity involves the trunk, the posture becomes bent, and turning, arising from a chair, or postural adjustment in bed becomes difficult or impossible. Patients in this stage often "freeze" when trying to initiate motor movement and often cannot walk until given a start. Frequently, when walking, they tend to accelerate their gait (festination) and cannot stop until they encounter some object or fall (propulsion). Speech is rapid and lacks inflection or volume. Ultimately, as the rigidity progresses, the patient becomes completely incapacitated by immobility. Even fairly early in the illness, the muscle rigidity interferes with work activity, and, as the illness progresses, self-care activities become difficult, necessitating adjustment on the part of the patient as well as the family.

Tremor in paralysis agitans is much less frequent but more striking and dramatic than is rigidity. It naturally is detected shortly after its onset. It is a coarse tremor of wide amplitude and of a rate of 4 to 5 per second. It most commonly implicates the distal parts of the extremities and produces in the hands the characteristic "pill-rolling" movement. As a result of this tremor, handwriting becomes tremulous and at times illegible. When extreme, this tremor interferes with all self-care activities and jeopardizes the patient's rest. Occasionally the tremor may involve the head or the jaws. When the latter is involved, the pounding together of the teeth may become very painful and distressing.

The course of paralysis agitans is usually slowly progressive over the years. However, the illness may run its course in a few years, resulting in rapid and complete invalidism.

Environmental adjustment

Because of the impaired motor activity, patients with parkinsonism must be aided in making considerable modifications in their normal living and work patterns. A discussion of some of the problems normally encountered might prove helpful.

Reduction of the patient's work load. Because of muscle rigidity, the patient's ability to accomplish many tasks slowly decreases. The patient is unable to complete his normal work load regardless of the effort applied. Any attempt to continue with the usual work load produces overfatigue and frustration. Understanding of

and adjustment to these limiting factors will help remove some of the emotional strain and aid in the comfort of the patient.

Home adjustment. These patients slowly develop difficulty with self-care activities which interferes with home adjustment and with general family routine. They eat more slowly, thus delaying the meal habits of the entire family. Unless the family has been briefed as to the nature of the illness and is willing to cooperate, extreme tensions can be created and the ultimate comfort of the patient reduced.

Personal adjustment. Parkinsonian patients have progressive difficulty in dressing and in simple self-care activities. At onset of the disease, such activities can be accomplished but are slowed. Later, the patient may need some help, even for the simplest tasks. This loss of personal independence can be distressing to most patients. Unless the family is extremely tolerant and understanding, the method by which they offer help can be detrimental and humiliating to the patient.

Emotional adjustment. Any increased emotional disturbance tends to accentuate the symptoms of paralysis agitans. It is, therefore, imperative that the physician work with the patient and the family to help both adjust to the illness and obtain the most satisfactory environmental status.

Drug therapy

A large number of drugs are now available for treatment of this disease. It may be necessary to try different drugs or different combinations of drugs before the best therapy is found. The patient may develop a tolerance or a toxicity to medication that formerly produced good results, necessitating a change of medication. Certain general precautions must always be kept in mind: (1) Drug tolerance tends to decrease with age, so that for older patients the drug dosage is smaller and is regulated more slowly; (2) Belladonna derivatives may prevent proper cooling of the body, and therefore dosage should be reduced in hot weather; (3) Systemic infections may reduce the patient's tolerance to these drugs and may precipitate toxicity in a previously well-controlled patient.

Belladonna derivatives. These were the earliest products used in the treatment of this disease and still comprise some of the most beneficial preparations available for therapy. The more common of these products are hyoscine, hyoscyamine, Rabellon, and Vinobel. The dose of each drug must be regulated for each patient in order to obtain the best tolerated dosage which offers the maximum improvement. The drug dosage is generally increased slowly until optimum results are obtained without causing toxic symptoms. Usually, the maximum dose is given at bedtime. In elderly individuals with decreased tolerance, dosage is increased very slowly in order to avoid rapid toxicity.

Toxic manifestations of the belladonna derivatives consist of dryness of the mouth, visual blurring, urinary retention, nausea, diarrhea or constipation, vertigo, and, rarely, confusion. Usually, dryness of the mouth is not considered sufficient to reduce the amount of medication. All the other symptoms suggest that the dosage should be reduced.

Parsidol (50 mg). The dosage of this drug must be separately determined for each patient, doses beginning with 50 mg. daily and slowly increased. Generally, the best therapeutic dose is over 250 mg. daily. Toxic symptoms are drowsiness, giddiness, and heartburn.

Artane or Pipanol (2 mg.). These are the same product under different trade names. It is one of the best tolerated of the antiparkinsonism drugs.

When it is used alone, the beneficial effects are apt to be transient. It is, therefore, advisable to use this drug in conjunction with one of the belladonna derivatives, such as Vinobel or Rabellon. The usual dose is 4 to 6 mg. daily. Toxic symptoms are dryness of the mouth, blurred vision, dizziness, nervousness, soreness of the mouth, and, occasionally, nightmares.

Pagitane Hydrochloride (1.25-2.5 mg.). The usual dose is 5 to 7.5 mg. daily. This product is relatively nontoxic. Symptoms, when they occur, resemble those produced by Artane.

Cogentin (2 mg.). This is an excellent product but tends to be somewhat toxic. The usual dosage is 1 to 4 mg. daily. Toxicity must be watched for carefully, and symptoms are drowsiness, confusion, ataxia, and gastrointestinal complaints.

Kemadrin (2.5-5 mg.). This product has not proved too helpful in the treatment of parkinsonism. It is relatively nontoxic and can be used to advantage in elderly patients. The usual dosage is 16 mg. daily.

Phenoxene (50 mg.). This is a nontoxic product that is most useful in elderly patients. When possible, it should be used as an adjunct to some of the belladonna derivatives.

Rotase. This is a combination drug composed of Mebaral, Amytal, Desoxyephedrine, and hyascine. Because of the small quantities of hyoscine, Rotase is well tolerated by elderly individuals with parkinsonism. Often, the sedative action of Mebaral is helpful in the control of the associated tension state.

Physical therapy

Generally, physical therapy offers no lasting benefits in this illness. It is most helpful to those patients who are confined to a chair or to bed. Mild massage and heat may reduce muscle soreness and relax rigidity temporarily.

Surgery

Surgical treatment for parkinsonism has received considerable popularity within recent years. As yet, the surgical procedures are still in the investigative stage. In younger patients who are extremely incapacitated by rigidity or tremor, surgery may be considered. Generally, it is not recommended as yet for older patients, particularly those with severe bilateral involvement.

WILSON'S DISEASE

A rare disease of the basal ganglia, hepatolenticular degeneration usually begins in the second or third decade of life; has a chronic progressive course; tends to occur in families; and is characterized by involuntary movements of the limbs, rigidity, and emotional disorders. It is now believed that this illness is an inborn metabolic disorder of copper metabolism which results in damage to both liver and brain. This is suggested by the increased excretion of copper and amino acids in the urine and the decrease in the serum copper.

As a rule, clinical evidence of liver damage is absent, although some patients may exhibit ascites or jaundice at any stage of the disease.

Tremor and rigidity are the predominant neurologic manifestations. The tremor may be of the alternating type seen in parkinsonism. Often, however, it is more bizarre, implicating chiefly the wrists and hands and assuming a wild, flinging motion resembling the beating of the wings of birds (wing-beating). The tremor is often absent during rest but is accentuated by movement or sudden changes of posture. It generally remains localized to the upper limbs.

Rigidity is almost always present and is generalized. It may predominate the clinical picture, producing parkinsonian-like manifestations, with expressionless facies and even speech disturbance due to spasticity of the laryngeal musculature. Mental symptoms are constant but variable in nature, and patients have emotional lability and mental dulling.

A Kayser-Fleischer ring in the cornea, when present, is diagnostic for this illness. It consists of a green-brown pigment ring visible in the cornea and generally best visualized by use of a magnifying glass or a slit lamp. The diagnosis can be further verified by the abnormality in the pattern of amino acid and copper excretion in the urine and the decreased copper content of the serum.

The course of the disease is slow but progressive. Remissions and exacerbations occur, particularly during therapy, but the final outcome is fatal.

Treatment consists of 2 mg. of BAL per kilogram of body weight intramuscularly every six hours. This therapy dramatically improves the symptoms, but improvement may not be retained, and the downhill course may continue.

SYDENHAM'S CHOREA

Chorea minor is a nonspecific encephalitis of childhood characterized by choreatic movements, frequent psychotic aberrations, and a propensity to tonsillitis, endocarditis, and polyarthritis. Rheumatic affection has been reported in 20 to 90 per cent of patients with chorea. Current opinion is that rheumatism is not a cause of the chorea but merely an integral component of the symptom complex, which includes repeated attacks of throat sepses, heart disease, rheumatic fever, and chorea. Over 80 per cent of cases occur during childhood and less than 8 per cent after the age of 20 years. Girls seem to be more frequently affected than boys.

Onset of the disease is usually gradual, occurring over a period of days or weeks, although it may appear suddenly after an emotionally charged experience. At the onset, the patient may show only excessive fatigability, irritability, and restlessness in sleep. The patient may appear to be inattentive and uncooperative. Soon movements become clumsy, objects are dropped, and the ability to execute such skilled acts as writing may deteriorate.

The characteristic feature of the disease is the appearance of the choreatic movements—rapid, irregular, purposeless movements which most commonly implicate small muscles of the limbs and face. The facial muscles may show peculiar twitching, with the production of smirking expressions and facial grimacing. In the limbs, the choreatic movements may remain limited to the hands and feet or may involve the entire extremity, resulting in flinging movements that interfere with the use of the limbs. The severity of these movements is accentuated by attention, excitement, or fright. When undisturbed, the child may remain quiet, with only minimal abnormal movement. Implication of the tongue and palate usually will interfere with speech.

There is often a definite weakness of voluntary

movement and an inability to maintain a sustained muscle contraction. This is particularly noticeable in the changing force of pressure when the child grips the examiner's hand. Occasionally, focal weakness of a limb may occur but generally clears up as the patient recovers.

Mental changes are usually mild and consist of disorders of attention and irritability. In acute cases, there is dullness of intellect, memory deficiencies, hysterical outbursts, and even psychotic behavior with hallucinations and delusions.

Acute chorea usually lasts from four to six weeks, with gradual and complete recovery in uncomplicated cases. Outcome is fatal in 2 to 3 per cent, particularly in those cases with severe hyperkinesias and rheumatic endocarditis. In 4 to 8 per cent of patients, mild choreatic movements of the fingers or ties of the face persist for years. Cardiac complications are seen in 20 per cent of cases.

There is no specific therapy for this disease. Rest, a placid environment, and the use of mild sedation are generally adequate in the milder cases. With more extreme involvement, heavy sedation may be necessary to control the motor manifestations. Fever therapy has been used but is of questionable value. Prophylactic oral penicillin as a precaution against rheumatic infection should be instituted and continued for many months after recovery from the illness.

HUNTINGTON'S CHOREA

Chronic progressive chorea is a strongly familial and hereditary disease that usually appears after the age of 30 years and is characterized by severe choreatic movements and mental deterioration. The disease is usually subtle in onset. The patients, over a period of years, become irritable and somewhat retarded.

The most characteristic feature is the choreatic movements, which are gross and implicate large muscle groups rather than smaller muscles. These gross, jerking movements produce saluting gestures, shrugging, and twisting of the body that interfere with gait. The facial expression becomes contorted and associated with clucks, grunts, and grinding of the jaws. These motor movements gradually become so violent that the patient is completely incapacitated and unable to care for himself.

The mental symptoms may precede or follow the motor component. Early, there occur irritability, forgetfulness, anxiety, and bouts of depression or fits of violence. As deterioration continues, the patient becomes slovenly, incontinent, and finally, completely demented.

Treatment is symptomatic. Reserpine may reduce the choreatic movements but does not influence the course of the disease. Often, because of the irritability and emotional instability, these patients must be committed early to state institutions for custodial care.

SPASMODIC TORTICOLLIS

This disease is a localized form of dystonia in which there is an involuntary pulling of the neck muscles to one side. The etiology of this condition is unknown. Although most cases no doubt are organically determined, some cases have been suspected as being psychogenic in nature.

This illness usually appears between the third and fifth decades of life, affecting both sexes equally.

At onset, there may appear to be a lateral tremor of the head due to spasm of the neck muscles on one side. The movements are slight at first but increase in frequency and severity until free intervals between paroxysms are few and very short. The head becomes pulled over to one side or rotated in a spasmodic, athetotic manner. In many cases, the head finally becomes permanently deviated and the sternomastoid muscle on the opposite side becomes tonic and hypertrophied. In some cases, dystonic contractions spread to involve the facial muscles as well as the muscles of the shoulder girdle and arm on one side. Fatigue and emotional tension accentuate the illness. The dystonic movements disappear during sleep.

The course of the illness is at first progressive but, in almost half the cases, becomes static after a period of years. Spontaneous remissions may occur during the first year of the illness.

Treatment is often ineffectual. Surgical procedures have been tried but are of questionable value.

DYSTONIA MUSCULORUM DEFORMANS

This disease is of unknown etiology, usually beginning in childhood, although adults are not exempt. It is characterized by slow, sustained, twisting, turning, athetosic movements that implicate any of the somatic musculature, with a predilection for the muscles of the trunk and limbs.

Onset is gradual but progresses, often with no orderly sequence of muscle involvement. When extensive, this disease produces an irregular, writhing distortion of the body, a twisting of the neck, and contractions and distortion of the limbs. The muscle spasms may result in a large variety of disturbances, such as facial grimaces, dysarthria, torticollis, and bizarre gait.

There is no true paralysis, but the muscle spasms prevent proper use of the limbs.

The course of this disease is progressive. At times, the involvement remains localized to certain muscle groups, but often it spreads to implicate the entire body, causing the patient to be bedridden in five to eight years.

There is no treatment for this illness. Recently, surgery has been tried, with some favorable reports.

BALLISM (HEMIBALLISM)

Hemiballism results from a vascular lesion of the subthalamic nucleus. Clinically, the symptoms develop acutely, usually in the older age groups, and consist of wild, flinging movements of the entire limb which continue to a point of exhaustion. There is no treatment for this disease, although an occasional case may subside spontaneously.

MYOCLONUS

This condition may result from many organic illnesses of the nervous system, such as multiple sclerosis, encephalitis, and so on. It also occurs as a rare familial disease associated with seizures and mental deterioration (myoclonic epilepsy).

Myoclonic epilepsy begins between the ages of 6 to 15 years, either with seizures or myoclonus. The myoclonic jerks involve primarily the muscles of the limbs but may also affect the trunk or face. They consist of quick, sudden jerks of a muscle resulting in gross muscle group or limb movement. Seizures may precede or follow the myoclonus and are grand mal in type. As the disease progresses, incoordination, intention tremor, and mental deterioration develop.

The course of the disease is slowly progressive. The seizures may be helped by anticonvulsive medication, but no effective therapy is available for the basic illness.

PNEUMONIA is the usual cause of pulmonary abscesses in pediatric patients, as in adults. Aspiration of foreign bodies and operations may also precipitate abscess formation.

Prominent symptoms are fever, cough, purulent sputum, weight loss, and hemoptysis. Chest pain appears to be less frequent in children than in adults.

Twice as many lesions occur in the right lung as in the left. The usual abscess is confined to 1 lobe, but 2 or 3 lobes may be affected. Streptococcus and staphylococcus infections account for most abscesses.

Pulmonary resection is the preferred treatment. All of 7 patients managed surgically survived. Lobectomies were done for 6 of the patients, removing a total of 8 lobes. For the other patient, treatment was rib resection with surgical drainage of the abscess.

Nonoperative treatment, including general supportive measures, transfusions, thoracentesis, bronchoscopic examination, tracheostomy, and postural drainage, was employed for 7 patients before antibiotics were available, all of whom died. Another 4 patients were treated similarly but with antibiotics, and 2 survived.

Brain abscess, meningitis, or both caused death most often. Other causes were hemorrhage, rupture of abscess into the tracheobronchial tree, pyopneumothorax, tension pneumothorax, and overwhelming infection.

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The C.V.D. Research Program of the Laboratory of Physiological Hygiene

An Explanation and a "Letter to Guinea Pigs"

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In 1947 the Laboratory of Physiological Hygiene, University of Minnesota, embarked on a research program, supported by the United States Public Health Service, aimed at providing clues about etiology and evaluating the prognostic significance for future heart disease risk of characteristics observed in health. The program involved following for some years a group of middle-aged business and professional men.

The subjects were recruited from Minneapolis and St. Paul, primarily through local business firms, which provided the names of 1,000 men of the right age who were considered permanent employees in responsible positions. Letters were sent to these men asking if they would join as "guinea pigs" in this research program, and 916 affirmative replies were received. In addition we had a list of about 30 men for whom a place was desirable because of considerations of friendship or public relations. This select group included the Governor, Luther C. Youngdahl, the late Dr. Archibald Cardle, then president of the state medical society, 11 leading members of the University of Minnesota faculty, and 10 other prominent professional men.

Our facilities and funds would provide for only about 300 men in the study. Selection was made as follows: First, those men were eliminated whose questionnaires indicated that they might be suffering from heart disease. Second, from data in these questionnaires, we selected the 50 most overweight and the 50 most underweight men, and another 50 men who were reported by the athletic directors of the local YMCA's and athletic clubs to be especially active in their programs. After including the select list, the remaining places in the group were filled by drawing names at random from the list of men available.

When the men were called in for their first examinations in 1948, several were found to have overt heart disease or other unacceptable disability. These men were excluded and their places were filled by men on the waiting list. The result was a final main study group of 285 men then aged 45 to 55. These "guinea pigs" were not an ideal sample of the Twin Cities, but there is no reason to suggest that they were seriously unrepresentative of the upper economic class.

They have been remarkably faithful to their pledge to come in for an annual examination. A total of 26 men has died. In 1961, contact was made with all 259 men in the surviving group. Examinations were carried out on 218 men. Of the remaining 41, 26 have been seen on 2 or more occasions in the last five years, 9 have moved out of town, and 5 men are known to be well and working but have, in effect, resigned from the experiment. There is a hard core of 198 men who have never missed an examination in fourteen years. Every year the examination includes a review of the interim history, physical examination, nude weight, chest roentgenogram, 12-lead electrocardiogram, urinalysis, and measurement of hemoglobin and serum cholesterol. Special tests, changed from year to year, have included exercise tests, cold pressor test, tilt-table test, ballistocardiogram, electroencephalogram, flicker fusion, basal metabolism, various meal tests, body density, subcutaneous fatness, sugar, uric acid, and protein-bound iodine in the blood, anthropometric details, and many evaluations of emotional status and personality.

All five authors are members of the staff of the Laboratory of Physiological Hygiene, University of Minnesota.

Besides the present senior staff of this laboratory, the following former staff members had major responsibilities in planning and operating this research program: Drs. Josef Brozek, now at Lehigh University; Carleton B. Chapman, now at Southwestern University Medical School; Austin Henschel, now with the U.S. Army Q.M.C. Research and Development Command; and Olaf Mickelsen, now at the National Institute of Arthritis and Metabolism.

During the followup through February 15, 1961, almost exactly 10 per cent (29 out of 285 men) have had a myocardial infarction or have died from coronary heart disease. Other deaths and serious disabilities have been remarkably few. The only item of observation so far found to be important in predicting their future health has been the concentration of cholesterol in the blood.

Except for a slight rise in the first few years, the average serum cholesterol concentration in this group remained relatively stable through twelve successive years. In the last two examinations, however, the cholesterol values have declined in a considerable number of the men, in some cases at least, because of dietary changes recommended by their physicians or induced by popular publicity. For the five years, 1955 to 59, inclusive, the average of the yearly medians was 238 mg. of cholesterol per 100 cc. of serum; the corresponding figure for the succeeding two examinations is 222.

Other reasons for believing that characteristics of these men may be changing are suggested by a tendency of some of the overweight men to reduce effectively, reports from a considerable number of men that they have stopped smoking, and an increasing number of men who are taking some medication to control blood pressure. Possibly these tendencies are current general characteristics of men of these ages in this community, but it is clear that this group is becoming increasingly health conscious and, therefore, possibly decreasingly representative of the whole population.

A LETTER TO "GUINEA PIGS"

Dear Friends:

Back in 1947 when we invited you to be "guinea pigs" in our C.V.D. (cardiovascular degeneration) study, we promised annual medical examinations but no direct medical advice. And so it has been for fourteen successive years. Each time we measured and tested everything we could to reveal the state of your cardiac health, and we advised your personal physicians about the findings. But we did not tell you what to do, we suggested no drugs or diets, we expressed no opinions about your doctors or their advice. Each year you received a letter which simply stated that we had examined your records and saw no special reason for you to consult your physician about our findings or, less commonly, that "it might be well" to get in touch with him.

This "hands off" policy did not mean we were unconcerned about your welfare. We simply could not do otherwise; our responsibility could not extend to the role of personal physician. Besides, it was essential to this research program that we remain scientific observers who would not interfere with your freely chosen mode of life and whatever that might entail.

Of course we could not always be so aloof. From time to time we spotted something disturbing enough to 'phone your doctors and, without alarming you, we tried to assure an early consultation. A suspicious spot in the x-ray of George 's chest led to prompt recall for more x-rays, persuasion to forego a vacation trip, and the eventual result that a very early lung cancer was successfully removed. And when we saw hypertension developing in some of you who were greatly overweight, we did not merely nod when you repeated your annual talk about reducing.

But now some of our views about the risk of coronary heart disease have spilled over from the medical journals to reach the public at large in such places as the cover story in *Time* magazine (January 13, 1961). We cannot really maintain you in your old habits anyway, so it is only proper that we attempt to answer some of your questions about the conclusions we are reaching.

Guinea pigs versus the actuaries. When we started this program, insurance company actuaries estimated the future mortality in your group. The actual experience in fourteen years has been far better than predicted. By now we had expected close to 50 deaths among the 285 men of the main group who were 45 to 55 years old in 1947 and who had no evidence of serious disease at that time. Actually, the number is only 26 deaths.

We make no claim that our examinations produced this gratifying result. Probably you were simply better "risks" to start with, though we did not preselect you on that basis. The kind of men you represent, mostly business and professional men with a high degree of home and job stability, may be generally better risks than the average insurance policyholder, even if many of you are overly sedentary and quite a few are certainly too fat. Perhaps also the very fact that you are in this group has made you unusually health conscious, less prone to foolish habits and disregard of danger signals, more apt to seek good medical advice and treatment.

Our expectation that coronary heart disease would be your major threat has been borne out, however. Among your group, 16 deaths have been caused by this disease; 13 other men have survived one or more heart attacks. Another man probably died from

a heart attack but we could not be sure (no autopsy). Other causes of death include accidents, suicide, leukemia, cancer, respiratory disease, stroke, and ruptured aortic aneurysm.

The bright side of the picture is the fact that at least three-fourths of the men in your group, first examined in 1947-1948, are very well indeed. A few nurse stomach ulcers, some complain of a little arthritis or hemorrhoids or lack of "steam," and many always get up to urinate in the middle of the night. But generally, at ages from 58 to 68, you are hale and hearty. We trust you will long stay that way to enjoy the good retirement programs most of you have.

The diet idea. You have noticed the increasing flood of public press, radio, and TV talks about the diet and heart disease. Basically, the main idea is that a diet rich in fats, especially of the "saturated" kind (butterfat, most meat fats, hydrogenated margarines and shortenings), promotes a high level of cholesterol and related fatty materials in the blood. This in turn favors the development of arteriosclerosis and, eventually, blockage of the coronary arteries and heart attacks. Moreover, it is suspected that the fat-laden blood resulting from a fatty meal may be unusually prone to clot, thereby increasing the risk of thrombosis, which can happen in the arteries in the brain as well as in the heart and elsewhere in the body.

Lately, manufacturers of liquid vegetable oils have blanketed the country with advertisements for their "unsaturated" fat products. In many cases the use of these fats in the human diet *does* lower the blood cholesterol level and the presumption is that the tendency toward arteriosclerosis will be lessened. The dairy and meat industries cry out in rage that reduction of *their* products in our diet is unwarranted and may be dangerous.

The vegetable oil merchants tend to imply too much about the "heart-saving" property of highly unsaturated fats. The major virtue in the use of those products seems to be the fact that, as ordinarily used, they replace some of the saturated fats in the diet which otherwise would keep the blood cholesterol level high. That is to say, a reduction in the saturated fats is more important than an increase in the use of vegetable oils in the diet. On the other hand, the dairy and meat propagandists go too far in their rear guard fight against the idea of the importance of the blood cholesterol level. Their propaganda for their kind of fats in the diet is more calculated to confuse than to enlighten the public.

We have discussed all this, and have provided practical advise for those who wish to lower their own blood cholesterol levels, in the book, "Eat Well and Stay Well," published by Doubleday & Co., Inc., New York. That book and the ideas it represents have been commended, and recommended to patients, by a large number of leading heart specialists in the United States and abroad. The general idea has been endorsed, too, in a report issued by the Central Committee of the American Heart Association in December, 1960.

Why the concern about cholesterol? Central in the present argument is the influence on arteriosclerosis of the concentration of cholesterol in the blood. Theories about this go back over fifty years, but in the last ten years a growing flood of research has greatly clarified the problem and provided compelling facts. This Laboratory has been in the forefront of much of this research. The threat of arteriosclerosis, heart attacks, and death from coronary heart disease sharply increases with rising blood cholesterol levels. This is seen in comparisons of populations all over the world as well as in the follow-up of men in groups such as your own in the United States.

Take your own group, for example. Each year we have measured the blood cholesterol in each of you and each year we classify you into the upper or the lower half of the distribution in regard to cholesterol. Among the 29 men in your group who have had definite heart attacks, including the 16 men who died from this cause, 22 have been in the upper half in regard to cholesterol before their heart attacks.

Four other studies like our own, that started later and involved more men, have uniformly given the same result. No one has found conflicting results.

Comparison of these various studies suggests one reason why your group has had a relatively favorable mortality. The average blood cholesterol value in your group is lower than that of men of your age in most of the other studies in the United States. And the frequency of heart attacks in your group has been correspondingly lower.

Our world-wide population comparisons are in complete agreement. In Japan, South Africa (Bantu), Southern Italy, the Island of Crete, and Dalmatia (Yugoslavia), we found really low blood cholesterol values and a remarkably low frequency of coronary heart disease. In Finland, Holland, and England we found much higher cholesterol values and much more coronary heart disease.

Overweight and obesity. Most of you believe that overweight or obesity carries a serious threat for future health, especially in regard to heart disease. Among those of you who are fat, this is invariably your chief health worry; those of you who are not fat take great comfort therefrom. You have got this idea from many sources, but the basis is almost entirely from life insurance company experience which has been publicized for many years.

Nobody denies the importance of the life insurance experience, which indicates, in effect, that men who are in the upper 10 per cent of the distribution of body weights for men of their age and height have about 50 per cent more risk of heart disease and early death than the rest of the policyholders. There are some technical questions about the evidence, but even if we accept it, overweight seems to be a much less serious threat than a high level of cholesterol in the blood.

This fact is emphasized by the follow-up studies mentioned above. Some of the studies indicate an increased risk for the most overweight men, but the much greater importance of the blood cholesterol is evident. In your own group, there was no surplus of heart attacks in the more overweight men.

We do not favor obesity by any means but it has been somewhat overemphasized as a health hazard. If you are overweight, reduce and stay reduced. But even more emphatically, if your blood cholesterol is up, do what you can to get it down. And by "up" we suggest that any value above 230 mg. per 100 cc. of serum is higher than we like; a value over 260 should not be accepted without action, and a value of 300 or more warrants serious attention. Your doctor can provide you with your average values from our annual report to him.

High blood pressure. In our yearly interviews all of you have shown a healthy respect for high blood pressure. You *should* be concerned, although except for truly hypertensive levels, the blood pressure seems to be less important than the blood cholesterol concentration.

In your own group when we divided the men into two halves with respect to blood pressure before heart attack, we found no significantly greater risk for those with the higher as contrasted with the lower blood pressure levels. This may be because you are really a rather small group and 29 men with coronary heart disease is not a large number. Moreover, at the outset we did not accept men who were already clearly ill with hypertensive disease.

The results in the follow-up studies elsewhere are in general agreement. They do not bear out the conclusions from the life insurance companies that mortality expectation is directly related to the blood pressure at all levels. Analysis of the life insurance data shows, in fact, that their blood pressure data must be treated with great skepticism.

If you have high blood pressure, which can be suggested by consistent readings of over 90 diastolic (or perhaps over 140 systolic), you and your doctor should consider the situation. Fortunately, new drugs make it possible to control without difficulty most tendencies toward high blood pressure. And, of course, you will follow the advice of your doctor about other things that may be done to help, including measures to promote relaxation and avoid undue excitement.

Exercise too. Besides worrying about overweight and blood pressure, many of you have expressed concern because you do not get enough exercise. Partly this seems to be because you feel better when you get some exercise; partly it appears that you have some idea about a connection between exercise and health. These are good reasons for you to try to get a reasonable amount of exercise. We recall a former medical mentor of ours who loved to state, stretched out on an office couch, that, "Sometimes I feel the urge to exercise but I find that if I then lie down quietly, after a while the feeling goes away." He died, at the age of 56, from a hemorrhaging peptic ulcer, which may mean nothing.

The importance of exercise, or its lack, as a cause of coronary heart disease, was proposed in England where it was found that bus drivers have 50 per cent more heart attacks than the bus conductors who go up and down the steps of the double-decker London buses collecting fares. More recently, medical examinations of the busmen have been made and it was found that, compared with the conductors, the drivers are fatter, more often have high blood pressure, and average higher in their blood cholesterol levels. There is no proof that the difference in exercise caused these other differences. Records of sizes of uniforms issued to busmen show that the London bus drivers are fatter than the conductors when they first go to work. This raises the question, of course, about the kinds of men who apply for jobs as drivers or conductors respectively. Does a difference in exercise cause the heart attack difference, or is it simply that different types of men, with different tendencies to heart disease, seek out different kinds of jobs?

In many parts of the world coronary heart disease is more common in the cities than among the rural populations. Rural men are also generally more active than their fellows in the cities. Does this explain the difference in heart disease? It is also found in many parts of the world that the rural diet is lower in fats than the city diet. These variables are so often intercorrelated that it is impossible to decide which is more important.

For several years we have been studying railroad employees from the Mid-West to the Pacific Coast. Mortality records show that the most sedentary of these men, the clerks, have a higher death rate from coronary heart disease than the more active switchmen who, in turn, are a little worse off than the section men who are even more active physically. Again we must ask whether these men would all be equivalent if they had the same activity habits. Why did they elect or drift into their respective occupations?

We approve of physical activity, and we regret that our current social environment makes it extremely difficult for many of us to get anything like a decent amount of exercise. And by "decent" we mean more than an occasional evening of bowling or a ride around in a golf cart on Saturday. We believe that most men will feel and look better if they maintain a higher level of exercise than is the current custom of the average businessman. At present it is not possible to decide how much protection this will give against coronary heart disease.

"Stress" and "tension." Many doctors share the recurrent popular belief that the "stress of modern life" is a major cause of our modern epidemic of coronary heart disease and that men in responsible positions are particularly threatened. There is little evidence to support these ideas. We are all impressed by reports of sudden deaths from heart attacks of prominent men who were busy with important affairs up to the moment of the attack. It

should be realized, however, that such sudden deaths are unfortunately common among all types of men in America today. A study of mortality in Chicago finds, in fact, that the death rate from coronary heart disease is *lower* among executives than among laborers.

The advocates of the stress theory have been driven to reply that the magnitude of business and public responsibility is not necessarily a good measure of stress, and there is no reason to think that laborers may not live under as much tension as anyone else. The real trouble with the theory of the importance of stress and tension is the absence of methods to measure such emotional factors.

Indirect evidence that stress may be a factor is offered in recent reports that under conditions presumed to be stressful the serum cholesterol level tends to rise in some men. The increase is not great and other factors, including the diet, were not properly controlled. The men studied and the stressful conditions involved were medical students preparing for examinations and tax specialists in the period before income tax deadlines. No heart attacks occurred and no study is reported on the persons who had to pay the income taxes.

If you feel harried under heavy pressure and "tense," this is obviously not the best way to live and at least you would be happier if you could find ways to avoid this stress. But no one knows whether this has much, or anything, to do with heart attacks.

Cigarette smoking. Several large-scale studies have found that heavy cigarette smokers have about 50 per cent more risk of dying from coronary heart disease than men of the same age who do not smoke or smoke very little. Further, it was found that former smokers who had stopped long ago had a lower death rate than continuing smokers. No information is available on other characteristics of the smokers and the nonsmokers. It is not known whether they tend to differ in occupation, relative body weight, blood pressure, diet, and no one knows why some men smoke and others do not.

So far there is no theory as to how cigarette smoking could promote hardening of the arteries or heart attacks and there is no proof at all that smoking itself really causes the excessive death rate among smokers. We were interested to find that heavy cigarette smoking is common in some populations, such as in Japan and Greece, in which the frequency of coronary heart disease is low.

Smoking can be condemned as being offensive, dirty, expensive, and an irritant to the throat and lungs. It causes an appreciable number of deaths from fire and probably is an important cause of lung cancer. If you smoke, you will probably be better off in several ways if you stop. But we cannot guarantee that you will be any less prone to a heart attack.

Alcohol. Men who have recovered from a heart attack or who suffer from angina pectoris are sometimes advised by their physicians to have a drink before dinner or at bed time. This is not because anyone believes that alcohol cures or prevents heart disease, but because it helps some people to relax and it does not seem to do the heart any harm.

However, alcohol is heavy with calories so if you are overweight bear this in mind. Two martini cocktails will run to around 300 calories and a 12-ounce can of "strong" (6 per cent) beer provides 200. Alcohol may have another possible danger for the man who has angina pectoris because it deadens pain and thus may remove a useful danger signal against overexertion.

Heredity. There is some tendency for coronary heart disease to run in families. Part of this is explained by the similarity of living habits and diet among members of a family but in some cases a true genetic or inherited tendency is involved. This does not mean that you are out of luck if your family has a history of coronary heart disease or sudden death at early age. With such a history it may be wise to be more careful than the next fellow. On the other hand, a "good" family history is no assurance that you are protected.

Better late than never. By middle age, most American men today have a considerable degree of hardening of the arteries as a result of their genetic make-up and their past mode of life. Ideally, a program to prevent or delay these arterial changes and the risk of heart attacks should begin in youth, but we insist that it is never too late to improve your prospects, even if you have a bad family history.

Your own good sense and the advice of your personal physician is your best guide. No one will argue against the general idea that it is wise to get regular but not violent exercise, avoid emotional upsets, and try to enjoy life without overdoing it. And, more specifically, guard against overweight and elevated blood pressure and try to correct your blood cholesterol level if this is high. "High" may be considered anything over 230 mg. of cholesterol per 100 cc. of serum, because men with such values are, on the average, at least three times more prone to heart attacks than men with lower levels. But high cholesterol values, even over 300, do not mean you have coronary heart disease or are doomed. You can bring it down, and, besides, individuals differ and you may be safeguarded by other factors in your make-up.

Drs. Henry L. Taylor, Henry B. Blackburn, Ernst T. Simonson, Joseph T. Anderson, Mrs. Nedra Foster, and the other members of the staff join in sending best wishes!

Sincerely,

s/Ancel Keys, *Director*

Chlorothiazide in Treatment of Arterial Hypertension

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CHLOROTHIAZIDE is a sulfamino derivative that may be given either orally or intravenously, although oral administration gives the best results. The synthesis of this product constitutes a notable advance in treatment with diuretics, since according to Ford,[1] it is the closest approach to the so-called "ideal diuretic."

Chlorothiazide inhibits renal reabsorption of sodium, chloride, and potassium with a minimum reaction on the concentrations of serum electrolytes. Because its molecule contains a sulfamido radical, some persons believe that it acts as a carbonic anhydrase inhibitor, causing excretion of a large quantity of sodium bicarbonate and potassium. However, it has an action similar to that of the mercurial diuretics in that it produces considerable excretion of chloride; hence it does not induce the hyperchloremic acidosis so often caused by carbonic anhydrase inhibitors.

The excretion of potassium produced by chlorothiazide is less than that produced by carbonic anhydrase inhibitors. Some authors point out that, since its effect on excretion is distinct from that obtained with the carbonic anhydrase inhibitors, chlorothiazide may have a different mechanism of action. Perhaps the carbonic anhydrase inhibitors block one of the tubular reabsorption mechanisms of sodium, the mercurial diuretics act on another mechanism, and chlorothiazide suppresses an unknown third mechanism.

When hypertensive patients were treated with chlorothiazide, it was found that this drug had a marked hypotensive effect in addition to its sodium diuretic property. As more evidence was accumulated, chlorothiazide was used less as a diuretic and almost entirely as a hypotensive agent. The works of Govea,[2] Freis,[3] and Wilkins[4] have been conclusive in regard to the hypotensive effect of this drug. The purpose of this paper is to augment these observations with a report of personal experiences with the use of chlorothiazide in the treatment of hypertension.

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MATERIAL AND METHODS

Chlorothiazide was given to 87 patients with primary or essential arterial hypertension, all of whom were ambulatory, since the effect of a hypotensive medication should be evaluated on casual pressure. A clinical history was taken and the following procedures carried out for each patient: (1) determination of the blood pressure in all four limbs; (2) cold pressor, Regitine, histamine, and Amytal tests; (3) amount of catecholamines in the urine; (4) electrocardiogram; (5) blood urea nitrogen determination; (6) determination of blood glucose; (7) blood tests; (8) urinalysis and phenosulfonphthalein test, (9) Addis test; (10) intravenous pyelogram; and (11) examination of ocular fundus.

According to Schroeder's classification, patients were listed as having slight, moderate, severe, or accelerated or malignant hypertension.[5] No changes were made in their mode of life or in their diet, except they were requested not to use salt, which kept the daily intake of sodium to about 4 or 5 gm.

Treatment was started with a dose of 0.5 gm. of chlorothiazide given twice a day. For some patients, the dose was increased to 1.5 gm. every twenty-four hours. The blood pressure was read at the office every other day for the first two weeks of treatment and once a week thereafter. In some cases of prolonged treatment, the blood pressure was read monthly. If a patient was receiving ganglionic blocking agents, his blood pressure was taken after he had been standing for five minutes. This pressure reading was used in adjusting the dose of chlorothiazide.

RESULTS

Response to chlorothiazide was classified according to the following criteria:[6]

Good—lowering of blood pressure to 150/90, or a lowering in the mean blood pressure of 20 or more mm. Hg

Slight—lowering of the mean blood pressure an average of 11 to 19 mm. Hg

No response—lowering of the mean blood pressure an average of less than 11 mm. Hg.

The mean blood pressure was considered to be the sum of the diastolic plus one-third of the differential blood pressures.

Of the 87 patients studied, 20 had slight, 45 had moderate, 15 had severe, and 7 had accelerated essential arterial hypertension.

Slight hypertension. Of the 20 patients who had slight essential hypertension, blood pressure was controlled by chlorothiazide alone in 15; response was good in 10 and slight in 5. The remaining 5 patients had good responses when reserpine, in average daily doses of 0.3 mg., was added to the chlorothiazide. In 4 of these patients, in whom control of blood pressure had been maintained with reserpine, in doses of 0.5 to 1 mg., it was possible to replace this medication with chlorothiazide.

Moderate hypertension. Only 8 of the 45 persons in this group responded to chlorothiazide alone. In the other 37 patients, other drugs, such as reserpine and ganglionic blocking agents, were needed. When reserpine was combined with chlorothiazide, results were good in 20 and slight in 5 patients. The average dose of reserpine which was needed was 0.45 mg. in twenty-four hours.

Those 12 patients who did not respond to the combination of reserpine and chlorothiazide were subsequently treated with mecamylamine, a ganglionic blocking agent. This was given 3 times a day, with an average total dose of 18 mg. Results were good in 8 and slight in 4 patients.

Control was maintained with a combination of reserpine and ganglionic blocking agents in 6 patients with moderate hypertension. On adding chlorothiazide, it was possible to reduce the reserpine dose by an average of 30 per cent and the dose of the ganglionic blocking agent by an average of 45 per cent.

Severe hypertension. All 15 patients in this group received a combination of mecamylamine, reserpine, and chlorothiazide. Response was good in 11 and slight in 2 persons. There was no response in 2 patients. To achieve a good response, the average dose needed of the blocking agent was 18 mg. per twenty-four hours and the average dose of reserpine, 0.8 mg. per twenty-four hours. In 5 patients, doses of reserpine were reduced by 40 per cent and doses of ganglionic blocking agents by 38 per cent when chlorothiaide was added to the regimen.

Accelerated hypertension. Responses were good in 3 of 7 patients with accelerated arterial hypertension treated with a combination of reserpine, mecamylamine, and chlorothiazide. The average doses were 1.2 mg. of reserpine and 38 mg. of mecamylamine. The remaining 4 patients in this group had no response.

Side effects. In general, chlorothiazide is a well-tolerated drug. The only side effects were vomiting in 3 patients, diarrhea in 2, rash in 1, anorexia and weight loss in 4, and profound asthenia in 3. No electrolytic alterations of the serum were observed. The patients with profound asthenia improved when treated with potassium chloride, 3 gm. daily, given orally.

CONCLUSIONS

Chlorothiazide is of great value in the control of blood pressure in the hypertensive patient. The recommended dosage is from 1 to 1.5 gm., taken in divided doses. In our opinion, it is the hypotensive drug that produces the fewest side effects, thus is well tolerated by patients.

When used alone, chlorothiazide is capable of controlling blood pressure in a considerable number of patients with slight or moderate hypertension. Therefore, treatment of slight and moderate hypertension should begin with this drug alone. If the desired response is not obtained, other drugs, such as reserpine and ganglionic blocking agents, may be combined with chlorothiazide.

As chlorothiazide in association with other hypotensive drugs allows a considerable reduction in the doses of the original drugs, the side effects caused by them are reduced or disappear. The hypotensor mechanism of the drug is supposed to be related to its sodium diuretic effect, which again brings to the fore the relationship of sodium metabolism to arterial hypertension.[3] Some authors believe that chlorothiazide acts upon the nervous structure apart from its direct renal effect.

In the present treatment of hypertension, we believe that, when such therapy is necessary, the best combination that can be used is chlorothiazide-reserpine-mecamylamine, with ambenonium chloride or Prostigmin to counteract constipation.

The chlorothiazide utilized in this study was supplied as Clotride by the Merck Sharp & Dohme Laboratory.

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Diagnosis and Treatment of Congenital Dislocation of the Hip in the Infant

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CONGENITAL DISLOCATION of the hip can be diagnosed in early infancy, and, if treatment is started during the first year of life, the hip develops normally in the great majority of cases. Upon the general practitioner, the obstetrician, and the pediatrician falls the responsibility for an early diagnosis.

DIAGNOSIS

Abnormality in the hip joint development can be observed in infants under 3 different clinical and roentgenologic syndromes. In the first group, the hip is very unstable and the joint capsule appears relaxed. The child may have a slight tightening of the adductors, but under relaxation it is possible to observe a click or snap in the hip when the thighs are abducted and the greater trochanter is pushed forward. This sign, carefully studied by Ortolani,[1,2] indicates that the hip is dislocated but is still easily reducible in the infant without anesthesia (figure 1). Anatomically, these hips are characterized by the presence of a shallow acetabular roof and a relaxed joint capsule, but the upper end of the femur and the femoral head are normal. Roentgenograms demonstrate that the upper end of the femur is widely separated from the acetabular cavity (figure 2). A severe dislocation will occur in all these cases unless treatment is started early in life.

A second group of infants have very tight adductors and asymmetry of the thigh folds, but the Ortolani sign is negative (figure 3). The roentgenograms in these cases show that the hip is not dislocated, but the acetabular roof is slanting in relation with the normal side. Most of these hips will develop normally even if not treated. On the other hand, subluxation may result which will not be apparent until later childhood or early adolescence.

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In a third group of patients, the hip is completely dislocated at birth, and the femoral head is lodged in a secondary acetabulum above the primary acetabulum. The adductors are very tight and the thigh on the involved side appears much shorter than the normal side, but the Ortolani sign is negative (figure 4). In these children, often severe anteversion of the femoral neck is observed. This deformity occurs often in children with other congenital deformities such as clubfeet or arthrogryposis. The reduction of these dislocations may be very difficult even in infancy.

Roentgenograms of the pelvis should be taken whenever any suspicion exists of maldevelopment of the hips. Clinical signs which point to an abnormality of the hip are: (1) asymmetry of the thigh folds, (2) limitation of hip abduction, (3) apparent shortening of the thigh, and (4) a snapping or clicking of the hip when the thighs are abducted. It may be difficult to diagnose a defect of development of the hip joint in roentgenograms of 1- or 2-month-old babies. At this age the femoral head and a great portion of the acetabulum are cartilaginous and thus not visible on the roentgenograms. Because changes in the hip joint may become apparent later on, a roentgenogram should be obtained at three or four months of age even if earlier roentgenograms were negative.

TREATMENT

The treatment of a congenital dislocation of the hip should be started as soon as the diagnosis is made. The treatment varies according to the type of congenital hip abnormality. The first group of children with a positive Ortolani sign can be treated with either a pillow splint applied between the thighs in order to keep the thighs abducted, or with an abduction brace which keeps the thighs in flexion and abduction position, thereby preventing redislocation (figure 5, A and B). These appliances are left on full

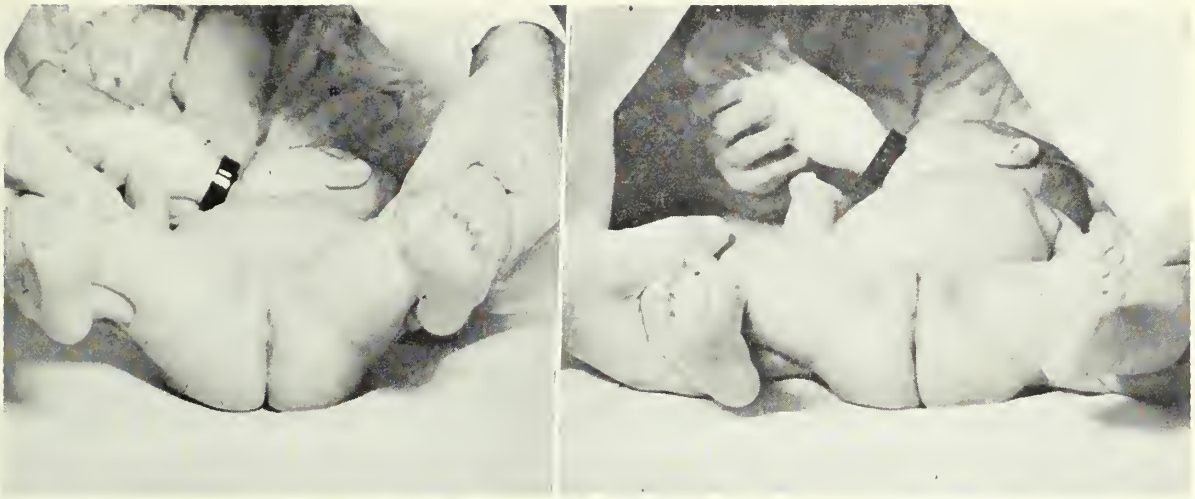

Fig. 1. "Snapping sign" of Ortolani. (Left above) Bilateral limitation of hip abduction due to hip dislocation. (Right) Hip abduction is free after femoral heads have "snapped" into the center of the acetabular cavities.

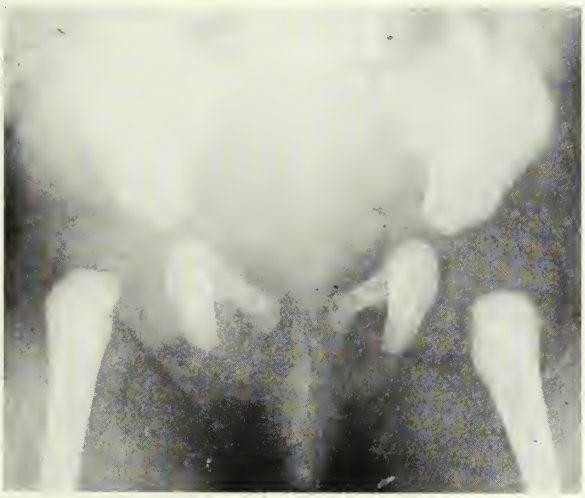

Fig. 2. Roentgenogram of the pelvis of 1-week old infant with positive snapping sign on the right. The upper end of the femur is more separated from the acetabular cavity on the right than on the left.

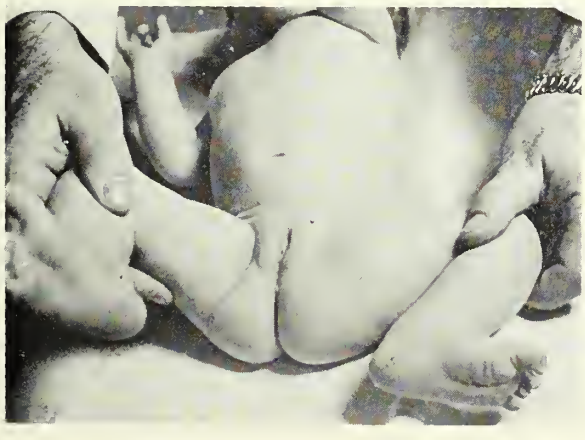

Fig. 3. Limitation of hip abduction on the right caused by tightness of the adductor muscle. The right inguinal fold was deeper than the left. The snapping sign was negative.

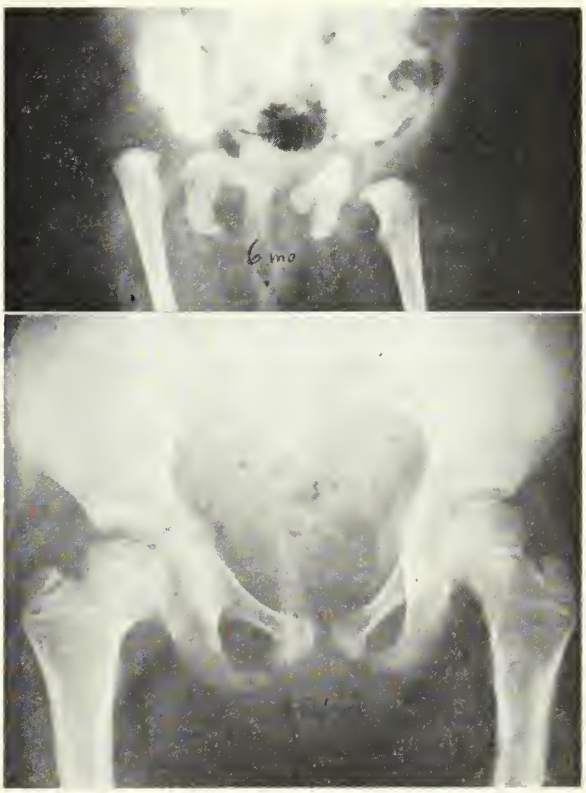

Fig. 4. Prenatal type congenital dislocation of the right hip in 6-month old infant. (Above) The head of the femur not yet ossified articulates with the secondary acetabulum above and separate from the primary acetabulum. The dislocation was reduced under general anesthesia and the legs immobilized in hip spica plaster cast extending to just above the knees for three months. (Below) When this child was 5½ years of age, the right hip was well developed although the femoral neck was in varus and anteversion.

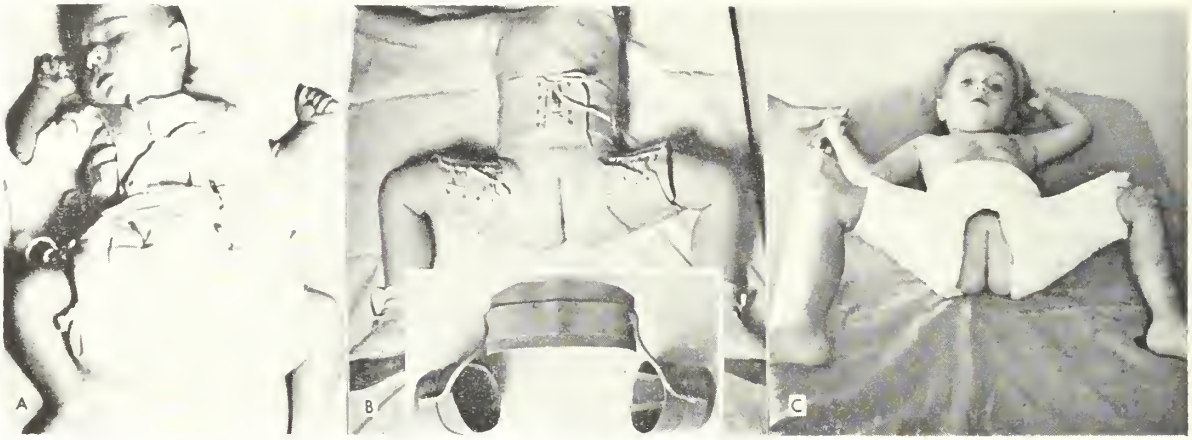

Fig. 5. Three types of bracing used in children initially treated prior to walking showing (A) Frejka pillow splint used in infants with mild hip dislocation or with tightness of the adductors. (B) Abduction brace used in infants with hip subluxation and dislocation. Insert shows posterior view of the steel frame and leather. (C) Hip spica plaster cast used in children with unilateral or bilateral hip dislocation or subluxation.

time for three or four months; then only at night and during napping hours for four to six more months. This treatment should be directed by an orthopedic surgeon since the first months of life are precious for rebuilding a new hip joint and any fault in the treatment must be avoided. The appliances are discarded only when the roentgenograms show a normally developed hip joint.

The second group of children, with shortening of the adductor muscles, should be treated only if the shortening is severe. The treatment may be delayed for two or three months as the adductor muscle shortening usually corrects itself. However, if it persists after 3 or 4 months of age, a pillow splint should be applied all of the time for three or four months until the thighs can be abducted freely. Treatment in these cases is imperative if the roentgenograms show a definite sloping of the acetabulum, and treatment should be continued until this is corrected (figure 6).

Children of the third group with a completely dislocated hip at birth are usually very difficult to treat, and only a well qualified orthopedic surgeon can deal with this problem. If the child has arthrogryposis or other severe congenital abnormalities, it is usually better not to attempt to reduce the hip joint. However, if the muscles of the hip are well developed and the dislocation is the only abnormality present in the child, a closed or even open reduction should be attempted. As a rule, a closed reduction under anesthesia with gentle manipulation should be attempted in all these cases, as a hip that appears irreducible on roentgenograms, often reduces easily when the child is under anesthesia (figure 4). After the reduction, the hip is immobilized in a hip spica plaster cast for two or three months (figure 5C).

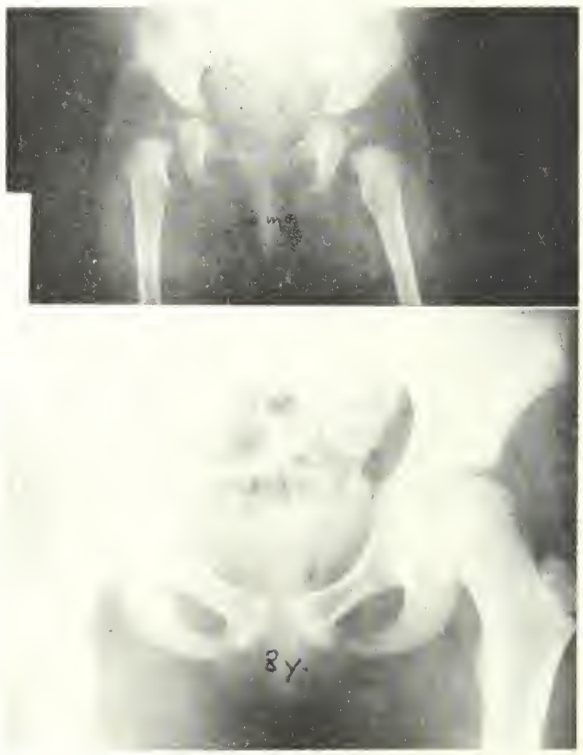

Fig. 6 (Above) Roentgenogram of a 2-month-old female infant with subluxation of the right hip. The Ortolani sign was negative. The acetabular roof was shallow and slanting. An abduction brace was worn full time for two months followed by application of a pillow splint for an additional six months. (Below) Result at 8 years of age. Both hips were well developed.

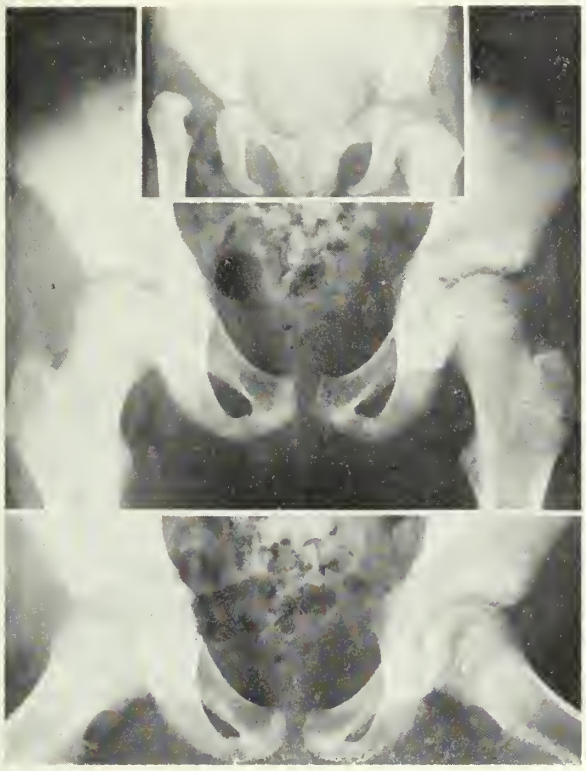

Fig. 7. Congenital dislocation of right hip in an 18-month-old girl. The hip was reduced under general anesthesia and a bilateral plaster hip spica cast was worn for three months. This was followed by application of abduction brace worn full time for three months and during night and napping hours for an additional six months. Roentgenograms taken at 8 years of age showed well developed hip joints.

In children with untreated congenital dislocation of the hip, walking is usually delayed for two or three months. The diagnosis of this deformity when the child begins to walk is very easy in unilateral dislocations, but may be difficult in bilateral dislocations. The gait of a normal infant is unsteady, but the child with dislocation of one hip has an asymmetric limp. When the dislocation is bilateral, this limp is symmetric and is called a waddling gait. It is often thought, by parents and even by doctors, that a slight waddling can be a passing gait abnormality. The medical profession should be sternly warned that a slight asymmetry of gait, swinging, or waddling should never be dismissed in a busy office practice but should be carefully investigated and roentgenograms of the pelvis should always be obtained.

The results of treatment of congenital dislocation of the hip are excellent in children treated before 1 year of age. The treatment is much more cumbersome and prolonged if started after the patient has walked, and some defective anatomic results will be encountered. Once the hip is completely dislocated, it must be reduced either by manipulation with the child under general anesthesia or gradually by traction. Most congenital dislocations of the hip seen in children under 20 months of age can be successfully treated by closed reduction under general anesthesia succeeded by the application of hip spica plaster cast extending to just above the knees and worn for three to four months[3] (figure 5C). The child then wears an abduction brace (figure 5B) full time for three more months and only at night and napping hours for another six months, or until the roentgenograms show a well rebuilt hip joint. These children can be treated as outpatients. Their stay in the hospital is limited to a few hours after reduction. The child is free to crawl while wearing the plaster cast or the abduction brace, and physical therapy is never used. Redislocations need never occur in patients treated properly (figure 7).

When the treatment is delayed until after 2 years of age, skeletal traction, open reduction, and derotation osteotomy of the femur may be necessary and the anatomic results will not be uniformly good. If the medical profession is well aware that a diagnosis of congenital dislocation of the hip can be made in infancy, there will be no more cripples observed in late treatment of this deformity.

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The Medical Ship S.S. Hope in Southeast Asia

Ampenan, Lombok
Indonesia
17 April, 1961

Dear Dr. Myers:

The S.S. HOPE is a charitable mercy ship, spending its first year of operation in far-off Indonesia. This archipelago, extending some 2,000 miles along the equator from the western tip of Sumatra to beyond the island of Timor above Australia, is a rich, tropical, lush series of islands filled with all the plant and wildlife one associates with Southeast Asian islands.

The idea for a HOPE-type project was conceived more than a year ago and was brought to fruition by Dr. William B. Walsh of Washington, D.C. (The central office of project HOPE is at 1818 M. Street, N.W., Washington 6, D.C.).

The HOPE is a converted hospital ship, the S.S. Consolation, taken out of moth balls. It sailed from San Francisco early last fall with a complement of 15 doctors, 1 dentist, and 30 nurses, with a total personnel of 75, including ancillary services. It is not a government enterprise. The funds have come solely from American business, industry, labor unions, civic groups, and John Q. Public. The only governmental help in this project consists of the loan of the hospital ship. The HOPE is operated at cost by the American President Lines, and the fuel for running the ship has been donated by the American Petroleum Institute. Drug houses, surgical instrument manufacturers, and others have all donated generously to make it a well outfitted ship with all the newest medicines, sutures, and equipment of twentieth-century medical care. The staff is augmented by rotating specialists who volunteer their services for varied periods of time.

When the ship arrived at its first stop—on the island of Java, at Djakarta, the capital of the Republic of Indonesia—an equal number of Indonesian doctors, nurses, and technicians were brought aboard as co-workers. Since then, it has island-hopped from Djakarta, Java, to Surabaja; Bali; Sumbawa Besar, Makassar, Sulawesi; Ambon; and, at the far eastern end to Kupang, on the island of Timor—200 miles from Australia. It has returned via Flores, Bima, and Sumbawa and is now on its way to Djakarta, stopping at Lombok and Semarang on the way.

Indonesia is said to be the sixth largest nation in the world, with 90 million people. Medical care is woefully lacking by the standards we use in America. Here there is one doctor for every 70 to 80 thousand people. At each stop, we have been pleased to find that the local doctors have been more than cooperative, friendly, and willing to take part in an endless round of seminars, lectures, movies, conferences, and other teaching routines. Medical and surgical treatment, of course, is the main purpose of the ship, but tied in with this is the teaching and demonstration program, which works both ways. It has been a liberal education in tropical medicine for all of the medical staff, and the occasional off-hours have been enjoyed observing the wildlife, customs, living habits, and all the other wonders of an exotic tropical isle.

Before the ship steams into a port, a prescreening has gone on by the local medical staff, so that, on the ship's arrival, the problem cases and difficult surgical entities are waiting at the local R.S.U. (Rumah Sakit Umum), the general hospital. Within an hour after the first early morning launch reaches the shore, a polyclinic is actively set in motion, with the patients registered, rescreened, and sent to the various specialists for evaluation. All departments are amazed at the unusual variety and type of problems with which they have to deal. Since the x-ray machinery, as well as some of the surgical specialty clinics, is aboard ship, the mass screening and special order x-ray evaluations and certain diagnostic routines are done on patients ferried to and from the ship. At only two ports have we been able to moor at a dock.

After the ship has been at an island for twenty-four hours, a regular routine of clinic visiting, surgery, and medical practice management, like that of any general hospital in America, is in operation. The local doctors assist in diagnoses and treatment, scrub in at surgery, or give their own conferences along with ours on mutual medical problems.

The case load is very bizarre. It's almost like looking at a turn-of-the-century medical book.

Hernias down to the knees, cysts and tumors the size of watermelons in every conceivable site, and routine problems magnified a hundredfold are taken in stride. In the last ten days, the ENT surgeon has repaired 25 cleft lips in adults and children. The General Surgery Department has removed cysts and tumors, each one larger than the last. In Eye, the cataracts are so mature and hypermature that only those patients with chalky pupils that react quickly to a light stimulus are operated upon. Trachoma, the most common disease in the Orient and Asia, is seen everywhere here. Unfortunately, in the later stages of the disease, the lids are so distorted that the lashes scratch the front of the eye. At least half a dozen corrective procedures are done for this every day.

The Internal Medicine Department finds that anemia is the rule rather than a rarity and is constantly transfusing people for surgery who have hemoglobins of less than 7 mg. per cent. Our blood bank on ship certainly must be one of the best in the Pacific, although the technicians admit they have to screen a great many people before they find suitable donors free from tuberculosis, malaria, and other problems.

Unexplained fevers, pains, parasites, hemoptysis, and palpable livers and spleens fill up the medical wards. This morning, a postoperative cataract patient of mine had an emesis episode and produced a 7-inch worm in the basin, which required a quick consultation.

Indonesians are small-boned people, with a friendly stoicism that stands them in good stead for all the treatment needed. Preoperative medication is habitually one-half to one-third the dosage we use at home. Rare is the child who is unruly, and they sit wide-eyed as they are being examined. I have done a bilateral cataract under local anesthesia on a 14-year-old boy, one of four under 20 years treated for the same condition in one family.

In this Moslem culture, one must be careful in suggesting an enucleation or an amputation. A devout Moslem has no desire to be reincarnated in the next world as a 3-legged water buffalo or a 1-eyed cockatoo. Amulets, charms, and tawizes play a great role in allowing the "will of Allah" to pull them through a serious illness.

Three days before the ship's sailing time, surgery stops, and the remainder of the time is spent going over again the postoperative care and the medical management that we hope can be in some way carried out after we leave. As the last launch leaves the shore for the ship, it has been a commonplace sight to see hundreds of cheering youngsters waving from the dock, surrounded by huge piles of foodstuffs—soap, rice, flour, and powdered milk—as well as the equivalent of a well-stocked pharmacy.

A realist's viewpoint of Project HOPE would state that our efforts are merely a drop in the bucket to that which is really needed. But a start must be made some place, and if such a thing can stem from a well-meaning American citizen's heart rather than by government direction, it probably will have some impact on Indonesian health as well as on international friendship.

Malcolm A. McCannel, M.D.

Henry E. Michelson, M.D.

An Appreciation

FRANCIS W. LYNCH, M.D.

St. Paul

Few dermatologists have exerted greater influence on their specialty in America, and none has in Minnesota, than Dr. Henry E. Michelson of Minneapolis. As is usual, little in his early educational and professional background would seem to have prepared him for this important role. Born on September 22, 1888, of Polish and German parents, Herman L. and Justyna Michelson, on their homestead near Bismarck, North Dakota, he received his early education in that city. In 1906, he came to the University of Minnesota, where he completed the usual premedical and medical training common to that period—two years of academic work and four years of medical school. He interned from 1912 to 1913 at City and County (now Ancker) Hospital in St. Paul. Immediately thereafter, he served for four years on the McIntyre Hospital Staff in Virginia, Minnesota, and was a "woods' doctor" there at a time when approximately 7,500 men were employed in timber production in the nearby forests.

Greater than average dermatologic interest became evident while Dr. Michelson was in medical school, and further contact with Dr. Charles D. Freeman during his internship increased this interest. A most friendly professional and personal association continued until the death of Dr. Freeman in 1952; several years previously, Dr. Charles D. Freeman, Jr., completed his dermatologic training under Dr. Michelson's direction.

Dr. Michelson's dermatologic interest was maintained during his general practice on the Iron Range. Perhaps his interest was stimulated further when a smallpox epidemic occurred there while he was assistant county physician. This interest in smallpox culminated a few years later in a study, with Dr. Kano Ikeda, of the clinical and dermatohistopathologic features of the disease as observed in an epidemic in Minneapolis.

It is also noteworthy that Dr. Michelson's first presentation of a scientific paper described "Syphilis in Childhood" at a meeting of the St. Louis County Medical Society. This paper was published in *The Journal-Lancet* in 1918. In 1917, he moved from the Iron Range to Minneapolis and limited his practice to the specialty of dermatology.

Dr. Michelson prepared for specialty practice in a manner different from many earlier dermatologists, as well as from his successors. Earlier, the usual procedure was to receive basic specialty training abroad, as postgraduate study, and then to return to associate with an established practitioner or, sometimes, to practice alone. By 1917, 6 or 8 competent dermatologists with this background were practicing in the Twin Cities. In Minneapolis, Dr. Michelson limited his practice to dermatology but shared office space with Dr. Franklin B. Wright, who was particularly interested in urology and venereology.

Dr. Samuel E. Sweitzer had taken charge of dermatologic teaching at the medical school of the university when the study of cutaneous disease was still intimately associated with venereology. Dr. Michelson found, at the University Hospitals' dispensary, a highly favorable opportunity for learning by association with Dr. Sweitzer, by clinical experience, and by teaching medical students. In 1921, Dr. Michelson, following the custom for American specialists, traveled in Europe to improve his basic knowledge of clinical dermatology.

Even during his period of practice in northern

Minnesota, Dr. Michelson had recognized the benefits to be gained from travel to medical centers. He had visited Cook County Hospital in Chicago several times and was particularly impressed by the clinical teaching of Dr. Oliver S. Ormsby, who later became the outstanding dermatologist of the Middle West—and, indeed, probably of the entire nation. In 1920, while attending a meeting of the Chicago Dermatological Society, Dr. Michelson met Dr. Norman Walker of Edinburgh, Scotland, a figure of international renown. This rather casual encounter led to a favorable introduction to European dermatologic clinics. It also led to a lifelong interest in cutaneous tuberculosis because, in 1921, Dr. Michelson visited Dr. Walker, who was then intensely interested in the relationship between cutaneous tuberculosis and the high incidence of bovine tuberculosis in Scotland. Dr. Walker asked Dr. Michelson to report, during his tour of the Continent, any new developments in that field.

Subsequently, Dr. Michelson spent considerable time in clinics with Dr. Moriz Oppenheim at Wilhelminenspital in Vienna. This institution adjoined the tuberculosis hospital where Volk was then pioneering with the therapeutic application of the carbon arc lamp. Dr. Michelson's report led Dr. Walker to introduce this therapy into the British Isles. From that time, Dr. Michelson maintained a vigorous interest in the literature and clinical problems of cutaneous tuberculosis. Perhaps this interest and collateral reading turned him early to an occupation with sarcoidosis and lupus erythematosus and impressed him with the importance of their systemic features.

In 1922, Dr. Kren of the University of Vienna was generally acknowledged as the foremost dermatohistopathologist. Dr. Michelson studied individually with Dr. Kren for three hours daily for several months, returning to Minneapolis with far more detailed knowledge of the subject than was possessed by others in the Midwest. Indeed, there were then few competent dermatopathologists other than Dr. Satenstein and Dr. Highman in the nation.

While attending medical school, Dr. Michelson had worked part time in the Department of Pathology and subsequently maintained interest and personal contacts there. When he returned from Vienna, his enthusiasm and his additional knowledge made him even more welcome as a regular visitor to Dr. E. T. Bell, head of that department. Over a period of many years, their almost daily conferences led to continued interest and investigational studies by Dr. Michelson, based upon his unusually broad understanding and knowledge of both general pathology and cutaneous histopathology. His dermatologic knowledge was greatly broadened when Dr. Oscar Gans spent three months in Minnesota in 1925 teaching a special course in histopathology. Dr. Michelson later did much to spur dermatologic interest in histopathology. Previously, at society meetings, in Chicago or the Twin Cities, clinical presentations had seldom been accompanied by demonstrations of sections from biopsy. Dr. Michelson's knowledge and interest in this field were also useful later, when he was an examiner on the American Board of Dermatology.

Dr. Michelson visited Europe again in 1929, this time spending more of his time in Paris, and he also enjoyed the satisfaction of visiting the clinics of Bloch and of Jadassohn. European dermatologic thought and activity strongly influenced his work as a teacher and a clinician.

In spite of the demands on time and energy which have resulted from his intense and absorbing interest in the clinical practice of dermatology, Dr. Michelson has maintained an equally intense and almost equally time-consuming interest in teaching dermatology at undergraduate, graduate, and postgraduate levels. He has been a most successful teacher, recognized internationally for his clarity in thought and presentation, both oral and written. Dr. Michelson began clinical teaching at the Medical School of the University of Minnesota in 1917 and worked closely with Dr. Sweitzer, who remained in charge of the program until he left the University Hospital service. Although trained more broadly, Dr. Sweitzer had early limited his interests to dermatology and venereology, leaving to others the nonvenereal aspects of urology. After leaving the University Hospital Clinic, Dr. Sweitzer retained his University appointment and instituted the Dermatology Clinic of the Minneapolis General Hospital; he continued to teach the medical students assigned there.

The friendship and cooperation between Dr. Sweitzer and Dr. Michelson have continued for forty-three years and, with their friendly association with Dr. Paul O'Leary while he was in charge of the Section on Dermatology of the Mayo Clinic, have contributed much to the continuing pleasant association of all dermatologists in this region.

In 1925, Dr. Michelson became head of the clinical service of the Division of Dermatology at the Medical School; he was appointed professor in 1928 and director of the Division in 1949. As emeritus professor since his retirement in 1957, he is active in undergraduate teaching at the Medical School, in graduate teaching both there and as a consultant at the Veterans Administration Hospital in Minneapolis, and in postgraduate teaching at the Continuation Study Center. He is active at meetings of the various dermatologic societies of which he is a member and as an invited speaker before other professional groups.

Under the direction of Dr. Michelson, the undergraduate dermatologic program at the Medical school became recognized as one of the most effective in the nation. His stimulation of dermatologic interest among medical students has been rewarded by the knowledge that more graduates of the Medical School of the University of Minnesota than of any other medical school have been candidates in the examinations given by the American Board of Dermatology during the past eight years.

Teaching at a graduate level was begun informally

early in Dr. Michelson's tenure as professor in the Division of Dermatology, and the first candidate for a graduate degree began training with him in 1930. Dr. Michelson has been responsible for all or a major portion of the dermatologic training of approximately 50 dermatologists now in practice in the United States, Canada, England, and Korea. Upon completion of training, his students generally have had an unusual degree of success in the examinations of the American Board of Dermatology. Through clinical and specialized research projects, many of these students have contributed to the scientific advance of dermatology during and subsequent to the time of their training at the University. This program of graduate instruction always had the willing cooperation and support of Dr. Sweitzer in his clinic at the Minneapolis General Hospital.

Among the most effective of Dr. Michelson's teaching efforts is the "Friday Session" of the Division; on Friday afternoons, for about thirty years, he regularly presented clinical discussions of interesting cases. In early years, the cases were drawn from patients seen during the week in the outpatient clinic or in the wards of the University Hospitals. Later, patients were also brought regularly from the Minneapolis General Hospital, then Ancker and, later, the Veterans Hospital. From the start, Dr. Michelson utilized patients from his private practice, and on many occasions he presented more interesting and more numerous private than institutional patients. Interns and graduate students welcomed an opportunity to attend these clinics regularly. Those graduate students who subsequently established practice in the Twin Cities continued regular attendance at these sessions; those at a greater distance returned periodically; and dermatologists who had trained elsewhere but practiced locally found themselves equally interested and welcome. The numerous visitors, whether or not members of the staff, were invited to bring private patients having unusual eruptions, and thereby both patient and physician received the benefit of Dr. Michelson's therapeutic as well as diagnostic attention without cost.

The intensity of Dr. Michelson's interest in teaching is well illustrated by the fact that, even in retirement from teaching, he continues regularly to send his private patients to the sessions conducted by his successor and frequently participates in or conducts the session on invitation. In addition to the assigned students, these Friday Sessions regularly attracted 20 to 30 dermatologists and other physicians who attended voluntarily.

Arriving in Minneapolis in 1917, soon after the founding of the Minnesota Dermatological Society, Dr. Michelson soon became a member and has ever since been most active in its programs and has served several times as president. For dermatology, both in Minnesota and in general, it was a fortunate coincidence that another young, able, and ambitious person entered the local dermatologic picture about the same time as did Dr. Michelson. Dr. Paul A. O'Leary, trained more formally at the University of Michigan in the "new" American manner, came to the Mayo Clinic in 1916 when Dr. John Stokes instituted the Section of Dermatology there.

These two, Dr. Michelson and Dr. O'Leary, of similar age and comparable ability but with different personal qualities, worked harmoniously and effectively for thirty-five years, until the death of Dr. O'Leary, and exerted tremendous influence on American dermatology, both individually and by mutual support of each other's efforts. Frequent, and sometimes wide, differences of opinion led to no rancor and were submerged readily when this was advantageous to dermatology. Their efforts were often closely allied with those of Dr. Francis E. Senear of the University of Illinois, the trio forming a powerful combination of soundly progressive Midwestern strength in American dermatologic organizations, particularly during their concurrent service on the American Board of Dermatology. Dr. Michelson was proud to be invited by Dr. O'Leary's successor, Dr. Louis A. Brunsting, to present the first Paul A. O'Leary Memorial Lecture in 1957. The address dealt with diseases of subcutaneous tissue, a subject that had long interested Dr. O'Leary.

Dr. Michelson became a member of the American Board of Dermatology in 1940, after its formative and early developmental periods, and served most responsibly for eleven years during its period of maturation of policy and program. He was president of the board in 1950 and is now an adviser of the board.

Aside from the satisfactions derived from work at the Medical School, probably Dr. Michelson's most pleasant professional association was with the Chicago Dermatological Society. He began visiting these clinical sessions in 1917 and attended each monthly meeting for many years; even now, he continues regular attendance. He has been present at each annual meeting since 1917. This important regional society honored him with its presidency in 1932, when his address was on the "Nodular Subepidermal Fibrosis," a simple, common problem that previously had been a subject of confused misunderstanding. Through association with this important society, Dr. Michelson came to know and to influence most of the dermatologists of the Midwest and to be influenced by close association with its leaders: Drs. Pusey, Ormsby, Mitchell, Ebert, Senear, Finnerud, Rothman, and many others. Many regard him as the society's most respected member. In 1953, he was invited to give the society's Pusey Lecture, choosing to present "A Review and Evaluation of Lupus Erythematosus."

Numerous additional honors and responsibilities have accrued to Dr. Michelson. For many years, he participated actively in the programs of the American Medical Association's Section on Dermatology and Syphilology and was its chairman in 1948, discussing "The Diagnosis of Cutaneous Tuberculosis." Upon the founding of the American Academy of Dermatology and Syphilology, Dr. Michelson be-

came a director of the organization for three years and a member of its Education (program and policy) Committee for twenty years. Having participated in the teaching program annually, often with several activities, it is likely that Dr. Michelson has contributed more than any other individual to the effectiveness of the teaching portion of the program of this, the largest dermatologic organization in the world.

Investigative studies at the University were largely clinical and histopathologic, but Dr. Michelson had great respect for studies requiring more detailed technical knowledge and he generously aided and encouraged the efforts of his students and associates. The Society of Investigative Dermatology recognized these interests by electing him president in 1946. His presidential address reviewed "The History of Lupus Vulgaris."

Election to the American Dermatological Association has long been a goal of ambitious American dermatologists and was achieved by Dr. Michelson in 1925. Until recently, he regularly attended and participated in the annual sessions. In 1951, he achieved the high honor of serving as president at its seventy-fifth anniversary meeting, discussing "The Boundaries of Dermatology" in a philosophic manner.

Other important dermatologic organizations have also honored Dr. Michelson. He was elected to honorary membership in the New York Dermatological Society, the Pacific Dermatologic Association, and the Austrian, British, German, and Venezuelan societies. He is a Corresponding Member of the Danish, French, Italian, and Swedish societies.

Very recently, Dr. Michelson received the Outstanding Achievement Award of the University of Minnesota reserved for former students who have attained high eminence and distinction in their respective fields. This award was presented on September 26, 1960, at the annual Minnesota Medical Foundation Day in connection with the fall opening of Medical School classes.

Dr. Michelson has participated actively at all levels of dermatologic literature. He continues as an avid reader, following closely the dermatologic journals in the English and German languages and regularly paging the French publications as well. He has contributed a total of approximately 200 papers of wide variety in form and subject. His investigational studies have been detailed and thorough, but perhaps his abilities have been most successful when he devoted himself to a thorough survey and review of a problem which previously had caused confusion or conflict of opinion. Examples of the latter type of presentation abound in his writings on clinical and immunologic aspects of syphilis, tuberculosis, sarcoidosis, and lupus erythematosus and in his more philosophic commentaries on cancer of the skin. These subjects occupied a major segment of his literary efforts.

Since 1947, Dr. Michelson has been an active member of the Editorial Board of the *A.M.A. Archives of Dermatology*, not content to be a figurehead but regularly corresponding with the editor and often contributing editorial comment. Dr. Michelson also served as an editorial adviser for *The Journal-Lancet*.

Before entering the field of dermatology, while still in practice in northern Minnesota, Dr. Michelson met and married Dalie Lindsay of Virginia, Minnesota, in 1915. They are rightfully proud of a daughter, Margery (Mrs. Scotson) Webbe, and a son, Robert L., and their spouses and three and two children, respectively. Dr. Michelson resides in Minneapolis and continues an active dermatologic practice there.

PUBLICATIONS BY HENRY E. MICHELSON, M.D.

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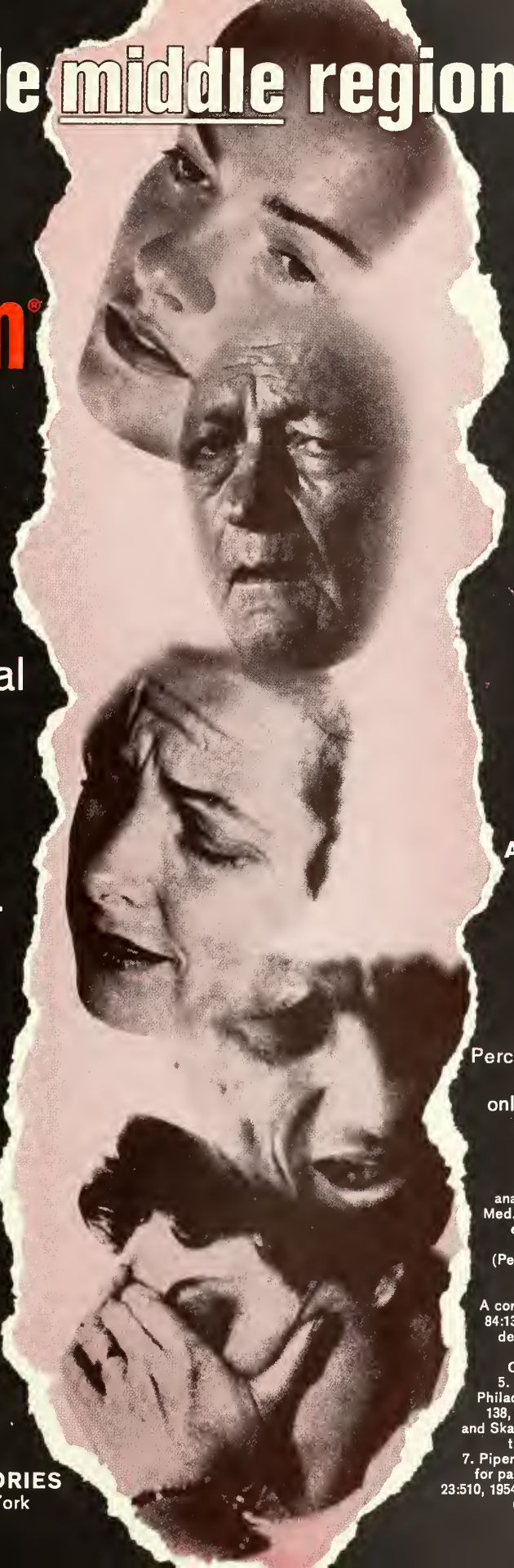
The occurrence of gout and diabetes mellitus in the same patient is more common than is thought, and the association of the two diseases may be more than simply coincidental.

Among 29 patients with gout, 25 were subsequently found to have diabetes, which suggests that the existence of gout in some manner affected the development of diabetes. The hypothesis that hyperuricemia may be one of the mechanisms postulates a defect in purine metabolism leading to the production of an alloxan-like compound in the body in some patients. The development of diabetes before the onset of gout does not annul the theory that hyperuricemia is also operative, as blood uric acid content may be high for years before gout is recognized.

Since gout improved with the onset of diabetes mellitus in 15 patients, the assumption that diabetes has an ameliorative effect on gout also seems tenable.

E. C. Bartels, M. C. Balodimos, and L. R. Corn: The association of gout and diabetes mellitus. M. Clin. North America 44:433-438, 1960.

in the wide middle region of pain



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Book Reviews . . .

French's Index of Differential Diagnosis

ARTHUR H. DOUTHWAITE, M.D., *1960. Baltimore: Williams & Wilkins Co. 1,111 pages. Illustrated. $24.00.*

Illness, to the man standing at the bedside, presents as a welter of confusing symptoms, signs, laboratory findings, x-ray changes, clues of all sorts, and descriptions. These are all nicely tabulated in their proper order in various texts under the heading of the disease in question. Thus the standard texts of medicine, surgery, pediatrics, and so forth competently answer the question, "What are the signs, symptoms, and other findings of the various named diseases?" However, the name of the disease is not written on the patient, nor may it be apparent to the clinician. How, then, is he to find the description of the anonymous pathologic process? Fifty years ago, Herbert French made a massive attempt to answer that question, producing the first edition of *An Index of Differential Diagnosis of Main Symptoms.* With the recurring printings, editions, revised and enlarged, occasionally "completely revised with many new illustrations," as advertised on the fly leaf of the 1960 eighth edition. French has become a classic beloved by students and practitioners.

Arthur H. Douthwaite has long since become the editor of the *Index.* With a group of 20 collaborators, mostly from London and the home counties, he has written with authority upon a myriad of subjects alphabetically arranged from "Accoucheur's hand" to, 1,000 pages later, "Weight, loss of."

The *Index* is a mine of information not to be read but to be quarried with a symptom or a sign as the handle of the search. The book is full of charts and tables, with lists of diseases to be considered in the differential diagnosis starting with any abnormal finding. In the study, for instance, of "Pyrexia, prolonged," the table under this heading and the succeeding article of 20 pages opens all the paths of investigation for this common cause of hospital admissions.

About 60 pages are devoted to pain in the various regions of the body. The common diseases are all mentioned, and many rare diseases are also considered. Inclusion of rare diseases in a compendium such as this is entirely justified since, in most instances, common conditions will spring to the physician's mind and he will be searching the *Index* for ideas for study of less common conditions.

In the paragraph, "Flushing," no mention is made of carcinoid, and this reviewer could find no mention of serotonin or 5-hydroxyindolacetic acid. That flushing is a symptom of carcinoid in fact, the only mention of carcinoid in the text—is under the heading, "Pulmonary stenosis." However, included in the *Index* is an enormous index of 150 pages with a heading, "Flushing of face due to carcinoid heart disease." So there it is, even though this reviewer would want to quibble about the fact that it is disease of the liver rather than of the heart that causes the symptom in question.

The work is well illustrated, although the subjects chosen for photographs are usually far advanced examples of disease. The *Index* is a necessary adjunct to the clinician's library. It is tempting to speculate upon future aids to the physician seeking a diagnosis to fit a collection of signs and symptoms. Transferring given symptoms into tables of diseases and producing a diagnosis by combining several symptoms and several tables to ferret out the one common factor are problems that can readily be programmed for a modern computer. Perhaps the metropolitan hospital at the end of our century will have in its record room such a computer connected by telephone to all wards. When a list of symptoms and signs is fed into it, the proper diagnosis will be regurgitated. For the time being, we still need *French's Index.*

REUBEN BERMAN, M.D.
Minneapolis

Pediatric Pathology

D. STOWENS, M.D., *1959. Baltimore: Williams & Wilkins Co. 689 pages. Illustrated. $20.00.*

In *Pediatric Pathology,* Daniel Stowens, pathologist of the Children's Hospital Society of Los Angeles, emphasizes the fact that there are cases of actual anatomic pathology in his practice—that not all are problems of colic, behavior, or enuresis.

The text is divided into the usual sections of discussion according to symptoms involved. Each discussion is followed by apparently adequate references to the world literature.

Many illustrations of low-power microscopic tissue sections are indistinct, heavy, black and gray masses that are of little value to the inquiring pediatrician. The higher-power illustrations are of better quality. The teaching value of many of the sections would be enhanced if arrow legends were used to point out characteristic pathologic changes.

This book will be of value in the hospital library alongside the other standard textbooks of pathology but alone will not be adequate for the pediatrician.

HERSCHEL J. KAUFMAN, M.D.
Minneapolis

Advances in Internal Medicine

WILLIAM DOCK, M.D., *and* I. SNAPPER, M.D., *1960. Chicago: Year Book Publishers. 353 pages. Illustrated. $10.50.*

The tenth edition of *Advances in Internal Medicine* represents the distillation of a vast quantity of current literature in the field of internal medicine, as evidenced by its index of 1,622 authors. Indeed, the fact that only 10 major topics are reviewed lends some justification to the attitude that the broad field of internal medicine is now beyond the capacity of the average internist to keep fully abreast, certainly while maintaining a busy practice.

The subject matter is organized with great care, and its lucid presentation makes comfortable reading. To this reviewer, the most impressive sections are those entitled "Diagnosis and Management of the Curable Forms of Hypertension" and "Cushing's Syndrome," although none of the remaining subject matter lacks comprehensive treatment of current progress. For example, the

(Continued on page 24A)

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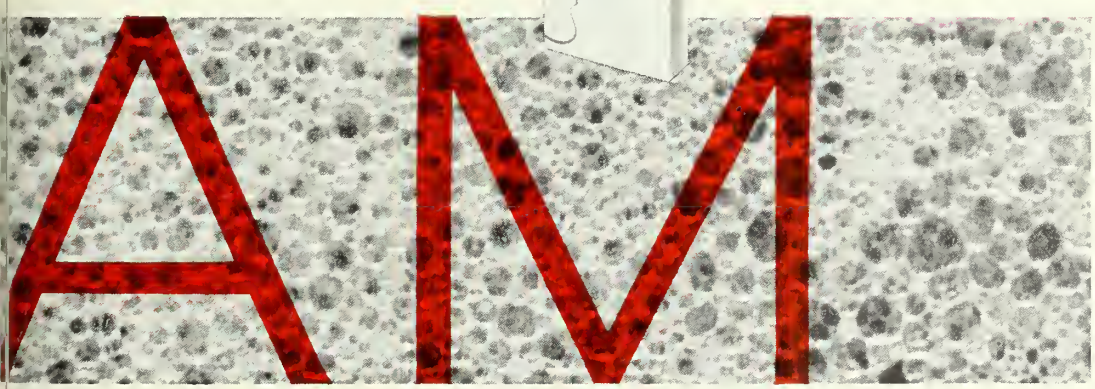

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(Continued from page 20A)

two sections on congenital heart disease—newer diagnosis and surgery—are couched in 253 references and should be required reading for every internist who cannot escape the ubiquitous challenge to distinguish the medical from the surgical congenital heart patient.

In purchasing this book, which is well worth its price, the reader may feel that its title should more appropriately be changed to "*Some* Advances in Internal Medicine." Its 353 pages represent about half the number found in the average year book of medicine, and the binding is of somewhat lower quality.

E. A. HAUNZ, M.D.
Grand Forks, North Dakota

Upper Digestive Tract

FRANK H. NETTER, M.D., *1959. Boston: Little, Brown & Co. 189 pages. Illustrated. $12.50.*

It is always stimulating to review one of the series of the *Ciba Collections of Medical Illustrations.* The splendid correlation between the anatomic, physiologic, and clinical evidences is most graphically demonstrated. They represent the combined effort of the clinical group and the artist.

In the section on lymphatic drainage of the mouth and neck, the reader can readily note the relationship of the thoracic duct to the lymph nodes and thus account for the frequency of a metastatic node in malignant areas drained by the thoracic duct.

The vascular outlines are exceedingly well done and are of importance in our increasing knowledge of carotid vessel disease.

The drawings covering the varicosities of the upper portion of the stomach and the esophagus are exceptionally well done and show their extent, which is much greater than we usually recall.

The systemic drawings for the various tests are outstanding. The correlation between x-ray studies and anatomic plates is most helpful. The utilization of these diagrams in demonstrating to patients their lesions has been very beneficial.

While some of the contributions are of a didactic nature, they are up-to-date and useful as a basic background for procedures and diseases. This text can be sincerely recommended for the gastroenterologist and the surgeon, as well as the general practitioner.

M. LUTHER MUSSELMAN, M.D.
Buffalo, New York

Cutaneous Manifestations of the Reticuloendothelial Granulomas

SAMUEL M. BLUEFARB, M.D., *Editor, 1960. Springfield, Ill.: Charles C Thomas. 442 pages. Illustrated. $14.50.*

This is one of the series of monographs on skin disease published by the Charles C Thomas Company. Its completeness is properly monographic. In contrast to most books in which different authors have written the chapters, there is a commendable lack of tautology and of jarring style changes from one chapter to the next. Fred Urbach discusses lipoidoses in 104 pages as fully as any English text. Systemic reticuloendothelial granulomas, including Letterer-Siwe disease, Schüller-Christian disease, eosinophilic granuloma, and their various synonyms, are covered in 82 pages by the editor. Sarcoidosis is reviewed in 55 pages by Harold L. Israel, Herman Beer-

man, and Murray Somes. Mastocytosis, or urticaria pigmentosa, by Felix Saugher and Zvi Evan-Paz of Tel-Aviv, involves 140 pages. Review and knowledge of the literature in all European languages by these Israeli authors is evident in the three-dimensional effect that makes this chapter outstanding.

This monograph will interest all academic-minded dermatologists and internists and many pathologists and research physiologists. Therapy for all entities may be summarized in a word—none. The tremendous accumulation of basic research, so thoroughly reviewed in this text, has not yet produced data suggesting a therapeutic approach. Future investigation of lipid metabolism and of physiology and chemistry of the mast cell may evolve rational therapy for lipoidoses and mastocytosis. Sarcoidosis remains an etiologic and therapeutic enigma, clouded by contradictions.

Illustrations throughout this book are profuse and well reproduced. They vivify the concept of the arcane diseases discussed and provide visual records of entities which, due to their excessive rarity, are often heard about but seldom seen, even by indefatigable attenders of meetings and conventions.

MURRAY C. ZIMMERMAN, M.D.
Whittier, California

Surgery of the Ear

GEORGE E. SHAMBAUGH, JR., M.D., *1959. Philadelphia: W. B. Saunders Co. 669 pages. Illustrated. $27.50.*

Dr. Shambaugh's book is a tremendous piece of work that should be a part of every otologist's library. It completely covers all aspects of aural infections and hearing problems which are treated surgically. The first portion of the book introduces the developmental and surgical anatomy of the ear, along with its radiologic examination.

The text is liberally and clearly illustrated, so that the reader is brought up-to-date on the most recent advances in otologic surgery. Dr. Shambaugh is to be congratulated for the concise and clear manner in which all subject matter is presented.

The historic portions of the text add to the completeness of this unusual book, which I consider to be a classic of our times on the subject of surgery of the ear.

ALAN A. SCHEER, M.D.
New York City

The Story of Dissection

JACK KEVORKIAN, M.D., *1959. New York: Philosophical Library, Inc. 80 pages. $3.75.*

This little book has 10 chapters: Antiquity, Classical Greece, Hellenistic Alexandria, Rome, Byzantium, Middle Ages, Renaissance, Baroque Period, Nineteenth Century, and Twentieth Century. The list of references consists of 3 books and 8 articles in scientific journals, 4 of the latter being in German.

The book is so short that it could not be expected to stand with such noncited treatises as *Lectures on the History of Physiology,* by Sir Michael Foster, published by Cambridge University Press in 1924; *Galen on Anatomical Procedures,* by Charles Singer, published in New York by Oxford University Press in 1956; and *Medicorum Graecorum opera quae extant,* 20 volumes, by C. G. Kühn, published in Leipzig in 1822.

An example of the lengths to which the book goes

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is a sentence from a paragraph about the clergy during the Renaissance (p. 42): "The death of Leo X again aroused suspicion of foul play, and his body, too, was therefore necropsied in 1521." The subject is dropped, without depicting some of the "goings on" in Florence and Rome in which the Medici played such important parts.

One wonders why the 9 or more split infinitives in Dr. Kevorkian's book were not rectified. Since we have them, we might do well to borrow and adapt Robert Frost's reply to critics of poetry, "The way to take a poem is not to kill it."

As far as it goes, *The Story of Dissection* is an interesting book.

LEMEN J. WELLS, M.D.
Minneapolis

Neurology Simplified

DAVID JOSEPH LA FIA, M.D., *1960. Springfield, Ill.: Charles C Thomas. 175 pages. Illustrated. $6.75.*

This book, written for general practitioners, has been prepared to remove some of the mystery of neurologic diagnosis. This has been no easy task, but the result should be generally appreciated by physicians. The book is organized on a basis of 3 steps: history taking, neurologic examination, and reasoning to the clinical diagnoses. The history is for the pathologic diagnosis. Step 3 is the combination of steps 1 and 2 and comprises the clinical diagnosis.

Part I of the book consists of chapters on etiologic diagnosis in neurology, neuroanatomic diagnosis, and methods of pinpointing neurologic diagnosis.

In Part II, space is given to pain syndromes, such as headache, in different parts of the body. Cerebrovascular disorders are presented briefly but fully enough to convey the author's ideas. Intervertebral disks and spinal cord tumors are treated similarly. Traumas of the brain, spinal cord, and peripheral nerves are discussed. Epilepsy is given consideration, as is multiple sclerosis. There is a chapter on brain tumors and a chapter on neurologic syndromes found in infants and children, which is illuminating. Infectious diseases are discussed, and a chapter on miscellany includes Ménière's syndrome, parkinsonism, and myasthenia gravis. The book is of value for almost anyone in the practice of medicine.

JOHN S. LUNDY, M.D.
Chicago

Hypothermia for the Neurosurgical Patient

ANTONIO BOBA, M.D., *1960. Springfield, Ill.: Charles C Thomas. 124 pages. Illustrated. $6.00.*

This book represents a timely treatise on the use of hypothermia for the neurosurgical patient. It is an application of a principle in a small text devoted to a special subject. This is a very valuable book and spares other authors the effort of trying to make their books complete with respect to trying to cover all aspects of anesthesia.

This book should be read by anyone who is interested in the subject of hypothermia and has not had the opportunity to become experienced with it. For those who are preparing for examinations in anesthesiology, it is a must. This book is indexed and printed on good paper.

JOHN S. LUNDY, M.D.
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Sampling of Cholesterol Levels in a Group of Unselected Office Patients

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MEDICAL LITERATURE contains voluminous amounts of material relating diet to health and to the etiology of atherosclerosis. Reviews of the role of cholesterol in diet point to a correlation of diet, cholesterol, and heart disease.[1–8] No averages of cholesterol are defined.

According to W. S. Hoffman, the average total plasma cholesterol concentration in a general population is about 185 mg. per cent.[9] Higher elevations have been noted in aging and older populations, but the data have been sparse for a general study of an average population. Some authors believe that values as high as 300 mg. per cent are normal.

We undertook a sampling of the average levels of cholesterol in a group of office patients to offer the clinician some suggestion as to what may be expected in such an ill-defined group.

METHOD

Total cholesterol determinations were done according to the method of Pearson and associates, who state that normal values range from 150 to 250 mg. per cent.[10] From a medical practice confined to internal medicine, 168 patients were sampled for cholesterol blood levels. No attempts at selectivity were made except that all patients were ambulatory and the majority of blood samples were taken from fasting patients. There were 92 male and 76 female patients ranging in age from 24 to 84 years.

RESULTS

The over-all average of total cholesterol readings was 297 mg. per cent, with a range from 155 to 440 mg. per cent. In patients 50 years of age or younger, the average reading was 280 mg. per cent; in patients over 50, the average was 365 mg. per cent, with a range from 290 to 440 mg. per cent.

Mattingly and associates have noted, in their study of 294 healthy male officers, that the serum cholesterol level was as informative as data from more elaborate procedures.[11] Mileh and associates observed that cholesterol values increased with age and noted a stability of the levels of cholesterol in the older age group.[12] These observations tend to confirm the findings of our admittedly small study group—the tendency to higher levels among the patients over 50. The predictive value of higher levels of cholesterol in the group under 40 suggests an accelerating atherosclerotic process.

No attempt was made in this study to correlate the lipid study with the more elaborate and expensive laboratory procedures involving the S_f 12-20 and the S_f 20-100 lipoprotein values of Gofman.

CONCLUSION

It would seem that the presence of an elevated serum cholesterol value in an otherwise normal

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adult under the age of 40 should encourage a search for further evidence of premature vascular disease.

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To prevent repeated infection and chronic illness, prompt recognition and treatment of acute inflammation of the prostate is necessary. The infection most often affects middle-aged men. The pathogenesis is obscure in most cases, although urethral instrumentation, hemorrhoidal injection, diabetes mellitus, and systemic infection are occasionally incriminated. Prostatic hyperplasia does not predispose to injection. Acute prostatitis is often caused by Escherichia coli, whereas both E. coli and staphylococci are commonly found with prostatic abscess.

Urinary frequency and dysuria always occur, and hematuria and urinary retention may develop. Pain is frequent with acute prostatitis and is always associated with abscess. The pain most often is referred to the rectum and is sometimes accompanied by a sense of fullness and tenesmus. Low backache and perineal pain are also common. Suprapubic pain is due to urine retention. Fever, chills, headache, muscle pains, and malaise are frequent systemic manifestations and may be the presenting symptoms.

Examination of the rectum reveals a tense, tender, and enlarged prostate gland: a boggy, soft area is indicative of abscess. The urine is usually cloudy from pus. The infecting organism is easily cultured from the urine if antibiotics have not been administered. Leukocytosis is detected in about half of patients with acute prostatitis and in all patients with prostatic abscess.

Symptomatic treatment of acute prostatitis includes bed rest, hot baths, local heat to the perineum, analgesics, and copious fluids with alkalies. Wide-spectrum antibiotics should be started immediately. If necessary, the drugs can be changed after culture and sensitivity studies are completed.

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Pharmacology of Pulmonary Circulation

With Special Reference to Drug Therapy of Pulmonary Hypertension and Pulmonary Edema

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In a recent article,[1] the effects of drugs on the pulmonary circulation were systematically reviewed. For completeness, coverage of each drug should include three major categories: (1) local action on the pulmonary blood vessels, (2) local action on systemic vessels, and (3) behavior of pulmonary blood flow or cardiac output. The available information is summarized in figures 1 and 2 in which each of the various drugs is characterized under these 3 categories. It is the purpose of this paper to discuss the considerations when drugs are used in the treatment of pulmonary hypertension and pulmonary edema.

PULMONARY HYPERTENSION

The most desirable action of a drug for the relief of pulmonary hypertension is pulmonary vasodilatation. The drugs that dilate the pulmonary vessels are listed in figures 1 and 2, below the horizontal axis of each figure. The vasodilatation of the pulmonary vessels is not a selective type of vascular action because all of these drugs act on the systemic blood vessels in the following manner: systemic vasodilatation for aminophylline, isoproterenol, acetylcholine and tolazoline, and systemic vasoconstriction for pitressin and the ethoxy derivative of methoxamine. A truly selective vasodilator for the pulmonary vascular bed has not yet been discovered, but selective vasodilators for other special vascular beds—coronary, cerebral, extremities—are similarly lacking. The discovery of a selective vasodilator for any one vascular bed will undoubtedly facilitate the development of drugs selective for the other areas.

The concomitant effect on pulmonary blood flow is not consistent with the nature of the systemic vascular action for all the available pulmonary vasodilators (figure 2). Three of them—isoproterenol, aminophylline, and tolazoline—usually induce an increase in pulmonary blood flow so that the combined action on pulmonary arterial pressure is variable. If vasodilatation predominates, a fall is to be expected, but if the increase in pulmonary blood flow is greater proportionate to the vasodilatation, a rise in pulmonary arterial pressure occurs. The most consistent pattern for a reduction in pulmonary arterial pressure is a reduction in pulmonary blood flow combined with vasodilatation, and this is the pattern for the ethoxy derivative of methoxamine and for pitressin. These two drugs have not been used for the treatment of pulmonary hypertension because the basic cause of the reduction in flow is cardiac depression, either directly or by increased vagal tone. If excessive, this depression may increase the left atrial pressure. The more desirable mechanism for a depression in pulmonary blood flow would be a reduction in venous return to the right side of the heart; the ganglion blocking agents cause such a reduction but they do not cause a consistent dilatation of the pulmonary vessels.

PULMONARY EDEMA

It is more difficult to outline the desirable actions of drugs for the therapy of pulmonary edema because of the lack of general agreement concerning the major causes of edema formation: increased capillary permeability or increased hydrostatic presure. The latter is more conducive to a discussion of drugs because drug effects on structures that will influence capillary hydrostatic pressures are known but drug effects on those that influence capillary permeability are not known. Drugs that relax the smooth muscles of the bronchioles and pulmonary veins should be expected to reduce the capillary hydrostatic pressure for the following reasons: a

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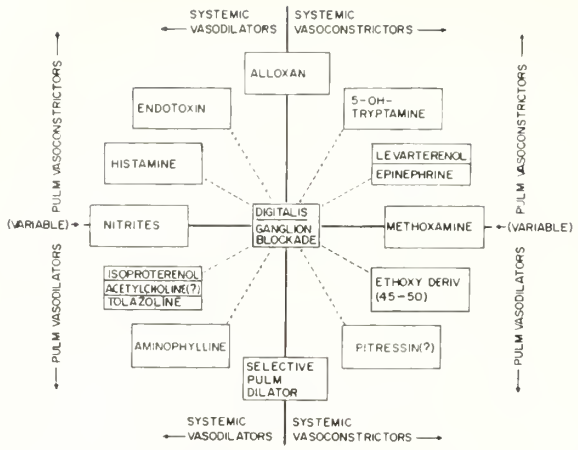

Fig. 1. Comparative effects of drugs on pulmonary and systemic vessels. Drugs below the horizontal line are pulmonary vasodilators, those above are vasoconstrictors and those on the line have variable effects. Drugs to the right of the vertical line are systemic vasoconstrictors, those to the left are vasodilators and those on the line have variable effects.

reduction in venous resistance will mechanically reduce the resistance to blood flowing from the pulmonary capillaries and bronchiolar dilatation will reduce the anoxemia which is known to cause an increase in pulmonary capillary pressure and edema by a complex series of mechanisms.[1]

There are some drug actions which are either desirable or undesirable in the treatment of pulmonary edema. Pulmonary arterial constriction

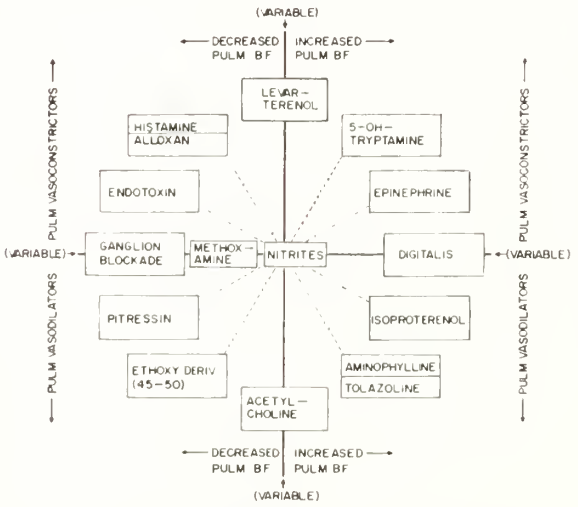

Fig. 2. Comparative effects of drugs on pulmonary vascular tone and on pulmonary blood flow. As in figure 1, the drugs below the horizontal line are pulmonary vasodilators, those above are vasoconstrictors, and those on the line have variable effects. Drugs to the right of the vertical line increase pulmonary blood flow, those to the left decrease pulmonary blood flow, and those on the line cause variable effects.

is desirable because of a protective action in the capillaries but would be undesirable if it would initiate opening of arteriovenous shunts and would contribute to anoxemia. An increase in left ventricular output would reduce pulmonary venous and capillary pressures, but an increase in right ventricular output would cause an increase in arterial and capillary pressures. A rise in aortic blood pressures would improve ventricular function by increasing coronary blood flow, but, on the other hand, would also mean an increase in left ventricular work and subsequent failure of the left ventricle.

The drugs that are used in the management of acute pulmonary edema will now be considered, based on the assumption that a rise in cap-

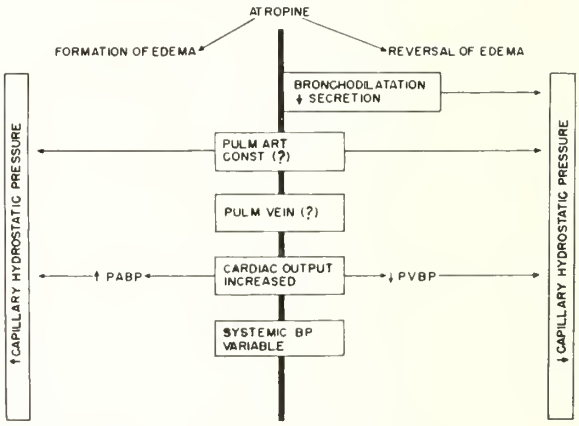

Fig. 3. Effects of atropine on pulmonary edema.

illary hydrostatic pressure will initiate formation of edema and a reduction in pressure will reverse its formation.

Atropine (figure 3). The pattern of action of atropine is as follows: (1) The paralysis of the vagal innervation to the tracheobronchial passages results in bronchodilatation and reduced bronchial secretion. (2) The pulmonary vessels, arteries or veins, are not dilated by atropine but might even constrict if the local dilator action of acetylcholine in human vessels[2] and the dilatation by electrical stimulation of the vagus[3] were extended to mean that parasympathetic pulmonary vasodilator fibers can be paralyzed by atropine. (3) Atropine causes cardiac acceleration and increased cardiac output in normal subjects[4,5] but information derived directly from patients with pulmonary edema is not available. The increase in cardiac output by atropine is not dependent on a reduction in circulating blood volume because Weissler, Leonard, and Warren[5] observed no increase in output when atropine was administered to subjects with blood pooled

in the extremities. (4) Systemic arterial pressure changes elicited by atropine are insignificant and probably unimportant in the consideration of pulmonary edema. In pulmonary edema associated with poisoning by cholinergic and anticholinesterase agents, atropine would be the most effective therapy.

Ganglion blocking drugs (figure 4). These agents were originally introduced in the therapy of pulmonary edema because of the supposition that they reduce circulating blood volume and consequently decrease hydrostatic pressure in the capillaries. Although this is their most probable effect, it may not be the only one. The ganglion-blocking agents are known to bring about the following actions: (1) bronchodilatation, by

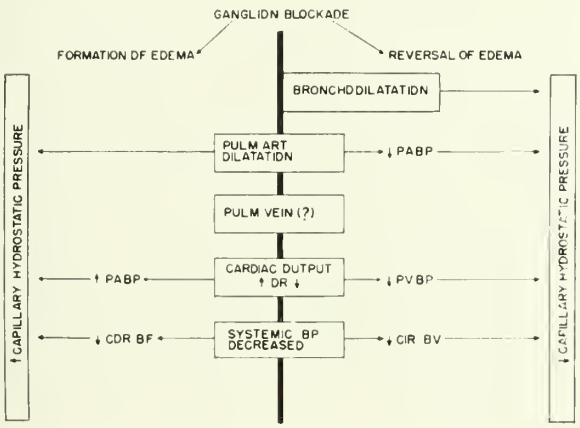

Fig. 4. Effects of ganglion blocking drugs on pulmonary edema.

paralysis of vagal innervation; (2) pulmonary arterial (and venous?) dilatation, by paralysis of sympathetic innervation; (3) increased or decreased cardiac output, from varied causes; and (4) systemic hypotension.[6] It is not possible to identify the most important action that is responsible for the relief of pulmonary edema.

Aminophylline (figure 5). Unlike the drugs already mentioned whose actions are mostly dependent on the autonomic nervous system, aminophylline acts directly on smooth and cardiac muscle. Its actions include: (1) bronchodilatation, which is one of the most widely known and important actions of aminophylline; (2) direct pulmonary arterial and venous dilatation, which is not as widely known although it has been repeatedly proved by lung perfusion experiments[7] and suggested by calculation of pulmonary vascular resistance in man; (3) increased cardiac output, a manifestation of the ability of aminophylline to stimulate the myocardium directly; and (4) systemic hypotension which may occur

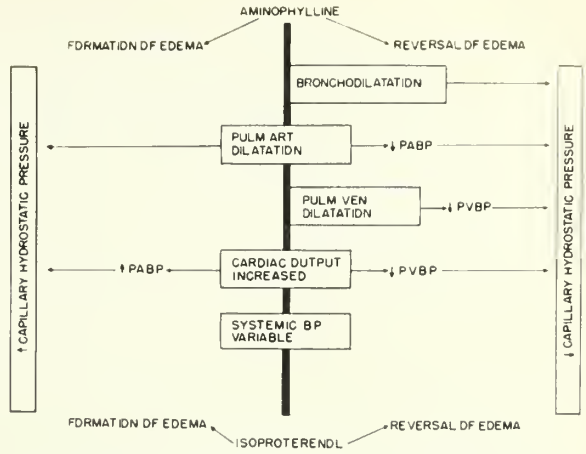

Fig. 5. Effects of aminophylline and isoproterenol on pulmonary edema.

if aminophylline is injected so rapidly that the systemic vasodilator action becomes apparent. Aminophylline is widely used in the therapy of bronchial asthma and paroxysmal cardiac asthma and the usual justification for its use has been entirely derived from its bronchodilator action. It has not been possible to assess the role of two other actions of aminophylline—cardiac stimulation and pulmonary vasodilatation.

Isoproterenol and other sympathomimetic pulmonary vasodilators (figure 5). The pattern of isoproterenol (Isuprel) is essentially the same as that of aminophylline: bronchodilatation, pulmonary vasodilatation, increased cardiac output, and systemic hypotension. Methamphetamine (Methedrine) and mephentermine (Wyamine) are similar to isoproterenol but lack bronchodilator and systemic hypotensive actions. None of these sympathomimetic drugs has been tested in clinical forms of pulmonary edema.

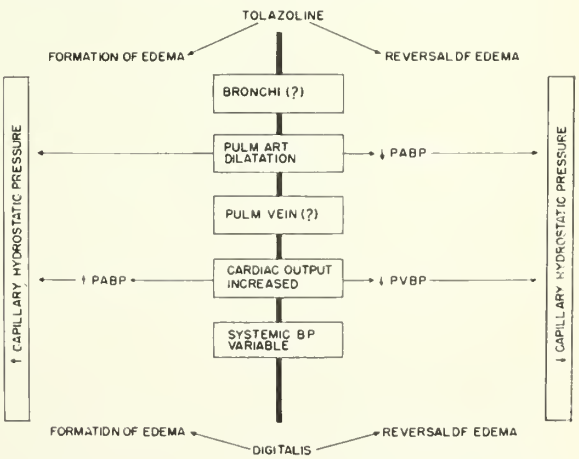

Fig. 6. Effects of tolazoline and digitalis on pulmonary edema.

Tolazoline (figure 6). This adrenergic blocking drug (Priscoline) was introduced by Wheatley[9] in the therapy of pulmonary edema secondary to acute left ventricular failure. The pattern of action of this drug in pulmonary edema would be about as follows: (1) The effect on bronchial musculature is not known, but, since adrenergic blocking action does not usually involve paralysis of sympathetic bronchodilator action, bronchoconstriction from a removal of adrenergic bronchodilatation would not be expected to occur. (2) Rose[10] failed to observe a local vasodilatation in the perfused dog lungs following the administration of tolazoline, but measurements of pulmonary vascular resistance in patients with pulmonary hypertension revealed a reduction which suggested a local vasodilator action.[11,12] (3) The cardiac output is usually increased by tolazoline, a response which is in line with its local stimulant action on the perfused mammalian heart. (4) The accompanying effects on systemic blood pressure have been variable, presumably because of simultaneous increase in cardiac output and dilatation of systemic vessels. Thus, tolazoline lacks one action characteristic of other drugs, bronchodilatation.

Digitalis (figure 6). The effects of digitalis are similar to those of tolazoline. (1) Digitalis has no important local action on bronchial musculature but the increase in vagal tone of the cardiac pacemaker (bradycardia) may also extend to the bronchioles (bronchoconstriction). (2) Although excised lung vessels can become constricted in response to digitalis,[13] calculation of pulmonary vascular resistance following digitalization in patients with heart failure indicates a reduction. This may mean that the vessels of the human lung behave differently from the excised vessels, that the increase in vagal tone during digitalization is sufficient to dilate the pulmonary vessels, or that there is an inactivation of the vasoconstrictor reflex from the left atrium to the pulmonary vessels as a result of the improvement in left ventricular function. (3) Cardiac output is increased consistently after digitalization of the failing heart. In spite of the increase in pulmonary blood flow, there usually is a fall in pulmonary arterial pressure largely because of the reduction in left atrial and pulmonary venous pressures, and also because of the probable vasodilation described under (2). If the right ventricle is failing due to cor pulmonale, digitalis may cause pulmonary artery pressure to rise. (4) The systemic arterial pressure is essentially unchanged in spite of the increase in cardiac output. The reduction in systemic vascular resistance is analogous to that described above for the pulmonary. The justification for using digitalis in acute pulmonary edema is to bring about an increase in cardiac output and therefore to reduce pulmonary capillary pressure. Its use in pulmonary edema complicating myocardial infarction rests on rapid improvement of myocardial contractility. Gorlin and Robin[14] report the successful control of pulmonary edema and systemic shock with ouabain intravenously (in subdigitalizing doses) in 3 cases of myocardial infarction. Because these agents may further augment the already existing tendency to increased myocardial excitability, such administration is dangerous, but the condition is a desperate one.

CONCLUSIONS

It is not yet possible to identify which particular drug is the most effective one in the treatment of pulmonary arterial hypertension or pulmonary edema. In the former, there are numerous studies on the reduction of pulmonary arterial pressure following a single administration of a drug but long term studies in pulmonary edema have been on animals exclusively and almost all drugs tested have been shown to be effective in one or more forms of experimental pulmonary edema.

It is difficult to apply such results in human cases of pulmonary edema unless studies are performed directly on patients, and this will be possible only if methods for assessment of human pulmonary edema become available.

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Injection of crystalline insulin four times a day may control labile diabetes that is managed inadequately by long-acting insulin or a combination of preparations. Such treatment reduces fluctuations in blood and urine sugar content, as well as frequency and degree of insulin hypoglycemia. Of 14 patients given injections before each meal and between midnight and 2 a.m., 10 improved.

H. L. Wildberger and H. T. Ricketts: Multiple injections of crystalline insulin in treatment of labile diabetes. J.A.M.A. 172:655-658, 1960.

Venous stasis is reduced by elevating the foot of the operating table or recovery room bed by 15°; thrombosis and embolism may also be prevented. Vigorous contractions of thigh and calf muscles with the body and lower extremities horizontal do not decrease stasis as effectively as elevation.

Venous stasis seems to be of primary importance in initiating thrombosis in leg veins. Thrombi are usually attached at or near the apices of valve pockets. Venous stagnation appears to cause minor changes in the lining endothelial cells, starting primary thrombus deposition. Microscopically, the greatest degree of organization of thrombi is at the apices, with more recent extension up the pockets.

Venous stasis was studied in about 100 subjects with normal lower extremities by cineroentgenographic and rapid cassette changer technics. A 25-cc. dose of 50 per cent diatrizoate (Hypaque) was injected in fifteen seconds into a dorsal vein of the foot after an initial 2-cc. dose. A tourniquet at the ankle directed the substance into the deep veins.

Dye retention in the horizontal supine position was especially apparent in leg pockets and venous saccules of calf muscles. Such retention tended to increase with advancing age of subjects. With an elevation of 15°, the greatest tilt at which most operations may be performed, the rate of flow was strikingly increased. In anesthetized patients, thigh and leg muscle contractions induced by percutaneous electrical stimulation were not as useful as voluntary muscle movements in speeding venous return. Little dye was noted in superficial veins of patients with normal valves when the injection was in the deep veins below the ankle. Addition of compression bandages at 15° elevation did not lessen venous stasis further.

A. D. McLachlin, J. A. McLachlin, T. A. Jory, and E. G. Rawling: Venous stasis in the lower extremities. Ann. Surg. 152:678-684, 1960.

Know Your Weeds

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Hay fever is caused by an allergy to the pollen of one or more certain species of plants, the species depending upon the idiosyncrasy of the individual. All other species do not affect that patient any more than they do a nonallergic person. The cause of the hay fever may be determined by finding out the exact days of the year the patient is afflicted. An observant patient will discover that this relationship is remarkably consistent from year to year, because every species of plant blooms at exactly the same time each year, almost to the day, in any given locality. Knowing when the local plants bloom, then, will give the answer as to which species of wind-pollinator is responsible for the hay fever. These findings should be confirmed by skin tests.

There are 3 specific pollen seasons. In North Dakota, trees bloom in April and May, grasses in June and July, and weeds in July, August, and September. In Minnesota, the seasons are essentially the same, except that the weeds bloom also in June. In South Dakota, the trees and grasses bloom a month earlier. Montana has the same seasons as North Dakota, except that grasses flower from May to September.[1]

Of the hundreds of species of flowering plants, only those pollinating by wind (anemophilous) are important in causing hay fever. These plants have flowers which lack showy color and are of small size, since they need not attract insects to ensure fertilization and reproduction. These flowers are very numerous on the plant and produce large quantities of pollen, since blowing by the wind makes the probability small that a given pollen grain will land on the female flower of another plant of that species. Those pollinating by insects (entomophilous) need not scatter their pollen where people inhale it in significant quantities. (An exception is the dandelion, which is more intimately tied to human beings because of its abundance on our lawns and pastures.) Moreover, of those wind pollinators, very few give enough trouble to be of significance. It is practical and easy to learn these few species. Gelfand[2] says, "It is important that the physician familiarize himself with the common hay fever plants of the community in which he practices." He was referring not only to the allergist but to the general practitioner, "since he sees and treats most allergic disorders." After finding out that he is allergic to a certain species, the patient will be interested and pleased to be able to recognize that species when he sees it. It is logical that the physician who treats hay fever should know what the hay fever plants look like.

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IDENTIFICATION OF PLANTS

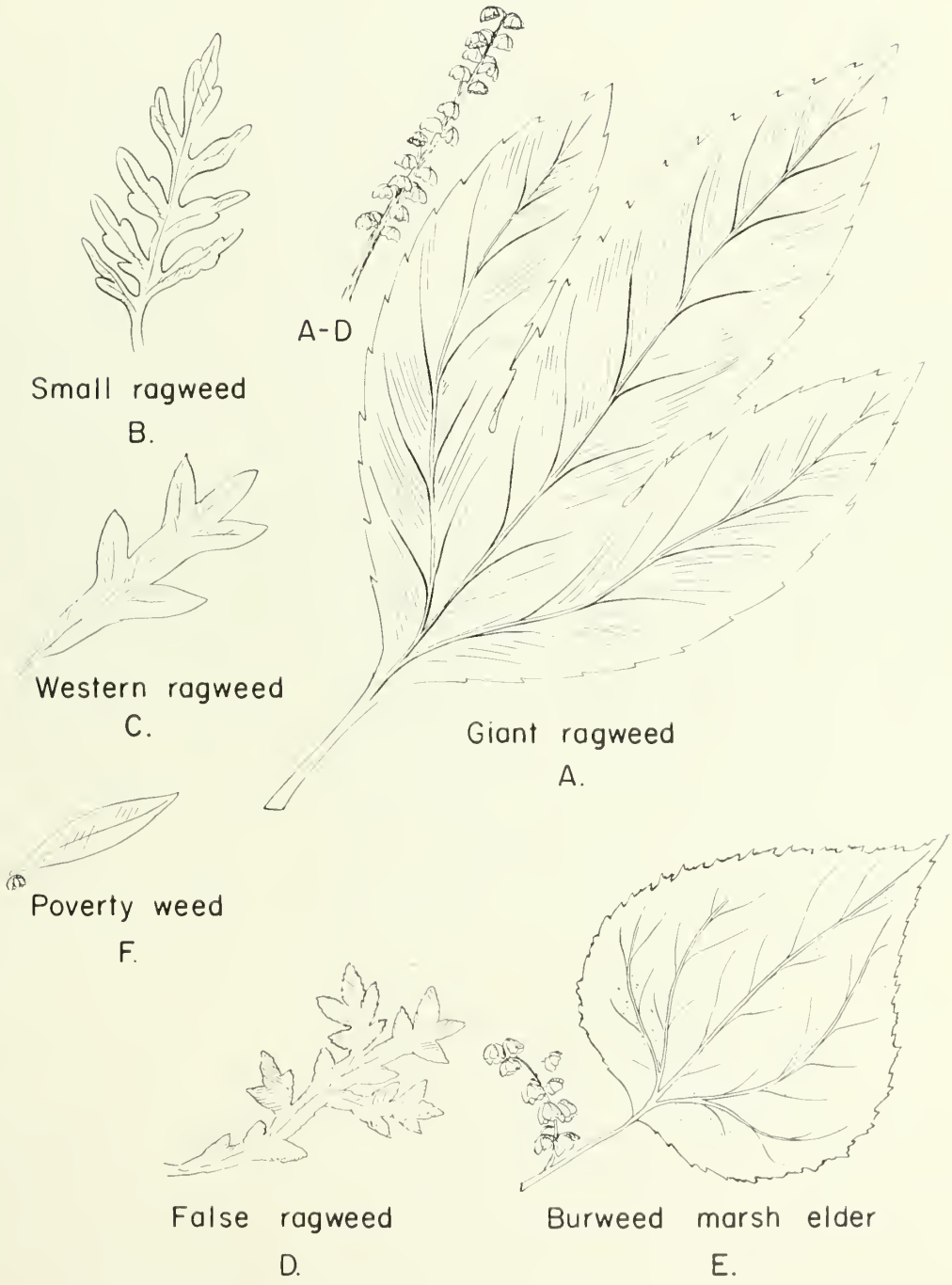
An excellent guide to identification of plants is the book by Stevens,[3] or that by Georgia.[4] But for the physician or his patient who is not familiar with plants or who does not have the background, or time, or inclination to master botanical terms, this paper is offered to help him recognize the worst offenders without using technical language. Most people know box elder, cottonwood, quaking aspen, birch, or pussy willow, so these are not mentioned. Grasses are harder to differentiate, but these don't cause hay fever as often as the weeds; furthermore, it has been stated that immunizing against one grass (timothy) will cross-immunize against the other allergenic grasses as well,[5] so that there is less practical need to be able to tell one from the other.

There are only a dozen weeds of importance which cause hay fever during the weed season in the Dakotas, Minnesota, and Montana. Of this dozen, the most important are the 4 ragweeds.[6] Three species are knee high, but one species, properly called giant ragweed, is head high.

The giant ragweed's scientific name is *Ambrosia trifida* (figure A). *Ambrosia* means "pleasing to taste or smell;" a hay fever sufferer would violently disagree with the botanist who pinned this name on it. *Trifida* recalls the shape of the hand-sized leaf, which has 3 large lobes or teeth, suggestive of a maple tree's leaf. It is common along roadsides and ditches in eastern North and South Dakota and Minnesota.

Weeds with Opposite Leaves:

Approximately ⅔ natural size



The common, short, or small ragweed, *A. artemisifolia*, has leaves resembling sagebrush; they are divided or lacy and almost as long as one's finger (figure B). This plant is common along roads and in fields in rich soil.

Western ragweed, *A. coronopifolia*, is a perennial and spreads by horizontal roots in dry prairie soil (figure C). Its leaf is narrow and has a thick, short lobe on each side. It is found only as far east as western Minnesota.

False ragweed, *Franseria acanthicarpa*, has several branches to its stem; the pollen-bearing heads grow in clusters instead of singly (figure D). Its leaves have lobes on each of their lobes and are broader and paler than the other ragweeds. It is an invader of North Dakota from the West and occurs in Little Missouri River country. It has pinhead-sized seeds with spines, which may stick to clothing.

Marsh elder, or burweed marsh elder, *Iva xanthifolia*, often growing taller than a man, gets its name by looking like a shrub, the elder (figure E). Its leaves look a little like cottonwood leaves. It grows typically in stockyards and around old strawstacks, as well as along roadsides and in neglected fields.

Poverty weed, *Iva axillaris*, grows in the Dakotas and Montana in soil too poor for much else to grow—hence its name (figure F). It is a perennial, with narrow, egg-shaped leaves 2 or 3 fingerbreadths long. These plants grow in dense patches and have an unpleasant odor.

These 6 weeds have their leaves and branches opposite on the stem—that is, where one leaf arises, a twin also arises at the same level on the other side of the stem. In the following 6 weeds, the leaves and branches alternate on the stem—that is, only one leaf grows at a given level, the next leaf growing on the other side of the stem at a higher level, resulting in a zigzag arrangement.

Of this group, the most common offender in hay fever patients in western Minnesota and westward is the Russian thistle, *Salsola kali*. The young plant is soft, but soon its short, narrow leaves turn into sharp spines as the branches round out into a small bush (figure G). In the fall, its stem loosens from the ground and the wind blows it away as a tumbleweed. One touch of the hand will distinguish this plant from all the others because of its spines.

Mexican fireweed, or burning bush, *Kochia scoparia*, also may be tumbled away by the wind after it has died. It looks like Russian thistle but has no spines (figure H). It receives its name from the red color of the leaves its ancestors had in the fall when they were planted for show in gardens. It is now common on neglected ground in western Minnesota, the Dakotas, and adjacent Montana.

Western water hemp, *Acnida altissma*, grows near water, mostly in South Dakota and southwestern Minnesota. Its flowers are prickly, and it has narrow leaves up to 3 inches in length (figure I).

A close relative is the rough pigweed, *Amaranthus retroflexus*, common in rich soil. Uniquely, it has a red root. Its leaf is egg-shaped, on a long stalk, and of rough texture (figure J). Its flowers are similar to those of water hemp, blooming in a thick, prickly cluster at the end of each branch.

Lamb's quarters, *Chenopodium album*, usually seen as a small weed on the edges of lawns, may grow 5 feet high. Its rounded, egg-shaped, or narrow leaves are grayish or bright green, and its stem has red spots and stripes (figure K).

Cocklebur, *Xanthium italicum*, is a relative of the sunflower, with miniature pollen-bearing flowers one-third of an inch wide on the top of the plant (figure L). The female flowers are lower on the plant, at the bases of the leaves. Each pair of flowers develops into a hard bur, with stiff, hooked spines which catch on clothing. It commonly grows on waste ground.

Sage may also be mentioned. Its gray-green color and distinctive smell when the leaves are crushed distinguish it from all other weeds. The prairie sage and pasture sages, *Artemisa sp.*, are common in western Minnesota and the Dakotas. A larger species, which is a shrub, is found in western North Dakota and Montana.

THERAPY

After the offending weeds have been identified, the following measures may be instituted:

1. Desensitization of the patient by injections of extract of the pollen. This is available commercially.

2. Removal of the patient from the allergic environment. He need not move his residence to a distant part of the country but may go on a vacation trip—perhaps less than a hundred miles' journey will be sufficient—for only that time during which the offending weed is pollinating in his community. This may be determined by driving out to where the weed is growing and noting its stage of growth. If the plant and its leaves and flower heads are small, it has not bloomed yet; if tapping it produces a shower of yellow dust, it is producing pollen; if the little knobs of flowers are dried and empty and the

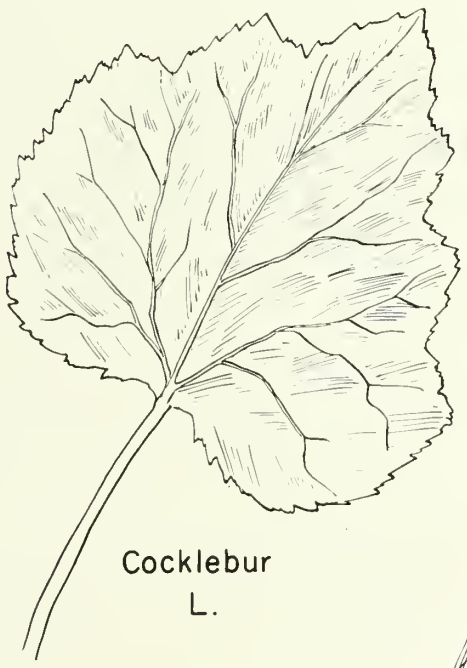
Weeds with Alternate Leaves:

Approximately ⅔ natural size

Western water hemp
I.

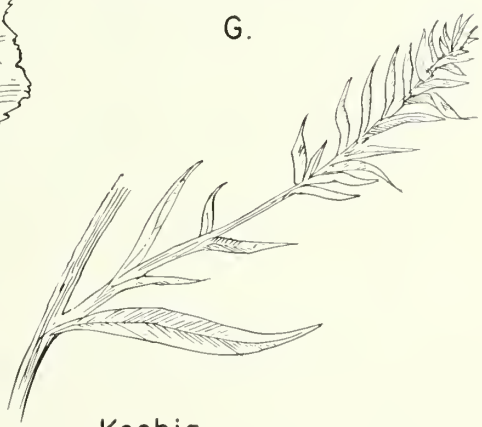
Lamb's quarters
K.

Rough pigweed
J.



Cocklebur
L.

Russian thistle
G.



Kochia
H.

leaves are withered, it is done with its pollinating. Picking a plant and setting it in a can near windows in a garage on a dark paper or cloth for twenty-four hours will reveal yellow pollen dust under the plant if it is actively pollinating; all plants of a specific species pollinate at the same time in a given community.

3. Growing of shelter belts. An arrangement of rows of trees on the windward side of the farmhouse causes the prevailing wind to rise over the house,[7] carrying its load of pollen overhead. Theoretically, this should cause the pollen to bypass the hay fever sufferer on the ground below.

4. Living on the leeward side of town. This will place the patient on the side of the city where the pollen count is lowest. The prevailing wind rises up and over a city because of the heat rising from the city, thus causing the pollen-laden air from the country to be diverted upward over the house level.[8]

5. Local eradication of the offending weed. This will cut down the pollen count in the air of the immediate vicinity, such as in the farmyard or the city neighborhood.

6. Encouraging the county extension agent and the farmers in their efforts at weed eradication on the farms. An indoctrinated hay fever patient can be an enthusiastic helper.

7. Installation of an air conditioner in the patient's bedroom. If he can enjoy a symptom-free night, he is more able to tolerate a day of symptoms.

8. Keeping doors and windows closed and staying indoors as much as possible during the hay fever season.

SUMMARY

Hay fever is caused by comparatively few species of plants. The physician who treats hay fever should be able to recognize the offending plants for his own edification and for the satisfaction of his patient. These plants may be identified easily by the novice by determining (1) whether the plant's flowers are tiny, green, and numerous; (2) in which month of the growing season it is blooming; (3) whether its leaves are opposite or alternate; and (4) the shape, size, and appearance of the leaves, as shown in the illustrations.

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Combined administration of chlorothiazide (Diuril) and methylprednisolone (Medrol) may induce sodium diuresis in patients with alcoholic cirrhosis and ascites refractory to other treatment. No complications occur with prolonged therapy. However, the steroid, in particular, should be administered only when other measures have failed. Neither drug alone produced significant sodium excretion in 18 patients, but combined administration promptly resulted in a mean twenty-four-hour excretion of 56 mEq. in 15. Weight loss usually was apparent within the first few days.

A. G. Redeker, O. T. Kuzma, and T. B. Reynolds: An effective treatment of refractory ascites in cirrhosis of the liver. Arch. Int. Med. 105:594-600, 1960.

Treatment of Alcoholism

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Recognition of alcoholism as a primary medical problem has increased rapidly during the past quarter of a century. Previously, legal agencies and religious groups took the lead in seeking approaches to the problem. Medicine was preoccupied mainly with treating the symptoms resulting from excessive drinking and with the organic pathology associated with the prolonged ingestion of alcohol.

In 1956, the Council on Mental Health of the American Medical Association presented a report to the AMA House of Delegates in which the principles were affirmed that (1) alcoholism comes within the scope of medical practice; (2) alcoholic symptomatology occurs in many personality disorders which may be properly admitted and treated in general hospitals; (3) the management of the alcoholic in the general hospital is much more feasible with the improved methods of treatment available; and (4) house officers need training in treating these patients to prepare them for later contacts when in practice.

Much of the delay in recognizing alcoholism as a primary medical problem stemmed from lack of clarity in differentiating social drinking, drunkenness, and alcoholism. This was further complicated by the strong emotional bias of many concerning drinking and the right to drink as a moral or religious issue. In addition, in the minds of many, the Skid Row drunk and the chronic drunkenness offender had become stereotypes of the alcoholic. It is true that some of these persons are alcoholics, but the overwhelming majority of alcoholics do not come from Skid Row. Until it was established that alcoholism is prevalent in all social and economic groups, there was an inadequate recognition that problems of alcoholism are intertwined with many problems preoccupying medical, psychologic, and social scientists dealing with all strata of society.

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DEFINITION

Alcoholism has been variously defined. Common to most definitions are the concepts of lack of control over drinking and drinking that continues in spite of its destructive effects on the individual's health and on his personal, social, and economic life. No satisfactory explanation has been found for this lack of control. Some workers have advanced the hypothesis that alcoholics have a physiologic idiosyncrasy in the way their bodies handle alcohol, but no factual evidence has been found to support this hypothesis. Most workers have looked for multiple factors in the areas of personality functioning or malfunctioning and of social conditioning.

Certainly, all who drink to excess are not alcoholics. Drinking of alcoholic beverages fulfills varied social functions in diverse cultures. Even drinking to the point of intoxication in certain situations meets social expectations and, to a greater or lesser extent, social approval. Many Skid Row men and chronic-drunkenness offenders are conforming to the way of life of their subculture. Their primary social relationships are dependent on sharing the drinking patterns of Skid Row. There are multiple reasons why these people are unable to find satisfactions in the main stream of society. Alcoholism may account for the presence of some men on Skid Row, but studies of Skid Row social groups suggest that many are there for other reasons.

What, then, characterizes the alcoholic? E. M. Jellinek gives a lucid description of the symptoms of alcoholism as seen in the United States. The alcoholic not only drinks more than other members of his group but more frequently. When drinking, he shows more behavior considered inappropriate to social drinking situations than do others. He may experience blackouts—

that is, temporary amnesias, during and after drinking episodes. He begins to express bizarre excuses or reasons for his drinking. He drinks more rapidly, frequently gulping his liquor. He "sneaks" extra drinks, hoping his companions will not notice the extent of his indulgence. He seems to "need" alcohol and extends the use of alcoholic beverage into times, places, and situations not considered appropriate by his associates. With greater frequency, the first drink is followed by loss of control, so that drinking proceeds to intoxication without regard for the damage done to his social situation. In an effort at control, he may change his pattern of drinking, using different beverages or drinking at different times of the day, in different places, or with different people. He may become a "loner." Eventually, he may no longer have "reasons" for needing a drink and simply deny that he drinks excessively. He may hide supplies in unusual places to avoid detection and to protect himself from being caught short if anyone tries to separate him from his usual source of supply. Finally, his growing incompetence, tremors, or episodes of delirium or stupor may bring him to medical attention.

MEDICAL MANAGEMENT

Advances in the medical management of hyperactive alcoholic states permit most patients to be handled at home or in the general hospital. The wide range of tranquilizing drugs has largely eliminated the need for sedatives of the barbiturate type. To many alcoholics, the attainment of rest with tranquilizers and the administration of fluids, vitamins, and other nutrients bring rapid restoration of physical well-being. Others, with impaired liver function, peripheral neuropathy, or evidence of brain damage, need medical attention over a period of many months. Stupor in a drinker must always alert the physician to the possibility that brain damage associated with a skull fracture may be a causative factor in the diminished responsiveness.

It is after the crisis is over that the physician must deal with the problem of how to help his patient avoid recurrence of the pattern of uncontrolled drinking.

Patient's attitude. The patient must first acknowledge that he is an alcoholic and has lost control of his drinking. All alibis and denials of its seriousness must be put aside before any real progress is made. It may be necessary to wait, even though the patient is in a hazardous situation, until he is prepared to take this first step. Sometimes he takes it only after enforced hospitalization. Sometimes, even while still in the community and still drinking, he accepts the fact that he is an alcoholic and needs outside help. In this case, he may be treated on an outpatient or office basis, but only if he remains sober for sufficient periods so that his problem can be discussed with him. There is no value in the physician's permitting an intoxicated person to lead him into endless discussions of the stresses with which he explains his drinking. The first aim of treatment is to attain and maintain sobriety, for it is only in the sober state that constructive work can be done.

The question then arises—how does the alcoholic reach the point where he recognizes his problem? Some alcoholics refer to a critical instance in their personal lives, such as a chance remark of one of their children, a wife, or an employee, or the threat of a major loss. Suddenly, something appears to bring the alcoholic to the point where, at least momentarily, he sees himself objectively and realizes the magnitude of his predicament. Many alcoholics refer to this experience as "touching bottom" and feel that it is essential to the beginning of sobriety, but no one appears able to bring this about with certainty for the individual alcoholic. It is a peculiarly personal experience.

Many have been helped to take the first step by the sharing of experience with another alcoholic who has attained sobriety. Others have taken it in a hospital where alcoholics are treated. Others have attained it on their own or through the help of a relative or friend. Relatives need the emotional support of the physician during the period they are waiting for this to occur. They must be helped to handle their feelings of guilt because of their powerlessness to help the alcoholic. They need help with their resentment when the alcoholic shifts responsibility for his drinking to stresses in the family, which may be secondary to his drinking. They need to know that reasoning, threats, and punishment are as futile in this as in any chronic illness. Frequently, they must simply wait until the alcoholic is ready himself to seek help unless the situation deteriorates to the point where enforced hospitalization becomes necessary.

Abstinence. The second step in treatment is the acceptance by both physician and alcoholic that the alcoholic can never return to social drinking. The principle that his goal must be one of maintained abstinence has been tested repeatedly and proved true. Each alcoholic would like to think that he is an exception, but when he tests this, sooner or later he finds himself back in the nightmare of uncontrolled drinking. The physician must emphatically maintain the goal of

complete sobriety during treatment and for the rest of the patient's life.

New patterns of living. There is another step that is even more difficult to take—this is the finding of other gratifications and other solutions to life stresses than through the "magic" of taking things by mouth. The alcoholic should not substitute reliance on another chemical to obtain satisfaction, but should find relief for his tension, depression, or anxiety through changes in his pattern of living and his interpersonal situation. This means that use of barbiturates or tranquilizers is not advised except for relief of physiologic symptoms of withdrawal. Long-term reliance on such medications leads to return to alcoholism or the substitution of some other form of drug addiction or drug dependency.

How, then, can the patient be helped to attain and maintain sobriety? There seems to be general agreement that there is little chance of maintained sobriety unless there is some sort of shifting of fundamental values on the part of the alcoholic and an associated reorientation toward himself and others. In some cases, this has been brought about through individual psychotherapy. Much more frequently, it has been brought about through group interaction.

Group therapy. Alcoholics are much more responsive to group than to individual psychotherapy. Many have done well in the type of supportive group situation offered by Alcoholics Anonymous without any traditionally organized group psychotherapy. Usually, help should be offered simultaneously in as many areas as feasible. This may mean support in maintaining sobriety through Alcoholics Anonymous; help with the wife's problems through her association with Al-Anon;* medical help from the family physician; psychotherapy if the aid of a psychiatrist or mental health clinic is available; pastoral help with spiritual problems; or social service help with financial, social, or employment situations.

Alcoholism is a serious, chronic illness. No avenue of approach should be neglected that might help in arresting its course. Even after sobriety has been continued for years, the alcoholic must continue to grow in maturity and in his skill in handling interpersonal problems if he is to maintain his status as an "arrested" alcoholic.

Alcoholics Anonymous. While members of Alcoholics Anonymous do not attempt psychotherapy in a formal sense, they emphasize in their approach to alcoholism many of the basic tenets of psychotherapy. They stress the need for the alcoholic to face realistically his personality assets and liabilities and to admit his responsibility for the direction his life has taken. He must experience a genuine desire for change. Great emphasis is placed on basic integrity and on his need to shift from preoccupation with self to concern for the welfare of others.

Alcoholics Anonymous stresses the need for spiritual guidance. This is formulated in such a way as to be acceptable to people of many faiths and even to those who profess agnosticism. However it is attained, some reorientation in fundamental values appears to be essential to the maintenance of sobriety.

Physician's attitude. If the physician is to be successful in his treatment of alcoholics, he must be aware of his own attitude toward the problem. Few can treat the alcoholic as objectively as they do a patient with chronic heart disease. Many physicians are handicapped by their insecurity over the acceptance of their own drinking habits. Others have not overcome a tendency, inculcated in youth, to look upon the excessive use of alcohol as a moral problem. Still others have an understandable but exaggerated pessimism regarding the constructiveness of what medicine can offer. Any of these attitudes tends to put the alcoholic on guard and interferes with the objectivity necessary for therapeutic effectiveness.

It is helpful to the physician if he can accept the fact that therapeutic effort must be maintained over a long period and that the course may be stormy with relapses into the former drinking pattern. There is no magic drug or procedure. Rather, the physician must help the patient understand his feelings, attitudes, and behavior in order to minimize what is unhealthy and to mobilize the healthy forces in his personality.

SUMMARY AND CONCLUSIONS

Each physician develops his own treatment methods, depending upon his personality and the setting in which he practices. Those who work predominantly in this field tend to stress the value of group psychotherapy and the utilization of all available therapeutic resources. Certainly, it is imperative not to minimize the problem but to assist the patient to a full acceptance of the fact that he is an alcoholic, with all this implies. It is wise to inform each alcoholic patient of the possibility of obtaining help through Alcoholics Anonymous and to give

*Al-Anon family groups are patterned after Alcoholics Anonymous to assist relatives to attain an understanding of alcoholics and of the emotional problems related to living with them.

thought to the pressing needs of the immediate family of the alcoholic.

With sustained effort and a multiple attack on the problem, the number of alcoholics maintaining sobriety has greatly increased in recent years. This has occurred despite the lack of critical studies of etiologic factors and scarcity of follow-up studies to evaluate specific therapeutic approaches. Only adequate research will give us basic knowledge to make major advances in this challenging field.

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Differentiation of fibrocystic disease from tumor is aided by simultaneous palpation of both breasts. Fibrocystic disease is frequently bilateral, with regions of increased nodularity disposed similarly in both breasts. In contrast, tumors are unilateral or, if bilateral, are not located in mirror-image position. Therefore, finding of a unilateral mass demands biopsy.

Current recommended methods of breast palpation do not stress simultaneous palpation. When the physician stands at the side of the supine patient, the hands may not be placed accurately for corresponding sections of the breasts, and amount of pressure on the breast tissue may be different with each hand. When the examiner stands behind the head of the patient, however, any significant difference in content of breast tissue can be determined easily by simultaneous comparison. If carcinoma arises in a region of cystic mastitis, diagnosis may be delayed until after late confirmatory signs appear, regardless of palpation technic used. However, a simple diagram of the regions of bilateral fibrocystic disease and repeated examinations at three-month intervals will reveal any enlargement in the affected region. Biopsy can thus be done at an earlier stage.

Simultaneous palpation should be used in addition to standard methods of breast inspection and lymph node palpation. For such examination, the patient is supine with arms fully abducted and forearms bent at right angles above the head. The examiner stands at the head of the table and gently presses the flattened, adducted fingers of each hand simultaneously on corresponding portions of each breast, palpating breast tissue against the rib cage.

Maneuvers are done in the following order: (1) Hands are placed laterally at the anterior margins of the latissimus dorsi muscles. As the hands are moved medially to the nipple lines, gradual palpation of the breast tissue raises any overlapping portions of the breasts, and tissue can be palpated against the chest wall. (2) Starting at the upper borders of the rectus muscles, the hands are moved superiorly, so that palpation includes the inframammary ridges and subareolar areas. (3) Hands are placed at the medial aspects of both breasts, and palpation progresses laterally toward the areolae. (4) Superior portions of the breasts are palpated, with movement of the hands inferiorly from the clavicles to include the free borders of the pectoralis major muscles and regions above the areolae. (5) The areolae are palpated simultaneously.

S. I. Gumbert: Simultaneous breast palpation. J. Med. 60:3065-3067, 1960.

Report of a Case

Villous Adenoma of the Rectum

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Villous adenomas, or papillomas, comprise between 0.1 and 6.6 per cent of all sigmoid and rectal tumors.[1,2] In the series of 37, 48, and 28 cases of villous tumor of the colon reported by Hines and assoeiates,[3] Sunderland and Binkley,[4] and Bacon and associates,[1] respectively, no mention was made of electrolyte imbalance. Since 1955, 9 eases of villous adenoma of the sigmoid or reetum causing fluid and electrolyte imbalance—hyponatremia, hypoehloremia, hypopotassemia, or a combination of two or more—have been reported in the literature,[2,5–11] and 8 of the cases were successfully treated by restoration of fluid and electrolyte balance and surgical resection; 1 of these had an in situ malignant change within the tumor.[11] One patient, who was treated for an ulcer, died with the villous adenoma going unrecognized until an autopsy was performed.[6]

This is a report of a case of a villous adenoma of the rectum resulting in dehydration, electrolyte imbalanee, aeidosis, extrarenal uremia, and death. The underlying eause was not recognized until after an autopsy was done and a recapitulation of the elinical picture was made.

So few cases have been reported previously that this interesting disease entity is not well known. Perhaps it oeeurs more often than is realized or documented in the literature. To alert us to think of and recognize this uncommon lesion, with its striking clinieal manifestations that are both eorrectible and eurable, is the purpose of this report.

CASE REPORT

S.F.F., a 70-year-old man, was referred to the hospital for treatment of eareinoma of the reetum by his family physieian on Deeember 30, 1959. The patient's ehief symptoms were anorexia, some weight loss, and obstipation for about one month before admission. More recently, he had nothing but watery stools and, when the urge to defecate oecurred, there would be preeipitate urgency.

Family history revealed that his mother had died at the age of 92 and that his father had died of cancer of the stomach at the age of 79. He had 4 brothers and 4 sisters. One sister died of a stroke and another of tuberculosis.

For five or six years, the patient had been troubled with frequency of bowel movements, which was attributed to nervousness. Three years before admission, he had a hemorrhage from the rectum treated with an instrument that "burned it out" and had no further bleeding thereafter.

Physieal examination revealed a thin, chronieally ill, elderly man with a blood pressure of 70/40 mm. Hg and a circular zone of irregularity, induration, and friability palpable reetally at the tip of the examining finger. Laboratory and additional elinical data are presented in the table.

On the day of admission, a sigmoidoscopic biopsy of the reetal tumor was obtained. The sections were reported as showing a classical adenoma of the filiform or fingerlike projeetion type without any evidenee of anaplasia or malignant change. Inasmueh as eareinoma of the reetum was suspeeted, additional tissue for further study was requested. In the meantime, the patient became confused, listless, lethargie, weak, and seriously ill. The intravenous fluids administered were alternate solutions of 5 per eent dextrose in 0.9 per eent normal sodium ehloride solution or 5 per eent dextrose in distilled water with Vicert (soluble B vitamins and vitamin C) and 20 mEq. of potassium ehloride. He had a few mild episodes of nausea, vomiting, and abdominal cramps. Frequent passage of liquid or watery stools containing mucus was reported almost daily in the nurse's notes. A low grade fever developed, and a downhill eourse resulted in death on January 13, 1960.

At autopsy, a soft, broad, flat, fungating tumor measuring 14 by 13 cm. in size was found almost eneireling the reetum. Its peripheral edge was

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	Dec. 31, 1959	*Jan. 5, 1960*	*Jan. 6, 1960*	*Jan. 8, 1960*	*Jan. 9, 1960*	*Jan. 12, 1960*
Serum sodium (mEq. per liter)		123	123	127		125
Serum chlorides (mEq. per liter)		61.6	64.7	61.6	65.8	69.2
Serum potassium (mEq. per liter)		2.6	3.5	3.2		3.9
Carbon-dioxide combining power (mEq. per liter)		19.2	14.6	25	18.4	10.2
Blood urea nitrogen (mg. per cent)		208	238	216	260	329
Fluid intake (cc.)	3,600	3,150	3,100	1,100	2,000	3,000
Urinary output (cc.)	500	450	1,150	1,025	500	450
Rectal discharges (cc.)			Not quantitated			
Hemoglobin (gm. per cent)	15.8	15.4	13			
Hematocrit	46	42				
White blood cell count (cu. mm.)	13,650		Normal differential			
Serum protein (gm. per cent)	7.4		Albumin-globulin ratio = 0.94 to 1			
Urinalysis			Negative; specific gravity, 1.033			
Serology			Negative			

raised, rounded, and well demarcated from the adjacent tissue. Microscopically, the lesion had the appearance of a villous papilloma without any malignant change (figure 1). Lung sections revealed a purulent bronchitis, some interstitial fibrosis, and focal areas of bronchopneumonia. Heart, kidneys (figure 2), pancreas, liver, spleen, adrenals, and prostate were histologically normal except for changes thought to be consistent with uremia.

DISCUSSION

One of the most unusual and uncommon causes of dehydration and electrolyte imbalance—hyponatremia, hypochloremia, hypopotassemia, or a combination of two or more—associated with acidosis and extrarenal uremia which may lead to death is a villous adenoma of the colon or rectum. The presenting clinical finding and diagnostic clue is a frequent rectal discharge of large amounts of mucus. Because of its liquid character or the mucus' mixing with the stool, the discharge may be mistaken for ordinary diarrhea. Therefore, it is important that stools of a patient with diarrhea be inspected personally if a reversible state of ill health such as this is to be recognized, especially since the tumor may be missed by digital examination because of its soft texture.

This entity usually occurs in the older patient.[5] In adding the present case to the 9 previously reported, the average age comes to 66 years. Other symptoms are those associated with fluid and electrolyte deficiencies and with tumors of the colon or rectum. That foci of carcinoma in situ or invasive carcinoma are commonly found in this tumor is well documented in the literature.[1,4,7,8,11–13]

These tumors are capable of secreting per day up to 3 liters of mucus containing relatively large amounts of chlorides, sodium, and potassium.[2,7,8,10,11] When associated with a decrease in dietary intake, vomiting, and a diminished renal function, the metabolic disturbance which develops may become very severe. Consequently, the lost fluid and electrolytes must be restored, and appropriate maintenance therapy for both the continuing loss and daily requirements of fluid volume and electrolytes must be given. The use of 5 per cent hypertonic sodium chloride solution is usually necessary,[8] and up to as much as 160 mEq. of potassium chloride intravenously daily may be necessary.[7] Inadequate replacement and maintenance therapy may result in death of the patient. As soon as the condition of the patient becomes stabilized, surgical excision or resection of the lesion does not appear to pose any problem.

ADDENDUM

Since this paper was submitted for publication, Findlay and O'Connor[14] have reported their experience with a villous adenoma of the large intestine with fluid and electrolyte depletion. They also refer to several other reports[15–19] on this syndrome, not included in the above bibliography. McKittrick and Wheelock[15] appear to be the first to have recognized the fact that these tumors could produce such a syndrome; that following correction of dehydration and electrolyte imbalance, surgical removal usually by resection of the rectum was the only satisfactory treatment

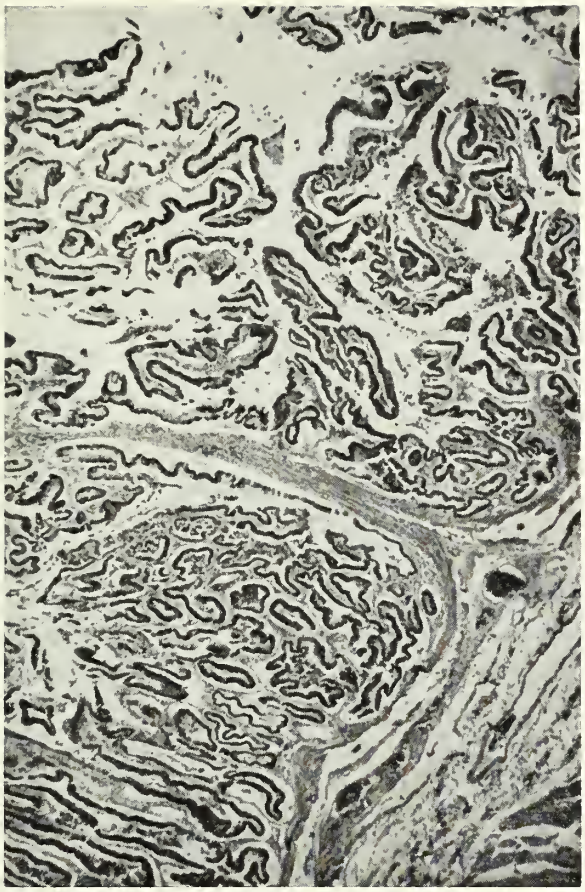

Fig. 1. Section of villous adenoma showing its branching and papillomatous nature; no evidence of malignancy.

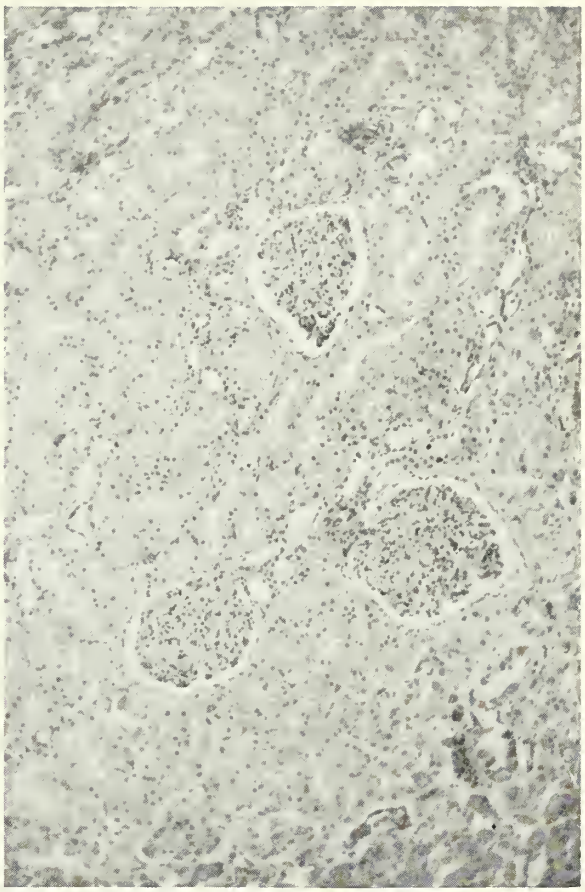

Fig. 2. Photomicrograph of kidney showing normal architecture histologically.

for both the prevention of carcinoma and any further serious fluid and electrolyte loss. Documentation in the literature of the fluid and electrolyte loss syndrome associated with villous adenoma of the large bowel will now reach a total of 18 cases, 3 of which have resulted in a fatality. The possibility that this disease entity may very well have been the cause of unexplained deaths in other instances in the past is well to bear in mind.

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Neurologic Aspects of Endocrine Disorders

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Manifestations from the nervous system as part of an endocrine disease may often become of great diagnostic importance. This is particularly true in the cases where neurologic symptomatology predominates at the early stage of the illness. Informations in regard to the above subject are very scanty in the literature and often omitted in regular textbooks. The report to follow is an attempt to review the material available and present the most important neurologic syndromes associated with endocrine disorders.

DISEASES OF THE THYROID GLAND

Hyperthyroidism

Neurologic syndromes in hyperthyroidism were described in the early literature almost a century ago and were reviewed by Sattler in 1908 in his classic monograph on Basedow's disease. The more recent literature has included the following neurologic and neuromuscular complications associated with hyperfunction of the thyroid gland:

Thyrotoxic myopathy, acute and chronic

Myasthenic syndrome in thyrotoxicosis

Periodic paralysis in thyrotoxicosis

Endocrine ophthalmoplegia

Optic nerve lesions and retinopathy

Thyrotoxic neurologic syndromes—thyrotoxic crisis, thyrotoxic encephalomyopathy, upper motor neuron syndromes, thyrotoxic electrocortical dysrhythmia and seizures, thyrotoxic tremor and chorea, and Parkinsonism in thyrotoxicosis

Thyrotoxic psychosis and psychoneurotic states

Thyrotoxic myopathy. Acute thyrotoxic myopathy is a rare complication of hyperthyroidism characterized by rapidly progressing muscular weakness, which often includes bulbar muscles. The patient may succumb from respiratory insufficiency. Objective sensory changes are absent, although pain and paresthesia may occur. Deep tendon reflexes are depressed, sphincters are intact, and muscle wasting is seen if symptoms persist. Improvement is usually striking after restoration to the euthyroid state. Encephalitic signs sometimes may accompany the paralysis.

Chronic thyrotoxic myopathy is the most common muscular disturbance associated with hyperthyroidism. It is manifested by progressive weakness more pronounced in the proximal muscles of the extremities. Associated symmetric muscular atrophy, involving primarily the shoulder and pelvic girdles, is common. Occasionally, severe atrophies of small muscles of the hands and fasciculations mimic progressive muscular atrophy. Deep tendon reflexes are normal, depressed, or show a quick but weak muscle contraction and relaxation.

The mechanism of muscle dysfunction is speculative, although electromyographic data suggest that the myoneural junction is the site at which alteration of neuromuscular function occurs. A number of biochemical defects have been suggested, including deficient reconversion of lactic acid to glycogen in the muscle after contraction and a defect in the ability of muscle to retain and store creatine. Although the pathogenesis of weakness is obscure, it is agreed that it is a direct effect of thyroxin and is promptly relieved by antithyroid therapy.

Myasthenic syndrome in thyrotoxicosis. Association of thyrotoxicosis and myasthenia gravis in the same patient is frequent enough to be outside of the statistical possibility of a chance occurrence. There is no general agreement as to whether the appearance of myasthenia and hyperthyroidism are closely related or coexist. The myasthenic paralysis is usually more noticeable in the eye muscles, although bulbar and peripheral musculature may be involved. The diagnosis should be supported by positive responses to neostigmine and other pharmacologic tests for myasthenia.

Although the progress of myasthenia common-

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ly parallels that of thyrotoxicosis, a physiologic antagonism between the two conditions has been described. According to these observations, myasthenia becomes worse as hyperthyroidism is subsiding and cessation of antithyroid therapy improves the myasthenic symptoms. Treatment in such cases is aimed at both myasthenia and hyperthyroidism, with the conventional measures available for these diseases. It is generally advised that, in the presence of advanced bulbar myasthenia, treatment of hyperthyroidism be instituted cautiously.

Hyperthyroidism and periodic paralysis. Several reports of simultaneous occurrence of periodic paralysis and thyrotoxicosis have been published since Shinosaki made his original observation in 1926. The attacks of paralysis are similar to those of familial periodic paralysis associated with low serum potassium. Evidence today indicates that hyperthyroidism and familial periodic paralysis are somehow linked, since the association of the two is more frequent than would occur by pure chance. Successful therapy of hyperthyroidism usually relieves or greatly improves the associated periodic paralysis.

Endocrine opthalmoplegia. Although impairment of ocular motility may be present in as many as 20 per cent of patients with hyperthyroidism, opthalmoplegia of significant degree is not as common. The degree of paralysis usually parallels that of exophthalmos; however, it is not uncommon for severe exophthalmos to occur without ophthalmoplegia, or extreme degrees of ophthalmoplegia with no demonstrable exophthalmos. A distinction is made between the ophthalmoplegia associated with malignant exophthalmos and that accompanying ordinary thyrotoxicosis. The usual mildness of systemic signs of hyperthyroidism with malignant exophthalmos, together with the fact that the associated ophthalmoplegia frequently is aggravated by relief of hyperthyroidism, has led authors to consider this syndrome as a separate type of thyrotoxicosis. The extraocular palsies may include any of the eye muscles individually or in unilateral or bilateral groups, although the elevators of the eyeball are more frequently involved. The underlying mechanism leading to ophthalmoplegia is not well understood. The exophthalmos per se is probably not the answer.

Optic nerve lesions and retinopathy. Papilledema with secondary optic atrophy or retrobulbar neuritis is a common complication in cases of progressive malignant exophthalmos and only rarely is seen in ordinary types of thyrotoxicosis. Retinal hemorrhages and exudates are also part of the picture in cases of severe exophthalmos.

Thyrotoxic neurologic syndromes. The most serious central nervous system complication is that of thyrotoxic crisis and coma developing when the patient can no longer adjust to the strain imposed by thyrotoxicosis. Infections, trauma, surgery, manipulations of the thyroid gland, withdrawal of iodine, and so on, are among the most common precipitating factors. The crisis is manifested by extreme tachycardia, hyperpyrexia, vomiting, diarrhea, and, occasionally, jaundice. Auricular fibrillation and congestive heart failure are not uncommon. The patient's mental condition may be either one of hyperirritability, confusion, and delirium or one of extreme prostration and mental apathy. Unless treated, the prognosis is extremely poor, with progressive stupor, coma, and death. Important therapeutic measures include control of hyperpyrexia, relief of anoxia, and use of iodine, propylthiouracil, and cortisone. Pathologic studies have failed to reveal any distinctive changes in the central nervous system.

Acute thyrotoxic encephalomyopathy is a form of thyrotoxic crisis in which neurologic and muscular manifestations predominate. Paralysis of bulbar muscles, especially pharyngeal, extreme muscular weakness, choreiform movements, confusional states, aphasic and apractic manifestations, and other focal neurologic signs may be present.

On rare occasions, hyperthyroidism may be associated with diffuse pyramidal tract signs. In the cases reported to date, complete reversal to the normal state was claimed upon relief of thyrotoxicosis.

True epileptic seizures in thyrotoxicosis have been described in the older literature, although it is hard to ascertain the cause-effect relationship between the two conditions. More recently, electroencephalographic abnormalities were reported in a significant number of cases in the form of paroxysmal spike discharge and slowing, generalized slow wave activity, or fast wave rhythms. After therapy of hyperthyroidism, such electrical changes usually subside. It appears that, since thyrotoxicosis can produce electrical dysrhythmia often assuming paroxysmal character, it is probably capable of precipitating a clinical seizure, at least in the presence of a preexisting irritative focus.

Tremor is the most constant and characteristic sign of thyrotoxicosis. Although more prominent in the fingers when arms are extended forward, it is actually a tremor of the entire arm and it is usually not intensified with voluntary movements. The oscillations are rapid, uniform, and of small amplitude. In severe cases, the tremor

may extend over the entire body and interfere with standing or walking. Choreiform movements are rare but have been reported. A number of cases with both parkinsonism and hyperthyroidism have been reported, the diseases occasionally developing during or soon after acute encephalitis. There is no evidence today for any direct relationship between parkinsonism and hyperthyroidism.

Thyrotoxic psychosis and psychoneurotic states. Nervousness, irritability, and mood changes are common and were described as early as 1840 by Basedow. Manic-depressive psychosis and, occasionally, a schizophrenic picture have been described. Older patients are more likely to develop depression, whereas younger patients commonly manifest manic symptoms.

Hypothyroidism

Hypothyroidism may be associated with central and peripheral nervous system manifestations. Muscular complications have recently been added. The following are the clinical syndromes described to date:

- Cretinism
- Organic mental deterioration and psychosis in myxedema
- Hypothyroid coma
- Hypothyroid ataxia
- Hypothyroid peripheral and cranial neuropathy
- Pseudomyotonia, myotonia, and muscle hypertrophy in myxedema

Cretinism. This condition results from thyroid deficiency developing during fetal life or early in infancy. Retardation of mental and physical development is the most striking manifestation, becoming apparent before the age of 6 months if thyroid function is completely absent. In partial cretinism, the symptoms may not appear until the age of 6 months or later. Early treatment is essential, although normal mental development is rarely achieved in severe cretinism, even with the earliest possible treatment. When hypothyroidism is acquired later in childhood, mental development is disturbed very little.

Organic mental deterioration and psychosis. Mental sluggishness, memory impairment, personality changes, lethargy, and slow speech are often prominent features in adult myxedema. Severe organic dementia is less common. In a few cases, overt psychiatric illness may range from anxiety to depression to extreme manic and schizophrenic behavior. The electroencephalogram in such patients may reveal slow alpha rhythm and diffuse slow wave activity of low amplitude. Remarkable improvement in the mental and psychiatric symptoms can be expected with restoration to the euthyroid state.

Hypothyroid coma. In severe untreated myxedema, progressive mental impairment with periods of irritability and even convulsions may lead to stupor and fatal coma, with characteristic hypothermia, hypotension, and bradycardia. The electroencephalogram in such cases reveals a greatly reduced electrical activity, which improves if a euthyroid state is attained.

Although the pathogenesis of myxedema coma is not well understood, it most likely represents an extreme depression of oxidative metabolism in the brain. Thyroxin apparently serves as a coenzyme in the oxidative enzyme system. Adrenocortical failure may play some role in the production of myxedema coma, which resembles the coma occurring with hypopituitarism.

Hypothyroid ataxia. Disturbed coordination in the form of unsteady gait and slow, clumsy movement of the hands may be associated with myxedema. It is not yet established whether these signs represent true ataxia or are due to associated asthenia and psychomotor retardation. There are no available reports to suggest cerebellar pathology.

Hypothyroid peripheral and cranial neuropathy. Impairment of peripheral nerve function is quite frequent and well documented in myxedema. Sensory neuritis is more common and is manifested by acroparesthesias and, in some cases, by objective sensory loss. Vibration sense tends to disappear before other modalities are impaired. Although subjective weakness is a frequent complaint, true paresis is rather uncommon. The picture is that of a mixed symmetric polyneuritis. The neuropathy is, as a rule, reversible by adequate thyroid therapy.

Impairment of cranial nerve function is not uncommon in myxedema. Decreased hearing, often with associated tinnitus and, less commonly, with true vertigo, may be among the early symptoms. Optic nerve atrophy, sometimes associated with bitemporal hemianopsia, is mentioned in the older literature and is attributed to pressure exerted upon the chiasm by the hypertrophic hypophysis that may accompany hypothyroidism. Retrobulbar neuritis and papillitis are rare complications, although nonspecific complaints of decreased vision are fairly common. Taste and smell may be significantly decreased, and atypical facial neuralgia has been reported. Changes in phonation in the form of husky, low-pitched, slow speech are common and are attributed to the soft tissue changes in vocal cords and tongue.

Pseudomyotonia, myotonia and muscle hyper-

trophy. The majority of patients with myxedema will show a delay in the relaxation of muscles when the deep tendon reflexes are elicited. This phenomenon, termed pseudomyotonia, is one of the most reliable diagnostic signs in hypothyroidism. It is ascribed to an abnormality in the contractile substance of the muscle fiber.

Occasionally, myxedema is accompanied by muscle hypertrophy and slow muscular relaxation after voluntary contraction. This type of myotonia, unlike myotonia congenita, does not decrease by exercise and does not give the characteristic electromyographic changes. The condition is often referred to as Hoffman's syndrome and, if muscular hypertrophy is the prominent feature, as Debré-Semelaigne syndrome. The latter is seen primarily in children.

Cerebral spinal fluid in myxedema. A characteristic increase in spinal fluid protein, usually around 100 mg. per cent, is seen in half the patients with myxedema. Although such a rise in protein can be seen irrespective of the neurologic syndrome, it is more common in patients with diffuse cerebral manifestations. On rare occasions, the cell count may be slightly increased and spinal fluid pressure moderately elevated. With thyroid therapy there is rapid reversal of the abnormal spinal fluid changes to normal.

DISEASES OF THE ADRENAL GLAND

The principal adrenocorticoid secretion important in neurologic symptomatology includes the C_{21} steroids, which include the glucocorticoids (hydrocortisone and cortisone), and the mineralocorticoids (corticosterone and aldosterone). The glucocorticoids induce glycogen storage, promote gluconeogenesis and protein catabolism, and exert a protective action against the effects of injury. The mineralocorticoids act at the renal tubule by increasing the reabsorption of sodium and chloride and decreasing the reabsorption of potassium. Both the gluco- and mineralocorticoids exert other effects on the total body economy which are not discussed here.

The adrenal medulla forms part of the sympathetic system and secretes adrenalin and noradrenalin. These hormones have effects similar to those produced by stimulation of the sympathetic nervous system.

Acute adrenal cortical failure

Acute adrenal insufficiency results from acute exacerbation of Addison's disease or severe destructive lesions of the adrenals. Adrenocortical failure manifested during periods of stress in patients chronically treated with ACTH or cortisone may also be included.

The acute crisis is heralded by muscular weakness that increases rapidly until the slightest effort becomes impossible. Restlessness and headache are often accompanying symptoms. Vomiting, diarrhea, abdominal pain, and peripheral vascular collapse are among the principal systemic manifestations. The patient becomes progressively lethargic and finally lapses into coma. Convulsions may occur. The electroencephalogram in such cases may show high-voltage slow activity, which often predominates over the anterior part of the hemispheres.

Chronic adrenal cortical insufficiency—Addison's disease

The onset of chronic adrenocortical failure is usually insidious and the course interrupted by acute episodes of adrenal crisis. Gastrointestinal disturbances, hypotension, diminished cardiac reserve, diminished resistance to infection and stress, and skin pigmentation are some common systemic symptoms. The nervous system complications are either purely organic or primarily psychiatric in nature.

Muscular fatigue and lethargy are early symptoms. Later actual weakness occurs, which may be so marked that the patient cannot lift his head off the pillow. Muscle cramps are common in this stage, as are generalized aches and pains. Episodic manifestations, such as confusion, epileptic seizures, and stupor, are the results of electrolyte disturbance, hypoglycemia, or hypotension, although several cases have been reported with normal blood pressure and chemistries which responded well after correction of the endocrine dysfunction. Electrical abnormalities may be present irrespective of neurologic symptoms in patients with Addison's disease and include generalized slowing, mostly over the posterior part of the hemispheres and occasionally assuming paroxysmal character.

Although the prevailing mood in Addison's disease is one of apathy and depression, the disease may manifest itself by acute excitation, negativism, and paranoid behavior. The incidence of emotional disturbance apparently is high, although the frequency of reactions reaching psychotic proportions is much smaller. The underlying mechanism for such manifestations involves disturbed electrolyte and carbohydrate balances, although in several cases no such disturbances have been found.

Cushing's syndrome

This syndrome is the result of excessive adrenocortical secretion due to tumor or hyperplasia of the adrenal cortex, in which the effects of gly-

cocorticoids predominate. The identical syndrome can be more or less produced by excessive doses of ACTH or cortisone.

Systemic manifestations of the disease include obesity, primarily involving the trunk, due to increase in storage of fat. The "moon face" and "buffalo hump" are characteristic signs. Protein depletion and connective tissue disturbance lead to fragility of skin and blood vessels and osteoporosis. Facial plethora is common. Increased glyconeogenesis leads to decreased carbohydrate tolerance and, occasionally, diabetes. Hypertension and peripheral edema are the results of sodium retention. Hirsutism and increased susceptibility to infections are common.

Neurologic manifestations include progressive weakness and hypotonia due to electrolyte disturbance and associated metabolic deficit in muscle protein. The latter may lead to marked muscle wasting and, in children, may result in cessation of growth and consequent dwarfism. A generalized feeling of illness and lethargy predominate. Some degree of mental disturbance is common, often marking the beginning of the illness. Psychosis may be dominant, simulating the psychotic episodes observed in patients treated with cortisone or ACTH. Persistent headaches, often assuming the malignant form, with associated papilledema may be the result of increased blood pressure. The prognosis in untreated cases is poor, death occurring from hypertension, infection, or extreme psychosis.

Syndromes induced by ACTH and corticosteroid therapy

Prolonged treatment with ACTH or corticosteroids is apt to produce symptoms simulating Cushing's syndrome. A number of peculiar manifestations have been reported, some of which have not been clearly described in cases of true Cushing's disease.

Muscle aching and asthenia, with or without bone and joint pain, may mark the onset of a neuromuscular syndrome. True peripheral neuropathy has been well documented, often associated with trophic changes which are usually the result of a vasculitis in the vasa nervorum as part of a more generalized mesenchymal reaction. This type of neuropathy, observed most often in patients with rheumatoid arthritis treated with cortisone or related compounds, is characterized by pain and paresthesias, followed by paralysis and sensory loss. The involvement begins at the distal part of the extremities, and the evolution of the symptom is usually asymmetric on the two sides. Occasionally, the condition may simulate Guillain-Barré syndrome. Similar types of peripheral manifestations, often associated with a systemic condition simulating lupus erythematosus or periarteritis nodosa, have also been described after withdrawal of steroids.

In addition to these neuropathies, paralytic episodes or persistent weakness may result from associated hypokalemia. A steroid-induced myopathy has recently been reported, verified by electromyography and muscle biopsy. Tetany has occurred in a number of cases during steroid therapy, caused by induction of hypochloremic alkalosis, hypocalcemia, or both.

Central nervous system complications during prolonged steroid therapy include convulsive seizures, psychiatric manifestations, and, occasionally, cerebrovascular disturbances. Convulsions during therapy with cortisone or ACTH have been well documented. The electroencephalogram becomes abnormal and is characterized primarily by slow alpha rhythm, generalized slowing, and, often, paroxysmal activity. Emotional instability, depression, irritability, or true psychosis of the manic-depressive or schizophrenic type may occur. The explanation for the convulsive activity and mental changes is not clear, although hypokalemia and sodium and water retention are held as important factors. In rare instances, cerebrovascular thrombosis has been attributed to steroids because of their hypercoagulative effect on the blood.

Aldosteronism

Primary aldosteronism is the result of an adrenal tumor or hyperplasia of the gland. Secondary aldosteronism is seen in chronic liver diseases, congestive heart failure, Kimmelstiel-Wilson syndrome, and a few other diseases. The deficit is an overproduction of aldosterone, which is the most active endocrine agent in regulating sodium metabolism. Aldosteronism should be suspected in a patient with hypertension and muscular weakness simulating periodic paralysis. Other symptoms include polydipsia, polyuria, nocturia, and diarrhea, especially during periods of muscular weakness. Hypokalemia is the most characteristic electrolyte disturbance. Urinary assays may reveal excretion of over 100 mg. of aldosterone diacetate in a twenty-four hour period, normal being less than 6 mg.

Muscular weakness due to hypokalemia may be present years before overt systemic manifestations occur and may be permanent or intermittent. Signs of tetany may be present when the patient has associated hypochloremic alkalosis. Other neurologic manifestations include severe headaches, especially at onset of illness, and occasional cerebrovascular accidents.

Pheochromocytoma

As the adrenal medulla forms only part of the adrenalin-secreting tissue, its destruction is not followed by significant physiologic disturbances. On the other hand, chromatin tumors of the adrenal medulla will produce profound disturbances in the body metabolism. The cardinal manifestations in pheochromocytoma are due to sustained or paroxysmal hypertension that results from a widespread vasoconstriction in response to an outpouring of noradrenalin and adrenalin. Characteristic neurologic signs occur with the paroxysmal syndrome and include throbbing headaches, often simulating migraine attacks, associated with extreme anxiety and palpitations. Trembling, vertigo, visual blurring, acroparesthesias, and pain in the extremities are usual symptoms. The attacks last for a few minutes to several hours and may occur several times a day. Long-lasting paroxysms give rise to acute hemorrhagic retinopathy and hypertensive encephalopathy. Cerebral hemorrhages may occur during acute attacks.

DISEASES OF THE ANTERIOR PITUITARY GLAND

Six hormones are now recognized as distinct entities of the anterior pituitary secretion. These include (1) the growth hormone; (2) adrenocorticotropin, or ACTH; (3) thyrotropin, or TSH; (4) gonadotropins, including the follicle-stimulating hormone (FSH); (5) the luteinizing, or interstitial cell-stimulating, hormone (ICSH); and (6) luteotropin, or prolactin. Only diseases with important neurologic manifestations will be discussed.

Pituitary gigantism and acromegaly

Excessive secretion of the growth hormone will result in gigantism during early life or acromegaly after adult body growth is completed and is due to an eosinophilic adenoma of the pituitary gland. Beside the well-known bony and soft tissue changes, a number of neurologic manifestations may be present. As a direct effect of the growth hormone upon the tongue and vocal cords, a deep, gruff, poorly articulated voice will result. Muscle mass obviously is increased. However, the muscle strength is not as great as is suggested by the bulk of the muscle. In fact, muscular asthenia is common. Heart failure and cerebrovascular accidents may occur due to the cardiac hypertrophy associated with myocardial ischemia and hypertension.

A number of symptoms result from associated endocrine disturbance. Diabetes mellitus may induce cerebrovascular disease. Cushing's syndrome may result from pituitary tumors of mixed cytology. In rare instances, thyrotoxicosis may develop and result in any of the neurologic complications previously described. The expanding pituitary tumor may cause pressure effects, including headaches, visual field changes, optic atrophy or papilledema, and hypothalamic or posterior pituitary symptoms. Failure of the anterior pituitary gland is a rare complication but can occur when the tumor undergoes degeneration after destroying the rest of the gland. The resulting condition in panhypopituitarism.

Pituitary hyperadrenocorticism

Excessive secretion of the adrenocorticotropic hormone (ACTH) due to basophilic adenomas causes changes indistinguishable from those of Cushing's syndrome of adrenal origin. These tumors rarely become large enough to erode the sella turcica and give a secondary pressure symptom.

Panhypopituitarism

Destruction of the anterior pituitary gland as a result of ischemic necrosis, tumor, or trauma causes functional failure of the glands under pituitary control. Usual endocrine manifestations include hypogonadism and signs of precocious aging, with atrophic skin and loss of hair. Although there is thyroid and adrenocortical insufficiency, the usual expressions of hypothyroidism and hypoadrenocorticism are indefinite, perhaps partly because of residual activity of these dependent glands, which form minimal amounts of hormone without the influence of thyrotropin or ACTH. Common neurologic manifestations are muscular weakness and excessive fatigue associated with marked lethargy. There is a tendency for orthostatic faintness and vertigo, with some mental confusion, especially on fasting. In the later stages, mental apathy, mental confusion, and psychosis are common.

An acute pituitary crisis may be precipitated by an infection or trauma and is heralded by changes in the state of consciousness. The crisis is due primarily to failure of adrenal and thyroid functions. If the adrenal dysfunction predominates, extreme muscular weakness caused by electrolyte disturbance and associated with drowsiness, seizures, and, finally, coma may result. If thyroid failure predominates, the patient gradually deteriorates both mentally and physically, while the body temperature falls below normal levels.

DISEASES OF THE PARATHYROID GLANDS

Both hyper- and hypofunction of the parathyroid glands may cause neurologic manifesta-

tions. Parathyrin plays an important role in the maintenance of normal calcium and phosphorus in the blood and bones, and the activity of the parathyroid glands is affected by changes in the equilibrium of these elements in the body. Sites of action of the hormone are the renal tubule, which inhibits the reabsorption of phosphorus, and probably the bone, which induces release of calcium and phosphorus. Removal of the parathyroid glands results in a rise of serum phosphorus and a fall of serum calcium, which are reversed by administration of the hormone.

Hypoparathyroidism

Primary hypoparathyroidism results from destructive lesions of the glands or their removal by operation. Secondary dysfunction may occur as the result of some other disorder involving calcium metabolism. Pseudohypoparathyroidism is an end organ disease associated with failure of the body to respond to parathyrin. As a result of decrease in parathyroid hormone secretion, there is a decrease in renal phosphorus excretion, a rise in serum phosphorus, and a fall in serum and urinary calcium.

Some systemic manifestations include cortical cataracts and defects in ectodermal structures in the form of malformed and brittle nails, coarse and dry skin, and thinning of hair. Recurrent fungus infection is common.

Most of the neurologic symptoms can be explained on the basis of hypocalcemia. Tetany due to excessive neuromuscular excitability is the cardinal manifestation. Early signs are paresthesias in the limbs and twitching of muscle groups, which give way to tonic spasms most commonly involving the hands and feet. The elbow and wrist are flexed, the thumb abducted to the palm; the metacarpophalangeal joints are flexed and fingers remain straight. The feet assume an equinovarus position. In more extreme cases, tetany is general, with widespread tonic spasm. If latent, tetany can be elicited by various maneuvers, including overbreathing, constriction of the arm to above the systolic blood pressure, tapping over the facial nerve, and so on.

Convulsive seizures, usually general, are not uncommon with hypoparathyroidism. Such seizures are the effects of hypocalcemia, either by direct excitability of the normal cerebral cortex or by decreasing the seizure threshold in a preexisting cortical lesion. The attack may simulate typical grand mal or even petit mal seizures or present a number of unusual features. The latter include attacks which begin or end with carpopedal spasm and present bizarre general convulsive movements with little or no disturbance in the state of consciousness. Sometimes the muscles assume peculiar movements reminiscent of extrapyramidal hyperkinesias.

Sometimes, papilledema and retinal hemorrhages are seen near the disk, leading to the suspicion of neoplasm, especially if seizures are associated. There is no good explanation for this alarming abnormality. However, it is thought to be the result of electrolytic imbalance with resulting cerebral edema and subsides with the administration of Parathormone.

Calcifications about the smaller vessels of the brain, especially basal ganglia, often are visible in skull roentgenograms and do not regress with therapy.

Psychotic manifestations may be seen in hypoparathyroidism, often as an acute schizophrenic reaction that responds to Parathormone therapy. Long-standing hypoparathyroidism may lead to mental deficiency.

Pseudohypoparathyroidism

Pseudohypoparathyroidism is a condition in which the symptomatology and biochemical findings are similar to those of true hypoparathyroidism but the parathyroid glands are normal or hyperplastic and there is no renal defect for the handling of phosphorus. An essential feature for its recognition is the absence of response to Parathormone. The failure of the hormone to induce hyperphosphaturia as it appears in cases of true hypoparathyroidism is characteristic. The disease presumably is due to failure of the renal tubules to respond to normally excreted parathyrin. The condition is transmitted genetically and is associated with certain developmental anomalies, including short, thickset stature; thickening of the calvaria; short, stubby fingers; and short metacarpals. The symptoms and signs include all those of true hypoparathyroidism. Pseudohypoparathyroidism has a higher incidence of mental deficiency than does true hypoparathyroidism.

Hyperparathyroidism

Excess production of parathyrin may result from primary disease of the gland or as a secondary response to certain diseases which lower the serum calcium, namely, rickets, osteomalacia, and chronic renal failure.

Biochemical changes include increased urinary phosphorus with consequent decrease in serum phosphorus. There results a relative undersaturation of the extracellular fluid with respect to calcium phosphate and a rise in serum calcium. Since there is no abnormal renal han-

dling of calcium, the urinary calcium excretion is elevated. The clinical manifestations result from the hypercalcemia and hypocalciuria and include gastrointestinal disturbances with episodes of anorexia, vomiting, diarrhea and nephrolithiasis with progressive renal damage, and demineralization of the bone with cystic bony changes. A number of symptoms and signs are purely neuromuscular and include general weakness, difficulty in swallowing, and loss of muscle tone. These are presumably a reflection of the known effect of hypercalcemia in depressing the electrical sensitivity of ganglia and peripheral nerves. High spinal fluid protein is possible, though infrequent, with hyperparathyroidism.

DISEASES OF THE PANCREAS

Diabetes mellitus

The neurologic complications of diabetes mellitus include a number of syndromes, which will be described under the following categories:

A. Diabetic neuropathies
   1. Symmetric peripheral neuropathy
   2. Asymmetric neuropathy
   3. Polyradiculopathy
   4. Visceral neuropathy
   5. Cranial neuropathy

B. Diabetic myelopathy and amyotrophy
   1. Diabetic pseudotabes and posterolateral syndrome
   2. Anterior neuropathy
   3. Anterolateral syndromes
   4. Acute vascular syndromes with myelomalacia

C. Diabetic cerebral syndromes
   1. Cerebrovascular accidents and diffuse vascular disease
   2. Diabetic coma

Although diabetic neuropathy has been recognized for a long time, there is still no adequate knowledge of the role of diabetes in its production. It is apparent from recent reviews of the literature that poor diabetic control is not a prerequisite for the development of diabetic neuropathy. The disease may develop during good diabetic control, may appear simultaneously with the onset of diabetes, or may occur in the prediabetic state. In rare cases, it may appear until diabetic control is established. Diabetic neuropathy usually assumes two distinct forms—the classic symmetric distal sensorimotor neuropathy or the predominantly motor asymmetric neuropathy or radiculopathy. Associated manifestations from the spinal cord often may accompany the neuritic involvement.

Symmetric peripheral neuropathy. This type of neuropathy is insidious in onset, is characterized primarily by sensory manifestations and by dull aching pain confined to the legs. It is usually seen with long-standing, poorly controlled diabetes. Paresthesias in the distal part of the extremities, generally the feet, usually accompany the pain. Objective sensory changes involve all sensory modalities in a stocking-and-glove distribution but may be absent, even with the most distressing diabetic causalgias. Motor deficit follows as damage progresses, although there may be complete sensory loss without paralysis. Trophic changes may appear in long-standing cases. Visceral neuritis with painless bladder distention and nocturnal diarrhea may develop in extreme cases.

Asymmetric neuropathy. This type of involvement may take the form of mononeuritis, mononeuritis multiplex, or radiculitis and is most commonly seen with early diabetes or in the prediabetic state. Onset is usually sudden and painful, with subsequent paresis and muscle wasting in the distribution of the nerves or roots involved. In radicular cases, pain may be the only presenting finding. Femoral and peroneal nerves are most commonly affected.

Polyradiculopathy. This type of involvement resembles the Guillain-Barré syndrome. The proximal segments of the extremities are extremely painful, and sensory disturbances, paresis, and loss of sphincter control are present.

Visceral neuropathy. Such neuritis is usually seen with acute diabetes and may appear alone or may accompany ordinary diabetic neuropathy. Symptoms include intermittent nocturnal diarrhea, incontinence, delayed emptying of the stomach, orthostatic hypotension, peripheral vasomotor changes, and so on.

Cranial neuropathy. This is relatively rare in diabetes and most commonly includes ocular nerve palsies, pupillary abnormalities, trigeminal neuralgia, and facial nerve involvement. Pupillary changes often simulate typical Argyll Robertson pupils. Optic atrophy and nerve deafness associated with diabetes recently have been described.

The pathogenesis of diabetic neuropathy is far from clear, despite the voluminous literature on the subject. There has been increasing awareness that diabetes is a complex systemic disease process of which the carbohydrate metabolic disorder is a single facet. Some authors considered the basic problem as a manifestation of an abiotrophy affecting the insulin-producing tissues and vascular system. Specific vascular changes were described in diabetic patients and included a microangiopathy that affected primarily the retinal and renal vessels. More re-

cently, a similar type of angiopathy was reported in the vasa nervorum in the form of luminal constriction due to medial deposits of material that stained like mucopolysaccharides.

It has been suggested that diabetic neuropathy is the result of a number of factors, among which is an operative toxic or metabolic deficit independent of the severity of the diabetic state. In contrast to this toxic-metabolic theory for the neuropathy, proponents of a vascular theory maintain that the basic mechanism lies in the interruption of the blood supply to the nerves as the result of an angiopathy. In support of this theory are recently reported specific changes in the vasa nervorum simulating retinal or renal angiopathy, increased incidence of neuropathy in the age group over 40, frequent association of vascular disease and diabetic neuropathy, and over-all high frequency of vascular disease and diabetes. The proponents of the toxic-metabolic theory emphasize that neuropathy is relatively rare in diabetic patients with acute and advanced obliterated arteriosclerosis, that it may occur in patients with no evidence of vascular involvement, and that it not uncommonly will clear in time, which is contrary to the process of ischemic neuritis. The theory was recently advanced that only the symmetric neuropathy seen with long-standing diabetes is related to a long-continued deficit in metabolism. However, the totally dissimilar asymmetric neuropathy is probably the result of an angiopathy in the nerve per se.

Diabetic myelopathy and amyotrophy. Involvement of the spinal cord often is associated with diabetic neuropathy. Posterior column degeneration occurs, as well as involvement of the dorsal roots. A specific syndrome termed diabetic pseudotabes closely simulates tabes dorsalis. Deep tendon reflexes are absent in the legs, proprioception is poor, and lightning pains are frequent. Argyll Robertson pupils and Charcot joints add to the confusion with syphilitic tabes. In contrast to the latter, however, muscle tenderness is normal and vesicle function usually is intact. Posterolateral syndrome due to degeneration of the pyramidal tracts and posterior columns may mimic subacute combined degeneration of the cord.

Flaccid paralysis associated with degeneration of the anterior roots and horn cells sometimes may accompany degeneration of the peripheral nerves and simulate progressive muscular atrophy. An anterolateral syndrome that may include bulbar paralysis simulating amyotrophic lateral sclerosis also has been described with diabetes mellitus. Pain and other sensory changes may be associated. Acute vascular syndromes due to vascular occlusions may cause extensive cord changes and acute deficit. Such pathology is not specific to diabetes and results from arteriosclerosis accelerated by the diabetic process.

Diabetic cerebral syndromes. Cerebral manifestations in diabetes mellitus include acute and chronic syndromes secondary to ischemia, thrombosis, and hemorrhages as a result of arteriosclerosis accelaterated by the diabetic state.

Ketoacidosis with coma is the most serious complication in the course of uncontrolled diabetes and is due to an increase in fat catabolism and an accumulation of ketone bodies far in excess of that which the body can handle. Coma without ketosis rarely is seen and probably is due to hepatocellular failure. Increasing weakness, dull headache, and hyperpnea are the common presenting signs. Kussmaul-Kien respiration follows, along with nausea and vomiting, with subsequent coma. The patient becomes dehydrated, pulse is rapid and feeble, and blood pressure drops. Anuria and peripheral circulatory collapse occur later.

Hyperinsulinism

Lesions of the pancreatic islet tissue capable of producing hypersecretion of insulin include adenoma, carcinoma, and hyperplasia of the pancreatic islet cells. The first condition is the most common cause of hyperinsulinism. The so-called idopathic hypoglycemia of infants and children probably is due to deficient formation of the hyperglycemic factor of the pancreatic islands. Beside pancreatic hypoglycemia, hypoglycemic states may result from pituitary or adrenocortical hypofunction or chronic liver disorders or may occur in von Gierke's disease. Finally, hypoglycemia may be associated with myxedema or may follow gastrectomy. Hypoglycemia with no anatomic lesion is due to functional-autonomic imbalance, which follows a meal especially high in carbohydrates. Symptoms are never extreme and consist of dizziness, faintness, sweating, and trembling.

The symptoms of hyperinsulinism appear after long fasting, characteristically before breakfast, and after long exertion. The patient usually has mild attacks for years before the disease shows a progressive course. However, some patients fall into deep coma shortly after the appearance of the first symptoms. Essentially, the clinical manifestations of hyperinsulinism are (1) episodic manifestations, (2) manifestations of a permanent deficit, and (3) hyperinsulinism neuropathy.

Episodic manifestations are most common and

most characteristic. In the early phases, mild attacks include signs of sympathetic excitability, with sweating, flushing, pallor, nausea, chilliness, hunger, epigastric pain, dizziness, increased blood pressure, cardiac palpitations, and syncope. Most acute attacks are characterized by episodes of confused behavior, slurring of speech, blurring of vision, diplopia, tingling around the mouth, and intense sweating. As the attacks become more frequent, extreme confusion, inappropriate laughing and crying, hallucinatory states, mania, and other psychiatric conditions are seen. In this stage, numerous focal neurologic disturbances, including aphasia, hemiparesis, incoordination, and so on, may occur. As the attack progresses, stupor and finally coma supervene. Convulsions of a major motor type also are common and may be the most important part of the attack.

Although the symptoms may be acute at the onset, it is more common for mild episodes to occur for months or even years before an attack of sufficient severity results in loss of consciousness. As the disease progresses, the episodes of coma become more prolonged, until the hypoglycemic attack leaves the patient in a state of decerebrate rigidity.

Epileptic seizures may be part of a multisymptomatic episode or may be the only manifestation. Onset of the seizures may occur early or several years after the first symptoms of hypoglycemia. Careful history will disclose the characteristic preictal apprehension, feeling of hunger, paresthesia, sweating, and even faintness.

The pathogenesis of these manifestations in hyperinsulinism involves a number of physiologic and biochemical mechanisms, not all of which are well understood. The most important are liberation of epinephrine and deficiency of cerebral oxidative metabolism as a result of the failure of the normal supply of glucose to be oxidized. Hypokalemia may play an occasional role. Disturbance of acetylcholine synthesis also has been postulated.

Episodes of focal central nervous system deficit simulating strokes were described as part of hypoglycemic attacks in adenomas of the islets of pancreas, as well as in other types of hypoglycemia. It was postulated that, in the presence of a relative area of cerebral ischemia due to arteriosclerosis, hypoglycemia may induce a localized reversible paralysis of neuronal function as the result of temporary decrease of metabolic supply.

Manifestations of permanent deficit. Although the hypoglycemic syndrome in hyperinsulinism almost always is episodic, a permanent deficit may be seen either as an acute fixed lesion or as the result of accumulating residual anatomic damage.

Prolonged attacks of hypoglycemia result in a variety of focal neurologic syndromes, such as hemiplegia, bilateral pyramidal tract syndromes, aphasia, hemiparesis, and incoordination, which may be due either to acute tissue softening or hemorrhages. Chronic progressive central nervous system syndromes include the progressive type of encephalopathy and myelopathy. The former usually is manifested by progressive organic dementia and variable focal signs of deficit. The myelopathies, generally in the form of progressive muscular atrophy from degeneration of anterior horn cells, usually are associated with involvement of anterior roots and peripheral nerves, commonly referred to as hyperinsulinism neuropathy.

Hyperinsulinism neuropathy. Peripheral nervous system manifestations may occur with hyperinsulinism as well as with other conditions with prolonged hypoglycemia. Because of the more dramatic cerebral symptoms of hypoglycemia, the peripheral manifestations are often ignored by the patient and the physician. Paresthesias over distal parts of both upper and lower extremities are usually the earliest symptoms, followed by muscular weakness and atrophy. Sensory changes are infrequent. Progressive muscular weakness and atrophy of the small muscles of the hands and feet with no apparent subjective or objective sensory changes may occur and closely simulate progressive muscular atrophy. Muscle fasciculations in such patients are not always present, although fibrillation potentials are seen commonly on electromyographic studies.

The peripheral nervous system syndromes of hyperinsulinism usually follow prolonged acute attacks of hypoglycemia and are reminiscent of the muscular weakness, paresthesias, and atrophy described in patients after injection of excessive amounts of insulin in the treatment of psychiatric illnesses. Removal of the pancreatic adenoma usually will arrest and improve the condition, although definite reversal to the normal state is not always successful. Although there has been some debate in regard to the role of hypoglycemia per se in inducing these peripheral manifestations, apparently, in most patients described, symptoms and signs began during acute episodes of hypoglycemia in the presence of hyperfunctioning adenomas of the pancreas, the removal of which arrested progress of the atrophy and paresthesias.

Present Status of the North Dakota State Medical Center

T. H. HARWOOD, M.D.

Grand Forks, North Dakota

The North Dakota State Medical Center was created in 1945 and provided with funds for its operation by legislative action in 1948. The mill levy, a tax on real and personal property, is earmarked for the Medical Center and brings in, at the present time, approximately $650,000 each year.

The Medical Center Law is very broad, deliberately designed so that its program might be adapted to changing needs and situations. It is under the administrative control of the University of North Dakota and the State Board of Higher Education. There is a Medical Center Advisory Council "to correlate health and welfare programs in the state." This council meets semi-annually and advises, consults, and makes recommendations to the administration. On this board are representatives of the Board of Administration, the Public Welfare Board, the Board of Higher Education, the State Health Officer, the state medical society, and the state hospital association and 3 members appointed by the Governor. The stated intent of the law encompasses the following:

1. The complete training of physicians
2. The training of nurses and public health nurses
3. The training of all other personnel concerned with the health of the people
4. The establishment of facilities for the care, treatment, and hospitalization of indigent and other patients
5. The fullest use, at a fee, of the Medical Center facilities by all agencies concerned with health and welfare of the people of the state to provide for the care of the indigent, those suffering from communicable disease, and those eligible for physical and vocational rehabilitation
6. The acceptance of gifts and matching funds
7. The "correlation, coordination, and extension of all facilities that pertain to the health and welfare of the people of the State of North Dakota and its political subdivisions."

It has therefore been the responsibility of the Medical Center to plan a program that will best carry out as many of the purposes of the law, insofar as the funds permit, as to best meet the needs of the people.

SERVICES PROVIDED BY THE CENTER

It was early evident that the funds of the mill levy were not adequate to support a four-year medical school, the minimum cost of which, at present, is about $1 million a year. We have therefore developed a high-grade two-year school. Our North Dakota residents are, of course, given first preference for admission, although nearly every year, from 4 to 6 places are filled with students from out of state. Our graduates transfer and do well after transfer. Each year, from 2 to 4 of our class of 36 are honored by election to AOA, the national honorary medical society.

The wisdom of this decision has been borne out by the recent trend of establishing more two-year schools, the graduates of which can help fill the 700 open places in the upper two years of our present four-year schools. The bottleneck in medical education is at the basic science level.

The program of training of medical technologists was established and has grown steadily, until we have now about 20 graduates each year.

A four-year degree program in nursing was established and is now being strengthened so that it may meet the standards of the accrediting agencies.

The North Dakota State Blood Bank, supported jointly by the State Health Department and the Medical Center, has been serving the state by providing community blood typing (the so-called "walking blood banks"), Rh typing, and antibody titration for the whole state.

We provide housing services without cost to the North Dakota State Health Laboratories serving the eastern half of the state.

We have developed a program of graduate education in the medical sciences which now numbers 22 students. The graduate program in

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anatomy is the only program in the country supported by funds from the National Defense Act. Dr. C. J. Hamre, professor and head of the anatomy department, is also Dean of the Graduate School.

A research program has developed in the fields of anatomy, bacteriology, biochemistry, physiology, and pharmacology that has brought well over $1 million of outside funds into the state. This money is used to employ technical assistants and to buy equipment and supplies; thus it is a positive addition to the economy of the state. No taxpayer's money is used for research. Two of our staff hold advisory positions at the national level, serving on boards which approve research grant requests made by other institutions. Dr. Hamre serves on the American Cancer Society Board and Dr. Cornatzer, on the board of the National Science Foundation.

Our pathology department staff provides free pathology services to all the institutions of the state. They have, for the past three years, been given the privilege of private practice, being paid only for their teaching.

Three years ago, our biochemistry department, under the direction of Dr. Cornatzer, began performing clinical chemistry examinations for physicians in the state. These tests are largely those not done in local hospitals, such as 17-ketosteroids and protein-bound iodines. This service grew so rapidly that it became necessary to employ 2 extra medical technologists to handle the work, and a charge is now being made to help defray the cost.

Last year we made our first venture in the field of postgraduate medical education, giving a one-day course for the Academy of General Practice. It is obviously not possible to give the usual clinical course, since our faculty is a basic science faculty, but with this start we plan to develop this field further.

SUMMER PROGRAMS

Each summer for the past five years, we have had a program of summer student research fellowships. Under this program, medical students may spend their summer vacations in a research laboratory working on a small project under the supervision of an experienced investigator. The student is given a fellowship of $600 from various outside sources to support him in this summer work. Many of our students could not otherwise afford to engage in this sort of activity. The students learn the basis of the scientific method, and some of them are encouraged to go on in this field as a career. Often, however, the reaction is, "It has been interesting and worthwhile, but I am now convinced that this is not for me. I know I want to practice." This has been a very successful program. There were 22 such medical students taking part in this program in the summer of 1960.

We have not only these students with us in the summer but a variety of others as well. Last summer, we had 2 high school teachers in programs designed to add to their knowledge and thus enable them to become better high school teachers. We also had undergraduate college students doing research work and high school students in a program to give them a taste of science and to enable them to make a better choice of college study. All these groups, with our graduate students, make for a busy summer. Many of our staff find it difficult to find time for a vacation.

Students and teaching still take up the majority of the time and effort of our full-time staff of 23 teachers.

BUILDING

The first two-fifths of our present medical building was built with $500,000 appropriated by the North Dakota State Legislature before mill-levy funds were available. With this as a start, surplus funds accumulated were used to add the central tower and the east end of the medical building. The cost of this was a little over $700,000, with an additional $424,000 for equipment. As our research program grew, we needed more space. We were given $75,000 through the generosity of Mrs. Ireland, which was matched with federal funds, enabling us to build and equip the present Ireland Laboratory for Cancer Research at a total cost of nearly $200,000.

This spring we applied for a federal grant of $528,000 for the construction of 2 more floors on the Ireland Laboratories under a program offering 100 per cent federal funds. We did not receive this grant because of lack of funds, although the project was approved. We plan to make further such applications.

Six years ago, the legislature advised the Medical Center to husband funds, planning for the eventual establishment of a four-year school. Surplus funds were available for some construction. While the possibility of a four-year school lies in the indefinite future, it was felt that it would be one step in that direction to construct a clinical facility on the campus. At one time, a chronic disease hospital was considered, but there is not a shortage of hospital beds in the state. A tuberculosis hospital was actually legislated, but, with the support of the medical soci-

ety, this legislation was reversed. It did not seem wise to build a hospital for tuberculosis when other states were closing down such hospitals for lack of patients. Furthermore, administration of such a facility would have been very difficult, since it would have to have been run by the Board of Administration, although built by and for the Medical Center.

However, the need for a clinical facility did exist. We have no facilities for the proper teaching of physical diagnosis. Our 2 local hospitals are active, busy hospitals, with a rapid turnover, meeting the needs of the community. They were not organized or built as teaching hospitals. It seemed that the construction of a rehabilitation center offering the team approach to disabled patients would provide us with teaching material—not only for medical students but for occupational therapists, nurses, speech therapists, social workers, and clinical psychologists. The North Dakota Division of Vocational Rehabilitation, a division of the Department of Public Instruction and therefore not a part of the Medical Center, had been sending patients to Minnesota and elsewhere for evaluation and therapy which was not available in this state. To meet these needs, a single story outpatient Rehabilitation Center was built in 1957. Two additional floors are presently under construction to provide inpatient facilities. They have funds in their budget for this purpose and, as a matter of fact, have been purchasing such services from us in our facility.

They have funds in their budget for this purpose and, as a matter of fact, have been purchasing such services from us in our facility.

Matching funds were available (46 per cent federal and 54 per cent Medical Center) through the Hill-Burton Hospital Construction Program earmarked for rehabilitation. With the advice of the State Health Planning Committee, the Medical Center Advisory Council, and the Board of Higher Education, an outpatient, 1-story facility was built and opened to patients in January 1958. The total cost was $347,000, of which $187,735 was from Medical Center funds. It is of interest that 12 other medical schools were similarly constructing rehabilitation centers for medical school teaching.

We have been in operation since. The case load grew slowly but leveled off at a point below our capacity. Two major problems existed. This facility was designed to serve the entire state. Patients from outside the local area had no place to stay while here for evaluation or treatment. The local hospitals cooperated, but this was costly. The services available far exceed the need since rehabilitation patients are not acutely ill and need only housing and feeding. Temporary arrangements were made, with the University providing dormitory housing for patients. This was highly unsatisfactory, partly because of the need of the rooms for University students but also because the patients had to travel across the campus, which in winter particularly is difficult and even dangerous for the physically handicapped. We are at present attempting to use motels, and there are many drawbacks to this arrangement, especially with adolescents. Hence the need for inpatient facilities seemed clear. Matching funds were available, and application for such funds was made and approved for the construction of 2 more floors on the present building.

The other lack was, and is, that of a physiatrist—a doctor of physical medicine—to head up the professional program. At present, we are employing 3 local orthopedic men on a consulting basis, but these men are busy practitioners and cannot devote the time necessary to expand the program. The program itself needs a physiatrist. Several physicians throughout the state are reluctant to use the facility until we get such a man.

FINANCES

At present, the program is only 25 per cent self-supporting, whereas most centers, once they become well established, are 60 per cent self-supporting. Most patients are treated under programs of vocational rehabilitation, welfare, or other agencies. Funds are therefore available to pay for the services rendered.

Our students after transfer find that the cost of education is considerably more than it is while they are here. The Post-sophomore Loan Fund established ten years ago by the Women's Auxiliary of this society is extremely valuable, but it is not enough to meet the need. It now totals about $22,000. We can loan only $500 per student per year from the amount available in this fund, and many of our students need $3,000 per year. To help meet this need, the state legislature passed a law in 1957 setting aside $75,000 each year from Medical Center funds to be made available to third and fourth year students, in loans of $2,000 per student per year. This amount may be increased to $2,500 if the student signs an agreement to return to the state to practice. Interest on these loans is 6 per cent, starting from the day the money is received. A forgiveness clause permits a student who returns to a town of 3,000 or less which is in need of a phy-

sician or an additional physician to have 20 per cent of his loan forgiven each year he is in such practice. Under this provision, the loan becomes a scholarship. We have to date loaned $262,700 under this program, and this last summer (1960), 11 graduates returned to the state to practice—the largest number ever to return at one time; 9 of these are located in small towns.

At this last legislative session, the law was broadened to include loans to dental students and the annual sum available increased to $100,000. The first of these dental student loans will be made this July.

Four years ago, the legislature also passed a psychiatric training bill. This provides a North Dakota physician with a stipend of $4,800 to $6,000 each year for three years of postgraduate training in psychiatry provided that he promises to return to the state for two years after his training to practice psychiatry in a state institution or program. We have 3 such physicians now on this program. The first, Dr. A. F. Samuelson, known to some of you, will return in August 1961 after his period of training at the Menninger School of Psychiatry.

We have, therefore, 5 major items in our budget, each of which, with the exception of the blood bank and rehabilitation, is rising in cost each year. The cost of medical technology, as well as the service courses we offer for nurses, dietitians, and physical education majors, lies in the medical school budget. We are budgeted for a significant increase in medical school salaries for this coming year, since our salary scale must advance as rapidly as that of other schools in the past four years. They are all in competition with us for personnel.

OTHER PROBLEMS

Several matters are of particular interest to the medical profession. First is the recruitment of well-qualified applicants. In common with the rest of the country, we lack a sufficient number of such applicants. If you have promising students in your community, we should be glad to provide you with information or have the student visit us. High school is not too early for a student to begin to prepare himself properly. A sound understanding of mathematics and a facility in English are most important. Also, many desirable students feel that the cost of a medical education is too high for them and exclude this career on this basis. We have this year, for the first time, money for scholarships. A grant of $10,000 will be received this summer from the Avalon Foundation to provide for nonrefundable scholarships for medical students. We plan to make this last for at least four years, making it available on the basis of need.

A recent letter brought another problem to my attention—the constant need for bodies for dissection. We have a small number of bodies willed to us each year by thoughtful people, but it by no means fills the need. We constantly face an insufficient number for teaching. Any body to be buried at public expense when there is no claimant is, by law, available to the medical school. The cooperation of the social agencies, the mortician, and the physician is necessary. We are prepared to defray the cost of embalming and shipping. You will each receive a communication in the near future about this matter, and we ask your serious consideration for help with this problem.

Each spring, students spend the last three weeks in the second year of school with preceptors in various parts of the state on a clinical clerkship. They work in the hospitals, see patients, and prepare themselves for the clinical years. This program has been very successful, thanks to the willingness of the physicians of the state to take on this considerable task. We are grateful to them and to the many hospitals which offer room and board to the student while he is on the clerkship. The introduction the student gets to North Dakota medicine should encourage him to return to the state to practice. North Dakota medicine is good, and the school is pleased that the students can be exposed to it.

Presented at the annual meeting of the North Dakota State Medical Association, May 8, 1961.

Richard M. Hewitt, M.D.

A Scholar-Physician

"And gladly would he learn and gladly teach."
CHAUCER: *Canterbury Tales*: Prologue

THERE WAS A TIME in the great age of the universities when a man who was a physician was also accounted to be a scholar. One of the most notable of these scholar-physicians was Thomas Linacre of England, who, on the one hand, was perfectly capable of founding the Royal College of Physicians in 1518 and, on the other, of turning out a Latin grammar for Princess Mary in 1523. These were the lettered men of medicine who brought the New Learning of the Renaissance to England from Italy, chiefly from "fair Padua, nursery of arts." Because of their vast learning, they came to be known individually as the "universal man" of the Renaissance of whom the prime example was Leonardo da Vinci.

Inevitably, as the lag in the sciences was gradually overcome, the 7 liberal arts represented by the *trivium* and *quadrivium* claimed less and less attention from the physician trained in the universities, and as his preoccupation with the sciences increased, the notion of the scholar-physician languished. Today he is a rare man indeed.

A few such men appear at times, however, and one of them is Dr. Richard M. Hewitt, for almost thirty years a member of the staff of the Mayo Clinic and for many years head of the Section of Publications in that medical center and associate professor of medical literature in the Mayo Foundation, Graduate School, University of Minnesota, until his retirement on October 1, 1957.

Imbued with the classical tradition in learning by exposure to the erudition of notable scholars in Wesleyan University and the Princeton University Graduate School, Dr. Hewitt took the degree in medicine in 1924 from the George Washington University after two years of clinical pathology in the Medical Department of the United States Army in 1917 to 1919.

Doubtless the call of active practice was strong, but the appeal of the printed word was more powerful, since he has always been convinced of the primacy of letters in the advancement of human knowledge. In 1925, therefore, he accepted the appointment of assistant editor of the *Journal of the American Medical Association*, and across his desk in Chicago flowed most of the advances, in manuscript form, of current medicine in America. Much of it, he saw, originally was in indifferent and sometimes execrable literary form, but after it had passed through the editorial department and the hands of Fred Bryant, it became a clear, logical, and useful piece of medical exposition, rescued from obscurantism and cleansed of verbiage.

In 1928, Dr. Hewitt was called to Rochester to become a member of the Section of Publications of the Mayo Clinic, and, in 1933, he became head of that section. The number of papers, chapters, and other medical works which have received his ministrations over the years probably is incalculable; 16 massive volumes of the *Collected Papers of the Mayo Clinic and Mayo Foundation* alone were issued under his direction.

However, the higher learning in medicine peculiar to the Mayo Foundation attracted his devotion from the beginning. He gave lectures in medical writing and presided at seminars in the technic of medical exposition for the benefit of increasing numbers of young men who held fellowships for graduate work in medicine in the Mayo Foundation, and he gladly scheduled consultations and private sessions in the art of communicating scientific ideas for the numbers of young physicians, as well as seasoned members of the staff of the Mayo Clinic, who sought his special knowledge and skill.

Dr. Hewitt was a consultant to the Office of the

Surgeon General, United States Army, in 1943 and 1944, and, in 1941 and 1942, he was a member of the editorial board of *War Medicine*. In 1944, he received the Alumni Achievement Award of the George Washington University for conspicuous achievement in medical journalism, and, in 1954, the American Medical Writers' Association gave him the Distinguished Service Award. In 1955 and 1956, he was president of the American Medical Writers' Association, and, in 1957, his book, *The Physician-Writer's Book*, compounded of the experience and accumulated wisdom of a lifetime in medical composition and literature, was published by the W. B. Saunders Company of Philadelphia. Reception of this practical and instructive work has been generally commendatory.

Remote from his native habitat of Connecticut and deflected, to a degree, from his original objective of a career in academic teaching, Dr. Hewitt has never deviated from his conviction that, just as a scientific result which cannot be reproduced successfully by others is of no great use to scientists, so also a scientific idea, however sound, which is not communicated clearly and effectively to others by way of the written word is of small use to science as a whole.

Fat ingestion does not appear to accelerate blood coagulation in healthy and hemophilic subjects. Results did not differ significantly in various coagulation tests on blood obtained before and three hours after feeding of 114 gm. of fat to 7 healthy subjects, 10 deficient in antihemophilic factor and 6 lacking in plasma thromboplastic component.

J. H. Lewis: Effects of a high fat meal on coagulation in hemophilia. J. Lab. & Clin. Med. 55: 245-249, 1960.

Accelerated destruction of circulating erythrocytes probably is the major cause of anemia in patients with liver disease. Survival half-times were determined for red cells labeled with radiochromium in 32 patients with portal or biliary cirrhosis, hepatitis, or malignant disease of the liver or bile ducts. For 28, values were less than twenty-five days, considered the lower limit of normal. Radioactivity in feces indicated significant alimentary bleeding in only 4 patients, and increased serum bilirubin values were correlated with diminished erythrocyte survival, tending to confirm the primary role of a hemolytic process. Apparent reduction in erythropoietic regenerative tendency as anemia progresses suggests that suppression of bone marrow activity may be a causative factor.

M. J. Cawein III, A. B. Hagedorn, and C. A. Owen, Jr.: Anemia of hepatic disease studied with radiochromium. Gastroenterology 38:324-331, 1960.

Book Reviews . . .

Eye Signs in General Disease

F. HERBERT HAESSLER, M.D., *1960. Springfield, Ill.: Charles C Thomas. 113 pages.*

It is difficult for this reviewer to conceive just what the author had in mind when he wrote *Eye Signs in General Disease.*

In approximately 100 pages, the author provides a collection of "ophthalmic findings of systemic disease which may be encountered in the course of the usual examination of patients." The book is divided into 3 sections, entitled "How to Look," "The Signs," and "Miscellaneous Essays." This book seems to be too sketchy to follow up on any one subject with authority, and, with the absence of any diagrams or pictures, it is difficult to comprehend just what type of sign the patient may evince. A man in general practice or a medical student probably would not have his interest held long enough to absorb some of the good points of the book.

Dr. Haessler's book, *Ophthalmologic Diagnosis,* which came out in 1953, is far superior. Here the author used copious illustrations, consisting of simple line drawings, which aided a great deal in explaining the text.

This book has little value to the practicing opthalmologist and only limited value to any other practitioner. Format, type selection, and layout seem to be very good.

MALCOLM A. MC CANNEL, M.D.
Minneapolis

Demonstration of Physical Signs in Clinical Surgery

HAMILTON BAILEY, *1960. Baltimore: Williams & Wilkins. 868 pages. Illustrated. $14.50.*

This is an expanded edition of an already renowned classic. It is directed primarily to the student and surgical trainee, and for such individuals, it is a graphic presentation of myriads of physical signs valuable in the elucidation of surgical problems. While they will find some material elementary, the practitioner and trained surgeon will still find the book of great value, both as a book to study systematically and a reference to consult. It is also an intriguing book to pick up for short periods of browsing. One can open the book anywhere, idly leaf through a short portion, and invariably encounter new signs, old ones long forgotten but well worthwhile, and remembered ones, beautifully illustrated. The profusion of fine illustrations is, in fact, one of the book's many fine attributes.

For anyone doing general surgery, the section on common acute abdominal conditions (perplexingly placed, it must be said, after sections on nonacute abdominal conditions, rectal and vaginal examinations, urinary organs, and male generative organs) is alone worth the price of the book.

There are few deficiencies. The small, fat size is unhandy (a larger and thus thinner book would have been better), and the price might be a deterrent to the student and resident for whom the book could be so valuable. In the section on the hand, there is almost nothing on the motor and sensory signs which should be elicited in diagnosing acute tendon and nerve injuries.

Beyond question, however, this is the best book of its type that exists and is enthusiastically recommended. We all pay lip service to the concept that the proper exercise of our senses in physical diagnosis is more important than using reports from the laboratory but often find this exercise not as rewarding as it should be because we have either forgotten or were never taught many physical signs that we can use. Here is a rich repository of such signs.

JOHN ROSENOW, M.D.
Minneapolis

Sexual Impotence in the Male

LEONARD P. WERSHUB, M.D., *and* RALPH E. SNYDER, M.D., *1959. Springfield, Ill.: Charles C Thomas. Illustrated. 107 pages. $5.75.*

The stated purpose of this book is "to impress the physician to (sic) the need of greater interest in the subject of sexual impotence in the male." With the tremendous advances in our knowledge of the reproductive processes, the stage has indeed been set for a profound and iconoclastic review of the subject of male impotence. However well prepared the stage, this brief volume fails even to ring up the curtain. The orientation of the authors is strictly urologic, and they deal with the more profound psychiatric aspects of impotence in a cursory, stuff-and-nonsense manner. The functional causes of impotence are handled in a manner the authors might use to explain the matter to a relatively bright patient.

A substantial portion of the text consists of direct or indirect quotations from the literature, the selection ranging with admirable impartiality from recognized authorities to what might best be classified as pulp "sexology" literature. Seldom do the authors venture more than agreement or disagreement with a quoted authority, and, when they do attempt greater profundities, the reader encounters such statements as "Many authors classify impotence as to varieties, . . . but this to me appears as superfluous for what may be temporary may also be permanent, as it is equally true that what is permanent is only permanent as such and could be temporary."

The section on organic causes of impotence is handled in standard textbook style. The major original contribution of the authors seems to have been a questionnaire sent to urologists asking for figures on the relative frequency of functional and organic impotence in office practice. On this basis, it is claimed that there has been "accumulated a great deal of pertinent data pertaining to the *over-all picture* of sexual impotence" (reviewer's italics). These data, except for a few anecdotal quotations, are nowhere to be found.

The editors have exercised remarkable restraint in preserving the authors' singular style. Amidst a scattering of split infinitives, repetitives, redundancies, and weary scientific clichés are such syntactical curiosities as "Also, added the most elaborate codes and rules, legal, moral, and esthetic, and in some cultures, sex has been made a central focus of human concern and endeavor, an almost obsessive preoccupation, with others favoring an

(Continued on page 14A)

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(1) Danowski, T. S.: Diabetes Mellitus, Baltimore, Williams & Wilkins, 1957, p. 239. (2) McCune, W. G.: M. Clin. North America 44:1479, 1960. (3) Ackerman, R. F., et al.: Diabetes 7:398, 1958.

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(Continued from page 344)

ascetic or celibate life." The 6 illustrations consist of clinical oddities dear to the heart of the specialist but of little over-all significance. Typography, paper, and binding are excellent.

JOSEPH W. GOLDZIEHER, M.D.
San Antonio, Texas

Photography in Medicine

ARTHUR SMIALOWSKI *and* DONALD J. CURRIE, M.D., *1960. Springfield, Ill.: Charles C Thomas. 313 pages. Illustrated. $14.50.*

The authors have set down in this volume the many special applications which photography has in the field of medical sciences. They have outlined the various aspects of medicine in which the use of photography will provide valuable records, and they have indicated many basic and sound technics which should be used in order to provide these records.

The various areas in which photography is used are discussed under separate chapter headings. These range from the organization of a department of photography and its related laboratory requirements through macro- and microphotography, gross specimen photography, photographic procedures for the operating room, the handling of patients, the requirements the various specialty fields demand in their photographic records, and photography in the physician's office to filing and indexing photographic records.

The book is well organized and filled with many photographs of fine quality, which illustrate the valuable records that can be obtained if the procedures described are put to use. With the photographs are many drawings, some of which portray in a schematic manner the proper placement of lights and camera and show the patient in various situations in which he might have to be photographed. Other drawings are detailed enough to provide working plans for the construction of certain pieces of special photographic equipment.

The information in this book will serve as a guide to the photographer, whether he is a beginner or well-established artisan, in the many aspects of medical photography. For the physician, this book presents the information on how highly technical this small segment of specialized photography really is. It does not intend to make a medical photographer out of the physician but rather to show him how it is possible to obtain good photographs in the office. It is more accurate to say that this book helps to point out to the physician what constitutes valuable and good photographic records and the many specialized technics that the photographer must know and practice in order to obtain photographic records of good quality.

HENRY MORRIS
University of Minnesota

Therapeutic Nutrition with Tube Feeding

MORTEN D. PAREIRA, M.D., *1959. Springfield, Ill.: Charles C Thomas. 51 pages. Illustrated. $3.75.*

In this monograph, Dr. Pareira of Washington University School of Medicine, St. Louis, Missouri, has discussed the use of tube feeding for all cases of undernutrition. The premise that many diseases precipitate extreme anorexia and that this may seriously interfere with the recovery of the patient is well documented. The physician is warned about dangers of acute starvation of hospital patients that are sometimes overlooked. The author clearly states the advantages of tube feedings for such cases of acute starvation.

This monograph has practical information for the clinician because it gives good, detailed instructions for the use of tube feedings, including kinds of equipment and general precautions to be taken. The history of tube feeding is particularly interesting and unique.

The results of using the recommended mixture for continuous drip feedings, intermittent tube feedings, and oral feedings are given for approximately 300 patients, representing 7,000 tube-feeding days. Nitrogen retention, weight gains, serum albumin regeneration, and hematocrit changes presented for these patients give a convincing picture of the efficiency of this method of alimentation.

The greatest limitation is that only 1 tube feeding mixture is recommended. This is a proprietary food that has been thoroughly tested by the author. It is available in a dry form and can be mixed at home as well as in the hospital. This method of preparation may be the most convenient, but it definitely limits the flexibility of feedings. For example, the ratios of protein, carbohydrate, fat, and calories cannot be altered without adding some other foods. The only changes that can be made from the recommended mixture are in the amount of diluent or the total quantity used. Since the proportion of protein to calories is quite high in the recommended feeding—23.5 per cent—there might be some pathologic states in which this mixture would be contraindicated. The author does suggest that more water might be needed in the mixture to prevent nitrogen retention in some semiconscious or comatose patients with impaired renal function.

The physician or dietitian might prefer to plan a tube feeding mixture from natural or processed foodstuffs to fit the nutritive requirements of the individual patient. This book would not give him any help in such alternative plans.

DOROTHY R. JUTTON
Madison, Wisconsin

The Chemistry of Heart Failure

WILLIAM C. HOLLAND, M.D., *and* RICHARD L. KLEIN, *Ph.D., 1960. Springfield, Ill.: Charles C Thomas. 116 pages. Illustrated. $5.50.*

In this book, an attempt has been made to gather together in a few pages some of the pertinent information on normal and failing hearts and the action of digitalis. This book has been written for the beginner as well as for the clinical cardiologist. It is especially interesting for physicists and chemists who are curious about the chemistry of normal and failing hearts.

The material has been organized on the basis of a discussion of (1) the elements of thermodynamics and chemistry of the normal heart, (2) the part played by free energy release and by electrolytes, (3) the chemistry of the failing heart, and (4) the nature of congestive heart failure and the mode of action of digitalis. Finally, a discussion is given on fibrillation—the theories, the ionic mechanisms, and the metabolic events.

The book is printed on good paper, is easy to read, and is indexed. This is a refreshing presentation of a subject that comes more and more to the attention of those who are concerned with the dramatic moment of life.

JOHN S. LUNDY, M.D.
Chicago

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Infections of the Urinary Tract

I. Pathogenesis, Symptomatology, Diagnosis, and Prognosis

WILLIAM J. MARTIN, M.D.

Rochester, Minnesota

INFECTION of the urinary tract is but a generic name for a group of diseases of differing pathogenesis, symptomatology, and prognosis. Since infections of the urinary tract may present as various syndromes, an extensive terminology has accrued, as witnessed by the terms "renal carbuncle," "perinephric abscess," and "pyelonephritis," among numerous others. Whatever the name, the basic disease is infection, the same infecting organisms are common to the various syndromes, and the essential purpose of diagnosis and treatment is eradication of the infection.[1,2] Further consideration of nosologic nuances at this time would contribute little to earlier recognition and improved management of urinary infections. The contention that they may rank second only to respiratory infections in incidence attests to their frequency. The total morbidity from infections of the urinary tract must be considerable and is appreciated with difficulty by an individual practitioner. Also, these infections are likely to cause, per se, and in a contributory fashion, an increased mortality rate which might not be immediately appreciated. Acute urinary infections usually are diagnosed with ease, since they are commonly manifested by localizing symptoms, but conversely, such symptoms may be lacking in chronic urinary infections, and consequently the latter may constitute the most commonly missed diagnosis in medicine today.

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ETIOLOGIC FACTORS

The first etiologic requirement is a uropathogenic strain of bacteria (table 1).[3] The 5 strains most frequently causative are (1) coli-aerogenes organisms, (2) streptococci, usually enterococci, (3) staphylococci, (4) protei, and (5) pseudomonades.

Structural abnormalities. Stagnation and infection may result from structural abnormalities along the urinary tract. In men more than 50 years old having urinary infection, the most probable abnormality is prostatism. Examination of men may disclose pinpoint meatus, phimosis, and the like; women may have pelvic relaxation, carcinomatous infiltration of the bladder, and so forth.

Urinary infections appear to be about twice as common in pregnant as in nonpregnant women. About half of those infected manifest frank symptoms sometime during the pregnancy; asymptomatic bacilluria may be noted weeks before any symptoms. In pelvic relaxation of surgical proportions, bacilluria is about 4 times more common than in otherwise normal women.

Susceptibility of host. Certain diseases, including diabetes mellitus, predispose to urinary infections. Presently, little is known about the role

TABLE I
SOME FACTORS ENHANCING INCIDENCE OF INFECTIONS OF URINARY TRACT

Uropathogenic strain of bacteria
Structural abnormalities of urinary tract: congenital (aberrant vessels, horseshoe kidney), hereditary (hereditary interstitial pyelonephritis, polycystic kidneys), acquired (pregnancy, prostatism)
Increased susceptibility of host (hypogammaglobulinemia, properidin deficiency, diabetes mellitus)
Sex: 3 times as common in women as in men
Multiple urinary catheterizations and instrumentations
Changes in chemical composition of urine
Changes in normal body flora
Trauma
Bacteremia with metastatic renal involvement
Increased functional demands on kidneys

of the properidin system of euglobulins, which appear related to hereditary immunity, in urinary infection.

Possible reasons why, in congenital hypogammaglobulinemia (defective acquired immunity), urinary infections are less common than are other infections, such as dermal, respiratory, and bacteremic infections, include these: (1) in this defect, infection with gram-negative bacilli, except hemophili, is less frequent than infection with gram-positive organisms, but urinary infections are more often caused by gram-negative bacilli; (2) newness of the syndrome, occupation to date with more obvious infections, and the fact that 50 per cent of urinary infections are relatively asymptomatic may have obscured their detection; (3) its victims are males, in whom urinary infection without obstruction is rare; and (4) formerly, those afflicted with hypogammaglobulinemia died in childhood, but in males, two-thirds of urinary infections occur after age 40.

Because of numerous respiratory infections caused by gram-positive organisms, metastatic renal involvement[4] seems possible in these subjects. Gram-positive organisms are more common in chronic infections, which may be asymptomatic or manifested as hypertension, azotemia, and the like, years after onset. Use of antibiotics and exogenous gamma globulin, by increasing longevity in these subjects, may allow more accurate retrospective determination of the incidence of urinary infections.

Concurrent hypogammaglobulinemia and urinary infection (1) may occur secondary either to retroperitoneal lymphoma causing obstructive uropathy or to multiple myeloma with superinfection of myelomatous kidneys or (2) may be linked to an allergic state that occurs in both sexes and that may further the female predisposition to urinary infection. However, in these situations, any role of the immunologic defect is obscured by the presence of other etiologic factors.

Sex. Infections of the urinary tract are 3 times as common in women as in men. About two-thirds of the infections in women occur before age 40, while, as mentioned earlier, two-thirds of those in men occur after age 40. Despite the higher clinical incidence of infection in women, the disease may be comparatively more lethal in men, since at necropsy it is almost equally common in the two sexes.

Catheterizations and instrumentations. Infections of the urinary tract follow single catheterizations in 2 to 4 per cent of cases and develop in many patients having indwelling catheters for several days, despite antibacterial prophylaxis and lavage of the bladder.[5] Indwelling catheters may facilitate infection via the fluid, composed of urine and exudate, forming around the catheter and serving as a culture medium. Clarke and Joress[6] point out that patients with catheter bacilluria may not have persistent infection if the factors favoring infections, aside from the catheter, are correctible and if patients are observed after removal of the catheter to assure that bacilluria is eradicated. In this same regard, among paraplegics with long-term indwelling catheters, only about one-third have pyelonephritis. There is a history of urinary manipulation or previous urinary infection in 50 per cent of patients with infection of the urinary tract; in noninfected patients, only 10 per cent have such a history.

Changes in chemical composition of urine. Infection may be facilitated by changes in the chemical composition of the urine of susceptible persons, making it a more productive medium for bacterial growth; conversely, Straffon and Engel[7] point out that potent nonspecific antibacterial substances have been found in normal urine. The fourth component of the complement is inactivated by ammonia, and the fact that the renal medulla produces ammonia from glutamine may explain its special susceptibility to infection.

Changes in normal body flora. Iatrogenic changes in the normal body flora may precipitate urinary infection. Thus, treatment with penicillin and allied drugs may cause suppression of

the gram-positive flora with overgrowth of gram-negative elements, or, conversely, treatment with tetracyclines or other drugs that depress the gram-negative flora may allow overgrowth of the gram-positive cocci, so that infections of the urinary tract occur because of the overgrowing bacteria.

Trauma. Trauma to the kidneys, as is common in highway accidents, may so injure these organs that resultant scarring renders them susceptible to infection.

Bacteremia with metastatic renal involvement. Metastatic infections as represented by bacteremias may cause renal implantation of bacteria; such might result from even transient bacteremia, occurring after cleaning the teeth, chewing tough meat, and so forth. Also, established bacteremia and subacute bacterial endocarditis can result in renal implantation of septic emboli. Schreiner[4] notes that the kidney, with its share of 20 per cent of the cardiac output and its glomerular capillaries constituting a large surface area wherein blood flow is slowed, is in an excellent mechanical position to receive emboli. There is a paradox to septic renal infarction in that, conversely, septic emboli may arise from the kidney and produce metastatic panophthalmitis, dermal pustules, and abscesses of the lung, liver, and brain.

Functional defects. Another factor perhaps enhancing the incidence of urinary infections is so-called functional defects. Various functional demands may mechanically exhaust the kidneys, to the point of decreasing their resistance to infection. Hypothetically, breakdown products of drugs being excreted by the kidneys, by constant functional overloading, may increase their susceptibility to bacterial invasion.

Although it is often assumed that chronic pyelonephritis results from acute pyelonephritis, this is not a necessary conclusion. In the series of Jackson and colleagues,[8] 50 per cent of patients had had an acute onset but 40 per cent had had the vague onset of chronic urinary symptoms and 10 per cent with chronic disease had had systemic symptoms without localizing ones.

MICROBIOLOGIC CONSIDERATIONS

Bacteria isolated from the urinary tract may be (1) pathogenic in the process at hand; (2) a manifestation of a histologically deranged kidney, that is, secondary invaders; (3) normal urethral organisms; or (4) contaminants.

Gram-negative bacteria are usually associated with acute infections; gram-positive bacteria are frequently isolated in chronic infections. Generally, however, infection is more commonly caused by gram-negative bacilli. Attempts at antibacterial prophylaxis against indwelling catheters by eliminating more susceptible invaders may increase the relative incidence of urinary infections due to the more resistant enterococcal, proteus, and pseudomonas organisms. It is common for pathogens to disappear during treatment, only to be replaced by others. Polymicrobic infections occur in about 10 per cent of patients.

There is a paucity of data suggesting renal involvement by viruses except that caused by the agent of yellow fever. Schreiner[4] has said that perhaps isolation of mumps virus in the urine heralds an era of viral nephritides.

Renal biopsy has revealed that the proportion of biopsy specimens that are normal decreases with the duration of infection; in only 10 per cent of chronic infections is normal tissue found. Renal biopsy has established (1) the existence of active pyelonephritis without urinary findings, (2) unsuspected pyelonephritis in association with such syndromes as toxemia of pregnancy and hypertension, (3) early micropathology of pyelonephritis in nonfatal forms, and (4) via successive biopsies plus necropsy studies, the progression of histologic lesions revealing a composite picture of pyelonephritis.

SYMPTOMS AND SIGNS

There are at least 4 clinical syndromes of infections of the urinary tract: (1) asymptomatic bacilluria; (2) acute infection, that is, fever, distress in the flank, and dysuria; (3) chronic urinary symptoms, both with acute episodes initially and periodically thereafter and without an acute episode initially and frequently without subsequent acute episodes; and (4) systemic reactions, such as hypertension, azotemia, and toxemia of pregnancy, in which local symptoms usually are absent.

Symptoms of urinary infection apparently depend on the pathogen's virulence and the host's urinary and general resistance. About 50 per cent of patients with chronic infections are relatively asymptomatic. In general, the shorter the duration of infection, the greater the likelihood of urinary symptoms. Infections manifested by chills, fever, and toxemia are usually associated with dysuria, or pain and tenderness in the flank, directing attention to the urinary tract. However, about 10 per cent of patients with acute infection and systemic reaction lack urinary symptoms. In the absence of localized signs, it is common to consider such an infection as a fever of undetermined origin; in such patients, it is well

to investigate the urinary tract not only for possible hypernephroma but also for occult infection. In this regard, in a febrile patient with or without urinary symptoms, excretory urography may disclose, in addition to hypernephroma, (1) neoplasm, especially lymphoma, which, if retroperitoneally located, may cause lateral ureteral displacement; (2) idiopathic retroperitoneal fibrosis, usually seen in middle-aged males, wherein there is fibrotic involvement of the lower part of the ureters; and (3) calyceal changes indicating pyelonephritis with or without an underlying cause such as renal calculi.

Diagnostic facets of acute infections of the urinary tract that may be confusing include infection in the renal pelvis which erodes into a blood vessel and produces gross hematuria that, if associated with cystic defects on urography, can be confused with tumors or cysts. In cases of infectious urinary syndromes that produce pain, such as septic renal infarction and abscesses, the pain may be referred to the dermatomes from which the innervation of the renal surface originates, and the distribution of these dermatomes is over the lower part of the abdomen. Therefore, if the patient has nausea, reflex ileus, and anemia, the pain may be confused with a bowel syndrome. Infections in the right kidney, including septic infarcts, may be manifested by fever, leukocytosis, and pain in the right lower abdominal quadrant which has been confused with acute appendicitis. Conversely, retrocecal appendicitis with adherence to the right ureter can simulate and cause unilateral right pyelonephritis. Also, cortical abscesses on the ventral aspect of the kidneys can both simulate and, by rupture, cause peritonitis. In older patients especially, infections of the left kidney, including septic infarcts and ventral renal abscesses, may be confused with diverticulitis of the colon. Leukemoid reactions may be produced by urinary infections such as acute pyelonephritis, renal abscesses, and metastatic infections to or from the kidneys.

Chronic infections also may masquerade as another entity (table 2). Chronic urinary infection should be considered in all cases of hypertension, so that early recognition may initiate corrective measures before the vascular response is irreversible. Kass[9,10] states that asymptomatic bacilluria is more common in hypertensive than in nonhypertensive subjects and that studies of hypertension should include a search for asymptomatic bacilluria. Schreiner[1] notes that congestive heart failure was the presenting syndrome in a number of his patients with chronic pyelonephritis and was most often due to intervening hypertension. In some of his patients, active signs of both pyelonephritis and hypertension had subsided at the time of heart failure, and in such cases pyelonephritis may be neglected as an etiologic agent. Some patients may present so-called malignant hypertension or encephalopathy with convulsions and rising diastolic pressures, especially during an acute exacerbation of the pyelonephritis. Chronic urinary infection may be more common than chronic glomerulonephritis and may be responsible for 15 to 20 per cent of cases of malignant hypertension. Pyelonephritis, healed or of a low-grade, smoldering type, may produce hypertension with remissions and exacerbations and is often confused with essential hypertension.

TABLE 2
INFECTION OF URINARY TRACT AS CAUSATIVE OR COMPLICATING FACTOR

Consider infection of the urinary tract as causative in:
Hypertension
Chronic renal insufficiency
Disturbed electrolyte metabolism
Nephrocalcinosis
Toxemia of pregnancy
Necrotizing papillitis
Consider infection of the urinary tract as a complication in:
Structural abnormalities of urinary tract (prostatism)
Increased susceptibility of host (diabetes mellitus)
Infection elsewhere in body (tuberculosis, brucellosis)
Prolonged use of indwelling catheters (coma)
Nephrosis (amyloidosis)

In such syndromes as salt-losing nephritis, uremia of obscure origin, and toxemia of pregnancy, the possibility of an underlying urinary infection should be considered. With extensive tubular damage and inability to conserve sodium, difficulties may be abetted by a low-salt diet. Prolonged renal failure caused by pyelonephritis may result in hyperphosphatemia, hypocalcemia, parathyroid hyperplasia, and bone changes. Since only one-fifth of the normal nephron mass suffices for the usual metabolic demands, uremia is produced with difficulty, and this may explain why ten to fifteen years of smoldering destruction sometimes is required. Urinary infections should be considered as possibly causative in toxemia of pregnancy when proteinuria, pyuria, and hypertension persist for more than seven days post partum.

Since urinary calculi predispose to infection and since one of the ultimate phases of healing in infection of the urinary tract is nephrocalcinosis, such calcification suggests the presence of infection. The exact genesis of nephrocalcinosis is not always apparent, but stone formation is abetted by an alkaline urine produced by urea-splitting bacteria. If nephrocalcinosis develops in patients with renal tuberculosis, brucellosis, or salmonellosis, secondary bacterial invaders may obscure the underlying process.

Necrotizing papillitis is another syndrome in which urinary infection is at least partially causative and should be suspected in diabetic patients with acute anuria or in patients undergoing instrumentation and having urinary infection. Schreiner[4] describes 2 fatal cases of necrotizing papillitis after retrograde pyelography in the face of infection. Manipulation of an infected urinary tract may also result in bacteremia and bacteremic shock if treatment is not given beforehand to control the infection. If fever occurs after urologic manipulation, both the urine and the blood should be cultured.

Schreiner[4] notes that urinary infections also complicate other renal diseases and cause confusion in conditions like amyloid nephrosis, glomerulonephritis, and intercapillary sclerosis. In cases of amyloid nephrosis, it may be hard to tell whether the infection is secondary to or is etiologic in the amyloidosis.

Pyuria is not an invariable associate of bacilluria; significant bacilluria may be present without pyuria. Bacilluria has been detected in significant numbers of patients who are otherwise normal.[10] The simplest way to detect it is to examine a stained sediment of the urine.

A count of 100,000 or more bacteria, cultured from a milliliter of urine, represents significant bacilluria and characterizes 95 per cent of the specimens of urine passed by patients with urinary infection. Less than 5 per cent of such patients have bacterial counts between 10,000 and 100,000 per milliliter; if the counts are repeated on a first morning specimen of urine, distinction between contamination and infection usually is evident. Counts of less than 1,000 bacteria per milliliter usually are not significant. Specimens with higher counts seldom contain urethral contaminants such as diphtheroids, saprophytic neisseriae, or sarcinae. Absence of large numbers of bacteria in the urine of a person with a classic syndrome of urinary infection suggests (1) precultural administration of antibacterial agents; (2) ureteral obstruction; (3) excessive hydration, perhaps manifested by low specific gravity of the urine; or (4) a *p*H of less than 5, which per se may be bacteriostatic. It is wise to request 2 quantitative counts of different specimens, if possible, before giving a definite opinion regarding the existence of urinary infection solely on this basis.

Duration of infection, not severity of symptoms, is the major factor in determining the degree of renal damage caused by urinary infections. Renal function is also poorly related to symptomatology but parallels structural changes. Concentration and clearance tests help to distinguish advanced infection from less serious renal involvement. Clearance tests may reveal diminished renal flow of plasma, reduced filtration fraction, or, possibly, decreased functioning tubular mass. If, after fluids are withheld during the night, the specific gravity of the urine passed on arising is 1.020 or more, renal function is probably adequate. Jackson and colleagues[8] note that chronic pyelonephritis sometimes can be distinguished from other causes of decreased function by its tendency to produce failure of concentration.

Kaitz and Williams[11] indicate that the correlation of asymptomatic bacilluria with unsuspected active pyelonephritis at necropsy and the finding of asymptomatic bacilluria before the appearance of symptoms of acute pyelonephritis of pregnancy[12] suggest that asymptomatic bacilluria and pyelonephritis are related.

During the annual session of the American College of Physicians recently held in Florida, a panel discussion of the association of pyelonephritis with hypertension, renal failure, and disseminated vascular disease was held; the panelists attempted to evaluate current evidence that there may be late consequences of persistent bacilluria. On the other hand, conceivably the scarred kidney is secondary to hypertension and disseminated vascular disease and in its wounded state falls prey to secondary infection. In this regard, certain data indicate the existence of a vicious circle that consists of urinary loss of potassium, increased vulnerability to renal infection, and eventual hypertension. Conceivably, any 1 of the 3 constituents of the circle might initiate the process and eventuate in the other 2.

Since about 50 per cent of chronic infections are relatively asymptomatic, about 10 per cent of acute ones lack urinary symptoms, and significant bacilluria may be present without causing pyuria, it is evident that a sizable percentage of infections do not cause urinary symptoms or abnormal findings on routine urinalyses. This clinical problem is accentuated by the high incidence of unsuspected pyelonephritis at nec-

ropsy. In view of the probability that persistent bacilluria rather than pyuria or symptoms is the essential sign of urinary infection, when predisposing states like pregnancy, diabetes, pelvic relaxation, and prostatism are encountered, one should recall especially the possibility of infection; actually, in view of these data, one is hard put to counter the advice to search for bacteria in stained specimens of urine of all patients before concluding that the urine is normal.

DIAGNOSIS

Exacerbations of chronic urinary infections should not be confused with acute recurrent infections. Another good rule to keep in mind is not to fail to exclude obstructive uropathy (or predisposing disease) when diagnosing acute recurrent or chronic infections.

So-called abacterial (amicrobic) pyuria does not always reflect tuberculosis but can be a manifestation of other diseases, such as brucellosis. There is also an idiopathic variety of abacterial pyuria, associated with hematuria and arthritis, from which hydronephrosis and contraction of the bladder may eventuate. Men who have had transurethral prostatic resection may have benign pyuria for years because of residual posterior urethritis and prostatitis in the remaining part of the prostatic capsule. Dehydration also produces pyuria.

Not all urine that burns is infected. In women with dysuria and normal findings on urinalysis, investigation may reveal urethrotrigonitis or interstitial cystitis, for which antibacterial therapy is not indicated; local treatment of the bladder is often helpful. Other conditions confused with urinary infections include prolapsed urethral mucosa, urethral carmncle or diverticulum, and post-irradiation cystitis. Senile vaginitis may produce dysuria and associated bleeding that is sometimes confused with hematuria.

Catheterization is not necessary in routine microbiologic study of the urine in men; examination of a second-glass specimen suffices. Although some physicians still prefer catheterized specimens from women, considerable data indicate that, in them, too, noncatheterized specimens may suffice, so that obvious physical, psychologic, and infectious hazards are avoided.[13–18] According to Hinkle and associates,[17] urine obtained from females by a clean-voided technic rather than by catheterization gives false-positive results in only 3 per cent of cases, which corroborates the work of Pryles and Steg[16] and Masters.[15] Many investigators now believe that catheterization for microbiologic diagnosis is unnecessary in persons of any age, since the results from quantitative culture of the urine are so dependable and correlation between the results from clean-voided specimens and those from catheterized specimens exceeds 95 per cent. Specimens should be studied for bacteria within an hour after passage or else the urine should be refrigerated, as storage at room temperature permits the number of bacteria to increase significantly. Urine generally supports multiplication of the usual urinary pathogens about as well as does nutrient broth. Urine may be stored at refrigerator temperatures for forty-eight hours without significant change in the bacterial population.

Staining of the urinary specimen by the gram method is very helpful in the preliminary diagnosis of infection of the urinary tract. The intrinsic error in this procedure is 20 per cent or less. If pyuria alone is used to indicate infection, the error approximates 50 per cent, since, in about half the cases, microbiologic investigation gives negative results.

In vitro studies of bacterial susceptibility to antibacterial agents need not be done routinely in acute infections, since they are time-consuming and expensive and may contribute no additional help. However, when an acute infection resists therapy, such studies in conjunction with urography and cystoscopy are indicated. Bacterial susceptibility tests performed by the disk-plate, or agar-diffusion, method are not as reliable as those accomplished by the tube-broth or cup-plate-dilution methods.

If the results of intravenous urography are unsatisfactory, the urologist may suggest that retrograde pyelography be done at the time of cystoscopy. Sometimes the urologist suggests that cystourethrography be done during voiding to demonstrate the presence or absence of ureteral reflux and the efficiency with which the bladder empties. If the bladder may be neurogenic, the urologist may perform a cystometrographic examination.

Antibody titers for specific bacteria, determined by the antibody-hemagglutination technic, have been studied in urinary infections. This technic utilizes the fact that erythrocytes, modified by bacterial antigens, become sensitive agents for the detection of bacterial antibodies. The technic has been used in attempts to differentiate bacterial contaminants from pathogens and, by periodic determinations, to evaluate the response to therapy.

PROGNOSIS

Although many urinary infections are simple and self-limited, they may do irreparable damage to

the urinary tract if not treated successfully. Relapse, either clinical or, to the patient's greater disadvantage, occult, may result from premature abandonment of treatment.

It is said that chronic urinary infections are found at 10 to 20 per cent of all necropsies but less than a third of them are diagnosed ante mortem. Kass[10] states that pyelonephritis is the commonest disease of the kidneys seen at necropsy. In about 3 per cent of necropsies, the urinary infection appears to have been a major cause of death. As MacDonald and colleagues[19] point out, however, all is not pessimism, since healed pyelonephritis is seen at necropsy about as frequently as is active pyelonephritis. Jackson and associates[8] have expressed the belief that, since the advent of modern antibacterial therapy, the incidence of urinary infections found at necropsy may have decreased.

Schreiner[4] puts it well when he writes that no figure can be offered for the number of patients with pyelonephritis in whom the diagnosis was made too late for effective therapy; without early diagnosis, treatment will more often be ineffective and, hence, the prognosis less good. It has been estimated that, clinically, about 75 per cent of the acute infections appear to respond to initial therapy; unfortunately, 50 per cent may recur. Also, it has been estimated that only about 25 per cent of chronic infections are controlled and about 75 per cent relapse. Evaluation of therapy, results therefrom, and, consequently, prognosis are essentially dependent upon the type of infection; from the viewpoint of prognosis, the types are (1) infections secondary to lesions amenable to surgical treatment, (2) infections intrinsically not susceptible to cure, and (3) infections without obvious cause. The number of recurrences is reducible by more intensive initial therapy, elimination of underlying uropathy, and intermittent use of a suppressive agent.

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Neurologic Aspects of Blood Diseases and Reticuloses

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In spite of extensive literature on the various blood diseases, little emphasis has been placed on the secondary neurologic manifestations encountered in these disorders. It is only recently that syndromes such as meningeal leukemia, encephalopathies associated with paraproteinemias, and peripheral nerve lesions in myelomatosis, have been described in some detail.

The purpose of this article is to outline the up-to-date and most commonly recognized neurologic complications in blood disorders and the reticuloses.

ANEMIAS

The neurologic complications in anemias include nonspecific manifestations common to all anemic conditions as well as certain symptoms and signs which are specific for only a few of these diseases.

The nonspecific symptoms in acute anemias include dizziness, general weakness, visual loss of central or peripheral origin, syncope, peripheral circulatory collapse, and coma. Focal cerebrovascular accidents are seen, especially in elderly people with pre-existing cerebral arteriosclerosis. In chronic anemias, general asthenia, paresthesias, vertigo, headaches, syncope, tinnitus, visual scotomas, and various emotional disturbances are the usual symptoms.

Hemolytic anemias. The hemolytic anemia of the Rh-positive newborn infant, due to the anti-Rh antibodies entering the fetal circulation during the pregnancy of an Rh-negative mother, may give origin to the picture of kernicterus. In these cases, cerebral symptoms appear shortly after the onset of jaundice but may be delayed a few days or weeks. Somnolence, muscular rigidity, opisthotonos, and convulsions are common manifestations. In the survivors, there is high incidence of residual effects, both mental and physical, usually in the form of incoordination, spasticity, extrapyramidal syndromes, mental retardation, and seizures.

In hemolytic anemias due to abnormal red cells or abnormal plasma factors, neurologic symptoms appear, usually during the "hemolytic crises," and consist of pain in the back and limbs, headaches, vasomotor disturbances, and Raynaud's phenomenon. In acute cases, especially those of sickle-cell anemia, disturbed state of consciousness, convulsions, cerebrovascular episodes, and retinal hemorrhages may be seen. Peripheral neuropathy and anterior horn-cell amyotrophy may accompany some cases of sickle-cell anemia, while a posterolateral syndrome may accompany congenital hemolytic jaundice.

Roentgenograms of the skull in some forms of hemolytic anemias, particularly thalassemia and sickle-cell anemia, may show a characteristic extension of the marrow through the outer table of the skull, giving the typical hair-on-end appearance.

Deficiency of vitamin B_{12}. The syndrome of vitamin B_{12} deficiency associated with Addison's pernicious anemia is due to primary failure of the glandular epithelium of the stomach to secrete an intrinsic factor necessary for the absorption of vitamin B_{12}. Secondary macrocytic anemias may result from a variety of conditions interfering with the intrinsic factor, such as gastrectomy or gastritis, or from inadequate intake or absorption of vitamin B_{12}, as in malnutrition and chronic intestinal disorders.

Of the conditions mentioned, Addison's anemia and macrocytic anemias due to secondary lack of intrinsic factor result consistently in combined system disease of the spinal cord, which is not as common in the other conditions, probably because the deficiency of vitamin B_{12} is not as complete.

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The onset of neurologic manifestations is insidious and may antedate the appearance of anemia. Symptoms include paresthesias of hands and feet, general asthenia followed by progressive ataxia from loss of proprioception, and spastic paresis from pyramidal tract involvement. Peripheral neuropathy is almost always present, while retrobulbar and optic neuritis or retinal hemorrhages are seen in a few cases. Mental symptoms in the form of organic dementia, confusion, and psychosis may complicate the picture in advanced cases.

Pathologic changes include degeneration of axis cylinders and myelin sheaths in the posterolateral columns of the spinal cord and peripheral nerves. A similar type of degeneration may occur in the brain.

Iron-deficiency anemias. Persisting paresthesias of the extremities and, occasionally, combined system disease of the spinal cord may occur in iron-deficiency anemias. With hookworm anemia, convulsions, psychosis, and dementia are common. However, the role of anemia in initiating these symptoms is not clear. In rare cases of infants with chronic iron deficiency anemia, roentgenograms of the skull may show the hair-on-end appearance seen in some of the congenital hemolytic anemias.

Aplastic anemia. The chief neurologic symptoms are due to intracerebral bleeding from associated thrombocytopenia. General weakness and associated multifocal central nervous system manifestations are the result of scattered areas of demyelination in the brain and spinal cord, due, probably, to the long-standing anemia.

HEMORRHAGIC DISEASES

Hemorrhagic diseases include the purpuras, thrombocytopenic and vascular, and the hemorrhagic conditions secondary to coagulation defects of the blood. The neurologic manifestations are primarily due to large or petechial hemorrhages into the nervous tissues. Associated thrombotic lesions are seen exclusively in thrombotic thrombocytopenic purpura.

Thrombocytopenic purpura. Essential thrombocytopenic purpura is a primary condition of unknown etiology. The chief neurologic manifestations are petechial hemorrhages, traumatic ecchymoses, and bleeding into various tissues. Such hemorrhagic manifestations into the central nervous system are particularly common in adults. Intracerebral hemorrhage is more frequent than subarachnoid or subdural bleeding. The course of the disease is characterized by remissions and exacerbations and may be mild or protracted.

Clinical neurologic signs include acute cerebral insults or signs of meningeal irritation. In the case of multiple petechial hemorrhages, progression of signs may be seen over a period of days in the form of multifocal or diffuse cerebral deficit. Retinal hemorrhages may be associated with or be independent of neurologic findings. The spinal cord and, occasionally, the peripheral nerves may be the sites of hemorrhage giving rise to corresponding acute syndromes.

In the secondary thrombocytopenic purpuras, caused by infection, drug allergy, or toxic or neoplastic injury to the bone marrow, the neurologic manifestations may be due to the primary disease or may be secondary to the purpura itself, simulating the syndromes seen in essential thrombocytopenic purpura.

In vascular purpuras associated with senility or due to acute infections, intoxications, and allergic reactions, bleeding into the central nervous system is not as common as with thrombocytopenic purpuras.

Thrombotic thrombocytopenic purpura. This is a rare disease of unknown etiology, although there is a suggestive relationship to collagen disorders. The clinical manifestations are the result of three basic defects: (1) a tendency for vascular occlusion by an amorphous hyaline thrombus, probably from agglutinated platelets or secondary to a primary lesion in the vessel wall; (2) hemolytic anemia, probably due to the action of an extracorpuscular hemolytic mechanism; and (3) thrombocytopenia, the result of an unidentified platelet autoagglutinin or, probably, a decrease in production of platelets.

The most common systemic manifestations include fever, general weakness, arthralgias, purpura, abdominal pain, nausea, vomiting, and jaundice. The neurologic signs are usually prominent and are caused by multifocal vascular occlusions and petechial hemorrhages in the cerebral cortex, basal nuclei, brain stem nuclei, and, less commonly, white matter. Seizures, mental changes, aphasia, cortical blindness, focal paralyses, bulbar signs, and pyramidal disorders are the most frequent symptoms. Mental changes occur in the form of organic dementia, confusional states, delirium, and coma.

Hemorrhagic disease due to coagulation defects. This group includes hemorrhagic disorders associated with deficiency of certain elements involved in blood coagulation. They are characterized by profuse bleeding, often following definite trauma.

In the hemorrhagic disease of newborn infants, which is associated with low prothrombin

level due to lack of vitamin K, intracranial hemorrhage is the most severe complication. Convulsion, decerebrate rigidity, and coma are the usual symptoms.

In acquired hypoprothrombinemia due to inadequate absorption of vitamin K, defective formation of prothrombin in liver disease, or interference with prothrombin synthesis by Dicumarol, hemorrhages may occur into the central nervous system or subarachnoid space. The same is true in cases of familial hypoprothrombinemia. Fibrinogen deficiency and a few other rare disorders also may lead to hemorrhage.

In hemophilia, where the primary defect is lack in plasma thromboplastinogen, hemorrhage into the central nervous system is rare. Bleeding into the spinal cord or its coverings may result from back injury. Peripheral paralysis may be due to nerve compression by hemorrhage into the muscles and most commonly includes the femoral and ulnar nerves.

Purpura hyperglobulinemia. This condition is characterized by recurrent purpura and associated increase in serum gamma globulin. Etiology is unknown. The hemorrhagic manifestations are most common in the extremities, especially the lower. Petechiae erupt in crops and are usually full-blown in a few hours. Burning paresthesias and pain accompany the appearance of petechiae.

POLYCYTHEMIA

Polycythemia secondary to recognized cause is distinguished from the idiopathic primary disease known as polycythemia vera. In both conditions, there is a sustained elevation of red cells and hemoglobin.

In the secondary type of polycythemia, the underlying cause is usually a cardiac or pulmonary disease that allows partially oxygenated blood to go into the major circulation. The decrease in oxygen tension stimulates a red marrow hyperplasia, with subsequent increase in the number of circulating red cells. Despite the increased oxygen capacity of circulating blood, the oxygen tension is less than normal. This, together with the underlying cardiac and pulmonary disease, results in poor tissue oxygenation, while the increased blood viscosity, retarding the cerebral blood flow, favors anoxic tissue damage and vascular thrombosis. In the cases of polycythemia associated with chronic mountain sickness, polycythemia develops as a compensation to the lowered oxygen tension of high altitudes. Although sufficient adaptation occasionally occurs, such balance usually fails, especially in the presence of chronic pulmonary disease.

In primary polycythemia, the excessive erythropoiesis has no apparent cause. The tissues receive adequate oxygen due to increased oxygen content and normal oxygen tension of the arterial blood. However, the excessive increase of blood viscosity results in diminished blood flow and a subsequent tendency to thrombosis and hemorrhage.

Outside of the primary and secondary polycythemias, there is a form of relative polycythemia that is due to dehydration or loss of plasma volume with resulting increase in red cell concentration.

Neurologic manifestations in polycythemia are mostly of central nervous system origin and due to ischemia, thrombosis, and anoxia. Anoxic symptoms are more common in secondary and relative types of polycythemia, whereas cerebrovascular manifestations predominate in polycythemia vera. The most common neurologic syndromes are (1) syndrome of chronic cerebral anoxia, (2) cerebrovascular syndromes, (3) polycythemia as part of primary neurologic disease, and (4) peripheral neuropathy.

Syndrome of chronic cerebral anoxia. Headaches, dizziness, vertigo, tinnitus, and scotomas caused by anoxia are common symptoms in patients with secondary polycythemia. Mental slowness, confusional states, profound lethargy, and even coma may be pronounced, especially in cases of mountain sickness. These symptoms usually clear when the primary disease is corrected or upon return to a lower altitude in the case of mountain sickness.

Cerebrovascular syndromes. Strokes resulting in fixed tissue damage are usually thrombotic, although cerebral hemorrhage may occur. Repeated multiple vascular accidents are even more characteristic. Transient episodes of cerebrovascular insufficiency may simulate internal carotid or basilar artery disease, and such manifestations are more dramatic in the presence of local impairment of circulation from arteriosclerotic changes. Of special importance is relative polycythemia, which is due to dehydration or increased water and electrolyte loss in elderly patients. The increased blood viscosity in such cases may become the initiating factor toward an acute vascular insult in the presence of poor cardiocirculatory reserve and arteriosclerotic brain disease.

Retinal changes in polycythemia are often dramatic and include venous engorgement and tortuosity, thrombosis of the central retinal vein, blurring of the disk margins, and actual papilledema.

Polycythemia as part of primary neurologic disease. Polycythemia often has been associated with disorders affecting diencephalic structures. The association has been close enough in some cases to suggest that the polycythemia was secondary to the diencephalic lesion. Infratentorial vascular tumors have had a high incidence of polycythemia, which, for the most part, clears after surgical removal of the lesion. The mechanisms involved in the production of polycythemia in such cases is not clear.

Peripheral neuropathy. Impairment of the circulation in the peripheral nerves may result in mononeuritis or peripheral neuritis. Occasionally, radicular involvement has been noted. Pain in the extremities is a usual accompaniment of the neuritis and may appear in the absence of neuritic manifestations. In the latter cases, it is probably due to peripheral arterial disease.

LEUKEMIAS

Neurologic symptoms of leukemia are produced by leukemic infiltrations and hemorrhages into the nervous system. Ischemic conditions from an associated anemia and secondary infections may often obscure the picture. Pathologic changes are much more frequent than is clinical evidence of neurologic involvement.

Cerebral complications and meningeal leukemia. Intracerebral or subarachnoid hemorrhages are common during blastic leukemic crisis and at the terminal phases of leukemias. Although it is more common to see multiple areas of hemorrhage, massive intracerebral bleeding or profuse subarachnoid hemorrage extending into the brain substance is not uncommon. The hemorrhagic areas are usually associated with leukostasis and leukemic nodules, although each lesion can occur independently. The clinical picture depends upon the size and location of the lesion. Convulsions, stroke syndromes, isolated paralysis, cranial nerve palsies, confusional states, and meningeal irritation are common manifestations.

The syndrome of meningeal leukemia results from leukemic infiltrations within the arachnoid and Virchow-Robin spaces, independent of hemorrhage, producing increased intracranial pressure, cerebral edema, and, often, overt hydrocephalus. It is usually seen in acute leukemia, especially the lymphatic form, and is more common during the active period of the disease, although it may develop during hematologic remissions. The symptoms are intense headaches, lethargy, vomiting, convulsions, stiff neck, and papilledema. Associated cranial nerve palsies and nonspecific neurologic signs may also result. The clinical picture may simulate that of pseudotumor cerebri, with pronounced papilledema and secondary optic atrophy. The skull suture lines are usually spread in children, and the spinal fluid shows increased pressure, pleocytosis of leukemic cells, and sometimes diminished sugar.

Dural infiltrations alone or associated with arachnoid infiltrations may give rise to focal cortical symptoms secondary to invasion of the cerebral cortex or to the formation of an epidural mass.

Spinal cord and peripheral nerve lesions. Spinal cord lesions are quite common and usually the result of epidural leukemic infiltrations with secondary root and cord compression. Infiltration of the roots and spinal cord per se is uncommon. Symptoms include back pain, rootlet pain, urinary difficulties, irregular paralyses, and signs of transverse cord involvement. In rare cases, the condition may resemble amyotrophic lateral sclerosis. The spinal fluid often contains large amounts of protein, leukemic cells, and, occasionally, low sugar.

Peripheral neuropathy is a rare complication due to extensive leukemic infiltrations of peripheral nerves. In chronic states of debilitation, peripheral neuropathies are usually due to secondary nutritional deficiency.

WALDENSTRÖM'S MACROGLOBULINEMIA

Waldenström's macroglobulinemia is a chronic debilitating illness affecting primarily men between the ages of 50 and 80. The usual life expectancy after the first manifestation of symptoms is two to ten years. Onset is insidious, usually characterized by progressive weakness, lassitude, weight loss, and pallor. Edema may be present. Hemorrhagic diathesis is present in at least two-thirds of the cases and is manifested primarily by epistaxis, gingival and retinal hemorrhages, cutaneous purpura (usually late), and, to a lesser extent, bleeding from other organs. Painless enlargement of the lymph nodes and hepatosplenomegaly are present in about half the cases. The laboratory profile reveals anemia, often associated with relative lymphocytosis and thrombopenia. In nearly all cases, the sedimentation rate is elevated. The bone marrow usually shows a characteristic lymphocytoid proliferation. Hyperglobulinemia associated with macroglobulinemia is characteristic. The Sia test is a useful screening diagnostic test for macroglobulins and consists of the formation of a white flocculum following addition of a drop of the patient's serum to a test tube filled with distilled water.

The etiology of Waldenström's macroglobuli-

nemia is unknown. Macroglobulinemia may coexist with multiple myeloma, leukemia, carcinoma, lymphosarcoma, nephrosis, and a few other diseases.

The neurologic manifestations appearing in 25 per cent of patients follow certain patterns, allowing classification into certain groups: (1) strokes or acute focal brain syndromes, (2) chronic brain syndromes, (3) peripheral nervous system syndromes, and (4) subarachnoid hemorrhage.

Strokes or acute focal brain syndromes. Acute cerebral lesions occur from a few days to several years after the onset of systemic illness. They are usually hemorrhagic in nature, although thrombotic occlusions may occur. Hemiparesis or hemiplegia is the most consistent sign.

Chronic brain syndromes. Neurologic symptoms include headaches, vestibular dysfunction, pyramidal tract signs, extrapyramidal or cerebellar tremor, ataxia, hemiparesis, slurred speech, facial paralysis, autonomic changes, hearing loss, and blurred vision. Pyramidal tract findings with or without paralysis and vestibular dysfunction in the form of dizziness or vertigo are the most consistent manifestations. The mental changes include organic psychosis, progressive personality change, lethargy, and clouding of the sensorium. Retinal changes may be seen in the form of retinal hemorrhages and, to lesser degree, venous engorgement, papillitis, and exudates. Spinal fluid examination may show a moderate increase of cells and, rarely, a high protein. The prognosis of this disease is grave. Most patients die less than one year after the appearance of neuropsychiatric manifestations.

Pathologic findings include lymphoid and plasma cell infiltrations, primarily perivascular, in the brain and the meninges and, to a lesser extent, multiple small hemorrhages in the brain.

Peripheral nervous system syndromes. This group includes cases of simulated Guillain-Barré syndrome, peripheral neuritis, and cranial neuritis, mostly of the eighth nerve. Spinal fluid protein may be elevated. Pain and tenderness are present in half the cases.

Subarachnoid hemorrhage. Subarachnoid hemorrhage has been reported occurring from two to twelve months after onset of the disease. It may occur alone or associated with other syndromes.

CRYOGLOBULINEMIA

Cryoglobulinemia is a condition with a variety of clinical manifestations due to increased blood viscosity and precipitation of cryglobulins in small blood vessels with subsequent stasis, hemorrhage, and thrombosis. Cryoglobulins are abnormal, high molecular weight proteins of low solubility which precipitate below 37° C. and redissolve by heating. Electrophoretically, they usually are found in the gamma globulin fraction. Primary or essential cryoglobulinemia is rare, whereas secondary types have been described in association with several diseases, including multiple myeloma, Waldenström's macroglobulinemia, lymphosarcoma, chronic lymphatic leukemia, collagen disease, chronic infections, and a few others.

The clinical manifestations are best studied in cases of essential cryoglobulinemia and include symptoms associated with ischemia, thrombosis, and hemorrhages. Raynaud's phenomenon; purpura; bleeding from the nose and mouth; ulcers and gangrene of the extremities; and multiple arterial and venous occlusions in the intestinal tract, lungs, retinae, and so on, are common manifestations.

Central nervous system syndromes. Among the most common manifestations from the brain are those of confusional states, psychotic episodes, and states of disturbed sensorium. Progressive loss of hearing and vertigo are the most common chronic manifestations, while focal cerebral insults occur in the form of acute cerebrovascular accidents.

Peripheral nervous system manifestations and retinal changes. Extreme pain in the extremities, usually of burning character, and cramps, occurring especially when exposed to cold, are often typical. Raynaud's phenomenon may be one of the earliest manifestations. True sensorimotor neuropathy is rarely seen and usually is associated with peripheral vasomotor disturbances. Retinal changes in cryoglobulinemia simulate those seen in Waldenström's macroglobulinemia and are the result of increase in blood viscosity.

MULTIPLE MYELOMA

Multiple myeloma is usually regarded as a type of plasmacytoma primarily affecting bones. In rare instances, plasmacytoma may infiltrate diffusely various organs and the blood and produce a true plasma-cell leukemia. In the usual cases of multiple myeloma, few plasma cells may be found in the circulatory blood, so that these cases may be considered as subleukemic plasma-cell leukemias.

Multiple myeloma generally is characterized by pain, usually referable to the back; destructive osseous lesions; moderate normocytic or macrocytic anemia; hyperglobulinemia; and, in many cases, Bence-Jones protein in the urine. Sternal puncture usually reveals excess of plasma

cells, some of which are immature. Roentgenograms reveal the eharaeteristie punehed-out areas in the bones. Autohemagglutination, spontaneous clumping of erythrocytes, thrombocytopenia, macroglobulinemia, or cryoglobulinemia may occur and accounts for the thrombotic tendencies or hemorrhagic diathesis of some cases.

Neurologic manifestations, most of which are due to the proximity of neural tissues to the involved bones, occur in about 50 per cent of eases. The following are the most common neurologie syndromes eneountered:

Cerebral syndromes
- Intracranial tumor syndromes
- Cranial nerve syndromes
- Cerebrovascular syndromes
- Intraorbital tumor syndromes, retinopathy, and optic neuritis

Spinal and radicular syndromes
- Spinal cord and root compression
- Myelopathies and muscular atrophies

Peripheral nerve compression and neuropathy

Intracranial tumor syndromes. There are two varieties of intracranial myeloma, both rare, one arising from myeloma of the skull and the other originating in the dura, with no obvious bony involvement. In both eases, the myeloma may be either a solitary mass or a multiple tumor formation. In rare instances, it presents a diffuse dural infiltration. The tumor grows in the epidural space, exerting pressure effects on the brain. Although it sometimes penetrates the dura, it does not invade cerebral tissue per se. Clinical symptomatology depends upon the location of the expanding mass. Increased intraeranial pressure may predominate, especially in the presence of multiple tumors.

Cranial nerve syndromes. Myeloma at the base of the skull gives rise to cranial nerve palsies. The site of origin is usually the bone and rarely the dura. The nerves are damaged by the pressure exerted from the mass expanding in the epidural spaee. Although all nerves ean be involved, the sixth, eighth, fifth, seeond, and seventh are the most frequently afflicted. The spinal fluid may be under increased pressure and may show a mild lymphoeytic pleocytosis or a mild to moderate increase in protein.

Cerebrosvasenlar syndromes. Subdural hematomas, intracerebral hemorrhages, or multiple petechial hemorrhages have been described as eaused by the hemorrhagic tendeney seen in 25 to 30 per cent of patients with multiple myeloma. Thrombosis of intracerebral vessels, related to the sludging of blood from the inerease in serum globulins, may also occur. Clinically, the eondition may simulate a hemiplegic stroke or present multifocal cerebral manifestations with confusional states or psyehotic manifestations.

Intraorbital tumor syndromes and retinopathy. Orbital myelomas are rare. The most common findings in such eases are a painless proptosis, decreased vision, optic neuritis, and diplopia. The myeloma may be primary or secondary. Thrombosis of the eentral retinal vein and retinal hemorrhages may be seen in the absenee of tumor formation. Such complieations are due to the inereased blood viscosity or hemorrhagic tendeney and may accompany eerebrovascular manifestations.

Spinal eord and root compression. The most common neurologic complication in myeloma, compression of the spinal cord, eauda equina, or roots which may be due to vertebral collapse or secondary to a growing epidural myeloma. The thoraeie spine, especially the fourth to sixth vertebrae, is the most common site of involvement. Invasion of the dura is rare, and infiltration of neural tissue does not occur. Root compression alone may be present, and herpes zoster is not uncommon. Compression of cord or roots is heralded by pain that may preeede the deficit by weeks or months.

Myelopathies. It has been claimed that ehronie myelopathy may oecur in the absence of direet involvement of the eord by myeloma. Cases with posterolateral syndromes, progressive museular atrophy, or Landry's paralysis have been described. The pathology in such eases is that of chronie degeneration and is thought to be the result of some type of toxie effect or secondary to the assoeiated anemia.

Peripheral nerve compression and neuropathy. Besides the cases of peripheral nerve compression by an adjacent bony myeloma, several eases of true neuropathy have been deseribed. There is no evidence to suggest myelomatous infiltration in sueh patients, and pathologie findings have ineluded degeneration of axons and myelin sheaths of the peripheral nerves and, to a lesser degree, of the anterior and posterior roots. The etiologic factors implicated include toxic influences by the abnormal proteins or effects of hyperglobulinemia or amyloid degeneration. Although the latter is a likely hypothesis, since primary amyloidosis known to produce neuropathy is common in myelomatosis, it lacks pathologic confirmation. The clinical pieture is one of peripheral sensorimotor symmetric neuropathy. Pain in the distal parts of the extremities, espe-

cially the hands, and muscle wasting are outstanding features. Occasionally, mononeuritis of vascular origin may be seen. The course of the neuropathy is rapidly progressive, usually producing irreparable nerve damage.

Cerebrospinal fluid in myelomatosis. Increase of protein is not infrequent in myeloma, irrespective of the neurologic complication, although compression of the spinal cord gives the highest protein values. The excess protein, except in the latter cases, is usually due to increase in globulin, which does not necessarily always correlate with an increase in serum globulin. Slight protein elevation can be seen, even in cases with no evidence of neurologic complication.

Some increase in the cellular content of fluid, mostly of lymphocytes, has been described, while increase in the cerebrospinal fluid pressure may be encountered in cases of intracranial myeloma.

RETICULOSES

Involvement of the nervous system in reticuloses occurs in about 10 to 20 per cent of cases, being most frequent in Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma. There is no single neurologic pattern typical of an individual reticulosis, so that all can be discussed together in order to avoid unnecessary repetition. The following classification covers the best-recognized syndromes:

- Cerebral involvement
  - Intracranial tumor syndromes
  - Meningeal reticuloses
  - Stroke syndromes
  - Cranial nerve syndromes
  - Toxic organic dementia
  - Progressive leukoencephalopathy
- Spinal cord involvement
  - Epidural granuloma with cord compression
  - Vertebral collapse with cord compression
  - Myelomalacia from segmental arterial compression
  - Toxic myelopathy
  - Meningeal reticulosis
- Peripheral nerve involvement
  - Herpes zoster
  - Compressive neuritis and radiculitis
  - Infiltrative and noninfiltrative radiculoneuritis (Guillain-Barré syndrome)
  - Toxic peripheral neuropathy
- Retinal involvement
  - Optic atrophy, papilledema
  - Retinal hemorrhages

Cerebral involvement. Although neurologic symptoms may occur early in the course of a reticulosis, involvement of the central nervous system usually indicates the final stage of the disease.

The most common form of intracranial involvement is through epidural deposits or by extension of lesions from the bones of the skull. The expanding lymphomatous mass may cause compression at various sites or invade the cerebral tissue per se. Primary lesions in the brain, mostly cerebellum, with no evidence of systemic lymphoma, are rare. The cerebral symptomatology depends upon the site of involvement, and the presenting picture is one of an expanding intracranial mass.

Meningeal reticulosis may simulate chronic meningitis or, in more acute cases, may take the form of pseudotumor cerebri, with increasing intracranial pressure and papilledema.

Acute pictures of stroke syndromes are usually the result of cerebral hemorrhage due to accompanying thrombopenia.

Involvement of cranial nerves may occur independent of other cerebral manifestations and is the result of lymphomatous masses invading the base of the brain by way of the foramen magnum or extension from bony involvement.

Occasionally, the presenting symptoms are progressive dementia, confusion, stupor and coma. Such cases have been described with no evidence of intracranial deposits of abnormal reticular tissue. A peculiar encephalopathy, characterized by widespread demyelination and relative sparing of axis cylinders, mostly over the posterior parts of the hemispheres, has been reported. It is postulated that some toxic-metabolic factors are responsible for the cerebral manifestations.

Spinal cord involvement. Spinal cord syndromes are the most common neurologic manifestations in reticuloses. The clinical manifestations depend upon the mechanism of cord involvement.

Epidural extension of lymphomas through the intervertebral foramina from mediastinal and retroperitoneal masses or via lymph channels may cause direct cord compression. The clinical picture is one of transverse cord compression and depends upon the rate of growth of the mass and the site of involvement. Anterior compression usually starts with pyramidal tract signs and sensory deficit of spinothalamic origin. Posterior lesions give rise to posterior or posterolateral syndromes. In the case of cervical or lumbosacral lesions, flaccid weakness and atrophies of the extremities mark the level of the lesion as

in any case of cord compression. Lateral lesions cause nerve root irritation, while retroperitoneal tumors may compress nerves outside of the cord, causing low back and leg pains. Herpes zoster is a common complication.

Involvement of vertebral bodies with secondary vertebral collapse causes a rapidly progressing paraplegia. The dorsal spine is the most common site of pathology.

Spinal cord syndromes of vascular origin may be due to occlusion of segmental arterial supply to the cord by mediastinal or retroperitoneal tumors. In such cases, the condition simulates occlusion of the anterior spinal artery.

Occasionally, cases of toxic myelopathy or subacute combined syndrome have been described during lymphoma. The pathologic substrate in such cases is myelomalacia or active demyelination and gliosis.

Spinal meningeal reticulosis may be seen in cases of reticulum cell sarcoma and may be part of a diffuse meningeal involvement.

Peripheral nerve and root involvement. Herpes zoster is a common complication, especially in cases of Hodgkin's disease. The lesion is distributed at various sites and commonly is associated with clinical evidence of active lymphoma corresponding to the root segment involved.

Enlargement of lymph nodes may give rise to local nerve and root compression. Horner's syndrome, brachial plexus involvement, recurrent laryngeal palsy, and lumbar plexus deficit are common manifestations.

Peripheral neuropathy may occur in reticulosis, in most cases as the result of diffuse infiltration of the nerves by reticular deposits.

Typical Guillain-Barré syndrome has been reported in Hodgkin's disease. In one case, it was associated with widespread infiltration of nerve roots and peripheral nerves by neoplastic cells. In another instance, the only changes found were comparable to an extensive neuropathy of allergic origin.

Retinal involvement. Optic atrophy may be due to direct invasion of the optic nerve from adjacent reticular deposits. Papilledema may accompany intracranial reticulosis and was described in a few cases with no evidence of increased intracranial pressure or intracranial lymphoma. Retinal hemorrhages are usually the result of accompanying thrombopenia.

Use of a shoe-raise often eliminates symptoms of short-leg syndrome, that is, low backache or leg pains caused by idiopathic or posttraumatic difference in leg length of more than ½ in. Age of the patient and mobility of the lumbar spine seem to determine, in part, the amount of relief possible.

Backache due to idiopathic short leg usually does not start until late adolescence or early adulthood. Strains of military service or minor injury, especially from lifting, may precipitate symptoms.

Short leg resulting from fracture of a lower limb may delay rehabilitation. To prevent limping and later degeneration of weightbearing joints, early correction of any shortening is essential. Posttraumatic short leg may cause low backache, even after many years; may aggravate other backache-producing conditions; or may be unrelated to symptoms. Trial use of a shoe-raise will determine whether pain is caused by the short limb.

Physical findings with leg length disparity are (1) shoulder held lower on the deformed side, (2) corresponding hip less prominent, (3) loss of the hollow of the flank, (4) gluteal fold lower than on the normal buttock, and (5) compensatory scoliosis and tilt of the pelvis.

Of 180 patients with orthopedic low backache, 22 per cent had a difference of ½ in. or more in leg length. Such disparity was found for 7 per cent of 1,007 patients without backache.

P. J. R. Nichols: Short-leg syndrome. Brit. M. J. 5189:1863-1865, 1960.

Practical Aspects in the Clinical Diagnosis of Congenital Heart Disease

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It is important to emphasize that, in the majority of cases of congenital heart disease, an accurate diagnosis can be made by routine clinical examination, and the seriousness of the lesion, as well as the operative risk, frequently can be predicted from a plain roentgenogram of the thorax, together with the electrocardiogram. It is true, however, that these studies do not always provide the correct answer and that we physicians then must proceed with cardiac catheterization and angiocardiography, and even after these examinations, the diagnosis may not be complete.

In congenital heart disease, the history is not as useful as in acquired heart disease, but it may be extremely helpful in providing diagnostic clues.

TYPE OF PATIENTS

The cyanotic child. A history of persistent cyanosis implies a right-to-left shunt of some type. If severe cyanosis has been present from birth, lesions, such as transposition of the great vessels, pulmonary atresia, aortic atresia, or tricuspid atresia, become good diagnostic possibilities, whereas, if cyanosis has appeared a few days, or weeks, or even months after birth, tetralogy of Fallot or pulmonic stenosis with intact ventricular septum and right-to-left shunt at the atrial level becomes more likely. It is well to appreciate that the degree of cyanosis in tetralogy of Fallot is dependent on the severity of pulmonic stenosis and may vary from minimal to severe, correlating with the oxygen unsaturation of the arterial blood. In patients who have had mild cyanosis since early in life, other lesions to be considered are Ebstein's anomaly, total anomalous pulmonary venous drainage, or a common mixing chamber, as occurs in a single atrium or single ventricle. In patients with cyanosis occurring later in life without intrinsic pulmonary disease, the condition to be considered is the possible development of pulmonary vascular obstruction with a right-to-left shunt at the atrial, ventricular, or aortic level. The reversal of blood flow through a shunt tends to occur much earlier in life when pressure in the shunts is high, as in communications such as a patent ductus arteriosus or ventricular defect, than when the pressure in the shunt is low, as in communications at the atrial level. There is nothing specifically diagnostic about general cyanosis, but the preceding are some of the abnormalities to be considered.

Differential cyanosis, by contrast, may allow a specific diagnosis. In patients with cyanosis of the face, head, arms, and trunk with pink lower extremities, the physician must suspect strongly the presence of transposition of the great vessels, together with patent ductus arteriosus. In the reverse of this situation, namely, pink face, head, and arms, with cyanosis of the lower extremities, reversal of a shunt through a ductus must be suspected when the great vessels are normally oriented. The 2 most common causes of this are coarctation of the aorta proximal to the ductus, so that blood shunts from pulmonary artery into a lower pressure-descending aorta, and pulmonary vascular obstruction, so that pressure in the pulmonary artery is raised above that in the systemic arteries and, again, causes a shunt from pulmonary artery to aorta.

Perhaps I should mention briefly the harlequin baby. Although this condition is not due to a congenital heart lesion, it may cause confusion in the newborn period. In the first few days of life, such a child has one side of the body pink and one side blue. There is apparently a lack of maturity of autonomic control of the peripheral vasculature, so that the dependent side of the child becomes cyanosed because of capillary dilation and stasis. This condition is easily diagnosed by changing the position of the child and observing a change in the distribution of the cyanosis.

Failure to thrive. A cyanotic child with a large left-to-right shunt at the ductus or ven-

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tricular level frequently is irritable, frequently sweats profusely, and may be markedly underdeveloped and undernourished. Diagnosis may be missed in these children because they often resist examination and the physician may be unable to hear a murmur because of their excessive crying. Indeed, with severe straining, the pulmonary pressure may rise sufficiently to lessen the left-to-right shunt and the murmur may diminish or even disappear at the time of examination. The diagnostic possibility of a large left-to-right shunt in this group should always be entertained, particularly if there is a history of repeated respiratory infections.

Apparently normal children. A third group of children to be considered are those who have been in good health but are found to have a murmur during routine physical examination. The diagnosis, which depends on the nature and site of the murmur, may be obvious. The lesions most often detected in this group are aortic stenosis, pulmonic stenosis, atrial septal defect, and small-to-moderate shunts at the ductus or ventricular level. Diagnostic murmurs will be considered a little later. The finding of elevation of blood pressure in the arm with a diminution in the femoral pulses and lowered femoral pressures will, of course, permit the diagnosis of coarctation of the aorta.

PHYSICAL EXAMINATION

In conducting the physical examination for assessment of congenital heart disease, it is wise to follow some system, so that interest in a particular clinical finding will not lead to failure to make a less spectacular but perhaps more pertinent observation. The following routine has no particular merit but has proved satisfactory to me and will serve as a basis for discussion.

While the physician is talking to parents in the office, he can observe many things about a child: Is his development normal? Is he cyanotic? Does he tend to squat while playing about the office? Does he appear breathless with mild or moderate exertion? When the child is on the examining table or in bed, the physician first observes the color of the child; in lesser degrees of cyanosis, it is necessary to examine carefully the fingers and toes. At this time, the presence or absence of clubbing of the extremities can be noted. In cyanotic congenital heart disease, clubbing is in proportion to the severity and duration of cyanosis, and clubbing without cyanosis is not a sign of congenital heart disease.

The next procedure is palpation of the radial and femoral pulses, followed by measurement of the blood pressure in at least the right arm and one leg; if there is any difference in pulse volume, the pressures in all four extremities should be measured. The diagnosis of uncomplicated coarctation of the aorta is so simple to make on the basis of palpation of the femoral pulses and the operation is so successful in good surgical hands that it is a great pity if this lesion is overlooked. Since the site of the aortic coarctation usually is close to the origin of the left subclavian artery, this vessel may be involved at the site of the coarctation and a comparison of the blood pressures in the right and left arms may show a lower pressure in the left than in the right arm. The site of the coarctation then can be predicted more accurately. Since the femoral pulses are not examined by physicians in all patients, it is certainly imperative to check them in any patient, whether a child or an adult, who has an elevated blood pressure in an arm. I recall a patient who was treated in a hypertension clinic for many years before a thoracic tumor was noted in a roentgenogram of the thorax and thoracotomy was performed. The surprised surgeon encountered coarctation of the aorta with an aneurysm of an intercostal artery.

Bounding peripheral pulses are not as helpful diagnostically as diminished femoral pulses, since a wide pulse pressure may have several causes, including excitement, peripheral vasodilation, and a rapid runoff from the aorta in such lesions as patent ductus arteriosus, aorticopulmonary window, ruptured sinus of Valsalva, true truncus arteriosus in some cases, and moderate to severe degrees of aortic insufficiency. Nevertheless, if the bounding pulses cause the physician to consider these possible diagnoses, they have served a useful purpose.

The abdomen is the next area of examination, and here the liver and spleen are of particular interest. Enlargement of the liver is one of the most valuable signs of congestive failure in children. An enlarged liver is easy to palpate through the relatively thin abdominal wall of a child, and the degree of enlargement is easy to measure from day to day. In this regard, examination of the liver provides a better index of congestive failure in children than does examination of the veins of the neck.

Although engorgement and pulsation of the cervical veins are easy to see in the older child, they may be extremely difficult to detect in a baby because of shortness of the neck and are especially hard to see when the baby is crying.

If the liver is enlarged, the veins of the neck must be checked carefully. An enlarged liver caused by heart failure will always be accompa-

nied by distention of the cervical veins, whereas an enlarged liver resulting from intrinsic hepatic disease such as cirrhosis or from inferior vena caval obstruction will not. This is a simple but valuable differential clinical point.

Enlargement of the spleen without associated enlargement of the liver is not secondary to congenital heart disease except when the patient also has bacterial endocarditis or bacterial endarteritis. A careful daily search for petechiae must be carried out on all patients with congenital heart disease who have an apparently unexplained fever. Blood must be drawn for cultures; a minimum of 2 cultures per day for three days should be made, unless a pathogenic organism is recovered in the early stages. Treatment then should not be delayed.

By simple observation of the patient and palpation of the abdomen and peripheral pulses, the examining physician can make considerable progress in diagnosis. At this point in the examination, he has decided whether the patient belongs in the cyanotic or acyanotic group, he has ruled in or out simple coarctation of the aorta, he has decided whether the child is in congestive failure, he has considered several diagnostic possibilities, and he has made an attempt to exclude bacterial endocarditis.

Now attention should be turned to the patient's chest, and several facts should be noted: (1) the general shape and development; (2) any disproportions of the two sides, since a large overactive heart often results in prominence of the overlying chest wall; and (3) the position of maximal pulsation, which may tell whether or not the heart is enlarged or overactive and in which side of the thorax the heart is situated. Percussion adds little to the diagnosis of congenital heart disease and seems to be performed more out of habit than because of any real benefit obtained. The roentgenogram of the thorax is a much better index of cardiac size and shape than is percussion.

Palpation by contrast is very productive. Careful palpation at the point of maximal impulse, along the left sternal border and at the upper right sternal border and in the neck, may be extremely helpful. Whether the heart is overactive, quiet, or normally active is easily determined. The physician decides whether the cardiac impulse is predominantly left ventricular, right ventricular, or combined ventricular in origin. A systolic thrill at the upper left sternal border strongly suggests pulmonic stenosis; at the upper right part of the sternal border, aortic stenosis; and at the lower left part of the sternal border, a ventricular septal defect. It should be remembered that a large patent ductus arteriosus in a small baby may be accompanied by a systolic thrill at the apex, anywhere along the left sternal border, in the left supraclavicular regions, or in the neck.

Palpation of the second heart sound is frequently possible in normal children, and the sharp slap accompanying severe hypertension in the pulmonary artery may be unmistakably abnormal. The examination so far has occupied only a few minutes and yet, without placing a stethoscope on the patient, a considerable amount of information has been gathered. The next step is auscultation of the heart.

AUSCULTATION OF THE HEART

Clinical auscultation of the heart requires diligence and concentration. Again, the physician should develop some form of routine, so that each phase of the cardiac cycle may be considered separately.

Auscultation of the heart is the single most important method in the clinical diagnosis of congenital heart disease. Frequently, murmurs are diagnostic of a specific lesion and, in many other cases, are highly suggestive. Because of the rapid heart rates encountered, auscultation is more difficult in small children and in babies than in adults. This is especially true if there is cardiac embarrassment of any degree. Many children cry or become restless during examination and are unable to cooperate in the temporary arrest of respiration which is so helpful when listening to the hearts of adults or older children.

Heart sounds. In the diagnosis of congenital heart lesions, study of the intensity of the first sound is rarely helpful. By contrast, close attention to the second sound in regard to the presence or absence of splitting and to the intensity of closure of the pulmonic and aortic valves may be most revealing. Obvious splitting of the second sound implies that there are two functioning semilunar valves, and this immediately excludes from consideration such lesions as aortic atresia, pulmonic atresia, or true truncus arteriosus. A single second sound does not necessarily mean that one semilunar valve is absent. It may result from the simultaneous closure of two valves or from accentuation of one closing sound so that the other is masked, or, conversely, one closing sound may be considerably diminished in intensity so that this particular sound is not audible. In some anomalies, the anatomic position of a valve may make

its closure difficult to hear. A normal second sound at the pulmonic area may be split from 0.03 to 0.05 second; the duration of the splitting increases to around 0.07 second on inspiration and may narrow to 0.02 second on full expiration. In atrial septal defect with increased pulmonary blood flow, the duration in the splitting of the second sound may be increased because of the increased duration of right ventricular systole secondary to the left-to-right shunt. Since the increased right ventricular blood flow may persist even at the end of full expiration, delayed closure of the pulmonic valve will persist, and this often is referred to as fixed splitting of the second sound. Widest splitting of the second sound occurs in patients with severe pulmonic valvular stenosis and intact ventricular septum. Under these conditions, right ventricular systole may be considerably prolonged and closure of the pulmonic valve markedly delayed. Two factors make this splitting difficult to hear: (1) a loud pulmonic systolic murmur, which tends to obscure aortic valve closure, and (2) a decrease in intensity of the pulmonic closure, especially when contrasted with the loudness of the systolic murmur. Another possible cause of wide splitting of the second sound is shortening of the left ventricular systole with early closure of the aotic valve in severe mitral insufficiency. Paradoxic splitting of the second sound in aortic stenosis is an uncommon finding in children. It occurs in severe aortic stenosis and results from delayed closure of the aortic valve secondary to prolonged left ventricular systole, with the result that closure of the aortic valve follows closure of the pulmonic valve. The delay of the latter with inspiration causes the duration of splitting to lessen rather than to widen, as usually occurs.

Careful evaluation of the intensity of pulmonic valve closure is of the greatest clinical importance. Diminution in intensity may result from pulmonic stenosis, either at the valve level or in the infundibulum, or from posterior displacement of the pulmonary artery. Increase in intensity results from increase in pulmonary arterial pressure, whether due to increased pulmonary blood flow or to increased pulmonary vascular resistance.

When heart sounds are being considered, the systolic ejection clicks should be mentioned briefly. These extra sounds occur early in systole; they are produced in the aorta or in the pulmonary artery in the presence of increased stroke volume, as in aortic or pulmonic insufficiency, in certain large left-to-right or right-to-left shunts, or in the presence of a dilated aorta or pulmonary artery, usually secondary to stenosis of the aortic or pulmonic valve. A third heart sound is a common finding in children and is of no specific diagnostic significance. Gallop sounds will not be discussed except to say that presystolic gallops caused by audible atrial sounds imply increased atrial pressure from any cause, whereas protodiastolic gallops imply ventricular embarrassment from any cause.

Systolic murmurs. The murmurs associated with congenital heart disease may be tremendously helpful in diagnosis. The rough stenotic murmurs at the upper left part of the sternal border in pulmonic stenosis and at the upper right part of the sternal border in aortic stenosis are difficult to mistake. In the interpretation of any murmur, the physician must be sure that the great vessels are normally oriented and that the heart is normally situated. The systolic murmur heard at the upper right part of the sternal border which is so typical of congenital aortic stenosis in vessels normally oriented also can be produced by pulmonic stenosis in a patient with corrected transposition of the great vessels or in peripheral stenosis of the right main pulmonary artery, but other factors in the cardiac examination should allow the differential diagnosis to be resolved.

Holosystolic murmur of ventricular septal defect heard over the lower left part of the sternal border is well known to all clinicians but occasionally may be missed because of unsuspected infundibular pulmonic stenosis or subaortic stenosis, which may closely resemble the murmur of a ventricular defect.

Continuous murmurs. The Gibson machinery murmur heard over the left upper part of the chest in patent ductus arteriosus is fairly typical, but other causes of continuous murmurs must run through the examiner's mind. These include (1) flow across a constricted artery in coarctation of the aorta or in some cases of peripheral pulmonary arterial stenosis, (2) collateral flow through the internal mammary arteries in coarctation of the aorta or through the collateral bronchial vessels in severe tetralogy of Fallot or in pulmonary atresia, (3) a continuous venous hum in total anomalous pulmonary venous drainage and in many normal children, (4) a large flow through pulmonary arteries in true truncus arteriosus, and (5) the much more common finding of a continuous murmur secondary to a previous Blalock or a Potts shunt for tetralogy of Fallot or for tricuspid atresia, which is encountered reasonably often. Other less common

causes of continuous murmurs are coronary arteriovenous fistulae, ruptured sinus of Valsalva, and pulmonary arteriovenous aneurysms. In the great majority of these instances, other factors in the clinical examination or in the thoracic roentgenogram and electrocardiogram will enable the clinician to make an accurate differential diagnosis.

Diastolic murmurs. True stenosis of the atrioventricular valves is uncommon in congenital heart disease, but relative stenosis secondary to increased blood flow through those valves is common and so, therefore, are mitral and tricuspid diastolic murmurs.

Any large left-to-right shunt at the ventricular or aortic level will result in increased blood flow through the mitral valve and will be associated with an apical, middiastolic, and, less commonly, a presystolic murmur. Any large left-to-right shunt at the atrial level via an atrial defect or in association with anomalous pulmonary venous drainage results in increased flow through the tricuspid valve and is associated with a tricuspid diastolic murmur.

Aortic diastolic murmurs are relatively uncommon in congenital heart disease. Mild aortic insufficiency may be noted in coarctation of the aorta with an associated incompetent bicuspid aortic valve and also in some cases of aortic stenosis, usually of the subvalvular type, but a more serious situation may occur in the combined lesion of ventricular septal defect with congenital deformity of the aortic valve. Severe aortic insufficiency then may be noted. Approximately half of this latter group of patients also have associated pulmonic stenosis, usually infundibular in nature. In an occasional child, aortic insufficiency is associated with Marfan's syndrome, in which there is dilation of the ascending aorta and of the aortic valve ring; in a few children, aortic insufficiency follows bacterial endocarditis superimposed on a bicuspid aortic valve.

Murmurs denoting pulmonic insufficiency are of 3 types:

1. Those secondary to dilation of the valve ring are (a) the so-called idiopathic group, (b) those sometimes associated with large left-to-right shunts, and now (c) those encountered after the insertion of a plastic prosthesis across the pulmonary valve ring in the complete surgical repair of tetralogy of Fallot.

2. This type of murmur may be secondary to greatly increased pressure in the pulmonary artery usually associated with increased pulmonary vascular resistance; whereas, in the first group, closure of the pulmonary valve is not accentuated except in the large left-to-right shunts with increased pressure in the pulmonary artery, in this group, pulmonic closure may be very loud.

3. This type of murmur is associated with deformity of the pulmonary valvular cusps, which may occur on a congenital basis, usually in association with tetralogy of Fallot, or on an acquired basis, secondary to surgical relief of pulmonic stenosis.

ROENTGENOLOGY

The plain posteroanterior roentgenogram must be considered a routine part of any cardiovascular examination and provides information on: (1) the position of the heart in the thorax and its general configuration; (2) the size of the heart in transverse diameter; (3) gross alterations from normal in the positions of the great vessels; and (4) pulmonary vasculature—whether it is normal, increased, or diminished.

The position of the heart in the thorax—that is, whether there is dextrocardia or levocardia and whether there is transposition of the viscera below the diaphragm—is important, since certain complex malformations are more likely to be present in isolated dextrocardia or levocardia.

The size of the heart is increased in lesions in which there is considerable increase in output of either the right or the left ventricle. Unless this is caused by persistent tachycardia, stroke volume is increased, as is the end diastolic volume of the affected chambers. Less striking degrees of cardiomegaly may be noted secondary to systolic overwork of a particular chamber, as in some cases of severe aortic or pulmonic stenosis. Cardiomegaly is much more severe when secondary to cardiac dilation than when secondary to hypertrophy. It is, therefore, more apparent in association with shunt lesions and valvular incompetence or with myocardial failure from any cause than it is in association with uncomplicated obstructive lesions.

Determining the position of the great vessels is helpful when these can be seen in the plain roentgenogram, especially if there is some obvious abnormality, such as poststenotic dilation or hypoplasia of the aorta or pulmonary artery. If the great vessels cannot be identified, then the physician is on less certain grounds, for if a vessel cannot be seen, he cannot be sure whether it is displaced, hypoplastic, or even absent. At times, oblique or lateral views are helpful, and fluoroscopy after a barium swallow is essential in patients suspected of having some form of vascular ring or when identification of the side of the aortic arch is necessary and in evaluation of atrial size. Notching of the ribs

with coarctation of the aorta is too well known to need reemphasis.

The pulmonary vasculature will be normal in obstructive lesions, such as coarctation of the aorta, aortic stenosis, and pulmonary stenosis, unless congestive failure is associated. The pulmonary vasculature may be increased in coarctation of the aorta or aortic stenosis with congestive failure but it may be diminished in pulmonary stenosis with congestive failure. It will be increased in any left-to-right shunt of moderate-to-large size, whether this be at the aortic, ventricular, or atrial level in acyanotic patients or associated with transposition of the great vessels or the pulmonary venous return in cyanotic patients. Diminished pulmonary vasculature will occur when there is severe obstruction to blood flow to the lungs, together with an intracardiac defect. This is seen most commonly in tetralogy of Fallot and tricuspid atresia but may occur in more complex lesions, such as single ventricle with pulmonic stenosis or atresia or transposition of the great vessels with pulmonic stenosis. In patients with pulmonary vascular obstruction in association with left-to-right shunts, there may be considerable disproportion between the size of the hilar vessels, which are prominent, and the size of the peripheral pulmonary vessels, which are considerably diminished.

ELECTROCARDIOGRAPHY

The electrocardiogram is extremely useful in the assessment of the severity of various forms of congenital heart disease, as well as in differential diagnosis. Apart from the usual observations concerning the rate and rhythm of the heart, the electrocardiogram is helpful (1) in determining left, right, or combined atrial hypertrophy; (2) in assessing right, left, or combined ventricular overload; and (3) in determining whether this overload pattern is secondary to increased blood flow, as in left-to-right shunts, or to increased pressure, as in obstructive lesions. In some situations, the ability to draw a frontal plane vector is extremely helpful.

A few examples of the usefulness of the electrocardiogram will be mentioned. In the selection of patients with ventricular septal defect for corrective surgery, it is important that the shunt through the defect be predominantly left to right and not balanced or predominantly right to left. If other causes of left ventricular overload, such as mitral insufficiency or aortic stenosis, can be excluded from this group, then left ventricular overloading, even in the presence of severe right ventricular overloading, is an indication of operability.

In a patient with uncomplicated ventricular septal defect, the electrocardiogram shows Q waves in the left precordial leads. If these Q waves are absent, and particularly if Q waves are present in lead V_1, a more complicated lesion, such as corrected transposition or single ventricle, must be suspected. Other patients whose clinical conditions resemble ventricular defect but whose electrocardiograms show left axis deviation with a counterclockwise frontal plane loop are more likely to have a form of atrioventricular canal with a different surgical prognosis. At times, a patient will be encountered who has all the clinical signs that are consistent with total anomalous pulmonary venous drainage; a counterclockwise loop in these circumstances makes possible the diagnosis of a single atrium.

Other examples of the usefulness of the electrocardiogram are ST depressions and T wave inversions seen in the left precordial leads in congenital aortic stenosis, which reveal that the disease is severe; corresponding findings in the right precordial leads in pulmonic stenosis indicate extremely high pressure in the right ventricle.

The P waves are less useful in differential diagnosis, but in one situation they may be most helpful. In an occasional cyanotic patient with a pulmonic systolic murmur and right ventricular systolic overload, it may be difficult to decide whether the right-to-left shunt is at the atrial or the ventricular level. Small P waves suggest that the shunt is at the ventricular level and very large ones suggest it is probably at the atrial level. There are many other possible examples of the diagnostic usefulness of the electrocardiogram, but these are some of the more common ones.

SUMMARY

This paper presents a brief review of the clinical approach to some of the more common lesions in congenital heart disease. No attempt has been made to discuss the more complicated lesions, since these are rarely diagnosed on a purely clinical basis. The procedures of cardiac catheterization and angiocardiography are not office procedures and so have not been discussed.

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Psychologic Factors in Hypertension

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In the nebulous area that surrounds the etiology and treatment of most types of hypertensive disease, it is somewhat presumptuous for a psychiatrist to attempt any clarification. Several points, however, are of interest.

First, let me draw attention to a question of therapy which most texts and articles do not fail to mention. Whatever else is suggested, the physician tells the patient that he should learn to relax, to be less tense, to take life a little easier, to drop some committees, to be less competitive, to control his temper and avoid getting angry, to take vacations more often, and so on. Thus it seems that, although no specific therapy is known, most physicians believe intuitively that emotions and tension play some part in the hypertensive process.

One can raise two pertinent questions based on this observation: Do physicians believe that emotional factors are important from a causative standpoint? Or, do they believe that emotional factors aggravate a condition that has its etiology elsewhere? It is, of course, possible that neither or both of these conditions are true.

PHYSIOLOGIC FACTORS

There are 3 major components involved in pressure within the arterial system: (1) the flow resistance imposed by the pipes or tubing; (2) the force of the pump; and (3) the composition of the fluid pumped, predominantly, the viscosity of the blood. Of these 3 components, it is generally felt that increased flow resistance within the smaller branches of the arterial tree due to vasoconstriction accounts for part of the rises in blood pressure seen under the impact of emotion. In the event that there is a proportionately larger degree of vasoconstriction than vasodilation to equalize the pressure, blood pressure will rise. This is thought to be an important cause of rises of pressure under emotional impact—that is, widespread vasoconstriction at the arteriolar level. This can sometimes be observed directly in the skin, as in blanching under the impact of anger, rage, or fear. We speak of "white with rage," which is constriction of small facial vessels. The quick rises of blood pressure caused by guilt or fear of discovery are used in lie detection work, along with changes in pulse rate, respiratory rate and volume exchange, and electrical potential differences measured in the fingers. This so-called psychogalvanic current, incidentally, probably measures electrical potentials set up by secretion of sweat glands, another vasomotor phenomenon related to emotions.

The second factor which is probably heavily involved in blood pressure rise under emotional impact is the force of the pump. Effects exerted through the hypothalamic-vagal-sympathetic routes are important factors in controlling the strength of the heart beat.

It is doubtful that blood viscosity plays a part in pressure changes related to emotion.

ROLE OF EMOTION

It is a fact that blood pressure may rise under emotional conditions. I assume it is also a fact that sharp rises in blood pressure may do damage to a patient who has hypertensive cardiovascular disease.

The major question that arises from a clinical and pathologic standpoint is most interesting but cannot be answered in the light of present knowledge. The question might read: is it possible that, if pressure changes resulting from the physiology of emotion are long-continued or particularly drastic, they will ultimately produce the pathologic changes in the arterial wall commonly associated with essential hypertension, atherosclerosis, and so on? Although there is no present answer to the question, is there anything that can be said about it?

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In the face of the current multi-factorial concept of the disease process, it would seem unlikely that a unitary factor—if emotional factors can be considered unitary in nature—would turn out to be the sole variable involved. Current evidence indicates that hypertension may arise from numerous sources, such as renal factors and certain endocrine disease. In the vast group of unexplained hypertensive and arterial diseases, probably the best guess is that emotion may be a piece of the whole etiologic pie and that such a factor, assuming it exists, would probably show large individual differences from patient to patient. Thus, emotional factors might be of utmost importance in the hypertension of patient A but negligible in patient B.

Interesting and important as this question is and much as one wishes there were factual data about it, it will have to await well-designed research of the future for its solution.

SUMMARY

In summary, if we come back to the observation with which we started—that doctors believe it helpful to advise hypertensive patients to relax—we must admit that this is probably based on the fact that blood pressure variations due to emotion may hurt or aggravate the patient—may, in fact, kill him—whatever the basic causes of the hypertensive disease may be. But it cannot be stated, as of 1961, that emotional factors are or are not important in the etiology itself.

LOCAL COOLING with ice water or ice-cold compresses is effective first-aid emergency treatment for burns of all degrees affecting less than 20 per cent of the body surface. Pain is relieved immediately; redness, blistering, and, probably, healing time are reduced.

Therapy should be started immediately, since the time between injury and treatment determines the result. The burned area is immersed, when possible, in a basin containing cold tap water, ice cubes, and hexachlorophene (pHisoHex). When areas like the head, neck, or chest are burned, cold wet towels, kept in a bucket of ice water, are applied. The ice cubes must be replaced continuously to keep the water at 5 to 13° C. Pain will return if water or packs become warm or treatment is stopped too soon. Thirty minutes to five hours of local cooling may be required before therapy can be discontinued without return of pain. Then, if absolutely necessary, minimal sterile debridement is performed, followed by conventional treatment as needed.

In almost every instance, 150 patients with thermal, chemical, or electrical burns of all degrees on less than 20 per cent of body area obtained instant relief of pain with ice-water therapy. Usually, pain was almost completely gone after two or three hours; with standard treatment, the pain with a first-degree burn ordinarily lasts a day or more. The total treatment time and number of office visits were reduced by about two-thirds. No infections occurred in patients treated within an hour of injury. In 1 patient, steam burns treated with ice-water compresses completely healed in one day while an overlooked burn patch remained painful, blistered, and crusted and required more than two weeks to heal.

A. G. SHULMAN: Ice water as primary treatment of burns. J.A.M.A. 173:1916-1919, 1960.

Eosinophilic Granuloma of the Lung

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EOSINOPHILIC GRANULOMA confined to the lungs was first reported by Farinacci and associates[1] in 1951. There have been 25 case reports[1–13] of this relatively rare entity until this time. This figure does not include case reports of eosinophilic granuloma of the lung which have had associated bone lesions[14–17] or diabetes insipidus[13,18–20] because the disease cannot be considered confined to the lungs when these manifestations are present. Although the histopathology of all these cases has been very similar, there has been considerable variation in symptomatology and response to therapy.

We have recently had the opportunity to study a case with a remarkably benign course despite extensive radiographic and histopathologic abnormalities. We believe that a report of this case and a discussion of the literature will aid in the clarification of this disease process and its delineation within the broad spectrum of diseases included in Lichtenstein's classification of histiocytosis X.[21]

CASE REPORT

E.F., a 44-year-old male x-ray technician, was first seen in October 1959 because of nonspecific changes found on a routine chest roentgenogram. The patient had had a posteroanterior chest film in July 1959, at which time the lungs appeared normal (figure 1). Two months later, another chest film showed nonspecific local infiltrative lesions in both upper lung fields, with prominent bronchovesicular markings throughout both lungs. Initially, these lesions were small and poorly defined, but subsequent films during the next two months showed progression, with increase in the size and number of the small infiltrates and coalescence in some areas (figure 2).

Skeletal survey was negative. There was no weight loss, fever, malaise, or sputum production. Mild, nonproductive cigaret cough was the patient's only symptom. He customarily smoked one-half to one pack of cigarets and at least one pipe per day.

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The patient, an Air Force sergeant, had been stationed in the southern United States and England during his seventeen years of service, before which he had worked for five years in an electroplating plant with some contact with powdered ferrous chloride. He had had an episode of atypical pneumonia requiring hospitalization eighteen years before the present illness. There were no family history or known contact with tuberculosis and no known allergies.

Physical examination revealed a slender but normally developed white man. Blood pressure was 126/74, pulse 88, and respiration 18. Examination of the chest revealed full and equal expansion bilaterally, with normal movement of both diaphragms. Breath sounds were slightly diminished but vesicular, without rales or rhonchi. The remainder of the physical examination was unremarkable. Laboratory work showed hematocrit, 47; hemoglobin, 16 gm. per cent; white blood count, 13,300, with 73 per cent neutrophils, 18 per cent lymphocytes, 5 per cent monocytes, and 4 per cent eosinophils; and urinalysis, normal. Coccidioidin and blastomycin skin tests were negative. First strength P.P.D. was negative, but intermediate P.P.D. and histoplasmin skin tests were positive.

In November 1959, with the patient under general anesthesia, surgical exploration of the left chest revealed nodularity throughout the upper lobe and in the superior segment of the lower lobe, the nodules varying in size from 0.1 to 1.5 cm. There was no significant hilar lymphadenopathy.

A wedge biopsy was taken from the left lower lobe. The biopsy specimen showed deep anthracotic staining and contained several almost spherical, firm, gray-white nodules, varying from 0.1 to 0.4 cm. in diameter. No cystic changes were evident, and the overlying pleura was smooth and glistening. Microscopic examination revealed these nodules to be composed of fibrous tissue, histiocytes, lymphocytes, and numerous eosinophils, as well as a few neutrophils, with destruction of the normal pulmonary architecture (figure 3). Clumps of eosinophils in these granulomas were particularly striking, although some nodules appeared more densely fibrous, with fewer eosinophils. The granulomas were moderately well circumscribed, but adjacent alveolar walls showed fibrous thickening. Vascular changes within and adjacent to the granulomas were prominent, with small arteries showing intimal proliferation and neutrophils and eosinophils within their walls (figure 4). Elastic tissue stains showed disruption of the elastica of these blood vessels. Several blood vessel lumens were completely obliterated by this process. Anthracotic pigment was prominent in the interstitial tissue as well as within numerous macro-

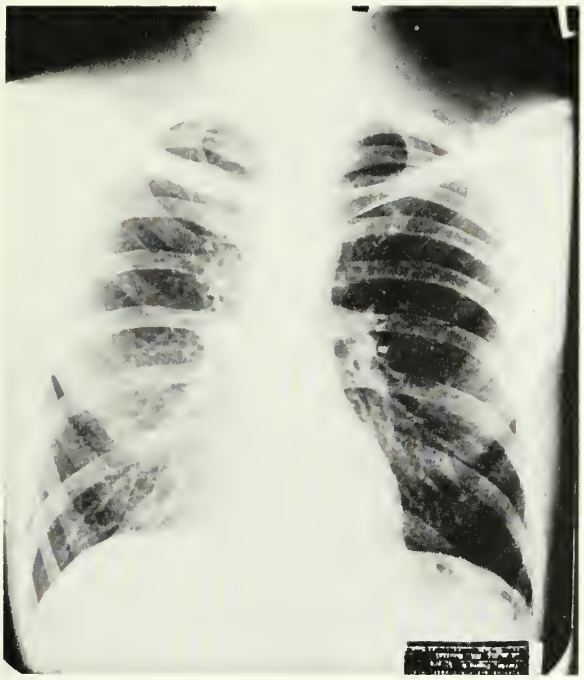

Fig. 1. Posteroanterior view of the chest in July 1959 shows a few calcifications in the right hilar area but is otherwise negative.

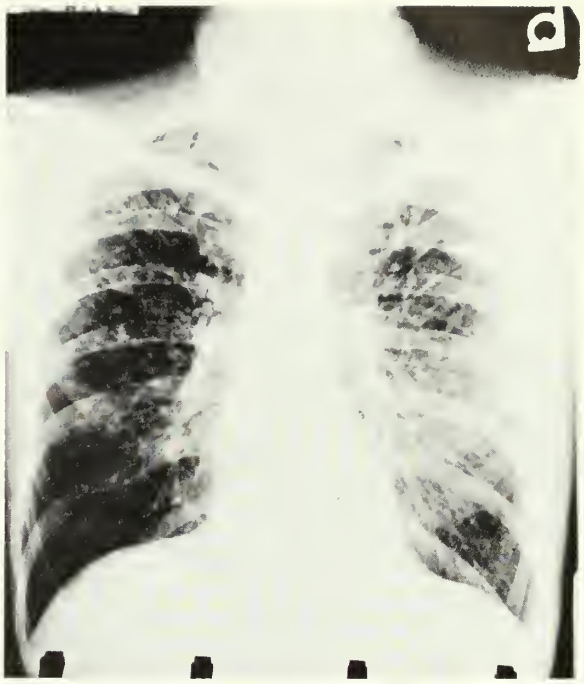

Fig. 2. PA view, October 1959, shows a widely disseminated bilateral reticulonodular infiltration; coalescence in several areas; a moderate amount of associated fibrosis.

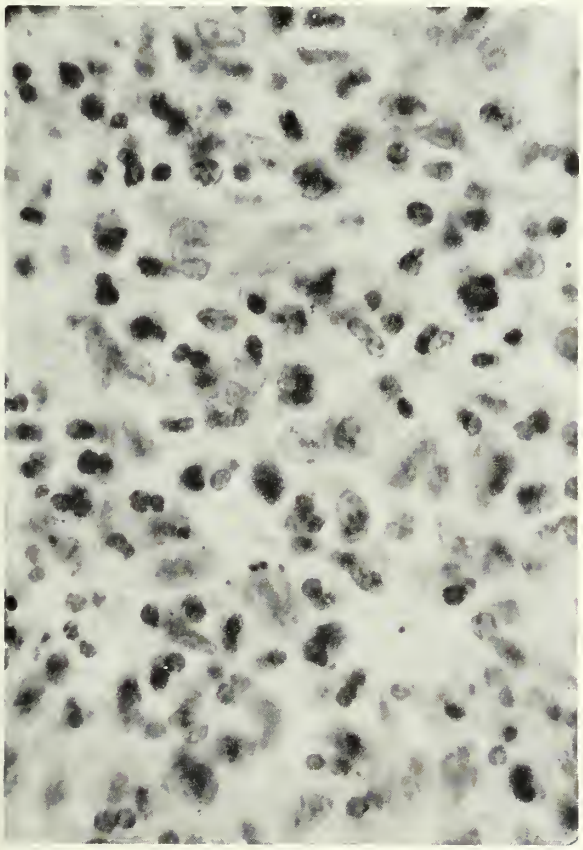

Fig. 3. Nodules are composed of histiocytes, plump fibrocytes, and numerous eosinophils, with occasional neutrophils and lymphocytes. Normal architecture destroyed.

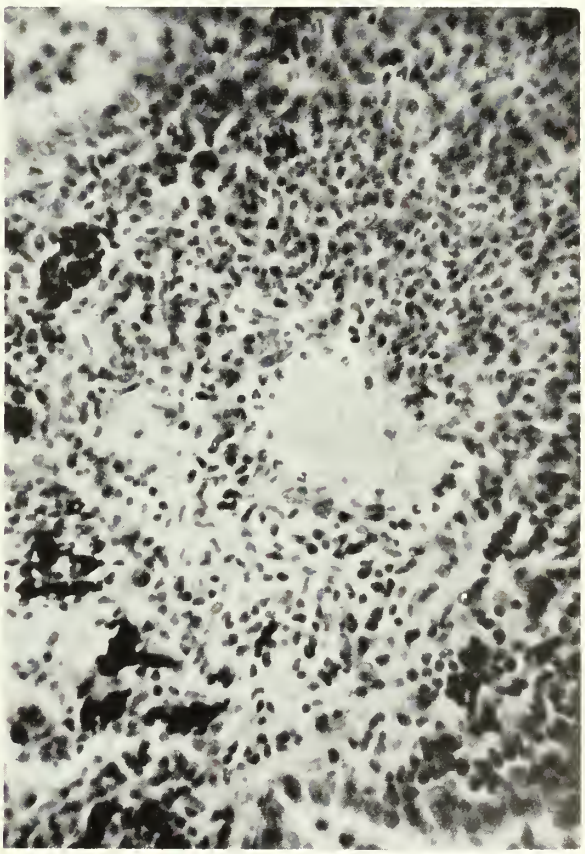

Fig. 4. Small artery within a granuloma shows neutrophils and eosinophils within its wall, with early destruction.

phages in the alveoli. Acid-fast, P.A.S. (periodic acid Schiff), and gram stains did not reveal any causative organism. Cultures for bacteria, fungi, and tuberculosis were negative, and guinea pig inoculation for tuberculosis was also negative.

The patient had an uneventful postoperative course. Within six to eight weeks after surgery, his cough became productive of a slight amount of yellow-white material and his weight dropped approximately 5 lb. Six months later, with no therapy, he had regained preoperative weight and was completely asymptomatic. Films taken during the early postoperative period showed further progression, with involvement of all lung fields, but the latest follow-up film, taken September 6, 1960, showed marked clearing, with almost complete disappearance of the infiltrative lesions (figure 5).

DISCUSSION

The 26 cases in the literature are summarized in table 1. The average age of patients reported is 34, with a range from 15 to 60; about half are in the third decade. Only 3 cases have been noted in women. This overwhelming male predominance may be partly explained by the fact that many of the case reports are from federal hospitals, where large groups of relatively healthy men are subjected to annual physicals and chest examinations. These institutions are also more likely to proceed to lung biopsy at the height of the disease to establish a diagnosis for determination of suitability for continued military service and eligibility for medical discharge and compensation. This factor alone is probably insufficient to account completely for the overwhelming male predominance, however, so that the greater frequency in men is no doubt a real one, even if less than indicated by published reports. The cases in the 3 females reported[7,10,13] were not remarkably different from those in the males, although the symptoms in 1 of the women[10] were more severe than in the average male.

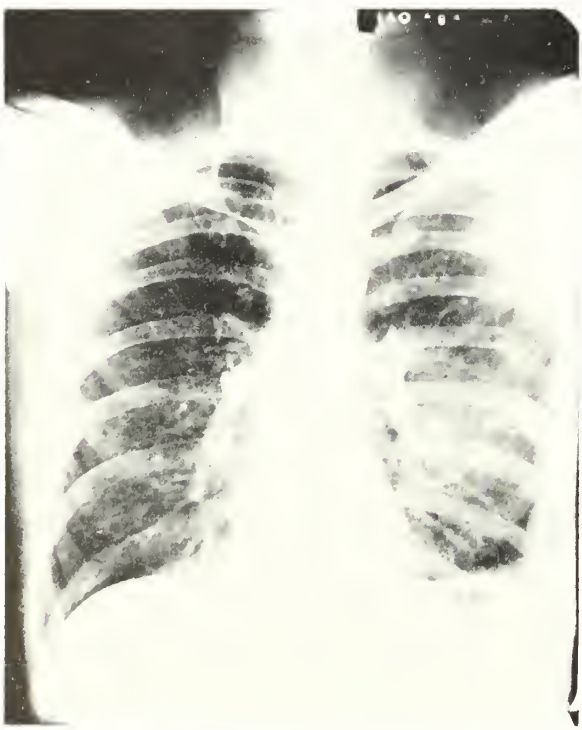

Fig. 5. Posteroanterior view of the chest in September 1960 shows marked clearing, with almost complete disappearance of infiltration. Note postoperative changes and slight residual fibrosis.

SYMPTOMS

Three patients were completely asymptomatic, suspicion of disease being raised from a routine type of chest roentgenogram. Symptoms of the other 23 patients are listed in table 2.

In most cases, the symptoms were not severe. However, a 57-year-old man[10] was bedfast and required intermittent oxygen, and a 30-year-old woman[10] had severe exertional dyspnea. The average patient had symptoms for ten months before diagnostic lung biopsy, with a range from one month to three years. Nonproductive cough was the most common symptom, usually of less than one year's duration. Of those with a productive cough, most produced only a small amount of sputum, although 1 patient[1] produced up to 120 cc. a day. The sputum was described as gray-white and mucopurulent, later as foamy white[2] or as yellow phlegm.[12]

Weight loss has varied from 5 to 40 lb., with an average of 14 lb., before lung biopsy and was not usually noted as a prominent feature, although, in one case,[6] a weight loss of 5 lb. was the only symptom of the disease.

Dyspnea may be only slight, more notable on exertion, but may be incapacitating, as noted in 2 cases,[10] 1 of which required intermittent oxygen. Fatigue was noted as a symptom in those patients with extreme dyspnea, prominent cough, or heavy weight loss.

Chest pain is an unusual symptom and is not of a distinctive type. One patient[11] noted occasional pain in the anterior chest wall during deep inspiration, while another[5] noted pain in the chest on raising his arm. Spontaneous pneumothorax occurred in 3 men. Hemoptysis was noted in only 1 patient[8] and was not a prominent feature. The afternoon fever in 1 case[1] was 99 to 100° F. during hospitalization. Palpitations or anorexia occurred in the 2 patients[10] most severely dyspneic.

Acierno[11] believes that the symptomatology is dependent upon 4 pathologic factors: (1) proportion of lung tissue destroyed, (2) degree of fibrosis and obstructive emphysema that may

TABLE 1

REPORTED CASES OF EOSINOPHILIC GRANULOMA OF THE LUNG

Case	*Author*	*Age*	*Sex*	*Symptoms*	*Therapy*	*Clinical course*	*Follow-up roentgenograms*
1	Farinacci et al.[1] (1951)	32	M	Fatigue, weight loss, productive cough	None	Not described	Clearing with residual fibrosis
2	Farinacci et al.[1] (1951)	24	M	Prolonged cough, weight loss	ACTH	Not described	Clearing with residual fibrosis
3	Mazzitello[2] (1954)	35	M	Productive cough, weight loss, exertional dyspnea	ACTH, cortisone	Became asymptomatic	Not described
4	Mazzitello[2] (1954)	23	M	Chronic cough	ACTH	Became asymptomatic	Not described
5	Virshup & Goldman[3] (1956)	15	M	Asymptomatic	Antibiotics	Continued asymptomatic	Moderate clearing
6	Arnett & Schulz[4] (1957)	26	M	Productive cough, weight loss	Antituberculosis therapy	Became asymptomatic	Clearing with residual fibrosis
7	Arnett & Schulz[4] (1957)	23	M	Nonproductive cough	Irradiation	Became asymptomatic	Clearing with residual fibrosis
8	Arnett & Schulz[4] (1957)	27	M	Asymptomatic	Cortisone, irradiation	Continued asymptomatic	No change
9	Arnett & Schulz[4] (1957)	35	M	Nonproductive cough	None	Became asymptomatic	Clearing with recurrence of nodular lesions
10	Arnett & Schulz[4] (1957)	52	M	Chronic cough, fatigue, weight loss	Antituberculosis therapy	Became asymptomatic	No change
11	Auld[5] (1957)	20	M	Chest pain, nonproductive cough	None	Became asymptomatic	No change
12	Auld[5] (1957)	23	M	Productive cough, spontaneous pneumothorax	ACTH, cortisone	Improved	No change
13	Auld[5] (1957)	24	M	Nonproductive cough, weight loss, spontaneous pneumothorax	Irradiation	Became asymptomatic	Some clearing
14	Thompson et al.[6] (1958)	45	M	Slight weight loss	Cortisone, ACTH	Improved	Almost complete clearing
15	Livingston[7] (1958)	21	F	Intermittent cough	Cortisone	Became asymptomatic	Eventual clearing
16	Myers[8] (1959)	28	M	Productive cough, hemoptysis (2X)	Not described	Not described	Not described
17	Pagan-Carlo & Haley[9] (1959)	59	M	Asymptomatic	Cortisone	Continued asymptomatic	Marked clearing
18	Anderson & Foraker[10] (1959)	30	F	Fatigue, weight loss, nonproductive congh, exertional dyspnea	Cortisone	Became asymptomatic	Clearing with residual fibrosis
19	Anderson & Foraker[10] (1959)	57	M	Fatigue, slight weight loss, nonproductive cough, exertional dyspnea	Cortisone	Marked improvement	Moderate clearing
20	Acierno[11] (1959)	21	M	Occasional chest pain	None	Became asymptomatic	No change
21	Mengis[12] (1959)	28	M	Productive cough	Cortisone	No significant improvement	No change
22	Nadeau et al.[13] (1960)	39	M	Mild cough, recurrent pneumothorax	Cortisone	Not described	Not described
23	Nadeau et al.[13] (1960)	60	M	Mild cough	Cortisone	Became asymptomatic	Considerable clearing
24	Nadeau et al.[13] (1960)	50	M	Mild cough	Cortisone	Became asymptomatic	Moderate clearing
25	Nadeau et al.[13] (1960)	39	F	Mild cough	Cortisone	Mild pulmonary insufficiency	No change
26	Burrows et al.	44	M	Nonproductive cough	None	Became asymptomatic	Almost complete clearing

TABLE 2
SYMPTOMS OF 23 PATIENTS WITH EOSINOPHILIC GRANULOMA OF THE LUNG

Cough	21
Nonproductive, 15; productive, 6	
Weight loss	9
Dyspnea	4
Fatigue	4
Chest pain	2
Spontaneous pneumothorax	3
Hemoptysis	1
Afternoon fever	1
Palpitations	1
Anorexia	1

follow bronchiolar infiltration, (3) potentiality of rupture of emphysematous blebs, and (4) progress of the disease process with extent of regression and degree of reparative fibrosis. The usual patient appears to be a young or middle-aged man with a chronic nonproductive cough and moderate weight loss of less than one year's duration.

PHYSICAL EXAMINATION AND LABORATORY FINDINGS

Physical examination is usually normal except for nonspecific rales in the chest, unless pneumothorax has occurred.[5] Bronchoscopy is not remarkable except that there may be diffuse erythema of the bronchial mucosa.[2,3]

Laboratory examinations are not diagnostic. Of those reports including a notation of white blood count, 36 per cent have had eosinophilia of peripheral blood and 41 per cent have had a total white blood count of over 10,000. Sedimentation rate may be elevated. Serum globulins may be elevated so that the albumin-globulin ratio is only slightly greater than 1 or may be reversed. Smears of sputum and bronchial washings may show large numbers of eosinophils.[1]

ROENTGENOGRAPHIC FINDINGS

The radiographic appearance of the lungs in primary pulmonary eosinophilic granuloma is identical with that of Letterer-Siwe and Hand-Schüller-Christian diseases. All cases show essentially the same roentgen findings, which consist of a widely disseminated, bilateral reticulonodular infiltration. The nodules vary in size from barely visible to around 1.5 cm. and are usually quite soft in appearance, with ill-defined, hazy margins.[1] There is usually a diffuse reticulated background indicating interstitial fibrosis. In the early stages, the infiltrate is generally nodular or miliary, while in the chronic phase, reticulations are more characteristic. The fibrosis usually increases as the disease progresses. Frequently interspersed between the nodular densities are small, local, cystic areas of emphysema, giving the radiographic appearance of the so-called honeycomb lung.

In several of the cases reviewed, the patient had had a negative chest film as recently as six months to a year before onset of the disease. In other cases, the roentgen changes occurred over a considerably longer period. Follow-up roentgen examinations in a few cases showed almost complete resolution of the pulmonary changes. However, in most cases, roentgen findings remained unchanged or showed clearing of nodular infiltration, with residual fibrosis persisting.

PATHOLOGY

All cases reported in the literature have required lung biopsy and histopathologic examination of lung tissue for definitive diagnosis. Despite a suggestive history and laboratory findings, together with a characteristic chest roentgenogram, the final diagnosis must rest upon lung biopsy.

The histopathologic lesions have been extensively described.[3–5,10,12,13,22] The lungs contain small, firm, gray-white nodules which are visible or palpable beneath the pleural surface. The overlying pleura may be puckered. These nodules are usually miliary in size but may be as large as 2 cm. in diameter. They are scattered throughout the lungs but may appear more confluent at the hilar regions. Their margins are indistinct and they do not show any special relationship to the bronchi. Cystic changes may be evident, ranging from small surface blebs to giant bullae.

Histologically, there is a diffuse granulomatous process in the form of both distinct nodules and thickening of the alveolar septa. There are numerous histiocytes and large groups of eosinophils in early lesions, and this may progress to a more fibrous lesion with elastic tissue destruction. The number of eosinophils is not considered a good indication of the age of the lesion. Occasional multinucleated cells may be present. While lymphocytes and plasma cells may be scattered in the lesions, they are never a prominent feature, thus distinguishing the lesion from chronic interstitial pneumonitis. Necrosis has been described[5] in the center of the larger lesions but has not been noted in most reports and was not present in our case. Numerous intra-alveolar macrophages containing anthracotic pigment is often a prominent feature[4] but is probably of no significance.

Vascular changes may be a prominent feature, with involvement of small arteries and arterioles.

There is intimal proliferation and disruption of the elastic tissue in the vessel walls, with fibrosis and eosinophils within the vessel walls. These arteriolitic changes narrow the vessel lumens so that it is somewhat surprising that necrosis is not a more prominent feature. The granulomatous nodules do not show any constant relationship to the vascular lesions.

Cyst formation is a variable feature and may represent the coalescence of disrupted alveolar walls and dilated bronchioles secondary to elastic tissue destruction and fibrosis.[22] Cystic changes may result from bronchiolar obstruction produced by granulomatous proliferation and interstitial fibrosis.[3] When necrosis is a prominent feature, it may be followed by cyst formation and fibrosis.[5] If the cyst formation is extensive, it may lead to a honeycomb lung.[18] Rupture of emphysematous blebs is the probable cause of the spontaneous pneumothorax observed in 12 per cent of patients.

THERAPY

Results of therapy with irradiation and corticosteroids have been variable; 14 patients received corticosteriods, with definite objective improvement in 10, no change in 2, subjective improvement in 1 despite no change in the chest roentgenogram, and no follow-up in 1. Of the 10 cases showing objective improvement with corticosteroids, 2 received ACTH alone; 1, ACTH followed by cortisone; 2, prednisone (Meticorten) alone; 1, prednisone followed by ACTH; and 2, cortisone. The exact corticosteroid was not noted in 2 cases. The 1 case with subjective improvement only received ACTH followed by cortisone, and 1 patient showing no response to corticosteroids received prednisolone. Objective improvement occurred from two weeks to eight months after medication was started, at least half the cases showing improvement within a month.

Radiation was given to 2 patients—1,000 r to the midplane of each lung in eighteen days in one case[4] and 600 r in air to each anterior and posterior thoracic region in the other case.[5] Both patients showed considerable clearing of the chest roentgenogram and became asymptomatic within two months. Nadeau and associates[13] expressed concern about treating a disease capable of causing pulmonary fibrosis with radiation that may also cause fibrosis.

Cortisone followed by radiation was given to 1 patient without any effect. Another patient received various antibiotics, and the chest roentgenogram showed some clearing in nine months. Therapy and follow-up were not noted in 1 patient.

Of 7 patients who did not receive any therapy, 4, including our case, showed spontaneous clearing of the lungs. Of these, 1 had recurrence of soft nodular lesions on chest roentgenography two months postoperatively despite the clearing noted one month earlier and 3 became asymptomatic postoperatively, although there was no change in their roentgenograms.

Regardless of the form of therapy or lack of it, it is unusual for the roentgenogram to show complete clearing. Evidence of a fine, diffuse fibrosis is still noted despite marked symptomatic improvement. No autopsy reports are available from this group of patients, so the histopathologic changes postoperatively and in response to therapy are uncertain. The extensive process noted in the lung biopsies would probably preclude complete restitution of normal pulmonary structure regardless of form of therapy and symptomatic improvement. Considering the histopathologic changes on lung biopsy, Auld[5] is understandably surprised that there is any regression at all in the chest roentgenogram after therapy.

Considering the relatively small number of cases in the literature, variation in type of therapy, and lack of long-term follow-up of many cases, it is difficult to be certain of the specific therapy, if any, that is indicated. Arnett and Schulz[4] cast doubt upon the need for any therapy, considering that there may be improvement without therapy and a chronic pulmonary fibrosis will inevitably develop. However, of the 26 patients reported in the literature, including our own, less than half had continued spontaneous objective improvement, whereas about 75 per cent of the group receiving corticosteroids improved. Both patients receiving radiation alone also showed a good response. Comparison of the group that did improve with or without therapy with the group that did not improve does not reveal any significant differences with regard to age, duration and severity of symptoms, x-ray picture, or histopathologic changes. This does not agree with Virshup and Goldman,[3] who believe that the older the patient at onset, the more benign the course. In contrast to the suggestion[9,22] that the process may be more reversible in an active proliferative stage, the patients with cystic changes of the pulmonary tissue were just as likely to show significant improvement. The 2 patients with the most marked symptoms[10] both improved with corticosteroids.

ETIOLOGY AND CLASSIFICATION

The etiology of eosinophilic granuloma of the lung is unknown. Weiss and Johnston[19] believe that the inflammatory nature of the disease sug-

gests an infectious agent. However, their cultures of lung biopsy tissue for viruses in the case they reported were unrewarding. Special stains and cultures from biopsy material for bacteria, tubercle bacilli, and fungi have been consistently negative. The histopathologic picture of eosinophilia, vascular changes, and clinical response to corticosteroids are consistent with an allergic etiology, although the patients have not had a remarkable allergic history and the disease has not followed immunizations or other manifestations of allergy. Auld[5] believes it may represent a chronic response to a low-grade antigen, probably an inhalant because of its limitation to the lungs and the diffuse pulmonary distribution of lesions.

Lichtenstein[21] has cast doubt upon the separation of this entity from the group of diseases that includes Letterer-Siwe disease, Hand-Schüller-Christian disease, and eosinophilic granuloma of bone, which he includes under the broad classification of histiocytosis X. When the disease it confined to the lungs, he classifies it as early, chronic, disseminated histiocytosis X.

There is much to recommend Lichtenstein's classification. There is no histopathologic difference from the lung that is the only organ involved and the lung that is involved together with skeletal sites.[15,21] The radiographic picture of the lungs is identical to those of Letterer-Siwe disease and Hand-Schüller-Christian disease with lung involvement,[4,15] and it is only the absence of extrapulmonary involvement that differentiates eosinophilic granuloma of the lung from this other group of diseases. Perhaps the ease of detection of pulmonary lesions radiographically in this era of routine chest roentgenograms has fictitiously singled out eosinophilic granuloma confined to the lung as a distinct entity. The lack of autopsy material in these cases prevents a final answer to this matter. Although many cases that have been reported have had a negative bone survey, Lichtenstein[21] does not believe that skeletal lesions should be necessary for the diagnosis of the Hand-Schüller-Christian type of disease, as they may be absent or may not be demonstrable until extraskeletal lesions are well advanced.

Despite the lack of autopsy material in these cases, there is a moderate amount of clinical evidence that eosinophilic granuloma of the lung may not be a distinct entity. Murphy and Baker[16] reported a case of eosinophilic granuloma of the lung in a 23-year-old woman which appeared earlier than and overshadowed the later development of a rib lesion. When typical pulmonary lesions are associated with diabetes insipidus, these cases should be regarded as a form of Hand-Schüller-Christian disease despite the absence of demonstrable skeletal lesions.[21] There have been 2 patients reported[18,19] with the typical features of eosinophilic granuloma confined to the lungs who also had diabetes insipidus. In a third case,[20] a 29-year-old man had cough and spontaneous pneumothorax with eosinophilia and characteristic roentgenographic and histopathologic findings of eosinophilic granuloma of the lung but also had diabetes insipidus and, later, a bone lesion in the calvaria. Weiss and Johnston[19] reported the case of a 22-year-old man who was treated for eosinophilic granuloma of the lung and in whom diabetes insipidus developed during the following year. Nadeau and associates[13] noted 3 patients who later suffered from diabetes insipidus; autopsy of 1 of these revealed pulmonary lesions and a hypothalamic lesion. May and associates[17] reported 3 cases of adults with typical pulmonary lesions on biopsy and characteristic roentgenograms, but all 3 had bone lesions and 1 also had diabetes insipidus. Other cases have been reported[14,15] of adults with a combination of pulmonary and skeletal lesions.

SUMMARY

A case of eosinophilic granuloma of the lung in a 44-year-old man is reported, together with a review of 25 previous cases in the literature in regard to symptomatology, physical and laboratory findings, roentgenographic interpretation, histopathology, and therapy. The average patient is a young or middle-aged man with chronic nonproductive cough and moderate weight loss of less than one year's duration. Radiologic findings consist of a widely disseminated, reticulonodular infiltration throughout both lung fields.

Final diagnosis usually rests upon lung biopsy and study of histopathologic changes, which are similar to those of the group of diseases within the broad classification of histiocytosis X. Although patients may improve without therapy, the best results have been obtained with corticosteroids or radiation. Symptoms and histopathology are not helpful in determining prognosis. The etiology is unknown, although some type of allergic response has been suggested. Considering the similarity of this disease process to other entities within the broad group of histiocytosis X, its delineation as a distinct disease process is somewhat questionable.

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This paper represents the personal viewpoint of the authors and is not to be construed as a statement of official Air Force policy.

Hypertension may be controlled by oral guanethidine sulfate (Ismelin), which does not block the autonomic ganglia and thus spares the patient the side effects of constipation, dryness of the mouth, impotence, iridoplegia, and risk of paralytic ileus. The pressure-lowering action, resulting from blockage of the sympathetic vasomotor system, is uniform throughout the day, except for a tendency to lower pressures in the early morning. Hypotension immediately after exercise may cause fainting and weakness, but reduction of dosage to avoid this effect may lead to imperfect control.

Oral doses range from 10 to 750 mg. daily, but most patients require 30 to 120 mg. Since guanethidine has a cumulative action, dosage is started with 30 mg. daily and increased by 30 mg. or more at three-day intervals until the desired effect is achieved. This regimen is designed for hospitalized patients.

Side effects of guanethidine are diarrhea; bradycardia, usually intensified by digitalization; dyspnea; lassitude; nasal obstruction and parotid tenderness; muscle tremor; and inability to ejaculate. Some patients retain fluid while taking guanethidine and thus are prone to congestive heart failure. If digitalis is given in addition to diuretics, the pulse rate, already depressed with guanethidine, may become alarmingly slow.

Oral guanethidine was used for nine months in 80 patients with extreme hypertension; more than half the patients had retinal hemorhages, exudates, or papilledema. Good control—a standing blood pressure of 160 100 mm. Hg or lower—was achieved in 34 patients, and 34 had fair control—a reduction in diastolic pressure of at least 20 mm. Hg. Retinopathy regressed steadily throughout the treatment period. Exercise hypotension limited control of blood pressure in 4 patients. In 8, treatment failed. Despite adequate control of blood pressure, 3 patients, uremic when treatment was started, died of renal failure.

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Max Seham, M.D.

EVERETT C. PERLMAN, M.D.
Minneapolis

Max Seham was born in Kovnow, Russia, on July 1, 1888, the only son in a family of 6 children. When he was 6 years old, the family, because of unfavorable and uncertain conditions in the homeland, emigrated to the United States. After a stormy and hazardous voyage, their ship landed on the east coast and the Sehams settled in the Carolinas. There was a severe epidemic of yellow fever in the area, and the mother contracted an acute form of the disease. The family was advised, after her partial recovery, to leave this region where the disease was so widespread and to move as far north as possible. On this advice, a further migration took place in 1895 to Minnesota. The family settled in a home in north Minneapolis, and Max went on to attend grade school, North High School, and the University of Minnesota. In 1910 he was graduated in good standing from the University of Minnesota Medical School.

After a year of internship at the Minneapolis General Hospital, he opened an office over a drugstore at Lyndale and Sixth Avenue North, where he struggled for four years to develop a practice among the people of that neighborhood. Upon the encouragement of Dr. Sedgwick, one of the pioneer specialists in pediatrics in this area, he was accepted at the Boston Infants' and Children's Hospitals in 1916, where he spent two valuable years as an intern in pediatrics. Part of this time was spent at Cornell University, where he studied intermediary metabolism and physiology. After serving as an extern in pediatrics at Mount Sinai Hospital in New York City, he accepted a residency in pediatrics at the Royal Victoria and Alexandria hospitals in Montreal. At the outbreak of World War I, he enlisted as a first lieutenant in the Medical Corps and received an assignment as assistant camp epidemiologist at Camp Dodge, Iowa. During this period, he encountered widespread epidemics of influenza and meningitis. Always interested in statistical research, he compiled and published an excellent statistical report of the epidemiology of meningitis.

Max returned to Minneapolis in 1919 and began his long period of service to the children of the community as a pediatrician. Early in his career, he became interested in the physiologic problems of fatigue in children. After many years of research and study, Dr. Seham, in collaboration with his wife, Dr. Grete Egerer Seham, a Ph.D. in chemistry, wrote and published the book "The Tired Child," a complete and exhaustive study of the effects of fatigue in children. He was also interested in the physiology of the heart and did much of the pioneer work in electrocardiography in children in this country. He was the author of the chapter on electrocardiography in children contained in *Abt's Compendium of Pediatrics*. In these volumes, he also wrote the chapters on congenital heart disease and on the physical examination of the heart in children.

Because of his interest, he was made the director of the childrens' heart clinic at the Minneapolis General Hospital as well as director of the Lymanhurst Heart Clinic, where he spent many years in the study of heart conditions in children and in stimulating the interest of interns and residents in this field. He was also on the attending staff of the pediatric and contagious services of the General Hospital, where his interest in the patients, students, and resident staff was legendary.

Dr. Seham has been a part of many pediatric organizations, to which he has given the same conscientious attention as that given to his young patients. In 1922, he was the consulting pediatrician

EVERETT C. PERLMAN *is on the attending staffs of Abbott and Mount Sinai hospitals and is clinical instructor in pediatrics, University of Minnesota Medical School.*

for the Jewish Sheltering Home, and from 1925 to 1927, director of the Franklin Nutritional Clinic in Minneapolis. He was health editor of the *Minnesota Public Health Nurse* in 1926, health editor of the *Junior House Magazine* from 1928 to 1932, and a member of the executive committee of the Hennepin County Medical Society in 1928. He was chairman of the Health Section of the Minnesota Social Conference in 1928 and on the Council for Crippled Children in 1928 and 1929. From 1925 to 1933, Dr. Seham was on the board of directors for the Infant Welfare clinics in Minneapolis. He served as a member of the Hoover White House Commission for Child Growth and Development, for which he was awarded a Certificate of Service in 1933.

In 1928, he was one of the charter members of the Minnesota Society for Internal Medicine and received a distinguished service award from that society for his research. He has been a member of the White House Conference for Child Health and Protection and, in 1937, as the principal speaker at the national convention of the American Public Health Association, he discussed "Screening of Behavior Disorders in Children." The Minneapolis newspapers asked him to report, in journalistic form, the proceedings of the meeting, which was of great national interest. His by-line appeared on daily articles in the local newspapers and in the University of Minnesota Daily.

Dr. Seham is a member of the Hennepin County and Minnesota State medical societies, the Northwestern Pediatric Society, the Minneapolis Pediatric Society, and Sigma Xi. In 1927, he was invited to join that select group, the American Pediatric Society, and in 1928 gave his inaugural paper on "The Relation Between Malnutrition, Fatigue, and Nervousness in Children." He is on the attending staff of Abbott Hospital, where he was chief-of-staff in 1946, and on the attending and consulting staffs of Mount Sinai Hospital, where he was chief-of-staff in 1952. At Mount Sinai, he has done yeoman service in organizing the pediatric department and in formulating many of the basic policies and plans for the hospital.

On his 70th birthday, Dr. Seham was honored at a testimonial dinner by the members of the Minneapolis Pediatric Society. In 1960, he was awarded a laudatory scroll by the members of the staff of Mount Sinai Hospital in appreciation of his accomplishments. In the same year, he was honored at the meeting of the Minnesota State Medical Society, and made a member of the "50" club.

At one of these testimonial dinners, many of Max Seham's colleagues and contemporaries spoke of his fine and humane qualities. The writer remarked that constant association with any person often reveals many faults unknown to those who see him casually in professional or social contacts, but in the case of Dr. Seham, quite the opposite was true. His warmth and understanding, his quiet sense of humor always near the surface, his appreciation of honesty and loyalty, and his unquestioned devotion to his professional oath are qualities to which we should all aspire. The love and devotion of his family, his friends, and his patients are not attributes that have come by chance. He has been an inspiring teacher to hundreds of medical students and residents who have always found an understanding ear to problems both professional and personal.

Even after many years of practice, when many professional persons tend to coast along on their past knowledge and experience, he continues to be inexhaustible in his interest in new developments and new therapies. He still spends time and regular study at the University Hospitals to better fit himself to understand and help those patients who need psychiatric care or advice in the solution of their behavior problems. Although Dr. Seham is now an emeritus professor of clinical pediatrics, he attends these classes as a student.

The life that Dr. Seham has led; his honesty in all matters; his interest in people and affairs; his tolerance of everything except intolerance; and his devotion to his profession, to his patients, and to his friends should be an example for all people.

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Despite the unquestioned benefits of treatment and the availability of drugs, application of prophylaxis against streptococcic infection in adults with rheumatic heart disease is inadequate.

Physicians attending such patients possibly have not been reached by educational programs of private and public health agencies. Infrequency of prophylaxis among rheumatic patients seen in teaching centers or given special treatment such as cardiac surgery suggests inadequate dissemination of basic information. Some private physicians may be unaware that a free supply of penicillin and sulfonamides may be available.

Of 101 adults with rheumatic heart disease or past rheumatic fever seen consecutively at a clinic between June 15, 1956, and May 1, 1959, only 28 were receiving prophylaxis prescribed by their physicians. The patient's age, degree of heart disease, and exposure to children apparently were not related to whether the physician instituted preventive treatment. Being treated in a teaching hospital decidedly increased the likelihood, but did not assure, that a rheumatic patient would receive prophylaxis.

Correlation was found between intensity of heart disease and recurrence of rheumatic activity.

R. Wiedland, J. Katz, and H. K. Hellerstein: Prophylaxis against streptococcic infection in an adult rheumatic population. J.A.M.A. 173:350-353, 1960.

Book Reviews . . .

Modern Perinatal Care

LESLIE V. DILL, M.D., *1959. New York: Appleton-Century-Crofts, Inc. 320 pages. Illustrated. $6.50.*

Modern Perinatal Care is an interesting book and, as its title connotes, is aimed at crystallization of present-day thought in the care of a woman in antepartum and postpartum states. The book has little material on the actual management of deliveries but quite thoroughly reviews the literature on many of the other aspects of modern obstetrics. There are interesting chapters on "Obstetrics and the Law" and "The Ethics of the Catholic Church in Obstetrics." It is somewhat similar to a yearbook of obstetrics except that the review covers a much longer period than a year. It is literally filled with recent references and therefore is valuable to the interested obstetrician or general practitioner from this point of view alone. The reprinted tables and charts, for the most part, are excellent and represent probably as much information as was available at the time the book was written. However, many of the sections on therapy include the opinions of many authors and therefore contain so many suggestions that many of us, I am sure, would not follow them.

In many instances, the basic works from which the review is drawn fail, in my opinion, to meet the test of adequate scientific investigation. Therefore, the conclusions that are derived are equally unsound. However, in the author's defense, it must be stated that when good material has been presented in the literature to countermand the preexisting misconceptions, this work has been reported.

This is an excellent reference book for information, good and bad, and should certainly have a place in the library of the obstetrician and general practitioner, provided frequent editions are made available. In the short time that has elapsed since the writing of the book, much of the information is outdated, although, in many instances, it is still very sound.

The format is interesting and makes reference easy. The paper is not of the best quality, but perhaps this has the advantage of keeping the cost of this book so low that no one would object to adding current editions to his library.

JOHN S. GILLAM, M.D.
Fargo, North Dakota

Electrophysiology of the Heart

BRIAN F. HOFFMAN, M.D., and PAUL F. CRANEFIELD, PH.D., *1960. New York: McGraw-Hill Company. 289 pages. $12.50.*

This book will be important to those persons interested in the electrical properties of the heart. The authors have had an intense and lasting interest in research concerned with the electrical properties of individual heart cells as studied by microelectrodes and modern recording technics. This is not a book that can be used for clinical diagnosis of abnormal electrocardiograms; that is, the book will increase the practicing cardiologist's depth of understanding of the electrical processes involved in the heart's action rather than give him a practical tool of immediate applicability.

The book opens with a summary of technics which have been used to get electrical records directly from the heart. Intracellular microelectrode technics are emphasized. A brief discussion of the ionic basis of excitation and conduction as applied to heart cells follows. It is properly pointed out that most of the research that gave rise to this type of explanation came from work on other cells, notably the giant axon of the squid. This treatment, however, allows various aspects of the electrical records from individual cells to be discussed in terms of possible individual ionic movements.

The main body of the book involves a description of the electrical properties of individual cell types, including cells from the sinoatrial node, atrium, atrioventricular node, Purkinje tissue, and ventricle. The peculiarities of each cell type are given. For example, it is shown that, in cells where pacemaker activity exists, there appears a continuous depolarization during the unexcited state of the cycle and that, when a certain potential difference between the inside and outside of the cell is reached, excitation becomes evident by the appearance of the spike of the action potential.

The last two chapters in the book cover the topics of excitability and general electrophysiology of the heart. In these chapters, many of the subjects taken up with respect to the individual cells are recapitulated in a more general setting. Of particular interest is the discussion of repolarization and the state of excitability at various periods in the recovery phase.

I feel that the writing is clear and that the authors have done a good job in presenting their ideas, especially in view of the fact that the field they are writing about is changing very rapidly.

JOHN A. JOHNSON
Minneapolis

Diagnostic Roentgenology of the Digestive Tract Without Contrast Media

BERNARD S. WOLF, M.D., MANSHO T. KHILNANI, M.B., *and* ARTHUR LAUTKIN, M.D., *1960. New York: Grune & Stratton. 174 pages. Illustrated. $8.75.*

This excellent monograph on roentgenologic diagnosis of the abdomen imparts considerably more information to the reader than the title would suggest. The initial chapter, entitled "General Principles," presents lucidly some of the physiologic and pathologic alterations responsible for x-ray changes in the abdomen. Important anatomic features are well discussed. The technic of comparing a barium contrast examination of the organ with its appearance on the plain roentgenogram is utilized liberally and effectively. Changes in the appearance of gas shadows with variation in position of the patient are empha-

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sized. The illustrations are of excellent quality, and the text is readable and easy to follow.

Each organ is considered in both its normal and pathologic states. As should be the case, the most common pathologic conditions are emphasized, but a "miscellaneous lesion" section is included with each organ and many interesting pathologic entities are discussed.

As the authors indicate in the preface, this monograph deals mainly with more chronic diseases of the gastrointestinal tract and not those generally seen in the acute surgical abdomen. The previous void in the literature regarding plain film diagnosis of important abdominal conditions has been admirably filled by this volume.

RICHARD GREENSPAN, M.D.
New Haven, Connecticut

Light Coagulation

GERD MEYER-SCHWICKERATH, M.D., *1960. St. Louis: C. V. Mosby Co. 111 pages. Illustrated. $9.50.*

This book is a brief but complete account of the development and use of high intensity light exposure to produce damage (and resultant scars) or destruction (when so desired) in the eye. Since the first reports of this technic by the ingenious author, Prof. Meyer-Schwickerath of Bonn University, there has been widespread interest in the method throughout the ophthalmologic world, since it offers a means of treating many detachments of the retina by simple and atraumatic means.

To detail the contents would be redundant. The book is concise, simple, and easily and quickly read. It is a must for most ophthalmic surgeons, certainly for any who have access to the required machine. Physicians in other fields might glance through it in the library, because this method has received some public attention and questions undoubtedly will come from patients.

As might be expected, such a method is developing rapidly, and indications and details of technic are constantly changing. More and more papers will be appearing in the current ophthalmologic literature on the subject. This book is basic to them all.

WALTER LEES HOFFMAN, M.D.
Minneapolis

Shaw's Textbook of Operative Gynaecology

Revised by JOHN HAWKINS, M.D., *1960. Baltimore: Williams & Wilkins. 177 pages. Illustrated. $20.00.*

Dr. Hawkins has given us a second edition of a superbly illustrated textbook originally prepared by Wilford Shaw, a world-renowned gynecologist and teacher. He states in his preface that, although much of the first edition remains, many chapters have been considerably revised and new ones added. In this revision, emphasis is placed on standard orthodox procedures. No attempt is made to include old operations no longer acceptable or untested innovations. The text is sufficiently comprehensive; no fault need be found regarding omissions.

Dr. Hawkins has been aided by some of his colleagues in the preparation of chapters on radiotherapy, anesthesia, blood transfusions, and cardiac arrest.

Consideration is given to pre- and postoperative preparation and care, concurrent constitutional disease, and choice of surgical instruments. The chapter on pelvic anatomy is well written and worth reviewing by all gynecologic surgeons. The various operative technics are carefully described and meticulously illustrated.

The chapters on pelvic relaxation and genital prolapse are outstanding. It has long been the practice of British surgeons to be more conservative in preservation of the uterus in these conditions. In judging current practice in this country, one cannot escape the conclusion that perhaps too many hysterectomies are performed. There is a middle course, and the writer adopts this in his choice of operations.

The reviewer recommends *Operative Gynaecology* to every surgeon treating gynecologic patients. The simple clarity of the author's writing, the large type of the text, and the logical presentation of the subject make reading this book a pleasure. "Each honest calling, each walk of life, has its own elite, its own aristocracy based on excellence of performance." The author impresses me as being a member of this select group.

G. WILSON HUNTER, M.D.
Fargo, North Dakota

Synopsis of Pathology

W. A. D. ANDERSON, M.D., *1960, fifth edition. St. Louis: C. V. Mosby Co. 838 pages. Illustrated. $9.25.*

There is an old saying that the best things come in the smallest packages. This is certainly true of Dr. Anderson's "Synopsis of Pathology," for this small volume, scarcely bigger than hand-size, has succeeded in its purpose of being "a concise but comprehensive presentation of pathology."

As a pathologist, I use reference volumes, including Dr. Anderson's "Pathology," primarily for bibliographies. For quickly reviewing some vague or woolly point, I prefer to start with the "Synopsis of Pathology," where all the major points are covered in a minimum of space.

As a former instructor in pathology, I found earlier editions helpful in organizing my approach to teaching. Almost anyone can ramble on and eventually cover, if not submerge, one topic; few can present it as concisely and as artfully as Dr. Anderson has done. My students found the "Synopsis" equally helpful in trying to encompass so broad a field as pathology in the all-too-brief time allotted to it.

The revisions in this fifth edition are surprisingly complete and up-to-date. The section on cytopathology is especially timely, as this field is becoming increasingly important in the light of our batting average in discovering and curing presymptomatic carcinoma in situ of the uterine cervix, as compared with results ten years or so later with symptomatic and invasive carcinoma of the cervix.

I feel certain that both the general practitioner and the specialist will find that this concise book, with its excellent illustrations and accurate index, will make reviewing lost and misplaced facts a real pleasure.

OSCAR M. WILBUR, JR., M.D.
Hibbing, Minnesota

First Aid: Diagnosis and Management

WARREN H. COLE, M.D., *and* CHARLES B. PUESTOW, M.D., *1960. New York: Appleton-Century-Crofts, Inc. 106 pages. Illustrated. $6.25.*

This volume is the fifth edition of a book that was first published in 1942—a fact indicative of its wide accept-

(Continued on page 24A)

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CM-4730

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ance and usefulness. Drs. Cole and Puestow, and the 16 other contributors, each an authority in his field, have assembled a body of information as comprehensive as anyone in the first-aid field needs to have and affords an excellent point of departure for the physician and surgeon who want to know more.

There are several excellent sections on the anatomy and physiology of various organ systems—circulatory, respiratory, urinary, digestive, nervous, and skeletal—all presented in easily understood language and in readable style and so integrated with the rest of the text as to make the whole more meaningful.

In this volume may be found, in clear and concise form, information about and instructions for the rational treatment of every conceivable form of trauma which may require first aid or more extended treatment. The book not only tells the first-aider what to do and why, but it also tells him (equally important) what not to do in order to avoid the many pitfalls attending such care.

I believe that the more generous use of illustrations would add to the value of this book. For example, illustrations would help differentiate types of wounds such as penetrating, perforating, lacerated, avulsed, and so forth.

This book should be in the library of every family, on the bookshelf of every physician, and in every Civil Defense Center. It is as valuable for military as for civilian or Civil Defense personnel. It is the best all-round book in this field that I have seen.

FRANK D. NAEGELI, M.D.
Minot, North Dakota

Cosmetic Surgery: Principles and Practice

SAMUEL ROMAN, M.D., *1960. Philadelphia: J. B. Lippincott Co. 642 pages. Illustrated. $27.50.*

In contrast to many specialized works, this book starts with detailed discussion of basic principles. Discussion of the foundations of plastic surgery before the more esoteric aspects of regional surgical procedures enables nonspecialists to follow the line of thought and learn easily from the author.

There are detailed chapters on pre- and postoperative consideration, anesthesia, and incision closure. The latter, especially, would be worthwhile reading for anyone who does surgery of any kind. A chapter on treatment of wounds is also excellent. These chapters, and a discussion of scars and tissue transplants, complete the first section.

The second section of the book, "Regional Cosmetic Surgery," consists of 400 pages, almost 200 of which are devoted to cosmetic operations of the nose. This seems too detailed, skimping the discussion of other areas, except for a plastic or ear, nose, and throat surgeon who wants a monograph on cosmetic rhinoplasties. In contrast, the material on skin operations, covering all sorts of cysts, tumors, wrinkling, and pigmentary faults, is less than 40 pages. Ear operations, cosmetic eye operations, maxillofacial surgery, and all cosmetic operations on the trunk and extremities are each covered in 40 pages or less. Discussion and explanation of procedures and the accompanying pictures combine to make the subjects easily grasped, with a minimum of rereading and pondering as to meaning.

The author is to be commended particularly on his omission of the cliché before-and-after pictures. These do not increase the teaching value but only the ego of a surgeon. Illustrations are either photographic and quite satisfactory or simple line drawings, which are excellent.

This textbook would be of greatest value to a plastic surgeon or to an ear, nose, and throat surgeon who did rhinoplasties. The surgical minded dermatologist would like its lucid exposition of all cosmetic procedures. Any surgeon who must disturb the integrity of the epidermis and then try to finish his operation with a minimum scar could read this with both interest and profit.

The erudition of the author and his acquaintance with early classical plastic surgery literature is shown by his inclusions, where pertinent, of diagrams and pictures from medieval texts. These add considerably to the interest of the book.

MURRAY C. ZIMMERMAN, M.D.
Whittier, California

Bleeding Syndromes

OSCAR D. RATNOFF, M.D., *1960. Springfield, Ill.: Charles C Thomas. 287 pages. $8.50.*

The author states in his foreward, "This book is a compilation of practical information about the clinical picture, pathogenesis, diagnosis and treatment of hemorrhagic diseases, written for the practicing physician. It is not intended as a laboratory manual for the differentiation of bleeding disorders, nor as a review of the current literature on the physiology of hemostasis."

Dr. Ratnoff is to be commended for adhering to his stated intentions and for the clarity of his presentation. For the practicing physician, this book brings a refreshing note of simplicity to a subject that is tightly clothed with a coat of semantic confusion. For the interested ones, an extensive bibliography is present.

It is an easily read and digested book. If there is to be criticism from the academic hematologic brotherhood regarding such things as brevity, please let it be noted that this book was written for the nonspecialist. With the daily increasing use of anticoagulants, this volume is most timely. It is a sound contribution to current medical literature. I can recommend this book highly to the practicing physician, resident, intern, and medical libraries.

J. Y. FEINSTEIN, M.D.
Minneapolis

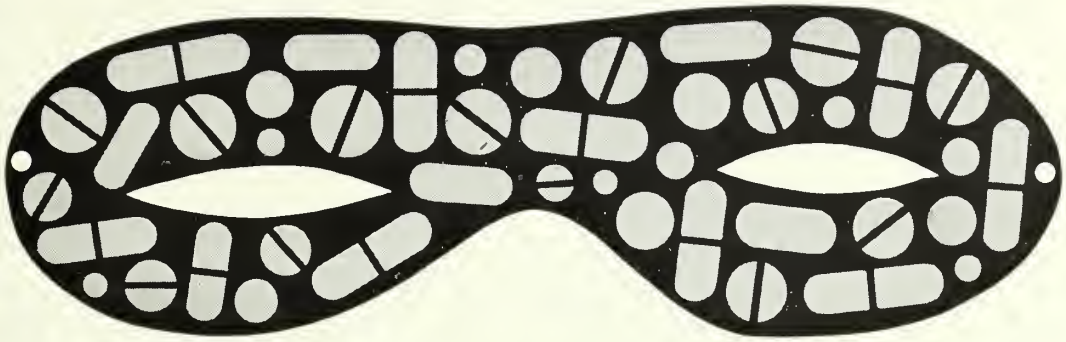
The Choice of a Medical Career: Essays on the Fields of Medicine

JOSEPH GARLAND *and* JOSEPH STOKES III, *Editors, 1961. Philadelphia: J. B. Lippincott. 231 pages. $5.00.*

Those who have occasion to receive the queries of youth on the subject of a career must have perceived that, in the last decade, the profession of medicine has suffered, in the eyes of the prospective college student, by comparison with the more exciting attractions of physics and biochemistry. Perhaps the current world-wide preoccupation with celestial physics has caused the young man in search of a career to regard the practice of medicine as a rather pedestrian vocation.

For these and other reasons, it is useful to have such a work as this one readily at hand, particularly since it reflects 21 viewpoints on the same number of branches of medicine by an authority in each field. The only work

(Continued on page 26A)



drugs anonymous

One of the several hastily conceived and potentially dangerous suggestions for reducing drug costs is generic-name prescribing. The proponents of generic-name prescribing claim that it will lower drug costs significantly and—through supervision by the Federal Government—provide quality equivalent to that of trademarked drugs. We maintain that these claims are false. Here are some authoritative answers to the principal questions posed by generic-name prescribing.

How much money would be saved if all prescriptions were written for generic-name drugs?

"The [Rhode Island] Division of Public Assistance examined 10,000 drug prescriptions for welfare recipients for the purpose of determining the actual savings . . . of generic versus trade-name drugs. The drugs had cost $28,000. Substituting generic drugs whenever possible would have provided a saving of less than 5 per cent. Syracuse has made a similar study of drug costs with comparable results."

Rhode Island Medical Journal,
January, 1961

Are the savings worth the risk of sacrificing quality?

". . . it is unsafe [to prescribe generically] because there is not sufficient policing of our standards. . . ."

Lloyd C. Miller, Ph. D.
Director of Revision of the U.S.P.

"The naive belief that, if a product was not good, the FDA would prohibit its sale is just not realistic. . . . it is completely impossible for the FDA to check every batch of every product of every manufacturer. . . . Hence the integrity and reputation of the manufacturer assume unusual significance where drugs and health products are concerned."

Albert H. Holland, M.D.
formerly Medical Director of the
Food and Drug Administration

Smith Kline & French Laboratories, Philadelphia

(Continued from page 24A)

of this nature in existence previously was an essay of 41 pages in "The Professions," by A. M. Carr-Saunders and P. A. Wilson (Oxford, the Clarendon Press, 1933, pp. 65-106)—a work reflecting much original investigation but intended almost entirely for a British audience.

The viewpoints in the present volume range from that of the general practioner to that of the specialist, and the inclusion is so extensive that such relatively new fields as administration and the more esoterie medical sciences are represented. The final chapter, by Dr. William B. Bean of State University of Iowa College of Medicine, is a provocative essay on the qualities of the heart and spirit in the ideal physician so prized by the patient but encountered so seldom. It is reminiscent of the genial wisdom of William Osler.

A prospective medical student could not but be impressed by this volume.

JAMES ECKMAN, M.D.
Rochester, Minnesota

Atlas of Anatomy and Surgical Approaches in Orthopedic Surgery

RUDOLFO COSENTINO, M.D., *1960, Volume II. Springfield, Ill.: Charles C Thomas. 264 pages. Illustrated. $14.00.*

About a year ago, Dr. Cosentino published the first volume of a proposed series of anatomic dissections which illustrated, through beautiful dissection and photography, the surgical approaches to the upper extremity. This second volume deals in a like manner with the lower extremity.

It is difficult to make actual dissection photographs take the place of a manual or atlas of surgical approaches illustrated by an artist. This volume is not, I am sure, intended to replace any other good atlas of surgical exposures. It is an excellent supplement, because it illustrates so well the dissected structures. It is a unique and superb supplement to the surgeon's anatomic library. It is not a complete atlas. It does not contain a dissection illustrating the hind quarter amputation or amputation of disarticulation of the hip. While its photographs of the ligamentous structures about the knee are excellent, there is no illustration of the two layers of the tibial collateral ligament.

This atlas of beautiful dissections is recommended highly for the library of any teaching institution in orthopedic surgery and for the practicing orthopedic surgeon.

JOHN H. MOE, M.D.
Minneapolis

Mitra Operation for Cancer of the Cervix

SUBODH MITRA, M. B., *1960. Springfield, Ill.: Charles C Thomas. 93 pages. Illustrated. $6.00.*

This monograph is one of a series called *American Lectures in Gynecology and Obstetrics.* The author, Subodh Mitra, is head of the Department of Obstetrics and Gynecology at the University College of Medicine, Calcutta University. The text describes the technic of an operation perfected by the author during the past decade. The Mitra operation combines extraperitoneal lymphadenectomy with radical vaginal hysterectomy.

Early in his career, Mitra turned to surgical therapy of cancer of the cervix because he was not satisfied with the results of radiotherapy. He chose the vaginal rather than the abdominal approach because the primary mortality for the Wertheim procedure was very high in those days before antibiotics and modern anesthesiology. The vaginal, Schauta, operation could be performed on obese and poor-risk patients with low primary mortality and very little danger of injury to the ureter or bladder. The main objection to the vaginal approach was that it failed to remove the pelvic lymph nodes that extend beyond the parametrium. In answer to this objection, the author added extraperitoneal lymphadenectomy preceding the radical vaginal hysterectomy. He also utilized the abdominal approach to ligate the uterine and ovarian arteries and thus make the vaginal approach more hemostatic.

The author reports the results of this combined procedure as performed by himself and his associates on 216 patients. The primary mortality rate was 3.6 per cent and the corrected mortality rate was 1 one per cent. The five-year cure rate for 42 patients without detectable involvement of the pelvic nodes was 73.8 per cent; for 15 patients with positive nodes, 26 per cent. The total cure rate for stages 1 and 2 in patients treated during 1950-1951 was 65.6 per cent for operated patients and 47.4 per cent for a comparable group treated by radiotherapy.

The text is well written and adequately illustrated. For those surgeons who contemplate doing radical pelvic surgery, the monograph is highly recommended. This reviewer agrees with the wise words of the author who states, "this type of surgery is not meant for the occasional operator but for those who have made it their life study and are regularly engaged in this type of surgery."

MELVIN B. SINYKIN, M.D.
Minneapolis

Neurology of Infancy

ANATOLE DEKABAN, M.D., *1959. Baltimore: Williams & Wilkins. 382 pages. Illustrated. $12.00.*

In this compact volume, Dr. Dekaban has succinctly presented the great majority of neurologic states, normal and abnormal, seen in infancy.

Among the few interesting states not discussed are the neurologic effects of hyper- and hypotassemia, the abnormal chromosome pattern in mongolism, and Echo and Coxsackie viruses. A section devoted to the technical details and indications for lumbar, subdural taps in the newborn infant; pneumoencephalography; and angiograms of cerebral vessels would be most helpful.

Some illustrations are well marked with a legend arrow, but many illustrations of x-rays and gross and microscopic sections could be made a hundredfold more instructive if arrowed legends were used. The bibliography is liberal in extent and detail.

The discussion layout makes for easy reading and ready review. This book is most valuable to the resident and physician preparing for board examinations. Most pediatricians, pediatric neurologists, and child psychiatrists will find this a valuable addition to their pediatric texts and more voluminous neurologic encyclopedias.

HERSCHEL J. KAUFMAN, M.D.
Minneapolis

News Briefs . . .

North Dakota

The North Dakota State Psychiatric Clinic, Bismarck, is administered by the recently established Mental Health Authority, under the direction of the state health department. The year-old clinic, designed to promote mental health services in the state, provides professional psychiatric, psychologic, and social services and performs mental health research and training. Dr. Victor Szyrynski is director of the clinic and consultant in psychiatry to the state department of health. Dr. Cecil G. Baker is psychiatric consultant to the clinic. Children, adolescents, and family groups are referred to the clinic through state institutions and welfare agencies. The clinic operates as a nonprofit service.

° ° ° °

Dr. D. Murray Cameron has discontinued his partnership at the Hettinger Clinic to specialize in radiology at Winnipeg General Hospital, Canada. Dr. Cameron had been associated with Dr. James Knickerbocker at the Clinic until 1960, and later with Dr. Robert G. Carter.

° ° ° °

Dr. Leonard W. Larson of the Quain and Ramstad Clinic, Bismarck, and president of the American Medical Association, was awarded an honorary doctor of science degree from Jamestown College. Dr. Larson spoke at the June commencement exercises and is a member of the Board of Trustees of the College.

° ° ° °

Dr. Kenneth J. Johnson of the Department of Internal Medicine at the Quain and Ramstad Clinic, Bismarck, has been elected an associate fellow in the American College of Allergists. Dr. Johnson practiced in Bemidji, Minnesota, before joining the Clinic in 1951. He received his medical education from the University of Minnesota and served as intern and resident at Wayne County General Hospital, Eloise, Michigan.

° ° ° °

Dr. Andrew C. Sawchuk, physician and surgeon at the Missouri Valley Clinic in Bismarck for the past year, has joined the staff of the Dickinson Clinic. A native of Canada, Dr. Sawchuk received his medical training at Queens University, Kingston, Ontario. He received his surgical training at the Chesapeake and Ohio Railroad Hospital, Clifton Forge, Virginia, and at Charleston General Hospital, Charleston, West Virginia.

Minnesota

A Radiation Survey of all dental x-ray equipment in Minnesota is in progress, administered by the Minnesota State Dental Association, the state health department, and the U.S. Public Health Service. Minnesota is one of 19 states to undertake such a statewide survey to reduce unnecessary radiation exposure without sacrificing diagnostic quality of x-ray pictures. As part of an educational program on methods of improving x-ray practices, the survey consists of 3 separate mailings to all dentists. A dental template for test exposure and 2 survey film packets designed to measure many characteristics of x-ray beams and to detect mechanical flaws in shielding of x-ray tubes are to be completed and returned for evaluation and interpretation. Reports of each phase will be sent to each dentist. The survey is to be completed by December 1962.

° ° ° °

The Center For Continuation Study of the University of Minnesota, Minneapolis, will offer the following medical continuation courses in 1962: Intermediate Electrocardiography for General Physicians and Specialists, January 2 through 6; Otolaryngology for Specialists, January 25 through 27; and Pediatric Neurology, February 12 through 17.

° ° ° °

Management of hypertension is the subject of an all-day seminar to be held September 23 at Methodist Hospital, St. Louis Park. Speakers at the symposium, which will be open to all physicians, will include Dr. Denton Cooley of Baylor University, Houston, "Surgical Management of Renal Vascular Hypertension;" Dr. Albert Brest of Hahnemann Medical College, Philadelphia, "Drug Therapy in Essential Hypertension;" Dr. Jesse Edwards of Charles T. Miller Hospital, St. Paul, "Pathological Changes of Renal Hypertension;" and Dr. Louis Tobian, Jr., of the University of Minnesota, "Mechanism of Drug Action in Hypertension." Panel discussions will follow the lectures, with a luncheon round-table planned. Visiting doctors and their wives will attend a dinner dance at Edina Country Club. Reservations for the seminar, for which Category 1 credit is approved by the American Academy of General Practice, may be made with the Methodist Hospital record office.

° ° ° °

Dr. Richard T. Henry has become associated with Dr. Clifford Stiles in Foley. Dr. Henry received his M.D. degree from the University of Minnesota and recently completed his internship at Springfield City Hospital, Ohio.

° ° ° °

Dr. Robert T. Hilker, specialist in internal medicine, has joined the Owatonna Clinic. A native of St. Paul, Dr. Hilker received his medical training at the University of Minnesota and served a rotating internship for a year at St. Mary's Hospital, Duluth. While in training at Veterans Hospital, Minneapolis, and Ancker Hospital, St. Paul, he served for three years as a fellow in internal medicine at the University. Dr. Hilker specialized in diseases of the heart, stomach, and liver, and in the interpretation of electrocardiograms.

° ° ° °

Dr. Norman W. Hoover, orthopedic surgeon at the Mayo Clinic, Rochester, is on leave of absence to join the SS Hope at Saigon, South Vietnam. He is serving as surgeon aboard the 15,000-ton floating medical teaching and training center.

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Dr. John W. Kirklin, head of a section of surgery at the Mayo Clinic, Rochester, and professor of surgery at the Mayo Foundation, Minneapolis, received an honorary doctor of medicine degree from the University of Munich during a recent visit to surgical centers in Germany,

(Continued on page 30A)

The Journal Lancet

SERVING THE MEDICAL PROFESSION OF MINNESOTA, NORTH DAKOTA, SOUTH DAKOTA, AND MONTANA

Series on PSYCHIATRY *for the* PRACTITIONER

The Doctor, the Relatives, and the Cancer Patient

RICHARD M. MAGRAW, M.D.

Minneapolis

THERE is something about the patient with cancer which is more disturbing to the doctor than the patient with diabetes, heart failure, or the like. For example, it is hard to conceive of a paper having a similar title on such a problem as Kimmelstiel-Wilson's disease, even though this complication of diabetes is just as inexorable, just as fatal, as cancer.

THE DOCTOR

I should like to begin by analyzing just what this threat is, since I think that, if the doctor can understand his own feelings, he will be better able to help the patient. At the outset, we need to remind ourselves of the obvious—that the idea of, in fact, the very word "cancer" is a frightening thing, partly because it suggests death. In our contemporary American society, as compared with earlier societies, there are not really very many things of which we have to be afraid. Saber-toothed tigers do not menace our dwelling places, the devils have all been exorcised, and we have indeed been "delivered" from the "ghoulies and ghosties and four leggedy beasties and things that go boomp in the night"* which frightened our forebears. But we still have cancer, polio, and schizophrenia, which fill us with dread. We doctors are not free of this culture-wide fear of this word and disease, although our familiarity with them diminishes our dread.

Probably no culture in the history of the world has had as little day-to-day contact with death as has ours. We manage to conceal the fact of death so that it is no longer a part of life. Thus, sick people are put into hospitals, and death, when it comes or becomes imminent, is dealt with behind closed doors of hospital rooms so that only those most intimately associated are aware of it in any immediate way. The rituals of funerals and death also tend to protect us from reality; thus the whole subject of death is swept under the rug. As stated previously, we doctors cannot help but be caught up in the usages of our culture. We are apt to have many neurotic and unrealistic attitudes toward death and have not always developed a philosophy which encompasses death and dying.

When cancer is diagnosed and this threat of death comes out in the open, confronting patients, family and doctors, any holes in our professional and personal philosophies are apt to become uncomfortably apparent. We doctors

RICHARD M. MAGRAW *is associate professor of psychiatry and neurology and internal medicine and is assistant dean and director, Comprehensive Clinic Program, University of Minnesota.*

*From an old Cornish litany.

sometimes do not have clearly in mind the fact that, while we may not be able to reverse the course of the disease, we can effectively treat the patient.

Moreover, cancer in the patient appears as a threat to the attending physician because it engenders feelings of helplessness and wrongdoing.

Helplessness. Cancer suggests suffering under an inexorable yet indeterminate sentence. One of the chief means by which we deal with anxiety is to "do something about it." Part of the strength of a doctor's role comes from his ability to "do something" about things which cannot be handled by other people without his special skill and knowledge. If he is confronted with a situation in which he feels "everybody knows" that nothing can be done, the doctor's attendance becomes an onerous, empty duty which he would like to fulfill as quickly as possible. At the same time, his professional role obligates him to carry on, and he may get into the position of going through certain motions which provide him with no sense of accomplishment and may only erode his feeling of effectiveness.

Sense of wrongdoing. The doctor feels reacted against as though he is somehow in the wrong. For one thing, he may feel guilty when, because of his habits of practice and usual level of diagnostic accuracy, he overlooks subtle signs of illness and only recognizes the presence of cancer when it unmistakably declares itself. Sometimes, lack of accuracy in diagnosis comes from our inevitable peaks of busyness, but, if we are honest, we must acknowledge that sometimes it results from slipshod or complacent methods of practice. If the doctor's conscience is not clear in this, cancer in his patient is indeed a threat to him. Needless to say, the only solution to this problem is careful medical practice.

However, even if the physician's diagnostic procedures have been exemplary, he may have a sense of being in the wrong because of what he has said explicitly or has allowed the patient to believe. Thus, if he has traded heavily on the somewhat omnipotent reassurance of his role in telling the patient with cancer that he will be all right, or if he has simply allowed the patient to fool himself or to deal unrealistically with the implication of cancer when symptoms occur, the trust between doctor and patient is impaired.

The doctor is in a real dilemma here. He knows that it is not desirable or professionally defensible behavior to worry the patient unduly. At the same time, he is in some degree pressed to be optimistic and magically reassuring by the patient's own needs. He has been taught to follow Osler's dictum, "Give the patient the benefit of your advice and keep your doubts to yourself." As I will point out later, the solution to this is to tell the truth and not be seduced into the easy, and apparently timesaving assumption of medical authority of saying, in effect, "You had a little tumor, but we got it all out and everything is going to be all right." The doctor must also take time to help the patient accomplish the necessary emotional healing, for, until the patient has assimilated and come to some acceptance of the situation, the physician's job is not done. Telling the patient in such a way that he is left alone to accomplish psychologic acceptance and healing is tantamount to walking out of the operating room after lifting out the gallbladder but leaving the clamps in and the wound open. The doctor must help the patient to become a partner in working for his own welfare and to accept the doctor at a level other than that of a parental figure who will intercept and ward off all painful threats.

THE RELATIVES

Relatives react with something of the same feelings as do the patients themselves, with, of course, a somewhat greater likelihood of guilt.

Guilt. It is extremely important that the doctor recognizes the different manifestations of guilt in order to forestall development of symptoms and illness in relatives as the disease unfolds. This is true just as much when it is likely that the patient has had a clinical cure as when the disease is slowly or rapidly progressive. The doctor must recognize the various guises which the relative's guilt may assume, such as depression, extreme oversolicitude, phobic fears for his own health, and projection of blame onto the physician. However, it is not likely to be helpful for the physician to make any direct interpretation of the reasons for the relative's behavior. What the doctor can do readily and successfully is to discuss in a conversational way the relative's feelings about the patient, particularly about some of the problems the relative has encountered in living with the patient. He can recognize, when appropriate, that "Things have been hard," or, "There were times when we thought of separating," or "The illness (or the sick patient) has been a burden to everyone involved." This implicitly accepts underlying anger and diminishes the occasion for guilt.

The doctor must be especially alert to the possibilities of preventive action in cases of lingering illness requiring a great deal of nursing care and he must help the wife, child, or parent of the sick person to recognize some of

the frustrations and discomforts he feels. The doctor should be aware of the common situation in which the oldest or most conscientious child is burdened with the major care. The oldest child is apt to be more guilt-ridden than his siblings and correspondingly vulnerable to distress. A few minutes of well-timed listening can prevent the development of disabling distress.

Anger. In a relative of a cancer patient anger may be a cover for guilt and may also serve as a defense against anxiety. Furious anger is sometimes a defense against the pain of grief and a forestalling of the painful work of mourning. It is important to help the relative work through such anger, for, until the grief has been resolved, it remains a kind of encapsulated emotional abscess and thus a potential source of pain and trouble.

Anxiety. At the outset, I alluded to the fact that cancer is a frightening concept. Some anxiety of relatives is normal and expected, for such illness makes us more aware of our own vulnerability. On the other hand, a lot of people are making a fragile adjustment to life—an adjustment which can be readily disrupted by anxiety heightened by such an illness. One such kind of fragile adjustment is the person who hides his uncertainty in bombast and who might be described as a kind of "paper tiger" moving through life as if he were in a jungle, beset by terrors on every side.

Grief. Certainly, grief is an appropriate response in relatives, not only when the actual bereavement occurs but also in the preceding period when it is clear that death is coming. There may be a kind of anticipatory recognition of this, resulting in some withdrawal of emotional investment in the patient. Close relatives are often aware of this and feel guilty about it. They may need to be helped to recognize that this is a necessary protective device to keep the loss from being overwhelming when it occurs.

THE PATIENT

The patient also is apt to react with one or a combination of the emotions of guilt, fear (anxiety), anger (resentment), and grief. Usually, he experiences several of these emotions together or at different times. We will understand them better, however, if we consider the emotions individually.

Guilt. Interestingly enough, patients not infrequently feel guilty about cancer, at least initially. One of their first reactions may be to justify the fact that they have not sought care sooner.

Anxiety. Like cancer, death is a fearful, unknown thing and is likely to be frightening as an idea. The major anxiety the patient experiences, however, may not be the fear of death but the fear of pain, the fear of the unknown, and, *above all, fear of being left alone.* This separation anxiety is, of course, frequently heightened by the tendencies which we all have to treat the cancer patient in a special, unnatural way so his usual closeness with doctors and relatives is diminished at the time he needs it most. The Germans have a phrase, "Torschluss-panik," which means fear of being locked out or locked in after everybody else has gone home. I think this depicts the central anxiety of many patients with cancer.

The patient has his own defenses against anxiety, which are sometimes surprisingly gross. Not long ago I saw a woman who had had a breast removed for cancer and, when I asked her, with a gesture to the missing breast, "How long ago did you have this operation?", she looked at me blankly and started the conversation off in another track. When I repeated my question after a few moments, I got the same response. She was denying not only the fact of cancer, but the fact that she had had an operation.

The doctor's major weapon in the face of the patient's anxiety is his own comfortableness with cancer and its implications and, in the words of Osler, his "equanimity in the face of disaster."

Anger. The patient often masks his anxiety and grief with anger. He may feel that life has been hard, that he has asked for little, and that his conscientious efforts to do the right thing have culminated in a disastrous illness which is scarcely a reward for the law-abiding, duty-oriented life he has been leading. Further, there may have been medical mistakes along the way. I am sure that one of the things that keeps physicians compulsively careful in medicine is the awareness of the disastrous consequences of casual or routine medical care.

Of course, dealing with anger in a cancer patient is no different from dealing with anger in any other part of medicine. It is important that the doctor be able (1) to practice medicine in such a way that he can minimize his mistakes; (2) to accept his mistakes without feeling so guilty about them that he has to shut himself off from the patient; and (3) to recognize that helping the patient express his anger about fate or failure of doctors to find his illness will give the patient relief.

I once knew well a federal judge in a neighboring state who for four years had gone to a

variety of excellent clinics thinking that he had cancer of the stomach. This was diagnosed as gastric neurosis after careful studies, and only after four years did an exploratory laparotomy reveal far-advanced malignancy which had originated in the cardia of the stomach. The patient had retreated to his room with the shades pulled and lay listless and disinterested; only when given a chance in a fifteen-minute interview to express his resentment toward doctors for missing this diagnosis and to sob out some of his feelings of loss did he get up out of bed and begin to read newspapers. He lived out the rest of the three or four months of his life in relative comfort and optimism. In telling the patient that this was a difficult diagnosis to make, I was not defending doctors or telling him he had no right to be angry but, rather, I was helping him to accept some of the inevitabilities of life.

Grief. Sorrow is a completely appropriate response for the patient with cancer because, whatever happens, he has lost something. Even if, as time passes, he finds he has a five-year cure or ten-year cure or can be presumed free of the disease, he has lost his sense of physical integrity and invulnerability. The patient whose illness and disability are increasing has a progressive kind of loss to acknowledge and accept and, hence, grief to work through.

The patient must progressively face loss in his capacities. He may, for example, no longer be able to go hunting, no longer be able to drive in a car to visit relatives, no longer be able to walk outside to enjoy the freshness of the day, and so on. Each step represents a new loss and fresh grief. The doctor can materially help the patient in this regard and, as the patient works through his grief, he is, in fact, being cured of a part of his trouble even at the same time that he may be dying.

In order to understand this, it would be well to review just what grief is. Grief is a healing process and may be regarded as a homeostatic mechanism which restores emotional equilibrium and health. Grief comes after we have been bereft. It represents a scabbing over of the wound in recognition and acceptance of the loss. Whether the loss be that of a friend, an idea, a part of the body, or a part of life or of health, the process is essentially the same. We have to hold the loss up and look at it, and in so doing, recognize its implication. Actually, grief has two elements: the pain and work of recognition of loss and the process of mourning in which an individual sobs out his sorrow and pulls back into himself that part of his life energy which had been invested in the person, thing, or idea from which he is being separated. This feeling of sorrow about leaving life is well expressed in Gray's *Elegy in a Country Churchyard*:

> For who, to dumb forgetfulness a prey,
> This pleasing anxious being e're resign'd,
> Left the warm precincts of the cheerful day,
> Nor cast one longing ling'ring look behind?

Now, what the doctor has to do in this situation with the patient is to be honest and to take the time that is necessary to treat the patient as well as to treat the disease.

It has become almost a vogue to discuss whether the doctor is to tell the patient that he has cancer. I think there is no question but what the doctor should be honest with the patient. The patient should be told the true nature of his illness, then helped with his feelings. This is not the same thing as informing him of the diagnosis in such a way that the doctor is relieved of further responsibility in the matter.

It has been said it "takes two to tell the truth." Because there are many misunderstandings about cancer and the word has many different meanings, the physician should not only tell the truth, but tell it in such a way that the patient hears the truth.

Since the doctor's own attitude will certainly be transmitted to the patient, it is extremely important that the doctor formulate for himself a philosophy which includes death as a part of life, not in any matter-of-fact or cold way, but as a recognition of some of the inevitable pathos resident in living.

If the doctor is able to see that, in helping the patient resolve his grief or anger, he is actually treating him, the doctor himself will not feel so futile and can support the patient by his own "equanimity in the face of disaster."

Infections of the Urinary Tract

II. Management and Comment

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Since acute infections are common, may be transient, and seldom require heroic therapy, treatment may be initiated empirically after preliminary identification of the pathogens by the gram stain. Acute uncomplicated infections often subside without specific treatment. Failure to eradicate the infection requires further investigation to exclude uropathy, predisposing disease, and so forth. It is serious to overlook chronic infection of the urinary tract with acute flare-ups and to consider them as episodes representing acute, simple infections. If investigation is unrewarding and if infection continues to recur, use of a suppressive agent, such as 0.5 gm. of a sulfonamide or 100 mg. of nitrofurantoin (Furadantin) four times daily for one week of each month for several months, may be helpful.

MANAGEMENT

Supportive and local treatment. General measures, such as rest and sufficient intake of fluid to produce a daily output of 2,000 cc. of urine may be stressed, except when intake is restricted in an attempt to keep the urine acid. Dysuria continuing beyond control of infection does not indicate further need of antibacterial agents; use of any of several bladder sedatives may be helpful, but sometimes lavage of the bladder is necessary. Paradoxically, if true infection is present, control of dysuria may result in a welcome decrease in the patient's vocal reaction but does not ensure beneficial effect on possible continued renal damage.

Antibacterial treatment. Infection secondary to stones, tumors, and the like may have value as a diagnostic feature of the uropathy; therefore, premature use of antibacterial agents without investigation may eventuate in a diagnostic loss. It may be wise to extend the duration of therapy in acute infections to two weeks after evidence of microbiologic cure and, in chronic infections, to four weeks thereafter.

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Generally speaking, combined streptomycin-tetracycline therapy is preferred in serious infections caused by gram-negative bacilli,[1] such as those of the coli-aerogenes group and proteus, alcaligenes, klebsiella, brucella, and most salmonella organisms. There are 5 possible exceptions wherein a single agent may be given: (1) novobiocin[2] in certain infections due to proteus organisms, (2) polymyxin B in pseudomonas infections, (3) erythromycin in some haemophilus infections, (4) chloramphenicol when Salmonella typhi is causative, and (5) a tetracycline alone in bacteroides infections.[3] Incidentally, a newer antibiotic, colistin sulfate, which is being marketed as Coly-Mycin, while less efficient weight for weight in vitro than polymyxin B, may be less toxic than that agent, and some investigators believe it may have sufficient potential to partially displace polymyxin B in clinical practice.

Streptomycin-tetracycline treatment for serious infections caused by gram-negative bacilli is preferable for several reasons. Streptomycin alone is inadequate because of the high failure rate following its use and because bacteria quickly become resistant to it. The onset of bacterial resistance may be delayed by use of multiple antibiotics. By means of combined therapy, an enhanced effect may be obtained; use of streptomycin may impart a bactericidal effect to the combination, since the tetracyclines alone are bacteriostatic. When streptomycin-tetracycline treatment is given after identification of bacteria and before inhibition tests are reported, broader antibiotic coverage is provided. In our experience at the Mayo Clinic, this type of treatment resulted in a lower relapse rate and the period of treatment was shortened.

It is worthwhile in certain severe infections caused by gram-negative bacilli unresponsive to tetracycline-streptomycin therapy to procure inhibition tests using chloramphenicol and kanamycin, with a view to substituting one or both agents. Also, in infections caused by gram-negative bacilli, if staphylococci are also present or if superinfection with them seems likely, use of

chloramphenicol, kanamycin, or both may avert further difficulties. A regimen of chloramphenicol-kanamycin is not used routinely in serious gram-negative bacillary infections because it has greater potential toxicity than does tetracycline-streptomycin. The restricted use of chloramphenicol makes it employable in these situations; its indiscriminate use not only increases the incidence of blood dyscrasias but also increases the number of resistant bacterial strains. Also rarely, polymyxin B, another agent of considerable toxicity and used mainly for pseudomonas infections, is employed in infections caused by coli-aerogenes organisms not responding to streptomycin-tetracycline therapy. Caution is required in using nephrotoxic agents like streptomycin, kanamycin, and polymyxin B in urinary infections; not only are they nephrotoxic, but delayed renal excretion of them allows their accumulation in the blood and furthers neurotoxic effects.[4]

Combined penicillin-streptomycin therapy is indicated for serious infections due to enterococci, for example, Streptococcus faecalis. Infections caused by other strains of streptococci, such as S. pyogenes and S. viridans, may respond to treatment with penicillin alone.

The treatment of staphylococcal infections depends largely upon results of in vitro susceptibility tests. If staphylococci are sensitive to penicillins G and V, they remain the drugs of choice; in mild infections, orally administered penicillin V[5] has been successful. In the recent past, alpha-phenoxyethyl penicillin potassium,[6] a semisynthetic penicillin, has been prepared for oral use and marketed as Syncillin and as Darcil. Some data were interpreted as indicating that the newer agent might supplant penicillin V as the preferred oral preparation of penicillin, since it provides higher concentrations in the blood. However, Nichols and I[6] have published data that corroborate the work of Griffith[7] and of McCarthy and associates[8] which indicate that there is, weight for weight, no difference in the antibacterial effects of the two drugs. In other words, although the semisynthetic penicillin provides higher blood levels, its ability to kill susceptible organisms, as indicated by the so-called serum bactericidal test, is not comparatively enhanced. To say it another way, when given in the same dose, penicillin V results in lower blood levels but its serum killing effect equals that of the newer agent, despite the latter's higher concentrations in the serum. Therefore, in infections wherein penicillin can be employed orally, penicillin V and the newer semisynthetic penicillin can be used interchangeably.

Still more recently, another semisynthetic penicillin, sodium dimethoxyphenyl penicillin, which retains its antibacterial activity in the presence of penicillinase and hence is effective against certain staphylococci resistant to other penicillins, has been marketed. The proprietary name of this latter drug is Staphcillin, and it must be administered parenterally. In vitro resistance to the agent can be induced. Even when in vitro susceptibility tests indicate that a staphylococcus resists other penicillins but is susceptible to Staphcillin and to other antibacterial agents, Staphcillin is not automatically the drug of choice, however, because of (1) the availability of other effective, orally absorbable, less toxic antibiotics and (2) the desire to minimize Staphcillin's use so as to minimize development of staphylococcal resistance to it.

Generally, if the staphylococci resistant to penicillins G and V are sensitive to erythromycin, then erythromycin, or its propionyl ester, is the agent of choice, since it can be given orally and is virtually nontoxic. Next, triacetyloleandomycin, which is absorbed orally and also is virtually nontoxic, should be considered, since there is about a 70 per cent chance that erythromycin-resistant staphylococci may be sensitive to its action.

Thereafter, the physician might consider novobiocin, since it is orally absorbed; although it causes drug rash, especially if its use is prolonged, so can Staphcillin, which must be given parenterally and which has a greater potential for hypersensitivity reactions, including anaphylaxis.

If erythromycin, triacetyloleandomycin, or novobiocin cannot be used, then Staphcillin may be the drug of choice. If Staphcillin is not applicable, as in patients who have previously exhibited allergy to a penicillin, kanamycin may be tried; kanamycin should be considered before vancomycin, since, although both are toxic to the eighth cranial nerve, kanamycin is given intramuscularly, while vancomycin must be given intravenously. Chloramphenicol follows vancomycin in the list of selections, even though it has the advantage of being orally absorbable, because of its propensity to depress the marrow; it should be considered before ristocetin, which can also depress the marrow but has the added disadvantage of requiring intravenous administration. Before or after consideration of chloramphenicol and ristocetin, depending on one's fear of ill effects on the marrow as well as on the laboratory facilities available, combined antibiotic therapy can be considered.

So-called combined therapy of staphylococcal urinary infections usually involves a bacteriostatic agent, such as erythromycin, novobiocin, or chloramphenicol, together with such bactericidal agents as bacitracin or neomycin. However, the need for such cumbersome therapy is rare in urinary infections. If such therapy is attempted, the organism preferably should be sensitive to both agents used. Excellent laboratory facilities are required for intelligent application of combined therapy. At the Mayo Clinic, we prefer to rely on the evaluation of combined therapy via the serum bactericidal test[6,9–12] during treatment with the two drugs that have been selected empirically rather than to rely on pretreatment in vitro susceptibility tests using various combinations of drugs for selection of the agents to be employed. If the physician relies on pretreatment susceptibility tests, he should perform serum bactericidal tests during treatment with the agents to verify in vivo that the effect predicted in vitro is being obtained.

Because of the profound effect of the tetracyclines on the normal bacterial flora and the possibility of consequent superinfection by tetracycline-resistant staphylococci and hemolytic streptococci, my colleagues and I avoid administration of these drugs as much as possible in hospitalized patients. Streptomycin, because staphylococci may develop resistance to it rapidly, and polymyxin B, which lacks significant antistaphylococcal action, usually are not considered in the treatment of staphylococcal infections. Of the chemotherapeutic agents, nitrofurantoin is used in mild urinary infections and, like the sulfonamides, as a prophylactic agent. Furaltadone (Altafur) has demonstrated considerable toxicity, and consequently its current application as an oral antistaphylococcal agent is uncertain. However, Nichols and I[12] have accumulated some data indicating that furaltadone, when administered intravenously, has a bactericidal effect; since the agent's toxicity is minimal when it is used for only a few days, one might consider employment of the drug parenterally in the initial phase of certain staphylococcal infections. Sulfonamides, because of the problem of resistance, play no major role in the definitive therapy of serious staphylococcal infections.

The physician must rely to some extent on sensitivity tests in the management of staphylococcal infections, but time does not always allow for such tests. When staphylococcal infections of a serious nature demand treatment before the results of such tests are available, we give an agent to which the staphylococci in our institutions most likely are sensitive. Novobiocin, Staphcillin, kanamycin, vancomycin, and chloramphenicol might be selected, in about that order of choice; after twenty-four to forty-eight hours, when the results of susceptibility tests are known, a more pertinent or less toxic agent may be substituted.

Consideration of the relative costs of antibacterial agents may help in deciding which is to be used, especially in mild infections. As an example, the cost of treating a patient with a sulfonamide is one-tenth that necessary for treatment with nitrofurantoin, tetracycline, or penicillin.

In some urinary infections, especially those without systemic manifestations, calcium mandelate may be used in amounts of 3 gm. four times daily; acidification of the urine is advised. Methenamine mandelate, in amounts of 1 to 2 gm. three times a day, which is also relatively nontoxic, may also be used, but its activity, too, is dependent upon the urinary *p*H, the activity decreasing sharply as the *p*H rises. Maintaining a low urinary *p*H is difficult because of the rather rapid renal adjustments to the acid load. However, decrease in urinary *p*H and lowering of bacterial counts in the urine may follow use of 12 to 15 gm. of methionine daily; methionine alone may be given for months if renal function is normal, and bacilluria may be thereby eliminated.

A combination of methionine and methenamine or calcium mandelate may be tried instead. Feeding of methionine leads to oxidation of its sulfur to sulfate, which in turn lowers the *p*H of the urine. The sulfate ion is efficient as a urinary acidifier to the extent that even alkaline urine of patients with proteus infections can be made acid, and the infection may be brought under control. Methionine, or a metabolite thereof, produces its bacteriostatic effect at a *p*H of 5 or lower. When attempts are made to keep the urine acid, it is wise to restrict fluid intake to 1,200 cc. a day and to avoid foods, primarily citrus fruits, and drugs, such as sodium bicarbonate and milk of magnesia, which increase the alkalinity of the urine. Also, the patient should periodically determine, by means of Nitrazine paper, whether his urine is properly acidic.

When so-called bacteriostatic or suppressive drugs are used, negative follow-up cultures of the urine should not cause relaxation of scrutiny, since the infection may recur shortly. In vitro, with concentrations of drugs unattainable in the body, agents may demonstrate a killing effect on bacteria, but we employ the term bactericidal to

designate drugs that may do so in vivo. The bactericidal agents include penicillin, streptomycin, bacitracin, neomycin, polymyxin B, ristocetin, kanamycin, and vancomycin. Although the terms bactericidal and bacteriostatic may not be ideal, one needs to be familiar with the concepts which they identify. Bacteriostatic agents are those whose concentrations in the body are insufficient to kill bacteria; they may be ineffective when used alone, except in acute, uncomplicated situations. The bacteriostatic agents include the tetracyclines, chloramphenicol, erythromycin, novobiocin, triacetyloleandomycin, sulfonamides, nitrofurantoin, calcium or methenamine mandelate, and methionine. However, when a combination of a bactericidal and a bacteriostatic agent is used, it may be bactericidal; this possibility should be determined in the individual infection and, as aforementioned, preferably by so-called serum bactericidal tests. The results of in vitro inhibition tests cannot be taken as dogma, since a bacteriostatic agent may seem to be indicated on this basis, but one may know empirically that, unless a bactericidal effect is obtained, treatment will be ineffective. Experience also may indicate that certain antibacterial agents will be effective, despite in vitro inhibition tests to the contrary. As an example of this, in treating infections due to proteus organisms, we noted that, despite in vitro resistance to tetracycline and streptomycin, eradication of the infection followed use of these agents.

In treatment of polymicrobic infections, several drugs may be given simultaneously—for example, penicillin and streptomycin in enterococcal infections and, simultaneously, a tetracycline against coli-aerogenes organisms. As it is difficult to say which organism is most important in polymicrobic infections, the physician gives broad coverage, since estimation of the infections capabilities of the individual organisms may be erroneous. However, one attempts to keep the number of agents to a minimum and rarely resorts to such an antibiotic umbrella. The use of multiple agents not only is unnecessary in many cases but might, some experimental data to the contrary, increase bacterial resistance more rapidly than if infections were treated with a single agent. In other words, restricted employment of combined therapy may delay the onset of bacterial resistance on the part of the individual pathogen, but indiscriminate use of multiple agents may increase general bacterial resistance, since such resistance is a direct function of the total amount of a given antibacterial used in a given area.

In diabetics with urinary infections, the possibility of ultimate necrotizing papillitis[13] makes vigorous therapy necessary.

It should be constantly recalled that antibacterial agents are not an unmixed blessing, because their use (1) entails extensive and highly technical bacteriologic study, (2) may distort manifestations of underlying uropathy if employed before diagnosis is established, (3) causes emergence of resistant organisms, (4) may lead to replacement of pathogens, (5) produces untoward reactions, including superinfection, (6) is expensive, and (7) may contribute to a false sense of security and to less comprehensive evaluation of patients. The most benign and easily administered regimens, such as use of an orally absorbable, relatively nontoxic, preferably inexpensive antibacterial agent, are reserved for acute simple infections and, paradoxically, for chronic, smoldering, relatively asymptomatic infections. More heroic therapy, such as use of parenterally administered, relatively toxic agents, employment of which requires much medical supervision and expense, is utilized (1) for infections characterized by a violent systemic reaction, (2) for infections not responding to more simple therapy, (3) for recurrent infections, and (4) for what is presumed to be the last chance to preserve the patient's relatively normal renal status, such as the postoperative condition wherein an organic lesion predisposing to infections has been eliminated.

Surgical treatment. In addition to relief of any obstruction to the passage of urine before antibacterial agents can become effective, surgical procedures such as drainage of an abscess or nephrectomy occasionally are necessary.

Toxic reactions to antibacterial treatment. Penicillin and allied drugs depress the gram-positive elements of the normal body flora and allow unopposed overgrowth of the gram-negative elements thereof, with consequent urinary infection, pneumonia, bacteremia, and other superinfections due to coli-aerogenes organisms and the like. Physicians are aware of antibiotic-induced overgrowth of gram-positive organisms, such as tetracycline-induced staphylococcal enterocolitis, but apparently are less aware of antibiotic-induced gram-negative infections resulting from penicillin and similar agents.

There is cross allergenicity between Staphcillin and other penicillins; adverse reactions to penicillins in the past or a history of other allergies, particularly asthma, may be more important than the results of skin testing in deciding to use these agents.

Penicillinase helps to combat allergic reactions to penicillin, but, conversely, penicillinase may also cause such reactions, including anaphylaxis. Use of penicillinase may not be effective in allergic reactions to Staphcillin, since the latter drug resists destruction by penicillinase.

Streptomycin is less likely to damage the auditory function of the eighth cranial nerve than is dihydrostreptomycin or a combination of the two substances. Although streptomycin may damage the vestibular function of the eighth nerve, this is not so calamitous as irreversible deafness, and the dysequilibrium may be compensated partially by ocular mechanisms. Dihydrostreptomycin should not be used except in the rare instance in which the patient has a real need for such an agent and cannot tolerate streptomycin but can tolerate dihydrostreptomycin. Other ototoxic antibiotics are neomycin, kanamycin, and vancomycin. Whether ristocetin is ototoxic is not certain. Concurrent and perhaps sequential use of ototoxic drugs should be avoided.

Streptomycin, penicillin, and the sulfonamides, particularly sulfathiazole, have been known to precipitate acute gouty arthritis.

Nephrotoxic antibacterial agents in addition to streptomycin are neomycin, bacitracin, polymyxin B, kanamycin, and the sulfonamides.

Streptomycin, neomycin, polymyxin B, colistin sulfate, and kanamycin produce acroparesthesia which, as an isolated finding, seldom warrants discontinuing the use of these agents.

Neomycin and kanamycin are cross-resistant; whether either has significant cross-resistance with streptomycin is uncertain.

Use of the newest tetracycline, demethylchlortetracycline (Declomycin), is not encouraged until its purported advantages and known disadvantages are clarified. Roberts and associates[14] find that the new agent does not produce significantly higher blood levels than do other tetracyclines and that it should be given in doses equal to those of the other tetracyclines. It is not at present reasonable to use this newer agent because its apparent advantage is disputed and it carries the additional hazards of photosensitization and, perhaps, increased gastrointestinal irritation when administered in the dose recommended by Roberts and his colleagues.

After oral administration of any of the tetracyclines, nausea, vomiting, and looseness of the stools may occur. However, when frank diarrhea develops in a patient receiving these drugs, specimens of stool should be examined by smear and culture for staphylococci. Staphylococcal enterocolitis[15] follows use of other agents, namely, sulfonamides, streptomycin, neomycin, polymyxin B, chloramphenicol, and kanamycin, which also depress the gram-negative flora and allow staphylococcal overgrowth. The factors predisposing to staphylococcal enterocolitis also operate in inducing staphylococcal superinfection elsewhere in the body; the physician should not only be alert to staphylococcal enterocolitis but also, in predisposing circumstances, should guard against staphylococcal urinary infections, staphylococcal pneumonia, and the like. As aforementioned, a considerable number of beta-hemolytic streptococci also resist the tetracyclines and may cause superinfection; also tetracyclines may not prevent rheumatic fever and glomerulonephritis following certain infections due to these organisms.

Gastric irritation from tetracyclines is less if they are given with cold milk. Use of milk may be undesirable in patients maintaining a low-residue or low-sodium diet; to them we give calcium carbonate, 5 gr. with each capsule of the agent. While calcium carbonate may tend to hinder the absorption of tetracycline, blood levels are considerably higher than when one resorts to the alternative of reducing the dosage of the antibiotic.

Antimicrobial agents in addition to chloramphenicol that are associated with blood dyscrasias are ristocetin, sulfonamides, and streptomycin. Actually, all antibacterial agents have been accused sometime of having depressed the marrow, but since victims of dyscrasias frequently received multiple drugs, conclusions about the other agents are established with difficulty.

Exogenous substances causing pigmentation and confusion with jaundice are novobiocin, Atabrine, and carotene.

Skin reactions, including angioneurotic edema, may follow use of any antibacterial agent, but among those commonly used, streptomycin, tetracyclines, and erythromycin are less likely causative; conversely, penicillin, novobiocin, and sulfonamides are most likely causative.

Antibacterial agents most likely to cause anaphylaxis are penicillin, streptomycin, and sulfonamides.

Any antibacterial agent given intravenously may cause local phlebitis, but the tetracyclines, ristocetin, and vancomycin are the most likely to do so.

Polymyxin B is most likely to produce pain on intramuscular use; the tetracyclines, bacitracin, and the 3 related drugs, streptomycin, neo-

mycin, and kanamycin, occasionally produce pain.

Any antibacterial agent given orally causes gastrointestinal irritation, apparently reflecting its chemical nature and the individual's tolerance; tetracyclines, nitrofurantoin, and sulfonamides most often generate such distress.

Moniliasis has not often complicated our attempts at antibacterial therapy, in contradistinction to the experiences of others.

Pruritus ani, in our experience, most often follows oral use of tetracyclines.

Any antibacterial agent can cause drug fever, but only penicillin commonly causes serum sickness.

Of cases of anaphylaxis, exfoliative dermatitis, and angioneurotic edema with laryngeal involvement, 10 per cent are fatal; 50 per cent of antibiotic-associated blood dyscrasias are fatal.

Hematuria may be due to 3 agents used in urinary infections: mandelic acid, sulfonamides, and chloramphenicol.

Sulfonamides have been associated with 5 potentially fatal syndromes: (1) nephropathy, (2) depression of bone marrow, (3) periarteritis nodosa, (4) exfoliative dermatitis, and (5) staphylococcal enterocolitis.

DISCUSSION

Bacilluria with or without pyuria may be asymptomatic. It is of increased incidence in patients with underlying conditions known to predispose to urinary infections, such as diabetes, pregnancy, obstructive uropathy, a history of urinary instrumentation, and the like. Necropsies indicate that asymptomatic bacilluria and infections of the urinary tract may be related phenomena. Asymptomatic bacilluria may be present weeks before clinical manifestations of urinary infections. Kass[16] notes that pyelonephritis of pregnancy occurs mainly in women having asymptomatic bacilluria at the first prenatal visit and if bacilluria is eliminated, usually by administration of 0.5 gm. of a sulfonamide daily for one to two weeks, pyelonephritis does not occur.

Bacilluria may persist in spite of therapy and, although infection may be reduced, may not be eliminated. Some such infections "burn out," some continue indefinitely without appreciable deterioration of renal function, and some culminate in renal insufficiency. It is obvious to practitioners with any clinical experience that not all urinary infections can be eradicated any more than can all disease in any sphere of medical endeavor, and failure to stop urinary infections should not generate pessimism sufficient to cause abandonment of all therapeutic effort. Therapeutic failures in urinary infections may depend on (1) lack of realization that infection may occur without local symptoms; (2) misinterpretation of the significance of pyuria, which is absent in 50 per cent of chronic active urinary infections and has causes other than infection in 50 per cent of cases; (3) lack of pathogens' susceptibility to the antibacterial agents employed; (4) errors in the selection, administration, and supervision of antibacterial regimens; (5) the patient's response to the pathogens and to the regimen; (6) underlying disease that may make recovery impossible; and (7) failure to realize that other investigative and therapeutic procedures are indicated if there is poor response to an appropriate antibacterial regimen.

The problem of urinary infections in patients with urinary retention requiring catheterization because of cerebrovascular accident or that induced by drugs required to relieve pain is common. Also, the physician may share the care of a patient whose urinary infection has followed urologic instrumentation or a surgical procedure. In such cases, acute pyelonephritis and fatal bacteremia may eventuate, and since the complications are iatrogenic, the doctor's responsibility for initiating the precipitating diagnostic or therapeutic procedures is obvious.

Routine administration of antibacterial agents in subjects without cardiovascular defects as prophylaxis against the 2 to 4 per cent chance that infection will result from instrumentation or operation is generally thought unwise. Conversely, control of known infections should be attempted before manipulation of the urinary tract. Objections to attempted prophylaxis with antibacterial agents in patients with indwelling catheters are that it may induce (1) emergence of drug-resistant pathogens, (2) superinfection, and (3) toxic reactions to the drugs employed.

The principles of management of urinary infections are (1) to identify pathogens by the gram stain and procure cultures in more severe, recurrent, or chronic infections; (2) if bacteria are identified, to initiate treatment with an antibacterial agent empirically if the condition of the patient warrants; (3) to re-evaluate if susceptibility tests later indicate poor choice of an antibacterial regimen but to continue the regimen unaltered if the patient is doing well; (4) in selected infections, to determine possible synergism of combined antibacterial therapy; (5) in severe infections, to obtain bactericidal tests to determine if the bacteria can be eradicated by the antibacterial regimen employed; and (6) to

correct any condition predisposing to infection—to ensure both free access of antibacterial agents to the site of infection and adequate drainage of urine.

Generally, with the numerous antibacterial agents available, acute simple urinary infections no longer present therapeutic problems, but chronic recurrent infections and persistent bacilluria continue to constitute clinical difficulties. Increased efforts at earlier recognition of the latter may aid in improved management of them; it may be difficult to maintain bacteria-free urine, but if a total review of the individual's problem makes vigorous therapy worthwhile and if renal function is acceptable, bactericidal drugs are superior to the bacteriostatic.

"Cure" is determined only by the patient's progress from both clinical and laboratory points of view after cessation of therapy.

Careful analysis of individual infections and the use of common sense in therapy are urged; there is no place for diagnostic or therapeutic dogma in the management of urinary infections. The physician should bear in mind constantly that at any stage of management of infections of the urinary tract, it may be necessary to re-evaluate, re-examine, and alter any regimen.

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Prolonged corticosteroid therapy at moderate or high doses often results in posterior subcapsular cataracts. Lenticular lesions appeared in 17 of 44 patients receiving corticosteroid therapy for rheumatoid arthritis but did not occur in 19 arthritic patients without steroid treatment. Cataracts formed in 8 of 18 subjects given moderate or high doses for one to four years and in 9 of 13 subjects given such doses for more than four years. None developed in patients who had taken low doses for any length of time or in those given any dose for less than one year. Cataracts were considerably more common in men than in women. Although impairment of vision was not serious, opacities were visible with an ophthalmoscope through the dilated pupils of 11 patients. For 3 of 5 subjects, initial lenticular changes were not arrested by decreasing steroid dosage, but such reduction seems advisable.

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Trauma to the Nervous System

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INJURIES TO THE HEAD are frequently associated with brain injury. Although cerebral injury is of prime importance, injuries to the scalp and cranium cannot be completely disregarded because they may open avenues for the spread of infection.

CRANIOCEREBRAL TRAUMA

Intracerebral complications may follow an infected scalp injury—with or without fracture—either by extension through the bone (osteomyelitis) or along the diploic veins. Head trauma is becoming one of the more common causes of cerebral damage as a result of injuries sustained in car accidents, industry, and sports. Such damage is caused from penetration by a missile; a blow to the stationary head; sudden arrest of the head while it is in motion; sudden movements of the head, such as are seen in whiplash-type injuries; or compression or crushing of the skull between forces.

The mechanism of brain injury may be caused by (1) direct injury to the underlying brain, (2) a contrecoup type of injury, (3) transient elevation of intracranial pressure with resultant cerebral anemia, (4) a direct type of trauma upon nerve cells, (5) acceleration-deceleration of the head, and (6) local shearing from passage of pressure waves.

Terminology

Considerable confusion exists in the literature because of the failure to define adequately the terminology used in discussing craniocerebral injuries. A large share of the confusion in terminology centers around the term "concussion"—a term which should be reserved for those cases showing transient loss of consciousness with no later evidence of localized brain injury. Concussion is a clinical term. The pathologic terms "contusion" and "laceration" are used to describe what happens to the underlying brain. Contusion describes a bruising of the brain and laceration, a tearing of the brain substances with hemorrhage and necrosis. Hemorrhagic complications of craniocerebral injuries may produce subarachnoid, subdural, or extradural bleeding. Skull fractures may be basilar, depressed, or compound.

Clinical Classification of Craniocerebral Injuries

The following clinical classification of craniocerebral trauma is of practical use:

1. *Transient or no unconsciousness with no persistent symptomatology.* In this type patient, headaches, vertigo, and mild confusion may be present and persist from a few hours to days. The electroencephalogram may be normal or show transient abnormalities which rapidly clear. Repeated head trauma of this type may be followed by permanent evidence of brain injury; for example, this is encountered in professional fighters who become punch drunk.

2. *Transient or no unconsciousness with persistent symptomatology.* A large number of patients fall into this group. The subjective symptomatology may be mild and unassociated with abnormalities in the neurologic examination or electroencephalogram or may be severe with varying degrees of such abnormalities.

3. *Prolonged unconsciousness—without shock and with shock.* The prognosis is worsened by the presence of prolonged unconsciousness, retrograde or posttraumatic amnesia, spinal fluid changes that show blood or elevated protein, persistent focal abnormalities in neurologic examination, or persistent abnormalities in the electroencephalogram.

Treatment of Acute Symptoms

During the acute stage of shock, general measures directed toward shock should be em-

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ployed. The patient should be moved as little as possible. Careful check should be maintained on the vital signs. Repeated neurologic examinations to detect the early development of complications are essential. Concerning fluid intake, it is best to maintain the patient as one would a surgical patient—with adequate fluid intake and output. Maintenance of an open airway is essential; in the comatose patient with a brain injury, serious consideration should be given to use of a tracheotomy. Tracheotomy can be lifesaving in severe brain injuries.

If a depressed skull fracture or a fracture of the temporal bone with the possibility of extradural bleeding is suspected, an early roentgenogram is indicated. If these complications are not suspected and the neurologic picture remains stable, a roentgenogram of the skull can be deferred until the patient is free of shock. Bleeding from the ear and nose indicates a basilar skull fracture.

If the patient becomes restless and irritable when the stage of shock has passed, this indicates the development of cerebral edema. The vital signs of a typical case of increasing intracranial pressure vary—the temperature and blood pressure rise and pulse and respirations decrease. If possible, the use of sedation for restlessness and irritability should be avoided. If necessary, restraints are indicated. Dehydrating measures, such as magnesium sulfate or sucrose, are probably contraindicated. This is because of the rebound in cerebral edema which follows the initial use of magnesium sulfate and the toxic effect which sucrose has on the kidney. A transfusion of salt-free serum albumin may be beneficial in reducing cerebral edema, particularly when such reduction is necessary for only a short time, as in preparing the patient for surgery. Urevert has some promise for combating cerebral edema.

In the face of increasing intracranial pressure with progressive coma of the patient, neurosurgical intervention with burr hole production and decompression are the procedures of choice. In some selected instances, lumbar puncture may be resorted to, but this carries the risk of postpuncture herniation of the brain. Supplementary use of oxygen may be of benefit in maintaining cerebral oxygenation. Careful attention to detail, intensive nursing care, and close neurologic supervision may be lifesaving.

Acute Complications

1. *Meningitis.* This may complicate a basilar skull fracture with bleeding from ears and nose, may complicate a penetrating wound, or may succeed an infected scalp injury. The usual signs of meningitis are accompanied by stiff neck, hyperthermia, and pleocytosis in the spinal fluid. Antibiotic treatment directed toward the organism responsible for the meningitis should be intensive.

2. *Brain abscess.* This may complicate a depressed fracture or penetrating wound of the brain. The clinical picture may be variable, but it is usually associated with elevated temperature and focal findings. Treatment with antibiotics until the abscess is encapsulated, succeeded by angiography and evacuation, are indicated.

3. *Rhinorrhea.* This complicates fractures of the cribriform plate of the nose or temporal bones. Many of these respond to conservative treatment—the patient lies flat on his back and avoids blowing his nose or coughing. If the rhinorrhea persists in spite of conservative treatment, it may be necessary to have the tear surgically closed. The use of antibiotics to prevent development of meningitis is indicated in cases of rhinorrhea.

4. *Aerocele (pneumatocele).* Air is encountered in the subdural and subarachnoid spaces or ventricles and is associated with severe headaches. Spontaneous recovery is the rule and no specific therapy is necessary.

5. *Cranial nerve damage.* The olfactory nerve is not infrequently damaged. When such damage occurs, it is usually permanent. Damage to the optic nerve complicates fractures of the nose —third cranial nerve symptomatology may be encountered either because of direct injury to the ocular motor nerves or to nuclei of the midbrain. Involvement of the trigeminal nerve produces sensory loss over the face. Eighth nerve involvement, causing deafness, tinnitus, and vertigo, may be encountered. Lower cranial nerves are uncommonly involved.

Chronic Complications

1. *Posttraumatic syndrome.* The symptomatology may be varied. Not infrequently headaches, vertigo, irritability, fatigability, memory impairment, and inability to work are the persistent symptoms.

2. *Subdural hematoma.* The picture may be extremely varied. Usually, headaches are encountered followed by drowsiness, confusion, progressive paresis of one side of the body, and evidence of increased intracranial pressure. On x-rays of the skull, pineal shift may be encountered. The electroencephalogram may show amplitude of asymmetry. The angiogram frequently reveals the hematoma. Treatment is surgical.

3. *Posttraumatic epilepsy.* This is a common sequela resulting from damage and scar formation at the surface of the brain; such damage often implicates the meninges. The first seizure may appear a few months or years after the injury. The incidence of posttraumatic epilepsy is higher in penetrating brain injuries and in patients with closed head injuries who have focal abnormalities in the electroencephalogram. The large part of treatment in posttraumatic epilepsy is conservative; anticonvulsant medications are used. Factors to be avoided are emotional stress, alcoholic ingestion, and activities in which the patient would be injured if he were to have a convulsion. A small percentage of patients require surgical removal of the focus.

4. *Mental changes.* These are indicated by personality changes, untrustworthiness, rages, irritability, sexual promiscuity, psychosis, emotional lability, and destructive tendencies.

5. *Intellectual changes.* Indications are defects in memory, comprehension, and judgment.

6. *Chronic brain syndrome.* This results from severe brain injury. Symptoms are loss of memory, confusion, emotional instability, slowing of reaction, unsteady gait, convulsions, slurred speech, lack of insight, and neurologic abnormalities. The electroencephalogram and pneumoencephalogram may be abnormal with the pneumoencephalogram demonstrating enlarged ventricles and cortical atrophy.

INJURIES TO THE SPINAL CORD

Mild Injuries of the Cord

This type of injury may result from a direct blow to the spine or from a blow along the spinal axis that is sufficiently severe to vibrate the spinal cord within the vertebral canal. A localized edema and small petechial hemorrhages are produced. The involved segment is in the state of shock, which causes moderate to severe sensory, motor, and sphincter disturbances below the lesion. However, recovery is rapid and is usually well advanced within twenty-four hours. Residual effects are mild, depending on the level and amount of tissue destroyed.

Whiplash Injuries

With the increasing incidence of rear-end collisions involving automobiles, whiplash injuries of the spine are more frequently encountered. It has been estimated that approximately 15 per cent of all automobile accidents resulting in death, injury, or property damage are caused by rear-end collisions. In this group of patients, the incidence of whiplash injuries is high. In the classic whiplash injury to the cervical spine, the head snaps back with the equivalent of several tons of force and with no support because muscular control of the neck has been caught off guard. The head then snaps back in acute flexion. In some, variance of this type of neck movement is encountered: when the automobile is struck from the side, a lateral motion of the head to and fro is produced. In a fully developed whiplash injury, injury to the cervical roots, vertebral artery, sympathetic nervous system, and spinal cord may result, in addition to the usual injuries of the ligaments and mechanical derangement of the spine, which most frequently is transient. Brain injury may result from this type of accident. The neurologic complication of whiplash injuries of the cervical spine falls into several large groups. These groups include (1) injury to the cervical nerve roots (traumatic radiculitis), (2) injury to the spinal cord, (3) injury to the sympathetic nervous system, (4) injury to the vertebral arteries, (5) brain injury, and (6) psychiatric disabilities.

Injury to the cervical nerve roots (traumatic radiculitis). This is the most common complication encountered—incidences as high as 70 per cent are reported. A typical cervical nerve root is composed of motor and sensory fibers. The symptomatology produced is determined by the degree of injury to the nerve root. Frequently the patient complains only of pain. Further involvement of the nerve root may produce reflex changes, sensory changes, and motor weakness. Not infrequently, the biceps and triceps reflexes are reduced immediately after the injury. The injury to the cervical root may be due to mechanical factors which occurred at the time of the accident. Persistent and progressive symptomatology of cervical nerve root involvement should suggest the possibility of a cervical disk or fibrosis about the cervical nerve root. The clinical picture of the cervical disk is well known: myelography will establish the diagnosis. Fibrosis involving the cervical nerve root produces an indistinguishable clinical picture and the myelogram may be inconclusive or negative.

Progressive bone formation initiated by the trauma may cause mechanical encroachment on the intervertebral foramina, which can be instrumental in producing progressive involvement of the cervical nerve. Involvement of the greater occipital nerves, which are branches of the posterior division of the second cervical nerve, may be responsible for a considerable part of the occipital headaches in some patients.

Injury to the spinal cord. Involvement of the cervieal cord may vary from mild to severe. In mild cases, involvement may be asymptomatic and ean be manifested solely by the presence of pyramidal tract findings on reflex examination. Initial involvement may be maximal with a stationary or gradually improving course. In this group of patients, initial insult to the cord is probably due to a partial and spontaneously redueed subluxation of the cervieal vertebra. In some more serious injuries, frank fracture dislocation occurs, produeing irreversible eord injury.

Injury to the sympathetic nervons system. Reflex stimulation of the sympatheties may give rise to such symptoms as blurring of vision, dilation of the pupils, loss of balance, headaches, swelling and stiffness of the fingers, tendinitis, and eapsulitis.

Injury to the vertebral arteries. The relationship of the vertebral artery to the cervical vertebra is such that, in some patients, there is meehanical impairment and even obstruction of the blood flow in the vertebral arteries. Undoubtedly some patients who complain of dizziness have this on the basis of vertebral artery insufficiency.

Brain injury. If routine electroeneephalograms are taken in patients with whiplash injuries, abnormalities in the eleetroencephalogram are not infrequently encountered. These may be transient or persist and change in character.

Psychiatric disabilities—posttraumatic neurosis. A large proportion of patients with whiplash injuries who present themselves for treatment have a nervous eomponent to their injuries. In some of these patients, a picture of posttraumatie neurosis develops whieh not infrequently proves refraetory to treatment. Persistence of pain from persisting neck pathology and presenee of abnormalities in the neurologie examination have proved to be poor prognostic factors in patients with posttraumatic neurosis.

Treatment of whiplash injuries. Treatment must be individualized according to the nature and severity of involvement. Mild cases respond to a few days of bed rest on a firm mattress plus the use of analgesics. In more severe cases, such measures as eervical collar, cervical traction, and physiotherapy are indieated either on an outpatient basis or in the hospital. Emotional support of the patient is important. These patients deserve careful consideration of their eomplaints and considerate handling. Nerve block direeted toward involvement of the greater occipital nerve may be of considerable benefit in relieving headaehes and neek pain resulting from this involvement. Cases with persistent symptoms of neek pain should be studied for protruded cervical disk.

Severe Injuries (Contusion, Lacerations, and Compression)

A variety of trauma may be responsible for severe injuries to the spinal cord. Such traumas are:

1. *Snddeu hyperflexion of the spine.* This results from blows to femur, buttoeks, abdomen, or chest when the head has been thrown forward. It also results from diving accidents with a blow to vertex or occiput. Most often, compression fraetures or dislocation oeeur at C4 to C6 or T11 to T12. The intervertebral disk is frequently pressed back against the cord in this type of severe injury.

2. *Sudden hyperextension.* Cervieal injuries result when the body is thrown forward and the head is unsupported or driven backward by a blow to the forehead. Lumbar and thoracie injuries are sustained from backward falls against angular objeets. Such forces tend to fracture the lamina, artieular faeets, and pedicles. Dislocation is severe when the anterior spinal ligament is torn. The posterior flaval ligament may herniate against the cord.

3. *Penetrating wonnds.* These may involve the eord directly and are caused by stab wounds, bullets, and high-speed fragments.

All degrces of injuries ean result from severe eord trauma. These can range from complete cord transeetion to smaller tears (lacerations) and to simple bruising (contusion). Such damage may be further compounded by compression. Most frequently, compression is caused by a fracture dislocation. Other causes of compression are displaeed bone fragments, herniated intervertebral disk, marked cord edema, intradural or extradural hemorrhage, or hemorrhage within the eord (hematomyelia). Isehemia with loss of blood supply to the cord segment for as long as one hour will produce irreversible infaretions, mostly in the gray matter.

In laeerations, all transected axis eylinders are probably permanently lost, even when closely approximated, because of rapid glial proliferation at the site of the injury. Sudden and severe compression abolishes all function within that seetion. Such eompression must be relieved within one to two hours or permanent damage will result. If compression comes on more slowly, the period of total paralysis may be much

longer before permanent damage is done. During the course of slow cord compression, the larger fibers of the pyramidal tract and of position sense are lost first. Pin prick is the last to go. If pin prick is present below a compression lesion, the prognosis is not hopeless provided the pressure can be promptly relieved.

The disability resulting from a complete transverse cord lesion varies according to the level at which the cord is transected. If the cord is transected at C4 or higher, there are quadriplegia and respiratory paralysis with usually fatal termination. Cervical lesions result in leg, trunk, and sphincter paralysis with various degrees of arm involvement. Thoracic cord lesions spare the arms. In transections of the cord, a condition of spinal shock develops that lasts several weeks to several months; in this condition, the distal cord acts as though it, too, were injured. All cord reflex activity is lost, including urination and defecation, sweating, and deep tendon and superficial reflexes. After the period of spinal shock, the lower segment of the cord becomes hyperactive. Toe signs become positive. The deep tendon reflexes become very active and marked clonus may be noted. Stimulation of the involved extremity may cause massive withdrawal or extension of one or both extremities, and defecation and urination may occur. The bladder detrusion reflex becomes very strong. Without proper care, the bladder rapidly loses functional capacity.

In an incomplete transverse cord lesion, the period of spinal shock is much shorter. The deep and superficial reflexes first appear within days or weeks and ultimately are typical of spastic paraplegia. Usually, neck sensation shows some return. Then motor function begins to reappear; it returns in varying degrees according to severity of the injury. At this time, sphincter control is likely to improve. The paraplegia may ultimately be asymmetrical and incomplete. With rare exceptions, the patient has complete paralysis of motion and sensation for some time after injury. Late recovery may occur at variable periods. Useful recovery has been seen when it began as late as five months after the injury. The incidence of the spasms varies in relation to the segments affected. Sixty to 70 per cent of all patients with spinal cord injuries have these spasms. They are present with all cervical lesions of the cord, with 75 to 80 per cent of thoracic lesions, with 31 to 44 per cent of lumbar lesions, and with 30 per cent of lesions of the conus and cauda equina. Spasms are not, of course, present with lesions of the cauda.

Therapy of severe cord trauma. The patient's neurologic examination should be done at the scene of the accident to establish, if possible, the level of the lesion and whether or not it is complete. Complete lesions are prone to slip into shock because of the lack of vasomotor tone below the injury. Careful watch must be kept on the vital signs and the Trendelenburg position, intravenous fluids and cardiovascular stimulants should be used as necessary to combat shock. The spinal injury patient should be transported like a "log of wood" with firm support, including head traction. In general, lumbar injuries are best carried prone and cervical injuries are best carried in the supine position. Roentgenograms of the skull and cervical, thoracic, and lumbar spine should be obtained. A spinal tap with Queckenstedt test is then performed to determine whether blocking of the spinal arachnoid space is present. If there is concomitant head injury and any suspicion of increased intracranial injury and pressure, the Queckenstedt test should never be done.

Indications for surgery in spinal cord injuries are (1) all penetrating wounds of the spinal cord, (2) all transverse lesions of the cauda equina, (3) complete loss of function with block, (4) incomplete lesions slowly developing further deficit or producing severe unremitting pain at same level, and (5) inability to reduce fracture dislocation with traction maneuvers. For a small group of patients in whom spasms are particularly painful and disabling during the chronic stages of cord lesions, the question of doing a rhizotomy deserves consideration. Unless the cord lesion has proved to be anatomically complete, rhizotomy should be done only on rare occasions when it would be a lifesaving procedure.

High cord lesions from T2 and up are best treated on a Stryker or Foster frame with cervical traction applied to Crutchfield tongs. A fracture dislocation at this level must be immobilized four to six weeks. Lower cord lesions may be handled supine in bed with blanket-roll support under a firm mattress. More serious lesions may require casts or spinal fusion—the usual degree of immobilization is two to three months. It is important to prevent decubitus ulcers. This is a major problem in cord lesions because the patient is unable to detect discomfort below the level of the lesion and is unable to turn himself to relieve skin ischemia. A Stryker or Foster frame rotated every two hours may help control pressure-point necrosis in the cervical fracture. A motor-driven alternating pressure air mattress is of great aid in a thoraco-

lumbar fracture. Frequent inspection and massage of all skin areas are essential, however.

Bladder training of the patient is very important. All patients with severe cord injuries must be catheterized within eight hours after the injury since, in the presence of spinal shock, the bladder can easily rupture from overdistention. If, after several days, the transverse cord lesion persists and is above S3, there is hope of establishing an automatic cord reflex bladder. If irreversible bladder contractures are to be prevented in the weeks ahead, a tidal drainage apparatus supervised by an expert is required. When the transection is below S3, an overflow bladder is the usual result and an indwelling Foley catheter connected to straight drainage is sufficient. Stones are best prevented by maintaining maximum physical activity commensurate with a cord injury. As soon as possible, the patient should be placed on the tilt table once daily and elevated to 45 degrees or more.

Paralytic ileus is common during the first few days of spinal shock. This is best handled by a rectal tube and the use of Prostigmin. Later, enemas every three days will establish reflex activity, after which a mild laxative combined with external stimulation, such as abdominal massage, will trigger fecal evacuation.

Rehabilitation usually requires long-term care at a specialized center. In general, goals are set to achieve maximum adaptation with surviving function. Persons with severe cervical injuries may achieve wheel-chair status and partial self-care; that is, feeding with special arm support mechanisms. When the lesion is below T8, an attempt is made to ambulate with the aid of long leg braces, back support, and crutches. Months of effort are spent in developing the arms and upper trunk to perform the necessary skillful and powerful motions.

The lower and less complete the lesion, the less difficult is the task. Once ambulation is achieved by wheel chair or crutches, efforts are made to increase self-care, namely, dressing, getting from bed to wheel chair, from wheel chair to lavatory, and so on. Many paraplegic patients ultimately are able to perform sedentary work. In each individual case, the physician must set a realistic goal and encourage the patient to achieve the maximum possible independence. Neurosis and depression are products of unrealistic guidance.

For patients with urinary retention, or when urine collection is unreliable, serum rather than urine may be used to estimate gastric acidity by the tubeless technic.

Venous blood is withdrawn fifty minutes after oral administration of azure A resin compound (Diagnex Blue). After treatment of aliquots of serum to change any colorless azure A to the oxidized color form, optical densities are read on a spectrophotometer at 630 μ with 0.035 mm. slit width. All azure A is then reduced to the leukoform by adding L-ascorbic acid, and the optical densities are redetermined. The difference between the 2 readings is used to calculate the azure A concentration.

Serum azure A values were inconsistent with gastric acidity estimated by the amount of dye excreted in urine for 3 of 60 subjects and were equivocal for 3.

H. L. Segal, R. P. Plosscowe, R. D. Gerle, and P. K. Russell: The blood serum azure A level in the determination of gastric acidity by tubeless gastric analysis. J. Lab. & Clin. Med. 55:815-819, 1960.

A Panel Discussion

Cancer Detection in Office Practice

MODERATOR:
VICTOR GILBERTSEN, M.D.

PANELISTS:
ALVIN SCHULTZ, M.D., J. P. COOPER, M.D.,
ROBERT A. GREEN, M.D., ROBERT NORD, M.D., and
ANN W. ARNOLD, M.D.

St. Louis Park, Minnesota

DR. M. A. SEGAL: As chairman of the symposium, I should like to introduce the panelists. Victor Gilbertsen, the moderator, is chief of the Cancer Detection Center at the University of Minnesota Hospitals. Dr. Schultz is an internist; Dr. Cooper, a urologist; Dr. Green, a hematologist and internist; Dr. Nord, a radiologist; and Dr. Arnold, a gynecologist. The panel will discuss various aspects of the subject of this symposium, "Cancer Detection in Office Practice." I shall ask Dr. Gilbertsen to open the discussion with a statement concerning the Cancer Detection Center. One of the questions frequently asked about patients coming to the Center is whether or not they really have symptoms.

DR. GILBERTSEN: Often patients who have obvious symptoms and who want a physical examination seek to be examined at the Detection Center. Do some of the patients who are seen at the Cancer Detection Center really have symptoms? The answer, of course, is "Yes, many of them do." Many of the symptoms, however, are brought out only by careful questioning by the examining physicians. Before a patient is given his first appointment, we insist, by form letter, that he certify that no symptoms suggestive of cancer or other serious disease are present.

Of each 1,000 new patients seen at the Detection Center, our pickup rate for cancer has been 12, that is, a little more than 1 per 100. In addition, for each 1,000 patients, we have found 250 precancerous conditions requiring correction. Of these, the most frequent were rectal or colonic polyps, of which there were 125. In addition, we have found 30 pigmented nevi in areas of irritation, 31 senile keratoses, 18 solitary nodules in the thyroid gland, and 3 instances of kraurosis vulvae per 1,000 new patients. Also, for each 1,000 new patients, 1,200 other "abnormal" conditions, of more or less severity, not related to cancer have been detected. For example, in each 1,000 patients, 56 hernias, 65 skin disorders, 58 patients with obesity, and 4 instances of previously undetected diabetes mellitus have been found; hypertension or some other cardiovascular condition was noted in 240, and 170 had ear, nose, or throat conditions. At this point, I should add that, in our twelve years' experience, we have had no success in the asymptomatic detection of gallbladder or pancreatic cancer; we have failed to diagnose at least 2 cancers of the gallbladder and 5 of the pancreas in the asymptomatic stage.

I should like to ask Dr. Schultz what plan of therapy he would recommend for a solitary nodule in the thyroid gland.

DR. SCHULTZ: This is a common problem that all physicians run into, particularly the solitary nodule of recent onset. There is considerable argument as to the incidence of nodular goiter and, in the group of nodular goiter, the incidence of cancer. The frequency of goiter reported in the mixed hospital population was 4 per cent, of which 75 per cent were solitary nodules. Many solitary nodules diagnosed clinically turn out, in surgery, to be multinodular. Once a nodule is felt in the thyroid gland, the question arises, should this be watched or should this be operated upon? Cole in Chicago reported a 20 per cent incidence of carcinoma in solitary nodules of the thyroid gland. Most studies have shown an incidence of between 5 and 10 per cent. The figure of 5 per cent, I think, is in itself a basis to excise all of these nodules. My feeling is that, if a solitary palpable lesion of the thyroid is found, it should be removed. The length

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of time it has been there is not much help. In the Mayo Clinic series, it was found that 20 per cent of the carcinomas had been present for ten years or longer as a known mass in the thyroid. I don't believe that these cases should be watched. This is a little like breast cancer—you cannot differentiate clinically benign from malignant.

DR. GILBERTSEN: At the University of Minnesota, about 1 out of each 50 solitary nodules has subsequently been found to be malignant; not all of the solitary nodules which have been detected, however, have been operated upon.

I should like to ask Dr. Arnold what the chances are that palpable ovaries, that is, ovaries which the physician notes as enlarged, are involved with malignant tissue.

DR. ARNOLD: We have been taught in gynecology for many years that tumors in the ovary or an ovary that is larger than 5 cm. is to be removed. However, we have a means of looking at the ovary with a culdoscope. I think, from a practical standpoint, that when the ovary is questionably enlarged in a woman between 40 and 50 who is still menstruating, she should be allowed to go through a menstrual cycle and then be reexamined. If she still has the tumor, culdoscopy or laparotomy is indicated.

DR. GILBERTSEN: Would you expect that eventually quite a few of those older patients, Dr. Arnold, will be proved to have a malignant lesion?

DR. ARNOLD: Age is a big factor in these tumors—that is, the older the woman, the more likely the tumor will be a neoplastic enlargement rather than a physiologic cyst.

DR. GILBERTSEN: I think everyone will agree that, in an annual physical examination for men, the prostate gland should be examined by palpation. I should like to ask Dr. Cooper for a suggestion regarding other procedures to be done on routine physical examination; what do you do, for example, when you palpate a nodule in the prostate gland?

DR. COOPER: A nodule in the prostate has been said to be the thing that everyone is supposed to look for. Routine examination of the prostate in any man over 40 should certainly be done once a year. A hard nodule or, more important, a fixed prostate that will not give as you try to manipulate it from side to side is apt to prove to be be a malignancy on biopsy. A relatively educated finger can be 70 to 80 per cent accurate in the diagnosis of carcinoma of the prostate.

Other studies include acid phosphatase, flat plate of the abdomen and pelvis, and, for definitive diagnosis, needle or open biopsy.

DR. GILBERTSEN: In certain cases, would you go ahead and treat a cancer of the prostate gland from digital examination data alone?

DR. COOPER: I believe that the needle biopsy is a conservative and simple procedure. It is done with procaine anesthesia and should precede definitive therapy unless there is other confirmatory evidence.

DR. GILBERTSEN: Dr. Green, I should like to ask you what sort of results of those blood tests which might be included as part of a routine physical examination would make one suspicious of the presence of leukemia, polycythemia, or some other malignant disease.

DR. GREEN: Routine studies that I should consider are hemoglobin, white blood count, differential count, sedimentation rate, hematocrit, and examination of the stained blood smear. Findings which might make one suspicious of malignancy in the blood or elsewhere are numerous. An elevated sedimentation rate may be quite important in terms of clinical findings. Leukocytosis in children is a common thing and can usually be explained by relatively benign conditions, but in the presence of anemia and unusual symptoms, one might well suspect malignancy. Of course, if immature forms are seen, further studies for leukemia are in order. There are changes in the presence of an elevated sedimentation rate, such as rouleaux formation, which should make one suspect multiple myeloma. Basophilia is a condition that almost always demands a further look because of its common association with leukemia. With our technicians or office assistants doing the blood counts and differentials, some of us forget what a normal specimen looks like. It is well to take a look at the peripheral blood smear.

When it is indicated, a bone marrow biopsy can now be done as a relatively innocuous procedure. If there are findings such as thrombopenia, basophilia, unexplained leukocytosis, and the like, then one certainly should do a bone marrow biopsy and send it to a hematologist for interpretation. I should like to add, in regard to bone marrow biopsy, that if you do send in such a specimen, be sure to include a peripheral blood smear taken at the same time. The pathologist or hematologist can give a much better opinion if he has blood to look at as well as bone marrow.

DR. GILBERTSEN: Dr. Nord, would you discuss the role of the chest roentgenogram in a cancer detection examination? Would you comment on the role of photofluorograms?

DR. NORD: In the first place, I think a chest film

has a place in any annual physical. The photofluorogram in the 4 x 5 size has proved fairly satisfactory as a good screening process. However, smaller sizes tend to sacrifice accuracy. For individual office practice, a 14 x 17 in. film is superior. Generally speaking, a solitary chest lesion is likely to be the primary lesion. Multiple lesions are likely to be metastatic. It is important to compare with old films, and in this day and age, most of the patients seen with lesions will have had previous chest roentgenograms. Calcium in the nodule favors benignancy. However, if you can't make up your mind, take it out and look at it under the microscope.

QUESTION FROM THE FLOOR: What about routine GI series, upper and lower, as part of an annual physical examination?

DR. NORD: Well, I'm not so certain that routine is good. I prefer a careful history first and then barium examinations if there is any indication. With a routine on everybody, I think the return is rather low; you encounter an economic factor there. I think your return would be low without any symptoms or familial history.

QUESTION: What is the rate in the cancer detection centers, with their routine GI series?

DR. GILBERTSEN: It is not entirely clear; as I look back over the statistics, it almost appears that we do these examinations routinely. From about 1,900 upper GI series which have been done, about 25 cancers of the stomach have been detected. This modest pickup rate thus makes a study project of this type economically unfeasible, I think, for ordinary private practice.

QUESTION: Should an annual upper GI series be done routinely in pernicious anemia?

DR. SCHULTZ: Dr. Rigler is a foremost exponent of doing routine GI series. At one time, he thought they should be done every six months in patients with atrophic gastritis and pernicious anemia. His incidence of cancer, as I remember, was somewhere around 5 per cent. My own feeling is that there is an increased incidence of cancer in patients with pernicious anemia and atrophic gastritis. I don't think they should have a GI series every six months, but I do think there is a basis for doing an annual GI series here.

QUESTION: Would you advise the routine removal of a gallbladder in the presence of gallstones without symptoms?

DR. GILBERTSEN: This is a question that has plagued many people. I think that most surgeons would advise routine removal of such gallbladders, most importantly to prevent trouble with *benign disease*, that is, with cholecystitis or choledocholithiasis. The operative death rates associated with removal of gallbladders with stones, although very low, usually are somewhat higher than the risk of death from possible future development of cancer of the gallbladder; in other words, when stones are present, I think that the gallbladder should be removed for the prevention of benign but severe disease.

QUESTION: I should like to ask Dr. Green if he thinks the Diagnex Blue test for achlorhydria should be a part of a routine annual physical examination?

DR. GREEN: I haven't done tests for achlorhydria as part of a routine physical examination. I think one should consider age factors, the history, and other findings. In other words, I should be selective about use of the Diagnex test. The Diagnex test has certainly simplified the problem of testing for achlorhydria and, although specifically not quite as reliable as a sample of gastric juice removed by tube, provides quite reliable information as to the presence or absence of free acid. In patients with anemia and a family history of cancer of the stomach, I should certainly perform a gastric acid test.

QUESTION: I should like to ask Dr. Green his technic for sternal marrow biopsy.

DR. GREEN: For the sternal marrow sample, the technic that I use is simple. I try to aspirate at least 1 cc. of marrow, and preferably 2 cc., so that a hematocrit tube can be easily filled with the marrow sample. We centrifuge the hematocrit tube for ten minutes and then prepare smears from the buffy coat. Direct smears of the marrow are made in the same fashion as thin smears of the peripheral blood, and these can be sent in unstained. There will be too much disintegration of cells if you send in the material in a paraffin-lined tube with anticoagulant. The anticoagulant of choice for marrow is an EDTA solution such as sequester-sol. Along with the bone marrow smears, as has been stated before, we should like to have peripheral blood films. It is very helpful also to have particulate material from the marrow for sectioning. What I have found to be a simple technic in preparing the particles for sectioning is to spread the aspirated marrow on a thin glass plate, aspirate the fluid portion from the particles, clump them with thromboplastin or thrombin, and put the clump in formalin. The fluid portion can then be centrifuged for buffy coat smears. The clump can be sent to the pathologist for sectioning.

DR. GILBERTSEN: I have a question for Dr. Cooper. It has only been in the last few months that microscopic urinalyses have been done at the Cancer Detection Center. In contrast, it is

interesting to me that tests for urine sugar have been done on 38,000 examinations, and I don't think that the detection of very many cancers have been facilitated by finding sugar in the urine. Dr. Cooper, how many red cells would you require to be present in routine urinalysis before you would suspect malignancy or would advise some additional diagnostic test?

DR. COOPER: This is one of the main points with which urology has to play. It is the simple subject of hematuria. Over-all, urologic tumors constitute about 20 per cent of adult male tumors—25 per cent in children. Hematuria is the most common symptom in any and all urologic problems. A 2-glass specimen certainly would be a logical next step with persistent hematuria. A persistent microscopic hematuria of only 5 to 8 cells is of importance, particularly if it is present in the second glass. An excellent article on this subject was written in the *Summary of the North Central Section Urological Association* by Dr. Green of Rochester in 1955.

DR. GILBERTSEN: What is kraurosis vulvae? Does cancer eventually develop in patients with this disease? What treatment do you recommend?

DR. ARNOLD: Kraurosis is not a diagnosis, it's a grab bag. I don't believe that kraurosis itself is a premalignant lesion. Kraurosis is a drying process usually seen in older women and has to be differentiated from local disease and general systemic disease; the problem of malignancy in connection with it is minimal.

QUESTION: What does Dr. Cooper think of routine catheterization of women on admission to a hospital?

DR. COOPER: The bulk of urologic literature is in favor of catheterized specimens. The big point here is whether or not the patient has obstructive uropathy. If the patient has no obstructive uropathy, catheterization probably will not cause any damage. People with recurrent bouts of urinary tract infection have obstructive uropathy until proved otherwise. Residual urine is an important thing. An estimation of it requires catheterization.

Before I sit down, I would like to return to the problem of microscopic hematuria. We now routinely, with ureteral catheters, collect bilateral specimens for centrifugation and cytology studies from each side. Right now I have a patient with an obvious pyelographic deformity on the left side and abnormal cells on the right side. What shall I do?

DR. GILBERTSEN: We try to refer most of those difficult cases to the Mayo Clinic.

THE FIVE-YEAR survival rate among patients with primary ovarian cancer may be significantly increased by immediate postoperative irradiation. Serous and undifferentiated carcinomas limited to one ovary or affecting the pelvic peritoneum or other viscera may be suppressed by roentgen-ray therapy. Cancer of structures above the pelvis and pseudomucinous carcinomas show no radiation reaction.

The best results are obtained when x-ray treatment is given after removal of uterus, ovaries, and as much of the tumor as possible. Benefits of irradiation often are maintained for twenty years.

Of 327 women with previously untreated primary ovarian cancer, 154 received immediate postoperative irradiation, 200 kv. with 0.5 mm. copper screening and a target distance of 50 cm., to the pelvis and lower abdomen. Portals of entry were 10 x 15 x 15 x 15 cm., both front and back, usually 2 to the lower quadrants and 1 to the lower back. The number of exposures was 12 to 20, and total doses at skin level varied from 3,000 to 9,000 r. Doses to the midpelvic plane varied from 1,400 to 2,600 r. The five-year survival rate was about 46 per cent, compared to 33 per cent for the 173 patients who received only surgical treatment.

S. W. KENT and D. G. MCKAY: Primary cancer of the ovary. Am. J. Obst. & Gynec. 80:430-438, 1960.

Notes from a Medical Journey

Opatija, Yugoslavia
24 April 1961

Dear Jay:

Time and distance have curious dimensions in this day of jet travel. The sombre buildings of Helsinki, half obscured by blowing snow, were surely more than three days away from my brief glimpse of the dogwood in flower in Atlanta, where I talked before the American Epidemiological Society. In between, there was the Research Committee of the American Heart Association at Atlantic City, three hours of television filming at New York, and a quiet evening with old friends at the home of Dr. Carl Johan Møllenbach in Copenhagen, after visiting the wonderful new hospital at Glostrup, where Danes, at the rate of several hundred a year, show that they, too, have no lack of myocardial infarctions.

At Helsinki Airport, Dr. Martti Karvonen greeted me with the news of the Russian space flight. Can Gagarin really understand that he flew around the world in eighty-three minutes? I recall flying from Bangkok to Bombay through the night once, and, though I must have crossed all of Thailand, Burma, and India, it had no real meaning. And the only reality of Bombay was the fact that the airport was desolate and dusty, the coffee bad, and we piled back on the plane weary for the next leg to Teheran.

In the sauna bath (at 235° F.!) in Helsinki, I forgot about Gagarin when I learned about the findings to date in the experiment in two mental hospitals in Finland -- one with the diet unaltered, one with the diet changed by substituting vegetable oils for butterfat. The serum cholesterol decline in the second hospital was soon notable (and was reported in the Lancet last year). Now, with the dietary difference maintained for nearly two years, there is a remarkable difference in mortality, and this is accounted for by a sharp fall in deaths from circulatory diseases. However, we shall wait another year before Prof. Turpeinen and his colleagues bring out the story with all statistical details.

After the snow in Helsinki, Stockholm in the spring sunshine was a delight from the top floors of the new Folksam Company skyscraper. The Folksam Insurance officials are nearly ready to start the research program I proposed a year ago, and soon we shall add some 6,000 Swedes to our international collaborative follow-up study. Dr. Lars Carlson is keen on serum triglycerides, as well as cholesterol, as a possible prognosticator of coronary risk, so they propose to add this item -- which means that all subjects must report in the morning without breakfast.

The diet-heart disease question is hot in Scandinavia, with top-level committees charged to produce reports both in Sweden and in Norway. The chairman of the Norwegian Committee, Prof. Ragnar Nicolaysen, is all for government action to reduce the intake of saturated fats, including possible forcing price differentials against butterfat. The information is that the frequency of myocardial infarction is increasing at a phenomenal rate in Norway, and recent serum cholesterol surveys show values similar to those in Minnesota. But in a large rural area not far from Oslo, serum cholesterol values and the intake of saturated fat in the diet are much lower -- and the mortality rate at ages 40 through 60 is scarcely half that of Oslo.

After Oslo came hasty and, I hope, fruitful business in London, Brussels, and Amsterdam, a lunch in Zurich; then 7 of us -- 2 Swedes, 2 Dutchmen, a Dane, Dr. Henry Blackburn, and myself -- were in a Yugoslav plane en route to Zagreb and wondering, as we saw the white peaks of the Alps poking through the clouds below, how we were to go on to Opatija that night.

Two small cars and a bus were the answer for five hours of pitch-black night, driving rain, and many patches of fog, which made the winding road through the mountains that much more interesting! And so to bed at 3 a.m. and up early enough to arrange my slides for a lecture that morning ("Risk of Coronary Heart Disease") before several hundred doctors at the Yugoslav Congress on Cardiology. Heart disease is now proclaimed, officially, to be a major health problem in Yugoslavia.

That night I was host and chairman at a dinner for 24 of my collaborators from 9 countries who spoke English -- except at the end, when I called for short talks with the promise that any talk would be out of order if it was in a language that could be understood by more than 4 people present. So we cheered impassioned remarks we could not understand in Croatian, Finnish, Flemish, Hungarian, Greek, Swedish, Copenhagen Danish, Dutch, and Neapolitan Italian.

More seriously, we learned that the frequency of infarcts in Zutphen, the Netherlands, is similar to that in Minnesota, and the serum cholesterol averages in middle age are practically identical. We also learned more reasons to distrust the diagnosis of angina pectoris and to wonder about the meaning of inverted T waves.

Today the rain continues, palms sway in the wind, and the

lovely Dalmatian coast is visible only on the postcards at the hotel desk. Phooey! Shortly, Drs. Puddu, Fidanza, Imbimbo, and I shall drive to Trieste to catch the night train to Rome; while Henry Blackburn, Orma of Finland, and Dontas of Greece go with the Yugoslavs to Slavonia to check the health status of 800 men, first examined in 1958.

The calendar says it is Monday, and I have been away two weeks; my plane tickets say I shall be home in Minnesota on Sunday. A week ago Sunday I spent the day with the Dr. Clarence Dennis family in Stockholm, where he does surgery on a sabbatical, and the whole family have learned Swedish to the extent that daughter Jane is engaged to a Swedish medical student. For desperate infarct cases, Clarence is attempting a pump bypass of the heart, which cuts out 90 per cent of the oxygen need of the myocardium and maintains a good pressure in the aortic arch (hence in the coronaries). And I continue to say prevention is the only answer.

And so off on the road again, with all good wishes to Minnesota.

As ever,

Ancel Keys

AK:ma

George Earl, M.D.

DELMAR R. GILLESPIE, M.D.

St. Paul

RARELY DOES ONE have the privilege of knowing a man with remarkable energy and with varied interests and activities who has made an outstanding success in numerous ventures in his lifetime. Such a man is Dr. George Earl, whose life has been marked by many diverse activities and accomplishments and who has that rare gift of handling numerous projects and problems, all seemingly at the same time, smoothly, rapidly, skillfully, and, to all appearances, without effort.

Dr. Earl jokingly says that he missed the prestige of farm birth when his father moved from Iowa to Minnesota shortly before he was born. He grew up in Minneapolis and acquired his B.A. and M.D. degrees from the University of Minnesota. During his years as a student at the University, he was active in numerous projects, such as the debate team. He was business manager of the *Alumni Weekly* through most of his college years, and soliciting ads for the *Weekly* on a commission basis helped to defray his University expenses. After finishing medical school and internship, he entered practice in St. Paul with his older brother, Dr. Robert Earl—a successful partnership that evolved into the Earl Clinic.

For many years, Dr. Earl served as chief of staff for both Midway and Mounds Park hospitals. He was constantly striving to keep both hospitals up-to-date in equipment and services, despite the depression years and the war years that followed. Midway Hospital was built just before the 1929 panic, which brought cancellation of most of its building pledges. It was largely his energies and foresight, together with those of Dr. Robert Earl and others, that carried the hospitals safely along financially and made possible the present hospital expansion program. As a member of the Board of Trustees of the Baptist Hospital Fund, Inc. which manages Midway and Mounds Park hospitals, Dr. Earl has held various offices on the Board and at present is its president.

Dr. Earl was a founder of the Association of Baptist Homes and Hospitals in the United States, serving as its first president until its active work was taken over by a full-time director in 1956. At this time, he was made honorary president of the Association, in recognition of the great effort that he spent in developing this needed and important organization. He also was active in laymen's work and at one time was president of the national group of American Baptist Laymen.

Over the years, Dr. Earl has taken an active interest and played an active part in the community. On moving to St. Paul, he first lived and practiced in the Dayton's Bluff district. With the help of others, he was able to establish a bank in that section of the city, becoming its first president and serving as such until this bank was taken over by the Northwestern Bank Corporation. Later, after moving to the midway district of St. Paul, he became active for a time in the Midway Club, becoming a member of its Board of Directors and at one time serving as vice-president.

Since 1940, Dr. Earl has served continuously on the State Appeal Board of Selective Service and as medical advisor to the State Director. He recalls that the first case to come before the newly formed Board of Selective Service was that of a young cobbler who specialized in orthopedic shoes and braces—the only one in St. Paul at that time. The question

DELMAR R. GILLESPIE *practices internal medicine in St. Paul, where he serves on the staffs of Midway, Mounds Park, Miller, and Ancker hospitals.*

was whether this young man was more valuable to the war effort if left at home or enrolled in the military service. Half a day was spent in discussing this one case alone, with the conclusion that the young cobbler should stay in St. Paul. In time, Dr. Earl told me, the Board learned to act with greater dispatch.

Dr. George Earl devoted time and energy to working for the University of Minnesota Alumni Association, as a member on the board of directors of the General Alumni Association for several years and as president for three years. He also was active in the organization of the Medical Alumni Association and served as a member of the group sponsoring the campaign for the Coffman Memorial Union.

He was secretary of the Mayo Memorial Medical Commission, which sponsored the building of a memorial to Will and Charles Mayo at the University of Minnesota. Many suggestions came to the Commission as to what the memorial should be—for instance, one advised statues of the Mayos in the state capitol area, and another, the creation of a beautiful park in a large tract of land containing Norway pines. But Dr. Earl felt that a Mayo memorial should be of real value in a medical way to the people of the state. He discussed his thoughts with Dr. Harold Diehl, then dean of the medical school, with the result that a new medical building was proposed as the Mayo memorial. Dr. Earl recalls that Dr. Cowling, former president of Carleton College, as chairman of the Mayo Memorial Medical Commission, did a most remarkable job in making this outstanding memorial a reality.

In 1953, the University honored Dr. Earl by conferring on him the Outstanding Achievement Award. He has had other educational interests, such as serving on the Board of Bethel College and Seminary, at one time as its chairman. At present, he is a member of the Board of Hamline Associates.

Early in practice, Dr. Earl showed great interest in organized medicine and especially in the state medical association, serving for many years as chairman of the Committee on Public Health Education, in which position he did an exceptional job. At that time, the need for public relations was not appreciated by the majority of our profession. The work of this most important committee was conducted generally by meetings with small groups of physicians throughout the state, as well as by meetings with county and district medical societies, necessitating a great deal of travel. Often, the Committee served as a grievance committee for local and state complaints and prejudices. In his travels throughout Minnesota, Dr. Earl had the opportunity to know many of the doctors in the state. He also had the opportunity of talking before their societies on matters of public health education and public relations, as well as on such surgical subjects as particularly interested him.

In 1930, he was elected councilor of his district and served for nine years on the Council of the Minnesota Medical Association, the last three years as chairman. In 1939, Dr. Earl was elected president of the state medical association. Following his term as president, he served as a delegate to the American Medical Association until 1958. Since 1941, Dr. Earl has been chairman of the Committee on Medical Economics of the state medical association. Although he tells me that the several subcommittees do most of the work, he and his committee have done a first-rate job in bringing to the attention of the physicians of this state the pressing problem of medical economics. In 1956, he was awarded the Distinguished Service Medal of the Minnesota Medical Association.

During all these years, Dr. Earl has carried on an active and large surgical practice, besides attending conventions and keeping up with new developments in medicine. In 1912, he studied in Vienna; in 1919, he took some months of postgraduate work at the Mayo Clinic; and in 1922, he moved his family to Philadelphia for postgraduate work at the University of Pennsylvania. He has also been the author of a number of medical articles.

Before the day of the specialty of urology as we know it, and before there were any urologists in St. Paul, George Earl learned to use the cystoscope and to do major urologic surgery as a part of general surgery. As the specialty grew, he gradually discontinued this type of surgery.

To accomplish his many and varied duties, Dr. Earl has developed that rare ability of holding a three-way conversation over the telephone, getting things done quickly and proficiently. On one of his trips, he received a card from the office showing a man holding phones to each ear and talking into a third.

In spite of all his community and professional activities, he has had time for recreation and travel. At one time, he was a member of both Town and Country and Midland Hills clubs and played a good game of golf. He usually went out very early in the morning, and often he persuaded Mrs. Earl to go with him. One day, after making a hole in one, she decided to give up the sport, her excuse being that she could not improve her game, but Dr. Earl felt that the real reason was that she did not like the early morning dew.

Dr. and Mrs. Earl have traveled extensively in Europe, Central and South America, the West Indies, Japan, the Philippines, Hong Kong, and Alaska, as well as throughout North America.

What of the future? Dr. Earl seems to us who know and work with him to be as interested as ever in his profession, in the future of medicine, in hospitals, and in the problems of health. He is presently deeply involved in an expansion program for the hospitals, as well as in a long-range program for the nursing school, in convalescent and nursing home care, and in continuing most of his past activities. There seems to be no immediate change in his pace or in his variety of interests. It appears that, unlike old soldiers, this active, energetic man will not fade away.

Transactions of the North Dakota State Medical Association

SEVENTY-FOURTH ANNUAL MEETING
Fargo, North Dakota, May 6, 7, 8 and 9, 1961

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CECIL BAKER — Bismarck
L. G. PRAY — Fargo
L. E. WOLD — Fargo
W. R. FOX — Rugby
M. A. K. LOMMEN — Bismarck

Committee on Aging and Rehabilitation
T. E. PEDERSON, Chairman — Jamestown
T. H. HARWOOD — Grand Forks
PAUL JOHNSON — Bismarck
M. W. GARRISON — Minot
LEE CHRISTOFERSON — Fargo
WILLIAM C. NELSON — Grand Forks
BRIAN BRIGGS — Minot
HANS GULOIEN — Dickinson

Committee on Foreign Trained Physicians
C. J. GLASPEL, Chairman — Grafton
JOSEPH SORKNESS — Jamestown
O. W. JOHNSON — Rugby
W. A. WRIGHT — Williston
J. C. FAWCETT — Devils Lake

Committee on American Medical Education Foundation
W. E. G. LANCASTER, Chairman — Fargo
K. G. VANDERGON — Grand Forks
T. H. HARWOOD — Grand Forks
A. R. GILSDORF — Dickinson
C. H. PETERS — Bismarck
T. E. PEDERSON — Jamestown
JOSEPH CRAVEN — Williston

G. W. TOOMEY — Devils Lake
P. H. WOUTAT — Grand Forks
V. G. BORLAND — Fargo

Committee on School Health
R. W. McLEAN, Chairman — Hillsboro
PERCY OWENS — Bismarck
M. H. POINDEXTER — Fargo
J. P. MERRETT — Valley City
R. E. DORMONT — Minot
J. V. MILES, JR. — Jamestown
W. C. DAILEY — Grand Forks
E. J. SCHWINGHAMER — New Rockford

Advisory Committee to the Public Assistance Division of the State Welfare Board
M. E. NUCENT Chairman — Bismarck
G. CHRISTIANSON — Valley City
G. L. COUNTRYMAN — Crafton
JOSEPH CRAVEN — Williston
R. M. FAWCETT — Devils Lake
V. J. FISCHER — Minot
A. C. FORTNEY — Fargo

Liaison Committee to the North Dakota State Bar Association
PAUL JOHNSON, Representative — Bismarck

Committee on Pharmacy
O. A. SEDLAK, Chairman — Fargo
R. H. WALDSCHMIDT — Bismarck
E. L. GRINNELL — Grand Forks
NEIL MACDONALD — Valley City
E. C. VINJE — Hazen

Liaison Committee to the Woman's Auxiliary to the North Dakota State Medical Association
V. G. BORLAND, Chairman — Fargo
E. H. BOERTH — Bismarck
J. C. FAWCETT — Devils Lake
WM. BUCKINGHAM — Bismarck
C. M. LUND — Williston

Liaison Committee to the North Dakota State Dental Association
DAVID JAEHNINC, Representative — Wahpeton

Medical Center Advisory Council
P. H. WOUTAT, Member — Grand Forks

Governor's Health Planning Committee
J. C. FAWCETT, Member — Devils Lake

State Health Council
Members: M. S. JACOBSON — Elgin
R. F. GILLILAND — Dickinson

Committee on Liability Insurance
R. H. WALDSCHMIDT, Chairman — Bismarck
JOSEPH SORKNESS — Jamestown
P. H. WOUTAT — Grand Forks
W. E. C. LANCASTER — Fargo
O. W. JOHNSON — Rugby

Liaison Committee to the State Board of Administration
JOSEPH SORKNESS, Chairman — Jamestown
G. A. DODDS — Fargo
P. O. DAHL — Bismarck
O. W. JOHNSON — Rugby
J. C. FAWCETT — Devils Lake
G. L. COUNTRYMAN — Crafton

Committee on Cardiovascular Diseases (Liaison Committee to the North Dakota Heart Association)
R. M. FAWCETT, Chairman — Devils Lake
H. C. WALKER, JR. — Williston
KEITH FOSTER — Dickinson
ROBERT STORY — Fargo
DAVID JAEHNING — Wahpeton
R. W. McLEAN — Hillsboro

Liaison Committee to Blue Cross-Blue Shield
O. A. SEDLAK, Chairman — Fargo
R. W. McLEAN — Hillsboro
RALPH LEICH — Grand Forks
E. J. LARSON — Jamestown
G. CHRISTIANSON — Valley City
ROGER SORENSON — Minot
GORDON ELLIS — Williston
E. J. BEITHON — Wahpeton
L. F. PINE — Devils Lake

Committee on Emergency Medical Service
RALPH MAHOWALD, Chairman — Grand Forks
DOUGLAS LINDSAY — Fargo
ROBERT NUESSLE — Bismarck
W. B. HUNTLEY — Minot
JAMES MURRAY — Fargo
J. K. O'TOOLE — Park River
DOLSON PALMER — Cando
C. M. GRAHAM — Grand Forks

REFERENCE COMMITTEES

1. To consider report of President, Secretary, Executive Secretary, and Treasurer:
F. D. NAECELI, Chairman — Minot
M. A. K. LOMMEN, Vice-Chairman — Bismarck
RICHARD LEIGH — Grand Forks
F. M. MELTON — Fargo
W. C. HANEWALD — Dickinson

2. To consider reports of Council, Councillors, and Special Committees:
R. B. TUDOR, Chairman — Bismarck
R. C. PAINTER, Vice-Chairman — Grand Forks
HENRY A. NORUM — Fargo
CLAYTON JENSEN — Valley City
JAMES LITTLE — Mayville

3. To consider report of Delegate to A.M.A., Medical Center Advisory Council, and Committee on Medical Education:
JAMES MAHONEY, Chairman — Devils Lake
L. G. PRAY, Vice-Chairman — Fargo
JOHN SANDMEYER — Grand Forks
M. W. GARRISON — Minot

4. To consider reports of Standing Committees, except Committee on Medical Education and Committee on Medical Economics:
J. V. VAN DER LINDE, Chairman — Jamestown
LEE CHRISTOFERSON — Fargo
DEAN R. STRINDEN — Williston
B. HORDINSKY — Drake

5. To consider reports of the Committee on Medical Economics, including Advisory Committee to Public Assistance Division of State Welfare Board, Committee on Rural Health, and Governor's Health Planning Committee:
A. C. BURT, Chairman — Fargo
C. L. COUNTRYMAN, Vice-Chairman — Crafton
EDMUND VINJE — Hazen
NORMAN ORDAHL — Dickinson
D. W. PALMER — Cando

6. Committee on Resolutions to include New Business.
R. E. MAHOWALD, Chairman — Grand Forks
MILTON NUCENT, Vice-Chairman — Bismarck
J. N. ELSWORTH — Jamestown
J. F. HOUCHTON — Fargo
A. F. HAMMARGREN — Harvey

7. Committee on Credentials:
FRANK MELTON, Chairman — Fargo
(Also serves on committee No. 1)
EDMUND VINJE, Co-Chairman — Hazen
(Also serves on committee No. 5)

PROCEEDINGS

of the House of Delegates

of the North Dakota State Medical Association

Seventy-Fourth Annual Meeting

The First Session of the House of Delegates of the North Dakota State Medical Association was called to order by the Speaker of the House, Dr. G. A. Dodds, at 3:30 P.M. in the Gardner Hotel, Fargo.

Dr. Melton, chairman of the Credentials Committee, reported that there was a quorum present and that all credentials were in order.

Secretary Buckingham called the roll. The following delegates and alternates were present:

Drs. A. C. Burt, Fargo; Frank M. Melton, Fargo; J. F. Houghton, Fargo; L. G. Pray, Fargo; Henry A. Norum, Fargo; Lee Christoferson, alternate, Fargo; J. H. Mahoney, Devils Lake; D. W. Palmer, Cando; C. L. Countryman, Crafton; Ralph Mahowald, Grand Forks; Robert Painter, Grand Forks; John Sandmeyer, Grand Forks; Richard Leigh, alternate, Grand Forks; F. D. Naegeli, Minot; A. F. Hammargren, Harvey; B. Hordinsky, Drake; C. J. Klein, alternate, Valley City; Edmund Vinje, Hazen; R. H. Waldschmidt, alternate, Bismarck; M. A. K. Lommen, Bismarck; Milton Nugent, Bismarck; R. B. Tudor, Bismarck; J. N. Elsworth, Jamestown; Dean R. Strinden, Williston; Norman Ordahl, Dickinson; W. C. Hanewald, Dickinson; James Little, Mayville; and John Van der Linde, Jamestown.

There were 24 delegates and 4 alternates present. The following also attended the House of Delegates meeting:

Drs. Pederson, Sedlak, Wright, Fawcett, Borland, Lund, Foster, Peters, McLean, Boerth, Gilsdorf, and E. J. Larson, and Mr. Limond.

The motion was made, seconded and passed that the reading of the minutes of the last session of the House of Delegates be dispensed with and that they be accepted as printed in THE JOURNAL-LANCET.

Motion was made, seconded, and passed that the reading of the reports as printed in the Handbooks be referred to the proper reference committees and that the reading of these reports be dispensed with.

REPORT OF THE PRESIDENT

It is customary for the president of the North Dakota State Medical Association to give a report regarding the important events transpiring during the year. I have attempted to keep you informed by means of newsletters regarding events of interest during the year 1960-61. In addition, you have been informed of the legislative sessions by our state office in Bismarck. Therefore, I think it would be needless repetition to burden you again with what has transpired.

The past eleven months in the affairs of the North Dakota State Medical Association have been far from uneventful. They have been extremely interesting, very enjoyable, and filled with challenges. In fact, every week seems to present new problems, some minor and some major. We were able to cope with some of the porblems whereas time prevented a solution to others. It is with regret that I leave this office with some of these unsolved problems passed on to the officers of the following year.

Most of you will recall that last year, when assuming this office, I publicly stated that the one object in mind during 1960-61 would be that of preserving and protecting our state organization against the intrusion of any type of socialistic medicine. In addition, we felt there was a dire need for a Department of Public Information and Education in our organization and lastly we were hoping that we could attempt to increase an interest among our profession legislatively, economically, and politically. Actually this is a continuance of the policy of my predecessors. I only hope we have not deviated from a course that you have expected us to follow.

Although our society is not large in number, it has far too many activities to be handled by 3 people in our Bismarck office. I believe the strength of our society is in our committees. I have attempted to choose strong committee chairmen and promising committee members. The various chairmen have been encouraged to activate their committees with new and in some cases daring thinking. We have had fine support from the American Medical Association in this respect. I can only think of one committee that has not received 100 per cent support from all of us. I attended most of the committee meetings during the past year and it was heartening to see the interest exhibited by the various members in spite of the long distances and the fact they had to travel at their own expense. As usual, the greatest burdens have fallen on the legislative, economic, and public relations committees but I am happy to say that most of the committees have been functioning well. I want to take this opportunity to thank them for their cooperation.

I did not attend the A.M.A. annual meeting in Atlantic City. I was also absent from the interim session of the A.M.A. and also the North Central Conference meeting in Minneapolis. I felt that I would be able to devote more time to the affairs of the association by working in the state. Furthermore, I was ably represented by Drs. Larson, Wright, and Pederson, and Lyle Limond. This also gave me the time to visit and inspect the various institutions throughout the state. I certainly want to encourage every doctor in our organization to take some time to visit the various institutions. It is both constructive and revealing.

I did, however, attend President Eisenhower's White House Conference on Aging, December 10 at Washington, D. C. This was arranged by the H.E.W. Department of the federal government and rather craftily planned so that the outcome bore resemblance of the will of the majority of the 2,700 delegates rather than a few. The medical profession was accused of "stacking" the session, whereas quite the opposite was true. I was amazed and shocked to find out in what low esteem the medical profession was held. I was told "medical ethics of the past are today a stone wall into which we are butting our head," and "the oath of Hippocrates no longer applies to present medical methods," and "many of the policies of the American Medical Association and state medical organizations are due for a direct about-face, especially those policies of public relations and excessive fees, if we hope to again recapture the favor of the public." (I was overwhelmed with arguments when attempting to refute these accusations.) How often have we heard the statement that the unions are pricing themselves out of work? Is this happening to the medical profession? I am happy to state that only two cases of excessive pricing have been called to my attention. Both of these were investigated and I found them to be of a minor nature. Doctors in North Dakota cannot be accused of charging excessive fees.

We have attempted to cultivate and improve relations between the Blue Cross, Blue Shield, and the North Dakota Hospital Association. In addition, other efforts have been made toward improving relationship between the State Medical Association and the State Health Department and Welfare Board. We must be constantly on the lookout for additional strength, support, and voting power. How futile it seems for the American Medical Association with a membership of 175,000 members out of 250,000 doctors in the United States to be combating the strength of the unions which total approximately 10 million people. In spite of this, it is remarkable how much power this small group is wielding in Congress. Think of the possibility of forming an organization composed of professional men, business men, and all of those who favor the private enterprise type of living and overwhelm the opposition with possibly 12 to 15 million members.

I feel some plan should be initiated in which to improve the organization of our state headquarters. At the present time we have a total of three, whereas we could easily use six employees. In addition, we should have a building of our own. This is being accomplished elsewhere and I see no reason why North Dakota cannot do this. There are various ways of raising funds for this need. I could mention that of a state medical periodical published monthly, from which the income from subscriptions and advertising over a period of time would take care of the added cost for such increase in our organization.

There are times when all of us are inclined to forget the good work that is being accomplished at our medical schools. We are apt to take for granted that, once having obtained a high standard, very little effort is needed to maintain this status. I have had the opportunity to ob-

serve at times what a discouraging task it is to be Dean of the medical school, attempting to obtain top men with a limited budget, etc. I have also witnessed the Dean appear before our state legislature in attempting to preserve the mill levy for the medical center when attempts were made to divert it elsewhere. Give the medical school a boost and a helping hand whenever you can. I also would urge you to give the same consideration and help to our American Medical Educational Fund which is being so ably handled by our past president, Dr. W. E. G. Lancaster. Remember, we have to replace ourselves in the medical profession as the other sciences and industries are grabbing our college graduates, offering them attractive salaries and fringe benefits to lure them away from a long and often disheartening medical course.

There are some committees, committee chairmen, members of the committees, and individuals in the society that I would like to single out as performing heroic work during the past year. This, however, would not be fair to all of the other members who have also given a splendid effort. So many doctors have uncomplainingly stepped into the breech when needed. I hope I will not show favoritism when I cite, for example, the work of the Bismarck doctors during the past legislative session. They were at the beck and call of the whims of the legislators at all times and did their work uncomplainingly. This type of response and sacrifice is the making of good society.

I would not be telling the truth if I did not state that I have enjoyed every day of my tenure. Being your president has been the highest honor I have ever received and ever hope to receive. I am thankful for the excellent support and cooperation that I have received from all the doctors in the state and also wish to thank our executive staff in our office in Bismarck for their kindness and patience in which they have received the added burden I have placed upon them.

CARROLL M. LUND, M.D., President

REPORT OF THE SECRETARY

The following report of the secretary is respectfully submitted:

MEMBERSHIP: The total membership for 1960 was 451. Of this number, 418 paid the regular membership fee, 5 were on a retired or limited basis, and 24 were honorary members. Four members were carried on a complimentary basis due to military service and age. Eight members passed away during the year and several have left the state. New members, however, are being steadily added to our roster.

Table 1 shows the annual membership for the past 5 years:

TABLE 1

COMPARISON OF ANNUAL MEMBERSHIP

	1956	1957	1958	1959	1960
Paid memberships	380	395	403	418	418
Honorary memberships	16	18	16	24	24
Retired and limited	12	9	9	4	5
Dues cancelled (military service and age exemption)	8	6	5	2	4
	416	428	433	448	451

Table 2 shows the annual dues for 1961 which have been coming in very slowly. There is still a very large number of members who have not yet paid their 1961 dues, and the district medical society secretaries and councillors are urged to use every possible means to collect the dues of these delinquent members.

TABLE 2

	May 1 1957	April 15 1958	April 15 1959	April 13 1960	April 17 1961
Paid-up members	328	313	309	335	348
Honorary members	18	16	20	22	27
To be honorary	2	3	4	5	2
Dues cancelled, military service	5	3	3	2	2
Limited			1	2	1
Retired	7	3	1	1	
	360	338	338	367	380

STATE ASSOCIATION MEMBERSHIPS

1960 —Total Membership 451

District	Regular	Retired	Limited	Comp.	Honorary
First	87			1	2
Second	28				2
Third	72			1	4
Fourth	66		1		4
Fifth	8				1
Sixth	72	1	2	1	6
Seventh	33		1		2
Eighth	18				
Ninth	24			1	3
Tenth	10				
	418	1	4	4	24

1961 Total Membership 378

District	Regular	Retired	Limited	Comp.	Honorary
First	80			1	2
Second	26				2
Third	49				5
Fourth	55				3
Fifth	10				1
Sixth	50				8
Seventh	32		1		3
Eighth	21				
Ninth	20			1	3
Tenth	5				
	348		1	2	27

A.M.A. GENERAL MEMBERSHIPS

	1960	1961
First	88	81
Second	30	28
Third	76	53
Fourth	70	57
Fifth	9	11
Sixth	80	57
Seventh	32	36
Eighth	18	21
Ninth	28	22
Tenth	10	5
	441	371

It is, of course, the wish of the association that all doctors practicing in North Dakota be members of our group. This, of course, has not been true in the past and probably will never be entirely true, but, nevertheless, it

behooves each of us to attempt to have our fellow physicians join and take an active part in the medical association.

As was noted previously, the dues this year have been coming in rather slowly. Failure to pay these dues when they become due on January 1 each year, creates unnecessary work for the secretaries of the constituent societies and the resultant uncertainty is disconcerting to the state office. Cooperation on the part of each member would expedite the early receipt of all dues payments.

W. M. Buckingham, M.D., Secretary

REPORT OF THE EXECUTIVE SECRETARY

GENERAL COMMENTS: Your executive secretary attended several state, regional, and national meetings in behalf of the association.

The routine of the headquarters office continues to show an increased tempo as each year passes. This increase is due to increased emphasis in the areas of medical economics, legislation, public relations, medicare, and general services to the members.

The affairs of your state office remain in the capable hands of Mrs. Margaret Fremming, office secretary. Part-time help is employed when the occasion warrants it.

LEGISLATION: Our greatest effort in this area was on the state level during January and February of this year. It is believed by this writer that the association had a very successful legislative session. The work done by Dr. C. H. Peters of Bismarck is to be particularly noted as he was ever ready to appear before house and senate committees, special conferences, and the like. Drs. P. O. Dahl, E. H. Boerth, Paul Johnson, and Robert Tudor, all of Bismarck, testified before committees. Drs. O. W. Johnson, Rugby; Rudy Froeschle, Hazen; C. M. Lund, Williston; and L. G. Pray, Fargo, also appeared before committees. Several members of this association and the woman's auxiliary made visits to the legislature and contacted their senators and representatives. All members who visited Bismarck wrote letters and made phone calls to members of the legislature are to be commended for their splendid efforts. Please note the listing of bills.

Last spring and summer were very busy on the national scene in combating the attempts to pass the Forand bill (H.R. 4700) in Congress. Organized medicine and its allies were successful in this regard with the passage of the Kerr-Mills bill which President Eisenhower signed into law on September 13, 1960.

With the advent of the Kennedy administration, organized medicine is now in a struggle against the King bill (H.R. 4222) which calls for benefits through the social security system to persons 65 years of age or older and naturally calls for an increase in social security taxes.

Here is the congressional status of bills of special interest to the medical profession at this writing:

King bill (H. R. 4222), as noted above.

Keogh bill (H.R. 10), to encourage through tax deferment the establishment of pension plans by the self-employed.

Aid for medical education, grants for construction and scholarships. Hearings not announced so far.

New appropriations, being considered by House Appropriations subcommittee in executive session.

Please note the report of the chairman (O. W. Johnson, M.D.) of the Committee on Legislation elsewhere in this handbook.

PUBLIC RELATIONS: Mr. George Michaelson was employed by the council as of October 1, 1960, when he assumed his duties as Director of Public Information and Education. He is leaving the employ of the association on May 10, 1961, in order to return to the national foundation.

While with the association, Mr. Michaelson visited 9 of the district medical societies, authored the booklet entitled, "The Positive Program of Health Legislation," drew up the newspaper advertisement in conjunction with Blue Shield for the centennial issue of the daily newspapers and wrote the legislative newsletter.

Our relationship with Blue Shield should continue on a firm basis with the employment of a qualified individual to take the place of Mr. Michaelson.

The North Dakota State Medical Association and Blue Shield can collaborate in a stepped-up program of public information and education in the following categories:

1. Newsletter to all daily and weekly newspapers
2. Speakers bureau
3. Radio and TV programs
4. Exhibits at state and county fairs
5. Press—radio and TV conferences
6. Public forums
7. Film library
8. Health columns in North Dakota newspapers and magazines
9. Paid advertising on occasions
10. Conferences with allied groups in the health field

PHYSICIANS' PLACEMENT SERVICE: Twenty-seven North Dakota communities and 10 physicians or groups are on file in the office in regards to a request for a physician and/or additional physicians.

The 27 communities are as follows: Anamoose, Ashley, Belfield, Buffalo, Casselton, Edmore, Enderlin, Esmond, Flasher, Fordville, Forman, Grenora, Killdeer, McHenry, McVille, Medina, Milnor, New England, New Salem, Page, Pembina, Portland, Rutland, Sharon, Strasburg, Willow City, and Wyndmere.

U.N.D. MEDICAL SCHOOL SCHOLARSHIPS: The 1960 winners of the association's scholarship prizes (totaling $500.) offered at the school of medicine were as follows: anatomy, first year, (tied) Reed Keller and Donald Foss; physiology and pharmacology, Douglas Miller; microbiology, William F. Belk; pathology, second year, Cecil Leitch; and highest scholastic average, first year, Reed Keller.

FINANCE: The treasurer's report continues to show an improved balance. The goal of having one year's operating budget in reserve was maintained last year when you consider the certificates of deposit in the headquarter's office account. It is hoped that this reserve can be kept at this level as it should be in the interests of good business practice.

Receipt of dues continued to be slow as in years past when you note the following listing as of April 19, 1961.

District Society	*No. of unpaid members*
First	9
Second (Devils Lake)	3
Third (Grand Forks)	24
Fourth (Northwest)	8
Fifth (Sheyenne Valley)	—
Sixth	24
Seventh (Stutsman)	—
Eighth (Kotana)	—
Ninth (Southwestern)	2
Tenth (Traill-Steele)	5
	75

MEDICARE: The Dependents' Medical Care Program (Medicare) commenced on December 7, 1956. Up to January 1, 1961, 4,174 claims had been processed by this office. The total sum paid to North Dakota physicians as of December 31, 1960, amounted to $303,636.00.

Each claim for services rendered averaged out at $72.79.

THOUGHTS FOR THE FUTURE:

1. Interest should remain high in the field of national legislation affecting organized medicine.

2. All members who possibly can should plan now to attend the association's diamond anniversary scheduled for Bismarck June 2, 3, 4, and 5, 1962.

3. In our public relations program, thought should be given to securing allies in combating the continued growth of the welfare state philosophy.

ACKNOWLEDGEMENTS: I wish to express my sincere appreciation to our president, C. M. Lund, M. D., for his efforts in behalf of this association. Dr. Lund made many trips both in and out of the state on association business.

My sincere thanks also go to those other members with whom this writer has had occasion to work this past year on committee assignments, lobbying activities, and the other programs of the association.

Lyle A. Limond, Executive Secretary

SENATE BILLS

8. State Health Department appropriation of $614,000 of which $80,000 is earmarked for a program under the new mental health authority bill. Supported. Signed by governor.

26. Public Welfare Board appropriation. Followed. Signed by governor.

36. Nursing preparation scholarships. Followed. Signed by governor.

37. State Commission on Alcoholism appropriation. Followed. Signed by governor.

46. Eliminates duplication in licensing or inspection of restaurants, motels, hotels, etc., by transferring authority from State Laboratories Department to local health authorities and in some areas to the State Health Department. Token support. Passed senate. Defeated in house.

47. Authorizes establishment of community mental health service units, provides for state aid and authorizes levy not to exceed 3/4th of one mill. One of the three bills dealing with mental health (SB 48 and SB 49). Token support. Killed in senate.

48. Transfers administration of Children's Psychiatric Clinic from Board of Administration to State Health Department. Supported. Became part of SB 49 when SB 49 was amended.

49. Mental health authority. This bill contains provisions of Senate bills 48 and 49. Certified psychiatrist to be administrator at Jamestown State Hospital. Mental health authority under State Health Council. Supported vigorously. Signed by governor.

70. Requires nonprofit corporations to file annual reports with Secretary of State and provides penalty. Followed with interest. Indefinitely postponed in the house.

89. Provides that arresting officer shall determine which chemical tests shall be given for determining intoxication to motorists, under "implied consent" law; strengthens interpretations of chemical tests. Supported with an amendment to protect doctors doing tests. Signed by governor.

96. The sum of $108,000 to be used with federal grant funds for construction and equipment of state public health laboratory at Bismarck. Supported. Indefinitely postponed in senate.

112. Provides for licensing of life, accident, and health and hospitalization insurance agents; appropriates $20,000 for administration; provides penalties. Followed. Indefinitely postponed in senate.

113. Sets up procedures for revision of rates of nonprofit hospital service corporations; provides that policy holders shall make up majority of board of directors. Opposed. Indefinitely postponed in senate.

116. Provides for licensing and regulations of charitable organizations which solicit funds. Provides penalty. Followed. Withdrawn.

119. Provides for licensing of sales representatives of non-profit medical service corporations. Supported. Signed by governor.

120. Three per cent (3%) surtax bill. Followed with interest. Killed in senate.

127. Changes limit of amount of state loans for nursing homes and homes for aged from one-third to one-half of cost of construction or reconstruction but not above $150,000 (now $100,000); makes eligible those facilities which receive loans or grants from federal government; appropriates $1,000,000 from public welfare fund to revolving loan fund. Supported. Signed by governor.

140. Regulates the labeling of certain hazardous substances for nonmanufacturing purposes which are intended or suitable for household use, provides penalty. Supported. Indefinitely postponed in senate.

146. Provides for licensing, registration, filing, and reporting of charitable organizations, excluding religious, which solicit funds. Token support. Signed by governor.

150. Provides for employee temporary disability insurance to be financed by deductions in employee salaries amounting to 1 per cent of wages up to $3,000.00. Opposed the provision in bill disallowing free choice of physician. Indefinitely postponed in senate.

158. Rewrites definition of special education to provide that such education may be provided in public schools and institutions. Followed. Signed by governor.

173. Establishes office of state toxicologist at North Dakota State University. Followed with interest. Signed by governor.

178. Provides for loans to dental students from medical center loan fund. Token support. Signed by governor.

179. Authorizes superintendent of public instruction to contract with nonprofit corporations for providing educational television in state, appropriates $46,356. Followed with interest. Signed by governor.

182. Requires hospitals to obtain approval of plans and specifications for major alterations, additions, and construction from State Department of Health, emergency. Token support. Signed by governor.

196. Authorizes president and secretary of district board of health unit to audit claims against health fund. Followed. Killed in senate.

197. Exempts from provisions of narcotics law those medicinal preparations authorized by federal law to be administered, dispensed, or sold at retail without prescription. Followed. Signed by governor.

207. Defines standard of care required of physicians and surgeons when rendering emergency care at scene of emergency, protects nonresident physicians and surgeons with respect to nonlicense. *Introduced* bill and supported same. Signed by governor.

217. Imposes 1½% surtax on net incomes of individuals. Followed with interest. Indefinitely postponed in house.

227. Medical Assistance for the Aged Act. *Introduced* bill and supported same vigorously. Signed by governor.

236. Authorizes chiropodists to participate in nonprofit medical service corporations. Opposed vigorously. Indefinitely postponed in senate.

265. Repeals all sections dealing with hospital service contracts. Opposed. Indefinitely postponed in senate.

268. Repeals all sections dealing with nonprofit medical service corporations. Opposed. Indefinitely postponed in senate.

283. Establishes state program of medical assistance for the aged. Welfare department bill. Opposed. Indefinitely postponed in senate.

303. Creates state milk board to supervise and regulate fluid milk industry, appropriates $130,000. Followed with interest. Indefinitely postponed in senate.

304. Provides for supervision of nonprofit medical service corporations by commissioner of insurance for licensing of sales representatives and requires majority of board of directors to be subscribers and persons other than licensed physicians and surgeons. Opposed. Indefinitely postponed in senate.

HOUSE BILLS

317. $366,000 for special education of exceptional children. Supported. Signed by governor.

332. $150,000 for the children's psychiatric outpatient clinic. Followed with interest. Signed by governor.

333. $30,000 for education of deaf-blind children outside of the state. Token support. Signed by governor.

341. Authorizes Board of Review to review examinations of any applicant failing exam for a license to practice any profession or occupation. Opposed vigorously. Indefinitely postponed in senate.

342. Removes mandatory requirement that certain persons be sterilized before being released from public institutions. Followed. Signed by governor.

343. Authorizes superintendent of Grafton State School to accept voluntary patients to school without necessity of court commitment procedures. Followed with interest. Signed by governor.

352. Deals with several boards and commissions and lightens duties of governor and superintendent of Public Instruction. *Opposed* amendment to the bill which would have placed a chiropractor on the State Health Council. Amendment removed. Signed by governor.

379. Requires person preparing or serving school lunches to file health certificate annually with school board or clerk. Followed. Signed by governor.

388. Requires cemetery owners or maintainers to submit plans and specifications for certain structures above ground to the State Health Department for review and approval. Token support. Signed by governor.

608. Provides for bonding of secretary-treasurer of Board of Massage; rewrites provision of those eligible for certification. Followed. Signed by governor.

685. Provides that revenue from 1 mill medical center levy shall be expended only upon prior appropriation of legislative assembly. Opposed vigorously. Indefinitely postponed in senate.

707. Makes it unlawful for any person to be employed in any school while suffering from any disease in communicable stage. Followed. Indefinitely postponed in house.

758. Authorizes creation and reorganization of hospital districts for acquisition, operation, maintenance, and administration of hospital and nursing home facilities. Opposed. Indefinitely postponed in house.

816. Prescribes powers and duties of State Public Welfare Board relating to child welfare and youth services for children and families. Opposed. Indefinitely postponed in house.

853. The sum of $800,000 to establish geriatrics hospital at Rugby. Followed. Indefinitely postponed in house.

887. Prohibits physician employed by state or political subdivision who receives more than $20,000 from engaging in private practice. Followed with interest. Indefinitely postponed in House.

899. Extends date when first installment of medical scholarship loan must be paid, if approved by medical center loan fund board. Followed. Indefinitely postponed in senate.

HCR-L. Submits to electorate constitutional amendment to repeal certain amendments setting up certain dedicated funds to provide that collections from 1 mill medical center levy from highway taxes and certain other collections go to general fund. Opposed. Indefinitely postponed in senate.

REPORT OF THE CHAIRMAN OF THE COUNCIL

The Council of the North Dakota State Medical Association held its regular spring meeting April 30 and May 1 at the Dacotah Hotel in Grand Forks. The regular interim meeting of the council was held on December 10 at the Gardner Hotel in Fargo.

The regular spring meeting convened at 1:30 p.m., Saturday, April 30. All of the councillors were present. Others present were: Drs. W. A. Wright, L. W. Larson, J. C. Fawcett, G. A. Dodds, E. H. Boerth, C. M. Lund, R. H. Waldschmidt, R. D. Nierling, R. W. Rodgers, C. J. Glaspel, and Mr. Lyle Limond.

The minutes of the previous sessions were approved.

Dr. John Fawcett, president of the North Dakota State Medical Association, appeared before the council and thanked them for their cooperation and great help during his year in office. He noted the increased interest and participation in political matters on the part of doctors throughout the past year. He felt that more attention should be given in general to these matters in the future.

Dr. L. W. Larson appeared before the council and informed them that he would be running for the office of President-Elect of the American Medical Association in June of 1960. He discussed certain legislative matters, particularly on the national political scene. He also advised the council of the important position that Dr. W. A. Wright holds with the American Medical Association House of Delegates and commended Dr. Wright for his excellent work. Dr. W. A. Wright then appeared before the council thanking them for the opportunity of serving them as delegate to the American Medical Association. He commended Dr. T. E. Pederson's work as alternate delegate. He then discussed the matter of the aging conference to be held in Washington, D.C. and stated that Dr. Pederson is the Chairman of the Committee on the Aging for North Dakota and asked the councillors and other members of the state association to support Dr. Pederson in this important work.

Several members of the North Dakota Pharmaceutical Association then appeared before the council to discuss certain problems and complaints that had come to them from the druggists in the state. Among those representing the Pharmaceutical Association were Mr. Alden L. Foss, president, Mr. Trom, Mr. Wagner, and Mr. Al Doerr.

After some discussion it was decided that the president of the North Dakota State Medical Association should appoint a committee to meet with a pharmaceutical association committee to work out solutions to mutual problems.

A motion was passed that the State Medical Association defray the traveling expenses of delegates to the White House Conference on Youth and the White House Conference on Aging.

The chairman of the council was requested to send a telegram of condolence to Mrs. D. J. Halliday because of the recent death of her husband who had served the North Dakota State Medical Association so well for so many years.

A motion was made and passed that the dates for the 75th anniversary meeting of the North Dakota State Medical Association to be held in Bismarck in 1962 would be June 2 through June 6.

Mr. Ronald Jydstrup and Mr. Truman Wold appeared before the council regarding the study of the 1959 discharges from North Dakota hospitals, a survey to be used by the Medical Association for their analysis and action as deemed necessary. It was agreed that the council would endorse this survey with the stipulation that the information would not be used for publication and that it be kept confidential by Mr. Wold and his assistant until mutual agreement for release is agreed upon by the North Dakota State Medical Association and Blue Cross.

The following resolution was introduced: Whereas, many physicians believe and various studies have shown that the goals, purposes, and accomplishments of the medical profession with regard to scientific, socioeconomic, and political developments in the field of medical care are poorly understood by the public; and

Whereas, greater public understanding and support are necessary if the best medical practice is to survive and continue to serve the public; and

Whereas, an effective public relations program is the best insurance that the purposes and performance of the Medical Association will be understood and appreciated by the people of our state,

Now, therefore be it resolved that the North Dakota State Medical Association activate its program to expand and accelerate public relations through the North Dakota State Medical Association's Public Relations Committee.

This was adopted and referred to the House of Delegates for action.

The following resolution was introduced: Whereas, it is the honored, ethical practice of the physician to aid all who are in need of medical care; and

Whereas, the physician does not turn away the person in straitened financial circumstances,

Now, therefore be it resolved that the members of the North Dakota State Medical Association reiterate once again through the association's ruling body, the House of Delegates, that no person in North Dakota is ever refused medical care based on inability to pay.

This resolution was adopted and referred to the House of Delegates for action.

Dr. Peters reported to the council that a new agreement is being worked out with the Division of Vocational Rehabilitation in North Dakota to accept the relative value schedule effective July 1, 1960, with a conversion factor of $4 per unit for medicine and surgery and $5 per unit for x-ray and laboratory.

At the second session of the House of Delegates, held on May 1, 1960, Dr. A. R. Gilsdorf was elected to the office of second vice-president. He, therefore, resigned as councillor and Dr. Keith Foster of Dickinson was elected as councillor to fill his unexpired term. Dr. V. G. Borland, vice-president of the council, called the meeting to order at 4:00 p.m. All of the councillors were present except the newly elected councillor from Dickinson, Dr. Keith Foster. Dr. F. D. Naegeli, newly elected councillor from the Fourth District, was present. Others attending this council meeting were: Drs. R. D. Nierling, J. C. Fawcett, E. H. Boerth, E. J. Larson, R. H. Waldschmidt, C. M. Lund, and Mr. Lyle Limond.

The new program planned for expanded public relations and education recently put into operation by the House of Delegates was discussed by the councillors. It was suggested that the president of the association be urged to appoint an active public relations committee without delay. This committee was then to investigate available prospects for the post of public education director and the council, acting with the advice of the Public Relations Committee is to hire such a man in the near future. A motion was made and passed that the council set aside $5,000 from the reserve fund to be used by the committee during the last six months of this fiscal year.

A letter written to Governor Davis by a member of the State Medical Association citing 3 instances where the Workmen's Compensation Bureau had reacted unfavorably to his interests was brought to the attention of the council. After some discussion the chairman of the council was instructed to set up a committee to meet with the Workmen's Compensation Bureau on this matter.

A motion was made and passed that the Council urge the president of the State Association to request that each committee appointed by him meet at least once yearly at a time other than the state meeting and that if such action is not taken, the chairman of that particular committee be replaced. Mr. Limond reported on the survey regarding the disability group plan and the dividend from the Union Central Life Insurance Company. They had received 80 replies from physicians in the state from 100 questionnaires sent out from his office. Forty-eight of the 80 asked that the dividend money be refunded to the policy holder. The council felt on this basis that the majority of the policy holders wished the money to be returned to them. Mr. Limond was requested to look into this matter and report back at the next meeting of the council.

Officers of the council for the current year were elected as follows: Chairman of the Council, Dr. V. G. Borland; Vice-Chairman of the Council, Dr. Glen Toomey; and Secretary, Dr. C. H. Peters.

The executive committee of the council was then declared to consist of Dr. Borland, Dr. Toomey, and Dr. Peters.

The next regular meeting of the council was to be held December 10, 1960, in Fargo, North Dakota, at 2:00 p.m.

A special meeting of the council was held in the Prince Hotel in Bismarck on August 6, 1960. This meeting was called for the sole purpose of employing a director of education and public information. After considering the information made available to us from the Public Relations Committee, Mr. George Michaelson was hired for this position at a salary of $7,500 per year.

The interim meeting of the council was called to order at 2:00 p.m. on December 10th at the Gardner Hotel in Fargo. All of the councillors were present. Others

present were: Drs. C. M. Lund, E. H. Boerth, William Buckingham, E. J. Larson, G. A. Dodds, O. A. Sedlak, O. W. Johnson, R. W. McLean, Mr. Charles Johnson, representing the American Medical Association, George Michaelson, and Mr. Lyle A. Limond.

The first item on the agenda was a discussion concerning the reception to be held for Dr. L. W. Larson in New York City on Wednesday, June 28, 1961, at the Statler-Hilton Hotel. The council unanimously approved underwriting the costs of such a reception.

The attention of the council was then called to a letter directed to Mr. Limond by Dr. James B. Murray, concerning a request made to him by the Governor's Committee for the Physically Handicapped. Each year the governor's committee sponsors an essay contest for high school students and the winner of this contest is sent to Washington, D.C. It was felt that the English teachers throughout the state would generate more interest in this contest if the teacher of the winning student could also go to Washington with the winning essayist. Since this was considered to be in the field of good public relations, the council approved supplying $250 toward defraying the expenses of the teacher of the winning student for the trip to Washington.

Dr. A. R. Cuadrado, Superintendent of the Tuberculosis Sanatorium at San Haven, North Dakota, then appeared before the council and discussed at some length the recent charges made against him from various quarters. A motion was made and passed unanimously that the council extend a vote of confidence to Dr. A. R. Cuadrado for his good work at San Haven.

The council regretfully accepted the resignation tendered by Dr. Keith Vandergon, who has long been a councillor from the Traill-Steele District Medical Society. The fact that Dr. Vandergon has moved his practice from Portland to Grand Forks prompted the letter of resignation. The motion was then made and passed that Dr. R. W. McLean of Hillsboro be appointed as a councillor from the Traill-Steele District Medical Society to fill Dr. Vandergon's unexpired term.

Dr. O. W. Johnson, chairman of the Committee on Legislation, addressed the council on some aspects of current and pending legislative problems.

Dr. C. H. Peters, chairman of the Committee on Medical Economics, discussed briefly some of the problems which had recently come before this committee. Attempts are being made to work out a new schedule with the Workmen's Compensation Bureau.

A request was presented concerning the North Dakota Chapter of the Multiple Sclerosis Society. Requests have been made by Mr. Don Albertson for a committee to work with the Multiple Sclerosis Society in a screening program. After some discussion the council felt that such a committee should be appointed and requested that Dr. Lund appoint the same.

After a brief intermission, the council reconvened at 6:30 p.m. for dinner. We were fortunate in having as our honored guest Governor-elect William Guy, who addressed the group briefly after dinner. After the guests excused themselves, the second business session began at 8:10 p.m.

A motion was made and passed that the names of Drs. V. J. Fischer, Frank Naegeli, M. S. Jacobson, and H. L. Reichert be submitted to the governor for his selection of two to fill unexpired terms of Drs. Halliday and Rodgers on the Board of Medical Examiners.

Dr. C. A. Arneson, president of the North Dakota State Board of Medical Examiners, addressed the council briefly on the problems of licensing foreign-born physicians.

Dr. Keith Vandergon, chairman of the Committee on Mental Health, reported at length on the actions of his committee which met at 9:20 a.m. Saturday, December 10. He read 3 bills, which had been corrected somewhat by his committee, that were to be introduced in the legislature at the coming session. A motion was made and seconded that the council approve the actions of the Committee on Mental Health.

A motion was made and seconded that the Committee on Public Relations, through the office of education and public information, be given the right and duty to quote the chairmen of various committees of the association on those matters affecting the various committees concerning the policies of the association. This motion was passed.

Dr. T. E. Pederson spoke briefly concerning the Joint Council To Improve the Health Care of the Aged. To underwrite certain expenses in connection with liaison committee meetings, outside funds are necessary. The Council approved Dr. Pederson's request for $100 to implement the program of the Joint Council To Improve the Health Care of the Aged.

At the request of Dean Harwood from the medical school in Grand Forks, the council went on record as opposing an addition to the McCannel Building at the University of North Dakota to be used as a tuberculosis hospital.

Dr. Carroll Lund, president of the North Dakota State Medical Association, next addressed the group. He discussed certain current problems in the political field, and stressed the importance of attempting to obtain qualified medical personnel for the office of State Health Officer and Superintendent at the Jamestown Hospital.

Mr. Limond reported on the refund moneys from the Union Central Life Insurance Company. He stated that he expected these funds to be in his office shortly and would then disperse them to the individual policy-holders.

Mr. Michaelson advised the council that there would be a presentation in the newspapers concerning the 100th anniversary of Dakota Territory with the centennial issue to be published February 28, 1961. He suggested that the Medical Association purchase space in this edition with a story of medicine in North Dakota, together with some background material on Blue Shield to be prepared for publication. A motion was made and passed that with the collaboration and consent of Blue Shield we buy one-quarter page in the centennial issue.

The meeting adjourned at 11:40 P.M.

V. G. Borland, M.D., Chairman

REPORTS OF COUNCILLORS

First District

The First District Medical Society held 7 meetings during the fiscal year from March 1960 through February 1961. It was necessary to cancel the meetings of March 1960 and November 1960 because of inclement weather. The meetings were held in the town hall of the Gardner Hotel in Fargo on the fourth Tuesday of each month.

On April 26, 1960, Dr. Jane Magill and Dr. Duane Nagle were elected to membership. Dr. Matthew B. Divertie of the Department of Internal Medicine at the Mayo Clinic gave a very instructive presentation on pulmonary carcinoma.

The next meeting was at 6:30 p.m. on September 27, 1960. Dr. Gerald Kavanaugh was elected to member-

ship. A resolution was passed approving the administration of Mantoux tests to food handlers, barbers, and cosmeticians in conjunction with the regular school Mantoux testing program.

Mr. Don Albertson, representing the North Dakota chapter of the Multiple Sclerosis Society, addressed the society briefly. Dr. Douglas Lindsay announced the receipt of equipment for a civil defense hospital in the Fargo area. A committee will be appointed to supervise and make plans for the use of this equipment in an emergency. Dr. Lee Christoferson requested that the society go on record approving the aims of the neuropsychopathic institute. A motion was made and passed that such a request be granted. Dr. Carroll Lund, as president of the North Dakota State Medical Association, Dr. O. W. Johnson, and Dr. C. H. Peters addressed the society and reviewed the political problems in the state of North Dakota. Mr. Mayo Christianson and Mr. Truman Wold reported on medical and hospital service in the Saskatchewan area. Mr. Ronald Jydstrup and Mr. Donald Eagles addressed the society on Blue Cross and Blue Shield problems.

The annual Long-Darrow lectureship was the occasion of the meeting on October 25, 1960, which was held at the Frederick-Martin Hotel. The speaker for this event was Dr. Arthur Curtis of the Department of Dermatology at the University of Michigan. He spoke on "Cutaneous Manifestations of Systemic Disease."

At the regular meeting on December 13, the following officers were elected for the year of 1961: president, Dr. G. Howard Hall; vice-president, Dr. C. M. Hunter; secretary-treasurer, Dr. M. H. Poindexter; delegates to the state meeting, Drs. Burt, Melton, Houghton, Pray, Norum, and Bacheller; alternate delegates, Drs. Jaehning, Thompson, Murray, Wold, Christoferson, and Schneider. New member of the Board of Censors was Dr. George Ivers.

A small dinner meeting was held at the Gardner Hotel on December 7, 1960, to which the legislators in the First District were invited. Many problems with which the legislature expected to be confronted were discussed and all those present felt that the meeting was worthwhile and mutually informative.

The next meeting was held on January 31, 1961. Drs. Neil S. Williams, Henry J. Wyers, Jerome P. Hager, Ralph E. Tarnasky, and Daniel Levson were elected to active membership in the society. Drs. B. C. Mahanti, Ralph Thomas, William T. F. Paul, and Dhia Allehverdi, physicians employed at the Fargo Veterans Administration Hospital were elected to associate memberships. Dr. Alice C. Peterson of the North Dakota Public Health Department and Dr. Eunice Davis of the Minnesota Public Health Department spoke briefly on the research project being carried out on phenylketonuria and requested the cooperation of the members of the society regarding babies born in Minnesota. Dr. T. H. Lewis who has practiced in North Dakota for fifty years was elected to life membership in the First District Medical Society. The speaker of the evening was Dr. Jack Spittell of the Mayo Clinic who spoke on "Problems of Blood Coagulation."

At the meeting on February 28, 1961, Dr. Robert Ivers was elected to active membership. Eighteen members of the society were designated as Blue Shield corporate members to represent the society at the annual meeting in May. Dr. A. C. Burt, Dr. L. A. Christoferson, and Dr. J. F. Houghton were appointed members of the board of directors of the North Dakota Physicians Service from the First District Medical Society. The untimely death of Dr. A. L. Klein was mentioned and the members stood for a moment of silence in respect for his memory. Mr. George Michaelson, Director of Public Information for the State Medical Society, spoke briefly on current legislative matters. The speaker of the evening was Dr. Charles Owens of the Mayo Clinic who gave a very interesting talk on "Diagnostic Applications of Radioisotopes."

Membership of the district is as follows: active members, 93; retired members, 1; honorary members, 1; limited members, 8; in-service members, 0; new members added during the year, 9; members who have left the state, Dr. C. V. Batemen, to Breckenridge, Minnesota, and Dr. W. C. Nellermoe to Portland, Oregon; deceased members, Dr. B. M. Urenn and Dr. A. L. Klein; and nonmembers residing in the area, Dr. H. B. Waydeman, Hunter, North Dakota.

V. G. Borland, M.D., Councillor

Second District

The Devils Lake District Medical Society held 9 regular meetings during the past year, including the one following the state medical meeting.

In May, a meeting of the society was held, after the meeting of the State Medical Society, at which time the society was given the reports from the delegates to the state convention and the councillor gave his report. At that time, we asked Mr. Floyd Gilliland of Devils Lake, chairman of the Governor's Aging Conference, to give us a report in October before going to Washington. There was no scientific session at this meeting.

On September 9, the Devils Lake District Medical Society was the guest of the doctors at Cando. Dr. Clayburgh of Grand Forks gave a paper on childhood and orthopedic problems in general practice. Dr. John Sawchuk of Rolette was admitted as a new member to the society.

October 6, a meeting was held in Devils Lake and was turned over to Dr. Lund, president of the State Medical Association, who introduced the speakers of the evening—Harvey Hanson, executive secretary of the Hospital Association, Mr. Jydstrup of the North Dakota Blue Cross, Mr. Christianson of the Blue Cross, and Mr. Finch of the Blue Cross. Their main topic was the impending hospital legislation. Mr. Lyle Limond spoke on contacting our legislators in our areas during the coming legislative assembly. Dr. O. W. Johnson gave a report on a meeting that he had had at Indiana at a gathering of the legislative committees of the various state societies.

November 3, Dr. Malcolm Cameron of Minot gave an interesting talk on surgical diseases of the chest. The application from Dr. McIntyre of Rolla had a third reading and he was unanimously voted into the society. A discussion followed as to whether the nurses of the health unit should do the Mantoux testing. It was unanimously agreed that they could. However, this particular program is to be reviewed on the yearly basis. Dr. McBane brought up the recent political meeting of the Ramsey County physicians with the political aspirants of both parties. We felt this was a very good move in regard to public relations.

December 1, Dr. Shea of Minot gave an excellent talk on the surgical aspects of deafness, followed by a brief film on the technic of stapedectomy. Mr. F. H. Gilliland of Devils Lake, Chairman of the Governor's Committee on Aging, gave us a preview of the Aging Committee

report which was to be submitted at the White House Conference in January.

January 12, 1961, Dr. James Houghton of the Dakota Clinic presented a paper on coronary artery disease. Following this, Dr. Neil Williams of Fargo discussed ocular injuries. The following officers were elected: president, Dr. Stuart Cook of Rolette; vice-president, Dr. E. J. Schwinghamer of New Rockford; secretary-treasurer, Dr. L. F. Pine of Devils Lake; delegates, Dr. Palmer, Cando; and Dr. Mahoney, Devils Lake; alternates, Dr. Hilts, Cando, and Dr. Seibel, New Rockford; and censor, Dr. Chris Johnson.

On February 2, the guest speaker was Dr. Macaulay of the Fargo Clinic, who spoke on skin diseases in infants. Dr. McBane and Dr. Mahoney reported on the investigation of maternal mortality and Dr. Corbett was reappointed to this committee. There was discussion regarding free choice of physicians, with particular attention to the United Mine Workers in North Dakota, the Blue Shield board of directors representative, Dr. Pine, reported on aspects of home and office visits.

On March 2, the guest speaker was Dr. Ralph Iver, who spoke on electrophoresis as related to neurologic problems. The society approved a special meeting with the Cancer Caravan on Tuesday, March 8, and also to meet with the Blue Shield representatives in April. The Devils Lake District Medical Society went on record as favoring the establishment of home and office visits to be underwritten by the Blue Shield on a rider basis.

On April 10, a meeting was held with the Blue Shield representatives from Fargo. A very spirited and interesting evening ensued.

We feel that the Devils Lake District Society has been very active during the year. The attendance at meetings has been excellent and all new members in the area have been brought into the society.

G. W. Toomey, M.D., Councillor

Third District

Since the last report, this district society has met on the third Thursday of each month, except during months of May, June, July, and August, with a total of 8 meetings.

On March 23, the scientific program consisted of a discussion of "Surgical Emergencies of the Newborn" by Dr. Tague Chisholm of Minneapolis. This was followed by discussion of the following topics: changes in the constitution of this district society, national legislative problems, representation to the North Dakota physicians service, organization of a Geriatric and Rehabilitation Committee for this society, a contribution of $125 to help defray expenses in sending the finalists of the State Science Fair to the national meeting, and the need for members to pay their annual dues.

On April 21, with 22 members in attendance, Dr. Channing Nicholas of the North Dakota State Department of Health discussed the results of the Bismarck-Mandan rheumatic fever study. Local society problems were considered, and there was again discussion of the national legislative situation.

At the September 15 meeting in Grafton, Dr. John H. Miller, Chief of the Section on Atherosclerotic Disease of the United States Public Health Service, spoke on their heart control program. Mr. Don Albertson, executive director of the North Dakota Multiple Sclerosis Society, presented methods of procedure for a Multiple Sclerosis Clinic scheduled for October 1960, in Grand Forks. Dr. Charles Porter of Grand Forks discussed the Blue Cross rate problems and the possibility of a mental health organization in Grand Forks county was considered.

The October 20 meeting was again held in Grand Forks with 48 in attendance. Dr. Lee Christoferson of Fargo discussed "Chemical Pallidectomy." The business session included the president of the State Medical Association, Dr. C. M. Lund, and representatives of Blue Cross and Blue Shield, whose discussions were primarily directed at North Dakota state legislative possibilities for the coming session of the legislature.

Fifty dollars in prize money was voted for the National Essay Contest sponsored by the Woman's Auxiliary.

On November 17, a movie and discussion of hypnosis was presented by A. A. Papermaster, D.D.S., of Fargo.

At the December 15 meeting, there was an illustrated travel talk by a local businessman who had recently made an extensive tour of Africa and Southeastern Asia. The business meeting was devoted to the North Dakota State Medical Association's legislative program and various local society problems.

On January 19, 1961, Dr. Wallace Nelson of Grand Forks reported on "The Papanicolaou Smear Survey" as carried out in the Grand Forks area.

The Grand Forks District Bar Association approached us regarding one or more joint meetings to discuss mutual problems and the professional and social relationship between the two professions. A committee was appointed to meet with a similar committee from their group, and preliminary discussions regarding possible joint meetings next year have been held.

The following officers were elected for 1961: president, Dr. William P. Keig, Grand Forks; first vice-president, Dr. Wallace W. Nelson, Grand Forks; second vice-president, Dr. Robert DeLano, Northwood; and secretary-treasurer, Dr. Richard Leigh, Grand Forks.

The board of censors consists of Drs. John Moore, Ted Harwood, and William Witherstine, Grand Forks. Delegates to the house of delegates are Drs. George Countryman, Grafton; Ralph Mahowald, Walter Dailey, Robert Painter, and John Sandmeyer, Grand Forks. Alternate delegates are Drs. William Powers, Wallace Nelson, Harold Evans, and Richard Leigh, Grand Forks, and Wellde Frey, Drayton.

At the February 16, 1961, meeting, Dr. G. B. Magill of Fargo discussed "Chemotherapy of Cancer."

The society has 80 members, including 1 retired and 4 at the air base. We lost 5 members through death or transfer to other communities and added 5 new members. The society was saddened by the death of Dr. H. E. French, dean emeritus of the medical school, who was beloved and respected by all who knew him.

The society is in good financial condition. No professional or ethical problems have come to my attention this past year.

P. H. Woutat, M.D., Councillor

Fourth District

This society had a successful year. The following new members were admitted to the society: Victor Cipolla, Minot; Edward Herba, Mohall; Dale Flickinger, Minot; Kenneth Kihle, Bottineau; Milton Herba, Harvey; and Thomas Wilson, Minot.

The following members transferred to other societies in North Dakota and elsewhere: Alexander Diduch, Stanley; Glen Brown, Bottineau; Martin Hochhauser, Garrison; William Kitto, Minot; F. Manzanero, Minot; Robert Whittlesey, Minot; and G. D. Anderson, Harvey.

At the start of 1960, the membership of the society numbered 72, of which 2 were honorary, and 70 were

active. At the end of 1960, the membership numbered 71, of which 2 were honorary and 69 active.

On January 28, 1960, Dr. Lucian Smith spoke on "Abdominal Pain." On February 25, 1960, Dr. Tom Chin spoke on "Enteric Virus Infection." On April 14, 1960, the North Dakota Cancer Caravan provided the program; Dr. M. M. Hargraves and Dr. C. A. Pascuzzi spoke on "Environmental Factors in the Production of Leukemia and Lymphomas." On September 28, 1960, Dr. Richard A. Daniels spoke on "Ochronosis." On October 27, 1960, Dr. Joseph Rushton spoke on "Convulsive Seizures." On December 8, 1960, a social meeting was held with the program provided by Dr. Darwin Kohl and a group of his musician friends.

F. D. Naegeli, M.D., Councillor

Fifth District

The Sheyenne Valley Medical Society held 7 dinner meetings during the fiscal year from March 1960 through February 1961.

At the first meeting on April 20, Dr. Robert Story of the Fargo Clinic, discussed the differential diagnosis of chest pain with special emphasis on spondylitis of the cervical spine.

Meetings without scientific programs were held on May 11 and June 8.

At the September 21 meeting, it was voted to send a tribute in memory of the late Dr. R. W. Rodgers of Dickinson. Mr. Don Eagles and Mr. Pezalla, representing Blue Shield, were dinner guests. Mr. Eagles spoke on the recent changes in coverage and fee schedules of Blue Shield.

Dinner guests on October 19 were Drs. James Hoyme of Oakes and Don Feist of Forman. Dr. James Cardy, pathologist at the University of North Dakota School of Medicine, reviewed the pathology and prognosis of malignant melanomas.

Another dinner and scientific program was held January 18, 1961, at which time the following officers for the ensuing year were elected: president, Dr. John Goven; vice-president, Dr. G. Christianson; secretary-treasurer, Dr. C. J. Klein; delegate, Dr. C. J. Klein; and alternate delegate, Dr. C. E. Jensen.

Dr. Ed Olmstead, internist and member of the faculty at the University of North Dakota School of Medicine, gave an instructive presentation of "Chronic Congestive Heart Failure."

Dr. Victor Szyrynski, psychiatrist, Bismarck, North Dakota, presented an informative paper on "Epilepsy" at a dinner meeting held February 15.

With the addition of Dr. Clayton E. Jensen, Valley City, and James Hoyme, Oakes, the fifth district now has a total active membership of 9 and 1 retired member.

G. Christianson, M.D., Councillor

Sixth District

The first meeting was held on April 7, 1960, in Bismarck, with vice-president, Dr. Rudy Froeschle, presiding in the absence of the president. Fifty-five physicians were present, including 5 guests. The program consisted of a discussion of leukemias and lymphomas by Dr. C. A. Pascuzzi and Dr. M. M. Hargraves of the Mayo Clinic, sponsored by the North Dakota Cancer Society.

At this meeting instructions to the delegates to the State Medical Association were given:

1. A motion was made, seconded, and rejected that a certain amount be deducted from the Blue Shield checks to the physicians for the purpose of AMEF.

2. A motion was made that the North Dakota Medical Association be requested to encourage the public of North Dakota to learn the dangers of accidental poisoning and to take such preventive measures as warranted by the seriousness of the danger, and be it further resolved, that the present labeling law of the state of North Dakota be amended to include all types of household poisons. The motion was seconded and passed unanimously.

3. A motion was made, seconded, and passed that the House of Delegates secure a physician as head of the State Health Department.

4. A motion was made, seconded, and passed that the House of Delegates may increase the state dues, not to exceed $25 for the sole purpose of public relations. An amendment to this motion was made, seconded, and passed that this fee be limited *solely* to this purpose.

5. A motion was made, seconded, and passed that a better relationship between the Workmen's Compensation Bureau and the doctors and hospitals be sought.

6. A motion was made, seconded, and passed that a physician of the state, or a group of physicians, write articles for monthly periodicals whose distribution is limited to the state. The above motion was amended and passed that these articles must pass through a board of the North Dakota State Medical Association and a by-line give credit only to the North Dakota State Medical Association.

In October, 1960, two separate meetings were held, one with the candidates for the November election of the Democratic ticket and a similar meeting with the candidates for the November election on the Republican ticket. Both representatives and senatorial candidates from both parties and several counties were invited to our district meeting, with approximately 10 to 12 candidates accepting this invitation from each party and meeting with approximately 40 physicians. A fellowship hour was followed by a dinner and an open discussion of many legislative, political, and medical problems. A thorough airing of the philosophy of both sides was obtained and a most informative evening was had by both the candidates and the medical profession.

At the December 7 meeting, the program was under the auspices of Merck, Sharp, and Dohme. Dr. Raymond Bunge, Department of Urology, University Hospitals, Iowa City, Iowa, spoke on "Problem in Sex Determination." Dr. Theofil Evangelista, McClusky, North Dakota, was elected to full membership in the society on April 7, 1960; Dr. John P. Sauer, Portgage County, Stevens Point, Wisconsin, was transferred to this society on December 7, 1960; and Dr. William Buckingham, Elgin, transferred on December 7, 1960, from the Southwestern District Medical Society of North Dakota.

Dr. Philip Dahl and Dr. Edwin Boerth, both of Bismarck, were elected to the board of directors of the North Dakota Physician's Service, Dr. Dahl filling the unexpired term of Dr. M. S. Jacobson, who resigned, his term ending in 1961. Dr. Boerth's term runs through 1963. Dr. Edmund Vinje and Dr. Carl J. Baumgartner were re-elected to the House of Delegates for a third term. Dr. Edwin Perrin was re-elected to the Board of Censors with his term ending in 1963. Dr. R. Froeschle was elected as incoming president; Dr. Paul Johnson, vice-president, and Dr. C. R. Montz re-elected secretary-treasurer.

The next regular meeting was held on February 28, 1961, with Dr. Rudolph Froeschle presiding. Dr. E. B. Save of the Baldwin County Medical Society of Milledgeville, Georgia, was elected to membership by transfer. Dr.

Carroll L. Birch of the University of Illinois Medical School spoke on her experiences during three years in India. Officers and staff of the North Dakota Physicians Services discussed abuses and overutilization and suggestions were made for prevention.

Membership in the district is as follows: The district society now consists of active members, 82; retired members, 1; and honorary members, 5. We gained 8 new members. One member transferred.

Members of the House of Delegates are Dr. M. A. K. Lommen, whose term expires in 1961; Dr. M. E. Nugent, 1962; Dr. R. B. Tudor, 1962; Dr. C. J. Baumgartner, 1963; and Dr. Edmund Vinje, 1963.

C. H. Peters, M.D., Councillor

Seventh District

During the past year 6 dinner meetings were held. The first meeting, on April 8, 1960, was the annual Cancer Caravan meeting and the guest speakers were Dr. M. M. Hargraves from the Mayo Clinic, who spoke on "Environmental Factors in the Production of Leukemias and Lymphomas," and Dr. C. A. Pascuzzi of the Mayo Clinic, who spoke on "Classification and Pathology of Lymphomatous Disease."

At the second meeting, on May 26, the state hospital staff and Mr. Henry Lahaug, superintendent, were hosts at the social hour and dinner. Reports from the Councillor and delegates to the state society meeting were presented. The program consisted of a paper on addicting drugs and the question of addiction potentials of common tranquilizers. Another paper was on "Multiple Meningiomata and Schizophrenia in the Same Patient, Presenting Diagnostic Problems."

At the first fall meeting, on September 29, we had as guests Dr. Carroll Lund, president of the North Dakota State Medical Association; Dr. Donald Schmidt of Gackle; Lyle Limond; Don Eagles of Blue Shield; Dr. Cliff Peters, chairman of the Medical Economics Committee; Mr. Jydstrup of Blue Cross; Truman Wold; Mayo Christianson; Steve Pezalla; George Michaelson; and 5 doctors from the state hospital. Don Eagles brought us up to date on Blue Sield contractural changes. Mr. Jydstrup of Blue Cross introduced Truman Wold and Mayo Christianson, who, with Dr. Young, had been on a recent trip to Saskatchewan. These men reported on the operation of the governmental hospital and physician program in the province of Saskatchewan. Dr. Clifford Peters, chairman of the Medical Economics Committee, then spoke on a survey of legislation which had been passed and proposed. Mr. Michaelson, the new public relations director, explained his plans concerning his office. Dr. Lund discussed briefly the board of administration problem at San Haven.

The next meeting, on December 8, was a dinner for our legislators, R. E. Meidinger of Jamestown; C. C. Tec, Ellendale; Milo Knudsen, Edgeley; Fred Rickford, LaMoure; I. C. Mueller, Oakes; Ed N. Davis, Monango; Clifford Lindberg and Mrs. Lindberg, Jamestown; Robert and Mrs. Reimers, Melville; and John Neukircher and Ralph Scott, Jamestown. The program was presented by Truman Wold and Mayo Christianson of Blue Cross, who spoke of their knowledge of the Saskatchewan hospitalization plan.

On January 26, 1961, the society was entertained at dinner by the state hospital staff and Superintendent Henry Lahaug. Dr. Victor Szyrynski, child psychiatrist at Bismarck, spoke on "Internal Medicine in Psychiatry," and mentioned the numerous medical diseases that can mimic psychiatric conditions.

At the next meeting, on February 23, Dr. Michael Koszalka of Fargo presented 12 cases that have been seen at the Veterans Hospital in Fargo and discussed the tentative diagnosis, differential diagnosis, and interesting facets of each case. The society voted to furnish the prize for an essay contest sponsored by the Woman's Auxiliary. There was a short discussion of current legislation.

The following officers were elected at the January 26 meeting: president, Dr. John Jestadt; vice-president, Dr. Clarence Martin; secretary-treasurer, Dr. Richard Nierling; delegates, Drs. J. N. Elsworth and John Van der Linde; alternate delegates, Drs. John Swenson and Robert E. Lucy; censors, Drs. Edwin Hieb, T. E. Pederson, and John Jestadt. Members of the North Dakota Physicians Service Corporation are Drs. R. L. McFadden, J. N. Elsworth, Ellis Oster, Joseph Sorkness, and J. M. Van der Linde.

Membership of the district includes 32 active members. The following members were admitted to the society during the past year: Drs. Waitzel, Lengyel, Sakai, and Rionx from the state hospital; Drs. Donald Schmidt of Gackle; Donald J. Feist of Forman; and Duane Clement of Jamestown. Dr. Waitzel transferred to Hawaii, Dr. John Palmer to Florida, Dr. Neville Turner to California, Dr. Hamilton to New York State, and Dr. Harris to Omaha.

T. E. Pederson, M.D., Councillor

Eighth District

The Eighth District Medical Society held 6 meetings during the calendar year of 1960.

On January 27, 1960, a dinner meeting was held at the Plainsman Hotel. The following officers were elected to serve: president, Dr. Chester Borrud; vice-president, Dr. H. Charles Walker, Jr.; secretary-treasurer, Dr. John Keller; delegate to state association, Dr. Dean Strinden; alternate delegate, Dr. E. J. Hagan; representatives to North Dakota Physicians Service, Drs. J. D. Craven and D. E. Skjei. The board of censors includes Dr. W. A. Wright, chairman, Drs. Chester Borrud, J. D. Craven, and Duane Pile.

On October 18, 1960, a meeting of the Eighth District Society was held with the society acting as hosts to several state Republican candidates for office. A round table discussion was held regarding legislation proposed which would affect medical practice. A similar meeting was held on October 11, with the society acting as hosts to several Democratic state politicians. It was felt that these meetings were mutually helpful and that the practice should be continued in the future.

Three short special meetings were also held during 1960.

On February 9, 1961, a dinner meeting was held at the Plainsman Hotel. The following officers were elected to serve the society in the current year: president, Dr. H. Charles Walker, Jr.; vice-president, Dr. John Keller; secretary-treasurer, Dr. H. Imess-Brown; delegate to state association, Dr. Dean Strinden; and alternate delegate, Dr. Duane Pile. The board of censors remains the same as recorded earlier in this report.

Dr. Sam Shea of Minot showed a very interesting movie and discussed the newest technics for the treatment of deafness.

The Eighth District membership consists of 20 active members, 1 honorary member, 1 non-member practicing in Eighth District, and 4 members added during the year.

Joseph D. Craven, M.D., Councillor

Ninth District

The yearly affairs of the Southwestern District Medical Society were conducted in 6 meetings. At the first of these, on June 11, 1960, we were guests at the home of Dr. Robert Hankins in Mott, North Dakota, for a social hour, followed by dinner at the Curve restaurant, with the business meeting at the Hankins Clinic following the social activities.

On September 12, the members of the society were deeply shocked and grieved at the news of the death of Dr. R. W. Rodgers, who apparently succumbed to a coronary attack while on a hunting trip in the Yukon territory. Dr. Rodgers was a bulwark in affairs of medicine in our area and in the state society.

In October, the members of the society were blessed with the attendance of their wives at dinner. Together we listened to the barnstorming barons present a complete discussion of the Saskatchewan plan for government hospital and medical care. Dr. Carroll Lund reported on his itinerary and visits about the state.

At our annual business meeeting on December 7, the following officers were elected: Dr. Norman B. Ordahl, president; Dr. Henry Slominski, vice-president; Dr. Walter Hanewald, secretary-treasurer; delegates to the House of Delegates, Dr. Norman Ordahl and Dr. W. C. Hanewald; alternate delegates, Dr. Robert Gilliland and Dr. Robert Hankins; councillors, Dr. K. G. Foster, Dr. Robert Thom and Dr. R. F. Raasch; members of the North Dakota Physicians Service, Drs. Ordahl, Gilsdorf, Gilliland, Foster, and Hankins. A memorial honoring Dr. R. W. Rodgers, in the form of a Dr. Rodgers Shelf, to be set up in the new library in Dickinson State Teachers College, was instigated. Dr. Joseph Cleary of Bismarck spoke on "Breech Presentation" and Dr. James Moses on "Carcinoma of the Prostate."

At our February meeting, Dr. Thomas Puckner of Minneapolis reported on the population studies done by Dr. Ancel Keys' group regarding diet and its effect on arteriosclerosis and coronary heart disease.

On Friday, March 31, the Cancer Caravan under the leadership of Dr. John Gillam, Fargo, was in Dickinson with its annual panel of physicians who presented the facets and interworkings of the cancer detection center.

K. G. Foster, M.D., Councillor

Tenth District

The Tenth District Medical Society held 5 meetings in 1960; three were scientific and two were business meetings.

It was our pleasure at the June meeting to have as our guests Mr. Mayo Christianson and Mr. Ed Drews to discuss with us the policies of the new Blue Cross contracts.

On September 30, our state president, Dr. Carroll Lund, Lyle Limond, George Michaelson, and their team of crusaders representing the Hospital Association, Blue Cross, and Blue Shield met with us to discuss the many problems throughout the state.

Many members of our society were very active during the year with meetings and talks with the general public and the legislators of our district. We were happy to have had representation in Bismarck during the legislative sessions.

Our present membership consists of 11 active members. Dr. K. G. Vandergon transferred to the Grand Forks District and Drs. Vistness of Cooperstown and Odegaard of Hatton were accepted as members of our society.

To our knowledge, there are no non-members residing and practicing in our district.

Officers elected for the year 1961 are as follows: president, Dr. D. N. Mergens, Hillsboro; vice-president, Dr. Russell Odegaard, Hatton; secretary-treasurer, Dr. R. W. McLean, Hillsboro; censor (3 years), Dr. R. C. Little, Mayville; censor (2 years), Dr. H. A. LaFleur, Mayville; censor (1 year), Dr. Mervin Rosenberg, Northwood; delegate, Dr. James Little, Mayville; and alternate, Dr. Kenneth Wakefield, Cooperstown.

In December 1960, Dr. R. W. McLean was elected by the Council to serve in place of Dr. K. G. Vandergon, who transferred to the Grand Forks District.

R. W. McLean, M.D., Councillor

REPORTS OF STANDING COMMITTEES

Committee on Medical Education

Report of meeting on April 30, 1960, at Grand Forks.

The medical school has accepted only 25 students for admission to the medical school this coming fall; last year 44 had been accepted by this time. The medical school will probably have only 32 North Dakota boys in this year's class. Dean Harwood stresses that the medical school needs more applicants from North Dakota.

For use of medical schools with unfilled quotas, the American Association of Medical Colleges is forming a list of suitable candidates for medical school who were unable to be admitted in their own states.

It was moved and passed that each district medical society appoint a committee to act as a liaison on medical education with local teachers and student counselors. The purpose of this committee would be to disseminate information in regard to medicine as a career to teachers and students. This committee would contact the various organizations and people connected with teaching in their districts and arrange for speakers to be available for the various meetings for a talk on medicine as a career.

It was suggested that the men on this committee be part of the state committee on medical education. It was also suggested that arrangements be made for the staff of the medical school to be invited to speak at the state teachers' convention on medicine as a career each year.

Nine students that had their first two years in our medical school and have completed their training and internship are returning to North Dakota to practice this year.

It was moved that the Legislative Committee try to get a law passed so that students who return to North Dakota for internship and residency be given credit on their loans the same as if they return to North Dakota to practice.

Dean Harwood informed the committee that junior and senior students are available for preceptorships at various times during the year if any of the doctors of the state desire students for this purpose. The medical school has received a significant donation from the American Medical Education Foundation.

* * * *

At the meeting on October 9, 1960, in Bismarck, the following doctors were present: Mahoney, Ulmer, Lund, Buckingham, Harwood, Christoferson, and Berg. Mr. Limond was also present. It was moved and passed that the Legislative Committee and the Council try to get a law passed so that the students who return to North Dakota for an internship be given credit on their loans the same as if they returned to North Dakota to practice. It was also moved that this same privilege be extended

to the students returning to North Dakota for their residency if the Legislative Committee and the Council felt that this was feasible.

The problem of obtaining more psychiatrists for the state was discussed.

Laschowitz's advocation of a four-year medical school was brought up and discussed briefly, but it was decided that nothing should be done about this at present. It was brought out that the Association of Medical Colleges advocated establishment of more two-year medical schools. At present, there are 600 to 700 vacancies for third and fourth year medical students in the United States that are not being filled.

Considerable time was spent discussing the problem of obtaining more interns in North Dakota.

Considerable time was also spent on a discussion of the examination for foreign medical graduates. There are 3,000 or 4,000 foreign graduates now taking training in this country who will have to return to their home countries without completing their training because they will fail to pass the foreign graduates' examination. It is thought that future good will in these countries will be jeopardized by forcing these students to return without completing their training. Most of these students were not informed at the time they were given American visas that they would have to pass this examination.

It was moved and passed that letters be written to the Council of Medical Education of the A.M.A., protesting that these men be required to return without completing their training. It was felt that a moratorium should be given all the students who are in this country and that they should be exempt from this examination and be allowed to complete their training.

The idea was also expressed that, in the future, students who have to pass this examination before coming to the United States do not need further training and that the men who really need further training would not be allowed to come, since they would fail to pass the examination. Copies of this letter were also to be sent to Drs. L. W. Larson, C. M. Lund, W. A. Wright, and T. E. Pederson.

Dean Harwood reported that the present freshman class consists of 39 members, 11 of whom are out-of-state, 9 from Montana. One out-of-state student is the son of a UND graduate and has many relatives in the state. One student is from Minnesota.

The prospective new medical school in St. Paul was discussed briefly.

Dean Harwood reported that they are losing some of their teachers at UND Medical School because other institutions are offering larger salaries and many fringe benefits.

The committee recommended that everything possible should be done to increase the salaries of the staff at the medical school. The opinion was unanimous that the salaries should be increased at least 10 per cent over the average in other schools as soon as possible.

Dean Harwood reported that an attempt should be made to have the $600,000 now earmarked for a tuberculosis hospital converted to an addition to the rehabilitation unit. At present, there are no facilities to house the people being treated in the unit. He feels that this money should be used to build an addition to the rehabilitation unit so that in-care could be provided. At present, these patients are being housed in motels in Grand Forks. Dean Harwood thought that, if this money were released for this purpose, it would be possible to obtain matching funds from Hill-Burton funds. It might require two or three years before Hill-Burton funds would be available.

It was moved that the next meeting of this committee be held at noon on Saturday, May 6, 1961, preceding the state meeting in Fargo.

H. Milton Berg, M.D., Chairman

LETTERS REGARDING EXAMINATIONS OF FOREIGN STUDENTS

North Dakota State Medical Association
Bismarck, North Dakota
October 20, 1960

Walter Wiggins, M.D., Secretary
Council on Medical Education & Hospitals
American Medical Association
535 North Dearborn Street
Chicago 10, Illinois

Dear Dr. Wiggins:

The Medical Education Committee of the North Dakota State Medical Association, at a meeting on October 9, 1960, passed the following recommendations to be sent to the Council on Medical Education & Hospitals of the American Medical Association:

1. That the present examination required of graduates of foreign medical schools to obtain training in this country is too difficult and that the number of failures is too high.
2. Many of the foreign graduates taking residencies in this country at the present time were not informed that they would have to take or pass this examination in order to take a residency at the time they were given their student visas. After arriving here and starting their training, they were informed about this examination. This is creating a difficult problem for these foreign graduates and causing much ill will toward the United States by their parents, relatives, and friends in their home country.
3. This committee recommends that all foreign graduates in this country at present be permitted to complete their training regardless of their grades in the foreign graduate examination. This recommendation is being made because this committee thinks the United States needs all the good will possible in all foreign countries. Sending these men home who fail to pass will cause a deterioration in our foreign relations for the future.
4. The passing grade for the foreign graduates examination being given in the graduates' own country before granting a student visa should be lowered. There are many doctors in foreign countries who need further training, much more than the brilliant student that is able to pass the present examination. This would permit many more doctors from foreign countries to receive residency training in this country and raise the standards of medical practice in their country.

Sincerely yours,
H. Milton Berg, M.D., Chairman
Committee on Medical Education
North Dakota State Medical Association

Educational Council for Foreign Medical Graduates
Orrington Hotel
1710 Orrington Avenue, Evanston, Illinois
October 29, 1960

Dr. H. Milton Berg, Chairman
Committee on Medical Education
North Dakota State Medical Association
Bismarck, North Dakota

My dear Dr. Berg:

Your letter of October 20th is acknowledged. May I comment on the four recommendations that your Medical Education Committee of the North Dakota State Medical Association is making to the Council on Medical Education and Hospitals of the American Medical Association.

1. Of the 8,713 foreign medical graduates taking our American Medical Qualification Examination, September 21, 1960, 71.5 per cent qualified and received certificates; 3,776 qualified with a score of 75 per cent or better and received standard ECFMG certificates; 2,456 qualified with scores between 70 and 74 per cent and received temporary two-year certificates. This does not bear out the statement that our examination is too difficult.
2. Most of the foreign medical graduates coming to this country to take internships or residencies, since October of 1957, have been warned that they will have to qualify with the ECFMG. Their exchange visitor visas have been renewable on a yearly basis and none of them has come over on long-term, iron-clad appointments.
3. It would not be fair to the patients in our hospitals to let some of the foreign medical graduates, who are now prac-

ticing as interns or residents, to continue to do so just because they slipped in before any attempt to screen them was made. In this group are some graduates of Ayurvedic schools in India, whose training has only been in the traditional Hindu, herb doctor medicine.

4. Our board of trustees and our examinations committee have on six different occasions given careful consideration to the lowering of the cut-off line for admitting foreign medical graduates to our internships and residencies. The conclusion has been against dropping the cut-off line below 70 per cent. It might be of interest to you to know that we have experimentally given this examination to nurses and we have already found that some nurses can pass our examination.

Sincerely yours,

Dean F. Smiley, M.D., Executive Director

SUMMARY OF EXAMINATION RESULTS

Examination	75+ N	75+ N	75+ %	70-74 N	70-74 %	70+ N	70+ %
March 25, 1958	298	152	51	51	17	203	63
Sept. 23, 1958							
United States	707	371	52.4	193	27.3	564	79.8
Abroad	137	47	34.3	33	24.1	80	58.4
Total	844	418	49.5	226	26.8	644	76.3
Feb. 17, 1959							
United States	1,278	616	48.2	341	26.7	957	74.9
Abroad	494	153	31.0	110	22.3	263	53.2
Total	1,772	769	43.4	451	25.5	1,220	68.8
Sept. 22, 1959							
United States	2,351	1,088	46.3	601	25.6	1,689	71.8
Abroad	717	282	39.3	141	19.7	423	59.0
Total	3,068	1,370	44.7	742	24.2	2,112	68.8
March 16, 1960							
United States	4,909	1,650	33.6	1,118	22.8	2,768	56.4
Abroad	1,146	347	30.3	235	20.5	582	50.8
Total	6,055	1,997	33.0	1,353	22.3	3,350	55.3
Sept. 21, 1960							
United States	7,308	3,222	44.1	2,084	28.5	5,306	72.6
Abroad	1,405	554	39.4	372	26.5	926	65.9
Total	8,713	3,776	43.3	2,456	28.2	6,232	71.5

Through September 1960, a total of 8,482 doctors had achieved scores of 75 or above. The statistics for the 70-74 category are masked by the fact that many in that category have now repeated the examination, achieving a score of 75 or above. An under-estimate of those presently in the 70-74 group is the number achieving such status in the September 1960 examination or 2,456. Thus, through September, a minimum of 10,938 doctors have received scores of 70 or above.

Report on Medical School 1960-61

Admissions. In contrast to the previous year in which 44 qualified North Dakota students were accepted to the school, only 31 North Dakota qualified applicants were available for September 1960. Indications are that this will improve somewhat but one of our basic problems common to all medical schools is lack of qualified applicants. Last year 9 students withdrew from the first year class for reasons of scholarship, or were dropped. This is 20 per cent of the class, which is considerably above the national average which runs between 4 and 6 per cent, and indicates that we are accepting borderline students each year on the basis that a North Dakota resident student deserves an opportunity and, if he does not make good, he has to be dropped.

Graduate program. This program continues to grow. At present, there are 23 graduate students in this school who are taking part in research and are definitely contributing to the stature of the school. The anatomy department has a $32,000 grant to support this program in the anatomy postgraduate area.

Medical technology. This year we will have about 16 students for clinical clerkships. This is the largest class we have had to date, having generally grown since the start of the program, ten years ago.

Faculty. Last year we lost 2 faculty members to other schools where considerably more attractive offers were made. We have, this year, in keeping with the general trend, made definite increases in faculty salaries to keep our good people. North Dakota is seriously lacking in fringe benefits. In February, Dr. Wasdahl resigned to go to Africa, where they are setting up a new school of medicine.

Research program. Two of our faculty have received national recognition. Dr. Cornatzer is a consultant for the National Science Foundation as one of the committee to pass upon research grant applications and assign funds. Dr. Hamre has a similar position with the National Cancer Society and is making top level decisions on a national basis. We are pleased with this recognition.

Scholarships. We were pleased to receive notice that this coming summer we will have $10,000 available to us for nonreturnable scholarships. There is no time limit set on this fund and no promise that it will be renewed. Our present thinking is that these scholarships should be given on the basis of need and we should probably try to make the money last for five years. A thorough investigation of financial need will be made in each case and we will try to carry on our basic philosophy that a promising student who has done his part in helping himself through school should not be denied an education for lack of funds. This money will be administered by our committee on loans and grants.

Medical Center loan fund. Through June 30, 1960, $200,650 has been loaned to third and fourth year medical students from this fund. In July 1960, 11 of our graduates came to the state immediately following internship to practice. Nine of them are in towns of 3,000 or less and therefore they will benefit from the forgiveness clause which forgives 20 per cent of their loan each year. There will doubtless be some changes in some of their locations. This is the largest group that has returned at a single time to the state. Other graduates have been returning through the year, some of them from the class of 1953, so at any given time it is impossible to say how many of our students are returning. The military and postgraduate education continues to tie up a large part of our graduates year after year.

Transfer situation. We are happy that very pleasant arrangements have been made with Minnesota in regard to transfer. They have agreed, as a start, to automatically accept one from each third of our class and, to date, a total of 5 students have been accepted for transfer at Minnesota. The new dean and his staff have been most cooperative and we look forward to increasing good relationships with our sister institution. More and more schools are requiring National Board examinations for transfer.

The Anatomy department has received a grant of $63,000 for the purchase and installation of an electron-microscope for teaching and research purposes. An application for an addition of three floors to the Ireland Laboratories is in process. This would complete the structure with 100 per cent federal funds.

We are still in the process of finding a Hill Research Professor in biochemistry. The money for this professorship is from the James J. and Maud Hill Foundation in St. Paul and consists of a grant of $15,000 a year for five years to support such a professor. We are also looking for two professors to be supported by the American Cancer Society.

Demands upon the biochemistry service laboratory have been steadily increasing. In the field of protein-bound iodine determinations, for example, the laboratory is now doing approximately 3 a day. These services are rendered at cost to referring physicians, clinics, and hospitals.

We are grateful for the support of the medical society in pointing out to the legislature the importance of maintaining our mill levy as it is. We are pleased that the legislature saw fit to leave these funds as they are now assigned.

We were all saddened by the death of Dr. French on February 4. He had been active in alumni affairs and on the loan committee since his retirement. He visited the school daily where he had an office and contributed wisdom and dignity to our school.

T. H. Harwood, M.D.
Dean, Medical School
University of North Dakota

Committee on Necrology and Medical History

I want to give to others hope and faith;
I want to do all that the Master saith;
I want to live aright from day to day;
I'm sure I shall not pass again this way.

ANONYMOUS

D. J. HALLIDAY, M.D.

Dr. David James Halliday, past president of the North Dakota State Medical Association and a physician and surgeon at Kenmare for 31 years, who retired from active practice in 1958, died on April 29, 1960, at his home. He was 61 years old. Dr. Halliday had been in poor health for the last five years, suffering from a heart condition.

Dr. Halliday was born November 2, 1898, at Gainsboro, Saskatchewan, Canada. He was graduated from the University of Manitoba with an M.D. degree in 1924 and engaged in practice at Grenora for a short time before locating at Kenmare, where he practiced until his retirement. He was a veteran of the Canadian Air Force.

Dr. Halliday was president of the State Medical Association in 1956, when the North Dakota and South Dakota associations, meeting at Aberdeen, South Dakota, observed the 75th anniversary of the forming of the first medical society in Dakota territory. He also was a past president of the State Board of Medical Examiners. Since 1935 he had been a member of the American College of Surgeons.

Long active in community affairs at Kenmare, Dr. Halliday was a past president of the Kenmare Association of Commerce, past master of the Kenmare Masonic lodge, past post commander of the Kenmare American Legion and a member of the Minot Elks Lodge. He was a director of the Kenmare State Bank and a member of the Methodist Church. He served as alderman on the city council from 1936 to 1940.

Dr. Halliday spearheaded the drive for the new $400,000 Kenmare Hospital, completed in 1959. In addition to medical practice, he had served as business manager of the Kenmare Deaconess Hospital and as president of the hospital board.

On May 2, 1925, he married Clara M. Allingham at Winnipeg, Manitoba. He is survived by his wife; three sons, Dr. David J. Halliday, Kenmare; Dr. Ross Halliday, a captain with the U. S. Air Force stationed at Minot; and Hugh Halliday, New York City; a sister and a brother.

A. C. ORR, M.D.

Dr. August C. Orr, a Bismarck physician since 1936 and Burleigh county health officer for the past fourteen years, died in a local hospital May 22, 1960. He was 57 years old.

Dr. Orr was born August 4, 1902, in New York City, but he was brought to North Dakota while still an infant. He attended grade and high schools in Rugby, taught rural school for one year in Pierce county, and graduated from Jamestown College in 1927.

Following graduation, he taught school at Watford City for two years and then attended the University of North Dakota Medical School at Grand Forks for two years. He received his M.D. degree from Rush Medical College in 1933.

After his internship, Dr. Orr was in general practice at Sarles, North Dakota, for two years and following special training at Harvard School of Public Hygiene, he became director of the division of child hygiene for the State Health Department. From 1939 to 1941 he was director of a district health department for the Michigan Health Department.

In May 1941, he resigned this position to return to Bismarck to become associated with Dr. R. W. Henderson in the practice of medicine with what was then known as the Henderson and Orr Clinic, now the Capital City Clinic.

Dr. Orr was a member of Alpha Kappa Kappa medical fraternity and a member of the Presbyterian Church. He leaves his wife, Doris, and one son, Robert, now of St. Paul.

G. F. DREW, M.D.

Dr. G. F. Drew, 86, retired physician and a former North Dakota state senator, died in Devils Lake June 8, 1960.

Born in Canada July 23, 1873, Dr. Drew came to Dakota Territory when he was 4, the family settling north of Grand Forks. When he was 11, they moved to Ardoch.

He was graduated from the medical school of the University of Minnesota in 1900. After a year of practice at Frazee, Minnesota, he went to Crary, North Dakota, and in 1912 came to Devils Lake. His specialty was eye, ear, nose and throat. He received an honorary membership in the 50-Year Club of the North Dakota State Medical Association in 1950.

He served four terms in the state senate, beginning in 1933.

He was preceded in death by his wife and a son. He is survived by two daughters.

B. M. URENN, M.D.

Dr. Bernard M. Urenn, 55, physician and surgeon with the Dakota Clinic, died June 26, 1960, in a Fargo hospital. His specialty was obstetrics and gynecology. Dr. Urenn had suffered from a chronic ailment a number of years but had been able to continue his practice until about a month before his death.

Born at Wolverton, Minnesota, July 14, 1904, he was the son of Mr. and Mrs. W. F. Urenn. The family moved to Iowa when he was a child and he grew up in Mason City.

He was graduated in 1926 from Upper Iowa University and received his medical degree at the University of Minnesota in 1934. He joined the Dakota Clinic in 1938.

Dr. Urenn was a member of Alpha Kappa Kappa and Alpha Omega Alpha fraternities and the North Dakota, Minnesota, and national medical associations and was

a past president of the Cass County Medical Society and the North Dakota OB-Gyn Society.

A member of Gethsemane Episcopal Cathedral parish, he also was a member of the Fargo Country Club and was an ardent hunter and fisherman.

Dr. Urenn had been wing medical officer of the North Dakota wing, Civil Air Patrol, and was a member of the pilot's association.

He married Edna K. Houge of Aneta, North Dakota, May 14, 1938, who survives him. He is also survived by two daughters and a sister.

L. H. KERMOTT, M.D.

Dr. L. H. Kermott, who began his career in medicine in Minot 54 years ago, died June 29, 1960, in a local hospital.

Dr. Kermott was born at Bowmanville, Ontario, June 5, 1878. He received his M.D. degree from the University of Minnesota in 1904 and was in the middle of three generations of medical men. His father, C. H. Kermott, was a doctor in North Dakota beginning in 1891, and his son, L. Henry Kermott, Jr., has been a practicing physician and surgeon in Minot since 1941.

He was a member of the Minot Elks Lodge, Masons, Kem Temple of the Shrine, Phi Rho Sigma medical fraternity, and the Minot Curling Association.

In October 1957, he was honored as one of 4 surviving charter members of the Minot Elks Lodge. The occasion marked the fiftieth anniversary of the Elks in Minot.

In June 1956, he was honored at a joint meeting of the Medical Associations of North and South Dakota for fifty years of service in the medical profession.

He also served on the general committee which worked successfully to bring to Minot the Veterans Hospital, now the John Moses Air Force Hospital.

His wife, the former Louise Feagles, of Minneapolis, preceded him in death. He is survived by two sons.

R. W. R. RODGERS, M.D.

Dr. Robert W. R. Rodgers, 57, well-known Dickinson physician and surgeon, died of a heart attack while on a hunting and fishing trip in Yukon Territory, north of White Horse, Canada, on September 12, 1960. He was accompanied on the trip by two companions who had to telephone from White Horse, informing Mrs. Rodgers that her husband had suffered a heart attack while fishing.

He was born in Elkhorn, Manitoba, on August 19, 1903. He received his M.D. degree from the University of Manitoba Medical College in 1926 and joined Dr. Sam Chernasek in a medical clinic in Dickinson in 1928 and in 1935 was joined by Dr. A. J. Gumper. The Rodgers-Gumper Clinic has since been formed.

Dr. Rodgers was president of the North Dakota State Medical Association in 1957-58 and was a member of the Board of Medical Examiners at the time of death. He was a past president of the North Dakota Society of Ob-Gyn. His specialty was general surgery. He was elected to the Dickinson Board of Education in 1950. In July 1951, he was named to serve as vice-president and in 1955 was elected president of the board. In June 1960, he was again elected vice-president. Dr. Rodgers was also well known in state Masonic circles and was given Masonic burial.

He is survived by Mrs. Rodgers, the former Beth Jones of Selkirk, Manitoba, and two daughters.

H. E. FRENCH, M.D.

Dr. Harley Ellsworth French, retired dean of the the University of North Dakota School of Medicine and prominent in North Dakota medical circles, died February 4, 1961, in a Grand Forks hospital. Dr. French had celebrated his 87th birthday December 7, 1960.

Dr. French devoted his life to the study, practice, and teaching of medicine. A native of Delphi, Indiana, Dr. French was born December 7, 1873. He attended the Kearney, Nebraska, elementary schools and the State College at Spokane, Washington, and the University of Idaho. He obtained his bachelor of arts degree in 1902, his M.D. at Northwestern University in 1907, and M.S. at the University of Chicago in 1911, and a doctor of science at the University of North Dakota in 1948.

Dr. French came to UND in 1911 from the University of South Dakota at Vermillion, where he had been professor of anatomy and physiology for four years.

Few medical school deans have served so long and faithfully under trying circumstances as did Dr. French. When finances were at a minimum, he maintained the highest standards of teaching, evidenced by the subsequent careers of the graduates. Working with a minimum of funds and equipment, he maintained the true spirit of education.

Dr. French was a member of Phi Beta Kappa, Alpha Omega Alpha, Sigma Xi, Phi Kappa Phi, and Nu Sigma Nu. He was past secretary of the North Dakota Board of Health, past president of the North Dakota Medical Society in 1921, the North Dakota Academy of Science, past president of the Franklin Club and also of the Fortnightly Club, and a member of Lions, the Shrine, and Masons. He was an emeritus member of the Association of American Medical Colleges.

Dr. French was active in civic, social, and fraternal affairs. In 1911, he started the custom of inviting medical students to an annual dinner at his home and this custom he continued after he became dean emeritus of the Medical School on his retirement. The program grew and attained reception size in recent years.

He married the former Mable Townsley of Vermillion, South Dakota, who preceded him in death. He is survived by a daughter and a son.

A. L. KLEIN, M.D.

Dr. Allan L. Klein, 55, physician and surgeon in Fargo, died February 18, 1961, in a Fargo hospital from an acute abdominal infection.

He was born in Winnipeg, Manitoba, December 26, 1905. After attending Manitoba University he received his M.D. degree in 1928 from Manitoba Medical College and interned in St. Paul.

A year of postgraduate work in obstetrics and gynecology at Columbia University, New York, followed. Dr. Klein practiced a year in Saskatchewan, then moved to Crystal, North Dakota. He practiced there three years and about eight years at McHenry, North Dakota, before coming to Fargo in 1940. On the staff of St. John's Hospital, he was chief of staff in 1951, and was also a courtesy member of the staff of St. Luke's.

A member of Temple Beth El, he been a trustee. He also was a member of Elks Lodge, the Masonic Lodge, and Scottish Rite bodies. He was a member of the American Academy of General Practice, First District Medical Society, North Dakota Medical Association, and the American Medical Association.

One of his favorite hobbies was playing bridge.

He is survived by his wife, the former Nellie Ellen Fitterman of Winnipeg, two daughters, and a brother.

E. H. Boerth, M.D., Chairman

Committee on Legislation

The Legislative Committee has been quite active this past year. Many things on the local as well as on the national scene have spurred this committee on in its work. Your co-chairmen attended 8 state meetings of the North Dakota State Medical Association Legislative Committee, along with other members of the Legislative Committee. Your co-chairmen traversed the state on a divided basis last spring for education of our members on the Forand bill. One of your chairmen, O. W. Johnson, attended the national political action meeting at French Lick, Indiana, last August 11, 12, and 13. Recently both chairmen attended the national meeting at Chicago called by the American Medical Association to attempt to educate the membership relative to the King-Anderson bill which is now pending in congress and which the administration has introduced to offset the Kerr-Mills bill, or medical assistance to the aged plan which was passed by the 86th congress.

The French Lick, Indiana, meeting was sponsored primarily for the purpose of educating the medical profession in political activity or political action. Probably our first responsibility should be to improve our image to the American public. Another facet discussed was the lack of physicians' interest in politics in general, both on the local and national scene. This interest was to be spurred to the extent that physicians would not only participate as citizens in local politics but also would become candidates for office. The recent meeting in Chicago was essentially one for the profession's approach to the King-Anderson bill (a partial reduplication of the Forand bill), which would replace the Kerr-Mills bill. The medical profession is presently in the squeeze by the politicians' approach to the old age assistance legislation problem, which essentially is a wedge for total socialization of medicine. This year and 1962 are the years that will spell the direction this country will take relative to the preservation of free enterprise. If the King bill fails in this session, it has an excellent chance to become an operative bill in the next session, unless a concerted effort is made to object to such legislation by our membership.

On the local-state scene, your committee met 8 times on state legislative matters. A total of 54 bills were watched with interest, some were supported, some were objected to, at the recent state legislative session. A summary of these bills follows this report. All together, this was a successful legislative year. We are thankful to our members for the support obtained at the recent legislative session. I believe we are now well enough organized so that we will become a voice in legislative matters in our state as well as in national legislative matters. The future indicates that all matters cannot be carried by your State Legislative Committee, but needs to be subsidized and supported by local legislative committee action within the local societies.

The summary of our activity on a state basis as far as legislation was concerned is as follows:

There were 8 House bills signed by the governor of which 4 were supported and 4 were followed with interest. The rest were defeated on the floor of the house. Of the 9 bills postponed indefinitely, medicine opposed 5 and followed 1 with interest; no opposition and no support of these. Of the 36 bills originating in the senate, 15 were signed into law by the governor. Medicine supported 8, followed the other 7 with interest. Of the balance of the bills, 3 were supported by medicine, but were indefinitely postponed. 4 bills were objected to by the Medical Association, and these were indefinitely postponed. The rest of the bills postponed indefinitely were followed with interest, but neither objected to nor supported. The total number of bills touching on medical fields again indicated that people are getting more security and health minded.

In summary:

1. There was increased activity by both state and local society legislative committees.

2. Organized medicine is taking more interest in local and national political activity.

3. There will be further attempts on the national scale to include physicians within the fold of social security and to include a fair segment of our population in medical social security legislation.

4. There will have to be more local activity if we wish to support the American Medical Association's stand—that is, the objection of the support of the aged segment by social security medical legislation.

O. W. Johnson, M.D., Chairman

Committee on Public Relations

The business of this committee was conducted under the leadership of Dr. R. W. Rodgers from his appointment in May 1960 until his death in September. Following the direction of the Council and the resolution of the House of Delegates in 1960, the committee met on June 25, 1960, to establish principles of operation under the expanded responsibilities of the committee and to review applicants for the position of director of education and public information which was created. No decision was reached on the selection of an employee and a subcommittee was appointed to further screen applicants. The subcommittee met on August 13, and, on September 1, decided to employ George Michaelson of Bismarck, effective October 1, 1960.

A Liaison Committee with the Board of the North Dakota Physicians Service was appointed and that committee held a short meeting on September 24 in Devils Lake.

The present chairman was appointed on October 1 to fill the unexpired term for the year 1960-61.

The second meeting of the full committee and the first meeting with the new chairman was held December 9, 1960, in Fargo. The committee invited Charles Johnson of the A.M.A. to present a summary of objectives of a public relations program as viewed by the A.M.A. and as practiced by other state associations.

President Lund reviewed the activities of the association in combating the proposal of Senator Van Horn of Mountrail County to initiate the Saskatchewan Compulsory Hospital Insurance Program and in other legislative matters throughout the fall.

Mr. Johnson stressed that areas of responsibility must be established since public relations cuts across all committee lines and activities and because publicity is not just a public relations program. He discussed the specifics of a public relations program under eight headings: (1) emergency call systems, (2) mediation or grievance committees, (3) press relations, (4) speakers bureaus, (5) indoctrination of society members, (6) medical care for all, (7) public service projects, and (8) citizenship activities.

(Detailed descriptions of these points will not be made

here because certain aspects of the presentation were accepted into the projects of the committee for the year).

Dr. C. H. Peters spoke as chairman of the Committee on Medical Economics and as co-chairman of the Legislation Committee on the plans and activities of these two committees, in particular, where a joint interest with public relations existed. Dr. T. E. Pederson outlined the activities of the Committee on Aging and Rehabilitation where a public relations joint interest existed. Dr. Pederson requested that the committee consider the problem of allowing a committee chairman to be quoted in refutation of incorrect or adverse information made to the public through the news media. The committee requested permission for this action by a proper committee chairman from the council of the association and the Council approved the request on December 10.

A program of materials preparation and continuing activities was presented to the committee by George Michaelson. The committee determined that activities of the director of education and public information should be directed most closely to the needs of the committees on legislation, medical economics, and aging and rehabilitation during the months following the meeting because of the impending North Dakota legislative session. The committee approved the projected plan of developing, for review by the committee, a code of relations among doctors, hospitals and news media, following the example of Wisconsin; approved the reinstating of medical press conferences; approved the development of several suggested institutional pamphlets; and noted the need for regular day by day contact with legislators, news people, and those who make opinions and attitudes toward health.

At the conclusion of the meeting, a discussion of intraprofessional relationships and their public relations aspects was led by the chairman, who appointed a subcommittee of Dr. R. E. Mahowald, chairman, Dr. R. E. Hankins, and Dr. R. B. Tudor to investigate this area and report to the next meeting of the committee on May 5, 1961.

Throughout the intervening period the directions of the committee have been carried out by the chairman and the staff. All printed materials have been distributed to the total membership throughout the year. Materials have been or are being developed for several committees of the association. Regular press and radio-television features are still in the planning stage. Work has been closely related to the various needs of the State Legislative Committee and the present campaign against the King-Anderson bill.

A review of the activities of the year and an analysis of the objectives of the coming year, plus the report of the subcommittee on intraprofessional relationships are on the agenda for the meeting of this committee to be held just before the meeting of the House of Delegates. The chairman will report on this meeting to the committee reviewing the public relations committee activities.

J. H. Mahoney, M.D., Chairman

Committee on Official Publication

At the last annual meeting of the North Dakota State Medical Association, The Journal-Lancet received a three-year contract. At the time of the meeting, discussion was had with two members of the publication staff regarding some recognition being given the North Dakota State Medical Association on the front cover of The Journal-Lancet, since this journal is recognized as the official publication of the Association.

After this, a letter was received from one of the members of the publishing staff of the journal, informing the Committee on Publications that this request would be reviewed by the publisher. The committee has received no comment from The Journal-Lancet regarding this.

The members of the committee feel that some recognition should be given the North Dakota State Medical Association in this respect.

It is also the opinion of the committee that, after review of this report by the Reference Committee, a copy of the Publications Committee report be sent to The Journal-Lancet along with any recommendations the Reference Committee may wish to make.

E. H. Boerth, M.D., Chairman

Committee on Public Health

The following is a report of the Public Health Committee for 1960-61. The chairman rather resents the fact that his report for 1959 was not accepted on the basis that the committee was asked to obtain a state health officer. In the first place, no such resolution was ever handed to the chairman of this committee. In the second place, I am wondering if the chairman of the Resolution Committee was not confused, since the Public Health Committee of the Medical Society had no authority to find a health officer, and I believe that this resolution should be sent to the North Dakota State Health Council.

As you will notice in the report on the meeting held on January 19, 1961, only one member besides the chairman attended. However, we did poll the members of the committee in regard to the secondary rheumatic fever prophylaxis program and I am enclosing the results of this in my report.

One meeting of this committee was held on January 19, 1961. A quorum could not be established for the meeting but the agenda was completed and such actions as were necessary were concluded by a poll of the members as noted below.

The committee reviewed the actions of the Committee on Cardiovascular Disease regarding the proposed program in secondary rheumatic fever prophylaxis which had been referred to the Public Health Committee by the House of Delegates at the 1960 meeting of the association. The program was outlined again by the State Health Department personnel present at the meeting. The program would be jointly sponsored and controlled by the Medical Association, the State Health Department, the North Dakota Pharmaceutical Association, and the North Dakota Heart Association.

In addition to the proposed program which was previously presented to the association, Robert Zimmerman, Ph.D., of the State Health Department outlined a suggested registry of RF patients in order to better supervise the project and to be alerted to any needed modifications.

After noting the action in 1959 and again in December 1960 of the Cardiovascular Committee of the North Dakota State Medical Association and the endorsement of the North Dakota Academy of Pediatrics, and the agreement of the 3 other participating agencies in the secondary prophylaxis project, the members of the committee present recommended a poll of the members of the Public Health Committee to determine their reaction to both the actual prophylaxis project and the registry project. The poll was conducted after sending each member samples of the actual materials to be used.

Nine of the 10 members of the committee responded to the poll and the acceptance of the two projects was unanimous. It is the recommendation of this committee, therefore, that the project submitted by the Committee on Cardiovascular Disease for a secondary rheumatic fever prophylaxis program in the state and a central registry of rheumatic fever patients in the state be endorsed by the association and that participation by individual physicians begin as soon as possible. It is noted that some form of secondary prophylaxis is carried on as a state-wide project in 40 states of the United States at present.

Mr. Mosser of the State Health Department offered to make available to each physician in the state a suggested treatment schedule for venereal diseases after the committee had noted his report of a rise in the incidence of the diseases in the state. The committee was polled on the desirability of the suggested schedule, and after reviewing it, agreed it would be helpful. The committee therefore suggests that Mr. Mosser be asked to distribute the schedule to the physicians in the state.

In other items of business at the meeting, the committee heard from Dr. Zimmerman that ASO and CRP blood tests are now being done by the State Health Department and, since rheumatic fever is a reportable disease, vials and forms will be sent to every physician in the state for these tests if samples are submitted during the acute stage of the disease.

The members of the committee at the meeting discussed the desirability of removing pneumonia from the reportable disease list but took no action until such time as a quorum could be present and a full discussion could be held.

PERCY L. OWENS, M.D., Chairman

VENEREAL DISEASE CASES REPORTED BY MONTH, 1960

	Syphilis	*Gonorrhea*	*Chancroid*
January	3	62	—
February	3	58	—
March	3	46	—
April	5	39	—
May	7	42	—
June	3	37	—
July	10	25	—
August	3	51	—
September	6	63	—
October	4	61	1
November	2	66	—
December	8	55	—
Total	57	605	1

North Dakota gonorrhea rate in 1960 is 95.6 per 100,000 population. North Dakota syphilis rate in 1960 is 9.0 per 100,000 population. Gonorrhea increased 22.96 per cent in 1960 over 1959. Syphilis increased 16.32 per cent in 1960 over 1959. There was a 12 per cent increase in gonorrhea in the teenagers (to 20 years) in 1960 over 1959.

Committee on Medical Economics

A meeting was held at the Gardner Hotel, Fargo, North Dakota, on October 1, 1960. The primary discussion at this afternoon and evening session was the prospect of introducing into the 1961 session of the North Dakota legislature a bill to provide a program of compulsory prepayment for medical care operated and administered by the state of North Dakota and based in large part on the Saskatchewan, Canada, plan. Mr. Truman Wold, the special projects coordinator of North Dakota Blue Cross, was called upon to report the survey team's findings regarding the Saskatchewan plan and the North Dakota Blue Cross plan. I feel the pertinent facts are as follows:

1. Cost of operation of Saskatchewan facilities is estimated at 80 per cent of North Dakota cost. (This percentage results from an analysis of per diem costs; cost per bed per annum, cost per case; and the October 31, 1959, salary survey report of the Saskatchewan Hospital Association.)

2. Saskatchewan residents are admitted to hospitals at the rate of 210 per 1,000 population compared to 183 per 1,000 in North Dakota.

3. Saskatchewan residents use 2,083 patient-days of care per annum per 1,000 population compared to 1,318 days for North Dakota residents.

4. Average length of hospital stay for Saskatchewan residents is ten days, compared to 7.2 days for North Dakota residents.

5. Saskatchewan has felt the need to provide 7.5 beds per 1,000 population compared to the 5.17 for North Dakota and 4.5 for the nation as a whole.

6. Total cost per capita (all sources) for hospital service is $34.90 for Saskatchewan residents compared to $33.09 for North Dakota residents. When these costs are weighted to the economy as reflected by the estimated cost of operation, the comparison becomes $43.625 (in terms of North Dakota cost) per capita for Saskatchewan against $33.09 for North Dakota.

Mr. Wold pointed out that three questions might be asked: Did a government prepayment program provide better hospital service? Did a government prepayment program provide cheaper service? Did a government prepayment program provide more equitable use of hospital services?

It was felt that these were the basic arguments advanced for a government program. The general attitude of personnel in these plans seemed to be that it would "solve the financial problems of hospitals." It was very clear that the political fortunes of the parties backing compulsory hospital and medical care plans in the provinces were closely related to the government hospitalization plan. They admit that they have not devised a system that does not have faults, but inferred that most of their troubles would be eliminated by changes to be made in the coming year, a statement that has a familiar ring to it, as we have heard it for the last fifty years.

Basically these changes were to be:

1. Initiation of a government medical services plan to cover doctor fees in much the same manner as hospital costs are presently covered.

Originally the hospital services plan (1947) operated on a single per capita tax of $5.00 and a family per capita tax of a maximum of $30. This climbed to $20 per individual with a family maximum of $45 in 1954-5-6. For the year 1959, the tax was $17.50 per person with a family maximum of $35. This tax paid about 27.5 of the total inpatient hospital costs for Saskatchewan residents.

For the year 1960, it is planned to increase the per capita tax to $24 per person and $48 per family to cover the addition of medical services.

Since general fund and other treasury contributions totalled $22,964,117 during the year 1959 to cover deficit from per capita tax for the hospital program, it can be expected that a considerably larger general tax contribution will have to be made to extend the program to medical services.

2. Elimination of depreciation allowance from hospital reimbursement and assumption by the government of cost of construction and modernization of hospital facilities.

The individuals responsible for these programs also stated "Doctors must be brought into line." Apparently by covering 98 per cent of the population with a compulsory medical care plan and so controlling doctor income, this is to be accomplished.

It was Mr. Wold's impression and that of the survey team that, after fourteen years of experience in Saskatchewan, this plan had not improved hospital service. Rather, as a result of government regulation of income; number and types of personnel; expenditures for food, supplies, and equipment, as well as a concerted attempt to control the population use of specific facilities, it is definitely felt that hospital service might well be downgraded.

The statistical facts above indicate definitely that the government compulsory plan has not resulted in cheaper hospital service in terms of cost to the public. Rather, it appears that the total bill to the public has been increased above the normal increase in hospital costs. Rather than providing more equitable hospital service to the public, this Saskatchewan Plan has resulted in profligate use of hospital facilities. The minister freely admitted that profligate use was evident but apparently accepted this as a necessary evil attendant to the humanitarian nature of the program. There are facets of a rigidly controlled and arbitrarily administered compulsory plan that are favorable but at what price appears to be the pertinent question.

Mr. Wold, the special projects manager for Blue Cross, also reported briefly on the status of the hospital use survey which has been going on for the past year and is about to be completed. There has been no analysis of the data accumulated so far, but this should be forthcoming shortly.

Mr. Donald Eagles, executive vice-president of the North Dakota Blue Shield, stated that the relative value schedule had been accepted quite satisfactorily to date with a minimal amount of difficulty and it has been in effect since July 1, 1960. He stated that there had been some misunderstanding by some physicians as to the amount of increase in fees. Some had felt that there was to be an increase of 15 per cent for each service given. However, this is not correct; it was to be on the basis of a 15 per cent rise on an average, but not for each specific item.

A re-survey of the relative value schedule was proposed and accepted by the committee. The re-survey will be done as early as possible in 1961, but has been delayed because of the legislative session through which we have just passed.

Mr. Herb Nilles, president of the North Dakota Blue Cross, also met with the economics committee and discussed the Blue Cross-Insurance Commissioner controversy, which has now been resolved apparently by the legislature's refusing to grant the insurance commissioner the powers that he wished, also by the fact that the state supreme court has denied him a mandatory injunction against Blue Cross.

Several other problems were brought up for discussion. Our Liaison Committee has been active in an attempt to work out with the North Dakota State Welfare Board a more equitable solution to report forms and to definition of procedures. This is a continuing problem and will need continued attention.

On January 4, 1961, a negotiating team of the Medical Economics Committee met with the Workmen's Compensation Board Commissioners in Bismarck and we proposed a new workmen's compensation schedule under the relative value study, comparable to Blue Shield Plan B, namely, that of a conversion factor of $4.00 per unit for medical and surgical services and $5.00 per unit for laboratory and x-ray services. This proposal is still under discussion. We have attempted to speed up their decision, but with the legislative session just ending and with the political turmoil that is now present, the decision has been delayed, although we hope that it will soon be ready.

In addition, a new medical assistance for the aged program was adopted by both houses of the legislature. It has now been signed by the governor, and it will go into effect July 1, 1961. This program is designed for those individuals who cannot qualify under the old age assistance program and whose income is sufficient for subsistence but not for medical care. It is not designed to take care of minor medical costs and will go into effect only after the individual has paid, or obligated himself to pay, $50 of medical cost in the twelve months prior to his need for further medical services. Medical services in this instance are defined as hospital, physician, nursing home care, drugs, etc. The program is also limited, in addition to the so-called $50 deductible, in that a single individual may have an income of $1,200.00 per year or a married couple $1,800.00 per year which will be disregarded so far as subsistence is concerned. If it is over this amount, then the extra amount must be taken into consideration in giving medical assistance to him. Another important section of this bill is that it defines by statute that each of these people should be given free choice of physicians, hospitals, nursing home care, druggist, etc., and lastly, it is spelled out by statute that the negotiations for a fee schedule should be carried on on the basis of the usual and customary fee for the community for that comparable economic group.

C. H. Peters, M.D., Chairman

Committee on Rural Health

There is no report concerning the activities of the Committee on Rural Health because of my losing a member from our medical group, which caused the work load to increase greatly.

I sincerely regret the fact that the committee did not meet.

M. S. Jacobson, M.D., Chairman

REPORTS OF SPECIAL COMMITTEES

Committee on Mental Health

This past year has been a relatively important year for mental health in North Dakota. After seeing our mental health program in the state regress for the past two years, we are again moving forward. This is a summary of events and the results obtained.

On September 30, 1960, a survey report of the mental health program of the state of North Dakota was completed by the National Institute of Mental Health Survey group and submitted to the Legislative Research Committee. The subcommittee on governmental organization then studied this report and submitted a report on mental health November 16, 1960, to the Legislative Research Committee.

From the Legislative Research Committee came 5 bills in which we were interested.

December 7, 1960, found 6 members of the North Dakota State Medical Association, including 3 members of this committee, attending governor-elect Bill Guy's informative meeting on mental health. The entire mental health field was represented and the tenor of the times was evident.

Nine members of the Committee on Mental Health and 8 other interested persons met in Fargo, December 10, 1960. The reports and bills previously mentioned were discussed and it was decided to make very positive recommendations concerning 3 of the bills.

A statement of policy concerning referrals to the state mental health facilities was composed at the request of the Board of Administration.

In view of the fact that a bill would undoubtedly be introduced in the 1961 legislature to establish a children's psychiatric hospital, Dr. Pray moved that the committee formulate a resolution to urge the establishment of a children's psychiatric hospital, that recommendations as to site and make-up would be worked on for the next two years with members of the committee and other interested people, and that specific recommendations be ready for the 1963 legislative session. Motion seconded by Dr. Lommen and carried. A resolution containing this motion was drawn up as follows:

RESOLUTION

Whereas, there is no inpatient facility in the state of North Dakota for the treatment of juveniles with serious mental illness, and

Whereas, the North Dakota State Medical Association believes such facilities are needed,

Now, therefore, be it resolved that the North Dakota State Medical Association urge the establishment of such a state children's psychiatric hospital in the future after a careful study of all facets and implications of such a hospital is made by the association and allied groups. A report of this study to be made to the legislature or the Legislative Research Committee in 1962-63, and

Be it further resolved that, in the interim, the North Dakota State Medical Association recognize the urgent need for a hospital for treatment of the emotionally disturbed child and recommends that a pilot program for hospital treatment for children and youth be set up as soon as possible at the State Hospital at Jamestown.

The 3 mental health bills were then considered and alterations made to make them more acceptable to medicine.

The most important activities then occurred in and about the Capitol Building in Bismarck. These activities were implemented by all the members of the State Medical Association.

Senate bill 49 passed, which (1) set up a state mental health authority in the State Health Department under the direction and supervision of a qualified psychiatrist; (2) incorporated SB-48 in this bill which transferred the psychiatric clinic in Bismarck from the control of the Board of Administration to the Mental Health Authority; and (3) the 1959 law allowing a lay superintendent of the state hospital was amended to read as follows:

"25-02-04. Superintendent to possess certain qualifications; employees. The superintendent of the state hospital shall be a certified psychiatrist. He shall appoint with the approval of the Board of Administration an assistant superintendent of administration who shall be under his supervision and who shall be a qualified and experienced hospital administrator. The superintendent shall appoint and employ the professional staff and define their qualifications and duties. The assistant superintendent shall employ such other personnel as may be necessary and shall define their qualifications and duties.

SECTION 5. Repeal. Chapter 39 of the 1959 session laws of North Dakota is hereby repealed."

There are very definite advances but they do not include such points that we did approve, such as, (1) under the mental health authority, we would like to see the authority to secure qualified personnel for state mental hospital, state school at Grafton, and all other state institutions in need of phychiatric services, and (2) authority to establish community mental health service units at a local level which would obtain guidance from state authority.

Bills concerning voluntary admission to Grafton State School and modification of sterilization laws concerning same school were also passed and are advances.

It is my feeling that good groundwork has been laid for further advances to be made in the subsequent years. We are committed to definitely get and present facts about a children's psychiatric unit. Once Senate bill 49 is implemented, we will have an M.D. coordinator in the State Health Department who can help in the furthering of the programs as recommended by the National Institute of Mental Health survey group. We also, for the first time in eight years, will have an M.D. in a state government office. This has not been true since Dr. Saxvik left the health department and became superintendent of the state hospital.

I would like, in closing, to thank all the men who so willingly gave of their time and efforts to enable such a program to pass and enhance our state mental health program. I know of the hours of time, the telephone conferences, the telegrams, the legislative committee meetings attended, the corridor conferences, etc., that made this possible and I'm proud to say I know these men.

KEITH G. VANDERGON, M.D., Chairman

Committee on Cancer

During the year 1960-61 your chairman attended the interim session of the American Cancer Society, June 5, 1960, at Los Angeles, the Regional American Cancer Society at Boise, Idaho, in September, the Fourth National Cancer Conference sponsored by the American Cancer Society in Minneapolis in September, the North Dakota state division of the American Cancer Society meeting in Fargo, in October, the annual American Cancer Society meeting in New York in November, several board meetings of the North Dakota Division, and a formal meeting of the Cancer Committee of the North Dakota State Medical Association, held in Fargo on December 10 in connection with our interim council meeting. Probably the most interesting and important of these conferences was the Fourth National Cancer Conference in Minneapolis, attended by cancer specialists from various parts of the United States and a scattering of foreign experts, who presented papers and group discussions on cancer on various areas of the body. The three-day session was divided into 3 group sessions and 14 panel sessions. Michael B. Shimkin, director of the National Cancer Institute at Bethesda, Maryland, gave the opening address on "Changing Concepts Concerning Cancer." One of the most interesting of the panels was that on "Cancer Etiology," in which Alexander Haddow, chairman of the Chester Beatty Research Institute of Cancer Research in London, discussed "Chemical, Physical and Viral Carcinogenesis." Also discussed were hormones and experimental oncogenesis, viral concepts of

the etiology of cancer, and radiation as an etiologic factor. We were left with the impression that, within a few short years, the research workers definitely expect a breakthrough in the treatment of leukemia and soft tumors.

The North Dakota division of the American Cancer Society, which is closely allied with the North Dakota State Medical Association, elected Dr. O. W. Johnson of Rugby, North Dakota, as chairman of the board and Dr. John Gillam of Fargo, North Dakota as chairman of the executive committee and also chairman of professional education. Dr. Gillam will, at the time of this writing, present a continuation of the North Dakota Cancer Caravan in various cities throughout the state. He has informed me that the caravan will emphasize the importance of cytology by means of lectures and demonstrations.

At the meeting of the Cancer Committee of the North Dakota State Medical Society on December 10, a thorough discussion was held regarding rumors of cancer quacks operating in the state and methods to prohibit this type of quackery. Your chairman was instructed to begin legal proceedings with a county attorney against a chiropractor who was advertising treatment of cancer in a Bismarck newspaper. As the State Medical Society has no legal counsel, correspondence with the A.M.A. legal department advised us that such a procedure would very likely defeat our purpose. It was therefore decided to obtain information from the Cancer Commission of the California Medical Society which has adopted state legislation that is practically ironclad against the practice of cancer quackery. From this information, we will draw up a proper bill to present at the next legislative session in hopes of obtaining a law which will end cancer quackery in North Dakota.

Another thought injected at the meeting was that of attempting to encourage lectures and demonstrations to doctors throughout the state so that the general practitioners, especially, become better acquainted with the facilities of cytology and the benefits derived from this procedure.

The Cancer Committee encourages all doctors in North Dakota to cooperate with and help out the local county commanders who are engaged in cancer education. You have given talks at various times and for this we are most grateful. We urge you all to be accessible for short speeches to the public regarding cancer information.

During the past year, the North Dakota Ob-Gyn Society, the North Dakota Surgical Society, and the North Dakota State Medical Society were supplied with speakers on cancer by means of grants from the North Dakota division of the American Cancer Society. We want to thank this organization for the speakers obtained and hope these valuable grants may be continued.

CARROLL M. LUND, M.D., Chairman

Committee on Veterans Medical Service

No special problems have been presented to this committee, and consequently the committee has not met during the past year and is making no recommendations.

A. C. FORTNEY, M.D., Chairman

Committee on Maternal and Child Welfare

The Maternal and Child Welfare Committee met in Bismarck on December 3, 1960, at which time the following matters were discussed:

1. It was considered advisable that the Maternal and Child Welfare Committee work in close harmony with the State Maternal Mortality Committee. It was the considered opinion of the members present that such action would result in more adequate dissemination of necessary information concerning obstetrical care to the members of the State Medical Association.

2. It was suggested that the following motion be presented to the State Medical Association for consideration: That the State Medical Association consider a formal study of perinatal mortality and morbidity, using the guide prepared by the Committee on Maternal and Child Care of the Council on Medical Service, American Medical Association.

The committee was represented in Chicago by its chairman at a multi-state meeting on maternal welfare and mortality sponsored by Section VI of the American College of Obstetricians and Gynecologists. The committee will be represented at the National Conference on the status of Maternal Mortality Committees to be held in Miami in the spring.

A meeting of the committee is planned early in May.

JOHN M. KELLER, M.D., Chairman

Committee on Diabetes

The Committee on Diabetes, initiated by Dr. Leonard Larson of Bismarck, has continued its primary function to encourage and coordinate annual diabetes detection drives throughout the state under sponsorship of constituent local medical societies. This function is a cooperative effort in support of National Diabetes Week, sponsored in November of each year by the Committee on Detection and Education of the American Diabetes Association, Inc. Increasing participation is in evidence among district medical societies throughout the nation. Last year, well over 1,000 societies held individual detection drives.

Although no detection drives were held throughout North Dakota by any of the district societies during 1960, at least 2 detection drives are planned for next year. Funds and supplies have already been allocated for a drive in Grand Forks sometime during 1961. Also, Dr. Edwin O. Hieb, chairman of the Committee on Diabetes Detection of the Seventh District Medical Society, has stated that his committee tentatively plans on a drive for 1961. Other societies have signified their intention to consider a detection drive in 1961.

It was pointed out by a member of the State Committee on Diabetes that more enthusiasm among younger physicians of the state is required to add impetus to the program of diabetes detection drives. The importance of carrying on such drives at least once every two or three years in all communities is pointed up by recent statistics of the incidence of diabetes, which indicate that there are at least 1.5 million known cases of diabetes under treatment and an additional 1.25 to 1.5 million unknown cases whose disease awaits discovery by routine diagnostic tests by physicians or mass detection drives. The latter, of course, provides a much higher yield. This follows the trend of a progressive rise in this disease which has been predicted by statisticians for many years.

Next year it is hoped that the Committee on Diabetes may prepare a specific recommendation for each medical society regarding the optimum frequency of detection drives, the most efficient methods of executing such drives, and the importance of keeping the program under the strict control of the medical profession. *It is well known that a number of public health organizations, including the Public Health Service, would be more than happy to invade the practice of medicine to the extent of finding these cases if we do not take definitive action ourselves.*

In conclusion, I wish to take this opportunity to thank the following members of the Committee on Diabetes for their cooperation and continued interest in diabetes detection throughout the state: Drs. A. K. Johnson, Donald Barnard, K. G. Foster, B. Hordinsky, P. Roy Gregware, W. H. Wall, and Kenneth Amstutz.

E. A. Haunz, M.D., Chairman

Committee on Crippled Children

A meeting of the committee was held at 9:30 a.m. on December 10, 1960, in the Gardner Hotel in Fargo. Present were Drs. Paul Johnson, L. B. Silverman, J. C. Swanson, D. T. Lindsay, A. E. Culmer, Jr., G. W. Toomey, B. A. Mazur, and J. J. McLeod. Others present were George Michaelson of the State Medical Association and William E. Unti, executive director of the North Dakota Society for Crippled Children and Adults.

The chairman, Dr. Paul Johnson, distributed 3 examples of reports on the fiscal year activities of the Public Welfare Board, Division of Children and Youth, and Crippled Children Services. He noted that there was an increase in operative and nonoperative strabismus case load in 1959-60, while other items covered remained about the same compared with the previous year. The chairman also noted a progressive increase in care for congenital heart malformations, crediting the reduction in the backlog of heart surgery at the University of Minnesota and at Rochester. This reduction was possible because other states were now able to provide surgery within their own states. He said that the diagnostic materials supplied from Bismarck were well accepted at the University of Minnesota and at Rochester. In orthodontia, only the most severe cases were now given assistance because the program was reaching saturation as was the case load of the orthodontists in the state.

The chairman reported, in answer to a question from the meeting, that 51 per cent of the CCS budget is now spent for hospitalization. The cost is increasing at a rate of 10 to 15 per cent each year, while physicians have received only a 15 per cent increase in seven years. He said that a new fee schedule would be ready soon after the meeting.

In a discussion on the hospital reimbursable rate, the point was made that hospitals are not sacrificing as much as are physicians in the fees for CCS because orthopedic patients are charged at the reimbursable rate which includes all laboratory and other ill-person fees, even though not receiving all those services. Most of the CCS patients are orthopedic patients. At present, the Mayo Clinic is allowing CCS charges at the private rate, less 25 per cent.

The second item of discussion was the question of a proper means test for CCS patients. Members of the committee noted that the means test in North Dakota varies from county to county according to the interpretation of the executive secretary of the County Welfare Board. In Michigan, the board allows each family to have a maximum of $750 in family savings and the state requires that a federal income tax report be filed voluntarily with the county board as a means test. The counties in the state, which administer the funds locally, do not have any financial participation in the program. The money in the program is received entirely from federal and state sources.

It was moved by Dr. Culmer and seconded by Dr. McLeod, that the chairman report to the appropriate sources that the Committee on Crippled Children recommends that participation in the program be reformed and that counties of the state be required to have a financial responsibility in the CCS program. The motion was carried unanimously.

President C. M. Lund, M.D., of the State Medical Society was introduced as a guest to the meeting.

The third item on the agenda was a consideration of cerebral palsy clinics in the state. None has been conducted since 1956, when the Public Welfare Board dropped sponsorship for lack of participation. The discussion proved an interest in having such clinics in the state again, with three years as the proper interval. For the Easter Seal Society, Mr. Unti offered to develop a program to meet the interest of the committee. He was requested to do so. The committee also suggested having Dr. Perlstein on the scientific program of the annual state meeting to present a paper on cerebral palsy once each three years with the possibility of a demonstration clinic at the annual scientific session of the association.

Mr. Unti requested the committee allow a subcommittee to be formed to serve Camp Grassiek to (1) review medical records before admission and (2) establish the medical policies for the camp. It was agreed that the chairman should appoint such a subcommittee for the 1961 camping session. Unti reported that the CCS program does not pay for physical therapy at the camp for children whose homes are within a 50-mile radius of a source for physical therapy. There were 8 children in this category at Camp Grassick in 1960 and this cost is part of the $12,000 deficit which the Easter Seal Society is forced to absorb this year.

After committee agreement, the following resolution of appreciation was voted unanimously:

RESOLUTION

Whereas: The State Association of the Benevolent and Protective Order of Elks in North Dakota and its members and member lodges have given generously of their resources and the resources and talents of individual members to create, support, and maintain Camp Grassick for physically handicapped children, and

Whereas: Camp Grassick has provided a valuable treatment facility within the state for crippled children and adults through the various camping and treatment projects, and,

Whereas: These various projects have contributed substantially to the rehabilitation of the campers,

Now Therefore Be It Resolved: The Committee on Crippled Children of the North Dakota State Medical Association expresses its sincere appreciation and gratitude to the State Association of the Benevolent and Protective Order of Elks in North Dakota and to its constituent lodges and members for the interest and the effective support for Camp Grassick, and congratulates the organization on its public spirit and forethought, and

Be It Further Resolved: Copies of this resolution be forwarded by the chairman of this committee to the president of the State Elks Association, the chairman of its committee on crippled children, and to each of the 11 lodges in the state.

The chairman noted that CCS will and does pay for local physicians care of patients and for follow-up care after hospitalization and that, therefore, the specialists in care of CCS patients are not receiving a disproportionate share of the fees paid by CCS.

Dr. Silverman noted that it was important that patients receiving welfare board assistance be informed as to the method by which doctors receive less than they normally would so that these patients realize they are not having a total doctor bill paid by welfare.

The chairman instructed George Michaelson to develop materials for a pamphlet which would be given to patients on welfare and that such suggested materials and a suggested special billing form be considered by the committee.

P. L. Johnson, M.D., Chairman

Committee on Aging and Rehabilitation

The committee make-up is essentially the same as last year's. The new year found the committee involved in the Governor's White House Conference on Aging. Four regional meetings of the Governor's Committee were held at Devils Lake, Minot, Dickinson, and Valley City in May and June. Your committee, interested colleagues, and informed, influential lay friends of physicians were in attendance at these meetings and at the final summary meeting in Bismarck in just sufficient numbers to counterbalance the expressed philosophies of North Dakota's welfare-thinking bureaucrats who were more than adequately represented. Before the final meeting, the committee formulated "Report of the North Dakota Medical Association to the Governor's Commission on Aging." This was in effect a statement of North Dakota physicians' philosophies and policies as related to the aged and was issued as such without House of Delegates approval. We felt the urgency justified this action. The final report of the North Dakota White House Conference on Aging was not too unfavorable to medicine's stated philosophies. Dr. Carroll Lund more than adequately represented the physicians of North Dakota as an elected delegate to the National Conference in Washington in January 1961. Drs. Leonard Larson and Willard Wright did not detract from our state's representation at this national meeting. Your committee expresses appreciation to all who helped by their presence at the regional and state meetings of the Governor's Commission and at Governor-Elect Guy's committee hearing on aging held in Bismarck in December.

The committee met in Fargo in October 1960. Emphasis was placed on the need for active committees on aging at the county society level as endorsed by the House of Delegates in May 1960. Attempts were made through the Easter Seal brochure to familiarize North Dakota physicians with the facilities for rehabilitation and restoration which are currently available. The committee feels much needs yet be done in this regard. A request from the State Welfare Board referable to prophylactic medical examinations of those enrolling under O.A.A. was referred to Dr. Nugent's Liaison Committee. The committee did not wish to expedite such a program at that time.

The major effort of the committee has been to furnish leadership in the development of North Dakota's joint council to improve the health care of the aged. Our association's participation in this endeavor was affirmed by the House of Delegates in May 1960. Three representatives each of the North Dakota State Medical Association, the North Dakota Dental Association, the North Dakota Hospital Association, and the North Dakota Nursing Home Association held 2 organizational meetings in Fargo in December. Your chairman was elected permanent chairman of this joint council. Howard Wells of Chicago, executive secretary of the joint councils to improve the health care of the aged, was present at one of our organizational meetings, and we benefited by his attendance. The avowed purpose of this joint council is to assist the principal purveyors of health services in their efforts to improve the health care of the aged. We feel that this council can be (1) a mechanism for exchange of information on activities and plans of organizations active in the field of aging, (2) coordination of related programs conducted by member organizations, (3) development, where indicated, of jointly sponsored projects, and (4) dissemination of accurate information on health care of the aged to the public.

At the final meeting of the joint council it was decided that our primary effort during the winter months of 1961 be directed toward implementing the passage of the MAA bill through our state legislature. It is the feeling of the members of your committee, that the joint council might expand its membership and act as a powerful cohesive force in the area of health care of the aged.

The scope and importance of aging on the national, state, and local level is ever-increasing. Your committee urges the implementation of active, knowledgeable committees on aging and rehabilitation in the district societies. Your committee wishes that all North Dakota physicians would become familiar with rehabilitative services available and more advantage taken thereof.

T. E. Pederson, M.D., Chairman

Committee on Foreign Trained Physicians

It was recently stated that the problem of the foreign medical graduate is only one phase of the whole postwar program of hospital and medical services to the country. Certainly, it is the most serious problem which confronts many hospitals and most medical licensure boards.

In 1948 when Congress passed the Educational Exchange Act, the State Department apparently did not consult competent medical authority regarding educational standards for admission. The open invitation to medical graduates throughout the world, regardless of their professional preparation, to come to the United States explains many of our present difficulties. In previous reports, your committee has called attention to the fact that, in many foreign countries, preparation in the basic sciences and clinical contact with patients is vastly inferior to ours. The value of lecture methods of teaching clinical medicine and the preparation of a thesis is vastly overrated.

It is unfortunate that this country is apparently in a position of having to depend considerably on physicians from foreign countries to fill positions in our state hospitals and to function as interns in our community and non-university hospitals. Since the U.S. graduates about 7,000 physicians each year and since there are now 13,032 approved internships, it is apparent that many of these must be filled by foreign graduates of varying degrees of professional competence, while many remain vacant. This gap had prompted an opinion that our medical schools should graduate enough physicians to fill all of these hospital positions; however, there is a stronger opinion that it is not the purpose of medical schools to do this. Rather, far more internships and residencies have been approved than merit such status. The purpose of both internship and residency is primarily educational and not for hospital service or convenience for the attending staff.

There are about 7,000 hospitals in the United States, but only about 1,300 have approved educational programs at the present time. We are forced to admit there are too many approved internships and residencies and not too few medical graduates. Elimination of hospitals which do not warrant approval because of one or more deficiencies is slow and often is subjected to various forms of pressure from many sources. It is somewhat comparable to the task the A.M.A. has had in the past fifty years in closing low standard medical schools in the United States.

It is regretted that figures stating how many foreign graduates enter the United States each year on an exchange student visa and how many depart are not available to State Boards. The fact is that the original pur-

pose of the program—to foster international good will and to improve the level of medical care in countries participating in the program—has been a complete failure, largely due to the fact that only a small percentage of these students return to practice in their native land. The presence of some 12,000 graduates of foreign schools from 91 countries who hold house staff positions in United States hospitals should substantiate this statement. Nearly half of all house staffs in New York City are graduates of foreign medical schools, with the largest number coming from the Philippines, Mexico, Turkey, and Korea, countries where there has not been opportunity to obtain a professional education comparable to United States standards.

The Educational Council for Foreign Medical Graduates, E.C.F.G., was first pioneered by the federation of state boards; however, because of lack of finances, it was necessary to call in the help of the A.M.A., the Association of American Medical Schools, and the American Hospital Association. Regardless of why it was developed, its real purpose is to insure that United States hospitals will obtain graduates of foreign medical schools with sufficient knowledge of clinical medicine and satisfactory command of the English language so they may be trusted to care for sick Americans. It is very difficult to evaluate the qualifications and competence of physicians coming from abroad. Some of the larger states have developed testing services and established postgraduate tutoring courses. The E.C.F.G. examination is a sincere attempt to appraise medical and English knowledge. The multiple tests to determine fitness and competence to treat sick people are the responsibility and the sacred duty of the various state boards of medical examiners.

The E.C.F.G. examination is completed in one day and consists of 350 multiple choice questions. Five hundred questions given to U.S. graduates are taken, and from that number 150 of the most difficult are deleted, with the balance used to make up the test. Because only 43 of the foreign graduates attain a mark of 75 or over, it has been suggested that the examination is too difficult. It also suggests how ineffective any method of examination can be in evaluating the education and training of the physician for, otherwise, even more would have failed. The chairman of this committee was disturbed at the recent meeting of the A.M.A. in Washington, D.C., by the reading of a letter from the Committee on Medical Education of the North Dakota State Medical Association which had been sent to the Council on Medical Education of the A.M.A. The statement was made that "it was their opinion that the E.C.F.G. examinations were too difficult and should be made easier so as to admit more foreign graduates to the United States." The Committee on Foreign Trained Physicians is opposed to making the E.C.F.G. examinations less difficult than those given United States graduates. If such a plan is adopted, it will mean we will soon have two standards of medical care in the United States—one on a high plane, rigid, exacting, and difficult, for United States graduates and the other substandard, with lax qualifications, for foreign graduates. Such a situation is certainly not in the best interest of Americans who are sick and who often must depend on foreign graduates to care for them. While the E.C.F.G. examination is by no means perfect (perhaps no method is), it is at least the best method we have at this time to screen the foreign graduate and to reject those who are deficient in medical knowledge and ability.

The Council on Medical Education has ruled that all foreign medical graduates serving as interns and residents in approved United States hospitals as of July 1, 1960, must be certified by the E.C.F.G. or licensed by some state board. The effective date of this regulation was then extended to July 1, 1961, in order to permit those who failed in September 1960 to take it over again. Then, in December 1960, the House of Delegates of the A.M.A. adopted a report asking hospitals to encourage special educational programs—another means of prolonging their stay in the United States. While the program must divorce such an intern or resident from any responsibility for patient care, there is no means mentioned to enforce such, and it is likely his duties would not change substantially. The United States State Department has set a limit of five years on the stay of foreign medical graduates serving as interns and residents because it is a moral obligation that such exchange visitors should return to their homeland. There is speculation that such a rule is not enforced. It is optimistic to think that most of these men can reach the professional standard and competence of graduates of United States and Canadian schools, regardless of how long they remain in the United States. The statement has been recently made that to return these physicians to their native land would foster ill will toward the United States. It would seem logical that just the reverse is true. Ill will is developed by keeping these men in the United States when they are urgently needed at home and could be of more value in their native land. That was the crux of the original exchange program act.

The greatest objection to the above "cut-off" rules naturally comes from New York State, which had 25 per cent of all foreign graduates, who total 34 per cent of filled positions of interns and residents in the state hospitals. Through the Medical Society of the County of New York and through Governor Rockefeller's office, tremendous pressure has been put on the Council of Medical Education to postpone any restricted decision. While New York City has a difficult problem, they have had two and one-half years to meet it, and in that time, have done nothing to correct the difficulty. It seems probable that most of these physicians will remain in the United States because they wish to and because there are many ways to circumvent the provisions of the act.

STATISTICS

Number of foreign graduates serving as interns and residents in the United States (3% of these are United States citizens educated abroad)	12,000
Number of foreign graduates taking ECFG examination in September 1960	8,713
Number who received 75% or over	3,776 (43%)
Number who elected not to take the examination (about)	2,000
Period 1958-1960: number passing 75% or over	8,432
Number of foreign graduates licensed in the United States in the past ten years	10,048

NORTH DAKOTA 1950-1960

(10-year period)

Number of foreign graduates who have been examined	60
Number of foreign graduates who have passed	41
Number of foreign graduates who have failed	19
Number of foreign graduates who failed, were re-examined, then passed	6
In 1960	
Number of foreign graduates passed	12
Number of foreign graduates failed	1

Canadians are not considered foreign graduates. The percentage of failures is considerably lower in North Dakota than in the E.C.F.G. examinations and is lower than the average pereentage of failures before all United States Boards. The reason for such is multiple, one being the North Dakota Board attempts to select the more competent who apply. Many foreign graduates are sadly laeking in knowledge of medieal ethies. They often refuse to take "No" for an answer and expeet the rules and regulations of the State Medieal Practiee Act and those of the Board of Medieal Examiners to be waived or ehanged to suit their individual eases. When sueh cannot be done, they appeal to attorneys and politieians instead of discussing it with the medieal profession of which they wish to beeome a part.

C. J. Glaspel, M.D., Chairman

Committee on American Medical Education Foundation

Last year remains our best year. We dropped about $640 below the goal we established in 1960. It is hoped that our new program of donating through Blue Shield will be reeeptive to our membership and provide an easy way of eontributing. Already, one Cass County physician has requested $25 per month to be so directed. He will never handle the money, yet at the year's end, he will have contributed $300 to a eause none of us has ever measured up to.

The Woman's Auxiliary eontinues to lend us its fine support whieh is increasing eaeh year. We should not only congratulate them, but try to emulate their fine example.

W. E. G. Lancaster, M.D., Chairman

Committee on School Health

The chairman of the Committee on School Health was happy to represent the state medical association at the Eighth National Conferenee on Physicians and Sehools, sponsored by the department of health education of the Ameriean Medieal Association. The conference, held in Chieago March 9, 10, and 11, 1961, had as its theme, Pertinent Problems in Sehool Health. The purposes of the National Conferenee were as follows:

1. To evaluate progress in the health and fitness of youth in relation to the national conferences on physicians and schools.
2. To discover effective methods of working together for the improvement of school health and physical education programs.
3. To explore in our present pattern of living the basic facters that influence the total health and fitness of youth.
4. To agree on policies for joint action by public health, education, and medicine that will lead to the development of essential services for health and fitness.
5. To point up and emphasize the fundamental responsibility of each family in promoting the health and fitness of youth.

Three major problems were discussed during the three-day session.

1. Child health needs and health education
   a. Growth patterns of children
   b. Health needs based on growth pattern
   c. Health education implications
2. The future of school health programs
   a. Healthful school living
   b. Health education
   c. Health services
   d. Physical education
3. Contributions of the home, school, and community to mental health
   a. Home obligations
   b. School opportunities
   c. Community responsibilities

A summary of the session was given by Dr. Helen M. Wallaee, Children's Bureau, Department of Health, Education, and Welfare of Washington, D.C. In addition to the numerous topics mentioned, small group diseussions were held on each subjeet.

The eonference representatives, from every aspeet of health edueation and medicine and from every department of the government, were vigorous and enthusiastic. I am sure this was a teaehing institute for us all.

It will take several months to eonsolidate the material diseussed and concluded at this eonference. It will then be published in booklet form by the A.M.A. It is the plan of the ehairman, when this is available, to meet with his committee to outline a coordinated program for presentation to the Public Instruction Department of our state and to develop an aetive health edueational system in North Dakota, with the eombined efforts of the medieal, edueational, and eommunity groups.

R. W. McLean, M.D., Chairman

Medical Advisory Committee to the Public Welfare Board

Regular meetings of the Medieal Advisory Committee to the Publie Welfare Board were held in July, Oetober, January and Mareh. At the October meeting, the committee met with the full Welfare Board.

In addition to the regular eommittee meetings, numerous eonferences were held between the director of publie assistance and representatives of the Medieal Advisory Committee.

During the year, many areas of difficulty arising between the medical profession and the Welfare Board were considered, and steps taken toward their solution. As a result of these meetings, a new chapter on medieal care for the social work manual was written and distributed to all physicians and county welfare boards. Further directives amplifying and interpreting the manual have also been sent to all physicians and county welfare boards. It is felt that at present there is the basis for a good working relationship between the Welfare Board and the medieal profession.

As yet there are still several areas in the field of medical eare where problems exist and where the Welfare Board is anxious to have the help of the Medieal Asso-eiation in their solution. Implementation of M.A.A., evaluation of nursing homes and nursing eare, drug eosts, and the policing of our own members to ensure conformity with the agreements between the association and Welfare Board are all problems that will confront this committee during the next few months.

M. E. Nugent, M.D., Chairman

Liaison Committee to the North Dakota State Bar Association

A medieal-legal conferenee was held at Fargo on Mareh 24, 1961. This was jointly sponsored by the North Dakota State Bar and the North Dakota State Medieal Assoeiation. There was a total registration of 73, eonsisting of 56 attorneys, 15 doetors, and 2 others representing medieal services.

It was felt that an exeellent program was presented, eovering topies eommon to law and medieine, as well as an attempt to further explain the interprofessional eode whieh was previously adopted by the two sponsoring organizations. Attendance, as far as the members of the State Medieal Assoeiation were concerned, was somewhat disappointing, but the remarks of Mr. Warren White of the legal staff of the American Medieal Associ-

ation indicated that he felt that medical-legal conferences were doing much to improve professional relations with the various bar associations. He felt that these should be continued and constantly improved as to content and time so that a greater attendance will result.

It is hoped that additional conferences of this type will be held and that suggestions regarding them will be forthcoming.

P. L. Johnson, M.D., Representative

Liaison Committee to the North Dakota Pharmaceutical Association

The meeting was called to order in the Gardner Hotel in Fargo on December 10, 1960. Present was the chairman, Dr. O. A. Sedlak, and committee guests, Drs. R. W. McLean, O. W. Johnson, and William Buckingham. The representatives of the North Dakota Pharmaceutical Association were Mr. Vernon E. Wagner, Mr. John Craven, and Mr. Al Doerr, executive secretary of the association. Also present was George Michaelson, education director of the North Dakota State Medical Association.

The chairman stated that the objective of the committee was cooperation between the two associations.

The Pharmaceutical Association representatives announced that they did not have any specific legislation which they hoped to introduce in the 37th legislative assembly. They did anticipate activity in the legislature on several items, however.

Over-the-counter sale of pharmaceuticals in places of business not controlled by a pharmacist was discussed. The Pharmaceutical Association hoped for support in asking eventually for either legislation or regulations to control such activities.

There was a first introduction of hospital pharmacy regulation No. 19 (based on such a regulation now operating in the state of Washington) which would limit the dispensing of drugs to specific personnel in hospitals. The Pharmaceutical Association said that they were beginning discussion of this matter now and, although they did not expect to introduce it now, after sufficient study and consideration, would appreciate support for some regulation in this area.

The chairman noted, with the concurrence of all attending the meeting, that it is desirable to share information and coordinate the activities of both associations in legislative activities and in negotiations or discussions with government organizations.

There was discussion of the need for more specific and proper refill labeling on prescriptions and need for specific refill requests in making those prescriptions by doctors.

It was agreed that the practice of sampling by suppliers has been over-used. Representatives of both associations agreed to discuss the good and bad of changing the labeling of pharmaceuticals.

The chairman and the chairman of the delegation from the North Dakota Pharmaceutical Association spoke for each association in agreeing that this committee should meet again.

The chairman recommends that the committee be continued and plan to meet at least once and possibly twice each year. It is hoped that more members of the association will become interested in the committee so that the two associations will increase their understanding and cooperation, as was accomplished at this meeting.

O. A. Sedlak, M.D., Chairman

Liaison Committee to the North Dakota State Dental Association

The medical liaison officer to the State Dental Association reports no activity in this field during the past year.

David Jaehning, M.D.

Report of Representative to the Medical Center Advisory Council

Your representative has attended the 2 regular and 1 special meeting of the Council held during the past year.

Medical students. The students continue to make excellent records on transferring for the last two years, and there has been no problem in transferring all of the graduates for a number of years.

Applications continue to come in slowly and the class for 1961 is not filled. We are informed that this is a nationwide problem and also applies in Canada. So far, it has been possible to fill a class of 40 with applicants from in-state and a few from out of state.

Medical student loan program. As you will recall, this program was not initiated by the Medical School or Medical Center Advisory Council but was instructed by the 1957 legislature. To date, from medical center funds, loans of $262,700 have been made to 84 North Dakota medical students. Of these, 13 have returned to the state to practice and 12 more are obligated to return. In the class of 1957, the first to have this program available, 10 have so far returned to the state and 1 or 2 more are considering it. We have had 2 previous classes from which 10 members have returned to the state so the effect of the medical student loan program on decisions to return to the state is far from clear. It will probably be a number of years before we know whether the availability of the loans and the provisions for forgiving them by practicing in smaller communities of the state will be an important influence on the decision of the young physician to return.

It will also be a number of years before we know how much money we can expect returned on these loans and how much is to be forgiven. It is probable that a much larger sum of money will be tied up in these loans before the fund becomes stabilized.

This last legislature instructed the medical center to include dental students in the loans and to use a considerable sum of money to provide loans to them. It should be recognized that the dentists have just as serious a problem as the physicians in getting qualified students from North Dakota to study and settle in the state. Representatives of the State Dental Association appeared before this Council and presented their problem, which is truly a difficult one. Whether availability of loans will answer the question, of course, will require time to answer, the same as in the medical student loan program.

Psychiatric training grant program. This is another program which the medical center was instructed to offer by the state legislature. So far there have been 3 fellows accepted in this program. We understand one is due to return to the state this coming summer to practice at the state hospital and that 2 more started training under it in July 1960, one at the Menninger School of Psychiatry and the other at the University of Nebraska College of Medicine. These men are obligated to return to the state, as their funds are in the nature of a subsidy, not a loan. The influence of this on the availability of adequate psychiatrists in the state would appear to be quite doubtful.

Faculty. A number of years ago our faculty pay levels ranked well above average for the country. During the last few years, however, in spite of salary increases, we have fallen somewhat behind and now rank well down in the lower third. This past year we lost four good faculty members, two for personal reasons which involved finances, and one to enter research. Two members of the Anatomy Department were lost to other medical schools because of increased pay, extensive fringe benefits, and to some extent the added prestige of the 4-year school. These have not yet been replaced.

Substantial pay increases are necessary across the board to keep and attract well-qualified faculty. This is now recognized by the medical school and the State Board of Higher Education and it appears that this will be corrected before the next school year.

Research facilities. The Ireland Laboratory space is entirely utilized, and it is necessary to enlarge it to give adequate research space for faculty members, for housing of the new electron microscope, and other uses. This building is constructed for the addition of 3 more floors. It is hoped that a 100 per cent federal research grant will be obtained for this expansion.

Graduate school. The graduate training program is growing and now includes 21 students in the departments of biochemistry, anatomy, bacteriology, and physiology.

Blood bank. The activities of the Southwest Blood Bank, have, of course, cut the activity of our blood bank somewhat, but it is still an important service. It provides services the Southwest Blood Bank cannot provide, particularly its Rh antibody titer testing program, and we have been urged by doctors in various parts of the state not to let this lapse. There is no thought of doing so. The blood bank people are in close contact with those of the Southwest Blood Bank, and we understand the cooperation is good.

Biochemical laboratory services. As in the past, these services are available on a state-wide basis. The policy is to attempt to provide laboratory services not generally available and not to compete with other laboratories in the state. This service program is heavy and is provided at a cost fee. The protein bound iodine tests alone during the past year have approached an average of 150 a month.

Medical technicians' school. This school at present has 24 students in the junior class. There were 11 who were graduated in the spring of 1960. The program appears to be growing. We are advised that 16 graduates are presently working in the state and only a few of them at the medical center.

The school of nursing. This school, providing a training program leading to a degree, will graduate 19 this spring. There are between 25 and 30 freshman students enrolled. This program is designed to train nurses for responsible positions in teaching and supervising in nursing schools and hospitals. I have been disappointed in the number of students enrolling and the relatively slow growth of this program.

Rehabilitation unit. We sense a lack of information on the part of many doctors in the state regarding the services available and general policies of the rehabilitation unit so this report is somewhat more comprehensive than in the past. If any desired information is not included, your representative and Dr. Harwood will be available for questioning at the annual meeting.

When a patient is referred to the rehabilitation unit for evaluation or treatment, the referring physician or agency is asked to supply all available medical and social information. The patient is usually seen first by a social worker who obtains pertinent information regarding physical condition, living arrangements, family status, financial ability, etc. This information is best supplied by the family physician, but, if not, it is acquired through him, family members, and other sources.

The few patients who attempt self-referral are urged to consult the family physician, or an attempt is made to contact the family physician, before admission. If the patient does not have a family physician, he is first seen when one of the consulting physicians is available for examination and recommendations regarding admission. Patients who appear without information as to their general physical status from the referring physician or agency are given a general physical evaluation under the direction of the consulting physicians to the unit.

Should the referring physician wish to follow and supervise his own patient, he may do so by sending a written prescription with the patient and revising it as indicated.

Reports of the patient's progress are sent to the referring physician or agency periodically and on discharge.

Services supplied. Available services include a prevocational exploration program, psychosocial services, physical, occupational, and speech therapy, and vocational rehabilitation. Patients can be referred for any one or more of the various services since the program is geared to the needs of the individual. All physical and occupational therapy is done under medical supervision and prescription. The physician may recommend other services but does not necessarily prescribe the manner in which they are carried out.

The staff includes qualified persons in all of these services and has available consultation from the University of North Dakota Speech Department and various other departments. The 3 qualified orthopedists in Grand Forks are on the active staff and are in attendance at least once a week and more often if necessary. In addition, consultation has been arranged with qualified men in other specialties available in Grand Forks.

As has been previously reported, a trained medical man in rehabilitation work would be a great asset, but such men are extremely difficult to obtain. They are usually employed in the large centers in which they train or to which they tend to go. The authorities at the school and the Medical Center Advisory Council are well aware of the advisability of such a man to head this program but are also aware of the problems in acquiring one. Until such a man can be obtained, it is the general opinion that the present program is working quite well.

Personal conversation with physicians in attendance at the rehabilitation unit indicates they believe that the work being done is of high quality and merits the confidence of the physicians and others in the state referring patients.

Volume of work. The patient load is increasing slowly and much more work can be done than is being done. One hundred forty-seven new patients were admitted during 1960 for various types of treatment. Lack of adequate housing facilities has been a handicap for patients living out of the immediate community.

Costs. Rehabilitation services are a costly part of medical care. Fees are charged by the center either to the patient or to the referring agency. No patient is denied care because of inability to pay unless he comes from out of the state. The Medical Center Advisory Council

has recommended that out-of-state patients should not be cared for until arrangements have been made for payment. The charges set are minimal rates. The charge for all services at present is $10 a day and is reduced depending on which services are utilized. If housing facilities are added, as seems likely, it is hoped that the program can be operated on charges of not more than $25 a day for all services including maintenance.

The rehabilitation unit is operating on a budget of approximately $86,000. Fees collected from patients and various agencies referring patients amount to around $13,000 a year. The rehabilitation unit received a federal grant of better than $20,000 for salaries each year. We are advised that most rehabilitation units build up to a point where at least 80 per cent of the budget is provided from fees. Collection of fees in our unit here has amounted to between 92 and 93 per cent to date.

It is hoped that increased utilization through adequate housing facilities will, in time, bring the income more nearly in line with other rehabilitation units.

There is included in this report a listing of the types of disabilities treated in the year 1960, the numbers of each, the course of referrals, and a listing of the towns from which patients are received. While by far the largest number come from the Red River Valley and Grand Forks area, many come from throughout North Dakota and from Montana and Minnesota. The lack of proper housing has been a big problem in caring for patients outside of the immediate Grand Forks area. Formerly, a small number of beds were available in one of the university dormitories, but these are now filled with university students and are not available. Boarding home facilities in Grand Forks have been tried and found lacking for various obvious reasons. The facilities of the local YMCA have been used and also those of the local hospitals. Probably a mistake was made in not supplying housing facilities at the time of construction. It is anticipated that housing facilities will be provided within the next year or two. The $600,000 previously impounded by the state legislature for possible construction of a state tuberculosis hospital has been freed for use of the medical center. We hope that some of these funds will be used for the addition of a housing floor and service facilities on the present building. A Hill-Burton grant is anticipated so most of this $600,000 will still be available for other needed uses such as augmenting faculty salaries. It is also probable that a considerable amount of these funds will be necessary to continue the medical student loan program, at least until such time as that program becomes stabilized. We will not know for a number of years how much of these funds will be repaid and how much will be forgiven.

The facilities of the rehabilitation unit are also used in teaching. University students in occupational therapy, social work, speech therapy, nursing, and psychology are receiving advantageous experience in this department.

There follows a listing of types of patients treated in 1960, and the source of referrals and residence of patients treated since the opening.

P. H. Woutat, M.D., Representative

SOURCE OF REFERRALS

72%	Physician
17%	Vocational Rehabilitation
2.4%	Workmen's Compensation
6%	Public Welfare
8%	Other

CATEGORIES OF DISABILITIES TREATED IN 1960

Hemiplegias with aphasia	13
Hemiplegias without aphasia	10
Cerebral palsy	13
Amputations	2
Shoulder disabilities	16
Injuries or paralysis of lower extremities	37
Injuries or paralysis of upper extremities	12
Injuries or paralysis of both upper and lower extremities	11
Speech and hearing	8
Back disabilities	18
Upper trunk disabilities including whiplash injuries	6
Cardiac	3
Hand deformities	6
Other, including brain damage, psychoneuroses, and mental retardation	13

TOWNS SERVED BY THE MEDICAL CENTER REHABILITATION UNIT

Grand Forks	141	Crystal	1
Gralton	20	Dickinson	1
East Grand Forks, Minn.	16	Emerado	1
Fargo	12	Edmore	1
Mandan	8	Esmond	1
Bismarck	5	Fairdale	1
Devils Lake	5	Fairview, Montana	1
St. Thomas	5	Fort Yates	1
Hillsboro	4	Forest River	1
LaMoure	4	Gardner	1
Michigan	4	Gilby	1
Clearbrook, Minn.	3	Glendive, Montana	1
Jamestown	3	Gwinner	1
Hazen	3	Hallock, Minn.	1
Langdon	3	Harvey	1
Mayville	3	Hatton	1
Northwood	3	Hensel	1
Reynolds	3	Hunter	1
Rolla	3	Johnstown	1
Thompson	3	Kenmare	1
Drayton	3	Kildeer	1
Cavalier	2	Kindred	1
Clifford	2	Kloten	1
Edinburg	2	Landa	1
Fertile, Minn.	2	Lancaster, Minn.	1
Garrison	2	Lidgerwood	1
Hettinger	2	Lakota	1
Hoople	2	Mahnoman, Minn.	1
Hope	2	Milton	1
Larimore	2	Minto	1
Leeds	2	Moorhead, Minn.	1
Lisbon	2	New Town	1
Minot	2	Oakes	1
Napoleon	2	Orr	1
Niagara	2	Oslo, Minn.	1
Park River	2	Page	1
Sheldon	2	Pekin	1
Thief River Falls, Minn.	1	Pisek	1
Walhpeton	2	Price	1
Williston	2	Red Lake Falls, Minn.	1
Rutland	2	Rugby	1
Stanley	2	Roseau, Minn.	1
Portland	2	Strandquist, Minn.	1
Bantry	2	Sawyer	1
Douglas	2	Sherwood	1
Ambrose	1	Spiritwood	1
Aneta	1	Streeter	1
Ardoch	1	Selfridge	1
Alvarado, Minn.	1	St. John	1
Bowbells	1	Twin Valley, Minn.	1
Belcourt	1	Tower City	1
Casselton	1	Walhalla	1
Cavalier	1	Washburn	1
Center	1	Wishek	1
Crary	1	York	1
Crookston, Minn.	1		

Because of the various circumstances of the several individuals involved, we have also had other patients whose residences are in Bombay, India; Fort Lauderdale, Florida; Atlantic, Iowa; Toronto, Canada; Silver Creek, New York; and Seattle, Washington.

It should be pointed out that a number of the physicians' referrals were not initiated by the physician himself but resulted from patients or families having made application to us of their own volition. They were then asked to obtain permission for referral from their family physician or local doctor. The "other" group includes self-referrals who had no local physician, special education, other individuals, etc. Although the public welfare and crippled children's program have referred very few patients, they have participated in the payment of care for others referred by private physicians and vocational rehabilitation services.

Report of Representative to the State Health Planning Committee

The writer attended a meeting of the State Health Planning Board on November 10. It was my first meeting with this committee, and I might say that this is quite an organization, with local pressure groups to be seen at their best.

Three projects were given preliminary approval: (1) a 35-bed general hospital to replace antiquated facilities of the Community Hospital at Mandan; (2) a 60-bed general hospital replaeement and hospital wing completion at the Good Samaritan Hospital at Rugby; and (3) a 2-floor addition of 38 and 41 beds with necessary related services to provide an in-patient care at the University of North Dakota Medical Center Rehabilitation Unit at Grand Forks. With final approval of the State Health Department and the Public Health Service, these projects will start construction in the spring of 1961.

Both the State Health Planning Committee and the State Health Council gave encouragement to a proposal for the construction of a Public Health Laboratory at Bismarck by the State Health Department. However, this proposal would require legislative appropriation, and so final determination would hinge on availability of state funds. There were about 8 other projects that were shelved for the present, because of lack of Hill-Burton funds to finance, or for other reasons.

J. C. Fawcett, M.D., Representative

Committee on Liability Insurance

No problems or matters requiring attention were submitted to the Committee on Liability Insurance of the North Dakota State Medical Association, and no meeting was held.

R. H. Waldschmidt, M.D., Chairman

Liaison Committee to the State Board of Administration

The full committee held 2 meetings at Jamestown with the State Board of Administration, at which the professional personnel at the state hospital at Jamestown and the hospital at San Haven were discussed. It was agreed that Dr. Cuadrado at San Haven was doing a creditable job and an attempt was made to get him a qualified assistant.

Your committee felt that the professional staff at the state hospital at Jamestown could only be improved if a qualified psychiatrist (preferably American trained) were superintendent of the hospital. The board felt that a qualified medical director could accomplish the same end. Therefore, no real agreement was reached at this time.

Your chairman met again with the Board of Administration on March 6 after the legislature had passed the bill requiring that the superintendent be a qualified psychiatrist. It was agreed that your committee would assist in selecting this man and also assist in delineating the duties and responsiblities of the superintendent and his assistant, who must be a qualified hospital administrator. It is our hope that Mr. Henry Lahaug would remain in this position as we believe he has amply demonstrated his ability in this field.

Joseph Sorkness, M.D., Chairman

Committee on Cardiovascular Diseases

A meeting of the committee was convened at 1:15 p.m. on December 10, 1960, by the chairman, Dr. R. M. Fawcett, at the Gardner Hotel in Fargo. Committee members present were Drs. R. D. Story, R. W. McLean, and Keith Foster. Others present were Warren Duntley, executive director of the North Dakota Heart Association, T. L. Burgum, field representative of the North Dakota Heart Association, and George Michaelson, education director, North Dakota State Medical Association.

The chairman outlined the history of the proposed program of secondary prophylaxis for rheumatic fever from the time it was approved at the first meeting of the committee until the present meeting. He noted that the committee had been represented at the meeting of the Council of the medical association in December 1959 and the Council had referred the program for further study by the cardiovascular committee. The North Dakota Heart Assosiation, when requested to investigate the program more thoroughly, appointed a committee of pediatricians, internists, and general practitioners, led by Dr. G. H. Heidorn of Minot. They recommended that such a program was needed, was workable, and should receive the support and cooperation of the State Medical Association. This report favoring the program of secondary rheumatic fever prophylaxis was submitted to the Council in May 1960 and they, in turn, referred it to the House of Delegates. That body referred it to the Committee on Public Health which will act on the proposal before the annual meeting in May 1961.

It was moved by Dr. Story and seconded by Dr. Foster that the Committee on Cardiovascular Diseases again approve the program for secondary prophylaxis in rheumatic fever prevention as outlined in previous minutes of the committee and that the Committee on Public Health of the state association be urged to review and approve the program during 1961. Motion carried.

The chairman reviewed a program to provide training in physical therapy to county public health nurses for work with stroke patients and training of patients' families. This project, under consideration by the North Dakota Heart Association, would be conducted by that organization in a manner similar to the program being used in the state of Georgia. The conclusion was reached that such a program would be very helpful in the many areas of the state where trained physiotherapists are not available and should receive the support and encouragement of the physicians of the state.

The committee suggested to the North Dakota Heart Association that its program of professional education could be wisely expanded through having at its annual meeting a scientific session on cardiovascular diseases. It was suggested that this program be arranged to qualify as credit hours for members of the Academy of General Practice. The committee felt that such a one-day

session under the sole sponsorship of the heart association would also increase interest of physicians in the heart association. The committee urged the heart association to establish such a project.

R. M. Fawcett, M.D., Chairman

Liaison Committee to Blue Cross-Blue Shield

Although no formal meetings of the committee were held during the year, the members were very active and devoted considerable time to visiting with the district medical societies in an attempt to get at the grass roots of the problems facing us today.

Of great concern to all of us, physicians, public, and health care plans, is the continuing high use of hospital facilities in the state. One reason why North Dakotans use hospital care more than others could be our large rural population. Another might well be the mean age of our population. Emigration of our young people to larger metropolitan areas has left us with a higher percentage of people in the over-60 age group than the nation as a whole.

But certainly the impact of Blue Cross and Blue Shield as well as commercial insurance is a significant factor. We know that people who have health insurance protection are more apt to be hospitalized than those without such protection.

We know that if this excessive use, or whatever name we apply to it, occurs in Blue Cross, it also carries over into commercial insurance. The degree to which patients who could be treated at the doctor's office or at home continue to be hospitalized will be reflected in greater costs of health care protection. Blue Cross-Blue Shield and the commercial carriers will be adversely affected as well.

The number one problem then, is what are we, as physicians, going to do about it? In a study made in 1955, for example, we learned that 10 per cent of a sample of 1,000 Blue Shield patients surveyed in the state received more services than were necessary or, possibly, would not have needed hospitalization. If this trend exists among Blue Cross and Blue Shield claims, most certainly it exists in commercial insurance.

The medical profession has the responsibility and control for hospital admissions. During the past year, Dr. A. C. Burt, Dr. M. H. Poindexter, and I visited with district medical societies in the state, recommending the immediate acceptance by the doctors of their responsibility to the public in active assurance that medical insurance is being economically used in North Dakota. We urge that committees be formed at once to carry out and fulfill this responsiblity.

This can be accomplished by 1 of 2 methods—by the expansion of tissue committees into medical review committees, or by setting up within each district medical society a special utilization committee to work with Blue Cross, Blue Shield, commercial insurance, the general public, and with other physicians to stop any excessive use of hospital benefits. All possible ways of providing and obtaining good medical care at the lowest possible cost must be explored. Doctors must forget how things were done in the past and learn how they can be done under present social and economic conditions. This committee feels that, unless the medical profession takes the necessary steps to establish a review committee, or utilization committee, call it what we may, someone else will be giving them the directives to do so, and, frankly, we refer to the government.

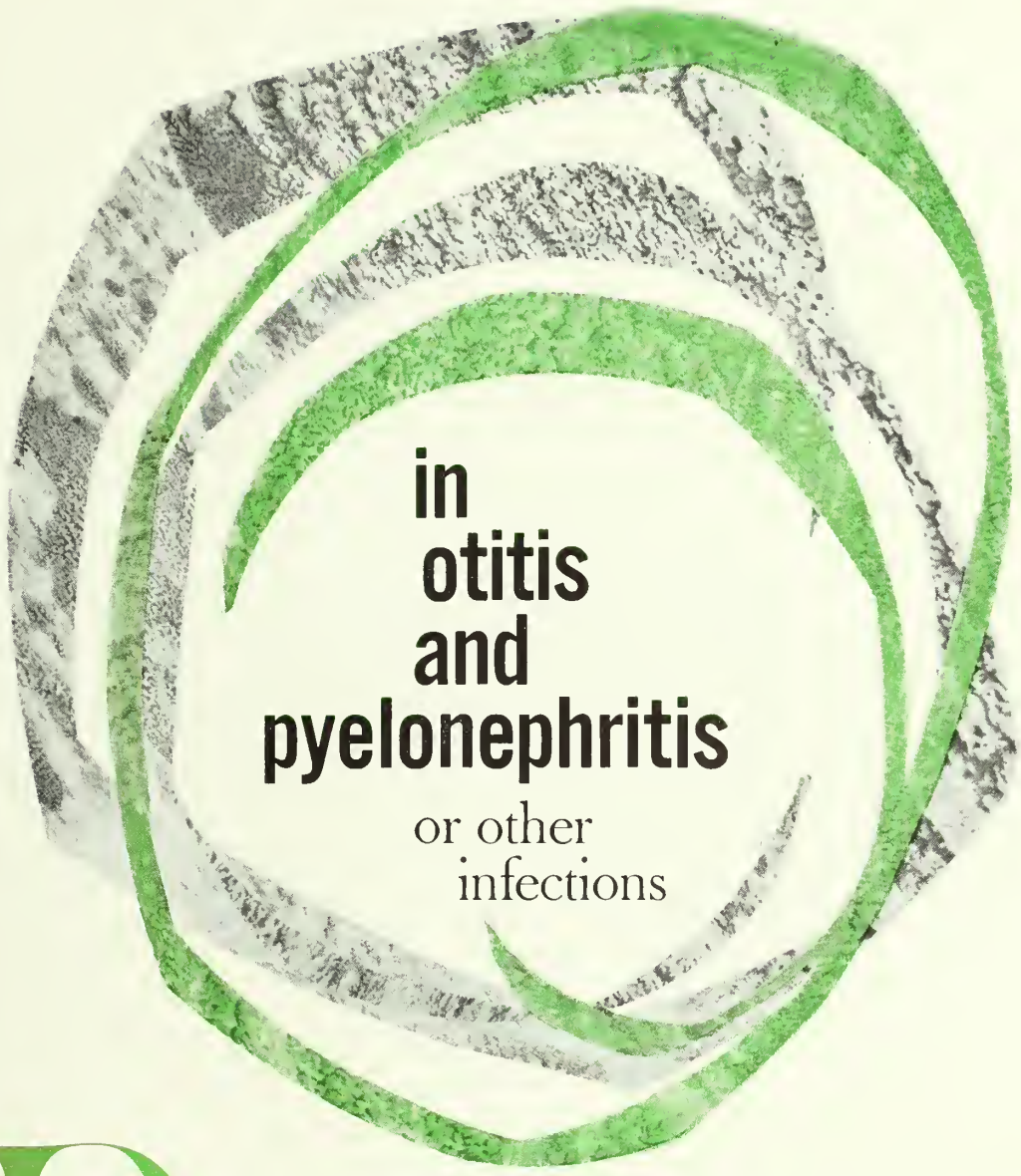
This committee would be charged with the responsibility of reviewing claims, Blue Cross and others, which either seemed exorbitant or out of line, then calling the attending doctor before the committee for explanation. Such matters as excessive drug charges, prolonged hospitalization, unnecessary hospitalization, and the like would have to be accounted for to the committee. If doctors are admitting patients to hospitals, when such hospital care is unnecessary, simply because the patient has health care protection, grounds certainly exist for disciplinary action.

There is no question but that much can be accomplished by doctors through their professional societies towards eliminating abuses in the use of hospital care which are causing the rates for such care to steadily rise.

In our visits with the various state medical societies, Dr. Burt spent much time going over the abuse—a naughty word but true nevertheless—of Blue Shield benefits. Dr. Poindexter pointed out how these abuses develop and what the damaging results amount to. Similarly, I pointed out the resulting effect of excessive, and often unnecessary, use of Blue Cross benefits. We were somewhat fearful of how our colleagues would take to our coming in, but we have been asked to come back for an encore, so we feel we did accomplish one or two things at least. The majority of the doctors have agreed that something must be done, and we are pleased with the results thus far.

O. A. Sedlak, M.D., Chairman

(The transactions will be concluded in the November issue)



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Book Reviews . . .

Laennec: His Life and Times

ROGER KERVRAN, M.D., *1960. New York: Pergamon Press. 209 pages. $3.50.*

The name of Laennec is immortal. As the discoverer of the stethoscope, as the developer of mediate auscultation, and as a clinician, pathologist, and morbid anatomist, he is one of the great men in medicine. But what of the man himself? What sort of human being was he? How did he become famous? What were the times in which he lived?

Dr. Roger Kervran has given us the answers to these and many more questions. His book has the classic plan of a biography—birth to death. The book is readable, comprehensive, and well edited. Only 3 minor criticisms are in order: (1) a map of France with the route of Laennec's travels would be helpful, (2) translation of the French quotations would give more continuity to some parts of the book, and (3) semantics and grammar have suffered slightly in the process of translation.

Laennec lived during the turbulent times of the French Revolution and Napoleonic era. He personally witnessed the use of a machine invented by a fellow physician, the guillotine. He saw the excesses of monarchy and revolution, but within this framework of chaos, he labored to alleviate the ravages of disease.

Personal suffering and debility were also a part of Laennec's life. Tuberculosis ravaged his body during most of his forty-five years. His intellectual accomplishments were attained against this background of physical decay. The great emotional strain from the savage and violent attacks by some of his colleagues aggravated this physical condition. His only respite was relaxation at his beloved country estate, Kerlouarnec.

In spite of the brevity of the book, the thoughts and observations of Laennec are in no way altered. In fact, as with all of the "old masters" in any field, Laennec's observations are as applicable today as they were one hundred fifty years ago.

I would heartily recommend this book for the busy practitioner of medicine.

THOMAS M. RECHT, M.D.
Minneapolis

Primer of Electrocardiography

GEORGE E. BURCH, M.D., *and* TRAVIS WINSOR, M.D., *1960. Philadelphia: Lea & Febiger. 273 pages. Illustrated. $5.00.*

Burch and Winsor's book has been one of the most popular introductions to electrocardiography since its first edition in 1945. This primer gives a clear presentation of electrophysiologic background and main clinical application, assisted by a profuse number of illustrations. The authors are careful to point out that this is an introduction for the beginner, and more comprehensive study of electrocardiographic literature is needed.

One has the impression, however, that a more thorough revision would have been in order for this fourth edition. A few examples may be sufficient for illustration. On page 149 is stated, "the single precordial leads employed today are 4F, 4R, 4L, 4B, and 4V leads;" and on page 150, "lead 4F is frequently employed clinically." All these apical leads are abandoned today. Precordial leads are discussed separately from limb leads. While this follows the historical development, it necessitates repeated discussion of the same condition. For example, myocardial infarction is discussed on pages 115 to 131 (standard leads), pages 171 to 186 (precordial leads), and again on pages 238 to 247, with reference to the initial QRS deflections in standard leads. The illustrations, figures 130 to 131 and 179 to 183, also are quite similar. Separation of limb and precordial leads does not follow the integrated interpretation of the 12-lead electrocardiogram. Wilson's original unipolar limb leads, VR, VL, and VF, are included, but not the augmented leads, although these are more frequently employed today. For the Q-T interval, Ashman's logarithmic formula is proposed, while the majority of electrocardiographers use Bazett's square root formula. The short introduction into spatial vectorcardiography is desirable. It is understandable that, in this short space, the presentation is limited to one lead system, i. e., the Wilson-Burch equilateral tetrahedron reference frame, but the claim that this is the most accurate lead system cannot be maintained (recent review by Pipberger, H. V., Progress Cardiovasc. Dis. 2:248, 1959).

All these objections are concerned with detail. The text is still, as it was before, a good introduction and can be recommended for the beginner.

REUBEN BERMAN, M.D.
Minneapolis

Practical Proctology

LOUIS A. BUIE, M.D., *1960, second edition. Springfield, Ill.: Charles C Thomas. 717 pages. Illustrated.*

Practical Proctology is a suitable title for this fine textbook. The author has drawn on the accumulated experience of forty years of the practice of his specialty to present a well-organized text, arranged in orderly and readable fashion. The opening chapter, entitled "The Responsibility of the Physician," pointed specifically at the proctologic examination, is valuable reading for any physician and especially for young practitioners and those not limiting their work to proctology.

All phases of proctologic pathology are well covered and discussed in readable fashion. No attempt is made to discuss all the various operative procedures for hemorrhoids and other anorectal operations, which would only serve to confuse the inexperienced operator. All procedures discussed are those which have been proved successful in the extensive experience of the author. There are adequate references to other authors in the bibliography to give the reader additional reading wherever he wishes it.

Operative procedures are adequately illustrated to give the reader a clear picture of what is discussed in the text. Of particular value are the color plates, which are used generously to illustrate conditions not satisfactorily shown by black and white illustrations.

The chapter on fistula in ano is especially good and points out the sequence of events that result in the for-

(Continued on page 26A)

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(1) Danowski, T. S.: Diabetes Mellitus, Baltimore, Williams & Wilkins, 1957, p. 239. (2) McCune, W. G.: M. Clin. North America 44:1479, 1960. (3) Ackerman, R. F., et al.: Diabetes 7:398, 1958.

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(Continued from page 24A)

mation of a complete fistula—a sequence frequently misunderstood by many practicing physicians.

The chapter on pilonidal disease also deserves special consideration. Dr. Buie, always a master of the choice of words and phrases, is responsible for the terms "jeep disease" and "marsupialization" in connection with this condition. I fully agree with Dr. Buie that the open method is the operation of choice in the vast number of instances.

This book, written in plain, forthright language by a man of vast experience—and one of the great teachers in the field of proctology—can well be taken as a basic guide for the fundamental principle in the diagnosis and treatment of proctologic disorders.

WALTER A. FANSLER and CHARLES A. NEUMEISTER
Minneapolis

Cirrhosis of the Liver

MARTIN SELER KLECKNER, JR., M.D., *1960. Springfield, Ill.: Charles C Thomas. 726 pages. Illustrated. $24.50.*

This book is a good compilation of most of the classical information now available about cirrhosis of the liver. The opening chapter summarizes the history of cirrhosis and reminds us that progress in the understanding of this disease, since at least 3,000 B.C., has been slow. Subsequent chapters deal systematically with the common forms of cirrhosis—portal, postnecrotic, biliary, and that which is often associated with other conditions such as ulcerative colitis, heart failure, and pancreatitis. Other chapters deal with special problems—portal hypertension, ascites, and hepatic insufficiency.

There is a good chapter on the proper technics of liver biopsy. The final chapter is on dietary management.

The book is well illustrated, with numerous photographs, photomicrographs, charts, and tables. The latter are of value in permitting the reader to make his own appraisal of the data discussed. Each chapter is followed by a generous reference list and there is an index. Designed primarily for the practioner, this volume will be a useful addition to the office or hospital library.

JAMES CAREY, JR., M.D.
Minneapolis

Cerebrospinal Fluid Dynamics in Health and Disease

DAVID BOWSHER, M.D., *1960. Springfield, Ill.: Charles C Thomas. 80 pages. Illustrated. $4.75.*

This small book is concerned with the dynamic aspects of the cerebrospinal fluid, embracing the borderlines of chemistry, physics, and physiology. This thesis deals with the newer knowledge and is applied to the understanding of the biologic formation, chemical composition, and physical absorption of cerebrospinal fluid, its secretion in the choroid plexus and ultrafiltration in the pia-arachnoid, its circulation and function in the body, the chemical nature of its control, the role of the blood spinal fluid barrier, the osmotic regulation of spinal fluid volume, and the mechanism of hydrocephalus. Isotopic studies demonstrate the dynamic behavior of cerebrospinal fluid but open new vistas of complexities in intracranial fluids as extracellular fluid systems of the body.

For those who find it advantageous to understand as much as they can of the nature of the cerebrospinal fluid, this book will be helpful. Although the index is very small, the bibliography is long and adds body to the presentation.

JOHN S. LUNDY, M.D.
Chicago

Fundamentals of Nerve Blocking

VINCENT J. COLLINS, M.D., *1960. Philadelphia: Lea & Febiger. 344 pages. Illustrated. $9.50.*

This book is a timely one, since the field of nerve blocking is not as popular as many think it should be. The intended field is rather well covered, and the effort to memorialize Dr. Rovenstine's field of activity in this direction is quite well done. This publication should be well received by anesthesiologists, since the majority of them need the information that is in this book. The book is indexed and printed on good paper.

JOHN S. LUNDY, M.D.
Chicago

The Natural History of Cerebral Palsy

BRONSON CROTHERS, M.D., *and* RICHMOND S. PAINE, M.D., *1959. Cambridge, Mass.: Harvard University Press. 296 pages. Illustrated. $6.75.*

This book, one of the first attempting to give a twenty-year follow-up—between 1930 and 1950—of 1,821 patients with cerebral palsy, succeeds in outlining the probably related etiologic factors, the neurologic deficit, and the mental, emotional, and dispositional statuses of over 600 patients that have been reexamined and reevaluated. In the first 4 chapters, the book delineates the proposed plan for following and investigating these 1,800 cases. The next 5 chapters deal with a simplified classification of cerebral palsies, as well as detailed etiologic and clinical evaluations of the various types of cerebral palsy. A thorough presentation of the various ancillary but necessary studies relative to electroencephalography, psychologic examinations, speech evaluation, and physical therapeutic approaches makes these procedures easy to understand.

The primary purpose of this book is to describe the outcome in a large group of patients who had cerebral palsy early in life. The modes of evaluation, therapy, and planning are discussed relative to the doctor, patient, parents, and community. The clarity of the definitions; the simple classification, with excellent illustrations of patients; and the informative tables and figures make this book very valuable not only to the general practitioner but to those who see children and adults who have sustained a brain injury early in life. The book is not only satisfactory for those who meet the problems on rare occasions but also of considerable value to the neurologist, neurosurgeon, pediatrician, orthopedist, and those in the allied fields, such as psychology and speech therapy. A copy of the book should be available in the offices of most physicians who encounter and counsel patients and parents relative to the problems of cerebral palsy.

The authors' analyses of previous works are numerous throughout the text and tend to point out the general consensus of opinion in regard to the various aspects of cerebral palsy.

Although the book is only 300 pages *in toto*, the bulk of the material is easily read and can be quickly referred to for brief reference.

J. T. JABBOUR, M.D.
Minneapolis

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Radicular Pain

A. B. BAKER, M.D.

Minneapolis

RADICULAR PAIN is a relatively common neurologic complaint and warrants careful evaluation by the physician as to its etiology. One of the first problems is to determine whether the pain is truly rootlet in origin. A number of features enable the physician to recognize rootlet pain and should be checked for in all cases of pain syndrome.

CHARACTERISTICS OF ROOTLET PAIN

1. Rootlet pain tends to be localized to the dermatome supplied by the affected nerve root. The pain may be limited to a small area or may be widely distributed throughout the dermatome. Characteristically, rootlet pain tends to be referred to characteristic areas of the body, such as C_3 to the shoulder, C_5 to the upper arm, C_7 to the thumb, T_{10} to the umbilicus, L_2 to the anterior thigh, L_3 to the knee, L_4 to the large toe, S_2 to the back of the leg, and S_5 to the anal region (figure 1).

Pain is occasionally referred from deep somatic or visceral structures to superficial areas of the body supplied by the same dermatome. This pain is called "referred pain" and sometimes is difficult to differentiate from true rootlet pain. Some common areas of referred pain might be described in order to help in this differentiation: heart to dermatomes C_3-T_8 (neck, shoulder, and upper back); stomach to dermatomes T_6-T_9 (mid-back or upper abdomen); ovary to T_{10} (umbilicus or mid-back); prostate to T_{10}-T_{12} (lower abdomen or mid-back); kidneys to T_{10}-L_1 (lower abdomen or lower back); and rectum to S_2-S_4 (groin, anal region, and genitalia).

2. Rootlet pain is increased by any procedure that suddenly increases intrathoracic or intra-abdominal pressure, such as coughing, sneezing, or straining.

3. Rootlet pain frequently awakens the patient at night after several hours of sleep and is often relieved by getting up and moving about.

4. Rootlet pain can be accentuated by maneuvers that stretch the involved roots. The lower lumbosacral roots can be stretched by the straight-leg-raising test (Lasègue's sign) or by bending forward to touch the floor with the knees held extended. The cervical roots can be stretched by bending the head so that the chin rests on the chest (chin-chest maneuver).

ETIOLOGY OF RADICULAR PAIN

The rootlets can be irritated to produce pain by lesions of any of the structures through which the rootlets pass. Hence, in any case of radicular

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pain, possible lesions of the vertebrae, meninges, rootlets, or even the spinal cord must be considered.

DISEASES OF THE VERTEBRAE

Trauma. This is one of the most common causes of radicular pain, particularly in the younger age group. The pain results either from a direct injury and swelling of the rootlet or from a compression of the rootlet by a lateral herniation of an intervertebral disk.

1. Injury to the rootlet. This occurs most frequently in sudden neck injuries, such as in jarring due to falls or in whiplash injuries following automobile accidents. The rootlets chiefly in the lower cervical region become swollen and hence compressed as they pass through the intervertebral foramen (figure 2A).

The clinical manifestations of rootlet injury are readily recognized. Symptoms may appear immediately after injury or may be delayed for twenty-four to forty-eight hours or more. In some cases, the only complaint is nuchal pain which radiates to the occipital region and is often mistaken for a tension headache.

More characteristically, the neck pain is soon accompanied by persistent pain or discomfort in the shoulder that radiates down the arm to involve the thumb or the middle three fingers. In some cases, the pain remains localized to the neck and shoulders but is associated with paresthesias or numbness of the hand region without radiation down the limb. The pain is usually accentuated by flexion of the head toward the side of involvement or by any jarring of the

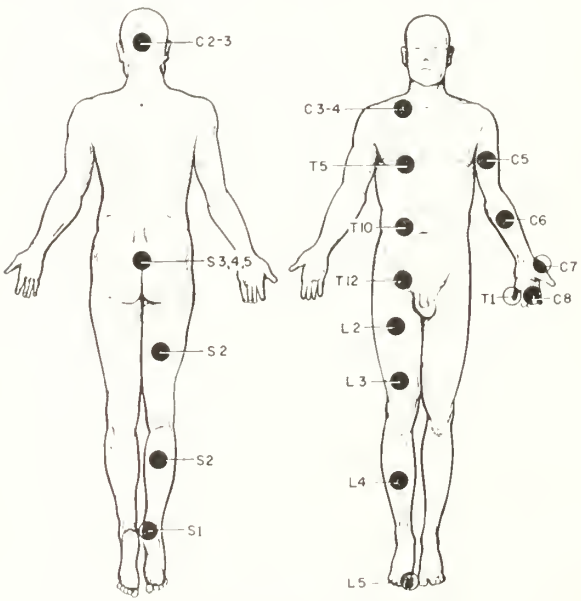

Fig. 1. Distribution of radicular pain.

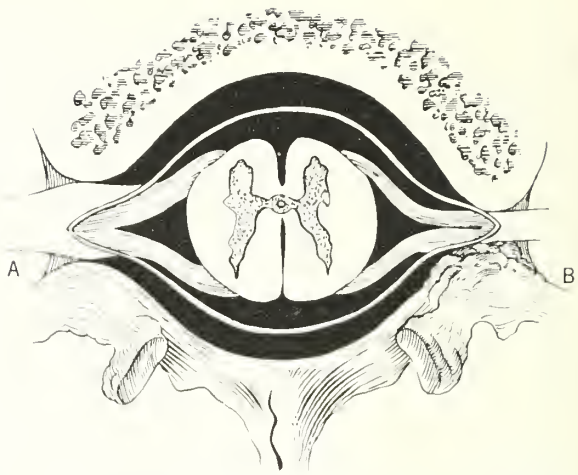

Fig. 2. Vertebral causes of radicular pain. (A) Swelling of rootlet due to injury. (B) Osteoarthritic narrowing of intervertebral foramen with compression of root.

body. It is often relieved by forced extension of the head. At times, weakness of the forearm musculature (triceps) may be present. This paresis may appear early or be delayed by weeks. Examination usually reveals marked tightness of the neck musculature, often a reduced triceps reflex and occasionally some paresis of the triceps muscle. X-ray examination of the neck is usually normal even on myelographic studies, and the spinal fluid is within normal limits.

The course of the illness is often unrelated to the severity of injury or findings. In some mild cases, if untreated, the symptoms persist and may result in severe incapacitation because of the constant head and neck pain. In other cases, the course appears progressive, and, after a few weeks of neck discomfort, radiating pain down the limb develops with some associated weakness. If the patient keeps active, the pain is usually constant and interferes with work and sleep.

Treatment usually is successful in alleviating the symptoms. In milder cases, placing a board between the patient's bedspring and mattress and removing the pillow during sleep often relieves the symptoms. In more intractable cases, the patient should be hospitalized and placed in cervical traction for about one week. The traction should be applied during the entire twenty-four-hour period, using not more than 3 to 4 lb. of weight. This procedure usually results in improvement. The patient can then continue traction for a few hours a day after returning home and to work. Muscle relaxant drugs may be tried but are of questionable value.

2. Herniated intervertebral disk. Rupture of an

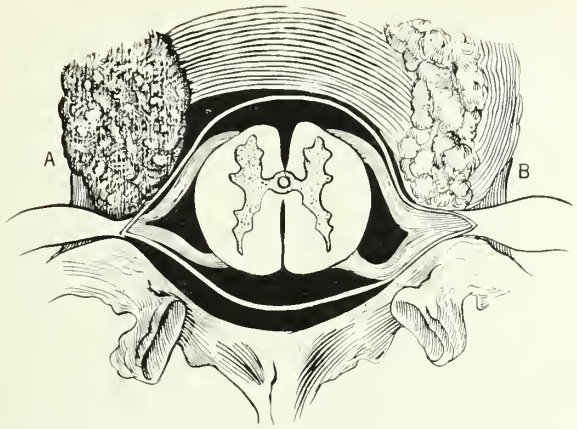

Fig. 3. Vertebral causes of radicular pain. (A) Metastatic carcinoma to the vertebra with compression of rootlet. (B) Herniation of intervertebral disk causing rootlet compression.

intervertebral disk is usually preceded by a history of back injury but may occur spontaneously without any available preceding etiologic history. The most common locations for ruptured disks are in the lower cervical and lower lumbar regions. The disk usually ruptures laterally and thus compresses the adjacent rootlet to produce the pain (figure 3B).

Cervical disk usually involves the lower cervical rootlets. The clinical manifestations are similar to those of rootlet swelling resulting from whiplash injuries. An acute onset of neck or shoulder pain develops followed in many cases by radiation down the arm to implicate the thumb or middle fingers. The neck muscles show marked spasm with a loss of normal neck curvature. The biceps and triceps reflexes are often reduced, and there may be some muscle weakness. Marked tenderness to deep palpation is often present just over the area of protrusion.

Clinically, it is often impossible to establish a definite diagnosis of herniated disk, and the spinogram must be relied upon to demonstrate the lesion.

In mild cases, treatment can be conservative and consists of bed rest, cervical traction, and a board placed between the bedspring and mattress. If the pain is very severe and persistent, surgical removal of the herniated disk fragment should be considered.

Lumbar disk herniation usually results from unusual backstrain or injury and manifests itself by the sudden onset of lower back pain or discomfort, which often subsides in a few days and may not recur for weeks or even months or years. Subsequent attacks may remain localized to the lower back or may radiate down the buttock to the posterolateral aspect of the leg. If the first sacral root is involved, the pain radiates to the lateral border of the foot to the little toe; involvement of the fifth lumbar root results in pain radiation to the anterolateral aspects of the leg across the dorsum of the foot to the middle three toes. Although the onset and distribution of pain is very characteristic, a diagnosis of lumbar herniated disk must never be made from the history alone. To substantiate the diagnosis, the patient must have some objective evidence of rootlet compression or irritation. These consist of the following findings:

1. Spasm or tightness of the lower back muscles. This is one of the most characteristic features of disk pathology, and, without its presence, one should not hazard a clinical diagnosis. Because of this muscle spasm, the patient walks cautiously with his back held rigid. The normal lumbar curve is flattened, and, on palpation, the spinal muscles are boardlike in consistency. Bending is impossible, and the patient walks stooped with the scoliosis away from the affected side.

2. Spine tenderness. This finding is also consistently present. The spine is tender to deep pressure directly over the involved interspace to the side of the midline.

3. Positive leg-raising test (Lasèque's sign). Raising the involved leg with the knee held extended usually precipitates severe pain. The level to which the leg can be raised is greatly limited on the involved side because of the muscle spasm as well as the pain. In chronic cases, the findings on this test may not be too striking. In contrast to this test, lateral manipulation of the hip joint (Patrick's test) is not involved.

4. Decreased deep reflexes. When the first sacral root is involved, the ankle jerk is usually decreased or absent. In higher lesions, the ankle jerk may be present but the knee jerk decreased.

5. Muscle weakness. In lesions of the first sacral root, there may be weakness in dorsiflexion of the large toe or even the foot.

6. Sensory changes. These are usually absent but, when present, may follow the course of the involved rootlet, usually producing hypesthesia over the dorsum and lateral aspect of the foot.

In the presence of a clear-cut clinical herniated lumbar disk, the spinogram will reveal a defect which corresponds to the clinical diagnosis. The spinal fluid often will reveal a mildly elevated protein.

Treatment may be conservative or surgical. Conservative therapy consists of continuous bed rest on a firm mattress, traction, and the use of

muscle relaxants. Surgical removal of the herniated disk should be considered: (1) if conservative therapy does not result in recovery after a few weeks, (2) if the patient is having frequent recurrent episodes which are disabling and incapacitating, and (3) if the acute attack is very severe and accompanied by muscle weakness.

Osteoarthritis. Most elderly individuals show osteoarthritic changes in the cervical spine. These changes often produce a narrowing of the intervertebral foramen (figure 2B). Radicular pain is prone to develop in such patients due to rootlet compression as a result of even mild neck strain or neck injuries. The clinical manifestations are very similar to those seen following a whiplash or cervical disk injury. Treatment by use of a hard mattress, no pillow, and, if necessary, cervical traction generally alleviates the pain.

Metastatic lesion to spine. This is the most common cause of radicular pain in the older age group (figure 3A). It should always be considered in any elderly patient with a history of weight loss or surgery for the removal of a primary lesion. In most cases, the involvement implicates the lower thoracic and lumbosacral regions, resulting in pain in the lower extremities. A number of features characterize the metastatic lesion and differentiate it from a ruptured intervertebral disk:

1. Pain often is bilateral, radiating down both legs.
2. Back muscles are often not tight, and the normal lumbar lordosis is not altered.
3. Pain occurs on direct palpation of the vertebral body involved, rather than by deep pressure lateral to the vertebrae as seen in the ruptured disk.
4. Pain is accentuated not only by the straight-leg-raising test but also by lateral flexion of the hip (Patrick's sign).
5. Sensory and reflex changes are much more irregular and often absent.
6. Roentgenogram often reveals the bony changes in the spine.
7. Spinal fluid contains a higher level of protein increase, often over 100 mg. per cent.

Treatment of a metastatic lesion to the bone is symptomatic. If the usual analgesics fail to offer satisfactory relief, chordotomy may have to be considered. Deep x-ray therapy at times has proved helpful.

Infections of the spine. Two infections characteristically implicate the spine to produce rootlet irritation. Fortunately, both are uncommon (figure 4B).

Brucellosis results in direct involvement of the lumbar spine with sclerosis and bony fusion. This bony involvement may produce rootlet irritation in the distribution of the sciatic nerve, which superficially may resemble the pain of a ruptured lumbar disk. The diagnosis is readily established by the history and x-ray findings. This condition responds promptly to the usual treatment for brucellosis.

Tuberculosis of the spine has become very uncommon. It may produce narrowing and destruction of the intervertebral disk and vertebral body with collapse of the vertebrae, resulting in a kyphos. It most frequently implicates the thoracic spine. This process may be associated with an epidural granuloma, which early results in rootlet irritation. Later, evidence of spinal cord involvement may develop, such as a slowly progressive spastic paraplegia with hyperactive reflexes.

The diagnosis is readily made by the roentgenograms as well as by the history associated with the kyphos or gibbus and the evidence of spinal cord compression.

DISEASES OF THE MENINGES

Metastatic lesions. The chief sources of the primary lesion are the bladder, prostate, kidney, ovary, or gastrointestinal tract. Usually, the thoracic or lumbosacral rootlets are implicated, resulting in pain in the region of the lower abdomen, pelvis, or lower limbs (figure 4A). Metastasis to the meninges with involvement of the rootlets may occur many years after a primary lesion has been removed. Often, at the time the pain appears, the patient has shown no other evidence of metastasis, such as weight loss,

Fig. 4. Meningeal causes of radicular pain. (A) Metastatic tumor of meninges compressing the rootlet. (B) Tuberculosis of the bone with secondary involvement of the nerve root.

anorexia, or even x-ray evidence of involvement of the chest or bones. The radicular pain may be the only complaint and is frequently not accompanied by other evidence of rootlet irritation, such as spasm of muscles, reflex changes, or muscle weakness. The course of the illness is prolonged. The pain may persist and remain localized for many years without any apparent evidence of extension or spread.

The diagnosis must be suspected from the history and findings. Often, substantiating evidence is absent. Spine roentgenograms and even spinograms will be normal. The spinal fluid protein often will be elevated above 100 mg. per cent.

Treatment consists of deep x-ray therapy and analgesics. High cervical chordotomy may be considered if all other methods of therapy fail.

Tabes dorsalis. This is a syphilitic inflammation of the dura of the spinal cord which often involves the associated spinal rootlets. The rootlet irritation manifests itself in severe bouts of muscle pain (lightening pain); recurrent episodes of visceral pain (visceral crises) referable to the heart, stomach, kidneys, and so forth; and girdle sensations consisting of constricting pressure around the chest or abdomen.

The diagnosis is readily established by the associated pupillary abnormalities and the evidence of posterior column involvement consisting of diminished ankle and knee jerks, impaired position sense with ataxic gait, bladder disturbances, and Charcot joint. The diagnosis can be verified by the spinal fluid serology or by a positive history of syphilis.

Treatment consists of the use of both penicillin and fever therapy. The penicillin dosage is 20 million units administered over a two-week period. Fever therapy employs chiefly malaria in a course of fifty hours of fever above 103° F. by mouth. Even the most intense therapy may not cure the radicular pain and chordotomy may have to be considered.

Fig. 5. Rootlet diseases resulting in radicular pain. (A) Neuroma of the rootlet. (B) Infection causing swelling and irritation of the rootlet.

Arachnoiditis. Adhesions between the pia and arachnoid may follow acute or chronic infections, trauma to the spine, intrathecal injections of serum, antibiotics or Pantopaque, or it may be of obscure etiology. The clinical features are most variable, since any part of the cord may be affected and since the lesions may be localized or diffuse. Radicular pain is often one of the earliest complaints and may be the only finding for a long period. The distribution of the rootlet pain is most variable and may implicate more than one rootlet area. Usually, as the disease progresses, there is evidence of spinal cord involvement. In the well-developed case, the neurologic examination reveals well-defined signs of local disease not only to the rootlets but also to the spinal cord.

The diagnosis is often impossible to establish from the examination alone. It is greatly facilitated by spinal puncture and myelography. The spinal fluid often shows a partial or a complete block with xanthochromic fluid. The myelogram reveals a partial block with droplets of oil arrested over a considerable extent of the spinal cord.

Spinal anesthetic. The introduction of a spinal anesthetic into the subarachnoid space results in irritation to the structures within the subarachnoid space, with subsequent rootlet irritation which may appear months or years after the anesthetic. In all cases of rootlet pain of undetermined etiology, a careful history should be obtained of possible spinal anesthetic or of various other types of intrathecal injections.

The involvement may occur at any cord level but most frequently involves the lower cord areas. The initial symptoms are rootlet pain followed by sensory changes corresponding to the involved rootlets. Muscle atrophy, hypotonus, and diminution of deep reflexes may also occur. The spinal fluid shows only a slight pleocytosis and some elevation of the protein.

DISEASES OF THE ROOTLETS

Tumors. The most common tumors implicating the rootlets are the neuroma and the meningioma (figure 5A). Both tumors are extramedullary but intradural in location and are benign lesions which, if diagnosed, can be totally removed. They grow slowly and often begin with rootlet irritation and radicular pain which may persist as an isolated finding for months or even years.

This pain is usually accentuated by coughing or straining. It is unilateral at its onset but may become bilateral or diffuse after a period of months. At this stage, the diagnosis may be difficult but should be suspected if a spinal puncture is done and the protein is found to be elevated.

After a period of time, evidence of spinal cord compression becomes evident and should promptly indicate the proper diagnosis. A slow progression of evidence of cord compression develops, consisting of spastic weakness which first involves one side of the body but soon becomes bilateral, a slowly ascending segmental hypesthesia, and, finally, sphincter disturbances. Any patient who presents with radicular pain and in whom a progressive spastic paraplegia later develops must be considered to have an extradural spinal cord tumor.

The diagnosis can usually be established by spinal puncture which reveals a partial or total block with xanthochromic fluid and a high spinal fluid protein. Myelography invariably demonstrates the lesion. Treatment consists of surgical removal of the tumor.

Herpes zoster. This is an infection of the dorsal root ganglia produced by a virus (figure 5B). The illness is introduced by a mild systemic reaction consisting of fever, headache, malaise, and a regional lymphadenopathy. At about the height of the systemic reaction, pain develops in the distribution of the one or more rootlets. This rootlet pain may persist as the only finding for days and then becomes associated with burning and erythema of the skin in the involved rootlet distribution. Vesicles soon appear in the erythematous area. These vesicles ultimately rupture, become dry and scaly, and result in a brownish pigmentation of the skin. The radicular pain persists for about ten days to two weeks and slowly subsides. In some elderly individuals, the pain may persist for years after recovery from the acute illness and resist all attempts at alleviation.

The diagnosis may be difficult prior to the onset of the skin eruption. However, the preceding systemic reaction and the regional lymphadenopathy should suggest the possibility of herpes zoster. Once the vesicular eruption appears, the diagnosis is no longer in doubt.

In most cases, the illness is self-limited and symptomatic treatment only is indicated. Adequate analgesics to alleviate pain and drying, soothing skin lotions are usually adequate during the acute illness. No adequate therapy has been found for the persistent postherpetic neuralgias seen in the older age group.

Diabetes. Radicular pain is a frequent manifestation of diabetes. It is often unrelated to the severity of the diabetes or to level of the blood sugar. The pain is usually temporary, lasting for weeks to months. It has a tendency to implicate certain rootlets, such as those innervating the trunk area and the anterior thigh regions. The rootlet involvement in diabetes appears to be recurrent, implicating different rootlets in each attack.

The diagnosis is readily suspected in the presence of a history of diabetes, glycosuria, elevated blood sugar, or symptoms suggestive of diabetes, such as fatigue, polyuria, and polyphagia. Occasionally, the radicular pain is the presenting complaint, and the diagnosis of diabetes is made only after the patient work-up for the radicular pain.

Treatment consists of rigid control of the diabetes and vitamin B_{12} given intramuscularly in doses of 500 μg. twice daily.

Guillain-Barré syndrome. This is not a disease but a syndrome, probably with multiple etiologies. Because of the nature of the illness, it is suspected of probably being toxic in origin. Many cases appear to be precipitated by an upper respiratory infection.

Radicular pain and exquisite muscle tenderness appear to be the most constant findings in this illness. The radicular pain is early in onset, often appearing weeks before the actual neurologic deficit. The pain may be widespread and difficult to control. Muscle tenderness also occurs early and persists until the onset of recovery. Calf and thigh muscles are most often involved.

Neurologically, any part of the nervous system may be implicated, resulting in muscle weakness with reduced reflexes, scattered sensory disturbances, bulbar involvement, and often bilateral facial palsy. The characterizing feature of the whole illness is the development of the entire symptom complex in the absence of any evidence of a systemic involvement. The patients are afebrile and show no leukocytosis and a normal sedimentation rate. The spinal fluid also shows no pleocytosis but often contains an elevation in the protein.

The course of the illness is usually favorable. Most cases level off after three to five weeks and show fairly constant improvement. In the more involved cases, recovery can be delayed for many months or even a year. In the bulbar form, the mortality rate is over 30 per cent.

Treatment consists of complete bed rest until

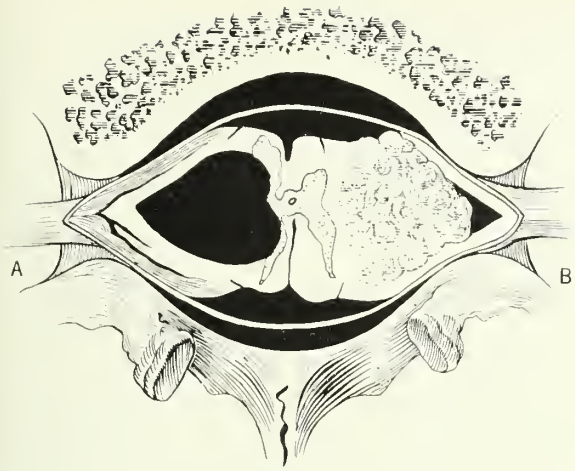

Fig. 6. Spinal cord disease resulting in rootlet irritation. (A) Syringomyelia with enlargement of the cord by a central cavity resulting in rootlet displacement. (B) Intramedullary spinal cord tumor causing rootlet irritation.

muscle pain subsides. A high protein diet and adequate vitamins should be given. In the presence of bulbar involvement, tracheotomy should be instituted. Steroids have been suggested but have not proved helpful in our experience.

DISEASES OF THE SPINAL CORD

Any lesion that results in a progressive enlargement of the spinal cord can produce displacement of the rootlets and radicular pain. This process is seen most often in intramedullary cord lesions, such as tumors and syringomyelia.

Tumors. Intramedullary tumors (figure 6B) are usually gliomas. These lesions frequently begin with segmental sensory disturbances at the level of the lesion associated with progressive pyramidal tract involvement below the lesion. If the lesion is situated in the cervical or lumbar enlargement, evidence of lower motor neuron involvement becomes prominent with weakness of the muscles of the limbs. Radicular pain is a late occurrence and is often dull and aching in nature. The progressive nature of the illness should suggest the diagnosis. Spinal puncture often reveals a partial block with increased protein. The diagnosis is established by myelography.

Syringomyelia. This illness (figure 6A) consists of a central cavitation occurring within the cord which begins as a slowly progressive benign gliosis and breaks down into a cystic cavity. The site of origin is usually the lower cervical cord with a primary involvement of the upper limbs. The lesion then tends to spread longitudinally up and down the cord.

Onset is usually before age 30. Dissociation of superficial sensibility—loss of pain and temperature with preserved touch and pressure—is the typical sign. The sensory loss is in the skin areas corresponding to the fibers interrupted and commonly takes a segmental distribution symmetrically. Painless trauma and burns with cigarettes, hot water, and so forth are frequent. Paresis early in the disease is of a lower motor neuron type with weakness and atrophy of the hand musculature. Horner's syndrome and trophic changes, such as a Charcot joint, may be present. Radicular pain occurs late in the disease after the spinal cord is markedly distended by the cystic cavity.

The course of this disease is prolonged over many years. Remissions may occur. The patient eventually becomes bedridden.

DIAGNOSIS of unusual pressure neuropathies depends upon investigation of attendant circumstances. Prolonged pressure on or injuries of various nerves, caused by conditions of occupation such as hod-carrying, automobile repair, carpet-laying, and the like, or by other circumstances, such as prolonged use of the telephone with the base of the receiver resting on the shoulder and the rim against the side of the face, use of crutches, the leg hanging over the side of the bed, and so forth, may be misdiagnosed as other disorders, for example, herniation of the third or fourth cervical disk, muscular dystrophy, cervical nerve root compression, syringomyelia, and the like. Thus, patients should reenact exactly the situation producing the paralytic state. The precise location of the lesion is determined by electromyographic examination.

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Neurologic Manifestations in 2 Cases of Ankylosing Spondylitis

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NEUROLOGIC LESIONS are rarely observed in ankylosing spondylitis except for mild radicular compression.[1] Sometimes, varying degrees of subluxation may develop with subsequent compression of the spinal cord at the atlanto-axial articulations, but rarely at lower levels.

Ankylosing spondylitis most characteristically begins with progressive ossification and fusion of the sacroiliac joints. At an advanced stage, the radiologic appearance consists of demineralization of the vertebrae, obliteration of the small intervertebral articulations, and ossification of the intervertebral ligaments, resulting in the classical bamboo spine. Peripheral joints may be involved.

The earliest report on ankylosing spondylitis was supplied by Conner in 1691, while basic clinical information was formulated by Strümpell[2] in 1884 and later by Pierre Marie[3,4] and Leri.[5,6] The papers of Bechterew[7,8] in 1893 and 1897 remain as classics for their description of the neurologic manifestations in ankylosing spondylitis. Polley[1] and Ludwig and associates[9] noted the rather frequent elevation of cerebrospinal fluid protein in patients with ankylosing spondylitis, particularly those with radicular pain. In 1959, Rouzaud and associates[10] described a case of ankylosing spondylitis with widespread muscular atrophy and asthenia secondary to an associated polymyositis.

The purpose of this paper is to emphasize some unusual neurologic manifestations observed in 2 patients with ankylosing spondylitis.

CASE REPORTS

Case 1. J.C.H., a 42-year-old man, was admitted to the University of Minnesota Hospitals in November 1959. The patient's chief symptom was inability to walk since 1954.

The patient had a long history of pain in his back beginning in 1934 with progressive difficulty in walking. In a few years, he assumed a stooped posture, and by 1942, he was forced to leave his job as a truck driver and undertake clerical work. Between 1951 and 1954, he was unable to work and was confined to bed for most of that time because of extensive weakness in his legs.

In 1954, his condition underwent acute deterioration and he was hospitalized in rural Minnesota. His temperature was reported to be 105° F., and he had profound generalized weakness, soreness of the muscles, and tender, swollen joints. His condition was diagnosed as rheumatoid arthritis, and he was hospitalized for a total of three years, during which time he was given cortisone and physical therapy, which resulted in some improvement in muscular strength and relief from pain. He was unable to walk in the hospital without assistance and, at the time of his discharge, was confined to a wheel chair.

The patient was first seen at the University of Minnesota Hospitals in 1959. Physical examination revealed generalized wasting, clubbing of the fingers, and slight edema of the lower extremities. The patient's spine was rigid and practically immobile. The rib cage was small and moved very little with respirations, which were essentially diaphragmatic in nature. There was slight limitation of movement of the proximal joints, but other joint signs were absent. Blood pressure was 150/90. The peripheral pulses were diminished.

Neuromuscular examination revealed moderate to severe atrophy of the upper extremities, shoulder girdles, and lower extremities. Marked fasciculations were present in the upper extremities and shoulders. Moderate weakness of the pectoralis major and shoulder girdles was noted bilaterally. Muscle power in the arms was only slightly impaired, with the exception of the extensor muscles of the left hand. The lower extremities were markedly paretic, especially distally. The deep tendon reflexes were slightly increased in the right leg and both upper extremities. There was a Babinski sign on the right side. Sensory examination was normal.

Roentgenograms of the spine revealed extensive changes characteristic of ankylosing spondylitis. A complete myelogram was normal. Routine blood work, urinalysis, serology, and C-reactive protein were negative. Electrophoresis of serum proteins was normal. Spinal fluid examination revealed protein, 18 mg. per cent; cells, 5; and a negative colloidal gold curve.

A muscle biopsy obtained from the right gastrocnemius revealed that sections of muscle tissue were replaced by

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tat. Most of the individual muscle fibers were quite atrophic and small in size, and some fibers showed loss of cross-striation. There was a grouping together of the muscle nuclei. The picture was suggestive of severe muscular atrophy.

Case 2. H.N., a 50-year-old man, was referred to the University of Minnesota Hospitals in July 1960 with ankylosing spondylitis associated with a progressive spastic gait. The patient's presenting symptoms upon admission were numbness in the lower extremities and inability to walk.

In January 1959, the patient had noted weakness of his legs and intermittent numbness of the left leg which eventually progressed to involve the other extremity. By the fall of 1959, he was quite incapacitated.

In February 1960, because of progressive weakness, a myelogram and laminectomy were performed at his home town. The surgeon reported thick adhesions between the dura and spinal cord at the seventh and eighth thoracic levels. These adhesions were partly freed by the surgeon. A rubber catheter was passed into the subdural space as far up as the middle cervical region and down to the cauda equina, with no further obstruction being encountered. Good pulsations of the cord were noted after the operation. Microscopic examination of the tissues removed revealed pieces of pia-arachnoid with areas of focal calcification and some fibrous proliferation but no evidence of active inflammation. A few scattered mononuclear cells were present. After the operation, the patient did well temporarily, but his symptoms recurred and progressed to the point where walking became nearly impossible.

The patient's history revealed that, in 1930, he fell from a truck and landed on his back but apparently did not suffer any disability. In 1937, he was told he had rheumatoid spondylitis. Of interest in the family history was that the patient's father had rheumatoid arthritis.

Physical examination upon admission to the University of Minnesota Hospitals revealed the patient to be clear and alert mentally. Blood pressure was 160/90. There was diminished movement of the thorax and the spine was rigid, with a slight forward bend. The remainder of the general examination was normal.

Neurologic examination revealed a markedly spastic gait. The patient required two canes for walking and even then could manage only a few steps. The deep tendon reflexes were markedly increased. Bilateral Babinski responses were obtained. A sensory level was present at the level of the tenth thoracic dermatomes. Spontaneous flexor spasms of both legs were elicited upon light stimulation. At times, the patient had some urgency on urination. The remainder of the neurologic examination was normal.

Roentgenographic examination revealed typical changes of ankylosing spondylitis throughout the spinal column. A second myelogram performed via cisternal puncture revealed complete obstruction at the border of the twelfth thoracic vertebra. The site of previous operation appeared clean.

On July 15, 1960, the patient had an exploratory laminectomy at the level of the eleventh and twelfth thoracic vertebrae. The dura and the arachnoid were very thick. The cord itself seemed to bulge posteriorly, and just anterior to this area was a large arachnoidal cyst, which was opened. The cord appeared somewhat soft in this area, indicating intramedullary cord damage. The cord was well decompressed after evacuation of the cyst, and resumption of normal pulsations was observed. The dura was partially closed.

After his operation, the patient improved gradually. He was given physical therapy and, upon discharge two months later, was able to ambulate with the aid of a cane.

DISCUSSION

The patients described in this paper showed severe neurologic deficit along with skeletal changes of ankylosing spondylitis. The first case was characterized by definite involvement of the spinal cord, especially the anterior horn cells; the second represented chronic arachnoiditis with features of progressive transverse myelitis.

A comparison of our cases with those described by Bechterew[7,8] reveals that certain similarities exist clinically and pathologically. Bechterew, in his original report in 1893,[7] described a chronic condition of the spine characterized by diminished mobility and by neurologic manifestations secondary to involvement of the nerve roots and spinal cord. Oppenheim,[11] in 1894, made reference to similar neurologic manifestations. Bechterew[7] was under the impression that he was describing a new disease, when in actual fact he was describing neurologic manifestations in ankylosing spondylitis. His findings included atrophy and paralysis of the muscles and loss of peripheral sensibility, primarily affecting the cervical segments. Bechterew at that time thought trauma to the back and heredity were important factors in this condition. His ideas in regard to the pathogenesis of the neurologic complications were finally formulated after the autopsy report of one of his cases in 1897.[8] He found pronounced posterior convexity of the thoracic spine, anterior fixation of the thoracic vertebra, disk degeneration, and adhesions at the vertebral foramina between the dura and spinal roots. Marked degeneration of the posterior roots and posterior root ganglia, as well as degeneration of the anterior roots and posterior columns of the spinal cord, was also noted. The pia overlying the posterior aspect of the involved segments of the cord was hyperemic and thickened. The peripheral nerves showed minimal degenerative changes. The atrophic muscles showed distinct fatty degeneration. On the basis of this autopsy, Bechterew thought that degeneration of the roots came from a chronic inflammatory process. Thickening of the meninges resulted in compression of the roots.

The significance of Bechterew's observations became somewhat confused after a report on heredotraumatic kyphosis by Pierre Marie[12] in 1897. This author described dorsal kyphosis related to trauma in an aged patient with a fa-

milial history of kyphosis. He arbitrarily classified this case with those previously reported by Bechterew and called the condition heredotraumatic kyphosis. Necropsy in his case revealed an old vertebral fracture and changes recognized today as senile ankylosing hyperostosis of the vertebrae. From that time, especially in France, the name of Bechterew has erroneously been attached to an ill-defined type of traumatic kyphosis that did not correspond to his original case reports. Although some injustice has been done to the work of Bechterew, it is generally recognized today that the conditions described by Marie, Strümpell, and Bechterew are essentially the same, that is, ankylosing spondylitis with special emphasis by Bechterew on unusual neurologic complications.

Our 2 cases seem to approximate the descriptions of Bechterew, although the neurologic involvement is somewhat more extensive. The appearance of neurologic manifestations in the first case especially with an exacerbation of rheumatoid arthritis suggests the possibility of a common and general disturbance of collagen tissue. The clinical appearance of extreme lower motor neuron involvement in this first case brings also to mind observations by Bannatyne[13] and Morrison and associates[14] on degeneration of anterior horn cells in rheumatoid arthritis. To what extent and under what circumstances ankylosing spondylitis was related to the arachnoiditis in our second case is difficult to ascertain. It is certainly reminiscent of the meningeal thickening described by Bechterew in one of his cases.

SUMMARY

Two cases of ankylosing spondylitis are presented for their unusual neurologic manifestations. The first case exhibited signs of diffuse lower motor neuron disease, along with some pyramidal tract involvement. The second case illustrated adhesive arachnoiditis with secondary cord compressions.

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Patients with rheumatoid arthritis have peptic ulcer 3 to 4 times oftener than the general patient population. The lesions are no commoner among arthritic patients treated with steroids than among those who are not. However, the incidence of gastric ulcers is higher in the patients who are treated with steroids.

Incidence of peptic ulcer was approximately 8 per cent in 2,114 rheumatoid patients, of whom 877 had received no systemic steroid treatment and 1,237 had received steroids in significant amounts. In the group receiving steroids, 18 per cent of all ulcers were gastric, whereas in the group receiving no steroids, 7 per cent were gastric.

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The Selective Use of Antidepressive Drugs in the Treatment of Depressive Disorders

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EMOTIONAL DEPRESSION is a common experience. Like pain, we have all felt it at one time or another; usually, it disappears in a short while. But if depression persists or becomes severe, it must be considered the symptom of an illness. Illnesses with mental depression as a prominent feature are very common, but it is a misleading oversimplification to lump such disorders together as though they were pretty much alike. They occur in a great variety of forms.

No satisfactory classification of depressive illnesses has been devised which would enable us to pinpoint diagnosis and treatment and predict results. Therefore, the psychiatrist today leans heavily on the concept of target symptoms in prescribing for the depressed patient—that is, he will aim the treatment at specific symptoms instead of prescribing according to general diagnostic categories. Thus, although depressions occur in a broad variety of illnesses, we still treat the depression as such.

As a starting point for our discussion of the use of antidepressive drugs, we can use the five categories of depressive diseases as offered by the American Psychiatric Association:

I. Involutional psychotic reaction
II. Manic-depressive reaction, depressed type
III. Psychotic depressive reaction
IV. Psychoneurotic depressive reaction
V. Depressive syndromes occurring in association with schizophrenia and other disorders.

1. INVOLUTIONAL DEPRESSIONS

Involutional depressions may be briefly identified as those disorders occurring for the first time late in life (age 45 or over)—that is, there is no history of previous attack. They are generally characterized by agitation and marked restlessness. Most other types of depression tend to spontaneous remission in a matter of a few months; not so a typical involutional melancholia. If physiologic therapy does not intervene, these miserable patients will continue to be ill for eighteen to thirty-six months or longer. Many of them become grossly delusional, and a small percentage will show more paranoid symptomatology than depression.

Early in the course of the disorder, the patient may be seen in office practice before the development of overt psychosis. The main problem presented is likely to be extreme tension and restlessness, with difficulty in sleeping, concentrating, and eating.

Etiology

There has been a great deal of misconception about the etiology of involutional depressions. Metabolic and other physiologic aspects of the "change of life" were once popularly held to be important causal factors in the development of these disorders. While these physiologic factors may play a role, they are no longer considered to be of paramount importance. It has been seen that identical clinical pictures occur years before or years after the menopause; also, treatment with hormones may relieve some vasomotor symptoms but has little or no effect on the depression.

While we do not have complete understanding of the genesis of depressive disorders, we do know that involutional depression and other types of agitated depression occur in persons who have an anxious, worrisome make-up. They tend to be rigid personalities with narrow interests. The agitated depressions of the older age group are often more severe. They are aggra-

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vated by the imminence of old age, the loss of valued biologic functions, and the realization that life is running out and that there will not be much further opportunity to make up for past failures and inadequacies.

Agitated depressions in the younger age group may be considered essentially similar to the involutional depressions, but, generally, they are not quite as severe. Because of their symptomatic similarity, the treatment of the two groups may be discussed together.

Treatment

1. *CNS suppressants.* Those patients who have large amounts of agitation and restlessness accompanying their depression (this includes most of the involutional group) are best treated with a central nervous system suppressant of the dibenzocycloheptene type such as imipramine (Tofranil) and amitriptyline (Elavil). The central nervous system stimulants are not used as this would result in an increase in agitation and insomnia which becomes intolerable to the patient. One of the most successful and widely used procedures is to treat the agitated patient with imipramine and to add thioridazine (Mellaril) or some other phenothiazine, to better control the motor overactivity. Imipramine is highly regarded, both in the United States and abroad, as a reasonably safe and effective antidepressive drug. It does, however, fail to help some patients. The nature and action of this compound have been discussed elsewhere.[1]

Amitriptyline is a newly introduced product which appears to be similar to imipramine in its actions and uses. It has the same slow suppressant type of action and the same dosage range. The pattern of side reactions will probably be similar to those occurring with imipramine; however, early claims indicate that it may be less troublesome in this regard.

Imipramine has a number of disadvantages which may be listed as follows:

a. It is slow. Though many patients respond favorably within seven to ten days, there are more who do not begin to show signs of improvement until they have been on the medication longer than this. Considering the misery and the suicidal potential of the depressed patient, it is often very difficult for both the patient and the physician to wait several weeks to see whether imipramine will be effective. The physician giving imipramine should consider three weeks as a minimum trial period. If the patient has not begun to show signs of improvement by three weeks and if the dose has been adequate, it can be assumed that the drug is not effective in this case.

b. Imipramine has a number of disturbing side reactions for some individuals. These usually are well tolerated but can be burdensome. The most common ones may be mentioned: dryness of the mouth, tremors, and perspiration may have to be endured until the dose can be decreased; postural hypotension is usually temporary but may necessitate reduction of dosage for a few days. This side reaction may be serious in older patients, who may faint and possibly suffer injury from falling; any tendency to constipation will probably be aggravated by both the depression and the drugs. Fortunately, this responds to the usual measures. Leukopenia and jaundice have been reported but are rare.

c. Imipramine alone does not control severe agitation. For this reason, it is often used in conjunction with a phenothiazine. Thioridazine with imipramine is the most commonly used combination.

d. The drug needs to be given for a long period. If the medication is discontinued too soon, the patient is likely to relapse. It seems highly probable that one of the main effects of imipramine is that of lessening symptoms until the depressive disorder has run its course.

As with other drugs of this type, there is considerable variation as to the patient's needs and tolerance. Geriatric patients require a low initial dose—30 to 50 mg. in divided doses—with gradual increases as tolerated. Otherwise, the minimum initial dose should be 25 mg. four times a day. If the patient does not respond but tolerates the medication, the dose can be gradually increased until about 200 mg. daily is given. Severely ill, hospitalized patients may require 300 mg. daily; 100 to 400 mg. of thioridazine may be added to control agitation. The total amount of these 2 drugs which can be tolerated will depend to some extent upon how quickly the symptoms respond and the severity of side reactions. Thioridazine may produce the same pattern of side reactions as imipramine, except for perspiration. After the patient has become more or less comfortable, the medication can be reduced if necessary to control side effects. Otherwise, it is best not to start reducing the dose for at least two months. After this, it should be reduced gradually over a period of several weeks with the physician, the family, and the patient being alert for the possibility of relapse. In that event, increasing the dose may once more be effective.

2. *Electroshock therapy.* Though imipramine

plus a phenothiazine is considered the most efficient pharmacologic therapy for agitated depression, virtually all physicians agree that it is not so efficient as electroshock therapy. This treatment is also "sedative" in type, and it remains our most reliable, tried, and proved antidepressive method. It has the advantage of working very rapidly, often providing relief in a few days. In competent hands, it is relatively safe, and the memory deficit which it creates is reversible. The typical agitated, depressed, involutional patient has an excellent chance to respond favorably. On the other hand, those who use this treatment will be very happy if and when an equally effective method is available so that they would no longer have to give electroshock. Although the death and injury rate from electroshock is low, deaths do occur, particularly in patients with heart disease. Memory disturbance is unfortunate for some types of patients, such as business executives and physicians. One of the cogent arguments against electroshock is the fact that the vast majority of persons who have received it have an aversion to the treatment which varies from mild dread to acute horror. In addition to all these objections is the fact that electroshock, too, has a great many failures. Even after twenty years' experience with this type of procedure, we cannot predict with certainty what the results will be.

On the whole, it is desirable to give the patient the benefit of a trial on drug therapy before instituting electroshock whenever this is possible. But if the patient is acutely suicidal and uncooperative, electroshock may be a more practical immediate step. There are other patients who do not appear to tolerate the drugs, and, of course, there are a fairly large number whom the drug therapy fails to help. In many of these cases, electroshock will be of benefit.

3. *Follow-up psychotherapy.* Other forms of treatment such as hypnotic drugs, psychotherapy, and activity programs are of value, but they are not the most critical issues in the treatment of involutional and agitated depressed patients. However, follow-up psychotherapy and management may help the patient attain a better perspective on his illness. He may learn to modify some of his patterns of living so that he is less likely to build up excessive tensions in the future.

The prognosis for most agitated depressions is good. Those with paranoid admixtures or those whose patterns are complicated by severe, chronic nervousness or alcoholism are less favorable. Of patients with the classic involutional depressions, the majority recover and remain well, though a small percentage may relapse or have a later recurrence.

II. NONAGITATED PSYCHOTIC DEPRESSIONS INCLUDING MANIC-DEPRESSIVE DEPRESSIONS AND OTHER RECURRENT DEPRESSIONS

This group is included in the commonly used concept of "endogenous depressions."

Characteristics

A depression of this type is easily recognized when there is a history of previous attacks of depression or elation. The attacks may occur several years apart, and the patient may be fairly well-adjusted between his spells. If he is having his first attack or does not admit to a previous one, the diagnosis may be more difficult. If the attacks are sufficiently severe, the patient may be considered psychotic. He may be withdrawn, retarded, or delusional. More often, the depression which occurs in the manic-depressive cycle is not an agitated one—in fact, the patient may appear slowed up and retarded.

Some patients are fortunate in that their depressive episodes are rather light and short-lived, and they may not need any special therapy for them. Some are able to keep working fairly effectively throughout their periods of depression, even though they may not enjoy life nor be as productive as when they are well.

Physicians and laymen alike seek an explanation from the patient's life situation and personality characteristics in an attempt to explain why he is depressed. For example, he may have suffered financial difficulties, or he may have a series of personal conflicts such as difficulty in handling hostility toward his employer, spouse, or someone else. Usually, it will be found, however, that he has had similar problems and conflicts in the past without becoming overtly ill. The pertinent stressful situation or personal conflicts may have acted as precipitating factors in the illness, but it is likely that some nonpsychologic factor is important in the causation of the disorder.

Treatment

Because these patients have a tendency to recover spontaneously, it is difficult to evaluate treatment. Many of the drugs available are new, and it will be some years before we have a clear idea as to their effectiveness. However, we do know that in this group both the dibenzocycloheptene antidepressants and the central nervous system stimulants have some success. The indirect and bimodal stimulants,[1] are of

definite value for the treatment of some individuals, though it is still impossible to predict which persons will or will not respond. The direct central nervous system stimulants[1] such as the amphetamines, which have been available for a number of years, have proved to be of very little value in the treatment of psychotic depressions because of their short duration of action.

1. *MAO inhibitors.* The most promising pharmacologic therapy of psychotic depression is with a nonhydrazine monoamine oxidase (MAO) inhibitor such as tranylcypromine (Parnate). This newly introduced compound has the advantages of (1) being the most potent MAO inhibitor available, (2) being relatively safe and trouble-free, and (3) because of its bimodal action, offering a rapid yet sustained effect.

Tranylcypromine is best given in the morning and around noon. If given late in the day, it may disturb the patient's sleep. The initial dose is generally 10 mg. twice a day. This dose is often sufficient but may be increased by 1 tablet every three days until a maximum of 6 tablets (60 mg.) is taken as a daily total.

Most depressions are not "pure" but are accompanied by anxiety, paranoid, or schizoid features. For this reason, the author also uses small amounts of a piperazine-type[2] phenothiazine such as trifluoperazine (Stelazine) or perphenazine (Trilafon) in addition to the antidepressive drug. The usual proportion is 1 mg. of trifluoperazine for every 10 mg. of tranylcypromine; such a combination tablet is not yet available commercially. Although the piperazine compounds are potent, these small amounts cause no trouble, while they do appear to enhance the antidepressant action.

Improvement usually begins to become apparent within the first week or ten days, although some patients need longer than this. The important point is that the patient should be kept on the medication two or three weeks if any sign of improvement occurs. The medicine is well tolerated by patients over a period of many months, and benefits which the patient derives appear to be sustained. Tranylcypromine is much easier to administer than the hydrazine MAO inhibitors, since it has little cumulative action, and thus the dosage is less troublesome to regulate. Because of its relative rapidity of action and safety, it is the first antidepressive drug to try in nonagitated patients.

There are very few troublesome side reactions with tranylcypromine. Overstimulation with insomnia may trouble some persons, and for this reason some patients do not continue on the drug. Postural hypotension, which may result in palpitation, dizziness, and even fainting, is temporarily disturbing to some patients, even though they may respond favorably otherwise. This side reaction can be managed by reducing the dose for a few days and then slowly increasing it.

As with other drugs of this type, other treatment procedures (psychotherapy and environmental treatment) should be used concurrently. The medication should be decreased slowly and under supervision after the patient has held his improvement for several weeks.

As mentioned above, it is logical to give a retarded, psychotic, depressed patient treatment with a relatively safe and rapid-acting drug such as tranylcypromine. Though this compound has only recently become available, it is apparent that it has definite advantages over the hydrazine type of MAO inhibitors; two of these, iproniazid and pheniprazine, have been taken off the market because of serious liver toxicity. The three which remain are isocarboxazid (Marplan), phenelzine (Nardil), and nialamide (Niamid).

The hydrazines have the following disadvantages: (1) they are not as potent as tranylcypromine, (2) they are much slower in action, and (3) they are much more likely to have disturbing side reactions. The hydrazines may be used immediately after tranylcypromine without danger. At the state of our present knowledge, however, it does not seem likely that they will be successful in very many patients where tranylcypromine is not. Further study on this problem will be necessary.

2. *CNS depressors.* There are many psychotic depressions which do not respond favorably to the MAO inhibitors. If circumstances warrant, the physician may wish to treat the patient with imipramine or amitriptyline before concluding that pharmacologic therapy will not benefit the patient. However, it is not safe to give imipramine or amitriptyline immediately after or in conjunction with any MAO inhibitor such as the hydrazines or tranylcypromine lest a troublesome and potentially serious atropine-type of reaction is precipitated.

3. *Electroshock therapy.* This is often effective in relieving the symptoms of recurrent depressions. There are many puzzling instances, however, in which it fails or in which the benefit is very short-lived. Unfortunately, electroshock appears to do nothing to prevent the recurrence of subsequent attacks. Maintenance electroshock once or twice a month apparently does have

some ability to lessen the cycle of attacks, but it must be kept up indefinitely, and, in the opinion of many patients, the treatment is just as bad as the disease.

4. *Supportive care.* When indicated, supportive care such as afforded by occupational therapy, hospitalization, and activity programs is useful. Psychotherapy probably does not have the ability to relieve the symptoms of this type of depression nor have much effect on the frequency of its occurrence. However, a psychotherapeutic program can help the patient become better adjusted to life and to his disease and help him recognize the attacks more readily and seek treatment earlier. This may help him "roll with the punch," as it were.

III. DEPRESSIVE REACTION

By far the most common type of depressive disorder is that large group of heterogeneous conditions loosely held together under the official term "depressive reaction." These are more commonly referred to as neurotic depressions. The patients suffer from some combination of the following symptoms: anxiety, indecisiveness, restlessness, fatigue, lack of confidence, and difficulty in sleeping. The patients are usually worried and preoccupied with their troubles and may have bodily complaints, lack of appetite, loss of weight, and constipation. These patients do not have delusions or other psychotic symptoms, although they may become suicidal.

Etiology

Psychogenesis is believed to be important in the origin of these disorders. Situational stresses can be of real significance in setting off this milder form of depression. Examples would be the death of a loved one and calamitous business or personal difficulty. While the patient may have a nervous predisposition or susceptibility, much of the symptomatology appears to be acquired. Patients often give a history of a nervous temperament. Distress over personal failures, personal losses, or personal conflicts commonly leads to prolonged tension. This in turn commonly results in the development of a depression. These individuals often "hold in" excessively—that is, they have difficulty with feelings of aggression or hostility. This repressed hostility is often an important factor in the development of their symptoms.

Many depressions in this group are very mild and of short duration; many clear up without any treatment at all. Since the same statement may be made about the milder form of manic-depressive and recurrent depression, it is probable that these are often mistaken for each other, particularly if the first attack of recurrent depression is a mild one in a young individual and also if there are apparently significant precipitating factors or environmental stresses.

Treatment

1. *Psychotherapy.* Though drugs may be very helpful, psychotherapy and environmental management are the most fundamental treatment for these patients. Most mild depressions are self-limiting. If the patient has a stable personality make-up with a good family, well-balanced interests, and a reasonably good personality organization, he will probably recover within a few weeks or months. The patient may benefit considerably by confidential discussion of personal problems with a physician, a change of pace in daily living, and the like. If the patient does not respond as he should or if his depression is complicated by prior nervous problems which impair his personal efficiency, he should be referred to a psychotherapist. The following article in this series deals with the psychotherapeutic approach in more detail.[3]

2. *Drug therapy.* Pharmacologic therapy of the neurotic depressions can be used successfully and concurrently with psychotherapy and other procedures.

There are three distinct types of pharmacologic action which may be brought to bear in the treatment of nonpsychotic depression. Partly because of the inability to clearly differentiate among the many varieties of neurotic depression which exist, we are unable to predict which of these pharmacologic modes of action will be the most beneficial for a given patient. Some patients improve dramatically with certain pharmacologic therapies, while other symptomatically similar patients do not. Possibly the answer does not lie in a refinement of clinical diagnosis but will have to await the development of psychometric or physiologic measurements. At the present state of our knowledge, the physician must rely on the trial-and-error method to a considerable extent, although clinical guide lines are beginning to appear.

The following are some of the pharmacologic actions which may be taken:

a. *Indirect or bimodal CNS stimulants.* The drug of choice here is tranylcypromine. A combination tablet (Parstelin) of 10 mg. of tranylcypromine plus 1 mg. of trifluoperazine[4] has been used with success in a fairly high percentage of nonpsychotic depressions. The addition of

small amounts of a major tranquilizer such as trifluoperazine appears to make this medication particularly effective in patients with any anxiety symptoms or any schizoid elements in the illness. In fact, the most impressive results have been obtained with less favorable chronic neurotics. The dosage and administration are the same as described above.

b. *Simple sedatives and minor tranquilizers.*[1] If the patient is tense and not seriously depressed, he may obtain some relief from sedative drugs such as phenobarbital or the tranquilosedatives such as meprobamate, meprobamate plus benactazine (Deprol), or chlordiazipoxide (Librium). These and other minor tranquilizers are more popular than the older sedatives. Their main advantage is that they appear to be a bit smoother in operation. The possibility exists that there is as yet some unknown fundamental difference in their action. For example, the muscle relaxation afforded by those mentioned may account for much of their success in this field.

c. *CNS suppressants with complex autonomic action.* Imipramine and amitriptyline have a central nervous system suppressant action and complex autonomic and other effects which are as yet poorly understood. One would not expect this type of compound to be indicated in the simpler depressive reactions, but, surprisingly enough, some patients respond quite favorably to this type of medication. Possibly such cases are unrecognized depressions of the recurrent or manic-depressive type.

IV. PSEUDONEUROTIC SCHIZOPHRENIA (BORDERLINE SCHIZOPHRENIA, MASKED SCHIZOPHRENIA)

As indicated above, all depressive reactions are not alike, and there is one subgroup that is differentiated from the depressive group only with difficulty. These patients are included in the designation "pseudoneurotic schizophrenia." The concept of pseudoneurotic schizophrenia was described by Hoch and Polatin in 1949.[5] It has become increasingly valuable in helping the physician differentiate the more favorable psychoneuroses from these more serious conditions. Most simple neurotic depressions improve spontaneously or clear up readily with help; not so pseudoneurotic schizophrenia. This type of patient often presents a picture of chronic neurosis with depression that has been rather resistant to treatment. While these patients may have significant psychologic conflicts or situational difficulties which contribute to their illness, it seems likely that there is some personality deficiency, possibly on a genetic basis, which contributes to their continuing psychopathology.

Characteristics

This type of disorder is difficult to describe briefly. The patients often tend to be more withdrawn than neurotic patients. They show much more severe ambivalence which is diffuse and occurs in many areas. They show an emotional disturbance often characterized by great inconsistency. For example, they may have cold self-control most of the time and yet may be hypersensitive and react to minor situations while overlooking major difficulties. They have commonly expressed hostility to the family and tend to show pananxiety with many kinds of anxious symptoms, such as tensions, anorexia, palpitation, vomiting, poor sleep, phobias, excessive-compulsive mechanisms, and depression. They frequently have difficulty in deriving real pleasure from anything. During interviews, these patients are verbal and talk freely about their complaints but are often vague and contradictory and tell very little about themselves. They may have short-lived psychotic attacks ("micropsychosis").[5]

All this sums up to chronically unhappy individuals assailed with fears, compulsions, and depressive symptoms. It is postulated that they have an underlying schizophrenic disorder hidden by a facade of neurotic manifestations with mixtures of anxiety, phobias, obsessions, depressions, hypochondriacal concerns, and brief psychotic-like episodes. As indicated above, many of the pseudoneurotic schizophrenics are mistaken for chronic neurotics or patients with chronic neurotic depressions.

Treatment

Tranylcypromine plus trifluoperazine is the pharmacologic treatment of choice for these individuals, although they need psychotherapy in addition. In many cases, the results have been dramatic, even when patients have been ill for years and previously failed with extensive treatments including psychoanalytic therapy, many varieties of drugs, electroshock, and long periods of hospitalization.

Pseudoneurotic schizophrenia, particularly in its milder forms, is a common disturbance. Patients with this disorder constitute a major medical problem, partly because they are characteristically refractory to treatment. However, these patients should not be confused with those with traditional schizophrenia. Patients with inactive and depressed forms of schizophrenia may benefit somewhat from tranylcypromine, but in

these cases large amounts of a phenothiazine and long-continued psychiatric management are also required.

SUMMARY

Although we cannot clearly differentiate among the varieties of depression nor predict therapeutic results, we can expect a pattern of responses:

1. Agitated depressions need physiologic therapy. Suppressant-type antidepressive drugs such as imipramine combined with a phenothiazine are the first choice. Such drugs have the disadvantage of being slow and uncertain. Nevertheless, electroshock should be reserved for those who fail on drug therapy.

2. In other types of psychotic depressions, MAO inhibitors have a good record. The preferred drug is tranylcypromine because of its safety and rapidity of action. Some patients will do better with imipramine or electroshock treatment.

3. In nonpsychotic or neurotic depressions, the best method is psychotherapy. Antidepressant drugs are an effective aid to psychotherapy and may do much to relieve the patient's discomfort. Three distinct pharmacologic actions may be used: (1) bimodal central nervous system stimulation; (2) simple sedation or tranquilosedation; (3) central nervous system suppressants with major autonomic effects. It cannot be predicted which of these three will give the patient relief or assistance. The bimodal stimulation of tranylcypromine is most likely to be helpful.

4. In pseudoneurotic schizophrenia, a serious psychotic type of personality deficiency is masked by a facade of neurotic symptoms including anxieties, phobias, and depression. Such patients make only a limited response to psychotherapy alone or to electroshock and most forms of drug therapy. However, they often improve dramatically with tranylcypromine plus trifluoperazine, after which they may be able to benefit from psychotherapy.

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Examination of bone marrow is useful for detecting metastasis and for differentiating malignant disease from primary hematologic disease. In addition, marrow findings aid selection and assessment of cancer therapy. Radical surgery may be futile if the marrow contains tumor cells.

Bone marrow is aspirated from the sternum with a syringe containing a small quantity of dilute heparin. If sternal aspiration is not successful, the posterior iliac crest is used. In some instances, specimens are obtained from sites of bone lesions revealed by roentgenograms. Sternal trephine biopsy is done if the aspirate contains only a few tumor cells.

Individual smears are made of 8 to 10 particles from the aspirate. The remaining marrow is centrifuged, and 4 or more smears are made from the buffy coat. The concentrated smear is most useful and is prepared even if no particles are obtained. A 9:1 mixture of Wright's and Giemsa stains is used for smears from bone marrow aspirates or trephine biopsies. Tissues are fixed in Zenker's solution with 5 per cent glacial acetic acid and stained with Giemsa and hematoxylin and eosin stains.

A syncytium or clump of tumor cells is diagnostic of malignant disease. If scattered abnormal cells are found, metastatic tumor can only be suspected. Sternal trephine biopsy generally shows malignant disease when satisfactory specimens cannot be aspirated from one or more sites.

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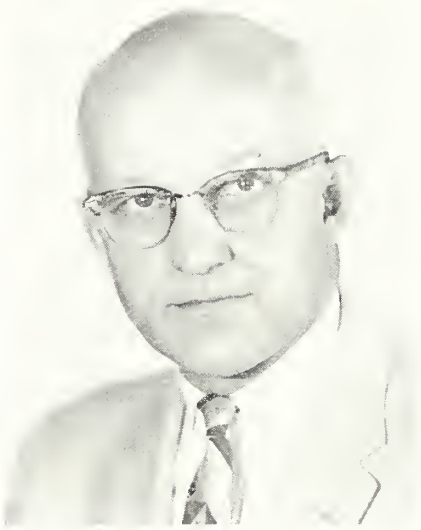

T. H. Harwood, M.D., F.A.C.P.

W. E. CORNATZER, Ph.D., M.D., F.A.C.P.
Grand Forks, North Dakota

Dr. Theodore H. Harwood came to North Dakota from Vermont to become dean of the University of North Dakota School of Medicine in 1953. The son of Elmer and Emma Harwood, he was born in Dorset, Vermont, in 1911, one of a family of 4. The Harwood family has contributed much to the practice of medicine throughout the years. In fact, Dean Harwood has 2 brothers practicing medicine.

After attending Burr and Burton Seminary in Manchester, New Hampshire, Dr. Harwood attended Hamilton College in Clinton, New York, receiving his bachelor of arts degree in 1932. He obtained his doctor of medicine degree from the University of Vermont in 1936, was a fellow in medicine at the Lahey Clinic in Boston in 1937, and was assistant resident in medicine at the Royal Victoria Hospital in Montreal. He returned to the Vermont College of Medicine in 1939 as resident in medicine, and his interest in teaching led him to accept an appointment as assistant professor in medicine in 1940. He was made associate professor in 1947.

In recognition of his administrative abilities, Dr. Harwood was appointed assistant dean of the College of Medicine, University of Vermont, in 1950. He held this position until he went to the University of North Dakota. He is a diplomate of the National Board of Medical Examiners and was certified by the American Board of Internal Medicine in 1943. Dr. Harwood was secretary of the Vermont State Medical Society from 1943 to 1945 and president of the Chittenden County Medical Society in 1951 and 1952.

In looking for a man to fill the position of dean upon the resignation of Dr. Wilbur Potter, the administration of the University of North Dakota saw in Dr. Harwood a man familiar with the problem of medical education in a sparsely populated state, similar to North Dakota, which was able financially to support a medical school. Dr. Harwood was already familiar with the University of North Dakota School of Medicine, for he first visited the state as a member of the Accreditation Survey Team from the Association of American Medical Colleges in September 1951.

Dr. Harwood began a diligent study of medicine in the state and undertook to clarify the role of the two-year medical school. With the growth of the University of North Dakota from 2,000 to 4,000 students, the two-year school has expanded into undergraduate and graduate courses. Since 1953, the preclinical sciences in the School of Medicine have awarded 7 Ph.D.'s—3 in biochemistry, 1 in anatomy, and 1 in pharmacology.

Dr. Harwood's objective has been to maintain the highest scholastic standards and the accumulation of a faculty for teaching and research. His office took over the admission problem, and Dean Harwood has been constantly working toward improving undergraduate premedicine. The dean's office has always been open to students and understanding of their problems, regardless of what they might be.

Under Dean Harwood's direction, the Medical School faculty began participating in lectures for general practitioners at the annual meeting of the North Dakota Association of General Practitioners. As evidence of his interest in medicine in the state and the role the Medical School might play in this, he was made a member of the State Health Planning Committee, the Blue Cross Board of Trustees, and the Governor's Committee on Aging and Rehabilitation.

Dean Harwood's interest in and study of the financial needs of the medical students led the North Dakota Legislature to pass a bill providing an annual

$75,000 loan fund for junior and senior students. Qualified students can borrow $2,000 per year from this fund. The objectives of this fund were to help bring back North Dakota boys for the practice of medicine. Many states have similar legislative bills.

Dr. Harwood has a great interest in the growth of the Medical School and has helped to attract and keep a superior preclinical faculty. His office has obtained funds for medical students to do research for faculty members during the summer months. During his administration, expansion of the research facilities of the Medical School has taken place, with the establishment of the $260,000 Ireland Research Laboratory in Biochemistry in 1959. Dean Harwood has helped to obtain the first full-time research professor in the Medical School in biochemistry with a grant from the Hill Foundation of St. Paul.

During his administration, the Medical Center has expanded to include a School of Nursing and a Rehabilitation Center. The University took over the Deaconess Hospital School of Nursing and has assembled a faculty for the school on the campus of the University. The Rehabilitation Center was constructed on a federal matching fund basis at a cost of $350,000 and was completed in 1958.

Dean Harwood's interest in research and the role of the Medical School in health agencies is evident by the fact that he holds membership in the North Dakota Cancer Society, Tuberculosis and Health Association, Society of Crippled Children and Adults, and North Dakota Academy of Science. He has served as a member of the executive committee of many of these organizations.

Dr. Harwood was married to Laura Jean Lathrop in 1936. They have 3 children: Judith Ann, a graduate of the University of North Dakota in June 1960; Theodore H., Jr.; and William Lathrop. Dean Harwood's hobby is his students. However, he is always ready to play his guitar and sing folk songs, and he is a member of the Presbyterian Church Choir.

Transactions of the North Dakota State Medical Association

SEVENTY-FOURTH ANNUAL MEETING

Fargo, North Dakota, May 6, 7, 8 and 9, 1961

(Continued from the October Issue)

Committee on Emergency Medical Service

A meeting of this committee was held on January 22, 1961, at the Gardner Hotel, Fargo, with the following members present: Drs. Ralph Mahowald, chairman, D. W. Palmer, W. B. Huntley, and Charles Graham. Others present were W. Van Heuvelen, Leonard Caverly, F. E. Murphy, and George Michaelson.

The meeting was opened by the chairman with a presentation of the priority needs and a summary of the check-points of the program. He noted that emergency medical service under the heading of civil defense needs would have to be judged by 3 criteria: Is it feasible? Will it overcome the unquestioned apathy? Does it meet the clearly great need?

The chairman said that the district medical societies will have to assume the leadership and teach the paramedical disciplines what medical defense is and what each group will be expected to do in emergency.

Mr. W. Van Heuvelen summarized the progress made in civil defense by the various parts of the State Health Department. Substantial progress has been made with plans in sanitation and nursing, and local community authorities had made plans for disaster programs. To his knowledge, no progress has been made with medical disaster. No complete civil defense program can be made without a staff; there is no full-time civil defense staff in the State Health Department, none at state, county, or city levels. A survey of the towns in the state as to terrain and underground water systems was completed some time ago, and good progress had been made in standardization of city equipment and fire materials. The State Health Department has one staff member who has had experience in dealing with atomic bomb testing and preventive measures. Staff members at the department have had regular civil defense training sessions, making full use of pooled knowledge and furthering cooperation of one department with another.

He noted that one of the greatest needs is local organization. The state plan book is completed and is on file in the State Health Department. The department has had joint meetings with Minnesota on the subject of

receiving evacuees into North Dakota. Manpower conferences have been held throughout the state and the organizations involved have distributed materials prepared by Washington on all phases of civil defense. Twenty-nine counties are organized for disaster nursing and county nurses have put a great deal of effort into the project called "How You Will Survive."

Van Heuvelen noted that 2 of the more pressing problems under consideration are mass feeding in case of disaster and the dissemination of information about sanitation. Dr. Huntley announced that there have been several disaster exercises in the Minot area and that all 3 hospitals in that city have their outline of action ready. Three trial runs were held with 60 children as simulated victims descending on the hospital.

Mr. Murphy, of the civil defense hospital group, announced the appointment of 4 directors for 4 areas in the state, assuring better coverage in the state. The civil defense staff is now on the merit system.

He presented a summary of the disaster hospital unit. There are 10 civil defense hospitals in the state stored in various cities and 2 more are set to be delivered. The hospital costs $27,400 and contains enough medical supplies for three to five days and a 200-bed capacity. They are being established in schools, public buildings, etc., in certain communities. Murphy's group has separated the emergency hospital unit into four 50-bed units to serve the smaller population areas since no smaller city has a place large enough to use 200 beds at one time. He reminded the committee of the January 24, 1959, issue of the J.A.M.A. which was devoted entirely to civil defense, and he announced that a new kit for preparing training aids is now available.

The committee agreed that the Walking Blood Bank was essential to a well-constructed plan and that preparation in Minot and Grand Forks was unique because of the air bases in those areas.

It was also agreed that ambulance drivers and assistants, police, and fire departments need additional first-aid training. The highway patrol has gone ahead in this area with a meeting in each of the 8 districts.

Dr. Palmer agreed that the Devils Lake area needs to split the emergency hospital unit into 50-bed sections because of the size of the communities in the area.

The chairman announced that only one critical target area, the Garrison Dam, was listed in North Dakota now, because Minot, Fargo, Grand Forks, and Bismarck have been taken from the list.

The committee agreed that the proposed congressional action to transfer civil defense into the National Guard was a bad bill because the National Guard would be gone from the state in a national emergency. It was further agreed that no state plan should be built around integration of guard or reserve elements because they will have a primary mission which cannot be relied upon to implement a state plan.

The committee agreed on the following basics of civil defense to be carried out in every hospital in the state:

1. Proper experience and adequate installation of the emergency hospital unit.

2. Sufficient supply of drugs and blood for a long-time disaster. This will be further expanded in detail.

3. Nursing service organization which would include controls over supply of nurses and other paramedical services.

4. Coordination of plans with the military.

5. Communications systems which can be put into use in emergency.

6. A transportation system for emergency.

7. A plan for emergency information dissemination to the public.

8. Organization of disaster teams for other communities.

9. Development and practice of evacuation procedures.

10. Consideration of first-aid teaching for firemen, policemen, ambulance personnel, and mortuary personnel; availability of first aid generally through Red Cross or medically-sponsored classes for the general public.

11. Urging the medical profession to read and use the J.A.M.A. of January 24, 1959, which is devoted entirely to the problem of Emergency Medical Care and its problems.

The chairman requested that each member of the committee develop a plan of action for the committee in implementing the civic and emergency needs and submit it to the chairman by March 1. He will summarize them and return the summary to the committee members for comments, then submit the suggested actions to the House of Delegates for approval.

RALPH MAHOWALD, M.D., Chairman

Report of the Delegate to the American Medical Association

Your delegate attended all sessions of the House of Delegates last year and many other meetings in connection with service on the Council on Medical Service and various committees of the association.

At the annual meeting in Miami Beach in June, I had the privilege of placing in nomination for the office of president-elect, Dr. Leonard Larson of Bismarck. As you know, he was elected by unanimous vote of the House and will assume the office of president at the annual meeting in New York next June. I'm sure we are all proud to have a member of the North Dakota State Medical Association occupy the highest office in American medicine. We know that Leonard is completely worthy of this office and will continue to be a great leader for medicine. He is going to need the wholehearted support of the entire medical profession during his year of service which may well prove to be the most critical year that we have ever faced.

For many years your attention has been directed to the fact that there is a continuous battle being waged for control of the medical profession, the practice of medicine, and the associated agencies involved in the care of the sick. During recent years this has been conducted at a stepped-up pace by a small, well-organized and highly vocal group well known to most of us. Leadership of this group comes from the ranks of union labor leaders, politicians, and increasingly from writers, reporters, newspapers, radio and television news purveyors. There is little evidence to show that this movement has the support of people as a whole.

The campaign against us is carried out in several different ways and, due to recent political developments, a number of the rabid leaders of this group are now in responsible positions in the federal government. As a major feature of the struggle for political control of medical and related care, we are being subjected to aggressive propaganda to downgrade our profession in the public eye. Attempts are being made by many to portray the doctor and allied health workers as mere technicians who, whenever results are not up to expectations, must have failed in the proper application of technical procedures.

Other unfavorable images of the profession regularly appear in periodicals, on the stage, TV, radio, and in novels. Sometimes, in reading the current crop of plays and novels, one is led to the belief that much that is best in our society is held up to ridicule, while dope addicts, gunmen, alcoholics and prostitutes seem to be glorified.

If the public attitude of general respect for the aims and aspirations of our profession can be changed to one of mistrust and suspicion, then the politicians will receive sufficient support so that they can take over control. Regrettably, this movement has become so effective that many talented young people are seriously questioning and, in many instances, rejecting medicine as a profession for them to enter.

There have been a good many questions both within the organization and among our general membership as to how effective we have been in meeting this tremendous barrage of criticism. It must be admitted that, in the past few months, we have had some extremely unhappy experiences, notably at the White House Conference and in a radio broadcast. Unfortunately, we are continually being placed on the defensive by these people who ignore all constructive accomplishments of the Association and endeavor to show that we are perhaps not completely worthy of the public's support. I regret that I do not know the complete answer to this, but it will be necessary for the Association to orient its thinking and practices to more effectively counteract this destructive propaganda.

We are again faced with the all-out attempt of the present administration to impose on this country a socialized medicine program under the Social Security System. The purpose of this program is not to provide medical care or even hospital care for the aged who need it, but to provide a federal mechanism on which can be built a complete socialized medicine program. It is believed that definite action will not be taken on this proposal at this session of Congress but it will have to be definitely decided during the next session.

Despite the formidable assaults on the integrity of the Association and its members we continue to devote most of the funds and energies of the Association to the promulgation of programs for the betterment of the health of the people.

At the December Washington session, the Council on Medical Education and Hospitals proposed and the House adopted an extensive program for help in recruiting qualified persons to enter the medical profession. As you know, the competition for top students in other fields has been detrimental to the supply of medical students. Accordingly, the A.M.A. has now set up two programs.

1. The formation of an honor scholar group composed of top students planning to enter medicine and the awarding of 50 scholarships in the amount of $1,000 per year to the members of this group whose need is greatest.

2. The A.M.A. will inaugurate and financially support a guaranteed loan program under which students in need may borrow money from their own bank, repayment of which is guaranteed by the A.M.A. fund.

Other recommendations which will be made by this council will include re-study of the medical curriculum and plans for better payment of interns and residents.

A three-year study conducted by the Committee on Medical Facilities of the Council on Medical Service was adopted by the House in Washington. This study points out that there is an increasing number of physicians engaged in professional activity other than private practice. It also notes that the membership in the A.M.A. for this group of physicians is rather low. Certain recommendations for improvement of this condition were adopted and these recommendations are now being forwarded to each state and county society. It is hoped that activity in the membership area will result in a stronger association.

At the same meeting, it was decided that the dues will have to be increased and the House adopted a report suggesting that there be an increase in the annual dues of $20 to be implemented over a period of two years: $10 on January 1, 1962, and $10 additional on January 1, 1963.

Again, at Washington, the House directed the Board of Trustees to proceed with an active program for national leadership in the prepayment insurance field. As a result of this directive, a number of meetings have been held and an active national organization representing the A.M.A., Blue Shield, and some related groups is being formed.

The Association has continued to be extremely active in supplying leadership and direction to those states which have been setting up provisions for implementation of the Kerr-Mills bill. The general provisions of this bill were originally suggested by the Committee on Indigent Care of the Council on Medical Service and much of the bill represents Association thinking. North Dakota is one of the first states to provide the necessary legislation to implement this bill, which is a sensible and constructive method to aid those who need aid and avoid the pitfalls of federal controls.

The complete reports of the actions of the House have been published in the J.A.M.A. and I would heartily recommend their perusal by our membership.

Again let me say that it has been a real privilege to serve as your delegate during the past year. While it is quite true that the officers and council and committee members of your Association have not been notably successful in solving all of the perplexing problems facing us, it is not for lack of effort and good will. As you all realize, we are faced with social changes and changes in attitude that are difficult to understand and deal with. I assure you that those who hold office have every intention of facing these problems and attempting their solution in as intelligent a manner as possible.

W. A. Wright, M.D., Delegate

NEW BUSINESS

Speaker Dodds read, in part, a communication from Mr. Penberthy, district supervisor of the Bureau of Narcotics, regarding a resolution which deals with the ambulatory treatment of narcotics addicts. One paragraph of Mr. Penberthy's letter stated, "I am attaching a copy of a draft form for your information. At the present time I have on my mind ambulatory treatment of addicts. To such a proposal, the Narcotics Division is very much opposed."

This correspondence and form of resolution was referred to the Committee on Resolutions for their action.

At the direction of the Devils Lake District Medical Society, Dr. Mahoney proposed a question to the Delegates. "Why does the Medical Advisory Board to the Medical Center and the Board of Higher Education feel it is wise to spend over $200,000 of the Medical Center 1-mill levy fund to expand the Rehabilitation Center? In view of the luke-warm acceptances of the present facility by the medical profession, it would seem reasonable to have polled the doctors of the state for their ideas on the matter of expansion of this facility. In view of the continuing loss of top-grade medical school staff, largely because of a non-competitive pay scale, it would appear that the medical center mill levy fund is being used in a questionable manner." This was posed as a question for open discussion which Dr. Ma-

honey was instructed to take back to the district society.

This proposal was referred to the Committee to consider the reports of the Medical Center Advisory Council and the Committee on Medical Education.

At the request of the chairman of the Medical Economics Committee, Dr. Nugent introduced a supplementary report of that committee, as follows:

Supplementary Report of Medical Economics Committee

At a meeting of the Medical Economics Committee held in Bismarck, April 15, 1961, the following resolution was adopted for presentation to the State Welfare Board:

RESOLUTION

The Committee on Medical Economics of the North Dakota State Medical Association resolved to offer the professional services of the members of the Association for recipients under the Medical Assistance to the Aged program, based on the present lowest fee schedule of the North Dakota Blue Shield, namely Plan A.

It was further resolved that a 10 per cent reduction of the Plan A fees will be given for services rendered to the recipients qualified under the provisions of Senate Bill 227 as passed by the 37th legislative assembly of North Dakota and signed by Governor Guy in March, 1961.

On a separate motion adopted unanimously by this committee, it was agreed that the resolution previously adopted concerning fees for services rendered MAA recipients be the first and final offer on the part of this committee in negotiating with the Public Welfare Board of North Dakota.

C. H. Peters, M.D., Chairman

The chair referred this supplementary report to the Reference Committee to consider the report of the Committee on Medical Economics, Dr. Burt, chairman.

Dr. Nugent presented a communication received by the executive secretary from Dr. Ralph O. Rychener, delegate to the American Medical Association from the section on ophthalmology, Tennessee State Medical Association, asking that the North Dakota State Medical Association consider the following resolution, and instruct the delegate to the A.M.A. from North Dakota, if we so wish.

RESOLUTION

Whereas, in 1959 there was introduced in the House of Delegates, Resolution No. 31 calling for the establishment of a Commission to Study the Relation of Medicine to Optometry, and to report to the House of Delegates, and

Whereas, the House of Delegates caused to be established a Subcommittee to Study the Relation of Medicine to Optometry, under the then Joint Committee to Study Paramedical Areas in Relation to Medicine; and

Whereas, the original Joint Committee to Study Paramedical Areas in Relation to Medicine has been succeeded by the Committee on Relationships of Medicine with Allied Health Professions and Services; and

Whereas, the optometrists are not ancillary to medicine, but are independent licensed practitioners, and therefore do not constitute an allied health profession; and

Whereas, there exists confusion in the public mind as to the distinction between medical care for patients with ocular complaints and optometric services; and

Whereas, the lack of understanding in this area is a threat to the welfare of the patient; therefore be it

Resolved that the House of Delegates establish a Commission on the Relation of Medicine to Optometry, to be appointed by the Speaker of the House; at least half the members of which commission shall be physicians practicing in the ophthalmological branch of medicine; and be it further

Resolved that it shall be the specific function of this Commission to conduct a broad study, from the standpoint of the public interest, of the problems involved in the present relation of medicine to optometry, and to explore all possible and desirable solutions to these problems; and be it further

Resolved that the Board of Trustees be requested to provide adequate personnel and funds for the proper performance of the duty assigned to this commission; and be it further

Resolved that this commission shall report to the House of Delegates not later than June, 1962.

The chair referred this to the Committee on Resolutions, Dr. Mahowald, chairman, and asked for further resolutions to be introduced.

Dr. Tudor presented a resolution from the Sixth District Medical Society, as follows:

RESOLUTION

Whereas, the complexity of claims submitted to Blue Cross, Blue Shield, commercial insurance carriers, and state and federal agencies, causes misunderstandings and confusions, and

Whereas, these matters could best be handled on the local level, where the hospitalization or visit to the physician's office occurred, and

Whereas, Blue Cross and Blue Shield have repeatedly asked for more and more cooperation in the handling and interpretation of their claims, and

Whereas, the Sixth District Medical Society has established such a review committee, now, therefore, be it

Resolved by the North Dakota State Medical Association that review committees be encouraged in each district medical society to handle these cases locally, and to assist physicians in the processing of their claims, and be it further

Resolved that the Council of the North Dakota State Medical Association implement this resolution through the direction of the councillors in each district.

The chairman referred this resolution to the chairman of the Committee on Resolutions, Dr. Mahowald.

Dr. Palmer next presented a resolution from the Devils Lake District Medical Society.

RESOLUTION

Under the date of March 2, 1961, the Devils Lake District Medical Society, in regular meeting, concluded a series of discussions with regard to contractual practice of medicine in the state of North Dakota and the following resolution was passed:

Be it resolved that the Devils Lake District Medical Society hereby reaffirms its belief in the right of all individuals to have free choice of physician for any medical and/or surgical treatment or any diagnostic procedure necessary for same, and be it further

Resolved that the North Dakota State Medical Association, through its Council, sponsor a bill at the next session of the North Dakota legislature, requiring any individual, company, corporation or society, giving, selling, or underwriting any form of diagnostic or treatment services to individuals or groups, be required to grant the privilege of free choice of physician in their contracts.

This resolution was referred to the Committee on Resolutions.

The chairman requested Dr. Christoferson to serve as a delegate from the first district in the absence of Dr. S. C. Bacheller, and to serve on the reference committee to consider the reports of the standing committees.

He instructed someone to contact Dr. Leigh with the request that he serve on the reference committee to consider the reports of the president, secretary, executive secretary, and treasurer.

The chairmen of the various reference committees were next called upon as to the time and place of their meetings.

Speaker Dodds presented to the assembled delegates the president of the Woman's Auxiliary to the North Dakota State Medical Association, Mrs. Robert W. McLean of Hillsboro.

Mrs. McLean: Mr. Speaker, members of the House of Delegates and guests: I am honored to bring you greetings from the Woman's Auxiliary and a brief report on our accomplishments of the past year.

To date, our membership totals 328. Our organization is made up of 10 districts, whose committees parallel yours. We adhere to the program outlined by our national organization, as it applies to our auxiliary. Geographical boundaries may limit some of our districts, but although their membership and program may be small, their enthusiasm is great.

"Legislation has been a major project for us, and we have worked as closely as possible with you, engaging in a campaign of letters to our congressmen, supporting the bills that would promote the advancement of medicine and public health, and working to defeat the legislation that would be detrimental to medicine.

"Our health careers program is active in several districts. This year the Future Nurses Club of Stutsman District received a certificate of honor from *Parents Magazine* in recognition of their community service.

"This is the fourth year we have supported the AAPS essay contest which we hoped would inspire high school students of our state to become interested in the national medical picture. Our endeavors have not met with success. We have found that this contest is not approved by the state board of education, nor is it disapproved. Although it has been welcomed in several schools, some teachers felt that the prizes were inadequate; others dwelt on the apathy of the student who will write only required themes. We invite your suggestions concerning our participation in this program.

"We have organized a committee on aging, and await your advice on how we can best serve you in this field.

"Community service has become a part of our everyday life, and it would be impossible to enumerate the hours spent by our members in the many facets of this work. Mental health receives our great interest and full support. Water safety and civil defense are also projects in which we are actively involved.

"We are happy to report that Sheyenne Valley is again a constituent auxiliary. For the past several years, they have had 5 members-at-large. This year they have reorganized and now have 13 active members.

"*News, Views, and Cues,* our State Auxiliary publication, is sent 4 times a year to our entire membership. In it are articles prepared by various state chairmen, district news items, editorials, and a message from the president of the State Medical Association.

"Financial aid in medical careers has long been a vital part of our program. We allotted $90 to the North Dakota chapter of SAMA. This year we contributed $815 to AMEF.

"The year 1961 marks the tenth anniversary of the sophomore student loan fund. Since its inception, the fund has provided aid to 53 students who had transferred from the University of North Dakota to a four-year medical school. Under the terms of the fund, no interest is charged until internship is completed, and then the rate is 2½ per cent. Loans are repaid one year later. This year the Woman's Auxiliary raised $2,352. Of this, $200 was a gift from Beth Rodgers in memory of her late husband. Our net assets for the past ten years now total over $20,000. This fund will remain an important project of the Auxiliary until the day when it can be self-supporting.

"We continue to look to you for guidance, encouragement, and assistance. All of us are grateful for the cooperation you, your president, Dr. Lund, Mr. Limond and his staff and Mr. Michaelson have given us. We are proud to be your auxiliary, and we hope we have served you well."

The secretary next read the names of the nominating committee as appointed by the president, Dr. Lund. Secretary Buckingham: Dr. W. E. G. Lancaster, chairman; Dr. R. H. Waldschmidt, Dr. O. A. Sedlak, and Dr. John Fawcett.

There being no further new business to come before the House, it was moved and seconded that the first session of the House of Delegates adjourn to reconvene at 2:00 P.M. on Sunday, May 7, 1961. Time of adjournment was 4:10 P.M.

PROCEEDINGS
Of the House of Delegates, Second Session

Speaker Dodds called the meeting to order at 2:00 P.M. The chairman of the Credentials Committee, Dr. Frank Melton, reported that there was a quorum present.

Secretary Buckingham called the roll. The following delegates and alternates responded:

Drs. A. C. Burt, Fargo; Frank M. Melton, Fargo; J. F. Houghton, Fargo; L. G. Pray, Fargo; Henry A. Norum, Fargo; Lee Christoferson, alternate, Fargo; J. H. Mahoney, Devils Lake; D. W. Palmer, Cando; G. L. Countryman, Grafton; Ralph Mahowald, Grand Forks, Robert Painter, Grand Forks; John Sandmeyer, Grand Forks; Richard Leigh, alternate, Grand Forks; F. D. Naegeli, Minot; A. F. Hammargren, Harvey; B. Hordinsky, Drake; C. J. Klein, alternate, Valley City; Edmund Vinje, Hazen; R. H. Waldschmidt, alternate, Bismarck; M. A. K. Lommen, Bismarck; Milton Nugent, Bismarck; R. B. Tudor, Bismarck; J. N. Elsworth, Jamestown; John Van der Linde, Jamestown; Dean R. Strinden, Williston; Norman Ordahl, Dickinson; and James Little, Mayville.

There were 23 delegates and 4 alternates present. Also attending the meeting were:

Drs. W. A. Wright, E. H. Boerth, O. A. Sedlak, W. E. G. Lancaster, V. G. Borland, C. H. Peters, K. Foster, A. R. Gilsdorf, R. D. Nierling, G. Christianson, T. E. Pederson, J. D. Craven, C. J. Glaspel, R. W. McLean, E. J. Larson, C. M. Lund, Dean Harwood, O. W. Johnson, and Mr. Lyle Limond.

The chairman declared the second session of the House of Delegates officially in session. As there was no objection, the reading of the minutes of the first session was dispensed with. Dr. C. M. Lund, president of the state association, was next introduced.

DR. LUND: I do not have many remarks to make at this time. Tuesday afternoon I will tell you what I think the doctors should do. There are a few pleasant things about this office; one of them will follow in a moment in the presentation I will make here.

We are inclined to forget some of our responsibilities. I hope in the future I shall be aware of these responsibilities of the doctor. I cannot single out any one doctor in the state to thank him for the things he has done, for they have all helped. They have all shown a deep interest. We have so many doctors in our organization who will go like fire if you put them on some job.

I had a lot of time to talk to the legislators this year, and I would not be at all fair if I did not tell you of the many kind words said of Lyle, and the good work he has done in our legislature—it was really outstanding. Also, Dr. Peters was tireless in his work on legislation. However, it is not fair to single out any one person, as I want to thank all of you. When you are called upon, please offer your services to Dr. Boerth. I shall certainly do so.

I think one of the things we often forget is our educational fund, to which we should all contribute. Dr. Lancaster is a tireless worker on this fund. He always reminds one of the obligation to the American Medical Educational Fund. Another obligation is to our Medical School. Those of you who are friends of the Board of Higher Education, please speak for our instructors at

the school, and tell the board that we must have more money to hire top educators for our medical school.

I also want to tell you how much we appreciate the help we got from Blue Cross, Blue Shield, and the Hospital Association. We were attempting to form a group that could give us a little bit more power, and they responded well to our appeal. When they ask us for help we should help them.

The ladies of the Woman's Auxiliary also did a lot of work during the session of the legislature. They have a terrific amount of power there. They are looking for things to do and they want to know what they can do for the aged. It is amazing, the amount of funds they have given to the Student Loan Fund. They want to help us, so we should call upon them when we can do so.

I hope that we can have a flexible policy without sacrificing any of our medical principles. We will do our best to smack down anyone who comes into our state with any ideas of socialistic medicine. I am glad Dr. Boerth will be our next president, as he knows what is needed. I hope we can improve our intraprofessional relations.

And now, I have a very pleasant task to perform. I have here a check to Theodore H. Harwood, M.D.—a check representing gifts from the American Medical Educational Foundation for the amount of $5,096.62, made out to the Medical School, signed by Dr. Blasingame. I would like to call on Dr. Harwood and present him with this check.

Dean Harwood: Thank you, Dr. Lund, and my thanks to all of you people. I am pleased to say that this check is many times its face value to us, as it comes without strings attached. It comes available as a fund which we can use for purposes for which we cannot use the state funds, such as travel. According to the Board of Higher Education, regulations limit travel to one person from a department to any one meeting. Therefore, from our state funds we can send only one anatomist a year to a meeting. I have always insisted that this money is for that type of thing. I have had a battle each time we changed governors. These doctors work hard, and you know that, unless you can attend a meeting, you very rapidly get stale. This fund also enables us to entertain prospective medical students. We can put on a ball so that our freshmen and sophomores can get acquainted. This is worth many times the $5,096.62 which is the face value.

The first order of business was the report of the Reference Committee to consider the reports of the president, secretary, executive secretary, and treasurer.

Dr. Naegeli, chairman, presented the following reports and their discussions, which were adopted section by section and as a whole:

1. *Report of the president.* The Reference Committee commended the retiring president, Dr. Carroll M. Lund, for his energetic activity in behalf of the association in a variety of fields. Because of his efforts, and those of others whom he inspired, socialistic perversion of medical practice was prevented and action was taken resulting in the implementation of the Kerr-Mills bill by the legislature of the state of North Dakota. This is an act which will benefit all the people of North Dakota.

His periodic news letter kept all members informed concerning matters of vital concern. His timely visits to, and inspection of, public institutions served to remind state and local administrators of the association's continuing interest in these institutions and demonstrated to physicians one of the duties of every good citizen.

His attendance at local, regional, and national meetings gave evidence of his and our interest with current medical and social problems. For these and other reasons, the Reference committee wishes to commend Dr. Lund for his untiring efforts on behalf of the association.

The Reference Committee agreed with the president that enlargement of the state headquarters and its staff would be desirable. Because this would involve considerable long-range planning and financing, the committee felt that the incoming president might wish to delegate such considerations to the Council, or an existing committee, or appoint a new one.

Without detracting from the praise of Dr. Lund, the committee wished to mention the activities of another dedicated and effective spokesman, a vigorous defender of the interests of the association, Dr. C. H. Peters. He and his Medical Economics Committee, their negotiations with the various state and federal agencies which the association serves, and the many hours spent with members of our legislature during its recent session, all demonstrate the sort of organized effort which the association must continue to have. The members more than held the line during the past year, but each year our responsibilities and the forces opposing them will increase. This portion of the report was adopted.

2. *Report of the secretary.* The Reference Committee reviewed the secretary's report and noted the significant number of unpaid dues. The committee suggested that all members resolve that such financial delinquency shall cease. It was suggested that the new secretary make a study of other states and see whether any more effective way of collecting dues exists. This portion of the report was adopted.

3. *Report of the executive secretary.* The Reference Committee studied the report of the executive secretary and commended Mr. Limond for the courteous and effective way in which he carried out the duties of his office and the directives of the association's officers and committees.

With respect to the public relations program of the association, the committee suggested that consideration be given to a carefully planned campaign of publicity which will present to the lay public a true picture of organized medicine and the association's concern for continuation of personalized good medical care. There seems little doubt that carefully planned education and coordination of the efforts of para-medical and other professional groups would yield many understanding friends who would be most helpful in the coming decisive battle over the socialization of medical practice. This portion of the report was adopted.

4. *Report of the treasurer.* The committee studied the several reports and statements of the treasurer, and noted his careful stewardship of the association's funds. The committee commended Dr. Nierling for his diligence in the preservation and investment of these moneys. This portion of the report was adopted.

The motion was made by Dr. Naegeli and seconded by Dr. Nugent that the report be adopted as a whole.

F. D. Naegeli, M.D., Chairman
M. A. K. Lommen, M.D., Vice-Chairman
Richard Leigh, M.D.
F. M. Melton, M.D.
W. C. Hanewald, M.D.

Reference Committee to Consider the Reports of the Council, Councillors and Special Committees

Dr. Robert Tudor, chairman, presented the following

reports and their discussions, which were adopted section by section and as a whole:

1. *Report of the chairman of the Council.* The referenee committe reviewed the report of the chairman of the Counеil and approved this report. The Council was commended for its work during the past year. This portion of the report was adopted.

2. *Reports of the Councillors.* The reports of the Councillors were reviewed and approved. The councillors were commended for their fine reports. The committee urged that the Pap Smear survey recently done in Grand Forks be repeated in the other distriets.

The committee also emphasized that meetings with Republican and Demoeratie legislators should continue on a yearly basis. This portion of the report was adopted.

3. *Report of the Committee on Aging and Rehabilitation.* This report was reviewed and approved by the committee. This portion of the report was adopted.

4. *Report of the Committee on American Medical Education Foundation.* This report was reviewed and approved by the committee. This portion of the report was adopted.

5. *Report of the Committee on Cancer.* This report was reviewed and approved by the committee. This portion of the report was adopted.

6. *Report of the Committee on Cardiovascular Diseases.* This report was reviewed and approved by the committee. This portion of the report was adopted.

7. *Report of the Committee on Crippled Children.* This report was reviewed and approved by the committee. The Committee on Crippled Children was commended for its emphasis on a proper means test for C.C.S. patients and for its recommendation that counties participate financially in the C.C.S program. This portion of the report was adopted.

8. *Report of the Committee on Diabetes.* This report was reviewed and approved. This portion of the report was adopted.

9. *Report of the Committee on Emergency Medical Service.* This report was reviewed and approved. This portion of the report was adopted.

10. *Report of the Committee on Foreign Trained Physicians.* This report was reviewed and approved. This portion of the report was adopted.

11. *Report of the Committee on Liability Insurance.* This report was reviewed and approved. This portion of the report was adopted.

12. *Report of the Committee on Maternal and Child Welfare.* This report was reviewed and approved. This portion of the report was adopted.

13. *Report of the Committee on Mental Health.* This report was reviewed and approved. This portion of the report was adopted.

14. *Report of the Committee on School Health.* This report was reviewed and approved. This portion of the report was adopted.

15. *Report of the Committee on Veterans Medical Service.* This report was reviewed and approved. This portion of the report was adopted.

16. *Report of the Liaison Committee to Blue Cross-Blue Shield.* This report was reviewed and approved. This portion of the report was adopted.

17. *Report of the Liaison Committee to the North Dakota Pharmaceutical Association.* This report was reviewed and approved. This portion of the report was adopted.

18. *Report of the Liaison Committee to the State Board of Administration.* This report was reviewed and approved. This portion of the report was adopted.

19. *Report of the Medical Advisory Committee to the Public Welfare Board.* This report was reviewed and approved. This portion of the report was adopted.

20. *Report of the Representative to the North Dakota State Bar Association.* This report was reviewed and approved. This portion of the report was adopted.

21. *Report of the Representative to the North Dakota State Dental Association.* This report was reviewed and approved. This portion of the report was adopted.

22. *Report of the Representative to the State Health Planning Committee.* This report was reviewed and approved. This portion of the report was adopted.

Dr. R. B. Tudor moved that the report be adopted as a whole. Motion seconded by Dr. Little and carried.

R. B. Tudor, M.D., Chairman
R. C. Painter, M.D., Vice-Chairman
Henry A. Norum, M.D.
Clayton Jensen, M.D.
James Little, M.D.

Reference Committee to Consider the Reports of the Delegate to the AMA, Medical Center Advisory Council, and Committee on Medical Education

Dr. James Mahoney, chairman of this committee, presented the following reports and their discussions, which were adopted section by section and as a whole.

1. *Report of the Committee on Medical Education.* The report was reviewed and Dr. Berg and his committee were commended for the efforts and activities involving medical education. The Reference Committee approved the recommendation that students who return to North Dakota for internship be given credit on their student loans.

Approval was given the intention of the Medical Education Committee in protesting that foreign medical graduates are being treated more abruptly than diplomacy might find wise. Foreign medical graduates are leaders in under-privileged countries and efforts to keep these men friendly to our way of life is worthwhile.

The Committee on Medieal Education has been concerned with Dean Harwood's problems including salaries for the staff at the medical school. The Reference Committee approves and supports the attitude of the committee in desiring comparable and competitive salary and fringe benefits in relation to medical schools across the nation.

The committee has also taken an interest in the rehabilitation unit and the finanees involved. Dean Harwood was requested to take the floor and enlighten the House of Delegates concerning this matter at the close of the session, since many had expressed interest in rehabilitation activities.

Dr. Mahoney added a supplemental report of the Reference Committee in conjunction to that of the Committee on Medical Education, concerning the intent of Dr. Berg's letter. He believes that these people desirous of coming to this country might very well be tested and checked in their own countries and thus screened before they come over here. On the other hand, the people who are over here, even though they are incompetent, have been in training of some kind. If they fail the examination and have to return to their home countries without completing their training, they would be sitting ducks for our opponents.

This supplemental report was added by the Reference Committee because of what appeared to be a conflict between the report of the Committee on Foreign Trained Physicians and the Committee on Medical Education.

This portion of the report was adopted.

2. *Report of the Representative to the Medical Center Advisory Council.* The committee commended the representative on a most comprehensive report. It was felt that the entire report should be read by each delegate in the House and reported to the Home District Medical Society. Pertinent points which the committee felt should be drawn to the attention of the House of Delegates were:

1. The medical center has loaned 84 North Dakota medical students $260,000 to date.
2. The last legislature has instructed the center to include dental students in loans when needed.
3. The medical center has a training program in the field of psychiatry which may develop a greatly needed specialty for the people of the state of North Dakota.

After studying the very detailed report on the rehabilitation unit, the committee felt the practice of urging the patient admitted to consult the family physician first, should be required rather than strenuously urged. This portion of the report was adopted.

3. *Report of the delegate to the American Medical Association.* The committee commended Dr. Wright for his efforts on behalf of free medicine. His report should be read, for he points up the difficulties faced in the national picture. He has the humility to state in this report that he does not know all the answers, but that he is continuing to devote his energy to the promotion of plans and program for the betterment of the health of the people. This portion of the report was adopted.

Dr. Mahoney moved that the report be adopted as a whole. Motion seconded by Dr. Pray and carried.

James Mahoney, M.D., Chairman
L. G. Pray, M.D., Vice-Chairman
John Sandmeyer, M.D.
M. W. Garrison, M.D.

Reference Committee to Consider the Reports of the Standing Committees

Dr. Van der Linde, chairman, presented the following reports and their discussions, which were adopted section by section and as a whole.

1. *Report of the Committee on Necrology and Medical History.* The committee noted with deep sorrow the passing of some our beloved colleagues—namely, Dr. D. J. Halliday, Kenmare; Dr. A. C. Orr, Bismarck; Dr. G. F. Drew, Devils Lake; Dr. Bernard Uremi, Fargo; Dr. L. H. Kermott, Minot; Dr. R. W. Rodgers, Dickinson; Dr. H. E. French, Grand Forks; and Dr. A. L. Klein, Fargo. Dr. Van der Linde requested the delegates to show their respect to the departed members by standing a moment in silence. Moment of silence adopted this portion of the report.

2. *Report of the Committee on Legislation.* This report was reviewed and the committee noted with great appreciation the activities of the Legislative Committee during the past year, a legislative year. This committee was one of the most active and productive; the legislative score of 1961 bears testimony to its efforts. The committee recommended more interest and activity by doctors in politics. They pointed out that this year, and 1962, may be the critical years in which the future of medical practice will be determined, whether socialization or free private practice will prevail. A total of 54 bills in the state legislature were watched with interest, a summary of which is in the committee's report.

The committee concluded its report with the recommendation that more local political activity is needed to support the AMA's stand against social security medical legislation. This portion of the report was adopted.

Dr. O. W. Johnson, chairman of the Legislative Committee, was called upon for a few remarks on the work of the Legislative Committee.

Dr. O. W. Johnson: I think that most of you fellows are aware of the fact that we have a problem. Medicine has a problem but it is nothing new to anyone. As the House of Delegates, I feel that you are holding the whip insofar as medicine in North Dakota is concerned. There is an old saying that there is no triumph in retreat. Medicine has been retreating the past few years. The image of medicine has changed a great deal in the past twenty years. It is up to us to change this image for a better one, insofar as "Joe" public is concerned.

Your committee has done a very good job insofar as legislation is concerned. There are certain things that the American Medical Association has requested of us. I think, primarily, the directives have been issued to me because I am the key legislative man in the state of North Dakota. The American Medical Association is doing a commendable job in many places all over the United States, watching consistently what is happening. In the last congress, there were 720 bills reported to congress that specifically affect medicine. The ratio has increased tremendously. The bills affecting medicine in North Dakota were increased some this past year. Why people have become medically minded is difficult to explain except that most of you fellows carry a good sized liability insurance policy.

The thing we face at the present time is the King bill. It is nothing more than a glorified Forand bill. You all know about the Forand bill and what it meant. Now, we are faced with another bill, after the Forand bill. Apparently, this is going to be a permanent thing. I think you had a directive from the state office that this is socialized medicine. There are many things I could tell you about the analysis of this bill, but I do not think we should take your time to do this now. The essential points of the bill have been sent to all of you through the state office. This bill calls for benefits through the social security system to persons 65 years or older, and naturally calls for an increase in social security taxes. All services rendered to these people will be billed by the hospital, even physicians' services. Medicine has been left out of this bill on a calculated basis. This will also increase the allocation of money into the social security coffers of all self-employed people. This probably will not pass in 1961, but has an excellent chance of passing in 1962.

I think you owe a vote of thanks to Dr. Peters and the other fellows that were working at the legislative session this year. This past legislative session in North Dakota was more favorable to medicine than many that we have had in recent years. I do feel that you must become cognizant of the fact that other people are watching medicine and watching you as a doctor.

3. *Report of the Committee on Public Relations.* This report was reviewed and the Reference Committee noted with appreciation the great increase in interest and ac-

tivity of this committee. The report reviewed its mandate by the Council, and the House of Delegates Resolution of 1960, and its selection of a director of education and public information, Mr. George Michaelson. At one of its meetings, the committee was briefed by Mr. Charles Johnson of the AMA on 8 specific points of a public relations program. The Reference Committee strongly feels that our public relations are mainly the result of each doctor's relationship with his patients. If each doctor's relationship with his patient is in the best interest of the patient, if each doctor deals fairly with his patient professionally and economically, then our public image would be what we want it to be. The rest of the report summarized the planning activities of the committee, and the Reference Committee requested permission to ask Dr. Mahoney to report on the most recent activities and plans of this committee.

Dr. Mahoney: If I could express how I really feel about this program, it would take forty minutes. We need this program. I feel that in North Dakota we may be able to lead national a bit, if they do not change some of their programs. As I visualize public relations, we need a well-trained man to help us. In public relations we are faced with a difficult problem. We cannot reach perfection, but we are going to strive to improve.

We are apart from the rest of the world. We have the most valued profession in America. We are doctors of medicine. People need us and we are privileged to be of service to them. If we all remember we are doctors of medicine, then I think our district societies will become important. If this fraternity can spread over the entire state, we still will be taking care of people, and they will be coming to us and respecting us. I think we can all go along and have differences and settle them.

This portion of the report, including the addition of Dr. Mahoney's remarks, was adopted.

4. *Report of the Committee on Official Publication.* This report was reviewed and the Reference Committee strongly endorsed its recommendation that the North Dakota State Medical Association be recognized on the front cover of The Journal-Lancet since it is our official publication. They further endorsed the suggestion of the committee, that a copy of its report be sent to the publishers of The Journal-Lancet. This portion of the report was adopted.

5. *Report of the Committee on Public Health.* This report was reviewed, and its consideration of the rheumatic fever prophylaxis program was noted with interest. In response to the actions of the Committee on Cardiovascular Disease and the House of Delegates action in 1960, the committee reviewed and considered the rheumatic fever prophylaxis program; was briefed by State Health Department personnel; and polled all 10 members of the committee before making a recommendation. The program would be jointly sponsored and controlled by the Medical Association, State Health Department, the North Dakota Pharmaceutical Association and the North Dakota Heart Association. In addition to the proposed program given to the association, the Health Department suggested a registry of rheumatic fever patients in order to better supervise the project.

The Public Health Committee unanimously accepted the two projects, and recommended that the project as outlined for a secondary rheumatic fever prophylaxis program be endorsed by the association and that participation by individual physicians begin as soon as possible.

The committee recommended that Mr. Mosser of the State Health Department be asked to send to each physician in the state a suggested schedule of treatment of venereal disease, because of a rise in incidence of venereal disease.

The Reference Committee strongly recommended that the North Dakota State Medical Association urge the obtaining of a doctor for the position of state health officer, and that an adequate salary be provided in order to attract candidates of high quality.

It was noted that the rheumatic fever prophylaxis program had been brought up in other sessions and nothing done about it. Also, nothing was done regarding the resolution to hire a state health officer.

This portion of the report was adopted. The chairman instructed the secretary to see that the motion of the house goes to the chairman of this committee, with a note attached for immediate attention.

Dr. Van der Linde, chairman of the Reference Committee, moved the adoption of the report as a whole. Motion was seconded by Dr. Countryman and carried.

J. M. Van der Linde, M.D., Chairman
Lee Christoferson, M.D.
Dean R. Strinden, M.D.
B. Hordinsky, M.D.

Reference Committee to Consider Reports of the Committee on Medical Economics, Advisory Committee to Public Assistance, Division of State Welfare Board, Committee on Rural Health and the Governor's Health Planning Committee

Dr. A. C. Burt, chairman, presented the following reports and their discussions, which were adopted section by section and as a whole.

1. *Report of the Committee on Medical Economics.* This report was reviewed and the committee commended the Committee on Medical Economics and all others concerned for their exposure of the deficiency and inefficiency of the Saskatchewan Health Plan.

They regretted that Truman Wold's survey of hospital costs and utilization was not completed at this time. They recommended that the analysis be completed and that the results be cleared through the Medical Economics Committee and made available to the individual physician and the hospitals throughout the state. It was recommended that the Medical Economics Committee and/or the Council seek funds from Blue Cross and Blue Shield for the completion of this survey.

The reference committee approved of the relative value fee schedule and suggested that it be accepted in principle with any further studies necessary to eliminate any present inequities.

It was felt that credit should be given to Blue Cross and its administration for defeating the recent limiting legislation.

The Reference Committee appreciated the efforts of the Medical Economics Committee, and the individuals concerned, to negotiate with the Welfare Department. It was realized that these negotiations are difficult, if not impossible, with the present welfare administration, but the time has come to take a firm stand and insist that the relative value fee schedule of Plan A Blue Shield be accepted as the usual welfare fee schedule.

The Reference Committee suggested that the Medical Economics Committee complete negotiations with the Compensation Bureau to accept the Plan B schedule of Blue Shield.

It was recommended that the Kerr-Mills bill be supported and that the Plan A schedule of Blue Shield be applied to this service. This portion of the report was adopted.

Dr. Nugent: This recommendation, that the Plan A Group Blue Shield be in effect for the MAA and Welfare Board, I think should be given consideration, Mr. Speaker. Senate bill 227, the MAA bill, is known as the doctor's bill in North Dakota. It was brought in and sponsored by the Medical Association. It is true that the Welfare Board would bring in a bill to implement this bill at the eleventh hour, but it is questionable if they would have brought it in, if medicine had not gone in first. In this bill it was agreed that medicine would ask for a fee schedule on the basis of the customary fee for the local community for that comparable economic group. The limiting factors for MAA eligibility are an income of $1200 for a single person, and $1800 for a couple living together, and that they would not have assistance if their income was in excess of $2500. If we are to keep faith, we should consider passing it on this Plan A Blue Shield, less the 10 per cent that was recommended by the Medical Economics Committee. I think we are in the public eye and if at this time we ask for a lot more money than was proposed, we would put our chairman of the Medical Economics Committee in a difficult position.

Speaker Dodds: What you are saying, in effect, is that we use Plan A Blue Shield, less the 10 per cent. Before we take action on this, do you have a supplementary report, Dr. Burt?

There was no supplementary report, and Dr. Peters explained this Senate bill 227, and also the offer of the Committee on Medical Economics for a fee schedule to the State Welfare Board, which is Plan A Blue Shield, less a 10 per cent reduction in the fees for services rendered to the recipients qualified under the Medical Assistance to the Aged Program. He also stated that this fee schedule offer had already been given publicity.

Dr. Peters: If you turn the Medical Economics Committee down, and rule that the Plan A Blue Shield must prevail without the reduction, you will tie the hands of the Medical Economics Committee as far as making any future negotiations. I believe you can understand the problem that we are going to have in public relations and at the next session of the legislature. Many of these things have to be decided on the spot. There was no time to contact the Council or any other members of the Association. We had to decide this immediately. We made the offer of Plan A, minus 10 per cent. If we adopt this program, and the Public Welfare Board will take it, you have a relative value fee schedule, even though they do not call it that. We cannot negotiate, if you adopt the idea that this Plan A Blue Shield should be applied to this service.

Speaker Dodds: A few years ago the House gave the authority to the Medical Economics Committee to negotiate the fee schedules at whatever they saw fit. Should this sentence read "we recommend that the Kerr-Mills bill be supported," and delete the rest, or would you like an amendment to include the 10 per cent?

Dr. Peters: We ask that this resolution proposed be adopted by the House of Delegates because we wish official action to back our stand. I would like to see the resolution presented to the State Welfare Board—that the schedule of the North Dakota Blue Shield, namely Plan A, with a 10 per cent reduction of the Plan A fees, will be given for services rendered to the recipients qualified under the provisions of Senate bill 227, as passed by the 37th Legislative Assembly of North Dakota—adopted by this House of Delegates. I should also like the second motion—namely, that the resolution adopted concerning fees for services rendered—to be the first and final offer on the part of the Committee on Medical Economics. If those fees are not acceptable, that we take care of these people as we have in the past, there would be no physician's service under the MAA bill.

Dr. Borland: "I would like to reaffirm what Dr. Peters has said. Those of us who have been on the Economics Committee negotiating team feel very strongly that we should support this Blue Shield Plan A, minus 10 per cent. If the Welfare Board refuses to accept this plan, it would mean that there would be no physician's services provided under this Kerr-Mills bill. It would mean there would be no physicians filling out any forms, and they could not operate without any forms. We do feel that we have them where they will be forced to accept this Blue Shield Plan A, minus the 10 per cent."

Dr. Lancaster: I believe that the Welfare Board would not accept Plan A, but there is a possibility that they will accept the Plan A, less the 10 per cent. I believe we can afford to take care of these people under this discount. I might also say, it looks to me as if we have some of Dr. Mahoney's philosophy in front of us regarding public relations. Perhaps we would do ourselves some good by making a little personal sacrifice. I hope the Reference Committee will see fit to change this resolution recommendation.

Dr. Boerth: The director of the Public Welfare Department has taken over this MAA bill as their baby. They were the ones that were dragging their feet and that is why the Medical Economics Committee came out on this, and also the Committee on Legislation. I think it was the intent of the committee that they would accept Plan A Blue Shield with the 10 per cent reduction, if it was not to be made by the Welfare Board, but by the individual physicians of the state.

Speaker Dodds inquired of Dr. Burt, as chairman of the Reference Committee, if he cared to recommend that the Kerr-Mills bill be supported and that the Plan A schedule of Blue Shield, less 10 per cent, be accepted. Dr. Burt replied that this would be satisfactory.

Dr. Ordahl withdrew his second to the first motion of adoption of the first report. He stated that the delegates should stand behind Dr. Peters and those who made the Plan A, less 10 per cent contribution by the doctors of medicine. Dr. Burt, chairman of the Reference Committee, made the following recommendation: "We recommend that the Kerr-Mills bill be supported and that the Plan A schedule of Blue Shield, minus 10 per cent as a contribution by the medical profession, be applied." Dr. Burt moved the adoption of this portion of the report, seconded by Dr. Ordahl, and carried, and this portion of the report was adopted.

2. *Report of the Committee on Rural Health.* There was no report this year from the chairman of the Committee on Rural Health.

3. *Governor's Health Planning Committee.* Dr. Fawcett's report of the State Hospital Committee was read and approved, except that the Reference Committee questioned the advisability of adding hospital facilities for the rehabilitation center in Grand Forks. This portion of the report was adopted with the exception of the addition of hospital facilities.

Dr. Burt, chairman of the Reference Committee, moved that the report as a whole be adopted, with the

change in the Reference Committee report on the Medical Economics Committee report regarding the Plan A Blue Shield, less 10 per cent. The motion was seconded by Dr. Palmer and carried.

A. C. Burt, M.D., Chairman
G. L. Countryman, Vice-Chairman
Edmund Vinje, M.D.
Norman Ordahl, M.D.
D. W. Palmer, M.D.

Report of the Reference Committee on Resolutions

Dr. Ralph Mahowald, chairman of the committee, presented the following resolutions:

RESOLUTION

Whereas, the members of the North Dakota State Medical Association attending the Seventy-Fourth Annual Meeting of the Association in Fargo have enjoyed the hospitality and kindness of the fair city and,

Whereas, the mayor of Fargo and his associates, the press, radio, hotels, and businessmen have made this session a memorable one,

Now, therefore, be it resolved that the House of Delegates express its appreciation by directing a copy of this resolution to the Honorable Mayor of Fargo.

This resolution was adopted.

RESOLUTION

Whereas, the exhibitors have shown great effort and interest in this meeting and former meetings in developing their exhibits and adding to the scientific interest,

Now, therefore, be it resolved that the North Dakota State Medical Association extend to them a hearty welcome and thanks, and

Be it further resolved that a copy of this resolution be sent to each exhibitor.

This resolution was adopted.

RESOLUTION

Whereas, Dr. Carroll Lund, president of the North Dakota State Medical Association for the year 1960-61, has given unstintingly of his time in the service of the North Dakota State Medical Association and has devoted himself to the furthering of the interests of the association through his news letters, his extensive legislative activities, and his many visits to all of the state institutions involved in medical care, as well as visits to each component medical society,

Now, therefore, be it resolved that the assembled delegates show their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this resolution.

RESOLUTION

Whereas, the members of the Seventy-Fourth Annual Meeting of the North Dakota State Medical Association have thoroughly enjoyed and profited by the excellent scientific program, and

Whereas, the host, the First District Medical Society, and the various chairmen and committeemen have excelled in providing the members of the association with the niceties of a gracious convention,

Now, therefore, be it resolved that the assembled delegates demonstrate their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this resolution.

RESOLUTION

Whereas, the ladies of the Woman's Auxiliary of the North Dakota State Medical Association have, through diligent and continuous effort raised the sum of over $20,000 for the Medical Student Loan Fund of the Medical School of the University of North Dakota, and, in the past year, have raised the sum of $2,352, and further have donated $815 to the American Medical Educational Foundation, and

Whereas, these funds have enabled many medical students to complete their medical training, and

Whereas, these gifts and other meritorious services have won for them certificates from the American Medical Educational Foundation and *Today's Health,* and, in this past year, through sponsoring the Future Nurses Club of the Stutsman County District, received a certificate of honor from *Parent's Magazine* in recognition of their community service, and

Whereas, these accomplishments in general have made for continuing good will for the medical profession in North Dakota,

Now, therefore, be it resolved that the House of Delegates of the North Dakota State Medical Association convey to the Woman's Auxiliary of the Association, their appreciation and thanks for their excellent work, and

Be it further resolved that a copy of this resolution be directed to Mrs. Robert W. McLean and her successor.

This resolution was adopted with the request to Dr. Lund that he read it to the Woman's Auxiliary at the time of his address to them.

RESOLUTION

Whereas, Dr. Leonard Larson, president-elect of the American Medical Association, Dr. Willard Wright, North Dakota delegate to the American Medical Association, and Dr. C. J. Glaspel, secretary of the North Dakota State Board of Medical Examiners, have worked unselfishly for the medical profession and have brought honor to the North Dakota State Medical Association,

Now, therefore, be it resolved that this association take this opportunity to pay tribute to these men for their endeavors on behalf of the North Dakota State Medical Association, and

Be it further resolved that a copy of this resolution be forwarded to each of these physicians.

This resolution was adopted.

RESOLUTION

Whereas, in 1959 there was introduced in the House of Delegates of the American Medical Association Resolution No. 31 calling for the establishment of a commission to study the relation of medicine to optometry, and to report to the House of Delegates, and

Whereas, the House of Delegates caused to be established a subcommittee to study the relation of medicine to optometry, under the then joint committee to study paramedical areas in relation to medicine, and

Whereas, the original Joint Committee to study paramedical areas in relation to medicine has been succeeded by the Committee on Relationships of Medicine with Allied Health Professions and Services, and

Whereas, optometrists are not ancillary to medicine, but are independent licensed practitioners, and therefore, do not constitute an allied health profession, and

Whereas, there exists confusion in the public mind as to the distinction between medical care for patients with ocular complaints and optometric services; and

Whereas, the lack of understanding in this area is a threat to the welfare of the patient,

Now, therefore, be it resolved that the House of Delegates establish a commission on the relation of medicine to optometry, to be appointed by the Speaker of the House; at least half the members of which commission shall be physicians practicing in the ophthalmological branch of medicine; and

Be it further resolved that it shall be the specific function of this commission to conduct a broad study, from the standpoint of the public interest of the problems involved in the present relation of medicine to optometry, and to explore all possible and desirable solutions to these problems; and

Be it further resolved that the Board of Trustees be requested to provide adequate personnel and funds for the proper performance of the duty assigned to this Committee, and

Be it further resolved that this commission shall report to the House of Delegates not later than June, 1962.

Your Reference Committee on Resolutions and New Business, having studied the resolution referred by the delegate to the American Medical Association from the section on ophthalmology, feels that no action in regard to this resolution is indicated. The committee recognizes that the problem referred to in the resolution concerning the education of the public in regard to optometry is one which needs the attention of all physicians, and we urge our delegate to the American Medical Association to support such measures as will help solve this problem.

This portion of the report was adopted.

RESOLUTION

Under the date of March 2, 1961, the Devils Lake District Medical Society, in regular meeting, concluded a series of discussions with regard to contractual practice of medicine in the state of North Dakota and the following resolution was passed:

Be it resolved that the Devils Lake District Medical Society hereby reaffirms its belief in the right of all individuals to have free choice of physician for any medical and/or surgical treatment or any diagnostic procedure necessary for the same.

Be it further resolved that the North Dakota State Medical Association, through its Council, sponsor a bill at the next session of

the North Dakota legislature, requiring any individual, company, corporation or society, giving, selling, or underwriting any form of diagnostic or treatment services to individuals or groups, be required to grant the privilege of free choice of physician in their contracts.

The Committee on Resolutions requested that this be referred to the Legislative Committee for study and action to be reported back to the House of Delegates in one year when adequate legal consultation has been completed.

This portion of the report was adopted.

RESOLUTION

Whereas, the complexity of claims submitted to Blue Cross, Blue Shield, commercial insurance carriers, and state and federal agencies causes misunderstanding and confusion, and

Whereas, these matters could best be handled on the local level where the hospitalization or visit to the physician's office occurred,

Now, therefore, be it resolved that the North Dakota State Medical Association recommend and urge each district medical society to establish a claims committee on a rotating basis to process controversial claims, and

Be it further resolved that the councillor from each district be instructed to promote the establishment of such a committee in his district.

This resolution was adopted.

RESOLUTION

Whereas, there has been no practitioner of the year selection in North Dakota medicine, and

Whereas, this is a definite honor which should be established on an annual basis, and

Whereas, there is a national selection of the general practitioner of the year by the American Medical Association,

Be it therefore resolved that the president of the North Dakota State Medical Association shall instruct the Council to designate a committee to select a North Dakota physician to be "Practitioner of 1961," and

Be it further resolved that due publicity be given to the selection of this practitioner, and

Be it further resolved that this selection be submitted to the American Medical Association as a nominee for the selection of the Practitioner of the Year, prior to November 1, 1961.

This resolution was adopted.

RESOLUTION

Whereas, the American Medical Association and the American Bar Association have had committees studying the problem of narcotic drug addiction, and

Whereas, the only adequate and successful treatment of narcotic addiction necessitates constant control in a secure institution affording a drug-free environment, and

Whereas, experience has shown that treatment of narcotic addiction by means of various types of ambulatory clinic plans has been universally unsuccessful, impractical, and scientifically unsound, and

Whereas, in all attempts of treatment of narcotic addiction by ambulatory methods, addiction has in fact increased, therefore,

Be it resolved that the North Dakota State Medical Association express the opinion that the ambulatory clinic plan for the treatment of narcotic addiction is inadequate and medically unsound, and

Be it further resolved that the North Dakota State Medical Association's delegate to the American Medical Association be instructed to oppose the development of any such ambulatory treatment plans, although it is not intended in any way to oppose, after complete withdrawal, follow-up treatment at rehabilitation centers, and to support (1) measures designed to require the compulsory civil commitment of drug addicts for treatment in a drug-free institution, (2) to advance methods and measures toward rehabilitation of the addict, (3) to establish methods for the dissemination of factual information on narcotic addiction to the members of the medical profession, and (4) it is not intended in any way to oppose, after complete withdrawal, follow-up treatment at rehabilitation centers.

This resolution was adopted. The chairman requested the secretary to notify Mr. Penberthy of the narcotics division as to the passage of this resolution.

RESOLUTION

Whereas, the state legislature passed a bill authorizing the establishment of a mental health authority, and

Whereas, the mental health authority is to be under the direction of a certified psychiatrist, and

Whereas, the Committee on Medical Education feels that this is an essential step in providing the opportunity for a postgraduate training program in psychiatry for the state of North Dakota,

Now, therefore, be it resolved that the House of Delegates of the North Dakota State Medical Association instruct the president to appoint an ad hoc committee to meet with the State Health Council and urge the State Health Council to contact the American Psychiatric Association for assistance in obtaining a well qualified psychiatrist to fill this most important position.

This resolution was adopted.

RESOLUTION

Whereas, the present status of political activity in the National Congress continues to be a dangerous threat to medicine, and

Whereas, the present activity centered around the so-called King bill which is to be implemented by use of the social security approach, and

Whereas, it is felt that this is a directly unfavorable and a determined activity to decrease the maintenance of the best possible medical care of the people of the state of North Dakota,

Now, therefore, be it resolved that the North Dakota State Medical Association strongly oppose this and all like legislation and that the state representatives be directly informed of this action, and

Be it further resolved that the activity of the Legislative Committees of the district medical societies be strongly directed to step up activity among their members.

This resolution was adopted.

Dr. Mahowald made the motion that the report as a whole, with the deletion of the resolution being referred to the Legislative Committee, be adopted. Motion seconded by Dr. Nugent and carried.

SPEAKER DODDS: Dr. Harwood, I would like to call on you to answer a few questions that have come up at this meeting this afternoon.

DR. HARWOOD: I would like to tell you how much I have been impressed by this meeting. I tell my staff that they must do two things—police their own ranks and get into their medical society work. I feel that organized medicine is now working on positive programs and I am very happy to have this chance to hear what is going on.

The question has been brought up about the feasibility and desirability of adding to our rehabilitation unit. Our medical center, as you know, is set up very broadly. It is by law designed to educate medical students through the postgraduate field, train nurses and public health nurses, and educate ancillary medical personnel. It is to provide for treatment of indigent and other patients, and to coordinate and extend all facilities that pertain to the health and welfare of the people of North Dakota. It has been the function of the Medical Center Advisory Council to develop a program which stays within the law and which meets the needs of the university, the state, and the law.

We have a two-year medical school, and in the foreseeable future it will continue to be a two-year school. Each year from 2 to 4 of our class of 36 are honored by election to AOA, the national honorary medical society. In addition to the medical school, we are supporting a school of nursing, and we run a school of medical technologists. We have the North Dakota Blood Bank. We have developed a program of graduate education in the medical sciences now numbering 22 students. A research program was developed in the fields of anatomy, bacteriology, biochemistry, physiology, and pharmacology which has brought outside funds into the state. No taxpayer's money is used for research.

All of these programs are expensive and, with the exception of the blood bank, they have become more expensive as time goes on. The blood bank remains fairly

constant at a cost of $25,000 per year. It does provide service to the entire state as far as testing is concerned.

The mill levy which is the source of our funds is relatively consistent but it has been rising slightly. It was never adequate for a four-year school, but is more than enough for a two-year school. About six years ago, the legislature said we should use funds toward the development of a four-year school. The talk of a chronic disease hospital was mentioned but it did not seem we were short of hospital beds in North Dakota. A TB hospital was mentioned some time ago, but we thought it would be a foolish move to build such a hospital when they were being abandoned everywhere else. We thought it was feasible and desirable to have a rehabilitation unit as a teaching facility not only for medical students, but medical technologists, medical nurses, and speech and hearing trainees. So, an institution was built which was an out-patient 1-story facility, and 46 per cent of the cost was taken care of by federal funds. We thought this would be good for a teaching hospital as the hospitals in Grand Forks are not set up for this. We thought the rehabilitation unit would help with our training program. It is interesting to know that at the time we laid our plans, 12 other medical schools had started this same set-up.

Then we found that, in order to house a patient coming in from outside Grand Forks, we either had to use the hospital, which is expensive, or a motel or the University dormitory, which has its drawbacks. So, we ended up by having patients coming from the motels in taxis. Therefore, it seemed that inpatient housing was necessary to make this available to the people of North Dakota. Our case load has leveled off. It is not feasible to have patients coming in if they cannot be housed. Therefore, plans were made and approved to build 2 more floors to provide inpatient housing for rehabilitation patients.

I know rehabilitation is highly controversial. Every program is going through growing pains, but the percentage for rehabilitation is with us. Our division of vocational rehabilitation, not a part of the Medical Center, had been sending patients to Minnesota and elsewhere for evaluation and therapy because this was not available here. I believe it is going to be more and more a team approach with these chronically crippled people to get them up and around and self-sustaining.

One of the statements made was that we should use the money to bring up salaries. Salaries at the medical school, when we started out, were reasonably high compared with other school figures. Each year raises have been given but the raises elsewhere have outdistanced ours a bit, and last year we were in the lower bracket of the schools as far as salaries go. This year a substantial increase in salaries was approved by the board and will go into effect. I think they will have to go up next year, and the time may come when our medical center funds will not be adequate to keep up with all of these programs.

Our blood bank, our nurses' school, the student loan fund, our psychiatric training program—all of these programs have increased in cost with a relatively fixed income. I think the time will come when our income will not meet our needs. I do not think we can stop inflation at the medical school level. We feel we have been trying to carry out a program which will give our students the best of instruction and provide a service that is useful to the state.

If you have any questions, I will be glad to answer them.

A discussion among the various members followed, with questions directed to Dean Harwood concerning costs, etc.

Speaker Dodds thanked Dr. Harwood for his comments and expressed his appreciation for his appearance. He then called for any new business which should come before the house.

Dr. Lommen: Last year, as an instructed delegate, I brought up the matter of better relations with the Compensation Bureau, and, with your permission, I would respectfully request a report as to what action was taken, in regard to a paragraph on page 34 in the handbook in the report of the chairman of the Council, which is as follows: "A letter written to Governor Davis by a member of the State Medical Association citing 3 instances where the Workmen's Compensation Bureau had reacted unfavorably to his interests was brought to the attention of the Council. After some discussion, the chairman of the Council was instructed to set up a committee to meet with the Workmen's Compensation Bureau on this matter."

The chairman called on Dr. Borland, chairman of the Council, to determine what action was taken.

Dr. Borland: Dr. Toomey was designated as head of a 2-man committee and Dr. E. J. Larson served on this committee. These men met with the Workmen's Compensation Bureau on this matter and reported that they had a satisfactory discussion and the Workmen's Compensation Bureau would cease these unreasonable acts. This was not by-passed. The bureau was informed of this and they promised to do better in the future.

Dr. E. J. Larson: Dr. Borland appointed Dr. Toomey and myself to meet with the Workmen's Compensation Bureau. We met with them and reported back to the chairman of the Council, Dr. Borland, and to the governor. We were very favorably met by the Workmen's Compensation Bureau. Some of these matters were misunderstandings and some of those concerned did not understand the law. We felt we were given complete satisfaction and now feel that we can have a lot of confidence in the Workmen's Compensation Bureau. They want to be on good terms with the physicians. I do not think they will be hard to deal with if you just write to them.

The next item of business was the matter of dues for the ensuing year. The chairman was not aware of any request for a raise in dues. Dr. Tudor moved that the dues remain the same. Motion seconded by Dr. Mahoney and carried.

The next order of business was the selection of a meeting place in 1963, since we must select our meeting place two years in advance. The chairman stated any invitations for a meeting place in 1963 would be entertained.

Dr. Hanewald: The Southwest District Medical Society issues an invitation to the North Dakota State Medical Association to hold their 1963 meeting in Dickinson, North Dakota. (He also produced telegrams from the Chamber of Commerce, the mayor, and the Ray Hotel of Dickinson, urging the Medical Association to hold their meeting there.) There will be a new auditorium built in Dickinson which will have adequate space and facilities for the scientific exhibits and lectures.

Dr. Palmer moved that the 1963 annual meeting be held at Dickinson. Motion seconded by Dr. Ordahl and carried.

The next order of business was the report of the Nominating Committee, Dr. W. E. G. Lancaster, chairman, made the following nominations:

President	E. H. Boerth, Bismarck
President-elect	E. J. Larson, Jamestown
First vice-president	A. R. Gilsdorf, Dickinson
Second vice-president	G. A. Dodds, Fargo
Speaker of the House	Lee Christoferson, Fargo
Vice-speaker of the House	C. H. Peters, Bismarck
Secretary	William Buckingham, Bismarck
Treasurer	R. D. Nierling, Jamestown
Delegate to the AMA	W. A. Wright, Williston
Alternate delegate to the AMA	T. E. Pederson, Jamestown

COUNCILLORS

Second District	G. W. Toomey, Devils Lake
Seventh District	T. E. Pederson, Jamestown
Eighth District	J. D. Craven, Williston
Ninth District	Keith Foster, Dickinson
Councillor-at-large	C. M. Lund, Williston

BOARD OF MEDICAL EXAMINERS

C. H. Peters	Bismarck
Rudy Froeschle	Hazen
V. G. Borland	Fargo
F. D. Naegeli	Minot

Dr. Pray moved that the nominations be closed and that the secretary be instructed to cast a unanimous ballot for the nominees. Motion seconded by Dr. Palmer and carried and the nominees on the nominating report were unanimously elected.

There being no further business, the meeting was adjourned at 5:00 P.M.

Scientific Program

Monday, May 8

Fargo Civic Memorial Auditorium

8:30 to 9:30 A.M. Registration
9:15 to 9:30 A.M. Greetings from the president of the First District Medical Society
9:30 to 10:00 A.M. "Present Status of the Medical Center," T. H. Harwood, M.D., Grand Forks, dean of the School of Medicine, University of North Dakota
10:00 to 10:30 A.M. "Surgical Management of Deafness," Ekrem Gozum, M.D., Minot, North Dakota
10:30 to 11:15 A.M. Intermission
11:15 to 12:00 noon "A Doctor's Impression of the Saskatchewan Socialist Hospital and Medical Plan," Bruce McCannel, M.D., Regina, Saskatchewan

NOON RECESS

1:30 to 2:15 P.M. "Physiologic Principles of Fluid Therapy," Daniel C. Darrow, M.D., Kansas City, Kansas
2:15 to 3:00 P.M. "Practical Aspects in the Diagnosis of Congenital Heart Disease," P. A. Ongley, M.D., Rochester, Minnesota. (Sponsored by the North Dakota Heart Association)
3:00 to 3:15 P.M. Intermission
3:15 to 4:30 P.M. "The Indeterminate Lung Lesion," Thomas J. Kinsella, M.D., Minneapolis, Minnesota. (Sponsored by the North Dakota Division of the American Cancer Society)

Tuesday, May 9

8:30 to 9:00 A.M. Registration
9:00 to 9:30 A.M. "Adrenal Disease by Case Histories," N. O. Brink, M.D., Bismarck, North Dakota
9:30 to 10:15 A.M. "Treatment of Urinary Tract Infections," William J. Martin, M.D., Rochester, Minnesota
10:15 to 11:00 A.M. Intermission
11:00 to 11:30 A.M. "The Management of Contact Dermatitis," Francis W. Lynch, M.D., St. Paul, Minnesota
11:30 to 12:15 P.M. "Management of the Painful Shoulder," Schuyler P. Brown, M.D., Lincoln, Nebraska

NOON RECESS

1:30 to 2:30 P.M. "Presidential Address," C. M. Lund, M.D., President, North Dakota State Medical Association
"Introduction: Honorary Members of the North Dakota State Medical Association"
"Inaugural Address," E. H. Boerth, M.D., president-elect, North Dakota State Medical Association
2:30 to 3:15 P.M. "Dysfunctional Uterine Bleeding," William C. Keettel, M.D., Iowa City, Iowa

PRESIDENTIAL ADDRESS

C. M. Lund, M.D.

The past twelve months have not only been filled with excitement and interesting events but with revelations and rewards. I have only one regret—that my experience could not have been shared by every member in this state organization. I have received many new images of the North Dakota doctor of which I was unaware, perhaps due to a selfish interest in my own well-being.

Fifty years ago the doctor's image was that of the family practitioner—the kind of man portrayed by Luke Fields in his famous painting, calmly seated at the bedside of a child, assuming all the responsibility but not doing very much. Medical education, specialization, improvement in hospital care, and growth of voluntary insurance have all helped to modify this nostalgic and romantic picture. With the coming of the machine age in medicine, laboratory, and research, the doctor required the help of technological specialists to make a diagnosis. Moreover, treatment changed. Instead of prescriptions containing somewhat futile remedies, "magic bullets" were created heralding the beginning of modern chemotherapy. The public became aware of the possibilities of preventative medicine.

Today, many other images of the doctor exist. There is still the general practitioner who sees a great variety of diseases, takes care of people in the office, home and hospital, and makes the choice when special services are required.

And there is the less clear image of the specialist. Patients question the greater cost for this service, not realizing the tremendously increased cost of equipment and education he must have to keep pace with new advances in medicine and surgery.

Another image is that of group practice. Some of my patients tell me that they dislike the businesslike environment, the numerous questions, the all too frequent failure to feel that the doctor who is taking care of them is a person and not a machine.

They look at the change in the hospitals, too. They long for the highly qualified, efficient nurses whose numbers are steadily diminishing. They resent the bill, even though they have Blue Cross or other insurance because there are always extras.

The modern doctor reflects on his various images—the man who spends the first thirty years of his life achieving his education and qualifications; the man who is frequently 40 before he begins to earn a living; the man who sacrifices early marriage, children, frequently his health, to engage in a profession which yields great incomes to a few, but, to most, less than is earned by men of 20 who begin by working in trades; and the man who is subject to more social control by legislation, medical organizations, insurance organizations, hospitals, welfare groups, and public opinion than a man or woman engaged in any other profession. This modern doctor ponders the various attitudes of the public and possibly becomes a bit confused when confronted in our popular magazines with charges of neglecting patients and with errors in diagnosis and surgery; he becomes a bit more confused when reading in newspapers of the vast sums awarded patients in malpractice suits. No wonder our

offspring balk at following in our footsteps when scholastic standards are increasing and the future appears rather unattractive.

After these reflections, the modern doctor becomes aware that the image of his predeeessor is not the only thing that has changed. A liberal form of government and medical care has slowly and unsuspectedly encroached upon his liberty and freedom—yes, that most eherished word in our national tradition—leaving him apathetie and unheedful of the cry that, on a global seale, hundreds of millions have exchanged freedom for the elusive and fraudulent promise of security, unmindful that men and nations sell their souls for a dinner pail. He must not forget that freedom is less a right than a gift, less a prerogative than an achievement. A doctor who covets it for himself loses it. A doctor who guards it for his colleague gains it.

At this moment, our nation appears to be fragmented by blocks of power, eaeh exereising what freedom it ean command in fierec loyalty to its local interests and with little responsibility to the national or common good. We go on blithely sneering with Cain, "Am I my brother's keeper?" Uneritieal of our self-interest, we heap abuse on our rivals and boast that this barbaric game is the way of freedom.

Exactly one year ago, we aeeepted the challenge of our foes to prevent their introduction of a socialistic type of medieine in North Dakota. Yes, I call them foes, as they have no concern for the nicctics of truth or honor or ethics. They are systematieally trying to undermine the eonfidence of the people in the frec institution of medicine to win their goal. The challenge and our efforts were futile in comparison to the huge problem we are confronted with on the national front.

The modern doctor again reflects and wonders if time has not run out or if possibly there is still something to do. It is diffieult for a doetor to throw in the towel when, to date, there has been no such word in our lexicon as defeat. The belated but vigorous battle the A.M.A. is waging in our behalf should, but does not, have the support of all the doctors in the U.S.A. At a recent Old Age Conferenee, our unpopularity was evidenced by "staeking the deek" against us and members of our own profession stating that "we are backing a jaded horse."

The medieal profession bears the brunt of the attack at the present time, but after us will come the dental, legal, pharmaceutieal, and other allied organizations; in fact, anyone engaged in private enterprise will feel the encroachment of soeialism, all too late.

Why ean't we colleetively form an organization—eall it whatever you wish—and wrest the initiative from the labor leaders and those in the government who are determined to destroy free medieine and free enterprise.

In the meantime, what can you as a physieian do? First, you cannot afford to close your eyes, hoping that when you open them again the whole unhappy business will have disappeared. You may open them again to the fact of government medicine. You can explain to your patients the truth about soeialistie medieine, the danger in tying medieal care to social security, the pitfalls in compulsory governmental medieine. You ean explain what it would cost the people in terms of taxes and redueed quality of medieine.

You can be prepared to talk about the problems before loeal civie groups and other organizations. You ean partieipate with your loeal medieal society in activities to inform the public. You can help persuade other organizations to join your eause.

You ean make sure that everyone in your community with a legitimate need for medical care gets it, regardless of ability to pay. All sorts of money has been spent for public relations to show people the true image of the doctor. But the only image that means anything is that one of him that is held by his own patients.

Introduction — Fifty-year Members

Now comes one of the most pleasant duties that I have had to perform during the past year. I want to present the fifty-year awards to outstanding members of the North Dakota State Medical Association: Dr. Spear of Dickinson and Dr. Charles W. Schoregge of Bismarck.

Dr. Schoregge was born May 21, 1889, in Sleepy Eye, Minnesota. He received his M.D. degree from the University of Michigan in 1911 and took his internship at Asbury Hospital in Minneapolis. He entered general practice in 1912 to 1915 at Henderson, Minnesota. In 1916 he had a surgical residency at the Bismarek Hospital and in 1917 he was lieensed in North Dakota. He joined the Quain-Ramstad Clinic in 1917 and became a partner in 1934. He retired as chairman of the partnership on December 31, 1954. His specialty was surgery. He is a diplomate of the Board of Surgery, a fellow of the American College of Surgeons, and a fellow of the International College of Surgeons.

Dr. Schoregge influeneed his son to go into medicine and his son is now associated with the Quain-Ramstad Clinic of Bismarck. I would like at this time to have Dr. Schoregge bring his father, Dr. Charles Schoregge, to the podium.

Dr. Sehoregge, I have here a certificate of distinction for fifty years of practice in the medieal profession. In addition to this certificate, we have a gold pin whieh is worn by only a few in this state. It gives me great pleasure to present these to you at this time.

Dr. Schoregge: Thank you, Dr. Lund.

Dr. Lund: The other award is for Dr. Albert E. Spear of Dickinson. He was born at Faribault, Minnesota, on January 29, 1882. He attended Pillsbury Aeademy, Owatonna, Minnesota, and received his bachelor of seience degree from Hamline University in 1905. He reeeived his M.D. degree in 1911 from the University of Minnesota Sehool of Medieine. He was licensed in North Dakota in January 1912. He first located at Belfield, moving to Dickinson seventeen years later. His speeialty was eye, ear, nose, and throat. He was a counecillor of the North Dakota State Medieal Association from the Southwest District from 1941 to 1943 and acting speaker of the House of Delegates in 1948-1949, replaeing the late Dr. A. P. Nachtwey. He was speaker of the House of Delegates from 1950 through 1953 and president of the North Dakota Medical Assoeiation in 1946-47. He is retired and resides at Dickinson.

I am so very sorry that Dr. Spear was not able to be here today, so I am sending him the certifieate and pin. I wish it were possible for me to deliver these to him in person.

The time has now arrived to step down and hand the baton to your next president, Dr. Edwin Boerth of Bismarek. I am very happy to see Dr. Boerth assume this offiee for many reasons. First of all, he is a native of North Dakota. He has lived in the state all of his life with the exception of a few years at Miehigan for his medical edueation. He is thoroughly familiar with all of the political, economie, and medical problems in the state, and a sworn foe of anything that smaeks of soeialistie medieine. In addition, he is a very hard worker and has already begun formulating his plans for our

joint medical meeting with South Dakota in June 1962.

Again, a thousand thanks for the high honor and the wonderful cooperation you gave me during 1960 and 1961. I am deeply grateful to all of you. I only ask that you extend the same spirit and effort to Dr. Boerth during 1961 and 1962.

INAUGURAL ADDRESS

E. H. Boerth, M.D.

Two major issues face the profession of medicine as distinct from the practice of medicine. These issues are of great concern to each of us in the practice of medicine. Without working forcefully for a solution of these two emergencies, there can be little hope of securing permanently a conservative, private, and free practice of medicine in our twentieth-century society.

The first problem to which I refer is the drastic shortage of students to take our place in practice. This shortage is not just in our state, although we certainly feel it strongly here, but it exists throughout the nation. According to the Association of American Medical Colleges, while our national population grew from 150 million in 1949 to 177 million in 1959, the number of applicants for admission to medical schools dropped from 25,500 to 15,000. I am sure we were all aware of this trend, but the shortages seem more alarming when we view them in the perspective of the increasing job medicine faces in providing health care for a growing population.

In our own medical school, the freshman class began with only 39 members last fall, whereas, the preceding year a total of 44 had been accepted by May 1st. In addition to the shrinking class, the number of those accepted from North Dakota is decreasing to the point that 11 of those 39 who began the freshman class were from outside the state.

Certainly, when we consider these figures, we can't say that we, as working members of our profession, have done everything possible to encourage our best young people to enter medicine. Another disturbing factor is contained in the medical school report. Indications are that the school is accepting students with lesser qualifications. The failure rate is rising, but the faculty has not reported a raising of the standards; therefore we must assume that the academic level of the students admitted is lower.

In our third and fourth years of medical schools around the country, there were between 300 and 400 vacancies which went unfilled this year. This is a figure I need not contrast with our experiences of less than five years ago. Many medical schools are now gratefully accepting North Dakota students who would not have been admitted five years ago. In fact, they are working out agreements for annual applications.

We have supported the projects designed to increase the number of places in medical schools for third- and fourth-year students; now we find ourselves without the students who should want to fill those places. There is no justification for building facilities that we cannot use and staff or for lowering the standards of medical practice. We must take the other road to finding the necessary students.

The reasons for the declining numbers of students are not hard to find. The cost of preparing for the practice of medicine has outrun the resources of families that are in relatively comfortable financial position. Therefore, assistance in loans, scholarships, and grants will have to be made available to halt the decline of students. The Association of American Medical Schools has estimated a need of 86 million dollars in the next five years. A committee of the association estimates that each year 2,150 medical students will need financial assistance at the rate of $8,000 for the four-year course.

To meet the cost problem, at least partially, the Kennedy administration has proposed an aid program, but, more important, contributions to AMEF are increasing slowly and the A.M.A. has begun a scholarship program. These will just begin to solve the problem.

Another reason for the loss of students is certainly the competition from industry for science students. By entering industry, a good science student can earn a better salary after only four years of training than he can by starting medical practice after eight or nine years of training. Furthermore, a science student candidate for graduate degrees has more financial assistance available to him. The cost of tuition and books for the four years of a medical education is $4,000 compared with $1,800 for a graduate student. The graduate students average $2,000 a year in assistance from various sources other than their own. Sixty-one per cent of the graduate students receive aid compared to about one-half of the medical students, and that at the rate of about $500 a year.

Now a new financial threat is appearing. A government program of aid to science research has already lured many medical school faculty members into government supported projects and threatens to take even more of them.

There is still another reason for lack of interest on the part of prospective medical students. Some of the blame must go to the attacks on our profession by those who would solve every problem by legislative fiat and who would eliminate the free practice of medicine. Let us put ourselves into the minds of these prospective students. To be told that the practice of medicine is antisocial and will be controlled by law is hardly an incentive to begin the long years of training for a profession that might not be the same when the student is ready to practice.

I think we must also note the loss of the close personal relationship of a student with a doctor of medicine, especially in the larger cities. This relationship was a very real part of the original incentive to enter medicine.

Some of these problems can be solved by attention to the simple matters that are with us every day in our practice; others will require vast sums of money and new solutions. To begin, it is up to each of us to take a personal responsibility for interesting more of our best young men and women in the practice of medicine.

We must increase our support of the aid to medical education fund. We must investigate the plans developed in Maine in which each physician donated to a scholarship fund and a recruitment project was begun by all schools of higher education in the state. We might further investigate the plan at Huntington, West Virginia, in which a loan fund has been established by a foundation for use by students in the hospitals in that city. Several states have developed growing programs for state scholarship aid.

In summary, each of us who believes in his profession must help to build a task force of new doctors who will support the system of private practice, with free choice, that has given this nation the highest level of health care the world has ever known.

I call your attention now to the second major issue which we must face as individuals and as a profession. This issue has two sides of equal importance. On the

one hand are the relationships within the profession, one doctor with another, whenever that relationship affects the economic well-being of a patient or his family. The attention of our opponents is always focused on our actions, so that all of these relationships must be above reproach. But these are things that can be attended to within the family. I am sure that these potential problems are being given attention.

The relationship of medicine, totally and individually, with the American people is no longer something that can be cared for within the family. Society is developing at a great rate. We are constantly called upon to integrate with that evolution, to adapt to the changing needs of a growing population as it becomes more urban through industrialization. This comes at a time when the volume of medical knowledge threatens to bury us under the need for study and continuing education.

I submit that we are accommodated to the changes in society and that we are prepared to meet the challenges of these changes. But, although we are prepared to meet new challenges with our present system of medicine, the people most affected are not educated on these subjects.

It has become imperative that we physicians must tell our individual patients and the collective electorate about the practice of medicine. They must learn the truth. When they know that truth, we will never need fear legislation to change the nature of medical practice and free choice. You may call this process public relations, human relations, or social engineering if you like, but, in the final analysis, what is needed is for us to sit with people and tell them the truth about our beliefs, the reasons for those beliefs, and the benefits derived by each citizen because of those beliefs. We must tell large numbers of people these same truths by continuing and expanding our public information program.

You have been told too many times that members of society love their individual physician, but do not like organized medicine. I remind each of you that the North Dakota State Medical Association and the American Medical Association are you. They are your voice in the state, the nation, and the world. Organized medicine reflects your ideas in amounts equal to your zealous and financial participation in the affairs of the organization. It seems to me only simple logic that each of us must start now to defend the organizations we have created whenever and wherever they are attacked. After all, the policies of organized medicine are the policies of the free practice of medicine in the only country left with free practice.

If we would have what the public relations specialists call a good climate of opinion, or a good image, then we must begin to create it. That image starts at the end of an examination or treatment when you take a moment to explain fees and hospital charges to someone, or when you bring the conversation around to the subject of the evils of social security medicine. Those little visits, coupled with the understanding and interest which you always give to that patient, are the most effective means available to us in combating the lack of understanding of our system of medicine.

Each of us must make an effort to interpret our policies to larger groups of people through speeches to service clubs and women's groups, not just when they ask us, but when they can be encouraged to do so.

In fact, the time has come for the doctor to take his case before the public, which benefits at least as much, if not more, than we do from our present system, and let them know that it is better than any other.

The practice of medicine has never been an easy life; now we must learn new skills of dealing with mass opinions and legislation technics. We must increase our efforts during the coming year to defend ourselves against offensive legislation in congress and we must increase our services to the state legislature by getting ready now for the 1963 session.

These, then, are the tasks that face us in the year ahead. These two major problems will not be eliminated in one year of work. If we don't begin now, the other side can very well reach their goal, and then our problem will not be to defend our free system, but to get our salaries from the federal government. I will put my efforts into the share of the job which must be borne by the president of the Association, and I shall call upon each of you to assume his share.

North Dakota State Medical Association Roster—1961

MEMBERSHIP BY DISTRICTS

First District

Amidon, Blaine F.	Dakota Clinic, Fargo
Armstrong, William B.	Dakota Clinic, Fargo
Bacheller, Stephen C.	Enderlin
Bakke, Hans	Lisbon
Barnard, Donald M.	Fargo Clinic, Fargo
Beithon, Elmer J.	Red River Valley Clinic, Wahpeton
Beithon, Paul J.	Red River Valley Clinic, Wahpeton
Beltz, Melvin E.	Wahpeton Clinic, Wahpeton
Borland, Verl G.	Fargo Clinic, Fargo
Burt, Arthur C.	405 Black Building, Fargo
Christoferson, Lee A.	702 1st Avenue So., Fargo
Christu, Chris M.	Fargo Clinic, Fargo
Corbus, Budd C.	314 Black Building, Fargo
Crim, Eleanor M.	1701 13th Street So., Fargo
Darner, Charles B.	Fargo Clinic, Fargo
Darrow, Kent E.	Dakota Clinic, Fargo
DeCesare, F. A.	Dakota Clinic, Fargo
Dillard, James R.	311 Black Building, Fargo
Dodds, G. Alfred	Fargo Clinic, Fargo
Donat, T. L.	Dakota Clinic, Fargo
Engstrom, Perry H.	Red River Valley Clinic, Wahpeton
Fercho, Calvin K.	812 Black Building, Fargo
Fortney, Arthur C.	Fargo Clinic, Fargo
Foster, George C.	15 Broadway, Fargo
Geib, Marvin J.	702 1st Avenue So., Fargo
Gillam, John S.	Fargo Clinic, Fargo
Goff, John R.	Fargo Clinic, Fargo
Goltz, Neill F.	Fargo Clinic, Fargo
Gronvold, Frederick O.	910 Broadway, Fargo
Gustafson, Maynard B.	702 1st Avenue So., Fargo
Hager, Jerome P.	Hankinson
Hall, G. Howard	Fargo Clinic, Fargo

Haugrud, Earl M.	304 Black Building, Fargo
Hawn, Hugh W.	Gate City Building, Fargo
Heilman, Charles O.	Fargo Clinic, Fargo
Houghton, James F.	Dakota Clinic, Fargo
Hunter, C. M.	608 Black Building, Fargo
Hunter, G. Wilson	Fargo Clinic, Fargo
Irvine, Vincent S.	Lidgerwood
Ivers, George U.	424 DeLendrecie Bldg., Fargo
Ivers, Robert R.	702 1st Avenue So., Fargo
Jaehning, David G.	Hotel Wahpeton, Wahpeton
Kulland, Roy E.	402 Sheyenne Street, West Fargo
Lancaster, W. E. G.	Fargo Clinic, Fargo
Landa, Marshall	Dakota Clinic, Fargo
Larson, G. Arthur	812 Black Building, Fargo
Lawrence, Donald H.	306 Black Building, Fargo
LeBien, Wayne E.	Fargo Clinic, Fargo
LeMar, John D.	Fargo Clinic, Fargo
Levson, Daniel N.	Fairmount
Lewis, A. K.	606 Ash Street, Lisbon
Lewis, T. H.	302 Black Building, Fargo
Lindsay, Douglas T.	Fargo Clinic, Fargo
Long, William H.	Dakota Clinic, Fargo
Lytle, Francis T.	Fargo Clinic, Fargo
Macaulay, Warren L.	Fargo Clinic, Fargo
Magill, Gordon B.	403 Black Building, Fargo
Magness, John W.	Dakota Clinic, Fargo
Mazur, Bernard A.	Dakota Clinic, Fargo
Melton, Frank M.	Dakota Clinic, Fargo
Miller, Herbert H.	509½ Dakota Avenue, Wahpeton
Murray, James B.	Dakota Clinic, Fargo
Nagle, Duane W.	Fargo Clinic, Fargo
Norum, Henry A.	Fargo Clinic, Fargo
Poindexter, Marlin H., Jr.	Fargo Clinic, Fargo
Poole, Ernest E.	Sasse Building, Lidgerwood
Pray, Laurence G.	Fargo Clinic, Fargo
Rogers, Robert G.	Dakota Clinic, Fargo
Schleinitz, Fritz B.	Hankinson
Schneider, Joseph F.	114 Broadway, Fargo
Sedlak, Oliver A.	Dakota Clinic, Fargo
Sessums, John V., Jr.	Dakota Clinic, Fargo
Shook, Lester D.	Fargo Clinic, Fargo
Spier, J. J.	1345 North 5th Street, Fargo
Stafne, William A.	Fargo Clinic, Fargo
Story, Robert D.	Fargo Clinic, Fargo
Swanson, Joel C.	407 Black Building, Fargo
Tarnasky, Ralph E.	Fargo Clinic, Fargo
Thompson, George R.	Fargo Clinic, Fargo
Traynor, Mack V.	Fargo Clinic, Fargo
Triggs, Perry O.	Fargo Clinic, Fargo
Ulmer, Robert J.	Dakota Clinic, Fargo
Veitch, Abner	502 Oak Street, Lisbon
Wall, Wendell H.	Wahpeton Clinic, Wahpeton
Wasemiller, E. R.	Wahpeton Clinic, Wahpeton
Webster, William O.	Fargo Clinic, Fargo
Weible, Ralph D.	Dakota Clinic, Fargo
Weyers, Henry J.	608 Black Building, Fargo
Williams, N. S.	Dakota Clinic, Fargo
Wiltse, Glenn L.	Wahpeton Clinic, Wahpeton
Wold, Lester E.	Fargo Clinic, Fargo
Zanner, Richard J.	708 Black Building, Fargo

Second District

Allport, F. W.	Towner
Cook, Stuart J.	Rolette
Corbett, Conner A.	Lake Region Clinic, Devils Lake
Coultrip, Raymond L., Jr.	McVille
Engesather, J. A. D.	Lakota
Eyelands, Jon V.	Rolla
Fawcett, John C.	Lake Region Clinic, Devils Lake
Fawcett, Robert M.	Lake Region Clinic, Devils Lake
Fox, William R.	Johnson Clinic, Rugby
Gilchrist, Milton R.	2288 Overlook Drive, Minneapolis 20, Minn.
Gorrie, William A.	Maddock
Hilts, George H.	Cando
Johnson, Christian G.	Johnson Clinic, Rugby
Keller, E. T.	Johnson Clinic, Rugby
Lazareck, I. L.	411 Fourth Avenue, Devils Lake
Longmire, L. T.	411 4th Ave., Devils Lake
McBane, Robert D.	Lake Region Clinic, Devils Lake
McIntyre, Donald G.	Johnson Clinic, Rugby
MacDonald, John A.	Cando
Mahoney, James H.	411 Fourth Avenue, Devils Lake
Munro, J. A.	Rolla
Owens, Clarence G.	New Rockford
Palmer, D. W.	Palmer Clinic, Cando
Pine, Louis F.	Lake Region Clinic, Devils Lake
Sawchuk, John	Rolette
Schwinghamer, E. J.	New Rockford
Seibel, Glenn W.	New Rockford
Sihler, William F.	Mann Block, Devils Lake
Terlecki, Jaroslaw	Minnewaukan
Toomey, Glenn W.	Lake Region Clinic, Devils Lake
Voglewede, William C.	Carrington

Third District

Benson, T. Q.	1600 University Avenue, Grand Forks
Benwell, Harry D.	Valley Medical Associates, Grand Forks
Campbell, Duncan W.	Grand Forks Clinic, Grand Forks
Cardy, James D.	U.N.D. Medical School, Grand Forks
Clark, Rodney	Grand Forks Clinic, Grand Forks
Clayburgh, Bennie J.	Grand Forks Clinic, Grand Forks
Countryman, G. L.	1004 Hill Avenue, Grafton
Culmer, A. E., Jr.	501 1st Natl. Bank Bldg., Grand Forks
Dailey, Walter C.	Valley Medical Associates Grand Forks
Deason, Frank W.	643 Cooper Avenue, Grafton
DeLano, Robert H.	Northwood
Doss, R. Douglas	1600 University Avenue, Grand Forks
Eaton, L. P.	Grafton Clinic, Grafton
Evans, Harold W.	Grand Forks Clinic, Grand Forks
Flaten, Alfred N.	Edinburg
Frey, Wellde W.	Drayton
Glaspel, Cyril J.	Grafton Clinic, Grafton
Goehl, R. O.	Grand Forks Clinic, Grand Forks
Graham, Charles M.	1600 University Avenue, Grand Forks
Graham, John H.	15½ South Third, Grand Forks
Grinnell, Ernest L.	Grand Forks Clinic, Grand Forks
Hardy, Nigel A.	Minto
Harwood, Theodore H.	U.N.D. Medical School, Grand Forks
Haugen, C. O.	Larimore
Hannz, Edgar A.	Grand Forks Clinic, Grand Forks
Helenbolt, Kenneth S.	1600 University Avenue, Grand Forks
Helgason, Norman M.	Cavalier
Helm, Richard K.	27½ So. 3rd Street, Grand Forks
Hill, Frank A.,	Grand Forks Clinic, Grand Forks

Jensen, August F.	1600 University Avenue, Grand Forks
Johanson, John F.	Cavalier
Kaluzniak, Nicholas	Langdon
Keig, William P., Jr.	1600 University Avenue, Grand Forks
Krahn, Henry	Walhalla
Landry, L. H.	Walhalla
Leigh, James A.	716 4th Ave. So., E. Grand Forks, Minn.
Leigh, Ralph E.	111 North 5th Street, Grand Forks
Leigh, Richard H.	1600 University Ave., Grand Forks
Levine, Leonard	Grand Forks Clinic, Grand Forks
Lorentson, Carl E.	Grand Forks Clinic, Grand Forks
McLeod, John	Grand Forks Clinic, Grand Forks
Mahowald, Ralph E.	1400 Grand Ave., Grand Forks
Mann, Hamish	1600 University Ave., Grand Forks
Marshall, Robert A.	27½ So. Third St., Grand Forks
Meredith, William C.	Drayton
Moore, John H.	Grand Forks Clinic, Grand Forks
Muus, Jacob M.	McVille
Muus, O. Harold	502 Commercial Exch. Bldg., Grand Forks
Nelson, Wallace W.	Grand Forks Clinic, Grand Forks
Nelson, William C.	Grand Forks Clinic, Grand Forks
O'Toole, James K.	Park River
Painter, Robert C.	Grand Forks Clinic, Grand Forks
Panek, A. F.	Milton
Peake, Frances M.	204 Widlund Bldg., Grand Forks
Peterkin, Frank D.	Langdon
Pettit, Samuel L.	Grand Forks Clinic, Grand Forks
Piltingsrud, Harold R.	Park River
Porter, Charles B.	Grand Forks Clinic, Grand Forks
Powers, William T.	Valley Medical Associates, Grand Forks
Prochaska, Leonard J.	517 1st Natl. Bank Bldg., Grand Forks
Rand, Charles C.	Grafton
Ruud, John E.	1st Natl. Bank Bldg., Grand Forks
Sandmeyer, John A.	Grand Forks Clinic, Grand Forks
Saiki, A. K.	U.N.D. Medical School, Grand Forks
Schafer, Thomas	Grand Forks Clinic, Grand Forks
Silverman, Louis B.	Grand Forks Clinic, Grand Forks
Tarpley, Harold I.	Valley Medical Associates, Grand Forks
Teevens, William P.	Grafton Clinic, Grafton
Thorgrimsen, G. G.	1600 University Ave., Grand Forks
Tompkins, C. R.	1004 Hill Ave., Grafton
Vandergon, Keith G.	1400 Grand Ave. Grand Forks
Witherstine, William H.	111 N. 5th St., Grand Forks
Woutat, Philip H.	Grand Forks Clinic, Grand Forks
Woytassek, Leonard E.	Larimore
Youngs, Nelson A.	Grand Forks Clinic, Grand Forks
Yury, Walter E.	1004 Hill Ave., Grafton

Fourth District

Amstutz, Kenneth N.	Northwest Clinic, Minot
Ayash, John J.	123 2nd Ave. S.E., Minot
Bermudez, Enrique	Garrison Clinic, Garrison
Blatherwick, Robert	Parshall
Boyle, John T.	Garrison
Boyum, Lowell E.	Harvey Medical Center, Harvey
Boyum, P. A.	Harvey Medical Center, Harvey
Breslich, Paul J.	Northwest Clinic, Minot
Briggs, Brian E.	Great Plains Clinic, Minot
Cameron, Angus L.	Northwest Clinic, Minot
Cipolla, Victor S.	Medical Arts Clinic, Minot
Cuadrado, Angel R.	San Haven
Devine, John L.	Great Plains Clinic, Minot
Dormont, Richard E.	Northwest Clinic, Minot
Erenfeld, Fred R.	617 2nd St. N.W., Minot
Fischer, V. J.	Medical Arts Clinic, Minot
Flath, M. G.	Stanley
Flickinger, Dale B.	Great Plains Clinic, Minot
Floch, John L.	Mohall
Gammell, Robert T.	Kenmare
Garrison, M. W.	Garrison Building, Minot
Giltner, Lloyd A.	Medical Arts Clinic, Minot
Goodman, Robert	Powers Lake
Gozum, Ekrem	123 2nd Ave. S.E., Minot
Greene, E. E.	Westhope
Halliday, David J.	Kenmare
Halverson, C. H.	1st Natl. Bank Bldg., Minot
Hammargren, A. F.	Harvey Medical Center, Harvey
Hart, George M.	Northwest Clinic, Minot
Heidorn, G. H.	Great Plains Clinic, Minot
Herba, Edward J.	Mohall Medical Center, Mohall
Herba, M. J.	Harvey
Hoopes, Lorman L.	17A So. Main St., Minot
Hordinsky, Bohdan Z.	Drake
Huntley, Wellington B.	Great Plains Clinic, Minot
Hurly, William C.	Medical Arts Clinic, Minot
Johnson, O. W.	Johnson Clinic, Rugby
Kaemerle, Harold K.	2318 Teviot, Los Angeles 39, Calif.
Kermott, L. H.	401 Main St. So., Minot
Kihle, Kenneth W.	Bottineau
Kohl, D. L.	123 2nd Ave. S.E., Minot
Lampert, M. T.	407 1st Natl. Bank Bldg., Minot
LaRochelle, William D.	Stanley
Larson, Richard S.	Velva
Leonard, Kenneth O.	Garrison Clinic, Garrison
Loeb, George L.	5407 26th Ave. So., Minneapolis 17, Minn.
London, Carl B.	Northwest Clinic, Minot
McCullough, William F.	Bottineau
McDougall, James R.	214 So. Main St., Minot
Naegeli, Frank D.	Northwest Clinic, Minot
Nelson, Leslie F.	410 Main, Bottineau
Olson, Burton G.	McCannel Clinic, Minot
Richardson, Gale R.	12 10th St. S.W., Minot
Rowe, Paul H.	Northwest Clinic, Minot
Sahl, Jens, Jr.	Northwest Clinic, Minot
Seiffert, G. S.	Northwest Clinic, Minot
Shea, Samuel E.	McCannel Clinic, Minot
Sorenson, Alfred R.	Medical Arts Clinic, Minot
Sorenson, Roger	Medical Arts Clinic, Minot
Towarnicky, Marvin J.	Fessenden
Uthus, O. S.	21½ 2nd Ave. S.E., Minot
Vaaler, Raymond A.	Professional Building, Minot
Veenbaas, Fred F.	Northwest Clinic, Minot
Wall, Willard W.	Northwest Clinic, Minot
Wallis, Marianne	St. Joseph's Hospital, Minot
Wilson, Herbert J.	New Town
Wilson, Thomas	Great Plains Clinic, Minot

Fifth District

Christianson, Gunder	117 N.W. Third, Valley City
Feist, Donald J.	Forman
Goven, John W.	117 N.W. Third, Valley City
Jensen, Clayton E.	117 N.W. Third, Valley City
Jensen, Warren R.	130 Central Ave. So., Valley City
Klein, C. J.	117 N.W. Third, Valley City
Macdonald, Alexander C.	130 Central Ave. So., Valley City

Macdonald, Neil A.	130 Central Ave. So. Valley City
Merrett, Joseph P.	117 N.W. Third, Valley City
Van Houten, J.	105 Main St. W., Valley City

Sixth District

Anderson, Freedolph E.	Underwood
Arneson, Charles A.	412½ Main, Bismarck
Baker, Cecil	408 Cowan Building, Bismarck
Baumgartner, Carl J.	Quain & Ramstad Clinic, Bismarck
Berg, H. Milton	Quain & Ramstad Clinic, Bismarck
Berg, Roger M.	Quain & Ramstad Clinic, Bismark
Bertheau, Herman J.	Linton
Bodenstab, William H.	520 Mandan St., Bismarck
Boerth, Edwin H.	Quain & Ramstad Clinic, Bismarck
Brink, Norvel O.	Quain & Ramstad Clinic, Bismarck
Buckingham, T. W.	405½ Broadway, Bismarck
Buckingham, William M.	Capital City Clinic, Bismarck
Cartwright, John T.	Missouri Valley Clinic, Bismarck
Cleary, Joseph W.	Missouri Valley Clinic, Bismarck
Curiskis, A. A.	Elgin
Dahl, Phillip O.	Missouri Valley Clinic, Bismarck
Daniolos, Demetrios P.	Quain & Ramstad Clinic, Bismarck
Diven, Wilbur L.	402½ Main, Bismarck
Dunnigan, Ralph J.	Capital City Clinic, Bismarck
Eriksen, Johan A.	Quain & Ramstad Clinic, Bismarck
Ewert, Arthur O.	Beulah
Fisher, Albert M.	922 8th St., Bismarck
Freise, Paul W.	Quain & Ramstad Clinic, Bismarck
Froeschle, Rudolph P.	Hazen
Gaebe, Otto C.	New Salem
Garrett, W. G.	Missouri Valley Clinic, Bismarck
Girard, Bernard A.	107 1st Ave., N.W., Mandan
Goodman, Edward	Napoleon
Goughnour, Myron W.	Capital City Clinic, Bismarck
Gregware, P. Roy	Quain & Ramstad Clinic, Bismarck
Griebenow, Frederick	905 9th St., Bismarck
Gutowski, Franz	Wishek
Hamilton, Charles A.	Quain & Ramstad Clinic, Bismarck
Hanson, Harris D.	Quain & Ramstad Clinic, Bismarck
Heffron, Maurice M.	405½ Broadway, Bismarck
Henderson, Robert W.	Capital City Clinic, Bismarck
Hetzler, Arnold E.	104 3rd Ave., N.W., Mandan
Hilts, Joseph A.	104 2nd Ave., N.W., Mandan
Icenogle, C. D.	State Hospital, Jamestown
Jacobson, M. S.	Elgin
Johnson, Kenneth J.	Quain & Ramstad Clinic, Bismarck
Johnson, Marlin J. E.	Quain & Ramstad Clinic, Bismarck
Johnson, Paul L.	Quain & Ramstad Clinic, Bismarck
Kalnins, Arnold	Washburn
Kling, Robert R.	Quain & Ramstad Clinic, Bismarck
Kuplis, Haralds	Turtle Lake
Larson, Leonard W.	Quain & Ramstad Clinic, Bismarck
Lindelow, Olaf V.	Missouri Valley Clinic, Bismarck
Lipp, George R.	405½ Broadway, Bismarck
Lommen, M. A. K.	Capital City Clinic, Bismarck
McGee, William J	1803 Linda Drive, Mandan
Montz, Charles R.	Quain & Ramstad Clinic, Bismarck
Morton, James R.	Quain & Ramstad Clinic, Bismarck
Nuessle, Robert F.	Quain & Ramstad Clinic, Bismarck
Nugent, Milton E.	Quain & Ramstad Clinic, Bismarck
Oja, Karl F.	Ashley
Orchard, Welland J.	Linton
Owens, Percy L.	Missouri Valley Clinic, Bismarck
Pearson, Lawrence O.	Wishek
Perrin, Edwin D.	Quain & Ramstad Clinic, Bismarck
Peters, Clifford H.	Quain & Ramstad Clinic, Bismarck
Peterson, Alice H.	State Health Department., State Capitol Bldg., Bismarck
Pierce, W. B.	Quain & Ramstad Clinic, Bismarck
Pierson, R. Warren	Quain & Ramstad Clinic, Bismarck
Quain, Eric P.	2075 Raynor St., Salem, Oregon
Sauer, John P.	Missouri Valley Clinic, Bismarck
Save, Ernest B.	Quain & Ramstad Clinic, Bismarck
Schoregge, Charles W.	Quain & Ramstad Clinic, Bismarck
Schoregge, Robert D.	Quain & Ramstad Clinic, Bismarck
Smeenk, H. Pieter	Quain & Ramstad Clinic, Bismarck
Smith, Cecil C.	101 Collins Ave., Mandan
Smith, Clyde L.	Missouri Valley Clinic, Bismarck
Spielman, George H.	305 1st Ave., N.W., Mandan
Stangebye, T. L., Jr.	Quain & Ramstad Clinic, Bismarck
Thompson, Arnold	Quain & Ramstad Clinic, Bismarck
Tudor, Robert B.	Quain & Ramstad Clinic, Bismarck
Van Drunen, Hendrika	Quain & Ramstad Clinic, Bismarck
Vinje, Edmund G.	Hazen Clinic, Hazen
Vinje, Ralph	405½ Broadway, Bismarck
Vonnegut, Felix F.	Linton
Waldschmidt, Reuben H.	Quain & Ramstad Clinic, Bismarck
Waldschmidt, William D.	Quain & Ramstad Clinic, Bismarck
Weyrens, Peter J.	Hebron
Zukowsky, Anthony	Steele

Seventh District

Beall, John A.	320 1st Ave. N., Jamestown
Bolliger, Eugene F.	Kulm
Clement, Duane	320 1st Ave. N., Jamestown
Craychee, Walter A.	205 Union Ave., Oakes
Cukurs, Paul	State Hospital, Jamestown
Elsworth, John N.	DePuy-Sorkness Clinic, Jamestown
Evangelista, Teofilo	State Hospital, Jamestown
Fergusson, Victor D.	Edgeley
Gronewald, Tula W.	State Hospital, Jamestown
Hieb, Edwin O.	DePuy-Sorkness Clinic, Jamestown
Hogan, Clifford W.	DePuy-Sorkness Clinic, Jamestown
Jansonius, J. W.	Medical Arts Clinic, Jamestown
Jestadt, John J.	DePuy-Sorkness Clinic, Jamestown
Klassen, Rudolph A.	LaMoure Clinic, LaMoure
Larson, Ernest J.	DePuy-Sorkness Clinic, Jamestown
Lengyel, Irwin	State Hospital, Jamestown
Lucy, Robert E.	DePuy-Sorkness Clinic, Jamestown
Lynde, Roy	Ellendale
McFadden, Robert L.	DePuy-Sorkness Clinic, Jamestown
Melzer, Simon W.	Woodworth
Martin, Clarence S.	Medina
Meunier, H. J.	Oakes
Miles, James V., Jr.	119 2nd Ave., S.E., Jamestown
Nierling, Richard D.	DePuy-Sorkness Clinic, Jamestown
Oster, Ellis	Ellendale Clinic, Ellendale
Pederson, Thomas E.	DePuy-Sorkness Clinic, Jamestown

Rioux, Berchmans	State Hospital, Jamestown
Sakai, Masahiro	State Hospital, Jamestown
Saxvik, Russell O.	10340 Wright St., Omaha 14, Neb.
Sorkness, Joseph	DePuy-Sorkness Clinic, Jamestown
Swenson, John A.	DePuy-Sorkness Clinic, Jamestown
Thakor, S. J.	State Hospital, Jamestown
Turner, Neville W.	1633 Marco Polo Way, Burlingame, Calif.
Schmidt, Donald J.	Gackle
Van der Linde, John M.	Medical Arts Clinic, Jamestown
Van Houten, Richard W.	301 Union Ave., Oakes
Waitzel, I. David	State Hospital, Jamestown
Woodward, Robert S.	DePuy-Sorkness Clinic, Jamestown

Eighth District

Berg, Milton O.	Tioga
Borrud, Chester C.	Harmon Park Clinic, Williston
Craven, John P.	411 Main St., Williston
Craven, Joseph D.	411 Main St., Williston
Ellis, Gordon E.	Harmon Park Clinic, Williston
Fennell, William L.	Crosby Clinic, Crosby
Hagan, Edward J.	411 Main St., Williston
Hoyme, James B.	Tioga
Inness-Brown, Hugh, Jr.	Harmon Park Clinic, Williston
Johnson, Alan K.	Williston Clinic, Williston
Johnson, P. O. C.	Watford City
Keller, John M.	Williston Clinic, Williston
Korwin, J. J.	120 Main, Williston
Lund, Carroll M.	Williston Clinic, Williston
McPhail, Clayton O.	Crosby Clinic, Crosby
Petty, Charles R.	411 Main, Williston
Pile, Duane F.	Crosby Clinic, Crosby
Skjei, Donald E.	Williston Clinic, Williston
Strinden, Dean R.	Harmon Park Clinic, Williston
Sussex, Thomas L.	Watford City
Walker, H. Charles, Jr.	411 Main, Williston
Wright, Willard A.	Williston Clinic, Williston

Ninth District

Ahlness, Paul	Bowman
Bush, Clarence A.	Beach
Carter, Robert G.	Hettinger
Dukart, Ralph J.	Dickinson Clinic, Dickinson
Foster, Keith G.	Rodgers-Gumper Clinic, Dickinson
Gilliland, Robert F.	Dickinson Clinic, Dickinson
Gilsdorf, Amos R.	Dickinson Clinic, Dickinson
Guloien, Hans E.	Dickinson Clinic, Dickinson
Gumper, Arnold J.	Rodgers-Gumper Clinic, Dickinson
Hanewald, Walter C.	Rodgers-Gumper Clinic Dickinson
Hankins, Robert E.	Mott
Hill, S. W.	Regent
Larsen, Harlan C.	Rodgers-Gumper Clinic, Dickinson
Maercklein, Otto C.	Mott
Ordahl, Norman B.	Rodgers-Gumper Clinic, Dickinson
Raasch, Richard F.	Dickinson Clinic, Dickinson
Reichert, Donald J.	24 West Villard, Dickinson
Reichert, H. Lawrence	24 West Villard, Dickinson
Schumacher, William A.	12102 Silver Fox Road, Los Alamitos, Calif.
Skwarok, Walter S.	Hebron
Slominski, Henry	Richardton
Smith, Oscar M.	P.O. Box 1188, Dickinson
Spear, Albert E.	610 1st Ave., W., Dickinson
Thom, Robert C.	Bowman

Tenth District

Dekker, Omar D.	Finley
LaFleur, Harold A.	Mayville
Little, James M.	Mayville
Little, Roy C.	Mayville
McLean, Robert W.	Hillsboro
Mergens, Daniel N.	Hillsboro
Odegard, Russell L.	Hatton
Rosenberg, Mervin	Northwood
Vistnes, Lars M.	Cooperstown
Wakefield, Kenneth M.	Cooperstown
Waydeman, H. B.	Hunter

TRANSACTIONS OF THE FIFTEENTH ANNUAL MEETING OF THE WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION

Fargo, May 7, 8, and 9, 1961

The opening session of the fifteenth annual meeting of the Woman's Auxiliary to the North Dakota State Medical Association was held in the Community Room of the Metropolitan Savings and Loan Building, Fargo, at 9:30 A.M., Monday, May 8, 1961. The meeting was called to order by Mrs. R. W. McLean, president.

The pledge of loyalty was led by Mrs. L. T. Longmire, president-elect, and repeated by the members. The invocation was given by Mrs. J. W. Jansonius, first vice-president.

Mrs. C. K. Fercho, Fargo, extended a welcome to the convention. The response was given by Mrs. Gale Richardson, Minot.

The following members answered the secretary's roll call:

State officers: Mrs. R. W. McLean, president; Mrs. L. T. Longmire, president-elect; Mrs. J. W. Jansonius, first vice-president; Mrs. R. H. Waldschmidt, second vice-president; Mrs. C. L. Smith, recording secretary; and Mrs. M. H. Poindexter, treasurer.

Committee chairmen: Mrs. J. M. Van der Linde, nominating committee; Mrs. E. A. Haunz, civil defense; Mrs. M. M. Heffron, publicity; Mrs. L. G. Pray, legislation; Mrs. O. M. DeMoully, historian; Mrs. B. A. Mazur, A.M.E.F.; Mrs. T. Q. Benson, parliamentarian; Mrs. R. L. McFadden, mental health; Mrs. R. D. Schoregge, health careers; Mrs. V. J. Fischer, by-laws; Mrs. J. C. Fawcett, safety; Mrs. M. V. Traynor, Jr., community service; Mrs. J. H. Mahoney, managing editor; Mrs. Robert Hankins, co-editor; Mrs. E. J. Larson, finance; Mrs. J. A. Sandmeyer, student loan fund.

District presidents: Mrs. Calvin Fercho, Fargo; Mrs. Gale Richardson, Minot; Mrs. R. H. Waldschmidt, Bismarck; Mrs. E. O. Hieb, Jamestown; Mrs. Robert Hankins, Mott; Mrs. D. N. Mergens, Hillsboro. Delegates: Mrs. W. L. Macaulay, Mrs. D. T. Lindsay, Fargo; Mrs.

Harold Evans, Mrs. T. Q. Benson, Grand Forks; Mrs. Ekrem Gozum, Mrs. Kenneth Amstutz, Minot; Mrs. T. L. Stangebye, Mrs. W. D. Waldschmidt, Bismarck; Mrs. C. M. Lund, Williston; Mrs. J. M. Little, Mayville. Councillors: Mrs. John Bond, Fargo; Mrs. R. C. Painter, Grand Forks; Mrs. L. T. Longmire, Devils Lake; Mrs. V. J. Fischer, Minot; Mrs. M. M. Heffron, Bismarck; Mrs. R. L. McFadden, Jamestown.

Dr. Carroll M. Lund, president of the North Dakota State Medical Association, brought greetings from the NDSMA and also the advice that we should "Blow our own bugle." He complimented the Auxiliary for its fine work in supporting the Student Loan Fund and the American Medical Education Foundation. He asked our help in combating adverse legislation and urged that a doctor's wife run for the state senate or house of representatives. He asked our help in the Committee on Aging. He closed with his thanks for the many auxiliary projects.

Mrs. R. H. Waldschmidt read the following "In Memoriam:" "We of the Auxiliary are saddened by the loss of one of our members, Olga Mayer Anderson, wife of Dr. F. E. Anderson of Underwood, who died October 25, 1960. She was in poor health for only seven months preceding her death. She was an active member of the sixth district, state, and national auxiliaries when we last convened, and an active participant in district activities last year. A native North Dakotan, she was born and went to school in Mercer. In 1932, she was married to Dr. Anderson at Valley City, and spent the following twenty-eight years as a resident of Underwood, where she was active in church, school, and local affairs, always ready to help out in any community project. She is survived by her husband, 4 children, 8 sisters, and 5 brothers. The two younger children, a son and a daughter, are still college students; the elder son, Dr. F. E. Anderson, Jr., is married and lives in Salt Lake City, Utah; the other daughter teaches in Minneapolis. Mrs. Anderson, still in the middle years of life, was almost at the pinnacle of her career as mother, doctor's wife, and community leader when she left us. We are still keenly aware of her absence."

Mrs. Clyde Smith moved that we accept the minutes of the fourteenth annual meeting of the Woman's Auxiliary to the North Dakota State Medical Association as published in the December 1960 issue of THE JOURNAL-LANCET. Motion carried.

Mrs. McLean then asked for the report of the state treasurer which follows:

Treasurer's Report, Financial Statement, 1960-1961

Income:		
June 1, 1960 Balance on hand	$1,749.32	
Dues: 326 members at $4.00	1,304.00	
3 associate members at $1.00	3.00	
1 delinquent member	4.00	
Student loan contributions	2,447.37	
Convention expenses (men's society)	200.00	
Sale of handbook	2.00	
1961 convention balance returned	219.55	
	$5,929.24	
Disbursements		
Mrs. Geo. Holt, AMA Convention	$ 25.00	
Mrs. R. W. McLean, state president	245.00	
Mrs. L. T. Longmire, president-elect	120.00	
News, Views, and Cues	285.43	
Standing committees	49.73	
Finance chairman of convention	200.00	
National treasurer (one honorary member dues)	330.00	
AMEF	25.00	
SAMA	90.00	
Convention extra (1960)	69.00	
President's pin	7.40	
Student loan Dean Harwood	2,447.37	
	$3,893.93	
June 1, 1961 balance on hand		$2,035.31
AMEF donations	$ 815.10	

MRS. M. H. POINDEXTER, Treasurer

PRESIDENT'S REPORT (as delivered to the House of Delegates)

I am honored to bring you greetings from the Woman's Auxiliary and a brief report on our accomplishments of the past year.

To date, our membership totals 328. Our organization is made up of 10 districts, whose committees parallel yours. We adhere to the program outlined by our national organization as it applies to our auxiliary. Geographical boundaries may limit some of our districts, but although their membership and program may be small, their enthusiasm is great.

Legislation has been a major project for us, and we have worked as closely as possible with you, engaging in a campaign of letters to our congressmen, supporting the bills that would promote the advancement of medicine and public health, and working to defeat the legislation that would be detrimental to medicine.

Our health careers program is active in several districts. This year the Future Nurses Club of Stutsman District received a certificate of honor from *Parents' Magazine* in recognition of their community service.

This is the fourth year we have supported the AAPS essay content which we hoped would inspire the high school students of our state to become interested in the national medical picture. Our endeavors have not met with success. We have found that this contest is not approved by the state board of education, nor is it disapproved. Although it has been welcomed in several schools, some teachers felt that the prizes were inadequate; others dwelt on the apathy of the student who will write only required themes. We invite your suggestions concerning our participation in this program.

We have organized a committee on aging, and await your advice on how we can best serve you in this field.

Community service has become a part of our everyday life, and it would be impossible to enumerate the hours spent by our members in the many facets of this work. Mental health receives our great interest and full support. Water safety and civil defense are also projects in which we are actively involved.

We are happy to report that Sheyenne Valley is again a constituent auxiliary. For the past several years, they have had 5 members-at-large. This year they have reorganized and now have 13 active members.

News, Views, and Cues, our state auxiliary publication, is sent 4 times a year to our entire membership. In it are articles by various state chairmen, district news items, editorials, and a message from the president of the State Medical Association.

Aiding medical careers financially has long been a vital part of our program. We allotted $90 to the North Dakota chapter of Woman's Auxiliary to the Student American Medical Association. This year we contributed $815 to AMEF.

This year marks the tenth anniversary of the Sophomore Medical Student Loan Fund. Since its inception, the fund has provided aid to 53 students who had transferred from the University of North Dakota to a four-year medical school. Under the terms of the fund, no

interest is charged until internship is completed, then the rate is 2½ per cent. Loans are repaid one year later. This year the Woman's Auxiliary raised $2,437, of which $200 was a gift from Beth Rodgers in memory of her husband. Our net assets for the past ten years total over $20,000.

We continue to look to you for guidance, encouragement, and assistance. All of us are grateful for the cooperation you, your president, Mr. Limond and his staff, and Mr. Michaelson have given us. We are proud to be your Auxiliary, and we hope we have served you well.

Mrs. R. W. McLean, President

Reports from committee chairmen were then called for by Mrs. McLean.

Membership Report

Membership in the Woman's Auxiliary to the North Dakota State Medical Association this year totals 329. Of this number, 3 are associate members, 1 honorary member, and 325 regular members. There are 10 organized medical districts in North Dakota, and 10 district medical auxiliaries, including one recently reactivated.

The Woman's Auxiliary has a membership of approximately 80 per cent of that of the men's group.

Mrs. Thomas Longmire, Chairman

Program Report

In order to "Preserve and enhance the heritage of American medicine," our programs for 1960-61 in North Dakota Medical Auxiliaries have been social, educational, and informative.

Legislation has been pertinent and interest-arousing. In Stutsman Auxiliary, legislators and their wives and doctors and their wives had a "legislative dinner." The evils of socialized medicine and the merits of the Blue Cross plan were discussed, followed by a question and answer period. This same Auxiliary felt that the talk on legislation by our state president, Mrs. R. W. McLean, followed by the TV viewing of the Dr. Annis-Reuther debate was our most rewarding program of the year. The Valley City members were our guests. One auxiliary had Lyle Limond as their guest speaker on the subject of "The Saskatchewan Medical Program." An interesting program reported by another auxiliary was a speech on "Communism in the U.S.—The Threat We Face."

Mental health programs have been presented including one of particular interest on "School for the Mentally Handicapped." Some of our members attended the Mental Health Conference in Fargo, which included panels on "The Changing Role of Mental Health," "Changing Pattern of Family Life," and "Mental Health Begins at Home." One auxiliary had a program on the needs of the occupational therapy program at the State Hospital.

Other programs have been films on travel, musical programs, "Let's Learn about the Stock Market," "The Doctor's Story," and, in one auxiliary, the 2 winners of the essay contest presented their papers. Fargo again staged their very successful annual benefit dinner dance.

Three auxiliaries sponsor Future Nurses Clubs. One auxiliary feels that it should limit its auxiliary program to one phase—the paramedical careers.

I especially wish to thank the district program chairmen who helped in the survey of the part program plays in attendance. Some quotes are: "I think our problems are similar to those of any other organization." "I don't think it would be possible to assemble our entire membership for any occasion, regardless of how interesting the speaker, nor how tantalizing his topic, even a social program with just sheer entertainment." Many felt that the state president's visit brought out their best attendance. Some felt that men speakers were their best attendance attractions. One auxiliary reported that their evening meetings were not well attended.

I very much agree with the suggestion by Mrs. Paul E. Rauschenbach that, since the activities that people take part in are the key to their interests, that we accent throughout the year the activities of our own members, making them the basis of our program.

Fern Jansonius, Chairman

Civil Defense Report

Seven districts replied to letters sent 9 districts requesting reports on their civil defense activities throughout the past year. Of these 7, 2 districts reported having a civil defense chairman and one district reported having a program on North American Air Defense. Four districts reported that, though they were not active as a group, their members had participated in their city defense programs.

On April 25, a letter was received from Mrs. Chester Farrell asking that we offer our assistance to the local and state civil defense directors in connection with the nationwide civil defense alert on April 28 and 29. Mrs. Farrell's request was forwarded to the District Auxiliary Civil Defense chairman and I shall attend the local meeting pertaining to this alert.

Mrs. Edgar A. Haunz, Chairman

Publicity Report

The following paragraphs summarize the information gleaned from publicity reports given by 8 districts. All 8 districts had notices or follow-up reports of district meetings published in local papers. Most had both; and several newspapers also noted the speakers and programs. The *Bismarck Tribune* even gave advance coverage to the content of Mr. Lyle Limond's speech to the sixth district about *"A Recent Study Comparing Hospital Services in North Dakota with those in Saskatchewan Under Compulsory Hospital Plan in Effect There."*

The Hillsboro and Devils Lake papers reported our selection of our state president and president-elect, and also publicized the trip made by these officers to the Chicago Conference. The *Hillsboro Banner* also noted Mrs. McLean's visits to various district and other medical meetings. A write-up on the fall board meeting appeared in at least 3 papers in the state, according to reports from Hillsboro, Bismarck, and Devils Lake.

At least 7 newspapers announced and explained the AAPS Essay Contest. The Minot, Jamestown, and Bismarck papers also published pictures of the contest winners. SAMA meetings and programs were listed in the *Grand Forks Herald*. The *Dickinson Press* publicized the Future Nurses Club projects sponsored by the district auxiliary, as well as auxiliary projects.

Fine photographic coverage was given by the *Fargo Forum* to the first district's preparations for their King Neptune Ball, which benefits Student Loan and AMEF, also to their state convention planning meeting. The *Forum* also published an explanation of our AMEF project.

Two other districts, Grand Forks and sixth, received newspaper mention of Student Loan Fund project or contributions. The *Bismarck Tribune* also published a report of last year's total state contribution to the Student Loan Fund.

In Grand Forks, the district president-elect's picture

appeared in the local paper. TV and radio newscasts from Fargo, Valley City, and Grand Forks included mention of our 1960 State Convention.

Auxiliary aims received further publicity when our state president spoke at a hospital auxiliary meeting in Hillsboro on "The Dangers of Household Poisons," using notes from a speech given at the 1960 Chicago Conference. Another boost was received when Mrs. Mergens, Traill-Steele district president, talked to the American Legion Auxiliary about the Kerr-Mills bill.

Several districts have no publicity chairman because of the small number of members and meetings which are essentially social. Councillors act as publicity managers in 2 districts, the secretary-treasurer handles publicity in another district, and the state president gave much auxiliary news to the papers in her district. In Northwest district, publicity and public relations are handled in combination by one chairman. The other 3 large districts have publicity chairmen.

Comments and suggestions for better publicity were solicited from district publicity managers and state officers, and those replying indicated that they felt newspapers were "most cooperative," "interested," and "gave excellent coverage." One chairman reported that a newspaper society editor suggested that we have more group projects if we want more publicity. It was suggested that the district councillors might be the logical choice for publicity chairmen in all districts. One district chairman who didn't need more assistance from a state level felt that just being encouraged to seek publicity is helpful. A state officer said that she thought that the form write-up of the fall board meeting and the state convention, prepared by the state publicity chairman for all districts, was helpful.

As a state, rather than a district, publicity project, the news release concerning the AMA Auxiliary Convention in Miami was presented to the Associated Press. At their request, the state chairman, assisted by the executive secretary of the State Medical Association, added details about Dr. and Mrs. Leonard Larson and some delegates from North Dakota who planned to attend the convention. The AP gave this news state-wide distribution. This year another state-wide publicity project will be attempted when, with the assistance of Mrs. B. C. Corbus, convention publicity chairman, and Fargo photographers and newspapers, we will try to provide every district with a picture, taken at the state convention, to publicize our Student Loan Fund project, on its tenth anniversary.

We have received more good publicity this year, which indicates that many districts are more publicity conscious, district chairmen have worked hard to prepare the good publicity and most newspapers are interested in our activities. The quality of publicity this year has been almost, but not entirely, good. Since we will continue to receive some publicity, good or bad, whether we plan for it or not, a more uniform state-wide plan for handling publicity in all districts seems needed, not only to forestall publicity that might be detrimental to good public relations but also to make it easier for the state publicity chairman to distribute material and procure reports. If it is necessary to spend more money for mimeographing, postage, or pictures to publicize our projects and contributions, it will be a good investment with returns in better public relations.

Mrs. M. M. Heffron, Chairman

Legislation Report

The Woman's Auxiliary to the North Dakota State Medical Association started work early last fall, with its members responding willingly and efficiently to support the presidential campaign. Seven out of 10 districts reported giving time and money to their local campaign headquarters. As accurately as can be figured, 100 per cent of eligible voters voted.

The defeat of the Forand bill and the passage of the Kerr-Mills law does not mean our federal government has given up the fight for compulsory medical care. The AMA and the North Dakota State Medical Association asked that our district auxiliaries have another letter-writing campaign, asking our Congressmen that the Kerr-Mills law be given a fair trial. Very few members have failed to write or wire their Congressmen.

To keep the district legislation chairmen informed, they were supplied with the following material: the 1960-61 summary of legislation program for county auxiliaries; information and encouragement to the get out and vote campaign; kits on "Health Care of the Aged," containing valuable information and suggested speeches; information regarding the "Health Insurance Benefit Act of 1961;" and pamphlets on "Positive Program of Health Legislation" and "Helping Those Who Need Help."

The chairmen will soon receive information regarding "Operation Coffee Cup" to oppose the King-Anderson bill.

Seven out of 10 districts are showing a keen interest and are taking an active part in medical legislation. We are cooperating with the AMA and the State Medical Association in the fight against socialized medicine.

Mrs. L. G. Pray, Chairman

Report on the Bulletin

North Dakota's response to the *Bulletin* in 1960-1961 was very good. Four districts out of the 10 subscribed 100 per cent, and the other districts made substantial improvements in their subscriptions. The main reason for this increase in subscriptions was the fact each district had a *Bulletin* chairman who gave her full-hearted support.

When you read in the January 1961 *Bulletin* that there are 179,333 active members of the AMA, with an auxiliary membership of 80,122, and that only 9,476 of the auxiliary members are subscribers to the *Bulletin* you feel something should be done about it. North Dakota will again go on record supporting the idea the *Bulletin* should be included with our national dues. We feel the AMA could afford to issue the *Bulletin* free of charge to the auxiliary in recognition of the support and assistance their auxiliary gives them. By so doing, the auxiliary would be a better informed and stronger group. The doctors receive their publication with their dues, why not the women?

Mrs. George H. Holt, Chairman

Report on the American Medical Education Foundation

This year, we did not have a state fund-raising project. Because of the diversity of size of districts, and the many other community projects of auxiliary members, it was decided to leave the method of raising funds for AMEF—whether by members' contributions, assessments, or district projects—to the various districts. We set a goal of $2 per member, as proposed by last year's chairman. With 328 members in the state, a total of $815.10 has been sent to the national office. One district was unorganized until recently and did not contribute. Twenty-five dollars was received from the state auxiliary. Of the

remainder, $260 was given through private donations as memorials, and $530.10 was contributed by 9 district auxiliaries. Money raising projects included the sale of stationery, the sale of cookies, a candy sale, a benefit ball (to benefit the Student Loan Fund as well as AMEF), members assessments, and district contributions.

Mrs. B. A. Mazur, Chairman

Mrs. Mazur then presented a Certificate of Achievement to the ninth district for the largest total and per capita donation to the AMEF. The Certificate was accepted by Mrs. Hankins.

Historian's Report

The fourteenth annual meeting of the Woman's Auxiliary to the North Dakota Medical Association was held in Grand Forks, on Monday, May 2, 1960, at the YWCA, with Mrs. Van der Linde presiding. Preconvention board meeting was held May 1, 1960, in the Gridiron Room, Hotel Ryan.

Official minutes are recorded in the December issue of The Journal-Lancet. The convention program, all minutes, and reports are filed in the archives. The fall board meeting was held in Fargo, October 18, 1960, at the Gardner Hotel, with Mrs. R. W. McLean presiding, and 23 members present.

Mrs. George Holt, Jamestown, North Dakota's delegate to the national convention, said her report of the convention had been printed in the September issue of *News, Views, and Cues*. Mrs. L. T. Longmire, president-elect, gave the highlights from her report on the Chicago conference, which was published in the November issue of *News, Views, and Cues*.

Guest speakers at the state convention were Mrs. Stephen Bacheller, north central regional vice-president of the auxiliary to the American Medical Association, Enderlin, and Dr. J. C. Fawcett, president of the State Medical Association. The registration at the state convention numbered 107 members, with a total auxiliary membership of 324.

Achievements on national and state level quoted from *News, Views, and Cues*: Mrs. B. A. Mazur, Fargo, was publicity chairman of the Mental Health Conference held in Fargo, October 1960. Mrs. S. C. Bacheller, Enderlin, is president of the North Dakota Heart Association, and Mrs. Paul Johnson, Bismarck, is secretary of the group.

R. Pearl de Moully, Historian

Program of the Woman's Auxiliary

SUNDAY, MAY 1, 1960

12:00 Noon. Registration. Ryan Hotel, Mrs. T. Q. Benson, chairman.

1:00 P.M. Nominating committee meeting. Gridiron room, Ryan Hotel. Mrs. V. J. Fischer, chairman.

2:00 P.M. Finance committee meeting. Gridiron room, Ryan Hotel. Mrs. Henry Kermott, chairman.

3:00 P.M. Sophomore medical student loan fund committee meeting. Gridiron room, Ryan Hotel. Mrs. R. H. Waldschmidt, chairman.

4:00 P.M. Preconvention board meeting. Mrs. J. M. Van der Linde, president, presiding.

6:30 P.M. Informal mixer and buffet supper. Grand Forks Country Club.

MONDAY, MAY 2, 1960

8:30 A.M. Past presidents breakfast. Mrs. G. G. Thorgrimsen, chairman.

9:00 A.M. Registration, Lobby, Ryan Hotel.

9:30 A.M. Opening session. Grand Forks YWCA. Mrs. J. M. Van der Linde, president, presiding.
Pledge of Loyalty: Led by Mrs. R. W. McLean, president-elect.
Invocation: Mrs. L. T. Longmire, first vice-president.
Welcome: Mrs. William P. Keig, Grand Forks.
Response: Mrs. K. G. Vandergon, Portland.
Greeting: Dr. J. C. Fawcett, president, North Dakota State Medical Association.
In Memoriam: Mrs. J. W. Jansonius, Second Vice-President.
Reports of State Officers, Chairmen, and District Presidents.

12:30 P.M. Luncheon. YWCA. Mrs. Charles Graham, chairman.
Mrs. R. W. McLean, president-elect, presiding.
Address: Dr. C. M. Lund, president-elect, North Dakota State Medical Association.

2:30 P.M. Second Business Session. YWCA. Mrs. J. M. Van der Linde, president, presiding.
Unfinished business, new business.
Election of officers.

6:30 P.M. Informal banquet. Nodak Room, Ryan Hotel. Mrs. Philip H. Woutat, chairman. Mrs. E. A. Haunz, Grand Forks, district president, presiding.
Honored guest and speaker: Mrs. Stephen Bacheller, north central regional vice-president of the Auxiliary to the American Medical Association, Enderlin.

TUESDAY, MAY 3, 1960

10:30 A.M. Brunch. Grand Forks Country Club, Mrs. W. P. Keig, chairman. Mrs. James D. Gardy, convention chairman, presiding.
Entertainment.
Installation of new officers.
Postconvention board meeting.
Transportation will be furnished to anyone so requesting.

1960-61 Officers and Chairmen of Standing and Special Committees

STATE OFFICERS

President—Mrs. R. W. McLean, Hillsboro
President-elect—Mrs. L. T. Longmire, 810 6th Street, Devils Lake
First vice-president—Mrs. J. W. Jansonius, 609 4th Ave. S.E., Jamestown
Second vice-president—Mrs. Ruben H. Waldschmidt, 600 N. Washington, Bismarck
Recording secretary—Mrs. Clyde Smith, 622 Raymond Ave., Bismarck
Treasurer—Mrs. M. H. Poindexter, 1350 So. 9th St., Fargo

STATE COMMITTEE CHAIRMEN

Organization (Membership)—Mrs. L. T. Longmire, 810 6th, Devils Lake
Program—Mrs. J. W. Jansonius, 609 4th Ave. S.E., Jamestown
Civil Defense—Mrs. E. A. Haunz, 1029 Lincoln Drive, Grand Forks
Nominating—Mrs. J. M. Van der Linde, 1016 4th Ave. N.E., Jamestown
Publicity—Mrs. M. M. Heffron, 320 Ave. B. West, Bismarck
Legislation—Mrs. L. G. Pray, 1701 S. 8th St., Fargo
Bulletin—Mrs. George Holt, 204 2nd Ave. S.W., Jamestown
Historian—Mrs. Oliver De Moully, 1715 Ave. E. East, Bismarck
A.M.E.F.—Mrs. B. A. Mazur, 1237 N. 3rd St., Fargo
Parliamentarian—Mrs. Theodore Benson, 1524 Walnut St., Grand Forks
Mental Health—Mrs. R. L. McFadden, 910 3rd Ave. N.W., Jamestown
Health Careers—Mrs. Robert Schoregge, 621 Ave. F. West, Bismarck
By-Laws—Mrs. V. J. Fischer, 303 8th Ave. S.E., Minot
Safety—Mrs. John Fawcett, 1125 5th St., Devils Lake
AAPD—Mrs. Theo. Keller, Rugby

CHAIRMEN OF STANDING AND SPECIAL COMMITTEES

Community Service—Mrs. Mack Traynor, Jr., 1020 S. 5th St., Fargo
Committee on Aging—Mrs. D. J. Halliday, Kenmare
Liaison to SAMA—Mrs. J. D. Cardy, 1110 Reeves Drive, Grand Forks
Student Loan Fund—Mrs. John A. Sandmeyer, 1005 Lanark, Grand Forks

OFFICIAL PUBLICATIONS

News, Views, and Cues—Managing Editor: Mrs. J. H. Mahoney, 601 8th St., Devils Lake. Business and Circulation Manager: Mrs. Charles Arneson, 714 N. 2nd St., Bismarck. Co-Editor: Mrs. Robert Hankins, Mott.

DISTRICT PRESIDENTS

First District—Mrs. Calvin Fercho, 1747 S. 7th St., Fargo
Second District—Mrs. George Hilts, Cando
Third District—Mrs. W. P. Keig, 501 17th Ave. S., Grand Forks
Fourth District—Mrs. Gale R. Richardson, 12 - 10th St. S.W., Minot
Fifth District—Members-at-large
Sixth District—Mrs. Reuben H. Waldschmidt, 600 N. Washington, Bismarck

Seventh District Mrs. E. O. Hieb, 300 - 6th Ave. N.E., Jamestown
Eighth District Mrs. John Craven, 403 - 3rd Ave. E., Williston
Ninth District Mrs. D. N. Mergens, Hillsboro
Tenth District Mrs. Robert Hankins, Mott

COUNCILLORS

First District Mrs. John Bond, 516 S. 13th St., Fargo
Second District Mrs. L. T. Longmire, 810 - 6th St., Devils Lk.
Third District Mrs. R. C. Painter, 1121 Belmont Rd., Grand Forks
Fourth District Mrs. V. J. Fischer, 303 - 8th Ave. S.E., Minot
Fifth District Members-at-large
Sixth District Mrs. M. M. Heffron, 320 Ave. B. West, Bismarck
Seventh District Mrs. R. L. McFadden, 910 - 3rd Ave. N.E., Jamestown
Ninth District Mrs. Mervin Rosenberg, Northwood
Tenth District Mrs. R. F. Raasch, Box 990, Dickinson

Report of Mental Health Committee

Early in March I wrote to the president of each of the 10 districts in the state asking them for their activities in the mental health program. Since that time I have had replies from 8 districts.

The First District reported: "The First District of the North Dakota State Medical Auxiliary has provided refreshments for the senior citizens' meetings twice each month. In addition to this group project, Mrs. B. A. Mazur is vice-president of the Cass County Mental Health Association and served as publicity chairman for the state Mental Health Conference held in Fargo last fall. Dr. Jane Magill was a member of a panel for this conference. During Mental Health Week in May 1960, Mrs. Mazur was area chairman for the state project 'Operation Friendship.'"

At the October meeting of the Fourth District, Captain Paul Kiell of the Air Force Hospital, Minot, spoke on "Mental Health" and the proper attitudes for facing everyday life, and the speaker in January was a local teacher of mentally handicapped children. Both these talks were followed by a question-and-answer period.

The March meeting of the Seventh District featured a program on mental health, with a film entitled "A Family Affair," procured through the State Health Department at Bismarck. This most cooperative department will send an up-to-date list of films available for such a program. There is no charge for this service, just return postage.

In July we will hold our yearly Auxiliary-sponsored State Hospital birthday party at which time we will supply cakes, gifts, and entertainment for patients at the State Hospital who have July birthdays.

The Tenth District president reported that the Medicorps of Mott, which is Auxiliary-sponsored, had sent several parcels to the Occupational Therapy Department at the State Hospital.

KATHERINE MCFADDEN, Chairman

Report of Health Careers Committee

Letters were sent out to the district chairmen requesting information regarding their local health career program for the year. To date, First and Fourth districts have not completed their reports as they have been working with their local schools on a career day program. Second and Third districts have had no project under way this year. Ninth District has proved that interest can be created and sustained through their Medicorps program and annual teas. Seventh District has had another successful year with their Future Nurse Club. The Sixth district heard of a medical career program that was instituted by the Lewis and Clark District nurses.

There are steps being taken by the State Health Careers to organize a statewide committee which will be known as the North Dakota Council on Health Careers. I attended one of the two meetings held each year and found their goals much the same as ours. The objectives are to provide information opportunities for service in the health career fields and to promote extension of scholarship resources.

Membership of the council will be open to duly designated representatives of all professional groups. The council hopes to provide brochures on all medical fields which will be placed in high school libraries throughout the state.

I feel being a part of this council would be helpful in accomplishing our aims and objectives. This letter is being submitted for discussion.

IRIS M. SCHOREGGE, Chairman

Report on State Safety Program

The safety program for the past year has been the "swat" project. With the tremendous activity in water sports, there has been an alarming increase in casualties as the result of careless use of boats and water equipment.

At the October 1960 board meeting we presented the project for a round table discussion. In a brief survey we found that some of the delegates, living near accessible lakes and rivers, have a governing body which exercises a safety control system. These delegates were to ask their respective auxiliaries to incorporate some of the ideas presented. Some delegates thought there should be more active promotion of safeguards in and about all sports areas.

Our national safety chairman, at last year's national convention, offered the following suggestions to be used by the auxiliaries:

1. Make posters illustrating water sports, captioned with catch phrases, and placed in store and office windows to attract the attention of passers by.

2. Ask that editorials on water safety appear monthly in local papers, especially during the summer months.

3. Present suggestions and ideas to PTA groups in the hope of reaching the parents, and through them, impressing the children of the caution necessary in water sports. Also urge active participation in supervised swimming lessons at city pools and summer camps.

4. Urge state and local officials who govern water areas to enforce more rigid rules and policing of these areas, to insure the safety of lives of the casual swimmer and boater, as well as the more active participants.

CLARE E. FAWCETT, Chairman

Report on AAPS Essay Contest

Last fall 174 "Packaged Libraries," each containing full information on the current AAPS Essay Contest, were distributed throughout the state.

The response was astonishingly small. The total number of essays written was 32, with 5 from second district, 1 from third, 15 from fourth, 2 from sixth, 4 from seventh, and 2 from tenth. I am confident the district chairmen did their utmost to make this contest a success and I sincerely thank each of them.

The committee of state judges was composed of Dr. John Hove, chairman of English; Dr. J. Frank Cassell, chairman of zoology and pre-med advisor; and Mr. Donald F. Schwartz, acting director of communications—all from the North Dakota State University.

The state winners, in ranking order, were (1) Susan Effertz, Bishop Ryan High School, Minot; (2) Janice

Evans, St. James High School, Grand Forks; and (3) Jeffrey Retzlaff, Jamestown.

Mrs. E. T. Keller, Chairman

Report of Community Service Committee

It is the purpose of the Community Service Committee to study matters of public importance relative to health education, and to correlate the work of the Auxiliary with that of other organizations.

Wherever there are doctors there are doctors' wives busy giving of themselves and their talents to enrich the life of their communities. It is extremely difficult to report in specifics the many community activities of our auxiliary members in North Dakota. In our larger cities, many of the activities suggested by the national committee are already sponsored by other local organizations (e. g., senior citizen programs, honoring outstanding citizens, etc.). In smaller district there is no need for a community service committee at all.

A few of the community service activities shared by more than one district are the following: financial support of AMEF and the Medical Student Loan Fund, sponsorship of or assistanee with some type of Senior Citizen program, health career programs in the schools, pre-natal and well-baby clinics, and AAPS essay eontest.

Perhaps our doctors' wives make the most impact as individuals. Each district's members include outstanding citizens in their various communities; they are active and hold offices in school organizations, in Camp Fire Girls, and in Girl and Boy Scouts. They serve as leaders and bloek workers in the various health organization drives. They are vital in our Mental Health program. In music and study clubs, in art and dramatics, they help enrich our cultural life. They are beeoming increasingly interested in the area of medical legislation. They serve on boards of welfare and edueational institutions, both public and private. They work in their churches and in their hospital auxiliaries.

Truly the North Dakota Medical Auxiliary can be proud of its members, for they have proved, as before, that they are active and loyal eitizens.

Mrs. Mack V. Traynor, Jr., Chairman

Report of District News Editor

News, Views, and Cues has put out 4 issues this year—October, December, February, and April. We have had excellent cooperation from District Councillors and reporters. We have heard from all 10 districts at least once, and the majority eontributed to all issues. Deadlines were met promptly and it was greatly appreciated.

The most pertinent column is "Meetings and Auxiliary Projects," which covers the programs of each district. "Membership" gives us a chance to welcome new members and say farewell to old friends. It also keeps us informed of the moves made within the state. "Community Serviee" shows that our membership is very aetive in numerous other groups and causes. We can tell that we have a young and vigorous membership in the long listing of new babies in "Progeny." The "Illnesses" and "In Memoriam" columns add a sad note but fortunately there is little to report in these categories.

"Travelogue" has presented a bit of eontroversy, also news of what children of members are doing—who is in school, their engagements, weddings, etc. We would like this problem to be brought to the Board of Directors or the House of Delegates to see what is really desired by the group. In all fairness I should mention that we frequently hear about members and even whole districts *only* through these columns. But on the other hand, it does tend to get bulky. There has been comment that some are reluctant to give this information and think it unnecessary. If you leave it up to the need for cutting, it is difficult to decide where to do the cutting. Also—few other state auxiliaries include such news in their state publieations.

One other suggestion is made as to *News, Views, and Cues*: Would it be possible to make this a rotating committee?

For instance: First year: Business and Circulation Manager—keeps up lists of current addresses and pays bills—should be mailing too, if possible.

Second year: District News Editor—makes contacts with councillors and reporters and types up District News Section for printer.

Third year: Editor-in-Chief—gets all national and state reports ready; responsible for makeup and printing (mailing too, when circulation manager is too far away).

If this is not feasible, at least have it understood that these posts are for three years and relief will come then, so that a president would have only *one* replacement to make on the staff each year.

Flo Hankins, Chairman

Report on Medical Student Loan Fund

Ten years ago, on June 13, 1951, the first check, representing the funds colleeted to start our Sophomore Medieal Student Loan Fund, was presented to the University of North Dakota Medical School. The amount of the check was $1,047.76. Ten years later the net worth of our fund is $18,400.22.

During this period of the fund's existence, 53 students have borrowed money. Of these, 21 are still in school or are interning. A fairly large number are in military service or are taking residencies, while 14 are now practicing in North Dakota. Of these 14, only 3 have set up practice in the larger cities of the state.

During the past calendar year of 1960, 9 loans have been made, totaling $4,285. Eight loans were for $500 each and the ninth one, granted on or about last Thanksgiving, requested $500 but had to be cut down to $285. That left exactly 29 cents in the fund. As of Deeember 31, 1960, the eash balance in the fund was $570.29. Our notes receivable now total $17,829.93. Interest collections in the past ten years have yielded $472.57. Thus, the current worth of the fund on December 31, 1960, was $18,400.22.

Since that date I am happy to report the following contributions which have been colleeted by the various districts and which will be added to that amount:

First District (Fargo) 72 members (dinner dance)	$300.00
Second District (Devil's Lake) 19 members (assessment)	76.00
Third District (Grand Forks) 57 members (Two benefit dinner dances)	491.37
Fourth District (Northwest) 42 members (assessment)	380.00
Fifth District (Sheyenne Valley) 10 members (assessment)	10.00
Sixth District (Bismarck) 57 members (assessment)	600.00
Seventh District (Stutsman) 21 members (assessment)	210.00
Eighth District (Kotana) 19 members (assessment)	100.00
Ninth District (Southwest) 20 members	50.00
Tenth District (Traill-Steele) 11 members (assessment)	20.00
Total members, 328; total contributions	$2,237.37

A further contribution came in the form of a memorial gift from Mrs. R. W. Rodgers of Dickinson and her daughters, Mrs. Keith Gardner and Mrs. Edwin Markel,

in honor of the late Dr. R. W. Rodgers. This gift made the total of our contributions to the student Loan Fund $2,437.37 for the year 1960-61 and should increase our net assets to the amount of $20,887.59.

Mrs. John Sandmeyer, Chairman

Resolutions Report

1. *Be it resolved* that this convention of the Woman's Auxiliary to the North Dakota State Medical Association extend to Mrs. Robert W. McLean its sincere thanks and appreciation for the service which she has rendered to that group in the past year.

2. *Be it resolved* that the Woman's Auxiliary to the North Dakota State Medical Association express its appreciation and thanks to the city of Fargo; to the First District Medical Society; to Mrs. B. A. Mazur, convention chairman; to managers and staffs of hotels and motels; to members of the press, radio, and television; to Mr. Lyle Limond and his staff; to Dr. Carroll M. Lund, president of the North Dakota State Medical Association; to Mrs. C. Rodney Stoltz, North Central regional vice-president of the Woman's Auxiliary to the American Medical Association; and to all other persons and groups who have contributed to the success of the convention.

3. *Be it resolved* that the Woman's Auxiliary to the North Dakota State Medical Association express appreciation for the help and co-operation from all persons, organizations, and agencies who contributed to the success of its program during the past year.

Mrs. Clyde Smith, Chairman

Auxiliary President's Report—First District

The First District Medical Auxiliary is still growing. We have 76 active members this year.

Four meetings were held in 1960-61, 3 luncheons and 1 dinner. Our luncheons were very well attended, the dinner, poorly. Our first luncheon was held October 31, at the new Oak Manor Lodge. Mrs. Robert Farris spoke on communism, "The Threat We Face." At the luncheon on January 30, at the Tree Top Room, FM Hotel, Mr. Rod Carlson spoke on the stock market in terms we could all understand. At our dinner meeting on February 28 at the Gardner Hotel, our own Dorothy Bacheller spoke, the title "Telling the Doctor's Story." At our last meeting on March 29, in the newly opened Biltmore Dining Room, speakers were Mrs. Robert McLean and Mrs. J. W. Jansonius. Officers were elected.

The Fall board meeting was held in Fargo as a convenience for Mrs. McLean. We were pleased to assist her with preparations.

Our largest undertaking this year was our benefit dinner dance held Saturday, February 4, 1961, with Mrs. F. A. De Cesare and Mrs. James Houghton as co-chairmen. An "Under the Sea" theme was chosen entitled "King Neptune's Ball." From profits we were able to contribute $400 to the Student Loan Fund and $150 to AMEF.

Our legislative chairman, Mrs. John Goff, urged us to write our congressmen to support the Kerr-Mills bill instead of the social security approach to medicine.

As a community service gesture this year, the auxiliary donated $30 to the Opportunity School for Handicapped Children to be used to enlarge their library. Again this year the Mental Health Committee furnished the Senior Citizens Group desserts for their bi-weekly meetings at the YWCA.

We have 16 Bulletin subscriptions.

The Para-Medical Careers Committee, headed by Mrs. J. B. James and her assistants, Mrs. Mack Traynor and Mrs. Gerald Kavanaugh, has been an ambitious one. This year we rented a booth at the Science Fair, held April 8 at the new Civic Auditorium and staffed it with auxiliary members' sons and daughters of high school age. Much literature on medical careers was distributed. The committee has also been working with the advisors in our local high schools, who have offered to set up a file of medical personnel who would be willing to advise high school pupils. The medical auxiliary would be the agency to administer the requests. This will be a continuing project for the auxiliary.

The chairman for the convention is Mrs. Bernard Mazur, assisted by Mrs. Charles Heilman. We are grateful for the help we are receiving from the Jamestown and Valley City auxiliaries under the new zone plan.

The officers for this year have been Mrs. J. F. Houghton, vice-president; Mrs. Mack Traynor, secretary; Mrs. David Jaehning, treasurer; and Mrs. John Bond, councillor.

Mrs. Calvin K. Fercho, President

Auxiliary President's Report—Second District

The Devils Lake District Medical Auxiliary held a social or dinner meeting once a month this past year. To encourage better attendance, these meetings were held on the same night the doctors had their meetings. Two of our dinners were preceded by a social hour to which the doctors were invited. Mrs. R. W. McLean was our guest of honor at the November meeting.

Our membership totals 19. Many of our members are active in community affairs, such as PTA, hospital auxiliaries, 4-H, March of Dimes, park board, and community chorus, and some members were actively engaged in the political campaign. A donation of $76 was made to the Student Loan Fund. This donation is based on membership. A $20 donation was made to AMEF. Many of our members received the *Bulletin* and *Today's Health*.

Flora Hilts, President

Auxiliary President's Report—Third District

Largely because of effort put forth by the chairman of the membership committee, Mrs. G. G. Thorgrimsen, our auxiliary increased to 57 members during the year 1960-61.

The program for our first meeting, held October 20, consisted of an excellent talk on civil defense and progress at the Grand Forks Air Base by Squadron Leader Douglas Bullock. We were entertained at the November 17 meeting by an attractive style show in which 8 members of our auxiliary were models. Because the state medical society was being held at the time, an invitation to attend this show was extended to and accepted by a number of women from other auxiliaries in the state.

The heart of our January meeting was an interesting and stimulating talk on legislation, particularly the Kerr-Mills bill, by our state president, Mrs. Robert McLean. At our final meeting, on March 16, a buffet dinner was followed by a demonstration by Mr. Kenneth Hall on various ways of arranging flowers.

Since 1960-61 was a vital year in American politics, many of our members contributed greatly to the over-all effort to block socialized medicine by actively working for candidates they considered opposed to it and by writing their congressmen on behalf of the Kerr-Mills bill and in opposition to any extension of the Social Security program.

The sum of $475 was raised this year for the medical students loan fund by having two dinner dances instead of the one traditional affair.

In spite of a valiant effort on the part of Mrs. John Graham, chairman of community service, our singular failure this year was in the promotion of the essay contest sponsored by the American Association of Physicians and Surgeons. Mrs. Graham encountered open, and probably justifiable, opposition from school officials in most of the 15 schools contacted on the basis that, by the very titles proposed, it was obvious that the AMA had an ax to grind. She was told over and over that these titles had not been approved by the National Board of Education. As a result of this opposition, only 4 students entered the contest from our district. It is our recommendation that if we are to promote this contest again next year, the AMA be contacted regarding changes in the titles that would make them acceptable to the National Board of Education.

The sale of note paper for AMEF produced the amount of $84.10.

If we accomplished anything this past year it was because of the complete co-operation, spirit, and friendliness of the entire board and committees. This has been a wonderful experience I will long remember.

Mrs. William P. Keig, President

Auxiliary President's Report—Fourth District

The Northwest District Medical Auxiliary held 3 evening meetings in the homes of members and 2 dinner meetings. At the first meeting in October on mental health, Captain Paul J. Kiell, psychiatrist of the U. S. Air Force Hospital, discussed the proper approach to our daily routine, and the psychotic criminal and his chances for rehabilitation into society.

In December, a dinner meeting was held jointly with the Northwest District Medical Society. Dr. Darwin Kohl provided a pleasant evening of musical entertainment.

Mrs. Melvin Olson, an instructor from the school for the mentally handicapped, spoke to us at our January meeting. We were informed that this school is supported entirely by donations, and so $25 was contributed to this worthy cause.

We were pleased to have our state president, Mrs. Ann McLean, to speak and visit with us at our March meeting. She was most encouraging to us in the proper approach to our duties and stressed continuing our legislative work encouraging a fair trial of the Kerr-Mills Law. Our legislative chairman, Mrs. Gertrude Shea, contacted all members to encourage them to write to our senators and congressmen.

A dinner meeting is planned in April to wind up any unfinished business, and for voting and installation of officers for the coming year.

There are 42 members and 2 honorary members in our auxiliary this year. We enjoyed having the Air Force Hospital wives at our meetings. Their help on our local projects is greatly appreciated. A $25 contribution was made to Camp Sioux in Grand Forks for diabetic children.

The members preferred to continue donating $10 each toward the Student Loan Fund. Thus far, we have collected $380. Subscriptions to the *Bulletin* and *Today's Health* are taken out of each member's dues. *Today's Health* is being placed in all schools and colleges in Minot.

A memorial fund has been used by our membership for AMEF. So far, we have collected $30 in memorials and added $50 to this to make a total of $80 for this fund.

We were pleased and happy to hear that one of our essay contest winners, Miss Carol Effertz, won first place in the state. We contributed $25 toward the prizes and the Northwest District Medical Society contributed $25.

The junior and senior high schools have "Careers Day" here in April. Mrs. Louise Heidorn, para-medical chairman, has been most helpful in giving us some worthwhile data as to how we may help in this program. This is and has been sponsored by one of the Business Men's Clubs.

Our publicity chairman, Mrs. Jens Sahl, has given us much publicity in our local news media as to meetings and projects. She also serves as a liaison between the auxiliary and other clubs and organizations. This includes serving and assisting both of the hospital auxiliaries and the foreign student exchange.

A proper form of bookkeeping has been organized and set up by the treasurer. These books are audited at the close of each year before being passed on to her successor. Each year the program committee plans the year's schedule and has printed a small pamphlet of all meetings, officers, committees, and hostesses. These are distributed to each member and all prospective members at the beginning of the year.

Mrs. Gale Richardson, Chairman

Auxiliary President's Report—Fifth District

In February 1961, the medical doctors' wives of Valley City were invited to the home of Mrs. Merrett for coffee. At this time we discussed dropping our status as members-at-large to become an organized active part of the North Dakota Woman's Medical Auxiliary. Since Valley City has acquired 3 new doctors, giving Valley 7 practicing physicians, it not only seemed feasible, but desirable to reorganize.

We plan to meet 4 times a year for dinner and at that time discuss and carry out any project we decide upon.

Our new officers are Mrs. Clifford Klein, *Newsletter;* Mrs. John Goven, councillor; Mrs. Clayton Jensen, secretary-treasurer; Mrs. Warren R. Jensen, president.

Mrs. Warren R. Jensen, President

Auxiliary President's Report—Sixth District

The Sixth District Medical Auxiliary held 4 meetings. At the first meeting, on October 31, 1960, at Municipal Country Club, new members were introduced and each chairman reported on the functions of her committee. Lyle Limond gave an inspiring talk on "Saskatchewan Medical Program," recent study of the comparative hospital service in North Dakota and Saskatchewan.

Our second meeting, held at the Steak House on December 7, was conducted by Mrs. M. A. Lommen and Mrs. Roger Berg. The program was given by flute pupils of Mrs. M. Nugent—Paula Johnson, Paula Quale, and Cheryl Johnson. A musical reading was given by Moira Heffron and Kitty Boyle.

On February 28, 1961, a potluck dinner was held at the Waldschmidt home. Our state president, Mrs. R. W. McLean, was present and gave us many helpful and favorable suggestions. Slides of Pan-Pacific Medical Meeting in Hawaii were shown by Mrs. Waldschmidt.

At the luncheon on April 22 at the Prince Hotel, Sandra Sims, Mandan, and Joseph Crawford, Bismarck, essay contest winners, read their papers and received their

prize money. Mrs. Richard Klein, one of the judges, was a guest.

New officers for the coming year were elected. They are: president, Mrs. Roger Berg; vice-president, Mrs. M. A. K. Lommen; secretary, Mrs. William Buckingham; treasurer, Mrs. Robert Kling. Mrs. T. L. Stangbye and Mrs. W. D. Waldschmidt were appointed delegates to the state convention in Fargo.

The Sixth District has 57 paid members and 1 transfer. Our policy still holds in regard to Medical Student Loan Fund: each member has the choice of donating $10 or raising the money herself. This year, $600 was sent to the fund; $38.70 was made through a cookie and candy sale to help pay $114 to AMEF. Subscriptions for the *Bulletin* netted $17.

Mrs. R. H. Waldschmidt, President

Auxiliary President's Report—Seventh District

The Stutsman County Medical Auxiliary, with 21 members, held 4 meetings this year. The first afternoon meeting, at the home of Mrs. John Jansonius, brought an excellent report on the National Convention from delegate Guneil Holt of Jamestown. It was agreed to raise our annual dues to cover a $2 per member assessment to AMEF, and $10 per member to the Student Loan Fund. Mrs. S. J. Thackor reported on the progress of the Future Nurses Club and their successful convention at the State Hospital on September 17, with 45 girls in attendance. Miss Gladys Wentland, executive secretary of the North Dakota Nurses Association, was the main speaker.

Our Christmas tea was at the home of Mrs. Ed Hieb; all members brought generous gifts of good clothing and toys for 2 needy families in our community. The main order of business included a resolution for a request for an honorary membership for Mrs. Philip Arzt, the first state president of the North Dakota Medical Auxiliary. Mrs. Guneil Holt reported a successful drive for *Bulletin* subscriptions. A decision was made to ask the doctors' wives in Valley City to join us at our February meeting in an effort to stimulate a reactivation of their group.

Mrs. John Jansonius entertained at a social hour in her home preceding our February dinner meeting, with our state president, Mrs. Robert McLean, as the honored guest. We were joined by 5 auxiliary members from Valley City. Mrs. McLean gave us a timely message on current legislation. The meeting adjourned to the home of Mrs. Hieb to watch the TV debate between Dr. Annis and Walter Renther.

At the final afternoon meeting in March, held at the home of Mrs. S. J. Thakor, plans for the state convention luncheon and the patients' birthday party at the State Hospital were discussed. Mrs. Thakor reported that the Future Nurses Club had received a certificate of honor from *Parents' Magazine* in recognition of their community service for the past year. In addition to the regular meetings, which have been of interest in many phases of health careers, the girls help with the juice cart in one of the hospitals and will assist with the Cancer Drive in April. A film on mental health was shown. Officers elected for the coming year are: Mrs. Clifford Hogan, president; Mrs. S. J. Thakor, vice-president; Mrs. J. Jestadt, secretary-treasurer; and Mrs. Robert McFadden, councillor.

Mrs. E. O. Hieb, President

Auxiliary President's Report—Eighth District

The Kotana District of the Medical Auxiliary has added 2 new members to its group this year, making a total membership of 19. We were happy to have Mrs. Milton Berg, of Tioga, and Mrs. Thomas Sussex, of Watford City, join us in January. Since we are still a small group, with many of our members living outside of Williston, it was agreed that we could not participate in all the fund-raising projects of the larger-city auxiliaries.

This does not mean, however, that our members are inactive. Each one of us contributes our share of time to the civic undertakings, health clinics, cancer and heart programs, polio, and crippled children clinics when they are held in Williston.

The Woman's Auxiliary usually meets two or three times during the year in conjunction with the Kotana Medical Society; this is always a dinner meeting. Following this, we have a business meeting for collecting dues and any other moneys which are due at that time, and a social hour is enjoyed at the members' homes.

The contributions for the year 1960 include:

Membership dues	$ 76.00
Medical Student Loan Fund	100.00
AMEF	10.00
Total	$186.00

Mrs. John P. Craven, President

Auxiliary President's Report—Ninth District

There are five meetings a year—the second Saturday of June, October, December, February, and April. The June meeting was held in Mott with dinner at the Curve with a social hour following. The October and December meetings were joint dinner meetings with our husbands. December's meeting was a dinner-dance Christmas party. In February we met for dinner at the Elks Club and for a business meeting at the home of Mrs. Guloien. Anne McLean was invited for the April meeting, with dinner at the Elks' and a business meeting at Mrs. Hannewald's. The president of the Future Nurse Club of Dickinson told what they have been doing this year. Appropriations were made for AMEF and Student Loan. This year, state and national dues were sent in for 20 members.

There are 2 Health Careers Clubs in the District, both in their fourth year. The Future Nurses Club of Dickinson has had advisers from the Auxiliary each year; this year they were Mesdames Hannewald, Gilsdorf, and Dukart. Mrs. R. Hankins continues as the adviser of the Medicorps of Mott. Both clubs have more than 20 members and have varied and interesting programs. Together they attended the rally in Jamestown in September, where they were royally treated by the Jamestown Future Nurses Club and the State Hospital. The Medicorps meets once a month all year round and the Future Nurses Club meets twice a month during the school year. The girls in Mott spend a week during their summer vacations at the hospitals in the area, since there is no hospital there. The Elgin hospitals, St. Joseph in Dickinson, and Bismarck Hospital have all taken many girls for a week. The district auxiliary has set aside $50 per year to help pay for trips and awards and the annual tea they sponsor at St. Joseph.

There were only 3 entries in the essay contest, one of which arrived too late to be included. Prizes of $15 and $10 were given by the medical association.

A $50 contribution was made to AMEF and $50 to the Student Loan Fund.

Mrs. R. E. Hankins, President

Auxiliary President's Report—Tenth District

We are a small social group organized for the purpose of supporting our husbands in their North Dakota Medical Association activities.

Traill-Steele District covers a rather large area and therefore the 11 members are so widely separated that no actual group activity is feasible. This year, from contributions by members, we donated $20 to the Student Loan Fund and $20 to AMEF.

Meetings are held in a centrally located town 4 times a year. The husbands and wives of the Tenth District have supper together, after which our business meetings are held separately. No minutes are kept of our meetings but we discuss topics of current interest and importance.

This year we have two new members: Mrs. Lars M. Vistness, Cooperstown, and Mrs. Russell Odegard, Hatton. We have also lost one member, Mrs. Keith Vandergon, formerly of Portland, and now of Grand Forks. She was our councillor and has been replaced by Mrs. Mervin Rosenberg, Northwood.

New officers for the coming year are: president, Mrs. J. M. Little, Mayville; vice-president, Mrs. Russell Odegard, Hatton; secretary-treasurer, Mrs. R. C. Little, Mayville.

Mrs. Daniel N. Mergens, President

Convention Report

Luncheon was served at the Biltmore Motor Hotel on May 8, with Mrs. L. T. Longmire presiding. Decorations, which carried out the convention theme, "Greater Horizons," were provided by members of Stutsman Auxiliary, with Mrs. E. O. Hieb as luncheon chairman. Mrs. Longmire presented Mrs. Hieb, who introduced the following persons seated at the head table: Mrs. C. K. Fercho, Mrs. Charles Heilman, Mrs. E. Boerth, Mrs. C. M. Lund, Mrs. R. H. Waldschmidt, Mrs. J. W. Jansonius, Mrs. C. R. Stoltz, Mrs. R. W. McLean, Mrs. L. T. Longmire, Dr. E. H. Boerth, Mrs Clyde Smith, and Mrs. M. H. Poindexter.

Mrs. Longmire read the names of the past presidents of the Auxiliary and introduced Mrs. Stephen Bacheller, Mrs. V. J. Fischer, and Mrs. J. W. Van der Linde, all former presidents. Mrs. Longmire then introduced Dr. Edwin Boerth, president-elect of the North Dakota State Medical Association.

Dr. Boerth read a resolution from the House of Delegates conveying appreciation and thanks to the Auxiliary for its excellent work. Dr. Boerth spoke of the drastic shortage of medical students. While our population is growing, there has been a drop in the number of medical students. At our own North Dakota Medical School there are 39 freshmen this year compared with 44 last year; 11 of these are from out of state. Students with lesser qualifications must be accepted to fill the quota. Third and fourth year classes at medical schools have 700 vacancies. Dr. Boerth feels that more loans and grants will have to be made available to induce more students to study medicine. He asked that we appoint a committee to help get medical students.

The Allen Trio, composed of 3 young men from Concordia College, sang several numbers.

The second business session was opened at 2:30 P.M. in the Community Room of the Metropolitan Savings and Loan Building, with Mrs. R. W. McLean presiding. Mrs. McLean asked for the report of the nominating committee and Mrs. J. W. Van der Linde, chairman, presented the following slate of officers for 1961-62:

President: Mrs. L. T. Longmire, Devils Lake

President-elect: Mrs. J. W. Jansonius, Jamestown

First vice-president: Mrs. R. H. Waldschmidt, Bismarck

Second vice-president: Mrs. Robert Hankins, Mott

Recording Secretary: Mrs. Clyde Smith, Bismarck

Corresponding Secretary: Mrs. J. H. Mahoney, Devils Lake

Treasurer: Mrs. M. H. Poindexter, Fargo

Since there were no nominations from the floor, Mrs. Richardson moved that the secretary be instructed to cast a unanimous ballot for the slate of officers. Motion carried.

Upon the recommendation of the preconvention board meeting, Mrs. Pray moved that the AAPS Essay Contest be dropped because of the poor response. Motion carried.

Mrs. Heffron moved that the councillor act as publicity chairman in districts which do not have publicity chairmen; also, in districts which do have publicity chairmen, the councillor shall be responsible for disseminating district and state publicity to her publicity chairman and shall also be responsible for checking publicity releases for accuracy. Motion carried.

Mrs. Longmire moved that Mrs. P. G. Arzt of Jamestown, first president of the Woman's Auxiliary to the North Dakota State Medical Association, be made an honorary member of the state auxiliary. Motion carried.

Mrs. Benson moved that the budget be accepted as read by Mrs. E. J. Larson, finance committee chairman, in the morning session. Motion carried.

Mrs. McLean brought before the convention the following matters which were called to the attention of the preconvention board meeting:

Mrs. Mazur, AMEF chairman, suggested contributions should be designated if they are to go to the University of North Dakota.

Mrs. McFadden, mental health chairman, said there are films on mental health available from the State Health Department for use on programs.

Mrs. Sandmeyer, student loan fund chairman, suggested that memorial gifts be made to the Student Loan Fund.

Mrs. Waldschmidt, sixth district president, asked if there might be some sort of honorary status for widows. It was recommended that such status be left to the discretion of the districts.

Mrs. McLean asked that lists of new officers from districts be sent in early enough to go in with the recording secretary's report to The Journal-Lancet.

Mrs. Fischer suggested the post-convention board meeting be held following the convention adjournment and preceding the banquet if time permits.

The editors of *News, Views, and Cues* announced they would send their first issue only to members, instead of to all doctor's wives as they did last year. They felt the additional expense and work involved did not produce the desired result of increasing membership.

Motion was made for convention adjournment.

Postconvention Board Meeting

Mrs. L. T. Longmire called the postconvention board meeting to order immediately following the convention adjournment. She announced she had made the following appointments:

Committee Chairmen

Membersbip (organization)—Mrs. J. W. Jansonius, 609 4th Ave. S.E., Jamestown

Program Mrs. R. H. Waldschmidt, 600 N. Washington, Bismarck
Nominating Mrs. R. W. McLean, Hillsboro
Parliamentarian Mrs. T. Q. Benson, 1524 Walnut St., Grand Forks
Legislation—Mrs. L. G. Pray, 1701 S. 8th St., Fargo
Mental Health Mrs. R. L. McFadden, 910 3rd Ave. N.W., Jamestown
Committee on Aging Mrs. D. J. Halliday, Kenmare
Liaison to SAMA Mrs. J. D. Cardy, 1110 Reeves Drive, Grand Forks
Civil Defense Mrs. Kenneth Amstutz, 505 9th Ave. S.E., Minot
Bulletin Mrs. George H. Holt, 214 2nd Ave. S.W., Jamestown
Historian Mrs. George Spielman, 1715 Ave. E., Bismarck
A.M.E.F. Mrs. Stuart J. Cook, Rolette
Health Careers Mrs. G. H. Heidorn, 1127 Valley View Drive, Minot
By-Laws Mrs. V. J. Fischer, 303 8th Ave. S.E., Minot
Safety Mrs. Gordon E. Ellis, 602 14th St. W., Williston
Community Service Mrs. John C. Fawcett, 1125 5th St., Devils Lake
Publicity Mrs. E. O. Hieb, 211 14th Ave. Drive N.E., Jamestown
Official Publication—*News, Views, and Cues*
Business and Circulation Manager Mrs. C. A. Arneson, 714 N. 2nd, Bismarck
Managing Editor Mrs. Robert Hankins, Mott
Co-editor Mrs. R. A. Vaaler, 1711 6th St. S.W., Minot
Finance Committee Mrs. W. L. Macaulay, 1410 S. 9th St., Fargo, chairman; Mrs. L. E. Wold, 1708 S. 9th St., Fargo; Mrs. W. P. Kieg, 602 Cherry St., Grand Forks; Mrs. E. O. Hieb, 211 14th Ave. Drive N.E., Jamestown
Medical Student Loan Fund Committee Mrs. G. R. Richardson, 12 10th St. S.W., Minot, chairman; Mrs. J. M. Keller, 910 4th Ave. E., Williston; Mrs. R. D. Nierling, 415 9th St. S.E., Jamestown; Mrs. Ralph Leigh, 301 Park Ave., Grand Forks; Mrs. Lee A. Christoferson, 1307 S. 6th St., Fargo
Reading Committee Mrs. Kenneth Amstutz, Mrs. Ekrem Gozum, Mrs. H. L. Kermott, Jr., and Mrs. S. E. Shea
Resolutions Mrs. J. P. Merrett and Mrs. W. R. Jensen

Mrs. Benson moved that the appointive slate be accepted. Motion carried.

The following members were elected to the Nominating Committee: Mrs. R. W. McLean, chairman, Mrs. C. A. Arneson, alternate; Mrs. H. L. Kermott, Jr., Mrs. S. C. Bacheller, alternate; Mrs. M. M. Heffron, Mrs. R. D. Schoregge, alternate; Mrs. B. A. Mazur, Mrs. John Bond, alternate; Mrs. E. J. Larson, Mrs. E. A. Hamz, alternate.

Mrs. Longmire announced cards would be sent early for convention registrations. The combined North Dakota and South Dakota auxiliaries and medical associations will be meeting in Bismarck in June 1962. Motion was made for adjournment of post-convention board meeting.

The closing banquet was held in the Top of the Mart, Frederick Martin Hotel, Moorhead. Decorations carried out an "Under the Sea" theme. Mrs. C. K. Fercho, first district auxiliary president, presided and introduced those seated at the head table: Mrs. L. G. Pray, Mrs. J. M. Van der Linde, Mrs. L. T. Longmire, Mrs. C. Rodney Stoltz, Mrs. J. W. Jansonius, Mrs. R. W. McLean, Mrs. R. H. Waldschmidt, Mrs. Robert Hankins, and Mrs. Clyde Smith.

Musical entertainment was provided by students from North Dakota State University who sang selections from the University's recent production, "South Pacific."

Mrs. C. Rodney Stoltz, regional vice-president of the Woman's Auxiliary to the American Medical Association, spoke on "A Is for Auxiliary" and emphasized how important it is for doctors' wives to be "attuned, alert, and active." She said the public's image of doctors is undergoing change and we must recognize it. People love their own family doctor but feel differently toward doctors as a group. "Organized medicine" has an unsavory flavor; it implies doctors are looking for more butter for their bread. One of the first steps to socialism and communism is in the field of medical care because health is so important.

American physicians provide free medical care amounting to 658 million dollars yearly. On the average, this is probably better than $1,000 worth of medical care given by each physician. Doctor's costs have risen only slightly, but people do not know how expensive government medical care is, nor do they know how much comes out of their pocket to pay "free for all care."

Mrs. Stoltz pointed out we must be attuned to our importance. Doctors' wives are open windows to the medical profession. They battle with the phone and the overdone meal, but they learn about the heart of the physician and are proud to be doctors' wives. She emphasized we must be alert to good public relations, to generous contributions to the Student Loan Fund and AMEF, alert to socioeconomic programs, and alert to our responsibilities and capabilities.

Finally, she declared we must be active. We forget the price we paid for freedom and must keep paying. We are becoming a hydromatic people, "shiftless and easy-going." She quoted a former AMA president who stated "One woman on her feet is worth three on her seat." The future rests in the hands of women. We have more time and opportunity to interpret our viewpoint to the public. Ronald Reagan has made a record for the AMA to use in their homes and play for friends which explains the dangers of government medical care.

Mrs. Stoltz then installed the following officers: Mrs. L. T. Longmire, president; Mrs. J. W. Jansonius, president-elect; Mrs. R. H. Waldschmidt, first vice-president; Mrs. Robert Hankins, second vice-president; Mrs. Clyde Smith, recording secretary; and Mrs. M. H. Poindexter, treasurer. The president's pin was presented to Mrs. Longmire by Mrs. McLean and the past-president's pin was given to Mrs. McLean by Mrs. Van der Linde. Mrs. Fercho presented a gift to Mrs. Stoltz. A standing ovation was given Mrs. McLean for her work as president.

District Presidents—1961-62

First District Mrs. Robert Story, 1315 S. 9th St., Fargo
Second District Mrs. George H. Hilts, Cando
Third District Mrs. James Leigh, 606 N. 3rd St., East Grand Forks, Minn.
Fourth District Mrs. Raymond Vaaler, 1711 6th St. S.W., Minot
Fifth District Mrs. W. R. Jensen, 521 4th Ave. N.W., Valley City
Sixth District Mrs. Roger Berg, 219 Ave. B. West, Bismarck
Seventh District Mrs. Clifford Hogan, 303 10th Ave. N.E., Jamestown
Eighth District Mrs. J. P. Craven, 403 3rd Ave. E., Williston
Ninth District Mrs. Norman Ordahl, Route 3, Box 805, Dickinson
Tenth District Mrs. J. M. Little, Mayville

District Councillors—1961-62

First District Mrs. R. J. Zanner, 1414 S. 6th St., Fargo
Second District Mrs. C. A. Corbett, 316 7th St., Devils Lake
Third District Mrs. R. C. Painter, 1121 Belmont Road, Grand Forks
Fourth District Mrs. V. J. Fischer, 303 8th Ave. S.E., Minot
Fifth District Mrs. J. Goven, 912 6th Ave. N.E., Valley City
Sixth District Mrs. M. M. Heffron, 320 Ave. B. West, Bismarck
Seventh District Mrs. Robert McFadden, 910 3rd Ave. N.W., Jamestown
Ninth District Mrs. Richard Raasch, Box 990, Dickinson
Tenth District Mrs. Mervin Rosenberg, Northwood

WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION
1961 MEMBERSHIP ROSTER

First District

Amidon, Mrs. Blaine F.	1325 S. 16th Ave., Fargo
Armstrong, Mrs. William B.	1710 S. 8th St., Fargo
Bacheller, Mrs. Stephen C.	Enderlin
Barnard, Mrs. Donald M.	1212 S. 7th St., Fargo
Beithon, Mrs. Elmer	429 N. 5th St., Wahpeton
Bond, Mrs. John H.	516 S. 13th St., Fargo
Borland, Mrs. Verl G.	1514 S. 9th St., Fargo
Burton, Mrs. P. H.	415 S. 8th St., Fargo
Christoferson, Mrs. Lee	1307 S. 6th St., Fargo
Corbus, Mrs. Budd C.	1257 N. 4th St., Fargo
Darrow, Mrs. Kent E.	716 S. 8th St., Fargo
DeCesare, Mrs. F. A.	1401 S. 9th St., Fargo
Dillard, Mrs. James R.	620 S. 8th St., Fargo
Dodds, Mrs. G. Alfred	1602 S. 10th St., Fargo
Donat, Mrs. T. L.	1109 S. 9th St., Fargo
Engstrom, Mrs. Perry H.	807 N. 2nd St., Wahpeton
Fercho, Mrs. Calvin K.	1747 S. 7th St., Fargo
Fjelde, Mrs. J. H.	1526 S. 8th St., Fargo
Fortin, Mrs. H. J.	1440 S. 8th St., Fargo
Geib, Mrs. Marvin J.	1219 S. 4th Ave., Moorhead, Minn.
Gillam, Mrs. John S.	1433 S. 7th St., Fargo
Goff, Mrs. John R.	1441 S. 8th St., Fargo
Goltz, Mrs. Neill F.	804 S. 8th St., Fargo
Gustafson, Mrs. Maynard B.	1201 S. 8th St., Fargo
Hall, Mrs. G. Howard	1748 S. 9th St., Fargo
Hanna, Mrs. J. F.	907 S. 12th Ave., Fargo
Hawn, Mrs. Hugh W.	1325 N. 1st St., Fargo
Heilman, Mrs. Charles O.	40 N. 18th Ave., Fargo
Houghton, Mrs. James F.	1707 S. 9th St., Fargo
Hunter, Mrs. C. M.	1434 S. 6th St., Fargo
Ivers, Mrs. George U.	1106 S. 10th St., Fargo
Jaehning, Mrs. David G.	823 N. 2nd St., Whapeton
James, Mrs. J. B.	1145 N. 10th St., Fargo
Kavanaugh, Mrs. Gerald J.	1242 N. 3rd St., Fargo
Lancaster, Mrs. W. E. G.	1332 N. 5th St., Fargo
Landa, Mrs. Marshall	1720 S. 8th St., Fargo
Larson, Mrs. G. Arthur	1538 S. 9th St., Fargo
LeBien, Mrs. Wayne E.	1353 N. 5th St., Fargo
LeMar, Mrs. John D.	1324 N. 5th St., Fargo
Lindsay, Mrs. Douglas T.	1545 S. 9th St., Fargo
Long, Mrs. W. H.	1438 S. 8th St., Fargo
Lytle, Mrs. Francis T.	1306 N. 1st St., Fargo
Macaulay, Mrs. Warren L.	1410 S. 9th St., Fargo
Magill, Mrs. Gordon B.	1312 S. 7th St., Fargo
Magness, Mrs. John W.	1711 S. 6th St., Fargo
Mazur, Mrs. Bernard A.	1237 N. 3rd St., Fargo
Melton, Mrs. Frank M.	1702 S. 7th St., Fargo
Murray, Mrs. James B.	1206 S. 15½ Ave., Fargo
Norum, Mrs. Henry A.	801 S. Drive, Fargo
Olson, Mrs. Donald D.	911 S. 8th St., Fargo
Pianka, Mrs. Wallace A.	Veterans Hospital, Fargo
Poindexter, Mrs. Marlin H.	1350 S. 9th St., Fargo
Pray, Mrs. Lawrence G.	1701 S. 8th St., Fargo
Rogers, Mrs. R. G.	1621 S. 7th St., Fargo
Schneider, Mrs. Joseph F.	1002 S. 13th St., Moorhead, Minn.
Sedlak, Mrs. Oliver A.	1019 S. 9th St., Fargo
Sessums, Mrs. John V., Jr.	1330 S. 18th Ave., Fargo
Shook, Mrs. Lester D.	1755 S. 10th St., Fargo
Stafne, Mrs. William A.	1409 S. 9th St., Fargo
Story, Mrs. Robert D.	1315 S. 9th St., Fargo
Swanson, Mrs. Joel C.	1220 S. 8th St., Fargo
Thompson, Mrs. George R.	421 S. 14th St., Fargo
Traynor, Mrs. Mack V., Jr.	1310 S. 9th St., Fargo
Triggs, Mrs. Perry O.	1401 S. 12th St., Fargo
Ulmer, Mrs. Robert J.	718 S. 19th Ave., Fargo
Varco, Mrs. B. W.	701 N. 29th Ave., Fargo
Webster, Mrs. William O.	823 S. 14th St., Fargo
Weible, Mrs. Ralph D.	1628 S. 9th St., Fargo
Weible, Mrs. R. E.	1630 S. 9th St., Fargo
Williams, Mrs. Neil S.	1707 S. 13th St., Fargo
Wold, Mrs. Lester E.	1708 S. 9th St., Fargo
Zauner, Mrs. Richard	1414 S. 6th St., Fargo

Second District

Cook, Mrs. Stuart J.	Rolette
Corbett, Mrs. Connor A.	316 7th St., Devils Lake
Eylands, Mrs. John V.	Rolla
Fawcett, Mrs. Robert M.	12th Ave., Devils Lake
Fawcett, Mrs. John C.	1125 5th St., Devils Lake
Fox, Mrs. William R.	315 Foster Ave., Rugby
Hilts, Mrs. George H.	Cando
Johnson, Mrs. Christian O.	Rugby
Keller, Mrs. Emil T.	Rugby
Lazareck, Mrs. Isadore L.	1032 5th St., Devils Lake
Longmire, Mrs. Lemuel T.	810 6th St., Devils Lake
Mahoney, Mrs. James H.	601 8th St., Devils Lake
McBane, Mrs. Robert D.	1106 4th St., Devils Lake
McIntyre, Mrs. Donald G.	Rugby
Palmer, Mrs. Dolson W.	Cando
Pine, Mrs. Louis F.	817 7th St., Devils Lake
Sawchuck, Mrs. John	Rolette
Terlecki, Mrs. Jaroslaw	Minnewaukan
Toomey, Mrs. Glen W.	Highway 20, Devils Lake

Third District

Benson, Mrs. T. Q.	1524 Walnut, Grand Forks
Benwell, Mrs. Harry D.	504 Reeves Drive, Grand Forks
Campbell, Mrs. D.	1007 Chestnut, Grand Forks
Cardy, Mrs. James D.	1110 Reeves Drive, Grand Forks
Clark, Mrs. R. G.	511 18th Ave. S., Grand Forks
Clayburgh, Mrs. B. J.	729 Reeves Drive, Grand Forks
Coultrip, Mrs. R. L.	Box 87, McVille
Culmer, Mrs. A. E., Jr.	101 Reeves Drive, Grand Forks
Countryman, Mrs. George L.	923 Kittson, Grafton
Dailey, Mrs. W. C.	1812 Belmont Road, Grand Forks
DeLano, Mrs. Robert	Northwood
Doss, Mrs. D. R.	419 23rd Ave. S., Grand Forks
Evans, Mrs. Harold	1024 Reeves Drive, Grand Forks
Flaten, Mrs. Alfred N.	Edinburg
Frey, Mrs. Wellde W.	Drayton
Fritzell, Mrs. K. E.	1120 Cottonwood, Grand Forks
Gertson, Mrs. G. D.	511 S. 5th St., Grand Forks
Goehl, Mrs. R. O.	1015 Reeves Drive, Grand Forks
Graham, Mrs. Charles	923 Almonte, Grand Forks
Graham, Mrs. J. H.	1125 Reeves Drive, Grand Forks
Grinnell, Mrs. E. L.	1207 Lincoln Drive, Grand Forks
Harwood, Mrs. T. H.	2704 Belmont Road, Grand Forks
Haugen, Mrs. C. O.	Box 436, Larimore

Haunz, Mrs. Edgar A.	1029 Lincoln Drive, Grand Forks
Helenbolt, Mrs. K. S.	2216 S. 10th, Grand Forks
Helm, Mrs. Richard	1505 N. 5th St., Grand Forks
Keig, Mrs. William P.	501 17th Ave. S., Grand Forks
Landry, Mrs. L. H.	Walhalla
Leigh, Mrs. James	606 N. 3rd, East Grand Forks, Minn.
Leigh, Mrs. Ralph E.	301 Park Ave., Grand Forks
Leigh, Mrs. Richard	1117 Lincoln Drive, Grand Forks
Levine, Mrs. L.	1006 Cottonwood, Grand Forks
Liebeler, Mrs. Frances D.	520 17th Ave. S., Grand Forks
Lorentson, Mrs. Carl	1716 Oak St., Grand Forks
Mahowald, Mrs. R. E.	606 S. 5th St., Grand Forks
McLeod, Mrs. John	911 N. 22nd St., Grand Forks
Moore, Mrs. John H.	1114 Reeves Drive, Grand Forks
Nelson, Mrs. Wallace W.	511 17th Ave. S., Grand Forks
Nelson, Mrs. William	1118 Reeves Drive, Grand Forks
Painter, Mrs. Robert C.	1121 Belmont Road, Grand Forks
Pettit, Mrs. Sam	625 Reeves Drive, Grand Forks
Porter, Mrs. Charles B.	1210 Chestnut, Grand Forks
Potter, Mrs. W. F.	2024 2nd Ave. N., Grand Forks
Powers, Mrs. W. T.	1509 Walnut, Grand Forks
Prochaska, Mrs. L. J.	620 Reeves Drive, Grand Forks
Ruud, Mrs. John E.	2221 Chestnut, Grand Forks
Sandmeyer, Mrs. John A.	1005 Lanark, Grand Forks
Schafer, Mrs. Thomas L.	1523 Cottonwood, Grand Forks
Silverman, Mrs. Louis B.	626 Belmont Road, Grand Forks
Stratte, Mrs. J. J.	109 4th Ave. S., Grand Forks
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(Continued on page 22A)

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Plans for 1962 already include the following Symposia, with more being arranged:

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January 8, 1962
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Wednesday, January 24, 1962
The Sheraton-Portland Hotel

ANCHORAGE, ALASKA
Saturday, February 24, 1962
The Westward Hotel

WINCHESTER, VIRGINIA
Wednesday, March 14, 1962
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Thursday, March 15, 1962
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Book Reviews . . .

The Surgical Treatment of Intracranial Meningiomas

COLLIN S. MACCARTY, M.D., *1961. Springfield, Ill.: Charles C Thomas. 69 pages. Illustrated. $4.50.*

This 69-page, well-illustrated book is very readable. It has numerous well-chosen references concerning the historical development of meningioma surgery as well as the current opinions of treatment.

The author's stated objective is the presentation of surgical methods for removal of intracranial meningiomas. This is accomplished in a unique and instructive manner, with each concise chapter devoted to each anatomic location of the brain and cranium where these tumors grow. Each chapter has an illustrative, documented case and particularly important technics derived from the author's experience are emphasized in each instance.

The writer's experience with his subject is ample to make this book authoritative. His knowledge has been accumulated over the years at the Mayo Clinic, where more than 1,000 meningiomas have been treated surgically. Generally, the operative technics presented are standard among neurosurgeons. This book is fundamental and suitable principally for younger surgeons.

LEONARD A. TITRUD, M.D.
Minneapolis

Textbook of Healthful Living

HAROLD S. DIEHL, M.D., and STEWART C. THOMSON, M.D., *sixth edition, 1960. New York: McGraw-Hill Book Co. 484 pages. Illustrated. $6.75.*

A leader in its field for nearly twenty-five years, Diehl's *Textbook of Healthful Living* has recently appeared in its sixth edition. For its preparation, Dr. Diehl collaborated with Dr. Stewart C. Thomson, a uniquely successful teacher of courses in personal and community health. The authors sought the suggestions of specialists in various fields of medicine and of many teachers in the field in selecting topics to be included in this revision.

The print is large and clear, the quality of the paper and binding is excellent, the subjects covered are appropriate and very well handled, and the diagrams for the most part are clear and accurate. Particularly outstanding are the chapters on communicable diseases, immunizations, and major health problems. The chapters on animals, insects and disease, sanitation, dietary dangers, stimulants and narcotics, and nutrition are good and the chapter on glands of internal secretion is very well done. The delicate subjects of choosing a physician and of what to expect from a physician, in the second chapter, are superbly handled. Reference and reading suggestions have been completely redone and include books and articles which have proved interesting to students in health classes.

Those who teach such courses take it for granted at times that the average student knows something about his body. Yet approximately 50 per cent of today's undergraduates have little or no knowledge of this kind. It is difficult to learn intelligently the abnormal without first having a working knowledge of the normal. Knowledge of some of the variations of the normal can allay many of the fears that disturb people today. Therefore, a more adequate coverage of the normal human anatomy and, particularly, physiology would seem desirable. Some common personal health problems of modern youth, such as skin infections, burns, lacerations, bleeding, and ingrown toenails, could be covered briefly with benefit.

There is an atmosphere conveyed by this book which is difficult to describe and yet makes it stand out above all others. There is nothing amateurish about it. The text obviously is written by men who know what they are talking about and who know how to write. Dr. Diehl's personality, evident in the previous editions, is manifest throughout this edition and is blended with that of Dr. Thomson, whose ability and popularity as a teacher in this field is widely recognized. They have created an outstanding book.

J. ARTHUR MYERS, M.D.
Minneapolis

Respiration: Physiologic Principles and Their Clinical Applications

PETER C. LUCHSINGER, M.D., *and* KENNETH M. MOSER, M.D., *editors, 1960. St. Louis: C. V. Mosby. 505 pages. Illustrated. $15.75.*

This 505-page book is unusual in that it was first written by 3 German authors in 1955, a second edition was published in 1958, and then the book was translated into English in 1960 by the editors.

The book is divided into 4 main parts. Part I, which deals with the normal physiology of respiration, goes into great detail concerning the pulmonary respiratory functions and the blood as a carrier of the respiratory gases, with the transfer of these gases from alveolus into the blood. Regulation of respiration and tissue respiration are also explained in this section.

Part II covers the methods for investigation and evaluation of pulmonary function, including determination of the blood gases. One chapter is devoted to the technic of cardiac catheterization and its normal values and calculations.

Part III discusses the pathophysiology of respiration and the different insufficiencies, including the shunts, alveolar hypotension, and so on. The last chapter of this section deals with the different forms of pulmonary hypertension and their classification.

Part IV describes the pulmonary insufficiencies, such as cor pulmonale, emphysema, bronchial asthma, tuberculosis, pneumothorax, atelectasis, thoracic deformities, and others, which occur in clinical practice. The last chapters take up the influence of various nonpulmonary factors, such as high altitudes, renal acidosis, congenital heart disease, pregnancy, anemia, and so forth, upon pulmonary function, and the final chapter deals with pulmonary function in the athlete.

An appendix, which has various equations, correction factors, reagents, and tables and an extensive bibliography of some 90 pages, conclude the book.

(Continued on page 28A)

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1. R. Lamb and E. S. Maclean, Penicillin V—A Clinical Assessment After One Year, *Brit. M. J.*, July 27, 1957, p. 191-193. 2. J. I. Burn, M. P. Curwen, R. G. Huntsman and R. A. Shooter, A Trial of Penicillin V, *Brit. M. J.*, July 27, 1957, p. 193. 3. J. Macleod, Current Therapeutics, *The Practitioner*, 178:486, April, 1957. 4. W. J. Martin, D. R. Nichols and F. R. Heilman, Observations on Clinical Use of Phenoxymethyl Penicillin (Penicillin V), *J.A.M.A.*, p. 928, March 17, 1956.

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For the student and research physiologist interested in the respiratory functions and system, this is an excellent and inclusive book. For the clinician, certain parts of it, especially Part IV, are interesting and instructive. The bibliography is of considerable value to anyone interested in this field.

RICHARD D. NIERLING, M.D.
Jamestown, North Dakota

The Concise Encyclopedia of Modern Surgery

JAMES HALE RUTLEDGE, M.D., *1960. Philadelphia: Chilton Co. 296 pages. Illustrated. $8.00.*

As the title implies, this book is obviously designed as a surgical reference work of rather general nature. Certainly it is not designed for physicians or surgeons, and its value even for preclinical medical students would seem rather doubtful. The author's comments on the jacket classifies it as a text and reference book to be used chiefly in nursing education and training for allied medical occupations. However, at least the first 4 chapters appear to be directed to the surgical patient and may indeed be of great value to some individuals confronted with the prospect of having an operation.

The text is well written in a simple, readable style, and the numerous illustrations by the author are diagrammatic and excellent. The book was submitted to the department of nursing at the College of St. Scholastica, Duluth, Minnesota, for evaluation as a textbook for nurses' training. The chairman, Sister Helen Claire, O.S.B., commented that, in the department's opinion, it would be a helpful addition to a ward library or for quick personal reference. The department members were particularly impressed by the excellence of the chapters dealing with the principles of surgical operation but were critical of a tendency to use terminology of subprofessional level, such as "paralyzed intestines" for paralytic ileus and "blood clots in veins" instead of venous thrombi or thrombosis. Also, some disagreement was expressed with the author's concept of the relative role of the professional nurse and the practical nurse, of present-day training requisites for nursing, and of the relative position of the nurse, either professional or practical, as a member of the medical team.

The book, in my opinion, would be a highly useful and valuable addition to a hospital library.

PHILIP F. ECKMAN, M.D.
Duluth, Minnesota

A Synopsis of Contemporary Psychiatry

GEORGE A. ULETT, M.D., *and* D. WELLS GOODRICH, M.D., *second edition, 1960. St. Louis: C. V. Mosby. 297 pages. $6.50.*

The increasing demand that family doctors treat emotional disorders and the expanding development of psychiatric knowledge and skills make urgent the need for ways to inform the physician. More and more postgraduate courses in psychiatry are being established, but physicians often do not attend these courses, either because they are too distant or because they believe they cannot spare the time. These physicians want a compact guide—a psychiatric Baedecker—to lead them through the maze of emotional illness and the ways of treating that illness.

Ulett and Goodrich therefore offer this *Synopsis.* Up-

to-date in the several matters with which psychiatry is concerned—including civilian disasters, military medicine, and courtroom testimony—this revised edition has been written with scrupulous attention to accuracy and balance among the often divergent theoretic and practical viewpoints in psychiatry. Furthermore, it reads smoothly and clearly.

In this synopsis of psychiatry, neurology and electroencephalography occupy a considerable amount of the carefully rationed space. Perhaps much of the space so used might better have been given to hints both on how to employ therapeutically the occupational therapist, the recreational therapist, and the chaplain and on how to utilize community resources such as social agencies and the patient's employer, clergyman, and friends.

Like all those who write synopses, the authors have set themselves a well-nigh impossible task—to be at once encyclopedic and concise, that is, to treat adequately not only all of psychiatry but also its related disciplines—clinical psychology, social work, nursing, neurology, and electroencephalography—without exceeding the confines of a "book small enough to fit in the side pocket of the clinic coat." Such a task requires the authors to limit their exposition to terse main points, with little clarifying elaboration.

The seasoned physician, therefore, who can supply such elaboration from experience in his daily practice, will read the book with more understanding and profit than will the medical student, intern, resident, student nurse, and others who are among its explicit intended readers. Even these latter, however, will find it a helpful survey of psychiatry—one that shows the field's subject matter and scope. The physician who has had psychiatric training in medical school or later, furthermore, will find it useful both for reviewing the field and for putting its facts into proportion. Many psychiatrists teaching postgraduate courses will use it.

One hopes, however, that neither this book nor any other will ever be considered an adequate substitute for an actual postgraduate or other course in psychiatry. In fact, the reader will surely find here ample evidence of the necessity for such formal education.

This book is needed—and it goes far toward meeting that need.

WILLIAM F. SHEELEY, M.D.
Washington, D. C.

Principles of Public Health Administration

JOHN J. HANLON, M.D., *third edition, 1960. St. Louis: C. V. Mosby. 686 pages. Illustrated. $10.50.*

This comprehensive publication, written by a distinguished authority in the field of public health, presents a most complete and useful volume on all phases of public health. The author presents his material clearly and logically in 4 parts.

The first part includes chapters on the philosopy of public health, world health problems, behavioral science and public health, social pathology and public health, and so forth. In this edition, the relationship of social pathology and public health is a new subject, and the subject of world health problems has been updated.

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The third part presents all the public health activities, not only those relating to the traditional services but

(Continued on page 30A)

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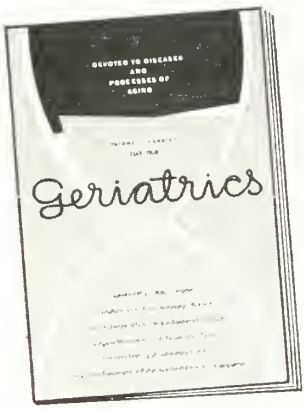

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(Continued from page 29A)

also those included in the newer concept of public health, such as social services and public health, housing and city planning, public health dentistry, rehabilitation, additional content of chronic diseases, adult health, and so on. Of special value are the new chapters on addictive diseases and public health, the private physician, and medical care.

In the chapter on public health nursing, there are new statistics and new definitions of functions, standards, and qualifications as defined by the American Nurses' Association, added since the last edition. The other chapters relating to the other activities and programs of public health are exceptionally well presented, with some improved arrangement, and are up-to-date.

In the fourth part, the author deals with the future, with the past as prologue.

This book is highly recommended as both a text and a reference—a must book for students, libraries, public health workers, teachers, voluntary health and welfare agencies, and all other persons interested in public health as now constituted.

HILBERT MARK, M.D.
Toledo, Ohio

Education for Nursing

JAMES GRAY, *1960. Minneapolis: University of Minnesota Press. 225 pages. Illustrated. $5.00.*

Exactly fifty-two years have passed since Dr. Richard Oling Beard envisioned and took the leadership in establishing the first program for the education of nurses on a college level in a state university. Few men have lived to see their dreams come true and flourish. Dr. Beard was one of the lucky ones!

The "Prologue: Emergent Profession" reviews the development of schools of nursing in the United States and the ardor and crusading efforts of the early nursing leaders in establishing schools of nursing and in raising the standard of nursing care. Recognition is given such leaders as Adelaide Nutting, Isabel Hampton, and Lillian Wold for their interest in and contribution to the program Dr. Beard was struggling to establish.

The author does not minimize the difficulties, the influences, and the obstacles Dr. Beard and the first director of the University of Minnesota School of Nursing, Bertha Eadmann, encountered in changing the status of the nurse from that of a pupil nurse to that of a student. He describes in detail the struggles of Dr. Beard and, later, Dr. Elias P. Lyon and their associates to strengthen nursing education, thus providing nursing leaders and teachers to improve nursing care of patients.

The contribution each director made to advance the program is well described. Special tribute is given Miss Louise Powell and her faculty in their timeless effort to establish the first five-year program leading to a degree of Bachelor of Science. This program was "designated to give the student a general education plus professional training."

The author pays tribute, and rightly so, to Miss Catherine Densford for her leadership in advancing nursing education in Minnesota and in helping nurses to become increasingly aware of their responsibility to the state, the nation, and the world.

The style of the author is concise. The book offers a rich source of historical material and should have a place in the libraries of schools of nursing.

IRENE DONOVAN
St. Paul

News Briefs . . .

General

Dr. Luther L. Terry, Surgeon General of the U. S. Public Health Service, has urged immediate influenza vaccination as a precaution against expected epidemics this winter. Vaccination is especially important for patients with chronic diseases, persons over 65, and pregnant women, as most deaths from influenza occur among these groups. Outbreaks of Asian and type B influenza are due or overdue this year, according to cycles that have been followed in the past, said Dr. Terry. A further warning was the prevalence of both types of flu in other parts of the world last year. A similar epidemic in England in 1951 reached this country the following year.

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The Atomic Energy Commission will offer 8 fellowships in industrial medicine, beginning in 1962, to citizens of the United States who are licensed to practice medicine in this country or one of its territories. The program, designed to satisfy specialty board requirements in occupational medicine, provides for two years of education at a university with an approved graduate course in occupational medicine and a year of in-field training at an AEC plant or laboratory or any other approved plant or industry. Stipends are $5,000 per academic year and about $7,500 for the in-training year, plus family allowance. Further information about and applications for the fellowship may be obtained from Dr. Henry Blair, Atomic Energy Project, University of Rochester School of Medicine and Dentistry, Rochester, New York. Applications must be submitted before January 1.

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The Medical Library Association will hold a Midwest Regional Group meeting in Rochester, Minnesota, October 27 and 28. Additional information is available from Mr. Thomas E. Keys, Librarian, Mayo Clinic, Rochester.

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The American Medical Association has issued a revised edition of *Medicolegal Forms with Legal Analysis.* Single copies are available from the AMA law department without charge to physicians and at $1.00 a copy to hospitals and laymen.

North Dakota

Dr. Ione E. Dzubur has joined Drs. Robert H. DeLano and Mervin Rosenberg at the Northwood Clinic. Dr. Dzubur received her medical degree from the University of Kansas School of Medicine, Kansas City; interned at Sacramento County Hospital; and took residency training at Merced County General Hospital, California.

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Jamestown Hospital has a new cardiac monitoring and resuscitation unit for the prevention and reversal of cardiac arrest. The unit consists of a cardioscope for monitoring all surgical procedures, a defibrillator, and a pacemaker to reestablish ventricular rhythm.

The Journal Lancet

SERVING THE MEDICAL PROFESSION OF MINNESOTA, NORTH DAKOTA, SOUTH DAKOTA, AND MONTANA

A large and significant part of the research in pediatrics in the United States has stemmed from the Upper Midwest, and in particular from the University of Minnesota under the inspiration of the late Professor Irvine McQuarrie, head of the Department of Pediatrics. His former students have now assumed positions of leadership throughout the nation's medical community. From them have come the papers making up this encomiastic issue. A biography and tribute to Dr. McQuarrie appears on page 552.

Physical Working Capacity of Children with Heart Disease

FORREST H. ADAMS, M.D., and
EDWARD R. DUFFIE, JR., M.D.

Los Angeles

Appraisal of exercise tolerance has long formed an integral part of the total evaluation of individuals with suspected cardiac lesions. This has become increasingly important with the advent of cardiac surgery and the consequent need for careful selection of operative candidates.

In the field of pediatrics, a child's tolerance to exercise remains an almost completely subjective symptom, evaluation of which is largely dependent upon the observations of the parents. Unfortunately, such observations are too often unreliable and at best are only a crude estimation by untrained and emotionally involved parties.

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This study was supported in part by United States Public Health Service Grants Nos. 2A-5292 *and* HTS-5449.

The present study represents an attempt to develop a method for a more precise measure of this function in children with heart disease. The response of the heart to known amounts of general work on a bicycle ergometer was employed for this purpose.[1–8] Similar studies, based on only a small sample of controls, have been reported in the literature by Kjellberg and associates.[9]

SUBJECTS

A total of 106 children and adolescents ranging in age from 5 to 20 years was studied; 72 were boys and 34, girls. Of the entire group, 84 had some type of rheumatic or congenital cardiac lesion. In the latter, a specific diagnosis was established in each case by cardiac catheterization. The distribution of the defects is presented in Table 1.

Subsequent catheterization studies in 18 and prolonged observation in the remaining 4 of 22 of the group initially suspected of having congenital cardiac defects showed no evidence of

TABLE 1

DISTRIBUTION OF CARDIAC DEFECTS IN 106 PATIENTS TESTED FOR PHYSICAL WORKING CAPACITY

Type of defect	*No. of cases*
Ventricular septal defect	22
Atrial secundum defect	16
Pulmonic stenosis	10
Patent ductus arteriosus	8
Aortic stenosis	6
Acyanotic tetralogy	4
Rheumatic valvular disease	4
Coarctation of aorta	3
Tetralogy of Fallot	2
Coarctation of pulmonary artery	2
Atrial ostium primum defect	2
Total anomalous pulmonary venous return	1
Idiopathic dilatation of pulmonary artery	1
Congenital mitral insufficiency	1
Ectasia of the aorta	1
A-V communis	1
None (innocent murmur)	22

organic disease. This entire group was eventually discharged with the diagnosis of "functional heart murmur, no evidence of organic disease."

METHODS

Before testing, a complete physical examination was made on each patient to rule out the presence of an associated illness. All were observed on the hospital ward for twenty-four to forty-eight hours as an added precaution. Only those who were free from associated disease were admitted to the study.

The surface area was calculated from the Du Bois nomogram.[10] The actual test in determining the working capacity was performed according to the method of Sjostrand[1] and Wahlund.[2] In this test, the subject was asked to perform consecutively 3 different work loads on an electric bicycle ergometer, in which the load is produced by a direct current generator.[3] The pedaling rate was maintained between 60 and 70 r.p.m., and each work load lasted six minutes. The apical heart rate was determined stethoscopically for thirty-second periods every fourth and sixth minute of each work load.

The work loads for each subject were such that, in normal children, the first would have produced a heart rate of 100 to 120 beats per minute; the second, 120 to 140 beats per minute; and the third, 150 to 170 beats per minute. These were previously determined to generally follow this code:

Weight range	*Work loads*
Under 30 kg.	100-200-300 kilogram-meters per minute
30-40 kg.	100-300-500 kilogram-meters per minute
40-60 kg.	100-300-600 kilogram-meters per minute
Over 60 kg.	100-500-800 kilogram-meters per minute

The working capacity was calculated by plotting on graph paper the heart rate at the end of each work load against the work load. A straight line was then drawn through the 3 points making the "best fit." The estimated amount of work that would produce a heart rate of 170 beats per minute was then recorded as the working capacity of that individual.[1] This was then compared to the working capacity of normal children of the same sex and size in terms of percentile.[11]

Of the patients, 10 had corrective surgery. The lesions in 3 were ventricular septal defects, in 2,

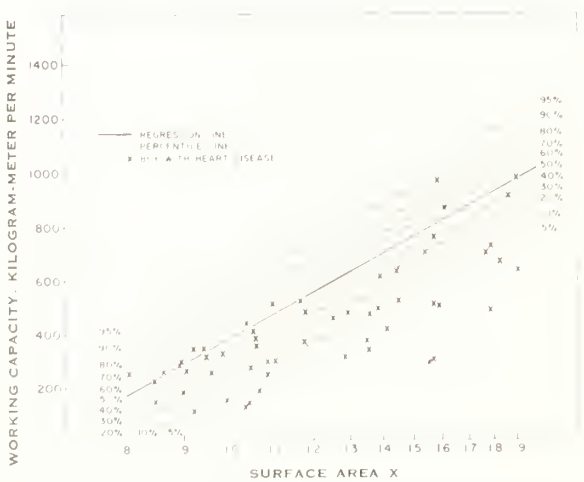

Fig. 1. Plot of working capacity against log of surface area in 56 boys with heart disease. Regression line and percentiles are for normal boys.

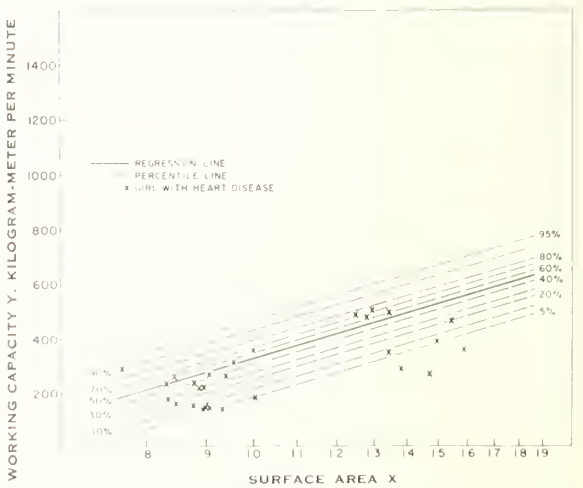

Fig. 2. Plot of working capacity against log of surface area in 28 girls with heart disease. Regression line and percentiles are for normal girls.

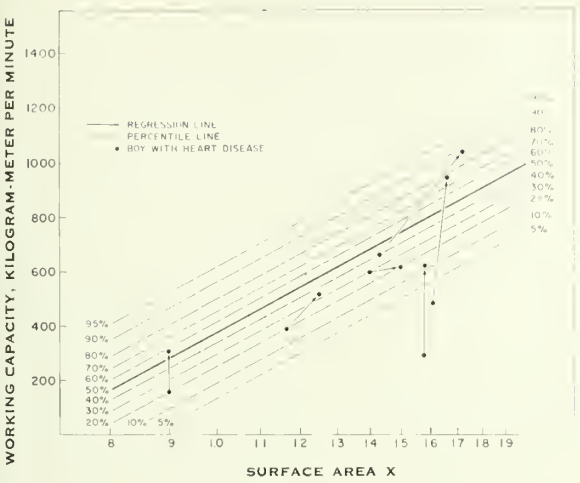

Fig. 3. Plot of working capacity against log of surface area in 6 boys with congenital heart disease. Values are plotted for each subject before and after operation. Regression and percentile lines are for normal boys.

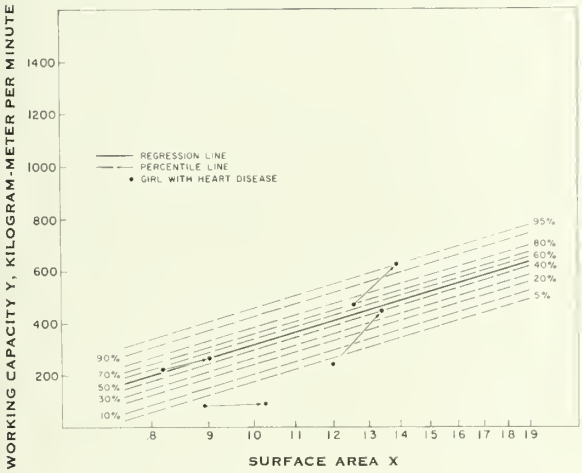

Fig. 4. Plot of working capacity against log of surface area in 4 girls with congenital heart disease. Values are plotted for each subject before and after operation. Regression and percentile lines are for normal girls.

atrial secundum defects; and in 1 each, atrial ostium primum, tetralogy of Fallot, total anomalous venous return, aortic stenosis, and pulmonic valvular stenosis. In each case, the physical working capacity was restudied six months to three years after operation.

RESULTS

Figures 1 and 2 show the physical working capacities plotted against the logs of surface area by sex in 84 children with cardiac lesions. Although there is considerable spread, the majority fall within the lower percentiles, the over-all mean being only 28.

Figures 3 and 4 show the working capacities of 10 children before and after definitive repair. The postoperative working capacity percentile showed an increase in 7 and the mean percentile of the entire group rose from 21 to 45. The 3 children in whom the working capacity percentile did not increase after surgery had ventricular septal defects. In 2 of these, severe pulmonary hypertension was present before operation. The possibility of residual pulmonary vascular disease may be a factor.

Figures 5 and 6 show the working capacities of the 22 children who were initially believed to have cardiac lesions but were subsequently found to have normal cardiac hemodynamics. The mean percentile in this group was 50.

DISCUSSION

Recent studies[11] performed on 243 normal Cali-

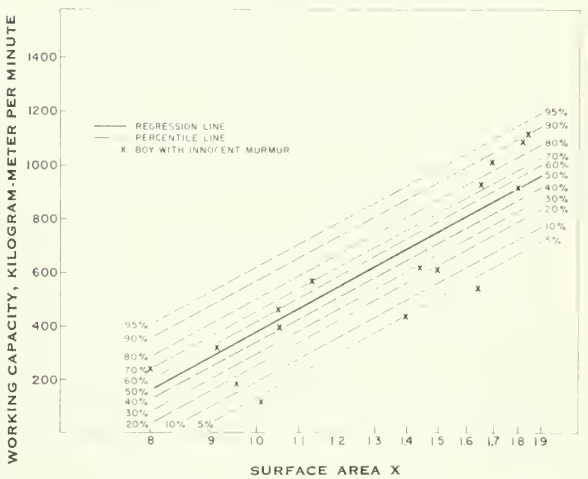

Fig. 5. Plot of working capacity against log of surface area in 16 boys with innocent murmurs. Regression and percentile lines are for normal boys.

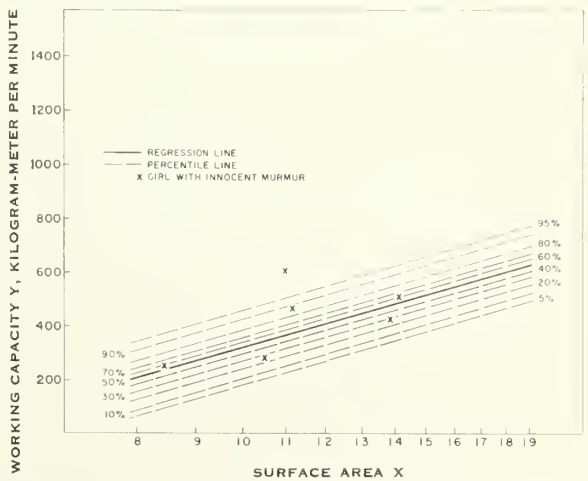

Fig. 6. Plot of working capacity against log of surface area in 6 girls with innocent murmurs. Regression and percentile lines are for normal girls.

fornia school children indicate that the physical working capacity increases with age and body size, correlating best with surface area. Boys possess a significantly greater working capacity than girls, even at the smaller surface areas.

The present results obtained in the 84 children with cardiac lesions, when compared with those obtained in normal children, according to percentiles for surface area, indicate that the physical working capacity is generally reduced. On the basis of longitudinal observations, corrective surgery was followed by a rise in the working capacity in 7 of the 10 children studied.

It is well known that the physical performance of children with cardiac abnormalities may be a reflection of a poorly trained state rather than the disease itself. The normal results obtained in the 22 normal children with initially suspected cardiac involvement suggest that the disease itself is the more usual determinant.

The modest sample size comprising the present series precluded the possibility of evaluation on the basis of the specific anatomic lesion or the degree of involvement. These were studied on a small scale by Kjellberg and associates,[9] who found that the physical working capacity was related to both the type of lesion and the degree of involvement. Thus, with coaretation of the aorta or atrial septal defects, it was generally good, whereas, with tetralogy of Fallot, it was usually low. With aortic or pulmonic stenosis, it was dependent upon the degree of obstruction, and with ventricular septal defects, upon the presence or absence of pulmonary hypertension. With complete heart block, the working capacity has been demonstrated to be normal.[12,13] Further studies along these lines are indicated, since the interpretations of Kjellberg and associates[9] were based upon only a small sample of controls.

SUMMARY

The physical working capacity was determined in 84 children and adolescents with proved cardiac disease and in 22 with suspected cardiac disease. In the latter group, subsequent studies established a functionally normal cardiovascular status in each case.

The average working capacity in the subjects with proved cardiac disease was below the mean for normal controls. In those with suspected but without organic disease, it was normal. Longitudinal observations in 10 subjects who underwent corrective operation showed a rise in the working capacity in 7.

These studies suggest that the working capacity test may be a valuable aid in the appraisal of cardiac suspects as well as in the selection of candidates for operative intervention. The results indicate that the disease itself rather than lack of physical training is the common determinant of physical performance.

The electric bicycle ergometer used in this study was manufactured by the Elema Corporation, Stockholm, Sweden.

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Physiologic Changes After Closure of Ventricular Septal Defects

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NICHOLAS MEYNE, M.D., and C. W. LILLEHEI, M.D.

Minneapolis

THE TECHNICAL SURGICAL ability to close ventricular septal defects has been well demonstrated in recent years at this and other medical centers throughout the world. The effect of closure of such defects on intracardiac physiology, and ultimately on life expectancy, has not yet been extensively studied or reported. The purpose of this study is to report the intracardiac physiologic findings in 57 patients after an average postoperative interval of one and four-fifths years and to make comparisons with the preoperative data.

Recent physiologic study of the natural history of isolated ventricular septal defect reveals that patients with this anomaly vary greatly in their clinical findings and symptomatology, with variation being related to differences in age of patient, size of defect, and status of pulmonary vascular bed.[1] In all likelihood, other unknown factors also exist which may influence the preoperative status of the patient and hence the physiologic results of surgery. Thus, any surgical group of patients with isolated ventricular septal defect is not a homogeneous group of patients. An ancillary purpose of this study, therefore, was to determine what measurable factors known before surgery favored maximal surgical benefit from closure of the defect, as measured in terms of return of physiologic findings toward normalcy.

MATERIALS AND METHODS

This report utilized the pre- and postoperative data on the first 57 patients surviving closure of an isolated ventricular septal defect in whom the postoperative data indicated complete closure. As such, it is a preliminary report, and additional data on a larger series of patients may be expected in the future.

The majority of the patients were studied both pre- and postoperatively at the University of Minnesota. Some patients had either the pre- or postoperative study performed elsewhere, and a few patients had both studies done at other centers.

Calculations of pulmonary pressures, mean pulmonary pressures, pulmonary blood flow, total pulmonary resistance, systemic blood flow, and cardiac index were possible in all patients included in the study.

Calculations of the pre- and postoperative physiologic indexes for each patient were first arranged according to each item of information available—for example, according to preoperative age, from the youngest to the oldest; from the highest to the lowest pulmonary artery pressure pre- and postoperatively; and from the highest to the lowest total pulmonary resistance pre- and postoperatively.

RESULTS

The data have been summarized by separating the 57 patients into 3 groups of 19 each, according to the value of the residual pulmonary artery systolic pressure: (1) patients with the highest residual pulmonary artery pressures, (2) patients with intermediate values, and (3) patients with the lowest residual pulmonary artery pressures. Patients in groups 1 and 3 might then be expected to show significant differences in regard to other variables, also.

Figure 1 shows a scattergram with superimposed bar diagrams, which represent average values, for the 3 groups so classified. The preoperative pulmonary artery systolic pressures are shown on the left. Groups 1 and 2 had similar average preoperative pressures. Group 3, the "best response" group, had significantly lower preoperative pressures on the average, though wide variation existed between patients.

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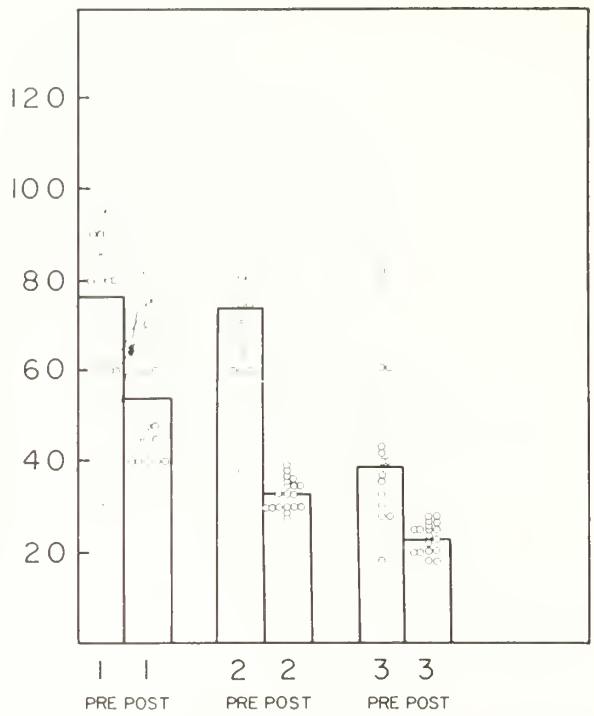

Fig. 1. Pre- and postoperative pulmonary artery systolic pressures plotted for groups 1, 2, and 3. Bar diagrams show mean values.

All patients exhibited a fall in pulmonary artery pressure after closure of the defect except for 3 group 1 patients, whose values are indicated by interconnected dots. Of these patients, 2 appear to have achieved good clinical results. However, they represent the earliest patients selected for surgery and are the only ones to have had their studies performed three to four years before corrective surgery. It is likely that their preoperative pressures would have been appreciably higher if measured close to the time of surgery, and thus their postoperative pressures would not have shown the increase already mentioned. They are included in the group for the sake of completeness. The third patient showing an increase in pulmonary pressure was unique in that he developed unexplained pulmonary insufficiency and right heart failure after surgery.

The median age was essentially the same for groups 1 and 2, but group 3 included more younger patients (figure 2).

The pre- and postoperative cardiac indexes (systemic flow per square meter of surface area) remained relatively constant, on the average, for all 3 groups (figure 3), the average value for all being approximately 4 liters per minute per square meter of surface area. The calculations of physiologic indexes in this study, including the cardiac index, necessitated estimations in a number of instances. For oxygen consumption in infants, mean pulmonary artery pressures were calculated if integrated values were not available, and 96 per cent oxygenation of pulmonary venous blood was assumed if systemic arterial samples were not available. The observation that the values of systemic flow are of similar magnitude indicates that such estimations were probably valid.

Pulmonary flow per square meter of surface area showed a wide range of variability in all groups preoperatively (figure 4). Calculations in a few instances gave excessively high values when differences in systemic and pulmonary artery oxygen saturation were small and hence greatly influenced by inherent errors in measurement. Group 1 showed the lowest pulmonary flow preoperatively on the average and the highest residual pulmonary pressures.

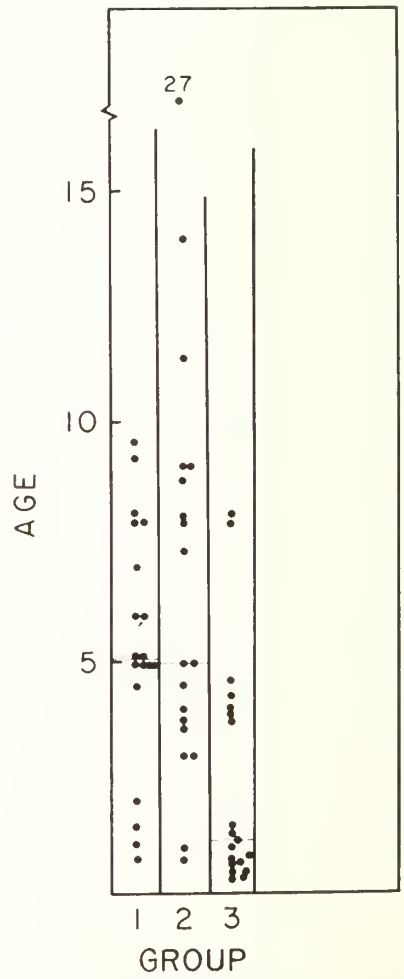

Fig. 2. Distribution of individuals by preoperative age. Dotted lines indicate median age.

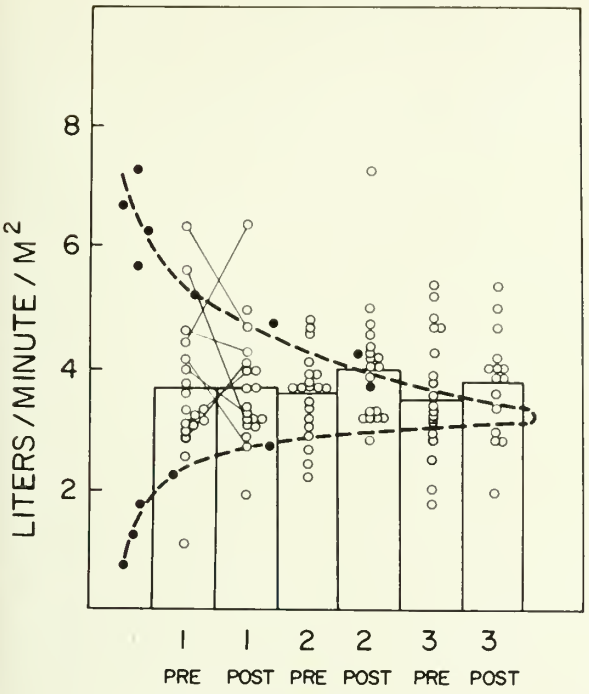

Fig. 3. Pre- and postoperative systemic flow values (per square meter) for groups 1, 2, and 3. Note similar mean values and similar range of values in all groups. Interconnected dots indicate measurements for selected individual patients.

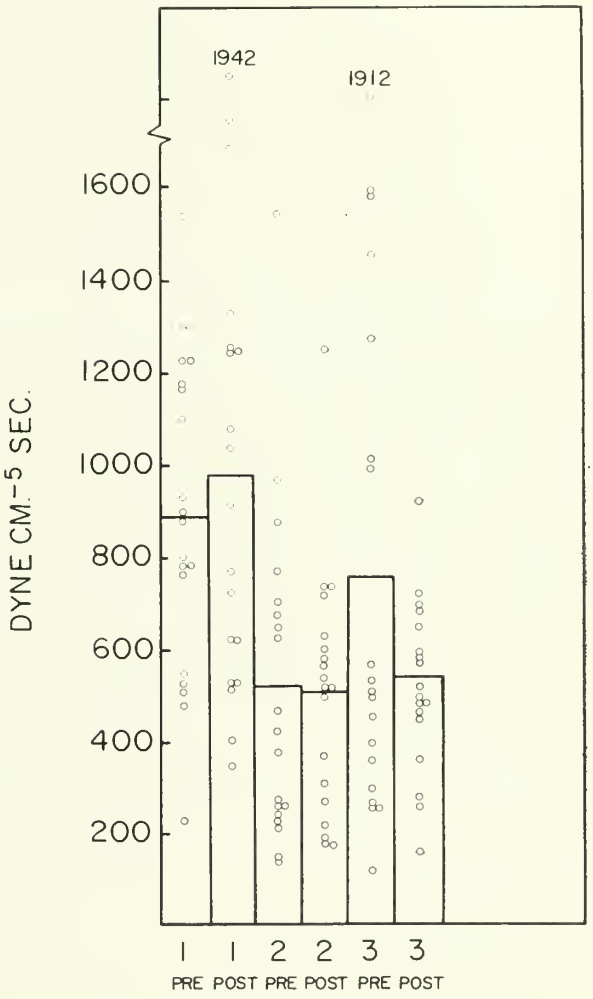

Fig. 5. Pre- and postoperative values for total pulmonary resistance. Wide scatter is attributed to great variation in age and size of children in each group, together with variation in individual cardiac status. Note similarity of pre- and postoperative mean values (bar diagrams).

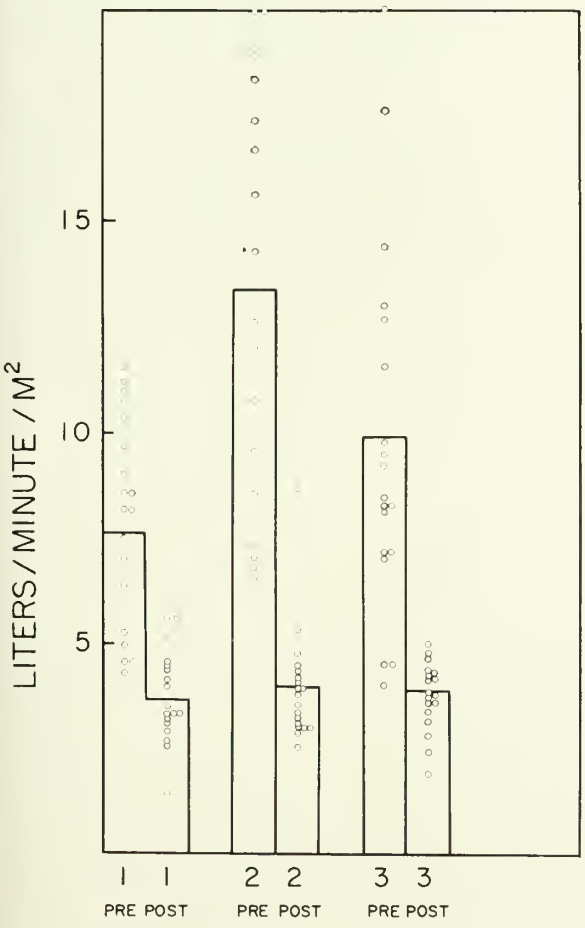

Fig. 4. Pre- and postoperative pulmonary flow values (per square meter) for groups 1, 2, and 3. Note wide range of preoperative values, indicating heterogeneity in physiologic status of patients in all groups.

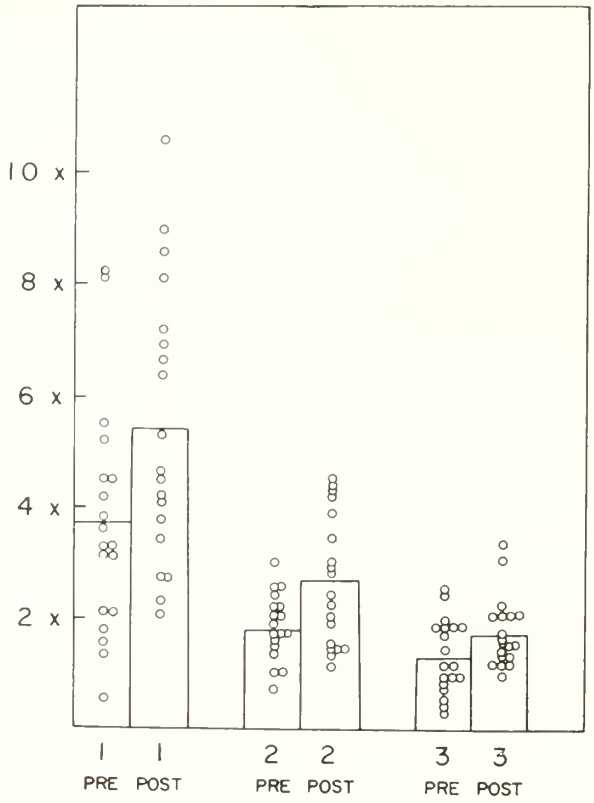

Fig. 6. Comparison of calculated total pulmonary resistance values to normal values.[2] Note that postoperative mean values tend to be higher.

The calculated total pulmonary resistance (dyne cm.$^{-5}$ seconds) also showed wide variations in all 3 groups both before and after closure of the ventricular septal defect (figure 5). This is to be expected in view of the inclusion in each group of children of widely different ages and body sizes and with wide variations in individual cardiac status. However, there was little difference between the average values before and after surgery.

In this study, therefore, there is no evidence that the status of the pulmonary vasculature was altered in the average one and four-fifths years after closure of the ventricular septal defect.

When the calculated total pulmonary resistance value for each patient was compared to the expected normal value for the same size child,[2] the scatter of values obtained was much less (figure 6). Similar comparisons for postoperative values showed mild increases in all groups. Though the latter finding may be within the errors of measurement, the increases might also be attributed to possible continued pulmonary arteriolar lumen narrowing, which was not influenced by closure of the defect.

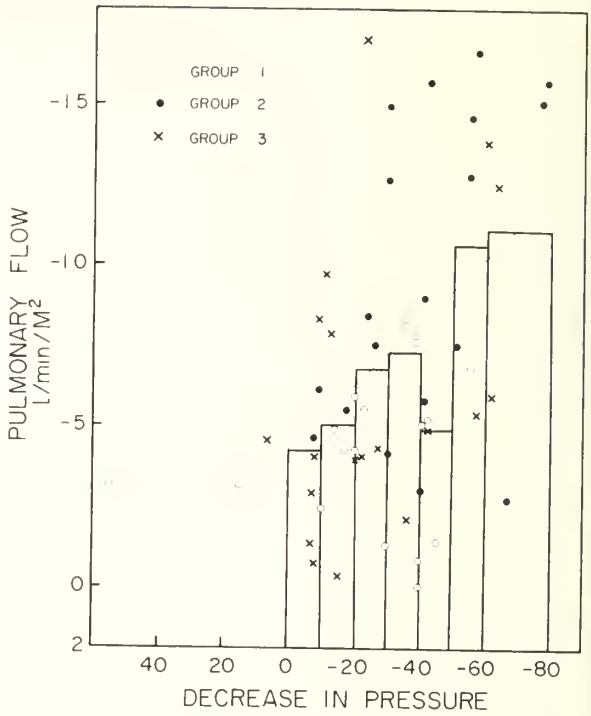

Fig. 7. Decreases in pulmonary flow plotted against decreases in pulmonary artery systolic pressure after surgery. Note that these values tend to be related in a straight-line relationship.

There is definitely no evidence from this study to indicate that pulmonary pathology has been lessened. The fact that no substantial change took place in the total pulmonary resistance indicates that the observed fall in pulmonary artery pressure in most cases can be

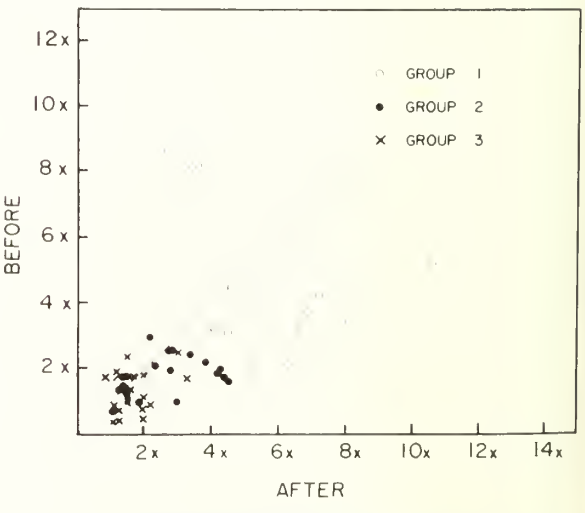

Fig. 8. Pre- and postoperative pulmonary resistance values. Note that group 3 patients had low resistance values both before and after surgery.

attributed only to the reduction in pulmonary flow after closure of the ventricular septal defect. This relationship is well demonstrated when the decrease in pulmonary flow after closure is plotted against the decrease in pulmonary pressure (figure 7). The average values approximate a straight line, pointing to a direct relationship of these two values.

The mere reduction of a high pulmonary flow does not insure a complete return toward normalcy of residual pulmonary pressure after closure of the ventricular septal defect. Low preoperative total pulmonary resistance values appear to offer the best indication that there will be a maximum return toward normalcy of postoperative pulmonary pressures (figure 8).

SUMMARY

Pre- and postoperative physiologic data are presented for 57 patients who have had successful closure of ventricular septal defects. These data demonstrate that the fall in pulmonary artery pressure after surgery is in direct proportion to the decrease in pulmonary flow effected by surgical closure of the ventricular septal defect. There is no evidence to indicate any regression toward normal of pulmonary vascular pathology in the first year or two after closure of the defect. The patients with the best results—those with the lowest residual postoperative pulmonary artery pressures—are those patients with the smallest elevation in calculated total pulmonary resistance before surgery. A near-normal total pulmonary resistance may exist at any age but is present most commonly in younger patients with ventricular septal defect.

This paper was presented in part at the meetings of the Society for Pediatric Research at Buck Hill Falls, Pennsylvania, May 1959.

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Sequential use of simple, established methods of therapy for incurable breast cancer, such as bilateral oophorectomy, irradiation, hormone administration, local excision, simple mastectomy, ancillary symptomatic therapy, bilateral adrenalectomy, hypophysectomy, and corticoid administration, is palliative in many patients. Of 146 patients treated in this fashion, 51 per cent had subjective palliation, that is, relief of pain, cough, or dyspnea; increase in appetite, body weight, and sense of well-being; and return of ability to work or perform usual activities, and 32 per cent had objective palliation, or measurable decrease in size of the breast, lymph node, or chest wall masses; epithelization of ulcerating masses; decrease in pleural fluid and pulmonary nodules; and healing of osseous lesions. In every instance, patients having objective palliation also had subjective relief.

In patients having objective palliation, average total period of palliation was forty months; 70 per cent had two years or more of relief and more than 20 per cent had five years or more. Subjective palliation lasted two years or more for more than 50 per cent of patients and five years or more for 15 per cent. Survival time from estimated onset of disease to death was five years for 38 per cent and ten years or more for 12 per cent of the patients.

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Relationship of Pneumonitis in Infants to Respiratory Syncytial Virus

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THIS SUBJECT WAS CHOSEN for the issue honoring Dr. Irvine McQuarrie because it was due to his stimulating influence in 1937 that an epidemic of pneumonitis in infants was considered to be a distinct entity, probably caused by an unknown virus. The respiratory syncytial (RS) virus recently described by Chanock and associates[1,2] in infants may be related etiologically to this disease. The virus was first recovered from chimpanzees with respiratory disease and was designated chimpanzee-coryza agent by Morris and associates.[3] Beem and colleagues[4] presented evidence of its widespread role in causing acute respiratory disease in children. More recently, Chanock and associates,[5–8] Hamparian and associates,[9] McClelland and associates,[10] and Reilly and associates,[11] in a series of papers, have clearly demonstrated the importance of the RS virus as a cause of a wide spectrum of acute respiratory diseases, particularly in infants and children.

During an epidemic of pneumonitis in infants in California in the early months of 1961, the RS virus was isolated from the majority of patients on whom virologic studies were performed. The epidemiologic, clinical, and pathologic features of the epidemic were similar in all respects to those of epidemics occurring in Minnesota in 1937, 1941, and 1945.[12–15] Unfortunately, direct proof of an etiologic relationship will never be had. However, many well-established entities in medicine are based on distinct epidemiologic, clinical, and pathologic findings. In this paper, further data of the clinical, epidemiologic, pathologic, and virologic studies of the epidemic which occurred in California will be presented. A preliminary report was made in June 1961.[16]

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CALIFORNIA EPIDEMIC

The epidemic first became evident early in January 1961, when the admission rate to the pediatric service of the Harbor General Hospital increased rapidly, largely because of acute respiratory disease in infants. Only the most extremely ill infants were admitted to the hospital. Symptoms were cough, dyspnea, and, occasionally, attacks of cyanosis. Fever was generally low grade and often absent, although occasional temperatures of 103° to 105° F. were recorded. A history of acute respiratory disease in other members of the family was a frequent observation. The epidemic continued through February and subsided during March (figure 1).

At the Los Angeles County Hospital during these same months, the average admission rate of approximately 100 per week to the pediatric unit more than doubled, with a peak of over 250 the second week in February. This striking rise could be accounted for largely by infants who were admitted with bronchiolitis or pneumonia, of whom there were 140 during the same week in February. During March, the rate fell sharply to approximately the average of 100 total admissions per week to the pediatric unit.

That the epidemic was largely related to the RS virus may be surmised from the fact that random virologic studies during the height of the epidemic revealed 8 isolations from 12 patients. The agent, readily recovered by growth on HeLa cell cultures, had all the characteristics of RS virus, including the formation of cytoplasmic inclusion bodies. Random samples from several patients after the epidemic failed to reveal a single viral isolation.

None of the influenza viruses has been isolated this season from patients in this area with acute respiratory disease. The para-influenza viruses likewise have been uncommon in this community this season, with rare isolations. These agents do not grow readily in the HeLa cell cultures, whereas all of the strains isolated from the in-

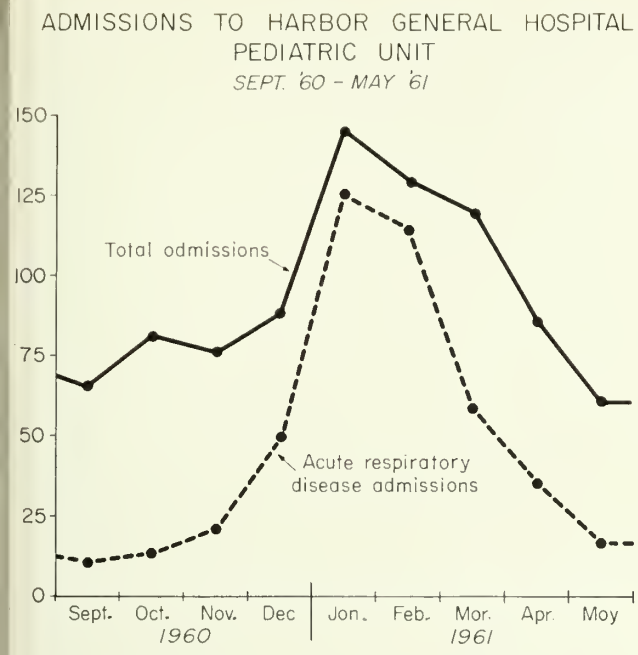

Fig. 1. Graph showing admission rate to Harbor General Hospital from September 1960 to May 1961. Sharp increase early in 1961 is due largely to acute respiratory disease in infants.

fants in the present epidemic did. Croup, which is common with para-influenza virus infeetions, was rare in the present series of cases. Other possible eauses of an epidemie of acute respiratory disease, such as the adenoviruses, are under study, but the present isolates do not show the cytopathic changes assoeiated with these agents and do demonstrate charaeteristie changes of the RS virus. No rash was observed in any of the patients, which serves to eliminate diseases such as measles.

The majority of the patients were between 6 weeks and 6 months of age, with a mean age of 10 weeks; very few were older than 1 year. Average length of hospitalization was eight days.

FINDINGS

Beeause this study is based on an acute hospital population, it represents the most severely ill patients who warranted admission to an already erowded ward. The symptom picture, therefore, is largely based on the most acutely ill and undoubtedly gives a biased cross section as far as age group and symptomatology are eoncerned.

The infants presented a picture of acute respiratory distress, with evidence of obstruction to adequate ventilation, which was frequently demonstrated by varying attacks of cyanosis. Physical findings consisted largely of fine rales over the lung fields. Roentgenograms of the chest revealed signs of overaeration, often with depressed diaphragms. There were indieations from these findings of trapped residue air in the lungs, with inadequate ventilation—a finding particularly charaeteristic of RS virus infeetion. Evidence of pneumonia or ateleetasis was not eommon but occasionally was demonstrated by an increase in shadows in certain areas of the lung, the right upper lobe being involved most often.

A ropy, tenaeious exudate was characteristically observed in many of these patients and may have served to aggravate the obstruetive symptoms. Cough was a striking symptom but was not eroupy in character. The fever was low grade in the majority of patients, some failing to register any elevations of temperature. This may have been due to the fact that the bronchial and bronchiolar areas of the respiratory tree were involved primarily, with little evidence of pneumonia. When fever is elevated, it is often an indieation of air-sac involvement, and signs of pneumonia may be evident.

Humidified oxygen administered by means of a tent was the main method of treatment. Antibiotics were given to 70 per cent of infants, who had roentgen evidenee of pneumonia. Steroids and digitalis were employed infrequently and thus cannot be evaluated.

PATHOLOGY

Pathologic material from the 1961 Harbor Hospital epidemie was limited to the study of 1 patient in whom signs of aeute bronchiolitis with minimal pneumonitis were evident. Cytoplasmie inelusion bodies were identified in this patient's lung sections. Lung sections from a patient with proved RS virus infeetion were kindly provided by Drs. F. H. Wright and M. Beem. A low-power photomicrograph from their patient (figure 2a) demonstrates peribronehial mononuclear infiltration, with destruction of lining epithelium. Inelusion bodies were demonstrated in sections, studied by the piero-Mallory staining method, of a few bronchial lining cells.

The patients from whom pathologie material was available were not cases which were proved to have RS disease but represent deaths which oeeurred from acute bronehiolitis and pneumonitis during the 1961 epidemic in California. They are therefore presented with epidemiologic evidence only. Figure 2b illustrates a small bronchus from such a patient with bronchiolitis and minimal pneumonitis. The same evidence is available from our previous detailed studies of the pathology of pneumonitis with cytoplasmie inclusion bodies.[12–14] The pathologic material is presented with the hope that future investigators

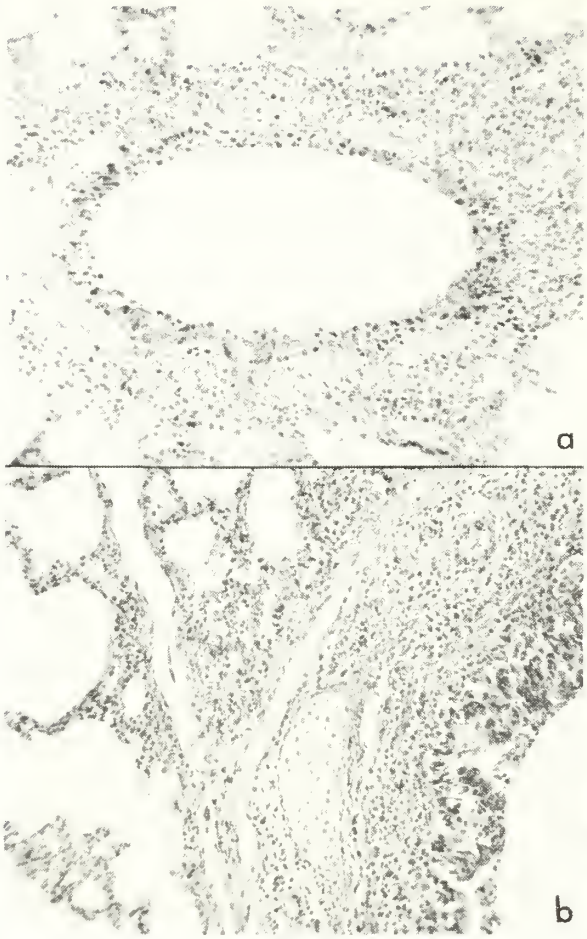

Fig. 2. (a) Low-power photomicrograph from proved case of respiratory syncytial virus infection illustrating minimal bronchiolar involvement with mononuclear reaction. × 160 (from material kindly furnished by Drs. F. H. Wright and M. Beem). (b) Low-power photomicrograph from patient in epidemic showing more extensive changes, with proliferation of bronchial lining cells. × 160

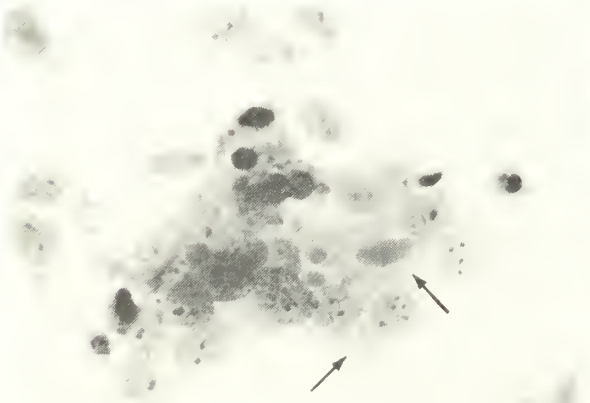

Fig. 3. Photomicrograph of HeLa cell culture showing typical syncytium caused by agent isolated from patient in epidemic. A giant cell is shown, with cytoplasmic inclusion bodies indicated by arrows. × 560

will go on to search for proved cases and thus establish RS infection pathologically.

Strong indirect evidence of the condition is provided by the similar cytopathic effects produced in human epithelial tissue culture and in monkey kidney cell cultures by the RS virus. Sections of HeLa cell cultures with cytopathic changes were illustrated in the preliminary publication[16] of the 1961 epidemic, and a further photomicrograph (figure 3) is presented here to illustrate a giant cell with cytoplasmic inclusion bodies.

Lung sections revealed a necrotizing bronchiolitis with peribronchial mononuclear infiltration. Photomicrographs of sections from a patient presumed to have died from this syndrome (figure 4) show typical cytoplasmic inclusion bodies stained with picro-Mallory stain. These same bodies also may be stained with hematoxylin and eosin. Details for these procedures were given in previous publications.[17,18]

Virologic studies were made during the height

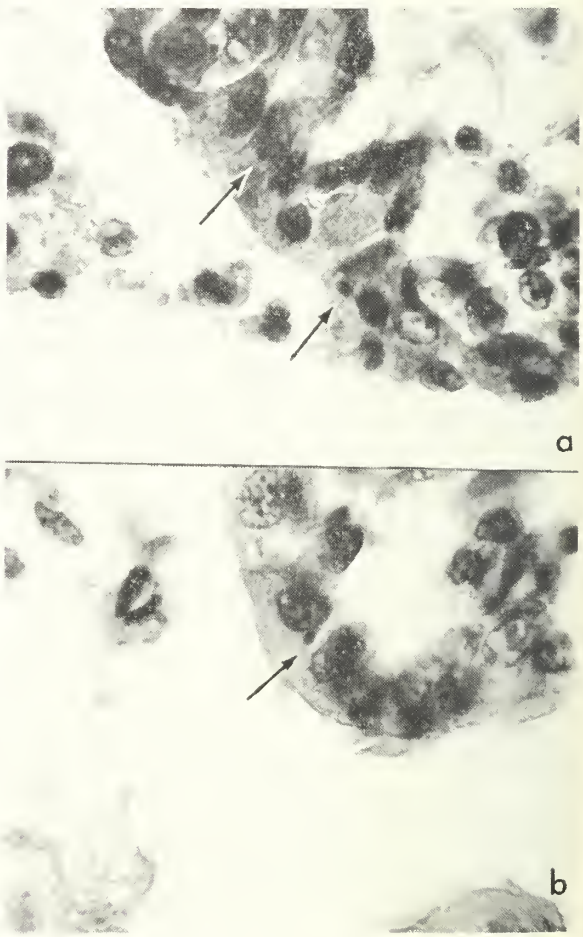

Fig. 4. Photomicrographs of lung sections from patient in figure 2b showing bronchial lining cells, with cytoplasmic inclusion bodies indicated by arrows. × 1,080

of the epidemic and consisted primarily of nasal pharyngeal washings, which were obtained by lavaging the nose and throat with a syringe bulb containing nutrient broth. The return was transferred immediately to cell culture preparations, which were brought to the bedside. Beem and associates[4] pointed out that the customary procedure of freezing specimens greatly reduces the possibility of isolation. This important finding we have been able to confirm.

The characteristic syncytium caused by this virus, and from which it received its name, occurred in five to nine days, with giant cells making up the syncytium. In the cytoplasm of the giant cells were seen cytoplasmic inclusion bodies, which varied greatly in size from minute bodies to masses 5 to 10 μ in diameter, usually round or oval in shape, with a clear zone or halo about them (figure 3).

The cytopathic changes were neutralized by known RS antibody and by convalescent sera from the patients from whom isolations were made, as well as from other patients in the epidemic. Complement-fixation tests with RS antigen performed on the acute and convalescent sera from patients known to have RS virus infection showed a fourfold or greater increase in titers. When the test was performed with the prototype virus of this epidemic, similar significant increases were observed. The agent also fixed complement when known RS antiserum was employed in the tests. These studies are still being carried out, as are experiments designed to eliminate other causes of the epidemic.

DISCUSSION

The studies reported here are still under investigation in the laboratory but are considered timely and of importance for stimulating further observations of this definite syndrome in infants and children. The discovery of the etiologic agent related to this disease makes possible definitive studies of the epidemiologic and pathologic data. Characteristic cytopathic changes caused by the RS virus, with the formation of giant cells and inclusion bodies, serve to link this agent with a form of pneumonitis in infants in which these striking changes occurred.[13,14]

Pharyngeal smear biopsies were made on a large number of the babies in the epidemic, and cytoplasmic inclusion bodies were seen in varying numbers in nearly every patient. The full significance of these will have to await further study, although they do occur in greatly increased numbers. Attempts to demonstrate an antigenic relationship by fluorescent antibody technics have to date failed to show a clear-cut association, largely due, we believe, to inadequate experience and technical difficulties. The association of increased numbers of inclusion bodies in infantile pharyngeal smears with bronchiolitis and pneumonitis was demonstrated many years ago.[14]

The experiences of the 1961 respiratory disease season point to the RS virus as one of the common causes of acute bronchiolitis and pneumonitis in infants. The clinical characteristics in the most severely ill patients are well defined and feature cough, dyspnea, and cyanosis, with few physical findings other than fine rales in the chest. Many extremely ill infants are actually afebrile, although they usually have fever at some time in the course of their illness.

Croup is a rare symptom, which tends to differentiate this disease from the para-influenza infections. Likewise, the clinical picture differs from the acute pharyngoconjunctival fever syndrome associated with the adenoviruses, in which tonsillitis, pharyngitis, and conjunctivitis are more striking and the tendency of bronchiolitis and pneumonitis to develop is much less likely. Influenza does not commonly involve the infant age group, as apparently occurs with RS infections; it is also characterized by acute pharyngitis; and rarely causes the pneumonitis so commonly found in the syndrome under discussion.

Many of these clinical differential points were observed by Reilly and his associates[11] in the epidemic recently reported by them, which included older children, the majority of whom were seen on an outpatient basis. However, they pointed out that 46 per cent of their patients had lower respiratory tract involvement, with resultant bronchitis, bronchiolitis, or bronchopneumonia.

The histopathologic changes are marked by destructive and proliferative lesions, particularly in the bronchioles. The presence of inclusion bodies and giant cells cannot always be demonstrated readily, as death frequently occurs early in the course of illness, probably before the development of the complete pathologic picture. These changes are much more commonly observed in patients who have prolonged illness before death. This same relationship was found to occur in experimental studies.[17]

SUMMARY

An epidemic of acute respiratory disease, occurring in California in the first three months of 1961, was characterized by severe symptoms of bronchiolitis and pneumonitis and, rarely, by death in infants. The epidemic apparently was

related etiologically to the respiratory syncytial (RS) virus, which has been isolated in HeLa-cell and monkey kidney-cell cultures. It caused a distinctive cytopathic change, the main features of which were a marked syncytium, giant cells, and cytoplasmic inclusion bodies.

Pathologic material from 1 proved case was presented. Additional material from patients dying in the epidemic illustrated a necrotizing bronchiolitis with peribronchiolar mononuclear infiltration and cytoplasmic inclusion bodies in the lining epithelial cells. The epidemic was similar in its epidemiologic, clinical, and pathologic aspects to an outbreak of infant pneumonitis first reported in 1941 which was characterized by giant cells and cytoplasmic inclusion bodies.

In the majority of the infants, humidified oxygen was the only method of therapy.

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Respiratory symptoms frequently antedate radiologic pulmonary abnormalities in men 45 years of age or older with lung cancer. For early detection of lung cancer, extensive radiologic and cytologic studies, as well as bronchoscopic, bronchographic, and clinical investigations, should be undertaken whenever respiratory symptoms arise in this vulnerable population.

The natural history of lung cancer was studied in 6,137 men 45 years of age or older by means of semiannual photofluorograms and questioning about symptoms. The observation period ranged from three and a half to seven and a half years. A total of 92 cases of proved lung cancer were found. Of these, 66, or 11 per 1,000, were visible on entry films. Hemoptysis was the commonest symptom among the 66 patients.

New pulmonary neoplasms developed in 26 patients during the observation period, an incidence of 1 per 1,000 per year. Of 15 patients who reported regularly or in whom the natural history of the disease could be delineated adequately, 10 had symptoms antedating x-ray changes by as long as five and a half years, with a mean of two and a half years. Most of the neoplasms were peripherally located. The incidence of new proved lung cancer was almost twice as high as the incidence of new proved active tuberculosis.

In patients who had smoked for more than twenty years, the cancer rate and degree and duration of smoking were definitely correlated. This correlation was not altered appreciably when age was taken into account.

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Growth and Development in Negro Infants and Children

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Until relatively recent times, a majority of the scientific investigations of growth and development have discussed racial differences in both physical and psychologic development without adequate documentation. Negro children were evaluated, in most instances, on the basis of norms which were developed from the study of white children.

The present study was undertaken to provide descriptive data on the anatomic, physical, and psychologic growth and development of Negro infants and children from birth through 5 years of age and to determine the effect, if any, of selected background factors upon growth and development. One basic assumption of the investigators was that many racial comparisons fail to take into account differences in background and living conditions, with particular reference to socioeconomic status. This led to the hypothesis that many of the so-called racial differences are, in fact, merely reflections of differences in socioeconomic status.

Some of the results of this study, which has been in progress since 1953, have appeared in print. It is the purpose of this paper to present briefly a description of the study design and to summarize some of our results to date, both published and unpublished.

AREAS OF INVESTIGATION

As stated above, it was felt that, in order to be complete, this study should include some evaluation of various background factors which seemed important in relation to the processes of growth and development. These are included in the following list of areas covered by this investigation:

1. *Nutrition.* Nutritional evaluations were obtained for the mother both pre- and postnatally. Prenatal evaluations were secured during the second and/or third trimester and postnatal evaluations, from six to eight weeks after birth. Evaluations also were made, at each interview period, of the nutrient intake of each child, beginning three months postnatally.

2. *Socioeconomic status.* An estimate of the socioeconomic status of the family was made on 2 occasions—at or near the birth of the child and when the child reached 5 years of age.

3. *Physical growth.* Physical growth of the subjects was measured by weight, height, head, and chest circumferences. Skin color of the child was also obtained at each interview.

4. *Anatomic growth.* Roentgenologic examinations of the hands, wrists, feet, and legs were made at each interview.

5. *Psychologic growth.* There were 4 different sets of tests used to measure psychologic development between birth and 5 years of age, and these may be listed as follows:

Age	*Psychologic measuring instrument*
Birth	Battery of reflex tests and postural responses*
3 to 30 months	Gesell Developmental Schedules
36, 42, and 54 months	Merrill-Palmer Scale of Mental Tests
48 and 60 months	Revised Stanford-Binet Intelligence Scale

*The reflexes and responses measured at birth include (1) activity, (2)Moro reflex, (3) tonic neck reflex, (4) rooting reflex, (5) muscle tonus, (6) ability to raise head from prone position, (7) ability to turn head from side to side, (8) crawling or swimming movements, and (9) stepping movements.

6. *Medical-social data.* This information was obtained from the mother in the hospital after the birth of her baby and includes the mother's medical history, height, and weight, and the skin color of both parents.

METHODS AND PROCEDURES

The original study design called for each child to make 14 follow-up visits after birth, at three-month intervals through 24 months of age and at six-month intervals between the ages of 2 and 5 years. At each visit, the child received physical, psychologic, and roentgenologic examinations.

All physical measurements were taken by a member of the pediatric staff of the Department of Pediatrics of Meharry Medical College. Psychologic examinations were administered by a psychologist in accordance with the respective test manuals. Nutritional histories were obtained from the mothers by a trained nutritionist or, in

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TABLE 1
INITIAL SOCIOECONOMIC DISTRIBUTION FOR TOTAL NEWBORN GROUP, PLUS COMPARISON OF NEWBORN AND 5-YEAR DATA ON 195 FAMILIES

Socio-economic group	All newborns		Families with newborn and 5-yr. data			
			Newborn		5-year	
	No.	%	No.	%	No.	%
I (low)	102	12.8	23	11.8	12	6.2
II	372	46.8	93	47.7	73	37.1
III	258	32.4	60	30.8	83	42.6
IV (high)	63	7.9	19	9.7	27	13.8
Total	795	100.0	195	100.0	195	100.0

the case of feeding histories of the infants, by persons instructed by the nutritionist. Medical-social data and the socioeconomic evaluation were obtained by a medical social worker. Details of method and procedure can be found in previous publications of this series.[1–11]

It was necessary in some instances to develop new technics or to modify existing technics for the measurement of particular characteristics. Where such was the case, these will be explained when the results are discussed.

Subjects. There were 873 children* in the major project, born between December 1953 and December 1958, the youngest of whom has now passed the age of 36 months. Participation in the continuing study was limited to those infants whose mothers resided in the city of Nashville and who were delivered at Hubbard Hospital, the teaching hospital of Meharry Medical College. Mothers were contacted before delivery, in the obstetrical clinic of Hubbard Hospital or by referral from an obstetrician, and were committed by agreement to participate in the longitudinal study.

The distribution of the subjects according to socioeconomic status is weighted toward the lower middle group, largely because of the preponderance of clinic patients accepted into the project. There is, however, a broad enough range to permit comparisons according to socioeconomic status. The distribution of the total group and of a group for whom both newborn and five-year information is available, according to socioeconomic status, is shown in table 1. It will be noted that, during the five-year period of study, there was a general improvement in the socioeconomic status of those 195 families represented here.

The socioeconomic score used in this study is derived from an index consisting of 8 items, each of which is scored on a 10-point scale—from 0, denoting low score, to 9, denoting high score—yielding a range of 0 to 72 points. The index is primarily a modification of the technic used by Kiser and Whelpton,[12] with the addition of a modification of Sewell's scale.[13] The complete index, with the scoring breakdown for each item, is shown in table 2.

*Information is available on more than 2,000 newborn infants and was collected from the following supplementary studies: (1) pilot study, (2) a study of nonproject infants born at Hubbard Hospital during a one-year period, which was conducted for comparative purposes, and (3) a study of nonproject premature infants, also conducted for one year in order to obtain additional roentgenologic information on premature infants.

RESULTS

Nutritional Evaluations

The prenatal nutrition scores of 483 expectant Negro mothers were analyzed, using a rough score to indicate adequacy of the prenatal diet. Each record was evaluated by a scoring technic based upon average values for weekly servings of food in 6 basic food groups. For scoring purposes, each food group was given a rating of excellent, good, fair, poor, or very poor, with each rating having a point equivalent such that total maximum score equals 100 and total minimum score equals 28.5.[4] Mean nutrition score for this group of mothers was 48.8. Only 19.1 per cent of the cases studied had scores approximating two-thirds or more of the daily allowances for pregnant women, as set forth by the National Research Council. Size of the family unit was not related significantly to prenatal nutrition, but number in the family was a determinant of total expenditure for food and of the amount spent per person. As size of family increased, total expenditure for food increased but amount spent for food per person decreased. This is in agreement with the findings of Murphy and Wertz.[14]

Although no consistent relationship was found between birth weight of the infant and prenatal diet of the mother, the average birth weight of female infants did increase consistently with increase in nutrition score, but the difference is not statistically significant. Moreover, prenatal diet was directly related to extent of prenatal care, socioeconomic status, and education of the mother. Excluding mothers with no prenatal care, there was a trend toward higher nutrition scores with prenatal care beginning early in pregnancy; as anticipated, nutrition scores were better, on the average, in the highest socioeconomic group, and there was a significant and direct relationship between education of the mother and nutrition score (table 3; figure 1).

Intensive analysis of the dietary records of 571 expectant mothers revealed results similar to those found using the rough score.[7] Figure 2 presents the average percentage of recommended dietary allowances supplied by the diets of

TABLE 2

SCALE FOR DETERMINING SOCIOECONOMIC STATUS

Score	Longest occupation of father*	Education of mother	Education of father	Average annual earnings of father*	Shelter rent at interview	Purchase price of car	Revised form of Chapin's scale	Modified Sewell's scale
9	Professional and semiprofessional	College 4	College 4	$4,500 and over	$90 and over	$1,350 and over	100 and over	110 and over
8	Proprietors, managers, and officials	College 3	College 3	$3,500-4,499	$80-89	$1,200-1,349	90-99	100-109
7	Clerical	College 2	College 2	$2,750-3,499	$60-79	$1,050-1,199	80-89	95-99
6	Skilled	College 1	College 1	$2,250-2,749	$50-59	$900-1,049	70-79	90-94
5	Semiskilled	Grade 12	Grade 12	$2,000-2,249	$40-49	$750-899	60-69	85-89
4	Protective service workers	Grade 11	Grade 11	$1,750-1,999	$35-39	$600-749	50-59	80-84
3	Service workers (exclusive of domestic and protective)	Grade 10	Grade 10	$1,500-1,749	$30-34	$450-599	40-49	75-79
2	Domestic service workers	Grade 9	Grade 9	$1,250-1,499	$25-29	$300-499	30-39	70-74
1	Farm laborers	Grade 8	Grade 8	$1,000-1,249	$20-24	$150-299	15-29	65-69
0	Unskilled laborers	Less than 8th grade	Less than 8th grade	Less than $1,000	Under $20	Less than $150	Under 15	Under 65

*In case of illegitimacy, mother was used.

mothers included in this analysis. Mean nutrient intakes were found to increase with higher socioeconomic status and greater educational attainment of the mother for the majority of the nutrients (tables 4 and 5). Meal patterns showed many variations, but relatively few bore signs of good meal planning. Studies by both Macy and associates[15] and Moore and colleagues[16] have reported lower nutrient intakes among Negro pregnant women than among white, and the adequacy of the diets reported here indicates that the prenatal diets of mothers in this study were considerably lower in nutrient intake than national recommendations.

Rating of the postnatal diet of 302 mothers, using the same rating scheme as employed for the prenatal period, was directly related to rating of the prenatal diet.[10] Differences in pre- and postnatal ratings are shown in table 6. Although there was no great shifting in dietary ratings between the 2 periods of observation, only 35.4 per cent failed to change categories; 28 per cent of the postnatal ratings were higher than the prenatal, while 36.1 per cent were lower. Mothers who were feeding their babies artificially by six to eight weeks postnatally had higher dietary ratings than did those who were still breast feeding.

For 388 mothers, no great divergence in breast-feeding practices was evident when this group was compared with similar studies in the literature.[10] Of these mothers, 55 per cent had done

TABLE 3

SOCIOECONOMIC INDEX ACCORDING TO MEAN PRENATAL NUTRITION INDEX

Socioeconomic index	Nutrition index		
	Mean	S.D.*	Number
Group I (low)	44.2	11.0	71
Group II	48.0	12.4	220
Group III	49.8	12.2	156
Group IV (high)	60.7	13.4	27
Total	48.8	12.8	474

*Standard deviation

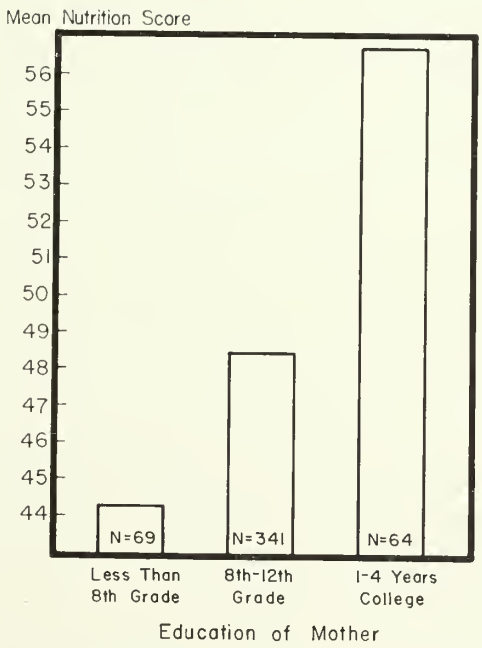

Fig. 1. Mean prenatal nutrition score correlated with education of mother

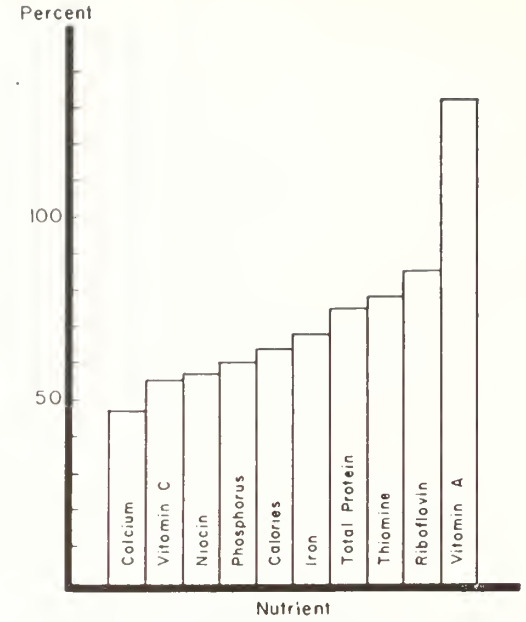

Fig. 2. Average percentage of recommended dietary allowances provided by diets of 571 pregnant Negro women.

some breast feeding, while the average percentage-incidences of breast feeding for the southeastern region of the United States and for Tennessee were, respectively, 43 and 62.[17] Of the mothers in this analysis who did any breast feeding at all, 35.1 per cent stopped in one month or less and 44.4 per cent, in 2 months or less. Although 69 per cent of the infants were receiving multivitamin supplements, the early addition of solid foods to the infant's diet was not practiced to any great degree by these mothers. Almost half the infants—45.9 per cent—were not receiving any type of solid food at 6 to 8 weeks of age. Cereal, however, was reported by 30.4 per cent of the mothers and strained fruits and vegetables, by 10.1 and 6.2 per cent of the mothers, respectively. The factors of socioeconomic status and education of the mother showed some relation to infant feeding habits. Mothers in the higher socioeconomic groups who breast fed weaned their infants earlier than did mothers in the lower groups; with advancement in socioeconomic status and education of the mother, a steady increase was noted, in most instances, in the percentage of mothers employing supplemental feeding (table 7).

Physical and anatomic development

1. Physical measurements. Thus far, the analysis of physical measurements has been confined largely to birth weight. Mean birth weight of Negro infants in this study has been shown to be less, for both male and female infants, than that reported in most studies of white infants.[1] It was also shown, however, to vary considerably, so that the range of differences in birth weight existing among Negro infants is similar to that shown when Negro and white infants are compared. The data tend to show that there is a direct relationship between small babies at birth and certain conditions more common to the Negro mother. Tandy[18] has shown that Negro mothers tend to be younger than white mothers, and studies by Michelson[19] and Peckham,[20] as well as this study, have revealed a direct relationship between age of mother and birth weight of infant. A similar relationship was observed for parity and birth weight in this study. It is interesting to note, however, that, although the higher socioeconomic groups have a lower mean parity, mean birth weight still shows a consistent increase from the lowest to the highest socioeconomic group. This would suggest that, in this study at least, the determining influence of socioeconomic status on birth weight is greater than the influence of parity. Figure 3 shows the cumulative percentage distribution of birth weights of 1,572 infants by socioeconomic group, while mean birth weight and mean parity by socioeconomic group are shown in table 8.

Type of prenatal care was also significantly related to mean birth weight, with mean birth weights of both male and female infants being highest for those mothers who had private care and lowest for those who had no prenatal care

TABLE 4

MEAN NUTRIENT INTAKE BY SOCIOECONOMIC GROUP FOR 530 NEGRO WOMEN IN THE THIRD TRIMESTER OF PREGNANCY

Socioeconomic group	*Number of subjects*	*Calories*	*Protein (gm.)*	*Calcium (gm.)*	*Phosphorus (gm.)*	*Iron (mg.)*	*Total vitamin A (I.U.)*	*Thiamine (mg.)*	*Niacin (mg.)*	*Riboflavin (mg.)*	*Ascorbic acid (mg.)*
I (lowest)	51	1,152	50.5	0.6	0.8	9.5	7,210	0.9	10.1	1.6	50.5
II	212	1,629	57.8	0.7	0.9	10.0	7,600	1.0	11.1	1.6	50.8
III	194	1,650	58.3	0.7	0.9	10.3	8,010	1.0	11.0	1.7	55.1
IV (highest)	13	1,971	69.6	0.9	1.2	11.5	8,520	1.2	12.8	2.2	73.6

TABLE 5

MEAN NUTRIENT INTAKE ACCORDING TO EDUCATIONAL LEVEL ATTAINED OF 530 NEGRO WOMEN IN THIRD TRIMESTER OF PREGNANCY

Educational level	Number of subjects	Calories	Protein		Calcium (gm.)	Phosphorus (gm.)	Iron (mg.)	Total vitamin A (I.U.)	Thiamine (mg.)	Niacin (mg.)	Riboflavin (mg.)	Ascorbic acid (mg.)
			Total (gm.)	Of animal origin (%)								
Less than 8th grade	70	1,389	51.6	64.4	0.6	0.8	9.1	7,380	0.9	9.9	1.6	41.6
8th grade	83	1,467	51.7	62.5	0.6	0.8	9.3	6,760	0.9	10.0	1.5	48.7
9th through 12th grade	289	1,698	59.0	62.5	0.7	0.9	10.5	7,640	1.0	11.6	1.6	51.6
1 to 4 years of college and over	88	1,860	67.3	68.2	0.9	1.1	11.0	8,920	1.3	12.3	2.2	66.7

TABLE 6

DIFFERENCES IN PRE- AND POSTNATAL DIET RATINGS OF MOTHERS

Rating on postnatal diet	Rating on prenatal diet (per cent)				
	Very poor	Poor	Fair	Good	Excellent
Excellent	–	0.9	–	–	–
Good	5.0	3.7	13.3	18.4	100.0
Fair	21.2	25.0	33.3	42.1	–
Poor	28.8	36.1	33.3	18.4	–
Very poor	45.0	34.2	20.0	21.0	–
Total	100.0	100.0	100.0	100.0	100.0
N	80	108	75	38	1

at all. The percentage of premature infants was correspondingly highest for those mothers with no prenatal care—19.8 per cent—and lowest for mothers with private prenatal supervision—7.6 per cent. When the incidence of prematurity is considered from the broader standpoint of socioeconomic status, the striking effect observed in figure 4 is the result.

Mean birth weights of 1,821 infants included in this analysis are shown in table 9 according to sex.

In a preliminary, unpublished analysis of growth data accumulated on infants during the first year of life, it was noted that the relation observed between birth weight and socioeconomic status also existed for weight at 3, 6, 9, and 12 months of age, at least at the fiftieth percentile (median) level. Median height and head circumference also tend to increase with socioeconomic status at the aforementioned age levels.

In comparing median weights of children in this study with those developed from comprehensive studies of health and development by Stuart and his associates[21] at the Harvard School of Public Health, Negro male infants were below the median weight of the Harvard study group at birth and at 9 and 12 months; Negro female infants were below the median weight at each age studied during the first year. Both Negro male and female infants were below the median height values at all periods, except Negro males at 6 months, whose median height was 0.3 cm. higher than that of the Harvard group. Median head circumference of the Negro infants was smaller in all instances. The number of cases included in these preliminary analyses varied from 700 at birth to 319 at 12 months of age.

2. Reflex development at birth. It has been suggested that Negro infants appear physiologically more mature when compared with white infants of the same size (weight) during the first months of life. No comparative studies have been found to affirm or deny this clinical im-

TABLE 7

PERCENTAGE OF MOTHERS EMPLOYING SUPPLEMENTARY FEEDING, ACCORDING TO SOCIOECONOMIC GROUP AND EDUCATION

Supplement	Socioeconomic group				Education of mother			
	I	II	III	IV	Less than 8th	8th grade	9th-12th grade	College 1-4
Multiple vitamins	52.2	53.3	64.4	71.0	50.0	53.8	57.9	71.2
Cereal	21.7	26.4	32.6	54.8	20.4	32.7	25.8	51.5
Fruit	8.7	6.0	12.6	25.8	11.4	9.6	6.7	21.2
Orange juice	39.1	33.0	43.7	32.2	34.1	34.6	36.8	42.4
Vegetables	8.7	4.9	4.4	12.9	2.3	3.8	4.3	13.6
Cod liver oil	13.0	5.5	5.2	0.0	6.8	3.8	5.7	4.5
Total N	23	182	135	31	44	52	209	66

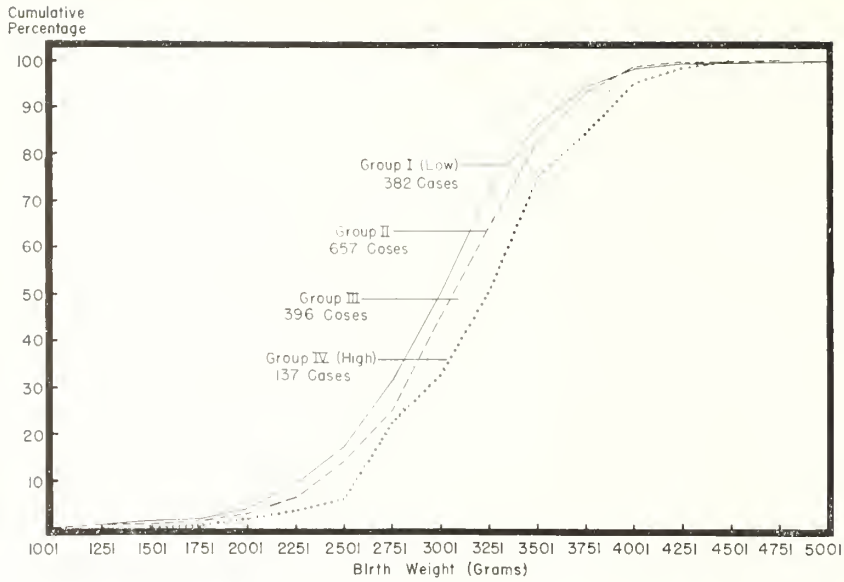

Fig. 3. Cumulative percentage distribution of birth weights of 1,572 infants according to socioeconomic group.

pression. It was therefore felt that assessment of the reflex responses or physiologic maturity of the infants in our study group would prove worthwhile. The babies were tested, accordingly, by means of a battery of reflex tests and postural responses, only 2 of which are considered here. The sucking reflex of 52 Negro female premature infants and 32 full-term newborn Negro infants was studied.[2] Heavier babies demonstrated a stronger and more effective sucking reflex during the first three days of life and thus achieved a higher maximal rate of efficiency. During the first week of life, the sucking rate of the premature infant—0.24 cc. per second—averaged less than 50 per cent of that of the full-term infant—0.6 cc. per second. The sucking efficiency of the premature infant appeared to follow a regular course of development with advance in postnatal age, the smallest infants generally achieving a maximal rate significantly later than larger babies. No relationship was found to exist between gestational age and maximal sucking efficiency of the 23 premature infants on whom complete data were available.

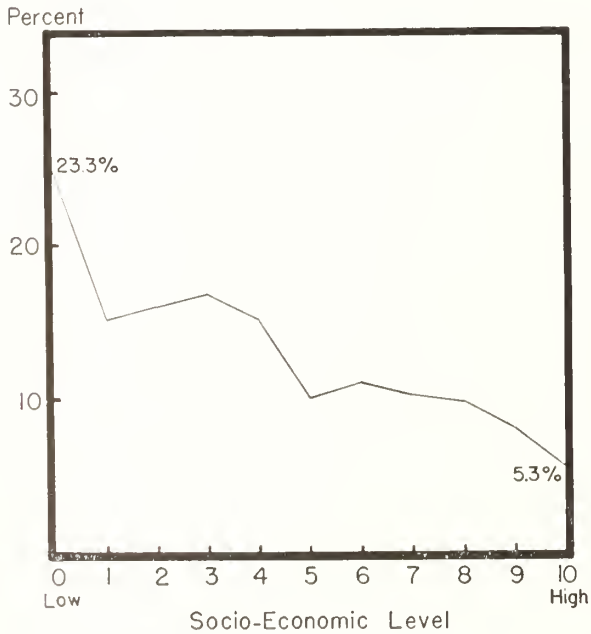

Fig. 4. Percentage of incidence of prematurity according to socioeconomic level.

TABLE 8

MEAN BIRTH WEIGHT AND PARITY ACCORDING TO SOCIOECONOMIC GROUP*

Socioeconomic group	*No. of cases*	*Mean parity*	*Mean birth weight (gm.)*	*Median birth weight (gm.)*
I (low)	382	3 (2.61)	2,960	2,994
II	657	2 (2.33)	3,038	3,058
III	396	2 (1.88)	3,106	3,116
IV (high)	137	1 (1.30)	3,193	3,236
Total	1,572		3,050	3,071

*Prematures included

TABLE 9

SUMMARY STATISTICS ON BIRTH WEIGHT OF 1,821 INFANTS ACCORDING TO SEX

Sex	*No. of cases*	*Mean birth weight*			*Standard deviation*
		gm.	*lb.*	*oz.*	
Male	947	3,227	7	1	± 409
Female	874	3,128	6	14	± 386
Total	1,821	3,179	7	–	± 401

The palmar grasp reflex of 527 newborn infants was studied (unpublished data), and the reflex was found to be absent for almost one-third of the group. A consistent increase was found in the percentage of infants who grasped as birth weight increased, with the difference being particularly notable between premature and full-term infants. As indicated by Halverson,[22] the activity level of the infant was directly associated with manifestation of the power to grasp.

3. *Skin color.* Numerous reports concerned with the importance of skin color among Negroes have appeared over the years. Among these are the studies of Myers and Yochelson[23] and K. B. and M. K. Clark,[24] which deal with the social and cultural importance of skin color, and studies such as Niedelman's[25] and Eller's,[26] which are concerned with the biologic and functional implications of this attribute. In the present study, careful determinations of the color of the skin were made on parents and on children at each interview, and the effects of skin color have been studied from two aspects.

The first analysis[3] dealt with the relation of skin color of 661 newborn infants and their parents to selected background factors. The social significance of skin color was indicated by the fact that the greater proportion of dark Negroes were in the lower socioeconomic groups and by the fact that, for 637 mothers, the percentage of unmarried mothers in each color group was 8.8 per cent among light mothers and 32.5 per cent among dark mothers (figure 5). (Myers and Yochelson[23] stated that "Greater opportunities for enhancement of status are offered to the light-skinned individual.")

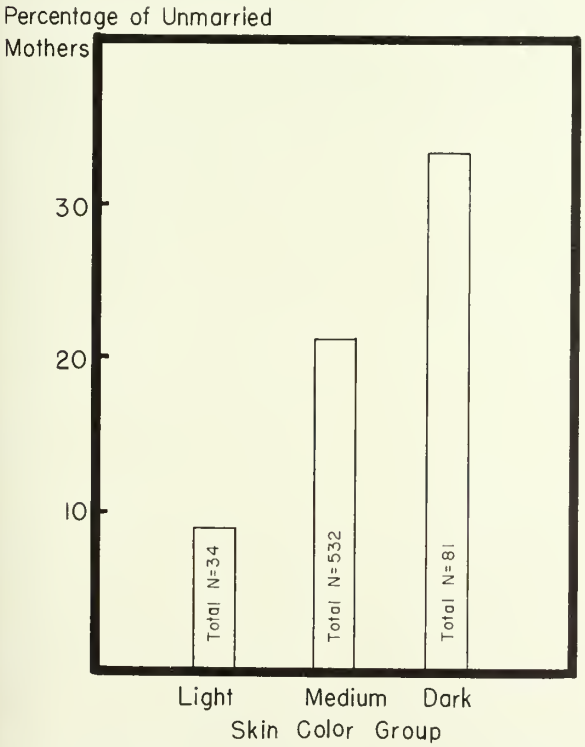

Fig. 5. Percentage of unmarried mothers according to skin color group

It was also revealed, in this study, that persons tended to marry persons in the same color group. In almost two-thirds of 448 families, both parents were within the same group. The skin color of infants was, in the majority of cases, neither significantly lighter nor darker than that of their parents. Slightly more than half the children born to parents of different color groups were lighter at birth than the darker parent, thus assuming an intermediate position colorwise.

In analyzing the relation between skin color and physical factors, it was found that lighter mothers tend to have heavier babies, which is probably a function of the relation between socioeconomic status and skin color. Other characteristics associated with the birth weight of infants, specifically, length of gestation and parity, had no such clear relationship with the mother's skin color, nor was there a consistent relationship between skin color of the infant at birth and birth weight or reflex maturity at birth.

Changes in skin color have also received considerable attention by others. Herskovits[27] states that "... all indications go to show that the pigmentation of the Negro becomes steadily darker with age." Results from the present study, comparing skin color changes of 51 Negro infants from birth through 3 years of age,[6] were not very conclusive in this regard. *Specific* color changes were observed in 35 of 48 children, but 36 of these 48 did not change color groups.* Generally, more fluctuation was observed in the medium color group. The correlation of children's color with that of their parents was found to be higher at 30 months of age than at birth and higher between children and their fathers than between children and their mothers. Some indication was found that children of parents of higher socioeconomic status tend to be lighter in color, but the relationship is not statistically significant. No association was apparent between psychologic development at 2½ or 3 years of age and skin color. Figure 6 illustrates the variations in skin color which occurred among 6 children at differ-

*The color chart used throughout this study consists of 9 color positions, ranging from (1) very light to (9) very dark. Color *groups* were defined as follows: positions 1-3, light; 4-6, medium; and 7-9, dark. The color chart was drawn up, and colors were reproduced by Aaron Douglas, internationally famous Negro artist.

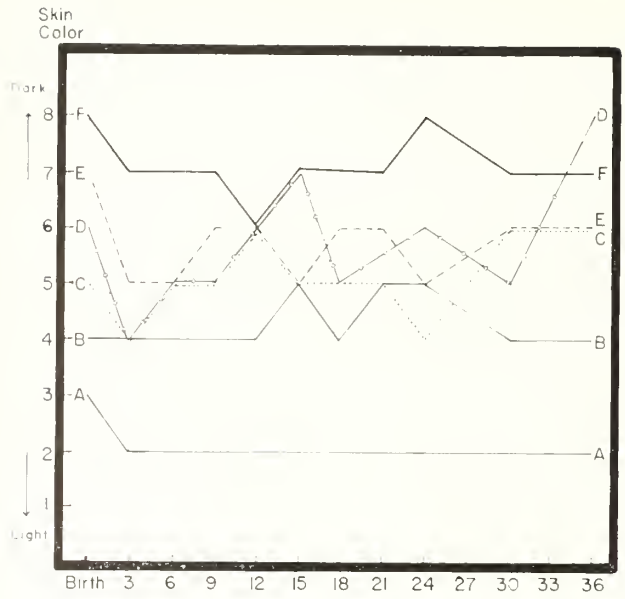

Fig. 6. Variations in skin color of 6 children during first three years of life

ent positions on the color scale during their first three years of life.

4. Osseous development. The frequency of appearance of certain ossification centers at birth has been studied for 997 Negro infants,[8] supplementing a relative dearth of information in this area. Centers studied were: distal femoral epiphysis, proximal tibial epiphysis, cuboid, primary center for middle phalanx of the fourth and fifth toes, capitate, and hamate. The frequency of appearance of the centers studied was found to be significantly associated with birth weight and length, parity, length of gestation period, and sex of infant. No significant association was found with reflex maturity index or skin color of infants or with prenatal nutrition, socioeconomic status, age, or height of the mothers. Infant factors thus showed a greater degree of association with ossification, reflex maturity and skin color notwithstanding, than did those of maternal origin. The expected precocity of female infants in osseous development was demonstrated, and the order of frequency of appearance for the centers parallels those reported in the literature[21,28,29] for the neonatal period and early infancy (figure 7). Table 10 presents the results of analyses involving the relation of presence or absence of each center to the various background factors which were considered.

Psychologic development

The regularity with which children participating in this study were seen has made available

TABLE 10

RESULTS OF CHI-SQUARE TESTS FOR ASSOCIATION BETWEEN PRESENCE OR ABSENCE OF SPECIFIC OSSIFICATION CENTERS AT BIRTH AND OTHER FACTORS*

Ossification center	*Length of gestation*		*Reflex maturity index*		*Birth length*		*Skin color of infant*		*Parity*		*Height of mother*	
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*
Hamate	0	0	–	0	2%	1%	0	–	0	5%	0	–
Capitate	1%	–		–	1%	0.1%	0	0	0	5%	0	–
Tibia	–	2%	–	0	0.1%	0.1%	0	*	0	–	–	–
Femur	0.1%	*	0	0	0.1%	2%	0	–	0	0	0	0
Cuboid	0	–	–	0	0	0.1%	0	0	0	0	–	–
5th toe	0	0	0	0	0	0	0	0	0	0	0	–
4th toe	0	0	–	0	0	0	*	0	0	0	0	–

Ossification center	*Prenatal nutrition Rough score*		*Age of mother at delivery*		*Socioeconomic group*		*Birth weight*		*Sex of infant*
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	
Hamate	0	*	0	0	0	–	–	0.1%	–
Capitate	*	0	0	0	0	–	5%	0.1%	–
Tibia	–	–	0	0	0	0	0.1%	0.1%	1%
Femur	0	0	0	0	0	*	*	*	2%
Cuboid	–	0	0	0	0	0	0.1%	0.1%	0.1%
5th toe	0	0	0	0	–	0	1%	–	–
4th toe	0	0	0	0	–	0	–	0	–

*Key to symbols: 0 = No consistent association; – = Consistent but not significant association; * = Could not make test due to small number of frequencies in some cells, but consistent association observed; 5%, 2%, 1%, 0.1% = Level of statistical significance*

Note. No attempt was made to test association where no consistent pattern was observed.

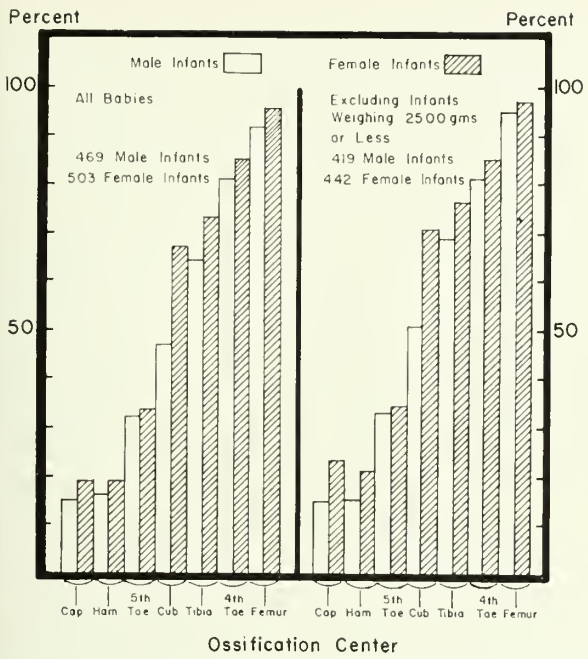

Fig. 7. Percentage of frequency, according to sex, with which specified ossification centers were present at birth

a large body of data relating to development in the psychologic area, much of which has not yet been evaluated. Some analyses have been completed, however, at all age levels.

Performance on the Gesell Developmental Schedules during the first year of life has been studied for all infants who were full-term at birth and on whom psychologic examinations were made during the first year of life, that is, at 3, 6, 9, and 12 months of age (unpublished data). The number of children seen at each age level varied from 556 at 3 months to 410 at 12 months. The subjects performed as well as the normative group at all age levels; their mean performance was, however, significantly better at 3 months than at 12 months. No significant sex difference was found in general maturity at any age level, although females had a significantly higher mean developmental quotient (DQ) at 12 months than did males (102.6 and 100.6, respectively). All infants were significantly more advanced in motor development than in the other areas—adaptive, language, and personal-social—studied throughout the first year. The infants tended to be slower in adaptive development. The most advanced group, however, displayed advancement in all areas rather than marked advancement in the motor area alone. Analysis of the data failed to show any statistically significant relationship between socioeconomic status or height and weight and performance on the Gesell schedules persisting at all age levels. Adaptive maturity was, however, related to socioeconomic status more often than was any other area of performance. Socioeconomic status was more often significantly related to the performance of male infants than to that of female infants. This disparity is not readily explainable in view of the relatively minor differences in the over-all developmental status of male and female infants.

Data on the Gesell schedules have been subjected to more intensive analysis in a study of child-rearing practices of mothers in Nashville. A group of 144 mothers and their children were studied, using data from Gesell schedules, in the areas of feeding, toiletry, and dressing between the ages of 15 and 30 months.[9] The median age at which children in this study achieved each of the items under consideration was found to be generally later than the corresponding Gesell norm in toilet training but earlier than the Gesell norm in feeding habits and dressing (figures 8 and 9), with one notable exception. Instead of discarding the bottle by 15 months (Gesell norm), mothers in this study continued to bottle-feed for at least an additional nine months. Davis and Havighurst[30] earlier studied child-rearing practices of Negro and white mothers in the Chicago area and reported a greater social class difference than color difference, although this

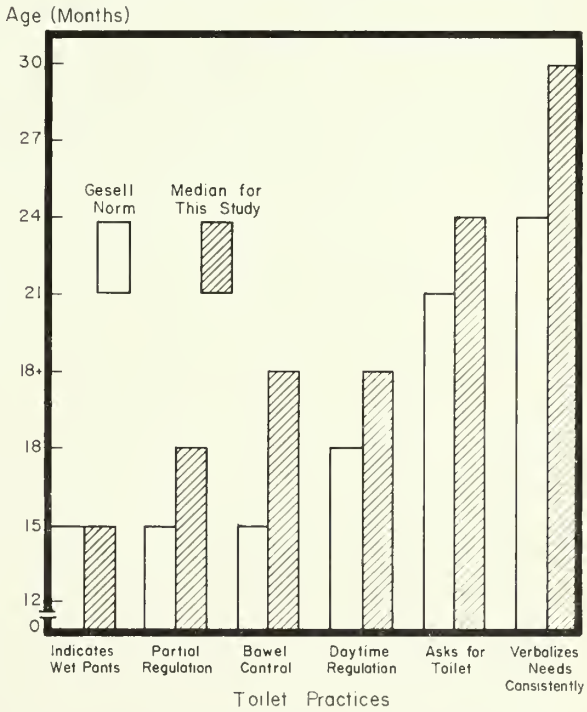

Fig. 8. Gesell norm for age by which various toilet habits should be achieved compared with median age of achievement in present study

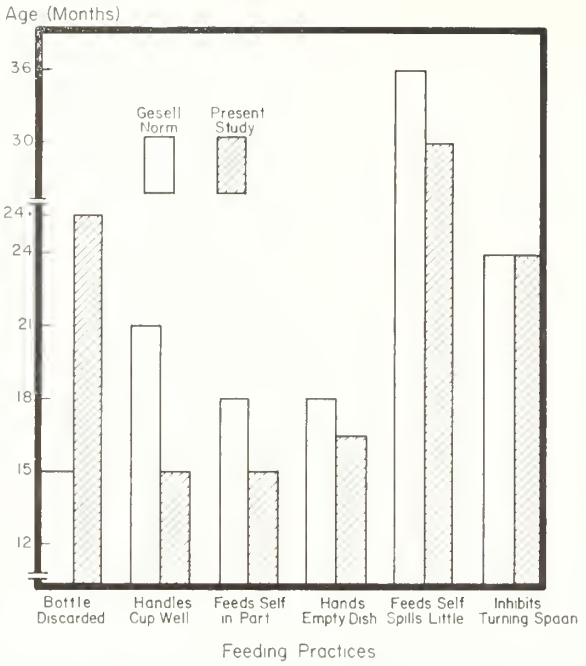

Fig. 9. Gesell norm for age by which various feeding habits should be achieved compared with median age of achievement in present study

over-all finding is not readily apparent when considering the toilet training and weaning data only. In the present study, child-rearing practices under consideration were not found to be significantly related to socioeconomic status, education of the mother, or number of older children in the family. There was a sex difference in the area of dressing—significantly more girls than boys were accomplishing the dressing tasks, such as putting on shoes and unbuttoning accessible buttons, by the age of 30 months. It is likely that some differences are masked, since, instead of ascertaining the exact age for each child, it was only possible to establish the age *by which* children "passed" a particular item, within a minimum range of three months, during follow-up visits. Findings suggest, however, that, though differences in attitude as well as practice may well exist among the mothers, they are not reflected in the development of the children in the areas of toiletry, feeding, and dressing, as measured by the Gesell schedules.

Analysis of developmental and intelligence quotients of 78 children in this study between the ages of 2 and 4 years yielded results (unpublished data) which were generally consistent with those found by other investigators.[31, 34] Using results from the Gesell Developmental Schedules at age 2, the Merrill-Palmer Scale of Mental Tests at 3, and the Revised Stanford-Binet Intelligence Scale at age 4, intertest correlations were in the same range as those between retests using the same measuring instrument, and average increments ranged from 7 to 15 points—within the range normally expected. As expected, there was a great deal of individual fluctuation, but it was sufficiently random that the mean scores for each test varied but slightly from one another. The relationships among the 3 tests were not, of course, strong enough to suggest that they can be used interchangeably. Differences between the individual child's pattern and the average pattern for the group were large enough to indicate that an IQ or DQ obtained from any one of these instruments might best be considered as an estimate of intelligence with little value for prediction, except within broad limits. Mean scores at 2, 3, and 4 years of age were 96.4, 93.2, and 98.8, respectively.

The final analysis of psychologic data which has thus far been undertaken concerns an evaluation of test performance (unpublished data) and backgrounds[41] of 76 of the study children whose scores were above or below average on the Merrill-Palmer Scale of Mental Tests at 3 years of age. Results of analysis of intertest performance indicate that performances of above- and below-average children can be descriptively differentiated on a performance test which involves manual manipulation extensively, even though such tasks are among the easier ones for below-average subjects. Form board and picture tests were found to be the most discriminating of the tests in the Merrill-Palmer system for this analysis. With regard to the backgrounds of the children, there was little indication that physical characteristics of the child were related to his development at age 3. Some of the family characteristics which were studied did suggest some association with test performance, notably, socioeconomic status, education of parents, parents' marital status, and number of siblings. Although these factors have long been recognized as affecting test performances of white children,[35] there has been a tendency to speak of test performances of Negro children without regard to intragroup variations. Socioeconomic status and education of parents tended to be directly related to test performance, and there was a distinct trend toward a smaller number of siblings among the above-average children. The proportion of disrupted legal marriages was greater among parents of below-average children.

SUMMARY AND CONCLUSIONS

It is apparent that there is a wide variation among Negroes in the majority of the character-

istics and relationships which are the object of investigation for this study. Analysis of factors affecting anatomic, physical, and psychologic growth and development of Negro infants and children between birth and 5 years of age has revealed that, by and large, intragroup variations among Negroes are similar, both in range and in factors relating to this variation, to those long accepted as existing among white children. In addition, socioeconomic status has been found to be directly related to most of the measurements of growth and development studied. Significant relationships were found between socioeconomic status and nutritional intake of the mother, feeding practices, weight of infants at birth and during the first year of life, skin color of infant at birth, and test performance at 3 years of age. Education of the mother generally was related to the preceding characteristics in the same manner as socioeconomic status. No relation has thus far been noted between socioeconomic status and (1) osseous development of infants at birth or (2) performance on Gesell Developmental Schedules (with consistency at all age levels) during the first year of life.

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Two-Dose Phenylalanine Tolerance Test for Detection of Phenylketonuric Heterozygotes

Value of Tyrosine Responses

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The determination of phenylketonuric heterozygotes by measurement of the plasma phenylalanine response to oral phenylalanine loads has been reported by Hsia and associates.[1,2] Using a precise method for determination of plasma phenylalanine, Knox and Messinger[3] suggested that the higher fasting plasma phenylalanine in heterozygotes provided a sensitive test for separating a group of heterozygous individuals from a group of control subjects. A higher fasting plasma phenylalanine and, after oral loads of phenylalanine, higher plasma levels and a limited rate of return to normal in the heterozygotes indicated a degree of abnormality under basal conditions as well as in the presence of excess phenylalanine, providing evidence of a partial limitation in the action of hepatic phenylalanine hydroxylase required to convert phenylalanine to tyrosine. While the differences in the mean fasting values between control and heterozygous individuals and between mean values obtained after phenylalanine loads were found to be statistically significant by previous workers, the degree of overlap of individual values did not permit separation of all heterozygotes from an unknown population with complete assurance.

Wang and associates[4] have presented what appears to be a more precise method for identifying the heterozygous individual on the basis of the plasma phenylalanine response after an oral load of phenylalanine. These workers applied the discriminate function analysis method described by Rao.[5] Discriminate function analysis was applied to the fasting, one-, one-and-a-half-, two-, three-, and four-hour postloading plasma phenylalanine values, and a classification error of less than 4 per cent was reported in the separation of the heterozygotes from normal individuals.

Measurement of the plasma tyrosine response after oral loads of phenylalanine has been suggested by Jervis[6] as possibly a more critical method of identifying heterozygous individuals. Postloading plasma tyrosine curves in phenylketonuric subjects were found by Jervis to be flat. Later, Jervis,[7] using a colorimetric method for plasma tyrosine, found that the plasma tyrosine increases at the two-, four-, six-, and eight-hour postloading times were only half or less than half of those observed for control subjects. Waisman[8] also measured the plasma tyrosine at one, one and one-half, two, three, and four hours after a single oral dose of phenylalanine—0.1 gm. per kilogram of body weight—and observed no difference between the fasting mean values of control and heterozygous individuals. However, significant differences in the mean values for the one-, one-and-one-half-, two-, three-, and four-hour times were found between the two groups.

These observations on the plasma tyrosine response to oral phenylalanine loads suggested the possibility of a more reliable method of identifying heterozygous individuals. It appeared from these studies that measurement of the metabolic product, tyrosine, produced by the enzymatic parahydroxylation step for L-phenylalanine, was possibly a more critical method of measuring a partial gene-enzyme deficiency.

MATERIAL AND METHODS

The present study was designed to investigate the value of a 2-dose phenylalanine tolerance test and the serum tyrosine response as a method

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TABLE 1

SERUM TYROSINE RESPONSES TO ORALLY ADMINISTERED 2-DOSE L-PHENYLALANINE TOLERANCE TESTS IN PHENYLKETONURIC HETEROZYGOTES AND IN CONTROL SUBJECTS

	Phenylalanine dose gm./kg. body wt.	Subjects (no.)	Serum tyrosine values (mg. per 100 cc.) — Fasting Mean	Fasting SD°	Fasting SE†	One hour Mean	One hour SD	One hour SE	Two hours Mean	Two hours SD	Two hours SE
Parent heterozygotes	0.05 x 2	6	1.27	0.14	0.06	1.92	0.23	0.09	2.18	0.38	0.16
	0.10 x 2	11	1.25	0.34	0.10	2.02	0.29	0.09	2.40	0.35	0.11
	Pooled data	17	1.26	0.18	0.07	1.98	0.27	0.06	2.32	0.36	0.09
Control subjects	0.05 x 2	3	1.61	0.05	0.03	2.57	0.40	0.23	3.38	0.26	0.15
	0.10 x 2	26	1.51	0.17	0.03	2.75	0.30	0.06	3.35	0.43	0.08
	Pooled data	29	1.52	0.18	0.03	2.73	0.38	0.07	3.35	0.42	0.08

Significance tests on differences between means		T‡	P§
	Fasting	3.84	0.01
	One-hour	7.10	0.001
	Two-hour	8.35	0.001
	(degrees of freedom = 44)		

°Standard deviation
†Standard error
‡Value of test statistic used to test null hypothesis that difference between means is 0
§Probability of obtaining T value

of identifying heterozygous individuals. Subjects consisted of 29 control male medical students; 17 phenylketonuric parents—8 men and 9 women; and 34 relatives of heterozygous parents—20 women and 14 men. Of the relatives, 3 were cousins and 2 were siblings of the phenylketonuric probands; the rest were uncles or aunts.

Of the control subjects, 26 were given an L-phenylalanine load of 0.2 gm. per kilogram of body weight and 3, a load of 0.1 gm. per kilogram of body weight. Of the parent heterozygotes, 11 were given a load of 0.2 gm. per kilogram of body weight and 6, a load of 0.1 gm. per kilogram of body weight.

Tests were begun between 8 and 9 A.M., after a fast since the supper of the previous day. Blood samples were drawn initially and at one and two hours after the oral load. L-phenylalanine was administered in cold orange juice in 2 equal doses. The one-hour blood specimen was drawn thirty minutes after the second test dose was drunk. The highly specific spectrofluorometric method of Udenfriend and Cooper[9] was used to determine the plasma tyrosine.

RESULTS

A comparison of the mean values for serum tyrosine obtained for control and parent heterozygotes during loading with the 2 different doses of phenylalanine is presented in table 1. It appeared that the one- and two-hour tyrosine values for both parent heterozygotes and control subjects in response to the larger dose of phenylalanine—0.2 gm. per kilogram of body weight—was not

TABLE 2

CONFIDENCE LIMITS (95 PER CENT) ON MEANS OF PLASMA TYROSINE VALUES OBTAINED AT FASTING, ONE, AND TWO HOURS IN L-PHENYLALANINE-LOADED CONTROL AND PHENYLKETONURIC HETEROZYGOUS INDIVIDUALS

	Number	95% confidence limits on means — Fasting	One hour	Two hours
Parent heterozygotes	17	1.13, 1.39	1.85, 2.11	2.15, 2.49
Control subjects	29	1.45, 1.58	2.59, 2.87	3.20, 3.50

significantly greater than the response to the smaller dose—0.1 gm. per kilogram of body weight. Significance tests calculated at the 5 per cent level of confidence to justify pooling the data obtained with both doses were applied, and no difference was found between the fasting, one-, and two-hour mean tyrosine values.

Statistical significance of the differences between mean tyrosine values was established in the following manner. The 95 per cent confidence limits on the means for all values were established (table 2). On this basis, no highest mean value for serum tyrosine at the fasting, one-, and two-hour times in the parent heterozygote group approached the lowest mean value found for the group of control subjects, indicating clear-cut separation of the parent heterozygote group from the control group. In addition, standard t-tests were performed on the differences between the fasting, one-, and two-hour mean tyrosine values, and the differences were found to be highly significant for all.

In spite of the excellent separation of the two groups on the basis of differences between mean values, tyrosine values for some heterozygotes

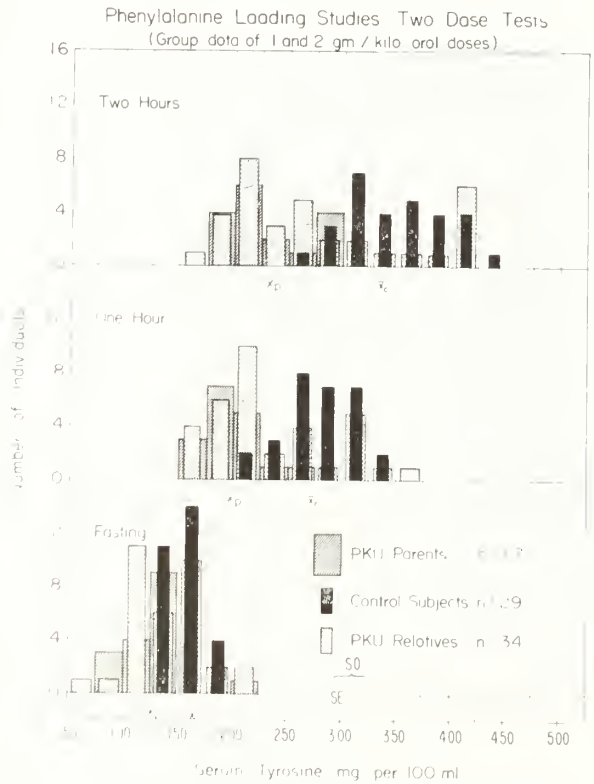

Fig. 1. Histogram presenting fasting one- and two-hour serum tyrosine values in L-phenylalanine–loaded control subjects, phenylketonuric heterozygotes, and relatives of phenylketonuric families.

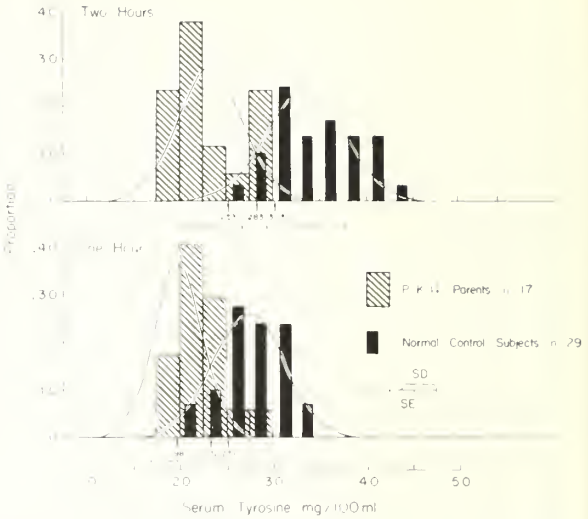

Fig. 2. Histogram of distribution of serum tyrosine values in L-Phenylalanine–loaded phenylketonuric relatives. Theoretic distributions, prepared from data on control and parent heterozygous individuals, have been superimposed. The ninety-fifth percentile in terms of two-hour tyrosine values on the parent heterozygote distribution was found at 3.03 mg. per cent; the intercept, at 2.83 mg. per cent; and the fifth percentile in terms of control distribution, at 2.53 mg. per cent. Theoretic overlap area was found to be 18.5 per cent of total area under both control and parent heterozygote two-hour tyrosine distributions.

and for some control subjects fell into an overlap zone in both the one- and two-hour distributions (figure 1). Proportional distributions for each group were constructed from the data, and assuring that the two groups were normally distributed, theoretical normal curves were superimposed (figure 2). The overlap area of the distribution of the one-hour tyrosine values was found to be 24.4 per cent of the total area under both curves. The intercept occurred at the ninetieth percentile of the parent heterozygote distribution and the fourteenth percentile of the control distribution.

More satisfactory separation occurred for the two-hour tyrosine values. This total overlap area was found to be 18.5 per cent of the total area under both curves and contained values from 4 heterozygotes and from 4 control subjects, or actually 17.4 per cent of the total population. The intercept for the two-hour distribution occurred on the ninety-second percentile of the parent heterozygote distribution and the eleventh percentile of the control distribution. This intercept value was found to fall at a two-hour serum tyrosine value of 2.83 mg. per cent. Actually, however, no two-hour tyrosine value for the control subjects fell below the fifth percentile of

the control distribution and no parent heterozygote two-hour tyrosine value was above the ninety-fifth percentile of the parent heterozygote distribution. Theoretically, selection of heterozygotes on the basis of those falling below 2.83 mg. per cent carries an error of 9 per cent. The fifth percentile on the control distribution for the two-hour tyrosine values was found to lie at 2.53 mg. per cent. Hence, two-hour tyrosine values falling above 2.53 per cent indicated the absence of heterozygosity with at least 95 per cent confidence. On the other hand, the tyrosine value found at the ninety-fifth percentile of the parent heterozygote distribution was 3.03 mg. per cent. Thus, any value below 3.03 mg. per cent indicated the presence of heterozygosity with at least a 95 per cent confidence.

There appeared to be little doubt that the 4 parent heterozygotes falling in the overlap zone of the two-hour tyrosine distribution, that is, between 2.53 and 3.03 mg. per cent, were truly heterozygotes. One was a father of 3 phenylketonuric children and another, a mother with 2 phenylketonuric children. The spouses of each of these 4 parent heterozygotes were most likely heterozygous, as their two-hour tyrosine values after loading fell well into the middle of the distribution for the parent heterozygote group. No history of phenylketonuria was present in the families of the 4 control subjects whose two-hour tyrosine values fell in the intermediate zone.

These critical two-hour tyrosine values were used to separate a group of 34 relatives into heterozygous or nonheterozygous individuals. Using the intercept value of 2.83 mg. per cent of the 2 distributions as the separating point, 19 of the 34 relatives were found to be heterozygous and 15 were normal. Such a separation, however, carried a 9 per cent selection error. More critical separation was possible by considering all individuals having a two-hour tyrosine value below 3.03 mg. per cent (ninety-fifth percentile of the heterozygote distribution) as heterozygotes and all above 2.53 mg. per cent as normal. Such a selection carried less than a 5 per cent error. However, this left 6 of the relatives—17.4 per cent—in the intermediate zone. On this basis, 17, or 60 per cent, of the group were clearly heterozygous and 11, or 40 per cent, clearly normal.

A comparison of the discriminating power of the fasting or postloading phenylalanine and tyrosine values in separating heterozygous from homozygous individuals was possible by the use of the formula D/S, where D = the difference

TABLE 3

COMPARISON OF DISCRIMINATING POWER, D/$\bar{S}$, OF VARIOUS PHENYLALANINE AND TYROSINE VALUES OCCURRING IN RESPONSE TO L-PHENYLALANINE LOADS

	Phenylalanine					*Tyrosine*		
	Present study°	*Wang*[4]	*Renwick*[33]	*Hsia*[2]	*Jervis*[7]	*Present study*° *pooled*	*Wang*[4]	*Jervis*[7]
Phenylalanine dose per kg. body weight	.2	.1	.1	.1	.3	(.1 + .2)	.1	.3
Fasting	.9	2.7	1.8	1.2	.7	.9	.3	
1 hour	1.2	.9	1.2	3.2		2.3	1.6	
1½ hour		1.2					2.1	
2 hour	1.5	1.3	2.4	2.7	.4	2.7	1.8	3.1
3 hour		2.2					1.7	
4 hour		2.1	2.7	2.5	.4		1.5	2.4
6 hour					2.1			
8 hour								2.2
Fasting; 1½, 2, and 3 hour		3.6‡						
Fasting; 1 and 2 hour						3.1‡		
1 and 2 hour						3.5‡		
Area (4-hour curve)†			3.2					

D/$\bar{S}$ = difference between mean values of control and heterozygous groups divided by average of 2 standard deviations

°2-dose tests

†area = ½ (fasting value + 2 × one-hour value + 3 × two-hour value + 2 × four-hour value)

‡calculated from discriminant score, Rao[5]

between the means of the two groups and $\bar{S}$ = the average of the two standard deviations.[10] The D/S has been calculated for the data obtained in the present study, and comparisons of the fasting, one-, and two-hour tyrosine values in the present study with those obtained from the tyrosine and phenylalanine values reported by other investigators[2,4,7,11] indicated equally good discriminating power for tyrosine. The D/S value of 3.5 obtained for the one- and two-hour serum tyrosine values in the present study and the value of 3.6 obtained from the phenylalanine values by Wang and associates[4] were derived by the discriminant function analysis method of Rao.[5] These have been presented in table 3.

Oral doses of phenylalanine larger than 0.2 gm. per kilogram of body weight appear to be undesirable because of the frequency of nausea and occasional vomiting. The use of a 2-dose test had a distinct advantage, as all subjects tolerated both the 0.1- and 0.2-gm.-per-kilogram doses well. While a slightly greater serum tyrosine response occurred with the 0.2-gm. dose than with the 0.1-gm. dose in both the heterozygous and control subjects, the differences were not statistically significant.

At present, the usefulness of the two-hour tyrosine value after a 2-dose test of a phenylalanine to identify the heterozygous individual must be confined to a maximum above which the two-hour tyrosine value is not likely to rise in heterozygous individuals and a minimum below which the two-hour tyrosine value for the control subject is not likely to fall. On this basis, two-hour tyrosine values above 2.53 mg. per cent would exclude a heterozygote with at least 95 per cent confidence and a value below 3.03 mg. per cent would identify the presence of heterozygosity with at least 95 per cent confidence. On the basis of comparison of the discriminating power of a single postloading phenylalanine or tyrosine value, it may be concluded that measurement of the two-hour serum tyrosine response is as valuable as any single postloading plasma phenylalanine value in separating the phenylketonuric heterozygous from the homozygous normal individual.

CONCLUSIONS

The two-hour serum tyrosine response to a 2-dose phenylalanine loading test has been studied as a method for determining phenylketonuric heterozygosity. Separation of heterozygous and nonheterozygous persons on this basis alone carried an approximate 9 per cent error. The critical value for the two-hour tyrosine was determined on the basis of the intercept of the two distributions and was found to lie at 2.83 mg. per cent. The 95 per cent confidence limit in terms of two-hour postloading tyrosine values was found to be 3.03 mg. per cent for phenylketonuric heterozygotes. Values under this would permit selection of heterozygotes with at least 95 per cent confidence. Similarly, the fifth percentile of the distribution of the control subjects was found to be 2.53 mg. per cent. Hence, two-hour tyrosine values above this level permit identification of the absence of heterozygosity with at least 95 per cent confidence.

The L-phenylalanine used in this study was provided by the Nutritional Bio-chemical Corporation, Cleveland.

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Evaluation of Electroencephalographic Tracings of Newborns

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As part of the perinatal research currently under way at the University of Oregon Medical School, routine electroencephalographic tracings are being made of babies born under adverse conditions, as well as of normal controls. The collaborative study, sponsored by the National Institute of Neurological Diseases and Blindness, aims to confirm known and suspected conditions and, if possible, to discover unsuspected causes of cerebral palsy, mental retardation, and other neurologic and sensory disorders of infancy and childhood.

The early discovery of brain damage or of developmental faults will assist in determining the onset of any neurologic deficit. The electroencephalographic tracing can also be a diagnostic tool that indicates the status of brain maturation at the time of birth.

METHODS

A transportable 8-channel Offner transistor electroencephalograph was available in the hospital nursery and on the ward for premature infants; 6 electrodes were applied over each hemisphere, specifically over the frontal, anterior and posterior parietal, anterior and posterior temporal, and occipital areas. A Grass photic stimulator was used for single or repetitive flash light. A clacker with inbuilt electronic signal and a Beltone Portable Audiometer, Model 10-A, were used for acoustic stimulation during sleep or wakefulness.

NORMAL RECORDS

The waking record of a normal newborn infant is notably different from the sleeping pattern. The amplitude of the waking record seldom surpasses 40 μv. No dominant frequency can be detected by visual analysis. The frequency varies between 2 and 22 cycles per second. Figure 1 gives an example in which the record was taken thirty-one hours after birth. The upper portion represents the waking state. The lower portion shows a normal response to acoustic stimulation during drowsiness.

The sleep record shows distinct stages.[1-7] When the infant glides from drowsiness into sleep, 16-cycle-per-second spindles usually are seen. At the same time, the slow wave activity, with increased amplitude, begins a burstlike discharge, interrupted by relatively depressed phases. In deep sleep, high-voltage, irregular waves alternate with flat periods of several seconds' duration.[8-10] This form of alternating tracing is characteristic of deep sleep in the neonatal period (figure 2).

PHOTIC STIMULATION

Photic stimulation by single flash evokes a prompt response by a potential in the right, left, or both occipital areas in 70 per cent of normal neonates.[11-13] The percentage of positive reactors can be increased when the test is repeated.

With the bipolar technic, the deflection of the evoked potential initially may be upward or downward, negative or positive, or biphasic. The latency was measured on calibrated electroencephalographic paper from the beginning of the stimulus artifact (superimposed on one of the channels) to the commencement of the deflection (figure 3). These measurements are shorter than those of Ellingson,[12,13] who counted the time from the artifact to the peak of a positive deflection of the ink writer.

In full-term babies with an Apgar rating higher than 6, the mean latency was 158 msec. (table 1). Premature babies had a significantly longer

TABLE 1

RESPONSE TO OPTIC STIMULATION BY SINGLE FLASH IN PREMATURE, FULL-TERM, AND POSTMATURE NEONATES

Birth	*Positive response (%)*	*Number of infants with measurable latency periods*	*Mean latency (msec.)*	*Standard deviation*
Premature	57	47	185.30	±26.40
Normal full-term	70	184	158.36	±27.31
Postmature	75	5	108.00	±22.27

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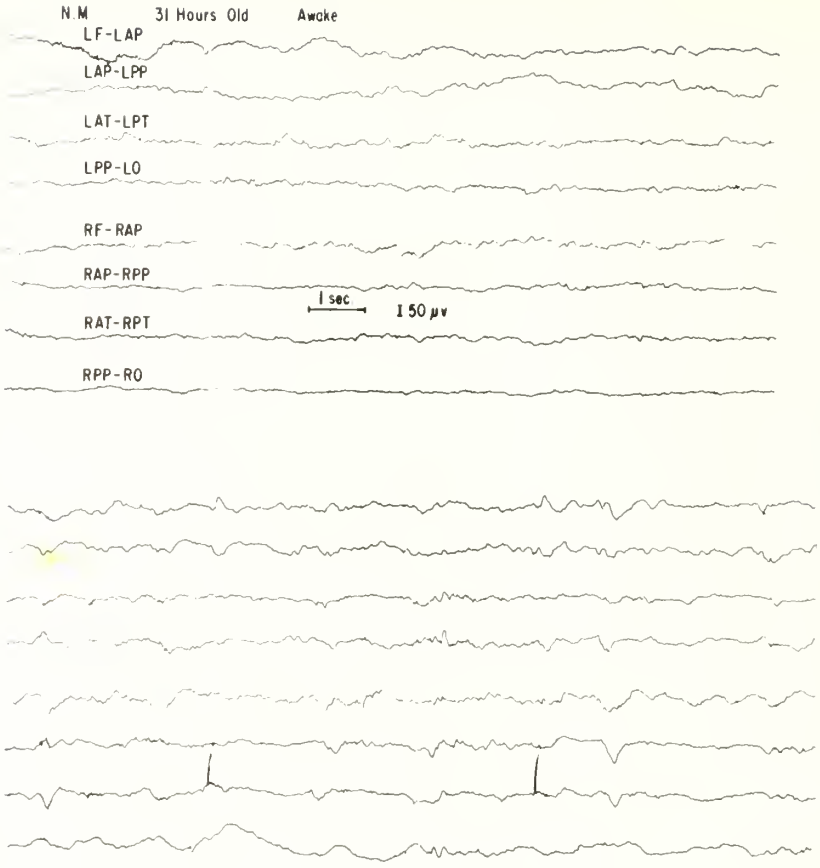

Fig. 1. Full-term newborn. Weight, 3,415 gm. Apgar score, 5. Cord was tight around neck, but no ill after-effects occurred. (Above) Waking pattern. (Below) Drowsy state. Shows increase in amplitude and amount of slow waves. Signal, superimposed on channel 7, indicates noise by clacker.

latency ($n = 229$, $p < .001$), and the few postmature babies so far observed had a mean latency period of only 108 msec., which also is significant ($n = 187$, $p < .001$).

A recent clinical experience, not yet included in the series, confirmed the importance of the observations. A dysmature baby, born thirteen days after the expected day of confinement, had a birth weight of 2,500 gm. The reaction to photic stimulation was positive, with a latency of 100 msec., indicating post- rather than prematurity, in accordance with clinical findings.

Illustrations of evoked potentials in the occipital area in a postmature (figure 4) and a premature child (figure 5) are self-explanatory.

Repetitive stimulation by flicker often gives, if the flashes are one second apart, individual reactions each time with about the same latency but not always with the same amplitude. Shorter intervals of the flicker usually show a marked "on" and a less marked "off" response when the stimulation comes to an end but only a slight increase of activity during stimulation. Temporary flattening of the background activity may follow. The observations of Ellingson[12,13] are fully confirmed. Figure 6 is an example of repetitive photic stimulation in a premature neonate during the spindling stage of sleep.

A group of 17 full-term neonates with lower Apgar ratings than 7 showed, after full recovery, a latency not significantly different from the reaction time of babies with ideal Apgar ratings.

ACOUSTIC STIMULATION

Acoustic stimulation[14,15] often causes a slow wave in one or both frontal areas which also may be seen as a response to photic stimulation (figure 7).

The slow wave in the frontal region is called the "non-specific EEG response."[16,17] A blink often accompanies the response, but frequently, during sleep, there is no movement detectable. Animal experiments indicate that the brain stem reticulum is essential for the occurrence of the unspecific waves after sensory and auditory stimuli.[18,19] Figure 8 is an example of such response to noise and to pure tone in a premature infant.

A general response to acoustic stimulation was positive in 87 per cent of normal full-term neonates, with a mean latency of 154.04 ± 23.56 msec. In premature neonates, the reaction time was not significantly different—mean latency,

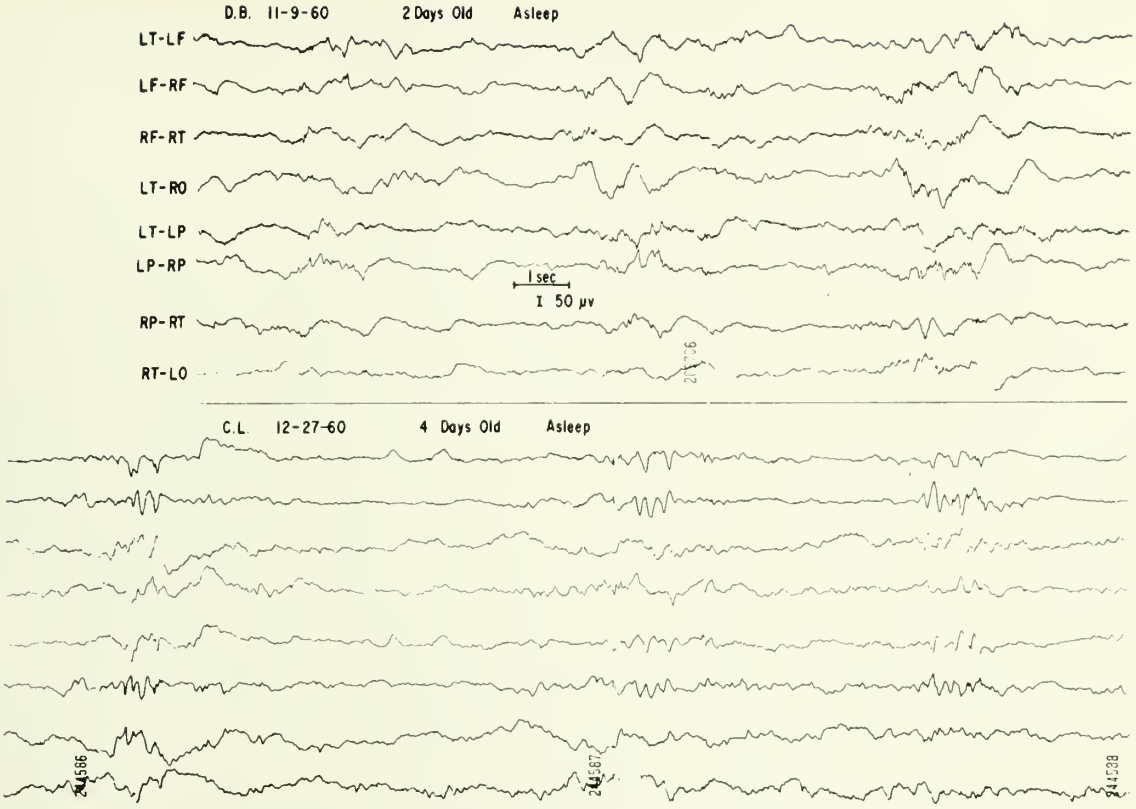

Fig. 2. (Above) Full-term neonate. Age, 2 days. Weight, 3,195 gm. First Apgar score, 9. Sleep spindles and beginning alternating tracing. (Below) Neonate delivered by cesarian section. Age, 4 days. Weight 3,270 gm. First Apgar score, 5. Normal alternating tracing in deep sleep

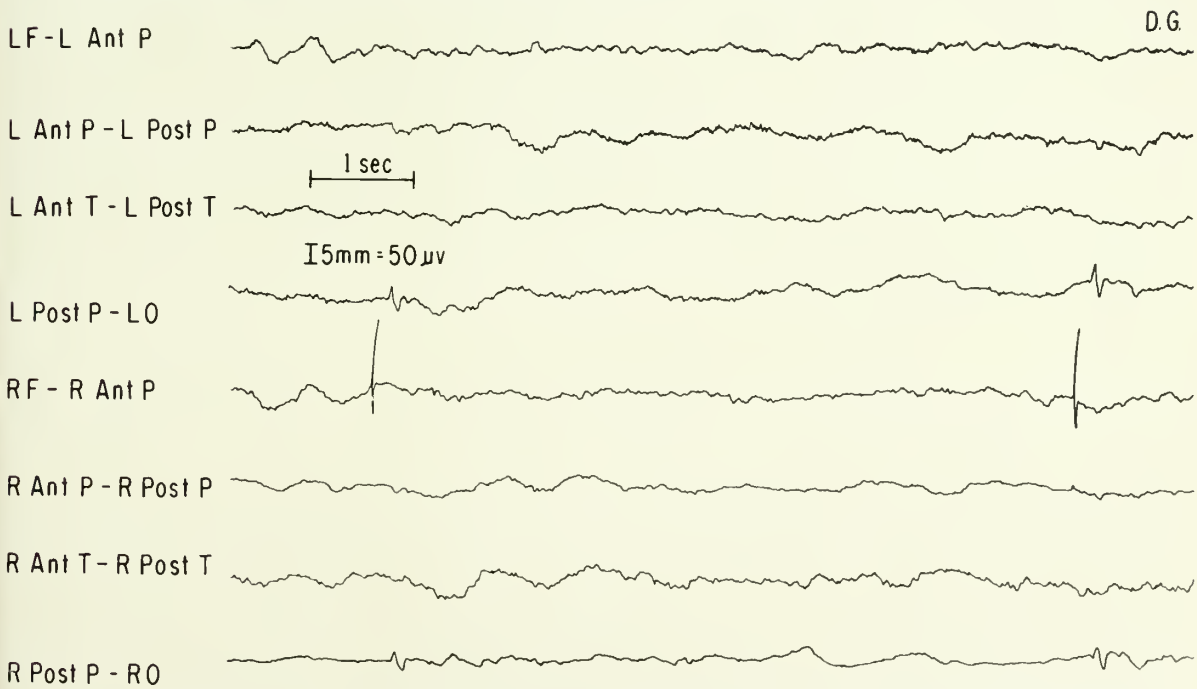

Fig. 3. Photic stimulation by single flash during wakefulness at twenty-two hours post partum. Breech delivery. Weight, 3,155 gm. First Apgar score, 7. Signal superimposed on channel 5. Evoked potentials over both occipital areas. Latency, 166 msec.

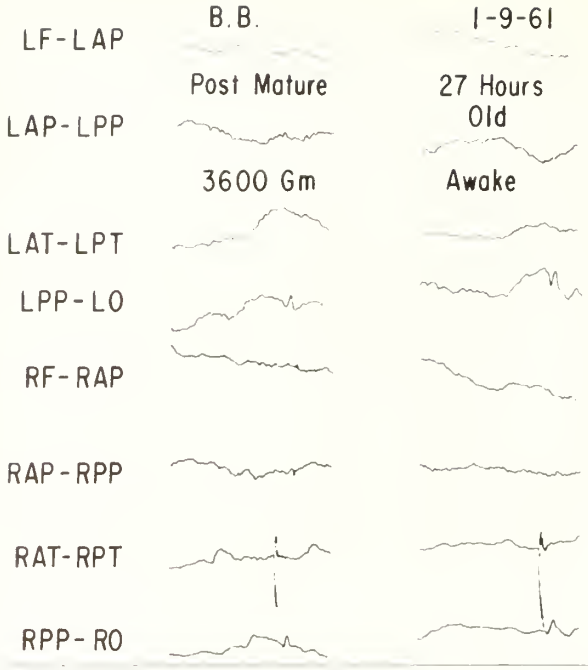

Fig. 4. Photic stimulation during wakefulness twenty-seven hours post partum in neonate postmature thirty-six days according to expected date of confinement. Weight, 3,600 gm. First Apgar score, 8. Latency period from beginning of signal (channel 7) to onset of evoked potential in both occipital areas, 110 msec.

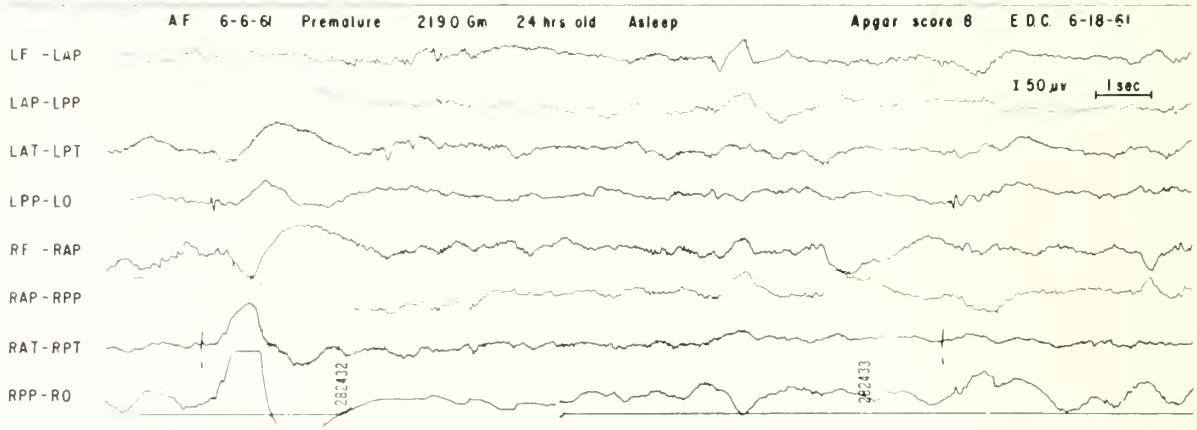

Fig. 5. Photic stimulation twenty-four hours post partum in premature neonate during sleep. Weight, 2,190 gm. Apgar score, 8. Latency period from beginning of signal (channel 7) to onset of evoked potential in left or both occipital areas, 200 msec.

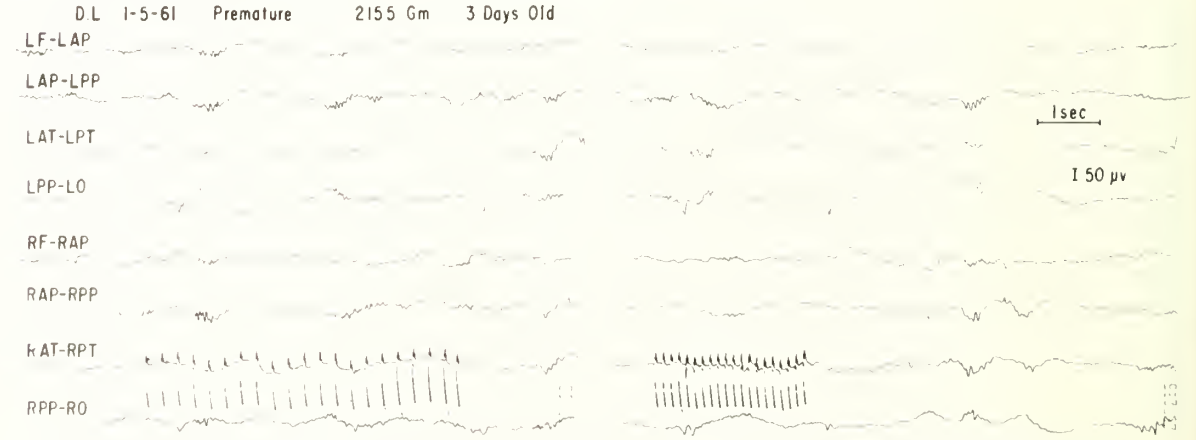

Fig. 6. Photic stimulation during sleep three days post partum in premature neonate. Signals superimposed on channel 7. Note sleep spindles and "on" and "off" responses. Weight, 2,155 gm. Apgar score, 9.

162.56 ± 30.52 msec. A positive response to stimulation by clacker was found in 68 per cent of pre- and postmature infants.

ABNORMAL CONDITIONS

The number of observations under abnormal conditions other than pre- and postmaturity is still too limited to draw general conclusions, but enough individual observations have been made to permit a basis for correlation between abnormal electroencephalographic tracings and neuropathology in the neonatal period.[21,22]

The most striking abnormalities are (1) voltage depression and (2) focal spikes and paroxysmal outbursts of seizure discharge.

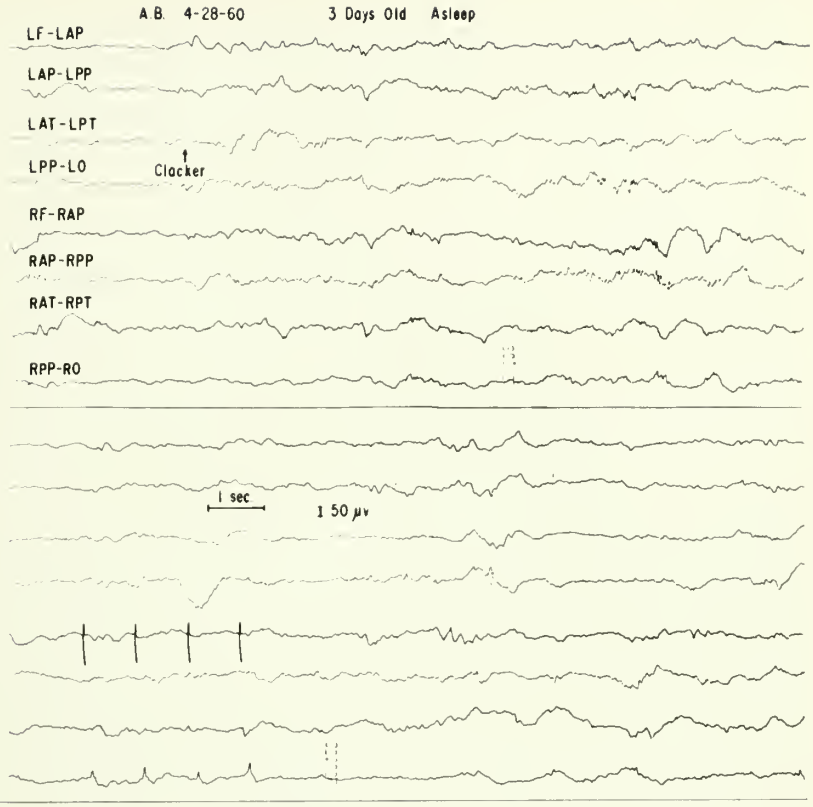

Fig. 7. Acoustie stimulation by claeker (Above) and repetitive photie stimulation, one second apart, in 3-day-old ehild. Weight, 2,806 gm. Apgar seore, 6. Flicker signal superimposed on channel 5. Note identieal slow waves in left frontal area after acoustie or first photic stimulation and evoked potentials in right oeeipital area after each flash. Spindling stage of sleep

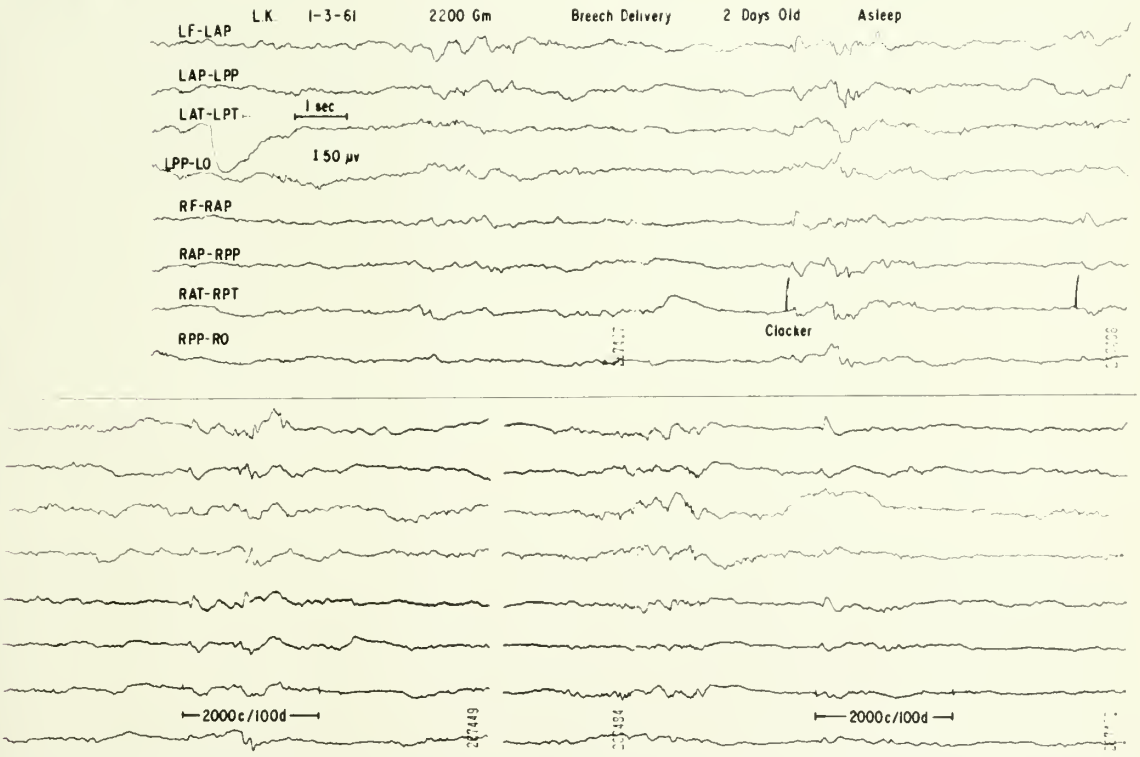

Fig. 8. Acoustie stimulation by clacker and by audiometer in 2-day-old infant during deep sleep. Signal superimposed on channel 7. (Above) Response to noise. (Below) Response to pure tone. Breech delivery. Weight 2,200 gm. First Apgar score, 6. Alternating tracing is present. Note frontal slow wave with each stimulus.

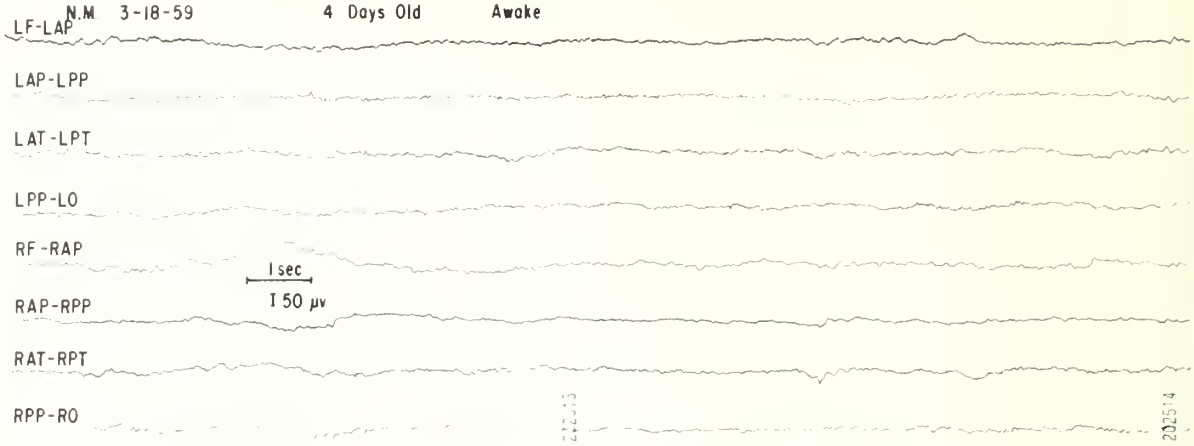

Fig. 9. Waking record of 4-day-old infant. Weight, 3,770 gm. Apgar score, 8. Note voltage depression.

Voltage depression. The voltage depression can be limited to one area or one hemisphere and can be recognized as a brain wave abnormality after exclusion of artifacts and skull anomalies.

A generalized low-voltage tracing poses greater diagnostic difficulties. Figure 9 shows an unusually flat tracing of a baby born with cyanosis of the extremities, caput succedaneum, and marked occipital molding. The amplitude occasionally reached 25 μv. and increased only slightly during sleep. Sleep spindles were not observed.

If, during sleep, the flat phase of the alternating tracing lasts an unusually long time, this

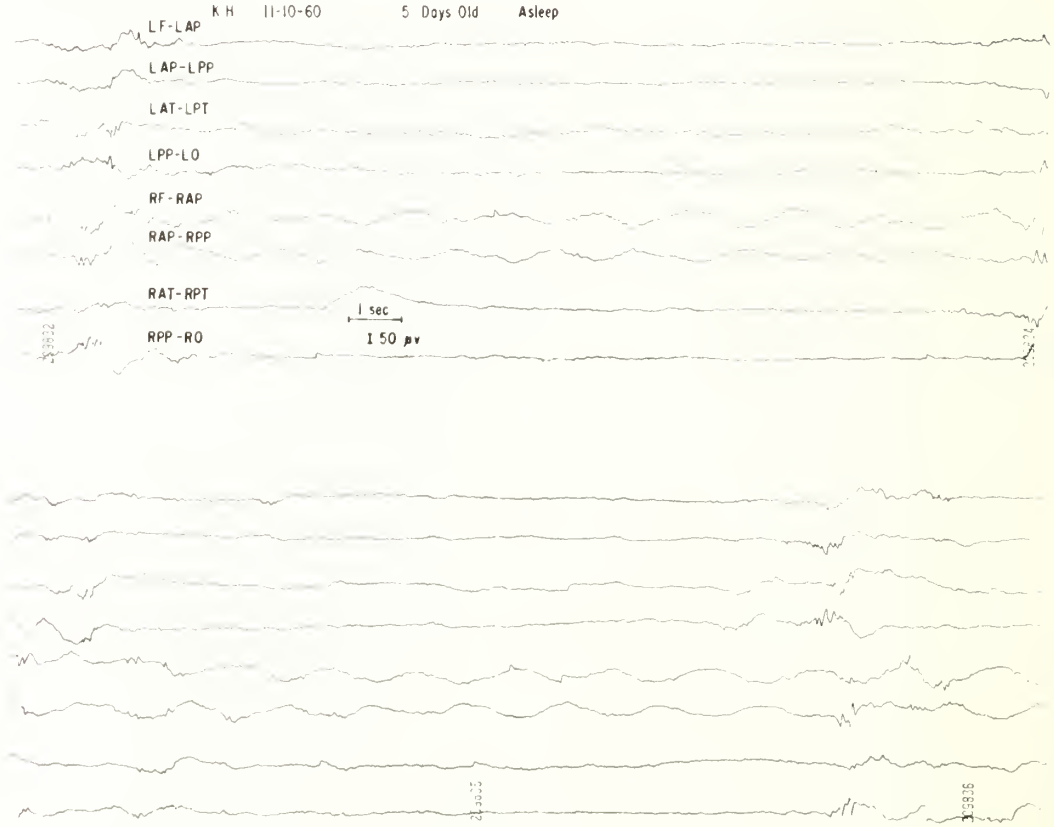

Fig. 10. Child, erythroblastotic because of Rh incompatibility. Bilirubin, 31.2 mg. per cent. Weight, 2,590 gm. Apgar score, 7. Continuous record during sleep shows alternating tracing with depressed phases of sixteen seconds' duration.

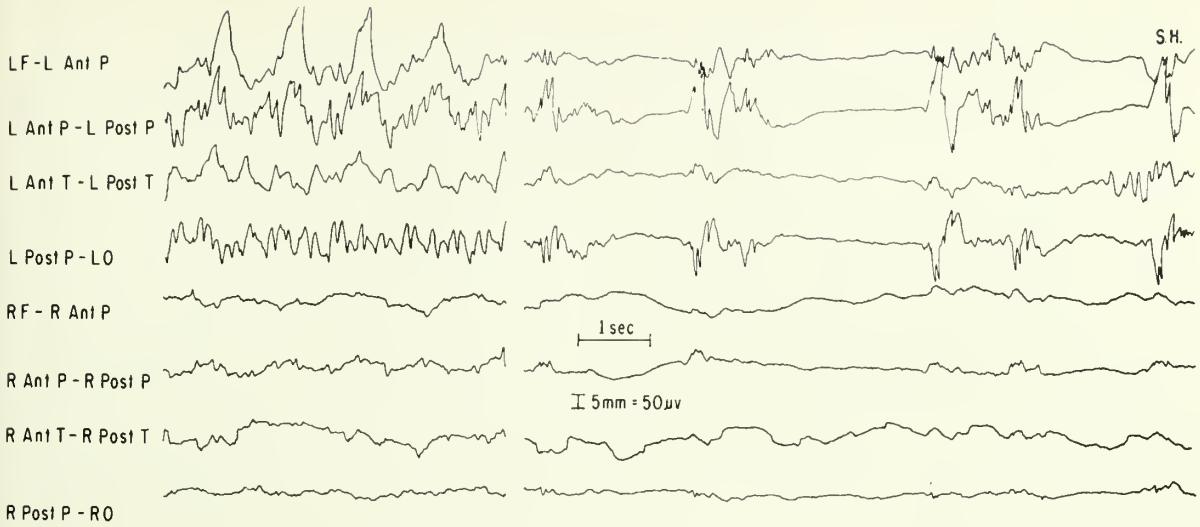

Fig. 11. Seizure discharge (left hemisphere) and depression (right hemisphere) in electroencephalogram of 5-day-old child after traumatic birth. Weight, 4,500 gm.

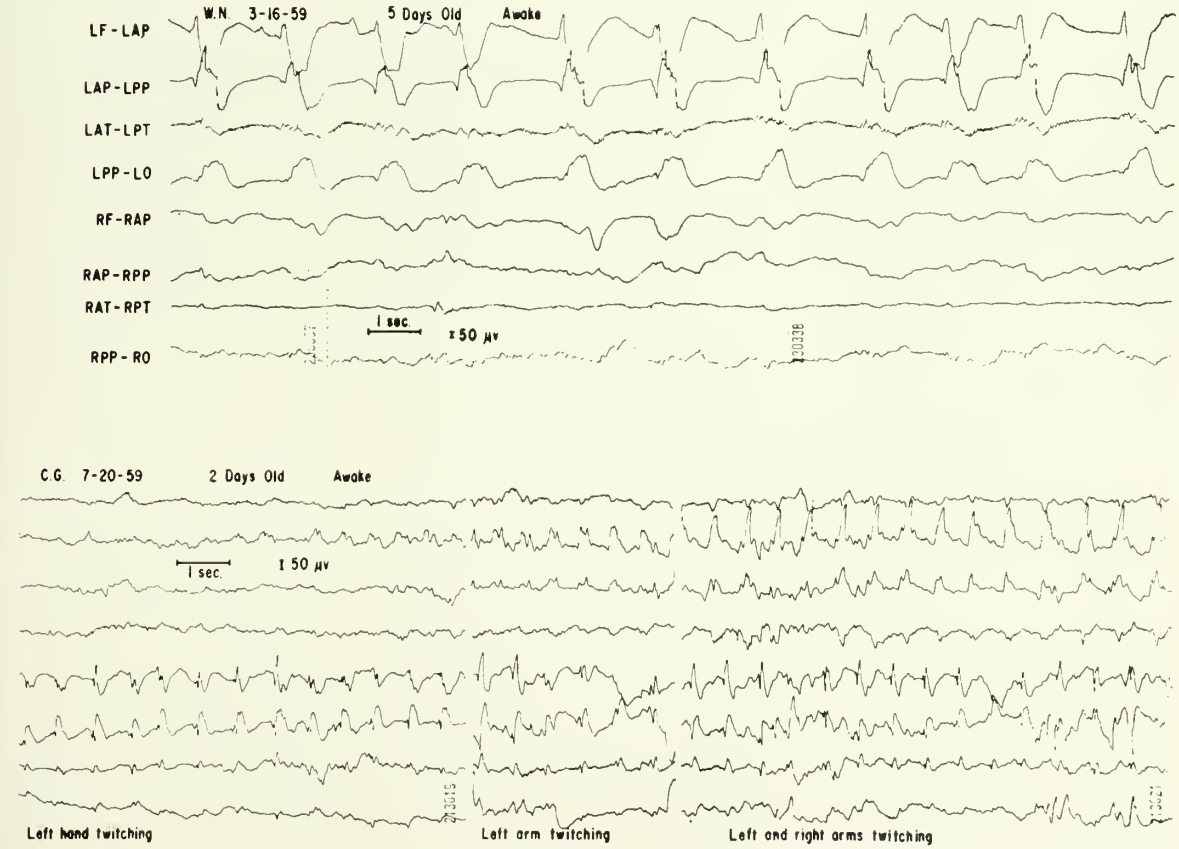

Fig. 12. (Above) Waking record of 5-day-old child with atresia of the aorta shows epileptic pattern over left hemisphere and depression over right side, especially over right temporal areas. Weight, 3,300 gm. (Below) Waking record shows onset and march of seizure of 2-day-old infant. Weight 3,150 gm. Apgar score, 3-4

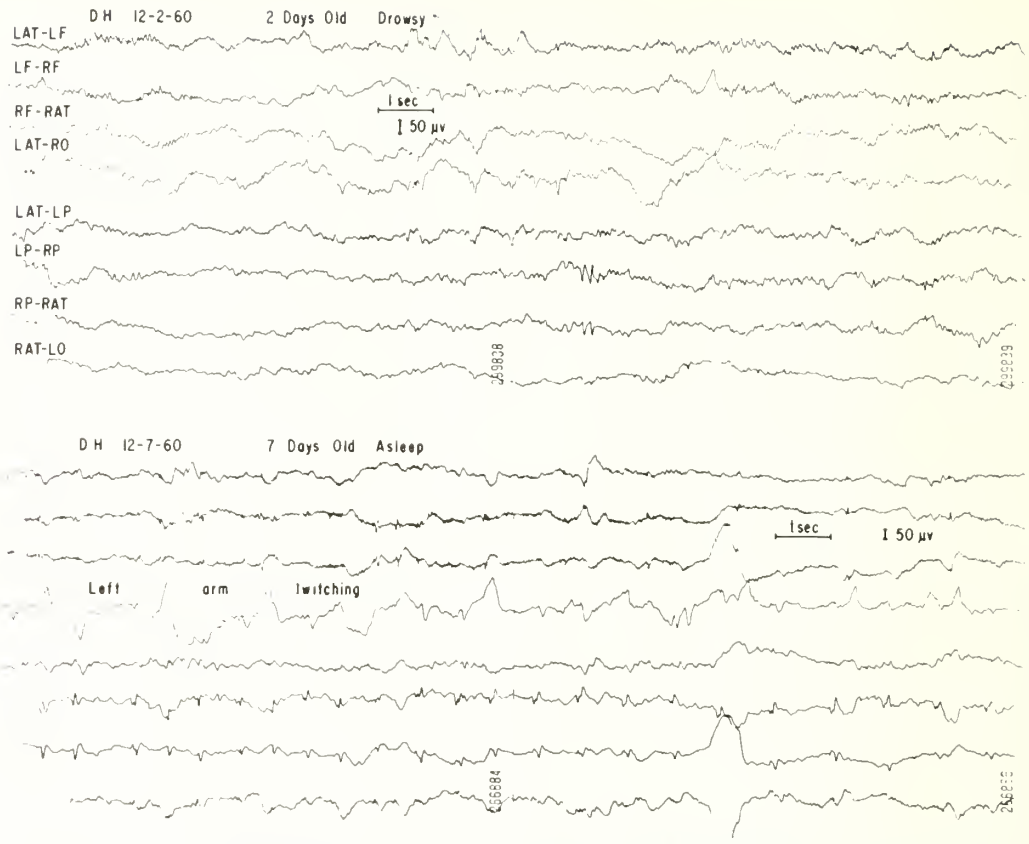

Fig. 13. Full-term neonate. Weight, 2,795 gm. Apgar score, 9. (Above) Age, 2 days. Drowsy. Note isolated spikes in right parietal and occipital areas. (Below) Age, 7 days. Continous spiking discharge over right hemisphere during left arm twitching. Calcium, 9.6 mg. per cent

might be an indication of depression beyond that of normal deep sleep. Figure 10 is an example of this category. It is taken from an erythroblastotic child during sleep on the fifth day. The serum bilirubin level at the time of recording was 24.8 mg. per cent. On the preceding day, it was 31.2 mg. per cent. The depressed phases during the alternating tracing lasted sixteen seconds. Three days later, the tracing became normal, and later the child developed normally.

Epileptic discharge. Voltage depression and seizure discharge often occur together. This is documented in figure 11, which represents the tracing from a 5-day-old boy who was delivered with a difficult double footling presentation. Resuscitation was prolonged, and when the baby became pale and listless and had Cheyne-Stokes respiration, he was transferred to the University Hospital. On admission, he was unresponsive except to painful stimuli. Erb's paralysis of the right arm was present. He began having intermittent seizures irregularly until death. Anatomic diagnosis was acute massive subdural and subarachnoid hemorrhage, particularly on the right, with displacement of brain to the left and herniation of the right gyrus cinguli under the falx cerebri. There were multiple, acute, small, intracerebral hemorrhages.

A similar pattern was seen in a 5-day-old infant with congenital heart disease (figure 12, upper tracing) who died the following day. The anatomic diagnosis was atresia of the aortic orifice and marked hypoplasia of the left heart and aortic arch. There were no malformations or inflammatory changes in the central nervous system. Anoxia must have been the cause of seizures and death.

The lower tracing in figure 12 shows the recording of a seizure of a baby born of a toxemic mother. The one-minute Apgar rating was 3. The entire body was stained with meconium. The cord was dark green. Occasional twitching of arms and legs was observed during the night before the recording. The record was taken in an incubator and shows the march of spreading convulsive discharge, accompanied by clinical symptoms. Calcium and sugar were normal. The seizures stopped on the third day.

Another seizure episode was observed during electroencephalographic recording of a 7-day-old child after isolated spikes already had been documented at 2 days of age (figure 13). This baby developed seizures and, at the age of 1 week, while a second tracing was being taken, twitching in the left arm.

Phenobarbital stopped the clinical seizures, but the isolated spikes remained. After discharge from the hospital, another convulsion occurred when phenobarbital was temporarily discontinued. No seizures have occurred since.

The electroencephalographic picture of tetany is similar to other convulsive disorders of the neonate, as illustrated in figure 14. In this case, the diagnosis was uncertain until the blood chemistry was reported; serum calcium was 6.4 mg. per cent. High-voltage spikes were observed over the left motor area, while twitching of the right leg began and increased to general paroxysmal outbursts with increasing voltage, so that the recording amplification had to be changed. Subsequently, acoustic stimulation by clacker caused a response with much sharper waves than are usually seen which might be indicative of tetany.

The examples presented here prove that reliable information can be gained by use of electroencephalography in the neonatal period.

DISCUSSION

The history of neonatal electroencephalography has not been discussed here. Most authors[6,21] agree that the immediate neonatal period appears equally sterile for the pediatric neurologist and for the electroencephalographer. Many experts[22] insist that a clear-cut distinction of waking and sleeping records cannot be made in the newborn period. It also has been stated that the response to photic stimulation is poor at that time.

More recent technics, using oscilloscopes and transistorized recorders with light-weight ink writers, have improved the sensitivity of our methods. With these apparatus, it is possible to see the difference between the waking and sleeping records and to recognize changes in depth of sleep in full-term and premature babies after the seventh month of gestation. Dreyfus-Brisac,[8] Dreyfus-Brisac, Fischgold, and associates,[9] and Samson-Dollfus[10] have demonstrated the developmental phases of the sleeping pattern and coined the term "tracé alternant," characteristic of deep sleep in the neonatal period.

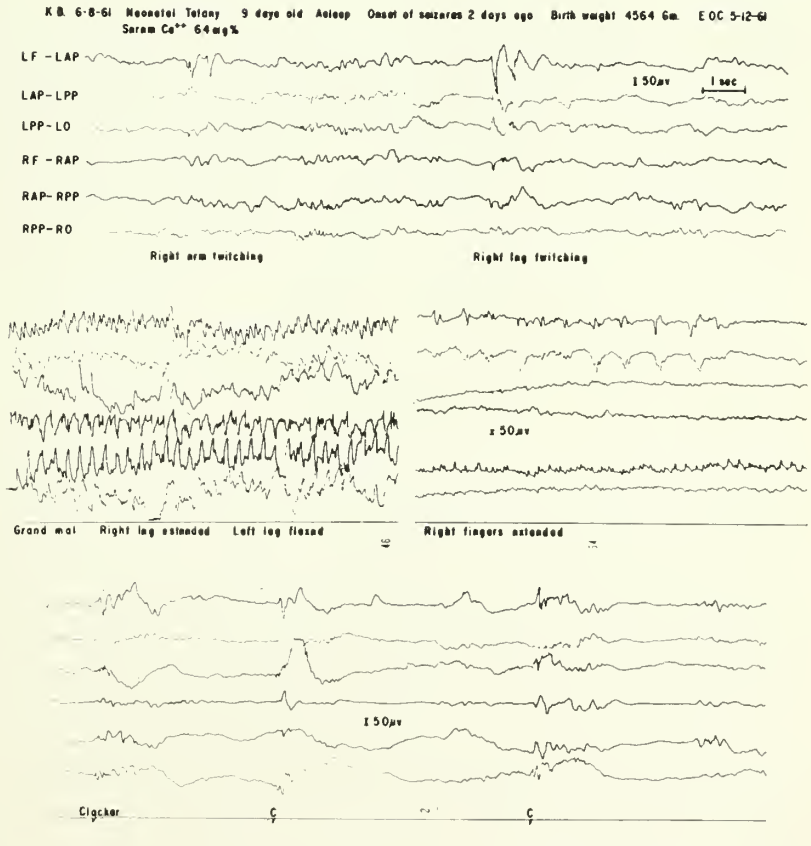

Fig. 14. Record of neonatal tetany. Weight, 4,564 gm. Serum calcium, 6.4 mg. per cent. Onset of seizures two days before electroencephalogram. Twitching of right extremities and grand mal seizure during recording. Response to acoustic stimulation by clacker (C) shows unusually sharp wave forms.

My presentation was aimed at demonstrating the practicability of electroencephalography in the newborn period, which can yield valuable information. The findings of Ellingson[12,13] have been confirmed. Pathologic, convulsive discharge was verified by clinical observation and pathologic findings. In the more difficult, questionable electroencephalographic abnormalities, repeated records should be obtained before sending out a report classified as abnormal. Longitudinal studies begun in the first days of life are most important. Close collaboration among obstetricians, pediatricians, neurologists, electroencephalographers, and anatomists is necessary.

SUMMARY

1. The electroencephalographic tracing in the neonatal period is very different during wakefulness and during different stages of sleep. Sleep spindles and/or alternating tracing indicates depths of sleep.

2. During sleep and wakefulness, optic stimulation evokes occipital potentials with a mean latency period of 158 msec., measured from the beginning of the signal to the commencement of the deflection in the occipital area in 70 per cent of full-term neonates.

3. Premature babies have a mean latency of 185 msec; postmature babies, a mean latency of 108 msec. The difference is highly significant in both cases and represents an additional scale for the evaluation of maturation.

4. Acoustic stimulation by clacker causes an unspecific slow wave or a blink in 87 per cent of normal neonates with a mean latency of 154 msec. Slight differences in reaction time of pre- and postmature neonates were not significant.

5. Abnormal tracings may show voltage depression that is either generalized or limited to a single hemisphere or area.

6. Focal spikes and/or paroxysmal outbursts of epileptic discharge are observed in the neonatal period.

The electroencephalogram provides valuable information and serves as an important diagnostic tool in studying normal and abnormal brain maturation in the neonatal period.

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The author wishes to express appreciation to Miss Christa Oltmann, R.N., and Mrs. Mary Sorenson, both electroencephalographic technicians, for skillful technical assistance and to Bruce Butler, Ph.D., for statistical analysis of data.

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Lipohistiodiaresis

A Syndrome of Lipodystrophy Universalis, Accelerated Growth, Lipemia, Hepatic Cirrhosis, and Insulin-Resistant Diabetes Without Ketosis

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In 1940, Hansen and McQuarrie[1,2] offered the expression lipohistiodiaresis to emphasize the total absence of body fat, the most notable feature of a bizarre, theretofore undescribed, clinical entity characterized primarily by general lipodystrophy, hepatic cirrhosis, and diabetes mellitus. McQuarrie[3] expanded the description in the 1944 Porter Lecture Series at the University of Kansas under the title, *Experiments of Nature and the Advancement of Medical Knowledge.* In the 1946 Oliver-Sharpey Lecture before the Royal College of Physicians, Lawrence[4] described similar clinical and metabolic features in an adult female subject, calling attention to the fact that the only other case in the published literature having clinical and laboratory abnormalities of a comparable nature was Hansen and McQuarrie's child.

Lawrence also cited Ziegler's[5] report of 7 cases of lipodystrophy, in which 1 patient, a 27-year-old woman, gave a history of development of a partial lipodystrophy when she was 14 years old. At that time, only the lower extremities were involved, but subsequently, the lipodystrophy became general and was accompanied by the development of brownish pigmented spots on the body, enlargement of the liver and spleen, and, ultimately, glycosuria with polydipsia and polyphagia. When seen by Ziegler, her basal metabolic rate was very high—+40 to +50. In 1951, Lawrence[6] offered the expression "lipoatrophic diabetes" for these 3 patients.

Corner,[7] in 1952, described a 14-year-old child with progressive general lipodystrophy, which had begun when he was 10 months of age, after an attack of pertussis. The muscles were prominent and powerful. The plasma lipids were very high, and cirrhosis of the liver was demonstrated early. Glucose and insulin tolerance test results were normal. Three months later, however, glycosuria and hyperglycemia developed and rapidly became resistant to insulin. During the eighteen months the child was under observation, ketosis never occurred. The basal metabolic rate was recorded at +45.

Berardinelli,[8] in 1954, reported 2 children with acromegaloid gigantism, strong athletic build, large hands and feet, wasting of subcutaneous fat, hyperlipemia, hepatosplenomegaly, brownish pigmentation of skin, corneal opacities, hypertrichosis, and prominence of the muscles and superficial veins. Two years later, Davis and Tizard[9] described a child who, at the age of 26 months, had lipodystrophy and infectious mononucleosis. In a personal communication, Davis stated that, during the next six years, this child grew abnormally rapidly. Height, weight, and bone age at 7 years simulated those of an 11-year-old child. When first seen, Davis' child had been noted to have straight hair; her hair subsequently became curly. She was a tall, muscular girl, with prominent veins and no subcutaneous fat, even on the face. Liver and spleen were enlarged. Serum cholesterol was 250 mg. per cent. The glucose tolerance curve was normal, but all blood specimens were lipemic.

Fontan and associates[10] have described an 8-year-old girl with general lipodystrophy. The photograph of the child accompanying the paper revealed abundant curly hair and prominent muscles and veins.

In 1957, we had the opportunity to observe a 13-year-old child with lipohistiodiaresis who was being studied by Gellis and later was the

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subject of a report by Schwartz and associates.[11] Complete absence of fat had been observed at 4 months of age, and hepatomegaly caused by cirrhosis was found at 2 years. During early childhood, accelerated growth with advanced bone age was observed, and at 12 years of age, hyperglycemia was demonstrated. The studies by these authors disclosed high levels for insulin-like activity of the plasma.

Seip[12] has recently described 3 children with clinical features strongly reminiscent of the patients here mentioned. The semblance of each child was strikingly similar to that of our patient, including the lipodystrophy; prominent muscles and veins; abundant, blondish curly hair; increased rate of growth; and advanced dentition. The brownish pigmentation, enlargement of the liver and spleen, and lipemia likewise were consistent with our observations, as well as with those of others.

Recently, Craig and Miller[13] cited data concerning 2 subjects studied by themselves, 1 by Witzgall,[14] and 4 known to them through personal communications. In all cases, the diabetic aspect of the syndrome was prominent. Of these patients, 3 were adults.

The increased frequency with which this clinical "experiment of nature" has been encountered in the past two decades and the repeated inquiries for promised additional data have impelled us at last to complete the report concerning our original patient. New concepts concerning the role of hormones in fat deposition and mobilization have added significantly to our equipment for dealing with the phenomenon since we originally reported it.

CASE REPORT

D. Z., 4½-year-old boy, originally was referred to us by Dr. G. F. Engstrom of Belgrade, Minnesota, who sought assistance in diagnosis of what was recognized as an extremely unusual clinical condition. The patient's mother stated that, for the previous three months, her child had been losing weight, gradually becoming more emaciated.

The patient was the product of a full-term normal delivery and was subsequently breast-fed without difficulty. About a month before he was weaned, the mother developed a breast abscess, but she continued to nurse him on the affected as well as the normal breast. At 6 months of age, the child had 2 abscesses on the buttocks and another above the symphysis pubis, all of which healed spontaneously. At 2 years of age, with no other symptoms, jaundice developed. This cleared after three weeks, but the mother stated that D. Z. never lost the jaundiced color entirely. Some months later, she noted that his abdomen began to enlarge.

When he was 3 years of age, his weight was 39 lb. His mother insisted that he had developed well until this age. About this time, wasting began. At age 4, D. Z. weighed only 36 lb.

Three months previously, he had developed what had been called mumps. However, the swelling in the left cervical region was incised and drained by the home doctor. About three weeks before admission, painful masses developed in the patient's cheeks, and two weeks subsequently, masses developed lateral to each eye, but all of these "lumps" had disappeared by the time D.Z. came to the hospital. Two weeks before admission, the referring physician had found an enlarged liver. The chief symptoms at that time were anorexia, enlarged abdomen, and weight loss.

Family history. The patient's parents were living and well. His maternal grandmother was reported as having diabetes mellitus. Of 8 other births to the patient's parents, 3 male and 5 female, 2 boys and 1 girl had died of unknown causes. Historical data were obtained from an older sister, who revealed that there was some possibility of consanguinity in the family.

Physical examination. When first examined by the writers, this quiet, 4-year-old boy presented a spectacularly striking appearance—a great shock of curly, reddish blond hair; markedly sunken cheeks; a moderate degree of enophthalmos; an enlarged abdomen; and a general absence of subcutaneous fat. The resulting conspicuousness of the superficial vascular tree and prominence of the skeletal musculature, with individual muscle groups clearly delineated, presented a composite suggestive of the classical painting of the anatomical man (figure 1). The liver was enlarged to about 5 cm. below the costal margin and on palpation had a finely nodular, firm texture. The spleen was slightly enlarged and firm. The

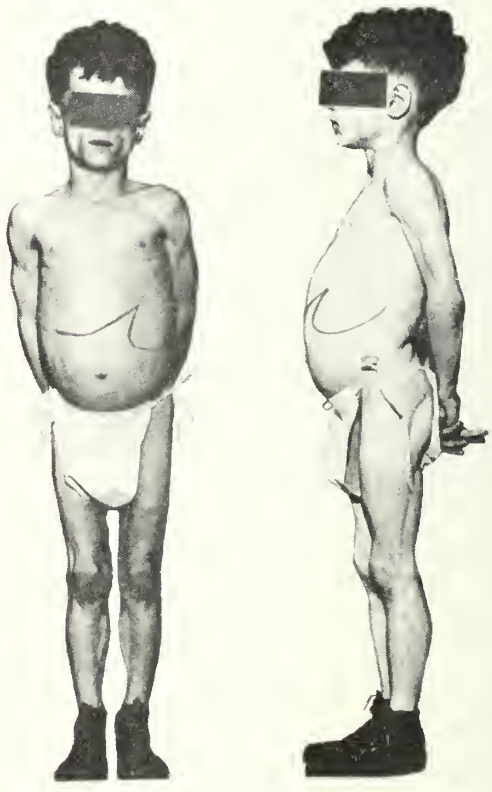

Fig. 1. Photograph of 7-year-old child (D. Z.) with lipohistiodiaresis, hepatosplenomegaly, and insulin-resistant diabetes mellitus. Note well-developed musculature and abundant curly hair.

skin and mucous membranes had a mildly icteric tint, and there was a small scar on the left side of the neck. Heart tones and breath sounds were normal. Epistaxis occurred on 2 occasions shortly after admission. Blood pressure varied between 95/65 and 112/74.

Laboratory findings. Numerous laboratory studies were carried out, many of which will be discussed in relation to various metabolic systems. Urine specific gravity varied between 1.001 and 1.016. The first specimen, which was nonfasting, had a 2+ reaction for reducing substance, but, during the next two months, fasting specimens repeatedly were found to be negative for reducing substance. Hemoglobin and erythrocytes, as well as leukocyte and differential white cell counts, were within normal limits. Bleeding and clotting times were normal, as was the platelet count. Fragility tests disclosed no particular deviation from control values. Wassermann reaction was negative. Stools were negative to guaiac tests and for parasites and ova. Fecal urobilin reaction was 1+. Icteric index was 11.8 on admission and 22 one month later. Urobilinogen in the urine was 24.8 mg. per day and in the feces, 15.2 mg. per day. Nonprotein nitrogen of the blood was 19.6 mg. per cent on admission and 29.2 mg. per cent six weeks later. Bromsulphalein test revealed 20 per cent retention. Serum calcium was 11.8 and phosphorus, 3.4 to 4.3 mg. per cent; sodium, potassium, and chloride values were 130, 5.3, and 100 mEq. per liter. Total plasma proteins were 7.2 gm. per cent on admission and 6.1 gm. per cent, with 3.6 albumin and 2.4 globulin, six weeks later. After two months, a total serum protein value of 9.4 gm. per cent was obtained. Fasting blood sugar values varied from 80 to 112 mg. per cent. Fasting values were higher, however, when glucose tolerance and epinephrine response tests were subsequently measured. Roentgenograms of the skull, including the sella turcica, and of the abdomen, chest, knees, wrists, cheeks, kidney, ureter, and bladder were all reported as normal. Intravenous pyelograms were negative. Biopsies showed chronic fibrosis in the axillary and hyperplasia in the cervical lymph nodes. Absence of fat cells was noted. A mild lipemia was discovered on admission, but there was no overt evidence of diabetes. Within two months, however, glycosuria was discovered and abnormal blood glucose tolerance curves were found. The intelligence quotient was reported by the psychologist to be 111 on the Stanford-Binet scale.

Course of disease. Progressive development of severe diabetes mellitus with marked insensitivity to insulin, increasing evidence of cirrhosis of the liver, and frequent hemorrhagic manifestations occurred during the patient's first hospitalization. During this nine-month period, 18 bouts of epistaxis were recorded. Temperature, pulse, and respiratory rates were essentially normal.

Approximately six weeks after discharge, the patient became listless, vomited, and noted sharp lower abdominal pain. He was readmitted two days later. Polyuria had occurred during the previous month, along with what were described as warts. After readmission, these raised, yellowish papules were diagnosed as xanthoma diabeticorum. On readmission, the fasting blood sugar was 268 mg. per cent and nonprotein nitrogen was 60.8 mg. per cent. The opthalmologic consultant noted lipemia retinalis. Dr. Hal Downey, the hematologic consultant, found no evidence of leukemia. The patient remained in the hospital for nine months, occasionally evidencing attacks of shock or temper tantrums and general convulsions, which responded to the feeding of orange juice.

After discharge, he was followed in the outpatient dispensary for the succeeding ten-month period. He was then again readmitted because of crampy abdominal pain and severe epistaxis of four days' duration. His weight on this admission was 48.5 lb. On this occasion, he remained in the hospital for only two weeks.

Three months later, D. Z. had his fourth hospital admission. Attempts to control the diabetic state were now found to be even more difficult. A skin biopsy specimen disclosed no noticeable change in the character of the panniculus adiposus. On this occasion, the patient remained in the hospital for six weeks.

Two months later, he was readmitted for a one-month period. Biopsy of the liver revealed thickening of the capsule and other evidence of chronic perihepatitis. The hepatic parenchymal cells showed large amounts of glycogen. The rhinologist could find no local explanation for the frequent attacks of epistaxis. Jaundice was increasing in intensity. The liver was gradually shrinking, while the spleen was enlarging. The venous pressure of the lower extremities was elevated.

One month later—four years after his first admission—D. Z. had his sixth and final hospital admission. The difficulty of controlling the diabetic state persisted. In spite of high values for the fasting blood sugar and glycosuria, the urinary acetone and diacetic acid reactions were recorded as negative to 1+. Administration of vitamin K did not influence the bleeding tendency. Eleven months later, terminal gastrointestinal hemorrhage occurred.

Clinical diagnosis. The interrelated anatomic and metabolic diagnoses of lipodystrophy universalis, progressive hepatic cirrhosis, and insulin-refractory diabetes mellitus were readily arrived at and well confirmed by the end of the first year of observation of this patient. Throughout the subsequent three years of his life, we were able to observe the clinical sequences and gradual progression of disease processes which combine these several abnormalities into a single diagnostic syndrome. It was then possible to reconcile lipohistiodiaresis with progressive cirrhosis of the liver and atypical diabetes mellitus and to rule out such disorders as lipodystrophia progressiva, Weber-Christian disease (nodular nonsuppurative panniculitis), and congenital muscular hypertrophy.

Autopsy. Postmortem inspection revealed the absolute lack of normal fatty pannicular tissue and the absence of fat pads in the cheeks and the soles of the feet. These deficiencies sharply accentuated the prominence of the muscles and skeletal structures. Also noted were sunken eyeballs, deep yellow sclerae, and healed scars on right upper quadrant of the abdomen. The skin was resistant and leathery to touch. The pathologists did not recognize this combination of features as being typical of any disease entity.

After the abdomen was opened, no adipose tissue was to be seen subcutaneously or in the omentum. The liver (950 gm.) edge measured 6 cm. below the xiphoid process, and the spleen (530 gm.) measured 4 cm. below the left costal margin. There were adhesions in the region of the splenic flexure of the colon, and the increased fibrous tissue caused resistance to cutting. Microscopic study showed marked fibrosis. Extreme cirrhosis of the liver lobules, which were separated by thick bands of portal fibrous tissue, was also found microscopically. Yellowish, firm nodular areas, 2 mm. to 2 cm. in diameter, were surrounded by fibrous tissue.

There were no varices in the esophagus, but punctate hemorrhagic areas were noted in the stomach. A diver-

TABLE 1

CERTAIN TISSUE LIPIDS IN PER CENT OF WET WEIGHT IN PATIENT (D.Z.) WITH LIPOHISTIODIARESIS AND IN CONTROL SUBJECTS (G.C., M.H., AND W.J.)

Tissue	Subject	Cholesterol		Total fatty acids			Acetone-soluble fatty acids			Acetone-insoluble fatty acids		
		Total	Ester	Amt.	M.W.†	I.N.‡	Amt.	M.W.	I.N.	Amt.	M.W.	I.N.
Perirenal	D.Z.	0.24	0.19	0.45	292	102	0.21	268	86	0.24	294	127
	G.C.	0.30	0.08	44.61	-	62	36.08	274	60	0.20	—	—
Subcutaneous°	D.Z.	—	—	—	—	—	—	—	—	—	—	—
	G.C.	—	—	51.14	279	66	50.08	278	65	0.31	—	—
Skin	D.Z.	0.16	0.03	0.31	276	68	0.21	—	68	0.13	—	—
	G.C.	0.10	0.03	10.03	274	64	10.03	274	64	0.16	—	—
Pancreas	D.Z.	0.41	0.11	1.21	293	113	0.77	294	117	0.30	294	103
	W.J.	0.27	0.07	—	—	—	0.70	—	93	0.60	—	102
Spleen	D.Z.	1.08	0.19	1.29	302	110	0.18	—	93	0.75	309	117
	M.H.	0.12	0.03	—	—	—	0.30	—	96	0.60	—	116
Liver	D.Z.	0.89	0.33	1.49	294	107	0.61	293	83	0.80	301	123
	G.C.	0.36	0.08	3.16	290	102	1.50	281	74	1.60	296	121
Kidney	D.Z.	0.48	0.06	1.22	292	121	0.37	287	114	0.71	299	119
	M.H.	0.36	0.05	—	—	—	1.20	—	72	0.50	—	100
Muscle	D.Z.	0.14	0.02	0.44	300	125	0.17	285	86	0.27	316	140
Heart	D.Z.	0.28	0.03	1.25	296	149	0.38	—	133	0.69	292	159
Adrenal	D.Z.	0.44	0.14	2.02	290	115	0.94	290	107	0.70	293	123
Brain	D.Z.	1.34	0.08	2.14	298	121	0.39	287	100	1.21	295	132

°No real subcutaneous fatty tissue found

†Molecular weight

‡Iodine number

ticulum, 3 cm. × 1 cm., was found in the ileum 40 cm. from the ileocecal valve, and a small amount of tarry-appearing material was found in the colon. The pancreas weighed 15 gm. and was moderately hard and rubbery. Microscopically, there was increased fibrosis, especially interlobularly; the acini appeared normal, but very few islands of Langerhans were seen.

Extensive study by a neuropathologist, Dr. A. B. Baker, revealed no gross brain abnormalities. All tissues, including several sections through the hypothalamic region, were microscopically negative. No special cell groups were found which could be identified either as the supraoptic or the paraventricular nucleus. Various smaller cells were present. Sections were checked also by Dr. A. T. Rasmussen, a neuroanatomist.

EVIDENCES OF DERANGED METABOLISM

Clinical and laboratory studies revealed evidences of aberrations in the metabolism of fat, carbohydrate, protein, and various hormones.

Lipids

Lipohistiodiaresis. The selective loss of fat deposition in adipose tissues indicates a profound disturbance in lipid metabolism in this subject. This was demonstrated by repeated antemortem skin biopsies as well as by the total absence of adipose tissue in pericardial, perirenal, peritoneal, omental, and other fat depots. The completeness of this fatlessness is emphasized by the absence of typical adipose tissue cells, even when special fat stains were used in microscopic study. By contrast, in normal individuals, adipose tissue may be found in relative abundance even under the condition of severe inanition, and in persons with ordinary lipodystrophia progressiva, typical appearing fat cells, though greatly diminished, are present even in the affected portion of the body.

The lack of fat is further confirmed by chemical analysis of body tissue lipids (table 1). Calculation of the ratio of cholesterol ester to the fatty acids in the acetone-soluble fatty acids gives strikingly low glyceride fatty acid values. Moreover, the high iodine numbers of the fatty acids in this fraction indicate that the saturated fatty acids were sparse in all the tissues. Most outstanding is the great difference between the amounts of total fatty acids in the adipose tissue (subcutaneous and perirenal) and in the skin—a difference caused by the decrease in glyceride fatty acids. The content of fat in the liver was only slightly less than in a normal child of this age. The differences in fat content of representative tissues are shown in figure 2.

Hyperlipemia. High values—528 and 642 mg. per cent—for the total fatty acids in the blood serum were found before the development of glycosuria. In spite of increased levels for the serum total fatty acids, the iodine numbers were high, an iodine number of 106 being found even when the total fatty acids were over 1,000 mg.

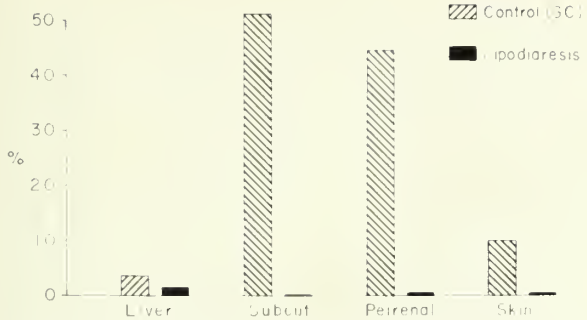

Fig. 2. Total fatty acids in tissues of child (D. Z.) with lipohistiodiaresis and of control subject (G. C.).

per cent. The increased values were in the glyceride fatty acids.

After the administration of a cream meal, fat was readily absorbed from the intestine into the blood stream. However, the iodine number of the serum fatty acids was found to increase at this time. Nevertheless, fractionation of the serum lipids revealed that it was possible for the patient to maintain excess amounts of saturated fatty acids in the blood stream in spite of their absence from the adipose tissue. The results of serum lipid analyses during marked hyperlipemia were remarkably similar to those of another child with poorly controlled diabetes mellitus. Both subjects had cutaneous xanthomatosis at the time. Calculations of the fatty acids present as phospholipids and cholesterol esters revealed that the triglyceride fatty acids equaled 1,500 mg. per cent. The fatty acids had essentially the same characteristics regarding the average length of the carbon chain and degree of unsaturation. Quite a different situation existed at the time of death, when values for the triglyceride fatty acids had dropped to an extremely low level and seemed to reflect, more or less directly, the lack of fat in the tissues.

Respiratory quotients. Our investigation into the nature of the metabolic mixture in D. Z. included study of respiratory quotients under different dietary conditions. These studies were carried on by Dr. Joseph Beber, who, with Dr. George O. Burr, was working on respiratory quotient studies in rats. The Carpenter form of the Haldane gas analysis apparatus was used. The data are presented in table 2. Although it was not possible to repeat the studies, the findings appear reasonable to us in view of the nature of the chemical composition of the tissues. The results may be summarized as follows:

1. On fasting, only 25 per cent of the calories were derived from fat, rather than the expected 50 to 55 per cent.

2. Only 15 per cent of the calories were derived from fat after a normal balanced meal.

3. The derivation of 77 per cent of the calories from fat after the ingestion of a fatty meal showed that fat was utilizable.

4. The increase of the nonprotein respiratory quotient to the neighborhood of 1 after a carbohydrate meal indicates that fat could be synthesized even though it could not be deposited.

5. The high fasting respiratory quotients indicate excessive utilization of protein.

Carbohydrates

Abnormal glucose tolerance. Since neither glycosuria nor high fasting blood sugar values were found when D. Z. was first seen, glucose tolerance tests were carried out to investigate the possibility of glycogen storage disease with he-

TABLE 2

RESPIRATORY QUOTIENTS UNDER VARIOUS CONDITIONS DURING FIRST HOSPITAL ADMISSION IN PATIENT (D.Z.) WITH LIPOHISTIODIARESIS

Date	*Dietary condition*	*Hr. p. c.*	*Respiratory quotient*	*Urine N_2 (gm./hr.)*	*Nonprotein respiratory quotient*	*Basal metabolic rate (cal./hr./M^2 body surface)*	*Food consumption (gm./hr.)*	*Fat calories (% of total)*
9/12	Fasting	0	0.840	—	—	—		
9/13	Fasting	0	0.819	—	—	—		
9/16	Fasting	0	0.819	0.620	0.809	39.50	0.83 C 0.68 F 3.88 P	25
9/14	Regular mixed	1.5	0.86	0.233	0.930	52.65	5.09 C 0.70 F 1.45 P	15
9/17	Carbohydrate meal	3	0.89	0.909	1.006	70.20	5.08 C 0.00 F 5.68 P	0
9/20	Fat meal	2 4	0.73 0.72	0.434	0.710	75.40	0.13 C 4.23 F 2.72 P	77

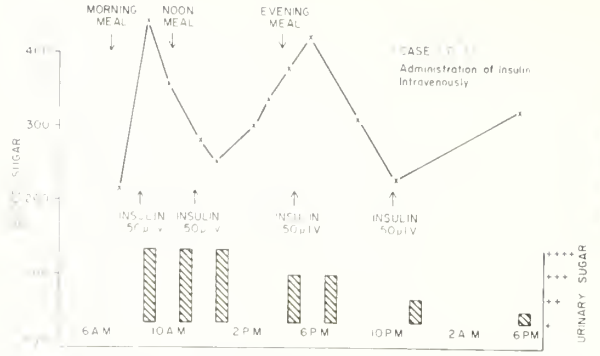

Fig. 3. Relative ineffectiveness of large doses of insulin administered intravenously in child (D. Z.) with poorly controlled diabetes mellitus associated with lipohistiodiaresis.

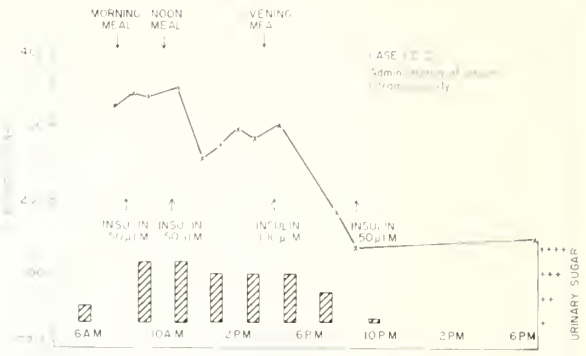

Fig. 4. Relative ineffectiveness of large doses of insulin administered intramuscularly in child (D. Z.) with poorly controlled diabetes mellitus associated with lipohistiodiaresis.

patic insufficiency. Somewhat later, the glucose tolerance test results were abnormal and of the diabetic type.

Response to epinephrine. Blood sugar increased after the administration of epinephrine. At the time of death, there was no chemical or histologic evidence of excess storage of glycogen in the tissues, although a microscopic biopsy of the liver early in the course of the disease had been reported to show an excess of glycogen.

Insulin resistance. Control of glycosuria and hyperglycemia was difficult. The child seemed to be equally insensitive to insulin whether the hormone was administered intravenously or intramuscularly (figures 3 and 4). Glycosuria persisted even with the administration of as much as 100 units of insulin three times daily with meals. The addition of a supplementary dose of 50 units after the evening meal produced no results. There were times when D. Z. received as much as 350 units of insulin daily.

The resistance to insulin increased as the disease progressed (table 3). Relatively early in the clinical course of the diabetic phase, each unit of insulin seemed to be able to metabolize 4 gm. —that is, dietary glucose minus the glucose excreted—whereas, late in the disease, this value decreased, 1 unit of insulin accounting for less than 1 gm. of available glucose.

Protein

Studies of the respiratory quotients under different conditions indicated preferential burning of protein. On one occasion, the total plasma proteins were found to be more than 9 gm. per cent. In view of recent findings by other workers, this may be of significance. On 2 other occasions, however, plasma protein values were found to be normal, as were the albumin-globulin ratios.

Growth

When D. Z. was first seen, his height was 42 in., which is in the ninetieth percentile according to Woodbury's weight-height-age chart; his weight was 33 lb., which is in the second quartile. According to the history, he weighed more at 3 years of age than he did at 4 years. His known measurements are charted on Stuart's grid (figure 5). A marked decrease is evident in the percentile levels for height, which was be-

TABLE 3

DEVELOPMENT OF INCREASING RESISTANCE TO INSULIN IN PATIENT (D.Z.) WITH LIPOHISTIODIARESIS

Date	*Weight*	*Diet Composition*				*Glucose value*	*Glycosuria (gm./day)*	*Insulin (units/day)*	*Ratio gm. glucose to units of insulin*
		Calcium	*Carbohydrate*	*Fat*	*Protein*				
9 20 35	16.0	1171	166	12	38	195	0	0	—
1 15 36	16.4	1130	150	50	66	186	0	38	1.8
8 23 36	18.2	1600	136	60	85	179	0	103	1.7
9 17 38	22.0	1701	150	60	96	195	trace	177	1.1
4 19 39	21.0	1800	165	60	100	210	0	284	0.8
6 29 39	23.7	2356	250	75	110	301	15.1	250	1.1
7 23 39	23.1	1561	128	11	92	163	0	230	0.7
8 1 39	22.8	1600	0	60	151	50	17.0	80	0.4

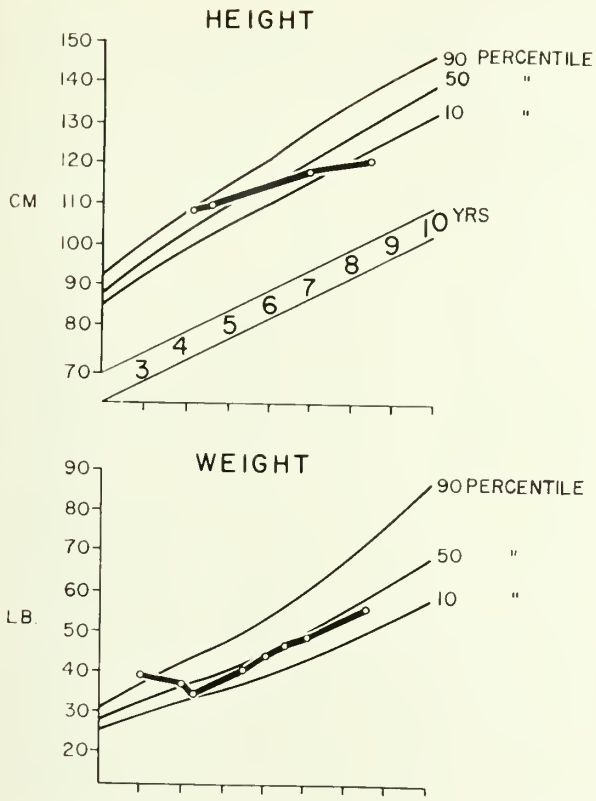

Fig. 5. Graph of height and weight curves in patient (D. Z.) with lipohistiodiaresis.

tween the fiftieth and seventy-fifth percentiles at 4½ years and less than the third percentile at 8½ years of age. This reduction suggests that the usual prediabetic growth spurt had occurred before we saw the patient. This feature seems to be of significance as evident of a somatotrophic stimulation early in the disorder, a phenomenon which has been surmised by other observers.

DISCUSSION

On the basis of available data concerning the 19 subjects reported in the literature to date, who have many rather bizarre signs and symptoms in common, it is difficult to decide whether the combination of symptoms represents a single disease entity or constitutes a fortuitous syndrome resulting from reactions to diverse metabolic stimuli. The most frequently encountered features are summarized in table 4.

It is quite clear that in all subjects there was an absence of fat from the tissues that typically are richest in lipid substance, namely, the panniculus adiposus. This feature is apparent clinically, histologically, and chemically. Moreover, the prominence of the musculature may not be merely a relative matter, as excess amounts of glycogen have been noted histologically. In no way, however, does the clinical picture represent that of congenital muscular hypertrophy, a condition associated with mental deficiency.[15]

TABLE 4

SUMMARY OF FINDINGS IN 19 SUBJECTS WITH A GENERAL ABSENCE OF FAT IN THE BODY (LIPOHISTIODIARESIS) (FROM REVIEW OF AVAILABLE LITERATURE[1,4,5,7-14])

	Symptom present			*Symptom absent*			*Not stated*		
	Total number	*Adults*	*Children*	*Total number*	*Adults*	*Children*	*Total number*	*Adults*	*Children*
Cases	19	4	15						
Male	6		6						
Female	13	4	9						
General lipodystrophy	19	4	15						
Consanguinity	2	0	2				17	4	13
Hyperlipemia	16	4	12	1	0	1	2	0	2
Growth accelerated	10	0	10				9	4	5
Muscles and veins prominent	19	4	15						
Large hands and feet	5	0	5				14	4	10
Genetalia enlarged	7	0	7				12	4	8
Hypertrichosis	8	1	7				11	3	8
Curly hair	10	1	9				9	3	6
Hepatosplenomegaly	18	4	14	1	0	1			
Glycosuria	13	4	9	1	0	1	5	0	5
Hyperglycemia	14	4	10	1	0	1	4	0	4
Resistance to insulin	8	1	7	6	3	3	5	0	5
No ketosis	9	3	6	3	1	2	7	0	7
Increase in basal metabolic rate	10	4	6	1	0	1	8	0	8

Hyperlipemia was present in all but 1 subject. Hepatosplenomegaly was also found in all but 1, and in many cases, hepatic cirrhosis was demonstrated grossly and histologically. In all cases observed during childhood, excessive growth was reported. Dr. Martin Seip[12] has compared in detail the size of 1 of his 18-month-old abnormal children with that of an average 18-month-old child (figure 6).

In some cases, advanced bone age and dentition have been demonstrated. The enlargement of the hands and feet noted in a number of the children supports the view of the possibility of growth hormone stimulation, or at least a disorder of the pituitary-hypothalamic axis, as was suggested by Berardinelli[3] and by Seip.[12] Enlargement of the genitalia was reported in only a few of the children, however. The possibility of important androgenic or estrogenic influences thus appears negligible.

Diabetes mellitus was reported in all of the adult subjects and in the majority of children. In a number of instances, the diabetic phase of the picture developed while the child was under observation; hence, one might expect that other children eventually would be found to develop this feature if followed for a long time. In nearly all subjects having glycosuria and hyperglycemia, there was resistance to the action of insulin, and, in one of the subjects studied by Seip,[12] there was an increase in the insulin-like activity in the blood plasma, although there was no evidence of diabetes mellitus. The failure to develop ketosis in spite of the severe diabetic manifestations is not unexpected, considering the paucity of fat deposits in the body.

In view of the absence of hyperthyroidism in any of the subjects, the elevation of the basal metabolic rate noted in many of the subjects is difficult to explain. The curly hair so prominent in many of the children is also difficult to explain.

An attempt to explain the metabolic defects in these cases of lipohistiodiaresis should account, then, for increased growth, insulin-resistant diabetes, hyperlipemia, triglyceridemia, and the absence of ketosis. The crucial role of the liver in the metabolism and utilization of both endogenous and exogenous fat is now clearly appreciated, although many gaps are still to be completed. Incoming exogenous fat from the lymphatics, in the form of chylomicrons, is taken up and transformed by the liver into lipoproteins of lower molecular weight and higher density, which can reenter the circulation as soluble lipoproteins. Depot fat is mobilized by a process known to be influenced by a number of hormones. The free fatty acids which are released

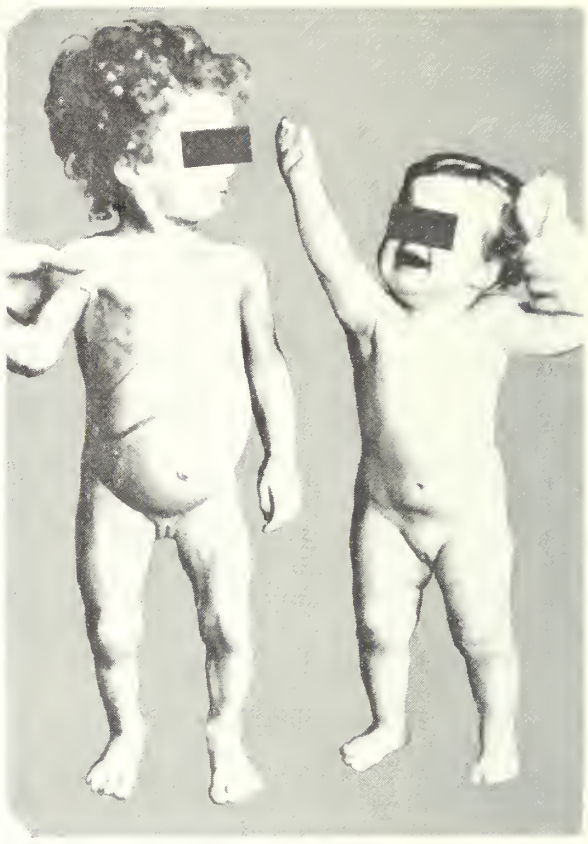

Fig. 6. Two infants, 18 months of age. Larger child has syndrome with general lipodystrophy. Other child is healthy control subject. (Courtesy of Dr. Martin Seip,[12] Rikshospitalet, Oslo, Norway.)

are available for tissue utilization. The liver utilizes these fatty acids either for energy or for the formation of triglycerides, phospholipids, and resynthesis into low-density lipoproteins, which then can be returned to the circulation. In view of this salient role of the liver in the handling of fat, it is not surprising that, in liver diseases, abnormal plasma lipid patterns are found.

The increased bone age and growth in these cases are almost certainly caused by increased secretion of growth hormone by the anterior pituitary gland. Evidence for the hypersecretion of other trophic hormones by the anterior pituitary is lacking, however. It may be relevant to note at this point that Rudman and associates[16] found that an extract of hog pituitary glands had a lipemia-producing activity when injected into rabbits. This fraction was free of recognized pituitary hormones.

It has become apparent that an antagonism exists between insulin and growth hormone,[17,18] although the exact site is as yet unknown. In vitro studies using rat adipose tissue have shown that, whereas insulin stimulates fatty acid syn-

thesis and CO_2 formation from glucose by the phosphogluconate pathway, growth hormone stimulates CO_2 production only and by a method not involving the phosphogluconate pathway. No antagonism studies have been carried out in vitro. It seems likely that competition for intracellular metabolites accounts for the antagonism of these two hormones.

In vivo, the action of growth hormone on adipose tissue involves a stimulation of mobilization of free fatty acids, whereas insulin is intimately involved in the utilization of glucose and in fatty acid synthesis. Insulin, moreover, is known to act on various tissues—mammary gland, muscle, and adipose tissue—but such action for growth hormone is not known at present. The well-known diabetogenic action of growth hormone is therefore presumed to be responsible for the insulin-resistant diabetes and the sequelae in the form of liver lipid derangement and absence of adipose tissue. The lack of opposition from other hormones to the action of growth hormone on the mobilization of fat from the adipose tissue may account for the hyperlipemia, since carbohydrate metabolism is greatly impaired.

The mechanism resulting in the complete depletion of subcutaneous fat remains unknown, but the metabolic effects as outlined above appear to provide the basis for this development. If growth hormone causes insulin-resistant diabetes by the inhibition of a single enzyme in the adipose tissue, then the absence of this enzyme may be responsible for observed effects—that is, no feedback mechanism is possible.

The absence of a ketosis in such a case of diabetes is caused by the absence of adipose tissue as well as by the diminished oxidation of fat.

SUMMARY AND CONCLUSIONS

Renewed interest in the subject of lipid metabolism during the past few years has prompted this more detailed consideration of clinical and laboratory data concerning a previously reported patient who presented an unusual clinical picture of general absence of fat in the adipose tissues of the body associated with prominence of musculature and accelerated growth. The child had cirrhosis of the liver and hyperlipemia; in later stages of the disorder, hyperglycemia and glycosuria, which became progressively resistant to insulin. Ketosis did not develop. Chemical analyses of the various body tissues confirmed the uniform deficiency of glyceride fatty acids, although glyceride fatty acids had been greatly increased in the blood serum early in the course of the disease.

Data from the literature, although incomplete in some instances, reveal 18 other patients with the essential features encountered in our patient. In the younger subjects, advanced growth, early hyperlipemia, and hepatosplenomegaly were observed before the diabetic picture appeared. In the adult subjects, growth acceleration was, of course, not a factor. However, insulin-resistant diabetes mellitus with no indications of ketone body formation was an outstanding feature. The clinical and laboratory findings in our patient and the details reported in the literature seem to warrant recognition of a syndrome combining lipohistiodiaresis, temporary advanced growth, hyperlipemia, cirrhosis, prominent musculature and veins, and diabetes mellitus characterized by insulin-resistance and lack of ketosis. Although the derangement seems to exist intrinsically in the adipose tissue and may be primary in nature, the possibility must be considered that the condition results, in part at least, from overactivity of growth hormone, possibly via the pituitary-hypothalamic axis.

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Congenital Complete Atrioventricular Block

Clinical Features, Hemodynamic Findings, and Physical Working Capacity

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CONGENITAL HEART BLOCK was at one time believed to occur almost invariably in association with gross anatomic cardiac abnormalities.[1–15] Only in rare instances was the pathology demonstrated to be of a purely microscopic nature.[15–20] Recent evidence has now established, however, that conduction defects of this type do frequently occur as a single isolated defect.[21–24]

Keith and associates[21] reported that 17 of their 23 cases of congenital atrioventricular (A-V) block were isolated. This was true also in 8 of 12 cases studied by Paul and associates.[22] Wright and colleagues[24] reported that 12 of 28 children with complete or advanced degrees of partial congenital A-V block had no associated gross anatomic cardiac abnormalities.

The purpose of this report is to describe the clinical and hemodynamic features of 6 children with congenital complete A-V block, 5 of whom had no gross anatomic lesion. In 4 of the children with the isolated type, physical working capacity was also studied. Evaluation of the physical working capacity in 11 children and young adults with this disorder was recently reported by Ikkos and Hanson.[25]

MATERIAL AND METHODS

Of the patients studied, 3 were girls and 3 were boys. The age range at the time of study was 3 months to 14 years. In 1 patient, the abnormality was suspected antenatally and confirmed by electrocardiogram at birth. In 2 patients, the diagnosis was established during the first year of life; in 2, during the second year of life; and in 1, at 3 years of age. All were in good health except the 3-month-old infant, who had failed to thrive since birth and died of heart failure at 5 months of age; autopsy examination showed a widely patent ductus arteriosus, with gross evidence of heart failure.

A 13-lead electrocardiogram and a roentgenologic examination of the heart were made in all 6 patients, and a vectorcardiogram was obtained in 4. Right heart catheterization was performed in 6 and high-speed biplane selective angiocardiography in 5 of the patients. These studies were made under basal anesthesia, using 10 per cent thiamylal sodium (Surital Sodium) rectally (22 to 33 mg. per kilogram of body weight). Blood samples were analyzed by Van Slyke and cuvette technics, and blood flows were calculated using the Fick principle.

Dynamic pressures were recorded using a 6-channel direct-writing Offner recorder. The frequency response of the entire system was 12 or more cycles per second, depending upon the size of the catheter. Peripheral arterial pressures, when measured, were obtained by direct cannulation of the exposed brachial or femoral artery. Mean pressures were obtained by electronic integration and by planimetry.

Oxygen consumption by the open-circuit method was computed in 4 patients by collecting expired air in a Douglas bag and analyzing the oxygen content with a Beckman analyzer, Model C2. The expired air was collected during catheterization in 2 of the patients and after the procedure in the others.

The effects of a constant infusion of isopropylarterenol (Isuprel) were studied in 1 patient. The drug was administered as a dilute solution in 5 per cent dextrose in distilled water, 1 cc. of the solution containing 0.8 μg. of isopropylarterenol. The rate of infusion was 0.8 μg. per minute initially and 2.4 μg. per minute terminally. The total dosage was 60 μg. and was given over a thirty-five-minute period. The heart rate was recorded by electrocardiogram, and the pressures were measured in the right atrium, right ventricle, pulmonary artery, and brachial artery before infusion and at the height of the

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physiologic response. During these same periods, blood samples for Van Slyke analyses were drawn from the main pulmonary and brachial arteries and expired air was collected for oxygen consumption tests.

The physical working capacity was evaluated in 4 patients. An electric bicycle ergometer was used for this purpose. The subjects performed at 3 different work loads, maintaining a pedaling rate of 60 to 70 r.p.m. The duration of each work load was six minutes. Oxygen consumptions were computed immediately before and during the last three minutes of the exercise. An electrocardiogram was made at two-minute intervals during the test.

Ordinarily, the working capacity is calculated by plotting on graph paper the heart rate at the end of each work load against the work load. A straight line is then drawn through the 3 points making the best fit. The estimated amount of work that would produce a heart rate of 170 beats per minute is then recorded as the working capacity of that individual. In these patients, however, because of inability to increase the heart rate much beyond 100 beats per minute, these criteria could not be used. The working capacity was therefore arbitrarily recorded as the maximal amount of work the patients were able to do without producing exhaustion.

CLINICAL FEATURES

Systolic murmurs were audible in all patients, were located along the left sternal border, and ranged in intensity from grade II to grade IV. A soft diastolic murmur also was audible in 3 of the patients, 1 of whom was the infant with patent ductus arteriosus.

The electrocardiogram showed complete A-V dissociation in all cases, the auricular rate ranging from 70 to 160 beats per minute and the ventricular rate from 40 to 60 beats per minute. The electrical axis was normal, and the duration of the QRS complex was 0.08 second or less in all tracings. Only in 1 patient did the electrocardiogram show evidence of chamber hypertrophy. In the tracing of this 5-year-old child, an SV_1 of 25 mm., an RV_5 of 17 mm., and a QV_5 of 7 mm. suggested left ventricular hypertrophy.

An interesting electrocardiographic feature which has not been previously pointed out in the literature was an unusually deep inversion of the T waves in some of the precordial leads. This was present in 4 of the 5 patients with the isolated form of the disease. In 2, the T wave was deeply inverted in V_1 through V_3; in 1, in V_1 through V_4; and in 1, in V_2 through V_5. The T waves measured up to 11 mm. in depth (figure 1).

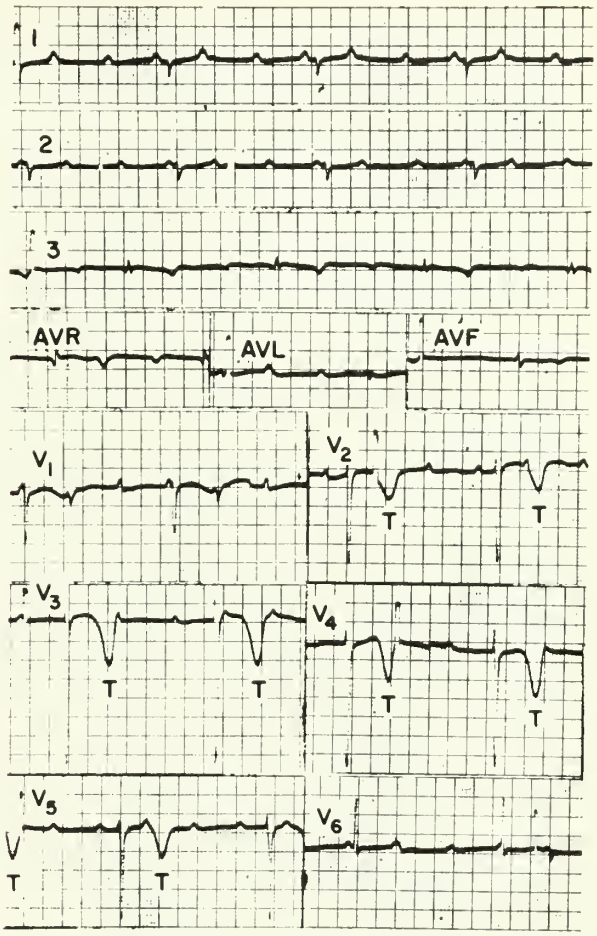

Fig. 1. Electrocardiogram showing complete A-V dissociation with deep inversion of T waves in V_2 through V_5.

Vectorcardiograms were obtained in 4 patients. In 3 of the tracings, the P loop showed a marked increase in the extension inferiorly and in 2, a prominent $T_{(P)}$ wave was present and oriented superiorly. The QRS loop was in a normal spatial position in 3 tracings. In the fourth, displacement of the loop superiorly and posteriorly suggested left ventricular preponderance, which was not evident in the electrocardiogram. In 2 patients, the QRS loop exhibited a figure-8 crossover in the midportion of the transverse and frontal loops.

Roentgenographic studies showed a moderate degree of diffuse cardiomegaly in 4 of the 6 patients. A roentgenogram typical of the finding is shown in figure 2. Selective angiocardiography was performed in 5 patients, and the only abnormality observed was moderate enlargement of the pulmonary and aortic trunks in 2.

HEMODYNAMIC FINDINGS

There was evidence of a shunt in only 1 patient. The data for this child suggested an atrial septal

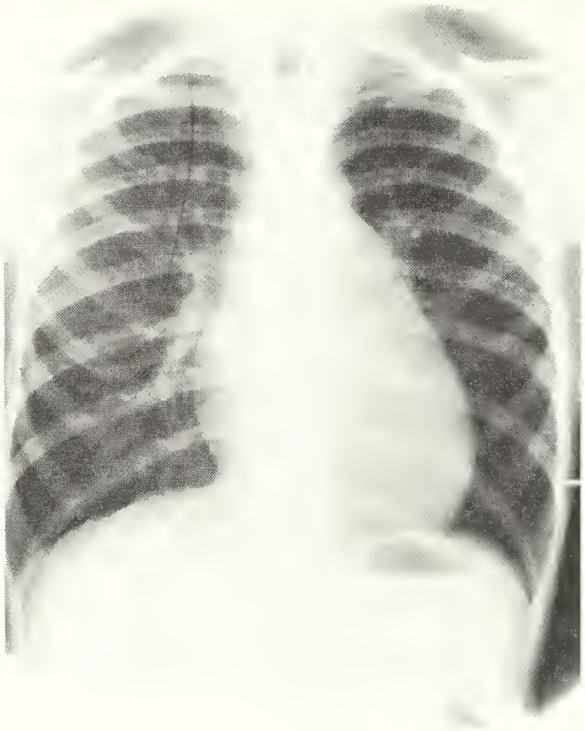

Fig. 2. Teleroentgenogram showing moderate cardiomegaly with congenital complete A-V dissociation.

defect, but study at autopsy two months later established that the atrial septum was intact but the ductus arteriosus was widely patent.

The values presented in table 1 indicate that the systolic intracardiac pressures, as well as those in the great vessels leading to and from the heart, were often increased. It is of interest, however, that the mean blood pressures in the pulmonary artery and in the right ventricle were within normal limits in each case.

Contrary to the findings of others,[24] an increase in pulmonary vascular resistance was not common. Calculated on the basis of the standard formula, the mean right atrial pressure being used as an approximate value when left atrial pressure was not measured, the vascular pulmonary resistances in the 4 patients studied were 0.8, 1.6, 3.2, and 5 resistance units. Thus, it was possibly elevated in only 1 case.

The arteriovenous oxygen difference ranged from 3.2 to 4.2 cc. of oxygen per 100 cc. and the systemic index, from 3.6 to 4.9 liters per minute per square meter. The stroke volume ranged from 60 to 83 cc. per square meter, with an average value of 72. This is more than the average value of 54 cc. per square meter reported by Wright and his associates[24] but less than that of 85 reported by Paul and associates.[22]

The effects of a constant intravenous infusion of isopropylarterenol are presented in table 2. Dramatic rises in ventricular rate (44 to 80 beats per minute) and in cardiac index (3.6 to 6.8 liters per minute per square meter) were observed. The arteriovenous oxygen difference dropped from 3.9 to 2.1 cc. of oxygen per 100 cc., while oxygen consumption and stroke volume

TABLE 1

HEMODYNAMIC FINDINGS IN 5 CHILDREN WITH CONGENITAL COMPLETE A-V BLOCK

Case	*Age*		*SVC*	*IVC*	*RA*	*RV*	*PA*	*LA*	*BA or FA*	*Ventricular rate*	*Cardiac index (L./min./M²)*	*Stroke index (cc./M²)*
			(9)*	(7)	(8)	(15)	(20)	(11)				
D.R.	5 yrs.	Pressure (mm. Hg)	12/7	11/6	11/6	48/0	31/9	21/9	—	60	4.9†	82
		Average O_2 sat. (%)	67	76	69	70	70	92	—			
			(6)	(9)	(5)	(17)		(13)				
C.P.	3 mos.	Pressure (mm. Hg)	10/2	12/8	10/0	54/0	—	26/6	—	60		—
		Average O_2 sat. (%)	45	57	58	59		89	—			
			(9)	(10)	(10)	(18)	(20)	(20)	(106)			
M.H.	8 yrs.	Pressure (mm. Hg)	13/5	16/6	16/8	17/0	40/8	36/10	148/70	50	—	—
		Average O_2 sat. (%)	72	72	67	64	61	94	94			
			(4)	(4)	(4)	(22)	(22)		(68)			
J.E.	7 yrs.	Pressure (mm. Hg)	6/3	7/2	8/3	30/0	25/7	—	100/54	60	3.6	60
		Average O_2 sat. (%)	76	78	77	77	77	—	96			
			(10)	(11)	(16)	(22)	(22)		(114)			
M.Z.	13 yrs.	Pressure (mm. Hg)	11/6	12/10	22/10	52/6	18/10	—	156/86	60	3.7†	62
		Average O_2 sat. (%)	65	60	67	62	65	—	98			
			(4)		(4)	(10)	(14)	(11)	(84)			
W.R.	8 yrs.	Pressure (mm. Hg)	9/0		9/0	30/0	30/0	18/0	132/74	44	3.6	83
		Average O_2 sat. (%)	73		73	73	73	93	93			

*Figures in parentheses represent mean pressures.

†Based on oxygen consumptions determined after catheterization procedure

TABLE 2

EFFECTS OF INTRAVENOUS INFUSION OF ISOPROPYLARTERENOL IN PATIENT WITH CONGENITAL HEART BLOCK (W.P.)

	Pressure (mm. Hg)				Ventricular rate	Cardiac index (L./min./M²)	Stroke index (cc./M²)	Oxygen consumption (cc./M²)	A-V oxygen difference (vol. %)
	RA	RV	PA	BA					
Before isopropylarterenol	(4)* 9/0	(10) 30/0	(14) 30/0	(106) 160/96	44	3.6	83	141	3.9
During maximal physiologic effect of isopropylarterenol	(8) 20/0	(16) 38/0	(20) 36/10	(80) 156/78	80	6.8	86	144	2.1

*Figures in parentheses represent mean pressures.

remained essentially the same. The pressure decreased in the brachial artery but increased in the right atrium, right ventricle, and pulmonary artery.

PHYSICAL WORKING CAPACITY

The response to graded exercise on a bicycle ergometer is presented in table 3. Based on average values for California children of the same sex and surface area,[26] 1 child performed at the thirty-eighth percentile, 2 at the sixtieth percentile, and 1 at the eightieth percentile levels. The heart rate increased in each subject, but in no case did it exceed 100 per minute. Pulse pressure and oxygen pulse increased in all 4 subjects.

DISCUSSION

Congenital A-V block is one of the less common cardiac abnormalities. In rare instances, it may be familial, and as many as 3 cases in a single family have been reported.[24,27] There is no sex predilection. The long-held view that it is usually associated with a gross anatomic defect of the heart is no longer valid, since recent evidence indicates that it commonly occurs as an isolated lesion of the conduction system. Including the cases presented here, hemodynamic studies of 69 children with this abnormality[21,22,24] have revealed that in 42, or 61 per cent, it was of the isolated variety.

The clinical picture in this disorder often simulates that of a ventricular septal defect. Systolic murmurs are almost a constant finding, and diastolic murmurs also are frequently present. Mild or moderate cardiomegaly is commonly demonstrated by roentgenogram.

The murmurs, cardiomegaly, and elevated systolic intracardiac pressures are presumably caused by an increase in stroke volume. Reported studies of the stroke volume, however, have been conflicting. Paul and his associates[22] found an increase in stroke volume to be the most consistent hemodynamic abnormality. Others[24] were unable to confirm this finding. The results of the present study support the contention that the stroke volume is increased in these children.

The electrocardiograms of the patients studied in this series showed normal intraventricular conduction, indicating that the block was located in or proximal to the main bundle. The commonly reported sites of involvement are the A-V

TABLE 3

RESPONSE TO GRADED EXERCISE ON BICYCLE ERGOMETER IN 4 CHILDREN WITH CONGENITAL COMPLETE A-V BLOCK

Case	Sex	Age (years)	Maximum work load (KgM/min.)	Work duration (min.)	Heart rate		Blood pressure (mm. Hg)		Oxygen consumption (cc./min./M²)		Oxygen pulse* (cc.)	
					onset	end	onset	end	onset	end	onset	end
J.E.	M	7	200 (38)†	10	50	100	110/60 (77)‡	120/58 (79)‡	109	367	2.5	4.3
D.R.	F	8	300 (60)†	18	50	84	—	—	199	359	3.7	4.0
M.Z.	F	14	600 (80)†	18	48	90	136/70 (92)‡	160/60 (93)‡	188	775	5.7	12.6
W.R.	M	8	400 (60)†	18	50	82	114/74 (87)‡	160/68 (99)‡	172	695	3.4	8.5

*Gross oxygen intake divided by heart rate

†Level of performance in percentile (on basis of studies of California children of same sex and surface area)

‡Mean pressure estimated by adding one-third of pulse pressure to diastolic pressure

node, the main bundle, or the bundle branches.[19] Involvement proximal to the A-V node apparently is rare.

Little is known about the physical working capacity of individuals with this abnormality. In a study involving 11 subjects, Ikkos and Hanson[25] found that it was normal or only slightly reduced. The present study demonstrated a response well above average in 3 of the 4 patients and within normal range in the fourth.

The way in which individuals with this abnormality adjust physiologically to increased work loads is not yet known. In normal individuals, an increase in the delivery of oxygen to the tissues may be accomplished by one or more of the following mechanisms: (1) an increase in arteriovenous oxygen difference, (2) an increase in stroke volume, and (3) an increase in heart rate.[28,29] The present data and those of others[25] indicate that children with this type of conduction defect compensate in part for the increased demands of exercise by a rise in the ventricular rate. The elevation in oxygen pulse, however, suggests that this mechanism in itself may not be entirely adequate. Measurements of blood pressure before and during active exercise suggest that the stroke volume increases. However, when exercise was simulated in 1 patient by a constant intravenous infusion of isopropylarterenol, the major changes were in the ventricular rate and the arteriovenous oxygen difference, the stroke volume remaining relatively unaltered.

Ikkos and Hanson[25] studied the response to exercise during catheterization in 2 patients with isolated congenital heart block. Cardiac output, ventricular rate, and arteriovenous oxygen difference increased in both patients. The stroke volume, however, increased sharply in one but decreased in the other.

As in normal individuals, then, the most constant circulatory adjustment to exercise is an acceleration in ventricular rate. Alterations in stroke volume or in arteriovenous oxygen difference apparently show more individual variation.

Until more is known about the basic physiologic mechanism in persons with isolated congenital heart block, the long-term prognosis must remain in doubt. During the neonatal period, the future is uncertain, because infants with slow ventricular rates may be unable to maintain an adequate cardiac output and may die of heart failure before physiologic adjustments can occur.

Beyond the period of early infancy, the prognosis is variable but in general appears to be good. Of the patients observed by Ikkos and Hanson,[25] 4 "engaged in usual athletics" and a fifth was an ardent ice-hockey player. The fact that 6 women with this disorder have withstood the demands of pregnancy and labor[16] is further evidence that many of these patients have sufficient cardiac reserve to live a normal life. The normal physical working capacity in the patients thus far studied suggests that, beyond the early period of life, isolated congenital heart block is not an incapacitating disease.

SUMMARY

Of 6 children with congenital complete A-V block studied, only 1 had an associated gross anatomic malformation of the heart. All had cardiac murmurs, and 4 had cardiomegaly.

The electrocardiogram showed unusually deep inversion of the T waves in some of the precordial leads—a feature which has not been previously described. The principal findings in the vectorcardiogram were prominent inferior extensions of the P loops and relatively minor abnormalities in the configuration of the QRS loops. The significance of these findings is not known.

Hemodynamic studies demonstrated elevated central systolic pressures, but the mean pressures in the right ventricle and pulmonary artery were normal. Pulmonary resistance was normal, and the resting stroke volume was increased.

The circulatory adjustment to exercise in individuals with this disorder is not clearly understood. A major mechanism is an increase in the ventricular rate. Alterations in arteriovenous oxygen difference and in stroke volume apparently show more individual variation.

The physical working capacity was estimated in 4 of the children, using graded exercise on a bicycle ergometer. The response was within the normal range in all, suggesting that the prognosis is favorable in these individuals. The long-term prognosis, however, must remain in doubt until more is known about the basic physiologic adjustments concerned.

The author is indebted to Dr. Samuel O. Sapin for his help in interpreting the electro- and vectorcardiograms.

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Diverticulitis is manifested by 2 separate syndromes requiring different methods of treatment: spasticity of the sigmoid colon is treated conservatively, but perforated diverticulitis requires prompt operation.

Sigmoid spasm may lead to (1) constipation, diarrhea, or both; (2) rectal bleeding; (3) pain in the left iliac fossa; and (4) subacute obstruction. Sigmoidoscopic or postmortem examination of the sigmoid mucosa reveals edema, congestion, and granular areas that bleed easily.

Conservative treatment with anticoliform antibiotics, sulfonamides, sedatives, and neuromuscular relaxants is generally effective. Patients with intestinal obstruction require gastric aspiration and parenteral fluids.

Diverticular perforation may cause general fecal peritonitis, which is highly lethal in elderly patients. In other instances, a small leak becomes sealed off, forming a pericolic abscess. The abscess may extend into adjacent viscera—bladder, small intestine, and loops of colon—causing internal fistulas. Intestinal obstruction caused by paralytic ileus frequently intervenes.

Treatment of perforated diverticulitis in patients extremely ill is limited to simple colostomy and drainage, when possible, with subsequent closure after an adequate healing period. Patients who can tolerate major surgery are best treated by resection and anastomosis. The whole sigmoid colon which shows tubular change and spasm must be resected. Occasionally, a perforated sigmoid loop can be exteriorized, leaving a double-barreled colostomy that can be closed at a second operation.

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Poisonings in Children

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As a very broad but perhaps pardonable generalization, poisonings in children can be divided into 2 major groups. The first consists of those in which the act and specific nature of the poisoning is known, and in which the only problem for the physician is that of therapy. The second, undoubtedly smaller but very important group, consists of those in which the fact of poisoning is *not* known or is even vigorously denied, but suggested or convincing to the alert physician because of characteristic symptomatology or other evidence. From this he deduces the nature of the toxic agent, then acts accordingly and promptly.

Despite the undoubted importance of such problems, the practitioner may not deal with more than infrequent examples of any one type or group of poisonings, and he may find it almost impossible to maintain awareness of the myriad toxic substances which come to a child's hand. Reading in "pure" toxicology may be relatively uninteresting to him; hence, very proper emphasis on establishment of helpful poison control centers and their improved reference sources makes the practitioner's responsibilities more tolerable. Yet a problem still exists in that most such reference sources simply describe or tabulate clinical features with regard to specific commercial products or their toxic ingredients; thus, in order to act intelligently, the physician must first have a reasonably good idea of the nature of the specific poisonous substance before he can proceed to proper confirmation and therapy. Somehow, then, he must first learn to suspect or recognize poisoning promptly when he meets it.

In recent years, joint teaching exercises in clinical toxicology between our departments of pharmacology and pediatrics have strengthened our conviction that most poisonings in children are followed by reasonably characteristic and chronologic sequences of symptomatology, despite variations relative to drug dosage, vehicles, or mixtures; to activity and age of the child; or to state of the intestinal tract at the time of poisoning. Often, such sequences can be considered as being similar to host-responses which predictably follow contact with a variety of known infections. Hence, in our collaborative and interdepartmental teaching, we have tried to emphasize to sophomore students, as well as to clinical clerks and house officers, that the natural history of poisonings can profitably be studied in the same manner as the important pharmacologic actions of drugs—by closely observing their effects in experimental animals.

Convictions as to the frequency, nature, manifestations, and importance of poisonings in children will naturally vary wtih experience. For example, a recent comprehensive textbook of pediatrics enumerates 78 potentially toxic chemical compounds in alphabetic order, together with the characteristic signs and symptoms of toxicity they produce. A more recent authoritative volume in toxicology considers only 45 such items important or interesting enough for inclusion. In our hospital house officer's manual, constructed on the basis of our own experiences, we felt obliged to include 145 different items!

Convinced that students and physicians learn best by experience and discussion of actual clinical problems, and in support of our collaborative teaching effort, we have assembled here a number of diagnostic puzzles, which might be called "pharmacologic experiments of nature" in that each of them represented reasonably adequate demonstrations of cause-and-effect relationships for particular toxic substances, even though none was consciously planned; in fact, in each instance, the possibility of poisoning was unknown to the informant or even denied. Informal self-scoring as to the nature of these poisoning episodes and the appropriate therapy for each patient described might be rewarding or provocative! Hmmh? Proof? Treatment?

Here are the problem-posing episodes:

1. A well-developed girl 19 months of age was recently admitted in flaccid coma, completely areflexic, with pale, moist skin, was salivating profusely, and did not respond to any stimulant. Her eyes exhibited peculiar vertical nystagmoid movements, the eyelids were twitching slight-

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ly, and her pupils were constricted; they did not dilate after instillation of Neo-synephrine or homatropine drops. Temperature was 100° F.; pulse, 102; respiration, 40; blood pressure, 124/50; and weight, 27 lb.

She had had a runny nose and had sneezed quite a bit for the past three days, but had not seemed at all sick. On the day of admission, she ate a good breakfast, spent the morning playing, as usual, at her aunt's house, and had seemed perfectly well when she came home after lunch for her usual nap. She was rushed to the hospital about an hour later, when she was found unconscious and covered with vomitus.

Family and past histories seemed entirely irrelevant; 4 older siblings and the parents were well. A routine hemogram showed only moderate leukocytosis, and urinalysis was negative except for a trace of albumin. Spinal fluid was entirely normal. Roentgenograms of the chest, skull, and long bones showed nothing unusual, and blood chemical values for urea nitrogen, glucose, sodium, potassium, cloride, CO_2, calcium, and phosphorus were soon reported as being within normal limits.

2. The mother of this first-born infant had mild preeclampsia, apparently satisfactorily controlled, when she went into normal labor about two weeks before the expected date. The infant seemed normal in all respects until about five hours after delivery, when the supervisor in the nursery noted that he was extremely lethargic, responded only sluggishly to any stimuli, and had slow, shallow, and irregular respirations, with slight cyanosis; the nose seemed "stuffy," but there was no obstruction to the passage of a nasal catheter.

3. This 8-lb. baby was delivered spontaneously and easily at term of a multiparous Negro mother who had no known complications prior to or during pregnancy and delivery; she received 100 mg. of meperidine (Demerol) hydrochloride and 120 mg. of secobarbital (Seconal) sodium thirty minutes prior to delivery. The baby breathed and cried spontaneously but seemed rather sleepy. Nalorphine (Nalline) hydrochloride was given, with no appreciable effect.

With continuing close observation and symptomatic measures directed against the respiratory distress syndrome, there was equivocal improvement for about six hours, after which respirations became more depressed and the infant appeared to be in shock and was more cyanotic. The Moro response was sluggish, and the cry was weak. The only other abnormal physical finding was a mild caput over the left parietal area; x-ray films of the chest and skull showed nothing unusual. Within fourteen hours, the infant again worsened, conspicuous nystagmus had developed, together with tetanic twitchings about the face and extremities; the caput by now was quite clearly a cephalhematoma. Subdural taps were negative, though the lumbar spinal fluid was uniformly bloody, with a deeply xanthochromic supernatant and almost all red blood cells crenated. The prothrombin time was twenty-eight seconds—more than twice the normal control.

Though the symptoms now seemed explainable by massive subarachnoid hemorrhage, the cause was still obscure. At this time, the mother was again interviewed, mainly to explain to her the gravity of the prognosis, while other "leads" were vigorously sought.

4. A 3-week-old baby had mild diarrhea, for which a physician had prescribed a hydrating fluid made of potassium chloride and sodium chloride, 1.5 gm. each, in simple syrup; this was to be diluted to 1 qt., and 3 oz. of the mixture were to be given every three hours, with no other feeding or medication. The mother had the prescription filled by a neighboring pharmacist, followed directions, and gave 4 doses as directed in the next twelve hours. She then noted that the child was becoming progressively blue about the lips and fingers, so she gave only one more feeding of 3 oz. and then brought the baby to the emergency room. On arrival, the infant was acutely ill, deeply cyanotic, but not dehydrated. Temperature was 99° F.; pulse, 180 per minute; respiration, 40; and systolic pressure, 68 mm. Hg. The routine hemoglobin was 12 gm. per cent, white blood count, 16,000, with a normal differential, and the brownish, murky, venous blood did not change color when oxygen was bubbled through it.

5. This 4-year-old girl went to play in a small fenced park across the street from her home. Two hours later, she returned and told her mother that her "tummy hurt." Almost immediately, she vomited profusely, had a large, loose, involuntary stool, and collapsed.

The frantic mother brought her to the emergency room, where stupor, pallor, clammy skin, thready pulse, and a barely obtainable low blood pressure were noted. Vigorously treated for shock, she responded as to vital signs but remained comatose, only moving now and then to retch up small amounts of bile-stained mucus. During the next hour, she had 4 watery stools, with apparent abdominal cramping.

6. This 21-month-old boy had apparently been "perfectly all right" until forty-eight hours before admission, when he began to vomit and retch. He was unable to retain any food or fluid, and soon low-grade fever and weakness developed. The patient was unable to support his own weight either standing or sitting and appeared "shaky."

The history seemed noncontributory except for the fact that the mother had been successfully treated with penicillin for prenatal syphilis. The infant had been repeatedly seronegative and free from any stigma of this disease.

On examination, the child appeared apathetic and had deep, rapid respirations, pallor, and poor tissue turgor. The head seemed slightly large in relation to the body. There was no deformity and no distention of the scalp veins. Temperature was 101° F.; pulse, 110 per minute; respiration, 46; blood pressure, 130/80; weight, 19 lb.; height, 32 in.; and head circumference, 18 in.

The pupils were equal and reacted to light, and the retinas appeared normal. There were no signs of meningeal irritation, and all reflexes were considered physiologic. The liver edge was palpable but did not seem enlarged; the extremities were obviously wasted.

Routine hemogram showed a hemoglobin level of 14.5 gm. and a white blood count of 15,000 per cubic millimeter, with 46 per cent polymorphonuclear leukocytes. Routine urinalysis was negative except for 1+ sugar; blood sugar, 136; urea nitrogen, 7 mg. per cent; and chlorides, 112 mEq. per liter. Sickling preparations were negative.

On admission, the patient was thought to have some form of acute gastroenteritis, perhaps slight residual arrested hydrocephalus, obvious malnutrition, and moderate dehydration. Given intravenous fluids calculated for replacement and maintenance needs, he was noted on the following morning to be opisthotonic, with cogwheel rigidity of the extremities and symmetrically hyperactive reflexes. The pupils and eye grounds again appeared normal and the blood pressure was unchanged, so a spinal fluid examination was carefully done; opening

pressure was 260 mm., so only a small amount of fluid was removed. No abnormalities were noted in levels of sugar or protein, cell count, and cultures.

The patient's status deteriorated rapidly to typical "decerebrate rigidity," with coma and recurring tonic fits. Repeated urinalyses again showed occasional slight glycosuria, a 1+ Sulkowitch reaction, and positive tests for coproporphyrins.

7. Until two weeks of age, this infant had been completely well. A diaper rash then developed, for which cortisone ointment, bichloride-of-mercury diaper rinses, and baking soda powders were prescribed elsewhere. Within three days, the rash was much improved, but the baby then had loose stools with occasional blood flecks, leading to a diagnosis of anal fissure, for which half of a rectal suppository (Medicone) was prescribed. Two hours later, the baby exhibited a peculiar color, which led the family physician to refer his patient to the hospital.

On admission, the infant was obviously cyanotic but in no apparent distress. Temperature was 99° F.; pulse, 160; and respiration, 88. There were residual healing impetiginous lesions about the buttocks and a very small anterior anal fissure. Urinalysis was negative; hemoglobin, 7.6 gm.; and white blood count, 9,000, with a normal differential.

8. This 2-year-old boy apparently had been perfectly well until sixteen hours before admission, when his mother noted that he was "breathing hard." Shortly thereafter, he vomited several times, so she took him to the family physician, who found nothing unusual and advised aspirin and castor oil. After a single aspirin tablet and 2 tsp. of castor oil, the child's condition further worsened, and he "got very sleepy." Again the physician was called; he found the child unconscious and referred him to us.

On admission, the child appeared moribund and comatose, with rapid, deep, panseless respirations, fixed pupils, and hyperactive tendon reflexes but absent superficial and corneal reflexes. There was no response to painful stimuli, and he was conspicuously hypotonic. Temperature was 97° F.; pulse, 180; respiration, 45; and blood pressure, 150/60.

9. A 9-year-old girl had been seen in the outpatient department over a three-day period for mild but otherwise typical gingivostomatitis, and her oral lesions had responded adequately to the usual symptomatic measures prescribed.

She returned on the third day because of severe leg cramps. Examination revealed all classical evidences and confirmatory signs of tetany. Qualitative test of the urine revealed no calcium. Serum calcium was 4.8 mEq.; pulse, 73 mg.; fasting blood sugar, 52 mg.; blood urea nitrogen, 14 mg.; and CO_2, 31 mM.

And now the answers:

1. Immediate suspicion of phosphate-ester poisoning led to aggressive inquiry and denial, despite which the child was promptly gavaged and vigorously bathed; intravenous atropine was given in doses up to 0.5 mg. every twenty minutes. Meanwhile, the father had been sent to the aunt's house, from which he shortly returned with an opened package of 25 per cent parathion. At a cumulative dosage of 3.6 mg. of atropine, the little girl was wide awake. Her reflexes were obtained, and her pupils were partially dilated. The drug was then tapered off and titrated against symptoms, while she made a completely uneventful recovery over a period of three days. Cholinesterase levels, very low in both red cells and whole blood at admission, gradually returned to normal (expressed as 1.5 to 2.8 mM. of acetylcholine hydrolized for whole blood and 0.7 to 2.2 mM. for red blood cells) as she improved clinically.

2. This reserpine syndrome is now reasonably familiar, this drug being commonly employed in treatment of preeclampsia nowadays. While it may be alarming, it is rarely lethal unless complicated by other insults, injuries, or anomalies. Babies have responded nicely to supportive measures, mild stimulation, and use of common nose drops.

3. The mother had taken "about two dozen" aspirin tablets *daily* for at least two weeks for a toothache and had not confided this information to her obstetrician! We have no information yet as to (1) the frequency of salicylate intoxication in newborns as a cause of bleeding or respiratory distress, much less the frequency of other manifestations that might be expected or (2) the distribution of salicylate in body fluids of the fetus or newborn after transplacental transmission. A catheterized urine was strongly positive for salicylate but was otherwise normal; the blood level was 8.5 mg. per cent just before the baby died at 30 hours of age.

Irrelevant to this discussion was the failure of measures employed in salicylate intoxication, management of hemorrhagic disease, or respiratory distress syndromes. The interesting point for speculation is the frequency with which congenital salicylism *may* exist or be at least partially accountable for some such distressing examples of perinatal wastage.

4. The cause for this methemoglobinemia was disclosed when the pharmacist was called, to discover and readily admit that he had inadvertently but undoubtedly put potassium chlorate rather than potassium chloride into the electrolyte mixture! Despite vigorous attempts at oxygenation, together with intravenous administration of ascorbic acid and methylene blue and an exchange transfusion, the patient died. Legal and philosophic implications in such an "honest error" leave much food for thought.

5. Despite vigorous denial of any such possibility, the physician held the conviction that this child had arsenic poisoning and therefore, on purely clinical grounds, initiated therapy with dimercaprol (BAL); analyses of stool, urine, and vomitus confirmed this impression. An aggressive search was then made for possible sources of arsenic in the child's environment and yielded only the information that the child *might* have eaten a packet of petunia seeds which the gardener in the park had been planting at the time she had been there playing. None of these seeds remained for analysis, though it was promptly learned that dry seeds are often sprayed with fungicides or insecticides for preservation, usually with mercurials or arsenicals. So far, our efforts to trace, through several national agencies, this interesting source of poisoning in children have been fruitless.

6. The presence of coproporphyrins in the urine led to further inquiries, revealing that the child had been eating paint scrapings for two weeks before admission.

Despite efforts to control his intracranial hypertension with hypertonic glucose, urea, and salt-poor albumin, along with attempts at chelating the circulating lead, there was no response, and he died within twelve hours of the time diagnosis was established. The important

autopsy findings consisted of massive cerebral edema with herniation of the cerebellar tonsils through the foramen magnum, focal atelectasis, and bronchopneumonia. The level of lead in the serum was 3.5 γ per cent and in the cerebral tissue, 84 γ per cent!

7. Methemoglobinemia was promptly established and attributed to ethylaminobenzoate (Benzocaine), of which about 60 mg. are contained in each of these suppositories. Infants seem more susceptible to methemoglobinemia than do adults, probably because of relative immaturity of the methemoglobin-reductase system, dependent on diphosphopyridine nucleotide.

Cyanosis and methemoglobinemia gradually cleared following an infusion of glucose and water; the methemoglobin level was 48 per cent at admission, 44 at three hours, 15 at sixteen hours, and only 4 per cent at forty hours.

8. Despite a negative urinalysis, including the qualitative test for salicylates, it was considered that this *had* to be salicylate intoxication, and peritoneal dialyses were initiated immediately after drawing blood for appropriate chemical determinations. The initial spinal fluid was entirely normal, as were the values for blood sugar, urea nitrogen, potassium, sodium, and chlorides. The blood salicylate level was returned at 44 mg. per cent; *p*H, 7.38; CO_2, 4 mEq.; and pCO_2, 15 mm.; subsequent salicylate tests of the urine were strongly positive. With dialysis, the patient's salicylate levels decreased stepwise to 21 mg. per cent at thirty-six hours, when he was clinically well and chemically "intact." He was alert and much improved, however, six hours after dialysis was started.

Subsequently, it was learned by paternal "detective work" that the child had probably gotten into and consumed at least 16 aspirin tablets about three hours before onset of the first symptom of "breathing hard." Whether because of laboratory error, *p*H of urine, or variations in distribution in body fluids, this is the third time we have seen such an initially false-negative test for salicylates in the urine. We believe that a hyperventilating, comatose child in the toddler age group deserves such prompt treatment for salicylate poisoning before proof of diagnosis when diabetic acidosis and increased intracranial pressure or central nervous system hemorrhage can be reasonably and promptly excluded.

9. On the advice of friends, and for several days before our therapy for the stomatitis was started, the mother had given this girl large but unmeasured amounts of baking soda. She hadn't volunteered this crucial information, and no one had inquired into such a possibility, until the occurrence of tetany led immediately to the obvious question! Everyone, we hope, learned something from the rather dramatic experience.

These conspicuously abbreviated protocols obviously do not contain all the details so commonly confusing or misleading in the actual clinical problems as they are encountered. The complete records were purposely "boiled down" in an attempt to emphasize the reasonably characteristic sequence of symptoms and physical findings in poisonings in which the possibility of such was unknown or even denied.

A SWALLOWED FOREIGN object, usually found in the esophagus, stomach, or large bowel and infrequently in the duodenum or lower small bowel, is rarely an immediate serious threat to the patient. Examination in the outpatient department and watchful waiting for a month or more, with another examination to make sure of elimination, are often adequate. Unusual delay in passage, however, may justify operation.

The most common points of arrest in the respiratory tract are the (1) cricopharyngeus, (2) aortic arch, (3) left main stem bronchus, and (4) lower portion, just above the diaphragm. Unless the object has widespread points, like an open safety pin, and is at or above the cricopharyngeus, 0.5 to 1 oz. of mineral oil given orally often will dislodge the foreign body and facilitate passage into the stomach. If the oil is unsuccessful, the delay is not detrimental and endoscopic examination can be performed.

When the foreign object is in the stomach, operation should be postponed to allow sufficient time for spontaneous passage. When the object has traveled beyond the pylorus, further progress ordinarily is rapid. A long foreign body that fails to navigate the short arc of the duodenum and hangs in a fixed position for a few days should be removed by operation. Anatomic anomalies anywhere in the alimentary tract may obstruct passage and require surgical correction. Objects in the rectum should not be removed digitally because of possible perforation.

G. N. SCATCHARD, D. O. DUSZYNSKI, R. W. MUNSCHAUER, and Y. RAMON PEREZ: The ingested foreign body. New York J. Med. 61:230-234, 1961.

Irvine McQuarrie, M.D.

Clinician, Investigator, Educator, and Beneficent Friend of Humanity

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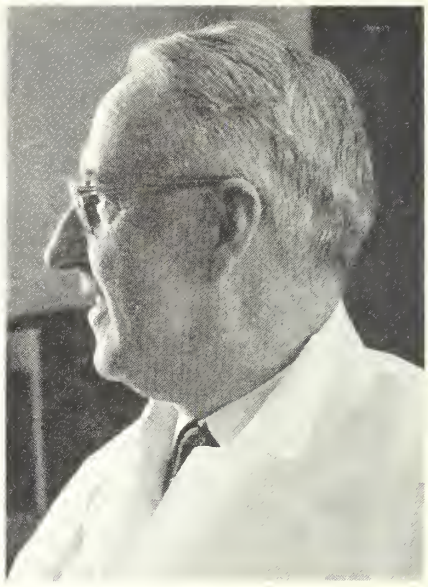

When Dr. Irvine McQuarrie reached his silver anniversary of service to the University of Minnesota in 1954, he was honored as few men before him have been, with a tribute which symbolized the philosophy of his life and his career-sharing with others. All who knew Dr. McQuarrie, then professor and chairman of the Department of Pediatrics at the University, agreed on the type of celebration that was to be a living testimonial of their high regard for him.

They chose a three-day pediatric grand reunion, which was held on the University campus. More than 200 pediatricians from all parts of the United States were in attendance. The celebration carried out the true McQuarrie tradition, for it was highlighted with a scientific program held jointly with the annual meeting of the Northwestern Pediatric Society. The program "shared achievements" by offering 39 scientific papers, including 14 presented by title. There was a compilation of papers by former students and associates of Dr. McQuarrie. Of the 26 papers read during the three days, 24 were contributed by these former students, now serving in full-time academic positions throughout the country. The papers were their acclaim to their "Chief," who had been largely responsible for the decisions of most of them to go into pediatrics and who had unselfishly provided the necessary support and guidance.

The grand reunion made history on the campus of the University of Minnesota in that it was recorded as being the first scientific meeting to be held in the amphitheater of the new Mayo Memorial Building. The reunion brought further acclaim to Dr. McQuarrie in the announcement of the establishment of a McQuarrie Pediatric Fund, to provide money for needs of the department not met from current sources. This fund came into existence through the efforts of a committee of founders, friends of the Department of Pediatrics and of Dr. McQuarrie. At the time announcement of the fund was made, more than $50,000 had already been raised from contributions and pledges.

The committee of founders also acted on the purposes of the McQuarrie Fund. They included provision for an annual lectureship in pediatrics in his honor; occasional pediatric fellowship stipends in unusual circumstances; certain items of equipment that might be needed for the department and other specific research needs, which may be stipulated by the donor; and other purposes within the department of pediatrics at the University of Minnesota as approved by the trustees of the McQuarrie fund.

The fund was described as a contribution to strengthen the University's Department of Pediatrics and to encourage those interested in pediatric education and research. It was to serve in the support of activities to extend pediatric knowledge and with the intent of contributing to the health and welfare of children. These purposes are those to which Dr. McQuarrie devoted his entire professional life. Trustees for the fund include the chairman of the Department of Pediatrics, chairman of the McQuarrie Fund Committee (sponsor of the fund), and a member of the Northwestern Pediatric Society appointed annually by its president. Trustees first named to serve on the fund committee were John A. Anderson, Minneapolis; George Kimmel, Red Wing, Minnesota; and the late Erling S. Platou.

The grand reunion program called for an open-house reception in the new McQuarrie lounge and library on the fourteenth floor of Mayo Memorial

Building, the pediatrics department's headquarters. Here again was an example of the Chief's sharing—Dr. McQuarrie had contributed his library of medical books and bound journals to the pediatric library.

Speakers at the sessions, in addition to those who read papers, were Drs. L. Emmett Holt, a former classmate of Dr. McQuarrie at Johns Hopkins University and friend and colleague for many years; Lee Forest Hill, fellow charter member of the American Academy of Pediatrics and fellow pediatric educator; and Roger L. J. Kennedy, professor of pediatrics, Mayo Foundation, University of Minnesota, and, at that time, president of the American Academy of Pediatrics.

As an outgrowth of the scientific sessions and the interest manifested in the reading of the papers, the grand reunion was made even more memorable by the papers being compiled in book form under the title, *Essays in Pediatrics*, in honor of Dr. Irvine McQuarrie. The volume was edited by Dr. Robert A. Good, research professor of pediatrics, Variety Club Heart Hospital, and an associate of Dr. McQuarrie since 1945, and by the late Dr. Erling S. Platou (Lancet Publications, Inc.). Many of the papers were published in THE JOURNAL-LANCET, the official publication of the Northwestern Pediatric Society. A tribute to Dr. McQuarrie by J. L. Morrill, president of the University of Minnesota, appears among the first pages of the book and includes the following excerpt: "Since little children are the living potential of the future, any contribution to the science of pediatrics has special significance of the whole challenge of medical teaching and research to a university committed in all its work and outlook to the better time-to-come. It is with this thought that we pay tribute to our distinguished colleague, Dr. Irvine McQuarrie."

EARLY LIFE

Dr. McQuarrie was born April 20, 1891, in Silver Reef, Utah, son of Robert Gray McQuarrie and his wife, the former Charlotte Anne MacFarlane. His grandparents, having heeded the pioneer West's beckoning allure, had left their native Scotland many years before. Whenever colleagues at the University of Minnesota asked Dr. McQuarrie about spelling his name Irvine with an "e" instead of "g," he would twinkle and reply, "Ask Dr. Stewart Thomson of the School of Public Health faculty about that." And Dr. Thomson, also of Scotch descent, always dutifully obliges with the following explanation: "During a visit to Scotland, I sought out the location where Dr. McQuarrie told me his ancestors were from. Down in the southwestern part of the country I found the town of Irvine, and the explanation of the spelling of his name." He notified Dr. McQuarrie of his discovery, sending a note, along with some sprays of heather, from the spot.

Young Irvine's father operated a gold mine. The boy spent many of his summers searching for and tracing streaks of gold ore. With this early experience and background, it seemed fitting that he go in for mining engineering at college. This he did, and, in 1915, he received a B.A. degree from the University of Utah.

Dr. McQuarrie married Miss Vira Perkins, also from a mining family, with similar background. There are 3 daughters—Mrs. William M. Balfour (Oane), Lawrence, Kansas; Mrs. A. Boyd Thomes (Maris), Minneapolis, Minnesota; and Mrs. Richard Nolte (Jeanne), Riverside, Connecticut.

EARLY MEDICAL CAREER

In the spring of 1915, upon graduation from college, McQuarrie changed the course of his career from the pursuit of mining to the study of biologic sciences. After receiving a Ph.D. degree in experimental medicine and completing two years of medical school and two extra years of research at the Hooper Foundation for Medical Research at the University of California, he went to Baltimore to attend the Johns Hopkins University School of Medicine. Dr. George H. Whipple was one of the outstanding men under whom he worked and who influenced him in his career while on the staff of the Hooper Foundation of the University of California as a research fellow. In addition to Dr. George H. Whipple, other world-renowned men at the University of California at that time were Herbert M. Evans, Phillip E. Smith, George W. Corner, Walter Bloor, and T. Brailsford Robertson, who likewise influenced his life and career. As Dr. McQuarrie himself was, for so many years, a pillar in encouraging students to go on in pediatrics, so he was guided by Dr. John Howland and other men distinguished in the field of pediatrics.

In 1921, he became affiliated with the Henry Ford Hospital, Detroit, first as house officer and, in 1923, as director of the section of endocrinology and metabolism.

By 1924, Dr. McQuarrie took the step to continue in the field of children's diseases, in which he became a dedicated worker. At Yale University, as an instructor in pediatrics, he was associated with Drs. Edwards A. Park and Grover F. Powers. He returned to Henry Ford Hospital as chief pediatrician, but not too much time passed before he was influenced by Dr. Whipple to return to university work, this time at the University of Rochester, New York.

Dr. McQuarrie's ventures had so far taken him from Utah to Berkeley, California, to Baltimore, Maryland, to Detroit, Michigan and to Rochester, New York. In 1930, he came to Minnesota as professor of pediatrics and remained as head of the department until 1956, the year of his retirement. Before coming to Minnesota, Dr. McQuarrie had become well-known for his proficiency in internal medicine and combined work on children's diseases. His research on convulsions at Henry Ford Hospital had already attracted much attention and was one of the many outstanding qualities which made him desirable to head the University's pediatrics department at Minnesota.

Honors came to him during and after his quarter of a century at Minnesota. One of the recognitions was the John Howland Medal and Award of the American Pediatric Society at the sixty-eighth annual meeting, May 8, 1958, in Atlantic City.

The introduction and presentation were made by Dr. Arild E. Hansen, a former colleague and friend, at the University of Minnesota from 1930 to 1944, now at Children's Hospital in Oakland, California. In the introduction, Dr. Hansen told of the early work of Dr. McQuarrie and also of the years of his association with him. He told of many of the qualities which made Dr. McQuarrie one of the "greats." He said, "Dr. McQuarrie believes that man is endowed with abilities to detect new things and is morally obligated to learn to understand life. To this end, he recognized that Nature herself supplies the clues but that the experiments of Nature must be studied so that man can advance." Dr. Hansen told how, by Dr. McQuarrie's following this philosophy all through his professional career, he made many great strides in pediatrics, both in its early development and after he came to Minnesota; how Dr. McQuarrie had recognized the importance of a closeness between the instructors and students and of the direction of the latter's career being guided throughout by the generousness of great physicians in sharing their knowledge and advice.

Dr. Hansen repeated a story that has long been a favorite on the campus: "One day a fine older woman came to the University to talk to someone about 'heart disease.' After having been given a sort of 'run around' by a number of other faculty persons, she landed in Dr. McQuarrie's office, she was listened to, and she, in turn, listened. Not too long after this visit and other happenings of similar nature, the Department of Pediatrics was the recipient of an endowment of over one and a half million dollars."

Dr. McQuarrie can be credited with sending to all parts of the country many fine trained pediatricians now holding professorships, directorships, or other high posts in educational institutions and hospitals. Dr. Hansen said, "In a routine photograph of the pediatrics staff at the University of Minnesota in the peaceful 30's, we find that some 50 per cent of the physicians there are nursing careers in science and teaching a decade later. There are no less than two score men who, in part or wholly, have been induced to follow the McQuarrie educational tradition, a dozen of whom occupy positions as heads of departments or the equivalent."

Dr. Hansen concluded his introduction with the following: "One of God's gifts to mankind is that energy cannot be destroyed, it can only be transferred from one form to another. In the pediatric world, John Howland stands out because of his works and because of his inspiring influence and spirit. Many received direct inspiration from this remarkable person. Today, we are honoring one who, in spite of his short exposure, received his full share and practiced the idealism for which Dr. Howland stood. Irvine, all of us, especially those of us who have been activated to live lives beyond our congenitally endowed potentialities, are grateful to you. We are happy to have you honored by receiving the medal which was named after one of the men who influenced you to make this world better and happier, because you have been what you are—an activator."

Dr. McQuarrie was always ready to give credit for his many accomplishments to the encouragement of scholarly medical teachers who served as mentors to him. A few of the many were Drs. Whipple, Howland, Evans, Corner, Park, Powers, Gamble, Kramer, Shohl, Ross, and Tisdall. In his response, Dr. McQuarrie said, "It is quite superfluous to emphasize the extent to which Dr. Park's direct influence contributed to my becoming established in the pediatric field. Through informal conversations carried on with him through long hikes in the woods and hills around New Haven, one was bound to acquire a lot of exact knowledge and Parksian philosophy. Similar associations with Dr. George Whipple, both before and after this period, first at Hooper Foundation and later at the University of Rochester, were invaluable."

OTHER ACCOMPLISHMENTS

This sharing of himself with others was Dr. McQuarrie's philosophy not only with his colleagues and students but also with his patients and their parents. The present century has been called the golden age of medicine, and if a list were to be compiled of the many prospectors in the field, Dr. McQuarrie's name would be among those who had gathered the most nuggets. In one of the papers printed in the volume, *Essays on Pediatrics*, the writer told of the ever-increasing responsibilities that came to Dr. McQuarrie and that much work had to be carried on by his associates. Of these young men, he wrote, "it is perhaps the brood of young pediatric eagles that he has raised and inspired that will be his greatest monument." The talents and vision of Dr. McQuarrie played a dominant role in the creation of the Minnesota Clinic, which has become an influence throughout the country and beyond.

In 1940, Dr. McQuarrie was a visiting professor of pediatrics at Peking Union Medical College. He made a three-month study of medical education, research, and hospitals in Japan for the Rockefeller Foundation in 1947.

Whenever Dr. McQuarrie's name is mentioned on campus or at many medical institutions throughout the country, the same reaction comes—"What a kind, wonderful man! Such talent, but never too busy to take time out for anyone who seeks him, whatever the problem." Those who worked with him in the pediatrics department tell of his being a "canny Scot," always alert to the expenditures but always willing to improve any facility when necessary for the good of the work.

Dr. McQuarrie was a prolific writer all through his professional career and published approximately 150 articles. He was editor-in-chief of *Brennemann's Praetice of Pediatries* and associate editor of The Journal-Lancet for approximately thirty years, the *Journal of Pediatrics, International Medical Digest, Quarterly Journal of Pediatrics, GP, Postgraduate Medicine,* the *Amerieau Practitioner,* and *Archives of Physieal Medicine.*

He was 1952-53 president of the American Pediatric Society and co-founder of the Society for Pediatric Research and the American Academy of Pediatrics. He was a member of 17 other American societies and an honorary member of 10 foreign organizations.

His great love for children was manifested not only in his constant work on childhood diseases but in his gentleness with patients. Miss Dorothy Jones, pediatrics recreation leader, Variety Club Heart Hospital, who came to the University the same year as Dr. McQuarrie, in 1930, tells of his great humbleness and sincerity in the presence of children. Once, when the doctor was making the rounds in the hospital, a small boy, the proud possessor of an autograph album, hailed him and asked for his autograph. The doctor smilingly consented and, after writing a note for the lad, signed it merely, Irvine McQuarrie.

Nor did his love for the outdoors change from his youthful prospecting ramblings in Utah. He owned a farm close enough to the University vicinity that he and his family could spend weekends and vacations.

Dr. McQuarrie retired from the University of Minnesota in June 1956, after having headed the University's pediatrics department since 1930. His retirement did not mean that he was to rest on his laurels, write his memoirs, and merely pleasure himself. He and Mrs. McQuarrie left almost immediately for the West and then Hawaii, where a new venture was waiting. Our new state had invited Dr. McQuarrie to become Director of Research at Kauikeolani Children's Hospital, Honolulu, where he served for the remainder of 1956 and 1957. Dr. and Mrs. McQuarrie revisited Hawaii in 1959 to attend the fiftieth anniversary celebration of the hospital. On his return to the mainland, he became Director of Research at Bruce Lyon Memorial Research Laboratory of Children's Hospital for the East Bay, Oakland, California. In addition to this title, he was honorary research consultant for the pediatrics department, University of Minnesota, and Kauikeolani Children's Hospital, Honolulu, Hawaii.

On November 20, 1960, Dr. McQuarrie had a cerebral hemorrhage, with total aphasia and corresponding paralysis. He and Mrs. McQuarrie returned to Minneapolis on January 20, 1961, and he died in the University Hospital on September 9, 1961.

PERSONAL GLIMPSE

Mrs. A. Boyd Thomes, 1 of his 3 daughters, kindly consented to provide the following glimpse into the life and professional career of her father and of his charming wife:

"Fifty years ahead of the current trend toward early marriages, Dr. McQuarrie married Vira Perkins, his high-school sweetheart. The first year after marriage, he continued his studies at the University of Utah, while she taught school to provide income and to repay some of the money they had borrowed to finish college. In his introduction of Dr. McQuarrie at the John Howland Award presentation in 1958, Dr. Arild Hansen referred to Mrs. McQuarrie as 'an attractive, capable and gracious "guide" of unlimited potential energy . . . who was similarly reared in an environment where adventure and pioneering were tantamount to life itself. To Vira, whom nature endowed with charm and perpetual patience, must be credited the understanding and indispensable role of fostering the development of her husband's career.'

"Her vigorous interest in political and community life was a fine complement to his scientific career, and she pursued it with comparable thoroughness and integrity. On several occasions, she was cited as one of the outstanding women of Minneapolis, and, upon their departure for Hawaii in 1956, a 'Statement of Appreciation' was presented to her by the Citizens League of Minneapolis and Hennepin County in gratitude and commendation for her services in the broad public interest.

"The early struggles for economic stability and academic proficiency did not leave Dr. McQuarrie much time to engage in leisure-time activities. Neither his golf game nor his wistfully voiced desire to 'learn a musical instrument' ever took firm shape. His hobbies, as it turned out, were his home and family.

"No doubt it was his boyhood background (the family orchard in southern Utah produced grapes, figs, almonds, and peaches) that sparked his interest in shrubs. At any rate, he was certainly the most enthusiastic and abandoned pruner in southeast Minneapolis. The two aged apple trees in his backyard were gradually reduced to cactus-like stubs, which eventually, out of sheer chagrin, he was forced to remove altogether. His yearning for 'a few acres' afforded him many happy visions of productive enterprise, though most of his pipe dreams foundered on the shoals of 'if only I had 6 sons. . . . ' His family always felt that he had been spared much disillusionment by this dearth of boys—who might not have shared his enthusiasms—and that the consolation of his 3 daughters more than made up for such unfulfilled desires.

"Birth dates and graduation dates, daughters and degrees, kept pace. Oane, the eldest child, was born the same year Dr. McQuarrie got his degree from the University of Utah and was awarded the Thompson scholarship; Maris, at Ph.D. time at the University of California and the Hooper Foundation Fellowship award; and Jeanne, hard on the heels of his M.D. from Johns Hopkins. The relationship with

his 3 little girls was full of tenderness and affection—and frequent picnics, storytime, and playtime provided happy respite from his work. Oane called his study bones 'daddy's dolls;' Maris, on one of his baby-sitting afternoons in Baltimore, protected, 'Daddy, you shouldn't give us cold milk! You know Dr. Holt says children shouldn't have cold milk.' And when he worked at the research laboratory at Yale or the University of Rochester on weekends, Jeanne made endless muddlers and big bubbles with glass tubing and bunsen burners.

"He drew horses and played horse. He told stories of when he was a little boy and instituted expeditions and adventures that provide his grandchildren now with stores of insight into his own and their mother's childhoods. Every summer, the family set out in one direction or another in tourist knickers and Model A's, in overalls and Essexes, to see Canada or New England, a national park, or the old stamping grounds in Utah or California. These trips were always rich in adventures, if not luxuries. And though the boiling radiators and peanut butter–and–tomato sandwiches loom large in retrospect, the physical and historic impressions are equally indelible.

"For several years, Dr. McQuarrie had watched with great interest and admiration the career of his uncle, M. J. McFarlane, one of his high school teachers who subsequently became an outstanding practicing physician and surgeon. During these same years, he had observed the onset and uninterrupted progress of his mother's illness with chronic arthritis, a disease for which, at that time, there was no more effective treatment than repeated doses of aspirin for relief of pain.

"Twin desires—to emulate his uncle and to contribute to the relief of suffering—not in his mother's case alone but in other disease areas as well, stimulated his inspirable nature to do more than just think about these problems.

The pursuit of a scientific career conflicted with the obligation to provide for his family and, at the same time, to 'get on in the world.' The financial burden of four years of regular premedical education, plus a sizable debt already incurred to finish college, loomed large—almost too large.

"It was at this juncture that good fortune intervened. What has since become one of Dr. McQuarrie's abiding interests, namely, scholarships for deserving and promising young scholars, operated in 1916 to make possible the realization of his own ambition. A competitive scholarship for Utah students at the University of California had been established by the parents of Willard D. Thompson, a Utah boy who had died while still a student at the university. McQuarrie applied for and was awarded one of these coveted scholarships. This enabled him to enroll in the University of California Graduate School, where he obtained a doctorate degree in pathology and biochemistry.

"Dr. McQuarrie was always on the lookout for and responsive to opportunities for enlarging and enriching experiences, conscious of the necessity both for education and the means of acquiring it. His hopes for his family's well-being seemed secure with the acquisition of 3 sons-in-law: Dr. William M. Balfour, research associate in physiology at the University of Kansas at Lawrence; Dr. A. Boyd Thomes, a practitioner of internal medicine in Minneapolis and a clinical associate professor of medicine at the University of Minnesota; and Richard H. Nolte, director of the Crane Foundation's Institute of Current World Affairs in New York."

TRIBUTES

Dr. McQuarrie was held in high reverence by all who have worked with him. Space permits brief expressions of only some of those whom he taught who became heads of departments of pediatrics.

The inspiration of Dr. McQuarrie was a result of his deep conviction about the academic, scholarly life. He rarely lost an opportunity and could always find time to discuss the simplest or the most complex problems in terms of what might be done to further our understanding of them. He could accentuate the thrill of discovery; it was this almost daily inspiration which emanated from Dr. McQuarrie that led many of his students, including myself, to seek to follow his example. He encouraged me to write and had the patience to edit every word and sentence. He would say, 'In ten or twenty years from now, John, you want to be proud of what you have written.' This has given me a sense of caution and regard for the truth which has been invaluable as the years sped onward. The inspiration for the academic and scholarly life he inspired in so many of us continues to fan out.

John M. Adams, M.D.
Chairman, Department of Pediatrics
University of California Medical Center

Dr. McQuarrie was a man who knew how to set standards for his colleagues and his students. His lucid explanations of the reasons behind his principles and practices as a clinician, an investigator, and an administrator were marvelously stated. I can remember nearly verbatim at least an even dozen of the impromptu commentaries which he found time to pass along to us at various stages of our training. More than anything else, I remain profoundly impressed with the effective image which he gave to us of the opportunities for service as academicians. No one doubted for a moment where he stood, and it was this clarity of purpose, combined with high standards and the ability to communicate with his colleagues at all levels, that inspired me to follow this career. I regarded Dr. McQuarrie with the greatest respect and admiration. He was a warm human being with great humility and dedication to the service of his fellow men.

Robert A. Aldrich, M.D.
Professor and Head, Department of Pediatrics
University of Washington

It has been suggested that a good teacher is one who says or does things you cannot forget. Dr. McQuarrie went beyond this in that I find myself on occasion judging things as I believe he did—applying his standards, as best I may, and yet trusting I will also be as tolerant. I doubt I would as easily put up with Allan Hill, Harvey

Hatch, and Bob Alway's leaving the Chief's rounds to pass time playing ping pong or billiards.

My wife saw another facet when we drove him to the Big Sur to see Dr. Gregg in 1955. We became increasingly worried about Dr. McQuarrie's apparent car sickness enroute—but, to our amazement, we found subsequently that he was most apprehensive as to the reception Dr. Gregg would give his idea for a medical school in Honolulu. We just could not imagine the Chief being overawed by anyone.

At least as important as Dr. McQuarrie's own teaching was the effect of those whom he had as loyal and effective associates. I suspect no little of their effectiveness was a further reflection of his expecting the best, so that one kept trying to improve so as not to disappoint him.

Robert H. Alway, M.D.
Professor and Head, Department of Pediatrics
Leland Stanford University

It is a real pleasure to have this opportunity to express an appreciation of Dr. Irvine McQuarrie for the privilege of many years of stimulating association and friendship. This privilege I enjoyed continuously from medical school days. My personal debt is so large, his gifts to me so many, that it is impossible to dwell upon all. Several aspects throughout this long period of association stand out clearly.

As you know, many of the leading practitioners of pediatrics, leaders in the field of pediatric education, research, and administration, who have been associated with him as friend or co-worker, are also indebted for guidance and stimulation that has directed them into their present pursuits. Through an intense and personal interest in the aspiration of his students and co-workers, he made each of us aware of potentials we did not as yet know were present. He keenly recognized in his associates a capacity to perform beyond that level which they had so far set for themselves. This helped his associates and students to define areas of study in which they needed strength and placed clearly before them the challenge presented by the vast areas of unexplored knowledge in medicine. This left no room for conceit, particularly when confronted with the continuous stream of unexplored problems in infants and children one encounters in everyday clinical medicine. This clearly emphasized that all physicians must be scholars continuously or they cease to be progressively effective.

Dr. McQuarrie's prodigious efforts to incorporate basic tools and new basic scientific knowledge into the clinical setting of pediatric care and research indicated to us that medicine can become a true science and that there is no separation of basic medicine from clinical medicine. Pursuit of any clinical problem always required an exhaustive search in depth for basic knowledge that could be applied at the bedside. As I now evaluate the present evolving structure of medicine, and anticipate the nature of its future, it is evident that Dr. McQuarrie saw, many years ago, the kind of knowledge that would be required of physicians to permit them to be increasingly effective. The unusual and incompletely explained conditions in infants and children which he chose to call "experiments of nature" now are being defined in terms of physical-chemical differences, molecular diseases, and inborn enzymic functional limitations. He foresaw a whole new future which will concern itself not only with the metabolic basis of clearly inherited diseases but with a fundamental knowledge which will help explain susceptibility to diseases. He clearly anticipated a truly scientific medicine.

Permeating the careers of each of his many students and co-workers now occupying responsible administrative teaching and research positions is clear evidence of the impact of these teachings and the tremendous, widespread influence that Dr. McQuarrie had on pediatric education and research.

John A. Anderson, M.D.
Professor and Head, Department of Pediatrics
University of Minnesota

In the years of our association at Minnesota, 1945 to 1949, Dr. McQuarrie's apt and favorite description of his department was that of a garden, in which his pediatric protégés could accomplish their potential growth and fruition. At the time, and ever since, I was aware of the very real privilege of living in that garden.

Those days were happy and richly stimulating for me, as for the several others in that situation. And these personal satisfactions stemmed directly from Dr. McQuarrie. His scholarly insight and vigor were consistently intermixed with a gentle and perceptive manner of leadership.

I gratefully join the Minnesota pediatric protégés in acknowledging Dr. McQuarrie's contribution to us and to our field as a person and as an inspiring example of humanity, scholarship, and leadership.

My appreciation continues, also, to the University and hospital which composed the environment within which such a man as Dr. McQuarrie could cultivate his garden.

James F. Bosma, M.D.
Formerly Professor and Head, Department of Pediatrics, University of Utah
now National Institute of Dental Research
National Institute of Health
Bethesda, Maryland

I first met Dr. McQuarrie in September 1943 in Minneapolis at the University and found him so replete with enthusiasm and zeal for scientific research and the zest for fullness and quality in living that it soon became apparent to me that here indeed was a splendid scientist, a great man. To know the Chief was to admire him for his dynamic personality and manly charm, to respect him for his tremendous appreciation of the possibilities of extending the horizons of medical knowledge, and to love him as a son for his munificent goodness, wise counsel, and keen sense of obligation for the comfort and welfare of all of his associates. To know and appreciate the fine qualities of Dr. McQuarrie, for me, has constituted a broadening experience infused with humility—an experience which I have proudly shared with my children and students. His contributions and stature in the field of experimental medicine are, of course, well-known and have spread his influence throughout this country and abroad.

E. Perry Crump, M.D.
Professor and Chairman, Department of Pediatrics
Meharry Medical College

Dr. Irvine McQuarrie's contributions to the field of pediatrics have been many and varied, always great. For me, however, one of his attributes stands out above all others—that of allowing a man to develop according to his own need and desires. Once Dr. McQuarrie decided

to add a new man to his staff, he supported him in every way possible but at the same time gave him complete freedom to pursue the course that best suited his own abilities. Among all the things that Dr. McQuarrie did and stood for in pediatrics, this was the most outstanding and important to me, and for his understanding, support, and guidance, I am very grateful.

Floyd W. Denny, M.D.
Chief, Pediatric Service
North Carolina Memorial Hospital

Other than birth and marriage, the most significant influence in my life was knowing Dr. Irvine McQuarrie. After several years in private practice, and just having returned from visiting pediatric centers in Europe, it was my good fortune to find an answer to a certain self-query concerning which lane I aimed to travel during my medical lifetime. As with most men, I had fully intended to pursue private practice and had chosen the field of pediatrics. At just the right time, it was my rare privilege to be introduced to Dr. McQuarrie. Although not yet in his 40's, he radiated charm and enthusiasm and preached the gospel of idealism. These qualities, coupled with his personal magnetism, influenced me, as well as many others, to consider seriously teaching and research as a life work in medicine. His never-ending desire to advance science and medicine had a great effect on pediatric life for the next three decades—not only in his own community but throughout many parts of the world.

In his intimate, personal conversations, he always demonstrated optimism for pursuing clinical investigation. To him, life itself was an experiment, and not to take full advantage of studying the experiments of nature was a disavowal of the assumption of Man's responsibility.

I cannot imagine anyone having a fuller, or more satisfactory, association than that which I had the pleasure of having during my fourteen years with him at the University of Minnesota. In assuming my duties to develop further the pediatric activities at the University of Texas school of medicine, there is no question but that his precepts were active in my attempts to carry on. Indeed, I was doubly rewarded—first to have had the opportunity to be with him in the flaming enthusiasm of his relatively early career and then, after another sixteen years, to succeed him as director of research in the Children's Hospital of the East Bay, after each of us had retired from our professorial positions. During the later years, the personal satisfactions were only exceeded by the thought-provoking gems which continued to break through during discussions concerning new ideas. Dr. McQuarrie felt that sound data are essential to man's advancement and that the ability to interpret them assists in the gratification which comes with the better understanding of life's infinite puzzle pieces.

Arild E. Hansen, M.D.
Director of Research, Bruce Lyon Memorial
Research Laboratory
Children's Hospital of the East Bay

I look back to my days with Dr. McQuarrie because of the inspiration gained from his management of problems. It has served as the driving force in my pediatric teaching. His interest in and warmth toward his men is something I will always remember.

Allan J. Hill, M.D.
(By Jane W. Hill)
University of Oregon Medical School

As the academic "offspring" of Dr. Irvine McQuarrie again signalize his inspiring example, it is appropriate to recall the Homeric admonition that few sons, indeed, measure up to their father and fewer still surpass him. This opportunity to include my own expression of appreciation and praise is most welcome.

In a lifetime devoted to the enthusiasms of teaching and investigation and crowned with achievement, he managed best to transmit the thrill and challenge of intellectual curiosity and the importance of the "quality effort." Those who came under his influence carried away this zeal as an integral part of their training, to be applied with equal aptness to the practice of medicine or the field of medical education and research. His impact was direct, personal, and evocative and lends emphasis to another ancient observation that, more than books and things, "men are my teachers."

Theo. C. Panos, M.D.
Professor and Chairman
Department of Pediatrics
University of Arkansas Medical Center

Looking back, it's continually amazing and stimulating to recall the bounding enthusiasm and genuine interest Dr. McQuarrie always displayed for the daily work as well as the long-term plans and objectives of each of "his boys." Realizing now, much more than then, the tremendous burden of administrative, teaching, and research obligations he continually carried so well, recollections of this inspiring attitude toward all we tried to do or did are particularly appreciated and still serve as a daily reminder of the faith he had, which we hope we all can now share in our *own* trainees and successors.

More than any other factor, I think his genuine and personal enthusiasm for each of us and our work explains why so many of us were stimulated to plan our professional careers along similar academic lines; though daily details and little anecdotes dim with time, this vivid recollection of his sparkle will remain as a continuing stimulus "to do unto others."

R. V. Platou, M.D.
Chairman, Department of Pediatrics
Tulane University School of Medicine

In reflection, it might be appropriate to consider which of Dr. McQuarrie's many fine attributes were chiefly responsible for his singular success as a leader in American pediatrics. Thinking over his enviable career and my own most pleasant contacts with Dr. McQuarrie, I feel that his accomplishments were only possible because of his ability to appreciate the future and to see well how it could best be served by highest academic achievements in his department and in the future activities of pediatrics. He well might have been considered an impractical dreamer by those with less ability than he to clearly see the future and with less willingness to accept the demanding challenge of achieving the highest goals of pediatric teaching and research. How well I remember his challenge to me when I joined the house staff of the University of Minnesota. During my first days there, Dr. McQuarrie often said that we must not concern ourselves with how pediatrics is practiced today—it is how pediatrics is to be practiced twenty years from now that is our responsibility. It was many years before I was able to realize that these were not the idle words of an unrealistic dreamer. That there would be those who would fail to appreciate fully a man of his

vision is understandable, but the appropriateness of striving to achieve such goals is attested to by the magnificent accomplishments of Dr. McQuarrie and the Department of Pediatrics at the University of Minnesota.

With each passing year, his influence, spread through his students throughout the country and, at the same time, his group at the University of Minnesota, became stronger and stronger. Young men were attracted to him and profited greatly from his situation and the opportunity he gave them to express themselves without interference through their investigative work and teaching assignments.

Dr. McQuarrie's retirement from the active scene of academic pediatrics was almost imperceptible. His influence now is as great as ever through the work and teachings of his many students. Although no longer on the wards or in the laboratory, in much of the United States, Irvine McQuarrie is still "Chief of Pediatrics."

Nathan J. Smith, M.D.
Professor and Chairman
Department of Pediatrics
University of Wisconsin

I remember Dr. McQuarrie as a people-watcher, in the same sense that others are bird-watchers. Throughout his term as professor at Minnesota, he watched, by day and night, with fascination, affection, and high hope, people.

He was a hard-headed, hard-boiled scientist in his own laboratory, self-critical and exacting with himself and his associates. But he was always willing to make concessions on behalf of the young fellow newly arrived and as yet untested, particularly the new young house officer. "Just wait and see," he would say, with the glee of a child before Christmas, "he's going to be good!" Sometimes he missed, but more times than any other chairman of his vintage can claim—many more times—he was right. This was an instinct of his, or a quick reflex, like the gift of instant perception that separates the superb bird-watchers from the tyros.

What Dr. McQuarrie had and used, as a kind of instrument, was an affectionate perception of quality in human beings. He took them all, as they came, with the same relish, zest, and fun. He delighted in his products, but here he was not the scientist; his was not the austere satisfaction of the botanist but the pleasure of the gardener.

Lewis Thomas, M.D.
Professor and Chairman
Department of Medicine
New York University–Bellevue Medical Center

Dr. McQuarrie holds a most unusual record in preparing physicians for high teaching and research positions. The following is an impressive additional list.

Adams, Forrest H.
Professor of Pediatrics
University of California Medical Center
Los Angeles

Adams, Paul, Jr.
Associate Professor, Pediatric Cardiology
Department of Pediatrics
University of Minnesota

Anderson, Ray C.
Associate Professor of Pediatrics
University of Minnesota

da Silva, Mauricio, M.
Medical Consultant
Pan-American Health Organization
Washington, D. C.

Dees, Susan C.
Professor of Pediatrics
Duke University

Diehl, Antoni M.
Associate Professor of Pediatrics
Pediatric Cardiologist
University of Kansas;
Cardiologist, Children's Mercy Hospital; Medical Director, Children's Cardiac Center, Kansas City, Missouri

Elwood, Paul
Medical Administrator
Kenny Rehabilitation Institute
Minneapolis

Ely, Robert S.
Assistant Professor of Pediatrics
University of Utah

Engel, Rudolph
Associate Professor of Pediatrics
Project Director, Child Development Study
University of Oregon

Erickson, Cyrus C.
Professor of Pathology and Microbiology
University of Tennessee

Good, Robert A.
American Legion Memorial Heart Research
Professor of Pediatrics
University of Minnesota

Good, Thomas A.
Assistant Professor of Pediatrics
University of Maryland

Grulee, Clifford G., Jr.
Associate Dean
Director of Graduate Medicine
Tulane University

Hilleboe, Herman E.
Commissioner of Health
State of New York

Jenson, Reynold A.
Professor of Psychiatry and Neurology and Pediatrics
Director, Division of Child Psychiatry
Department of Psychiatry and Neurology
University of Minnesota

Kelley, Vincent C.
Professor of Pediatrics
University of Washington and
Director of Research
Children's Orthopedic Hospital
Seattle

Lowe, Charles U.
Research Professor of Pediatrics
University of Buffalo

Luzzatti, Luigi
Associate Professor of Pediatrics and Preventive Medicine
Director, Pediatric Outpatient Department
Stanford University

May, Charles F.
Professor and Head of Department of Pediatrics
University of Iowa

Moss, Arthur J.
Associate Professor of Pediatrics (Cardiology)
U.C.L.A. Medical Center
Rambolt, Raymond R.
Director, University Hospital School for Severely Handicapped Children
State University of Iowa
Smith, Richard J.
Professor and Chairman
J. Hollis Miller Health Center
University of Florida
Ulstrom, Robert
Associate Professor of Pediatrics
University of Minnesota
Wannamaker, Lewis W.
Professor of Pediatrics
Career Investigator of the American Heart Association
University of Minnesota
Worthen, Howard
Associate Professor Pediatrics
Cornell University Medical Center
New York City, New York

Dr. McQuarrie's great goodness was not limited to his undergraduate and graduate students and his staff but extended to a host of others whom he was ever ready to assist and encourage. I personally was the recipient of innumerable acts of kindness and helpfulness, and words could never express my deep indebtedness to him.

Soon after his arrival as chief of the Department of Pediatrics at the University of Minnesota, I came in contact with him, through the kindness of Dr. Chester A. Stewart, also of pediatrics fame. For ten years, Dr. Stewart and I had been making longitudinal observations on tuberculosis in children, the results of which did not bear out a considerable number of current theories. Therefore, reports of these observations were meeting with considerable opposition, not only locally but from afar. When Dr. McQuarrie saw and analyzed our data, there was no question in his mind but that theories had been replaced by facts, whereupon he became a firm supporter of these newly established facts and without hesitancy cast aside previously held theories. That was approximately thirty years ago, and his support and teaching of these newly established facts were abiding.

Throughout the years, he lost no opportunity to promote our studies on pediatric tuberculosis, as well as on tuberculosis in adults. At every opportunity, he voted for research funds for that purpose. For many years, he was chairman of the Committee on Grants from the Research Fund of the Graduate School of the University. Throughout those years, his committee never failed to recommend the amount requested for our work, after which he would nearly always state that the request was far too small.

In 1951, he and William Braasch of the Mayo Clinic and Foundation, as members of the Executive Committee of the Minnesota Tuberculosis and Health Association, formulated a motion which, if passed, would provide a specified sum annually through the Greater University Fund for longitudinal studies in tuberculosis. There was no dissenting vote. Throughout the years, he took great interest in the accomplishments made possible through that fund.

For approximately a quater of a century, he was a member of the Editorial Board of The Journal-Lancet, always making valuable recommendations so as to improve the pediatric contributions of the journal. Indeed, for a number of years, he not only assembled but edited all the manuscripts for the special May issues on pediatrics.

When the time came for a multiple-authored book on tuberculosis and other communicable diseases, which had long been contemplated, it was Dr. McQuarrie who kindly consented to list the diseases which he considered most important and to name the physician he felt was best qualified to prepare each chapter. When the manuscript was completed, he wrote the introduction.

Several times each year from 1930 until his retirement, when one or more guest physicians from this country or abroad arrived, a small group of genial physicians assembled at 6 o'clock for an evening of discussion of mutual problems. The last of these sessions was an evening in October 1960, when Dr. McQuarrie was in Minnesota on a visit. He never failed to attend these sessions and was always the outstanding good-will ambassador.

After he returned to Minneapolis, although unable to speak, items pleasing to him elicited the same characteristic sparkle so familiar to his students. Throughout the preparation of this profile and of this special McQuarrie issue of The Journal-Lancet, that sparkle betrayed his deepest feelings and admiration for those whose letters of appreciation were read to him. He also exhibited a great sense of satisfaction when told of his former students having accepted invitations to contribute to this special issue of The Journal-Lancet.

Through his most exemplarly life and work, Irvine McQuarrie contributed mightily to the health and welfare of children everywhere. He informed, stimulated, and inspired large numbers of physicians through short and long periods of direct contact and many others through his contributions to medical literature who are working not only in this country but also in many other nations. The fires he kindled in them are burning brightly. From them, many others have been and will continue to be lighted, ever-increasing and extending knowledge, until Irvine's vision of generations of healthy children everywhere will be realized.

The author wishes to thank Miss Dorothy Riley for her assistance in the preparation of this manuscript.

Family Outbreak of Acute Nephritis Associated with Type 49 Streptococcal Infection

LEWIS W. WANNAMAKER, M.D., and

HOWARD C. PIERCE, B.S.

Minneapolis

THE DEVELOPMENT of acute nephritis among several members of a family within a relatively short period has been observed by a number of physicians.[1] The data from some of the better-documented instances in the literature[2–5] are presented in table 1. In these families, the attack rates of both respiratory disease and acute nephritis were high among the siblings. When urinalysis was performed in the clinically unaffected children, evidence of subclinical nephritis was often found. The interval from the onset of the first case of nephritis to that of the last in a family is not clearly indicated in all reports but appears to range from nineteen days to seven weeks.

The present report concerns a family of 7, seen at Minneapolis General Hospital, in whom acute nephritis developed in the father and in 4 of the 5 children within a period of three weeks. The renal disease was preceded by streptococcal infections, some of which were accompanied by scarlatinal rash. The nephritogenic strain of streptococcus has been identified as a new serologic type—type 49.

CASE REPORTS

Case 1. V. S., a 31-year-old truck driver, was seen in the outpatient clinic on August 16, 1953, because of exposure to scarlet fever. A culture of the throat on this visit was negative for beta hemolytic streptococci.

On September 6, he was admitted to the hospital. Two weeks previously—about one week after his outpatient visit—he suffered from a sore throat. Five days before admission, he noted swelling of the face around the eyes and discomfort in the back, followed the next day by nausea. The urine decreased in volume and he experienced frequency without dysuria, pyuria, or bloody or smoky urine. Two days before admission, he was treated for pyelitis with sulfisoxazole (Gantrisin). On the day of admission, he awoke with pain in the right upper quadrant and lower right anterior chest. His backache was more severe, particularly in the right costovertebral angle. He had minimal nonproductive cough and fleeting pains in the knees.

Past history revealed that he had been treated for syphilis, after which he became seronegative. He had had no definite urinary symptoms, but a 4+ albumin had been found in his urine one year before and he had previously had sudden onset of severe lumbar and costovertebral angle pain on the right.

Physical examination revealed a well-developed, well-nourished white male with a blood pressure of 125/95/65. An old choroiditis was noted in the inferior quadrant of the left eye. There was relative dullness to percussion over both bases and flatness over the lowermost portion of the right base. Moist inspiratory rales were heard over the right anterior inferior chest. The heart was not enlarged and there were no murmurs. The liver was down 3 cm. The spleen was questionably palpable. There was an appearance of swelling in the right upper quadrant, with tenderness in this area and over the rib cage. There was no muscle spasm or rebound. Minimal shifting dullness with a fluid wave was found. Minimal costovertebral angle tenderness to percussion was observed on the right.

Daily urinalyses for the first three days revealed a clear or slightly cloudy urine, with a specific gravity varying from 1.011 to 1.019, a trace of albumin, occasional granular casts, up to 15 red blood cells, and 22,010 white blood cells. Admission hemoglobin was 11.7 gm., and white blood count was 6,450, with 61 neutrophils, 35 lymphocytes, 2 monocytes, 1 eosinophil, and 1 basophil. Sedimentation rate was 53 mm. in one hour (Westergren uncorrected). Throat culture was negative for beta hemolytic streptococci. Sputum smears were negative on 3 occasions for acid-fast organisms but showed gram-negative diploeocci and gram-positive cocci in pairs, clusters, and chains. Gastric washings were also negative for acid-fast organisms. Blood culture was sterile. Blood chemistries included albumin, 4.2 gm.; globulin, 2.4 gm.; thymol turbidity, 7.8 units; and blood urea nitrogen, 22 mg. per 100 cc. Chest roentgenograms showed a normal-sized heart, with left ventricular prominence, bilateral pulmonary congestion, and free pleural fluid in the right hemithorax. The x-ray picture was considered consistent with congestive failure. The electrocardiogram showed a heart rate of 67 and a P-R interval of 0.17, with sinus rhythm. There was slight elevation of $ST_{1,2}$ aVF, and $V_{2,4,5,6}$. T waves were normal. Circulation time was thirteen seconds and venous pressure, 15 cm.

The patient had an afebrile clinical course. The blood pressure did not rise above 114/70. Daily urine volumes

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TABLE 1

DATA FROM SOME FAMILIES REPORTED IN THE LITERATURE

Author	*No. of siblings in family*	*No. with respiratory infection*	*Nature of respiratory infection*	*No. developing nephritis*		*Relationship of siblings with nephritis*	*Interval from onset of first to last case of nephritis*
				Clinical	*Subclinical*		
Thomson and Macauley[6]	8	8	"influenza"	4	?	1 brother, 3 sisters	? 1 month
Ernstene and Robb[3]	10	8	sore throat	6	0	3 brothers, 3 sisters	7 weeks
Schuricht[1]	11	7	scarlet fever	3	4	unknown	19 days
Tudor[5]	4	4	sore throat or URI	2	1	2 brothers, 1 sister	?

ranged from 800 to 2,000 cc. The patient was put on a low-salt diet and bed rest. His weight decreased by 10 lb. during the first three days of hospitalization. The urine sediment became negative on routine examination, and the sedimentation rate dropped to 23 mm. per hour. The patient continued to improve and was discharged on the eighteenth hospital day. An Addis count on discharge showed 252,778 casts, 22,993,750 red blood cells, and 8,125,000 white blood cells in a twelve-hour specimen.

Three weeks later, the patient was readmitted because "he needed rest" and because the sedimentation rate had risen to 37 mm. per hour. He had had a transient intercurrent sore throat four days before readmission. Physical examination revealed a blood pressure of 130/70. There was no edema and no costovertebral angle tenderness. Heart and lungs were negative. Chest roentgenogram showed a normal-sized heart, with no evidence of fluid or congestion. The electrocardiogram showed $ST_{1,2}$ aV_F, and V_6 still elevated. A pyelogram revealed normally functioning kidneys. Hemoglobin was 12.8 gm. and white blood count, 5,300. A throat culture revealed numerous colonies of beta hemolytic streptococci. A twelve-hour Addis count showed 305,000 casts; 57,318,000 red blood cells; and 1,894,000 white blood cells.

The patient received procaine penicillin for ten days in connection with dental extractions. He was discharged against advice but continued to do well except for tiring easily. An antistreptolysin-O titer on January 21 was 250 units, and a throat culture was positive for group A beta hemolytic streptococci. On February 8, 1954, approximately five months after the first manifestation of renal disease, his Addis count showed 19,733 casts, 155,277 red blood cells, and 2,094,222 white blood cells.

A physical examination on November 22, 1955, was negative. Blood pressure was 128/80. Hemoglobin was 13.5 gm.; white blood count, 5,800; sedimentation rate, 24 mm. per hour; blood urea nitrogen, 8 mg. per 100 cc.; albumin, 5.4 gm.; and globulin, 3.0 gm. Urine showed a trace of albumin, occasional red blood cells, and 1 white blood cell. Another urinalysis on January 11, 1956, showed 1+ albumin and very occasional red and white blood cells.

Case 2. Mrs. T. S., a 27-year-old white female, was admitted for delivery on July 18, 1953. She had had no prenatal care. Delivery was without complication. No symptoms referable to the ears were recorded on this admission, although she subsequently stated that she had a "running ear" that flared up with each pregnancy. On physical examination at the time of confinement, no discharge from the ears was noted and the tympanic membranes were reported as intact.

A routine urine examination on September 26 was negative.

On October 1, 1953, the patient was seen in the outpatient clinic with "sore ears" with yellowish discharge of one month's duration. A diagnosis of bilateral draining otitis media had been made one week previously, at which time group A beta hemolytic streptococci were isolated from both ear cultures. She was given 7 daily injections of penicillin. Ear cultures on this visit revealed staphylococci and Pseudomonas aeruginosa. The patient received, in succession, oxytetracycline (Terramycin) orally, streptomycin intramuscularly, and polymyxin locally. After one month of treatment, drainage stopped and the ears healed.

A throat culture taken on January 21, 1954, was negative for beta hemolytic streptococci. Antistreptolysin-O titer was 317 Todd units.

The patient was subsequently seen in the outpatient clinic on July 15, 1959, at which time hemoglobin was 12.1 gm.; white blood count, 10,100; and urine, negative. Two months later, she was admitted for removal of an adenomatous thyroid nodule.

Case 3. J. S. This white male infant was born on July 18, 1953, after an uncomplicated delivery. Physical examination was not remarkable. At 1 month of age, he had a granuloma of the umbilicus and was noted to be "fussy." At 2 months of age, hemoglobin was 10.7 gm. and white blood count, 9,200, with 27 polymorphonuclear leukocytes, 72 lymphocytes, and 1 monocyte. Blood urea nitrogen was 15 mg. per 100 cc. A twelve-hour Addis count showed no casts, 186,700 red blood cells, and 467,000 white blood cells. Antistreptolysin-O titer was 1,585. Antidesoxyribonuclease B (anti-DNAse B) titer was less than 10, and antidiphosphopyridine-nucleotidase (anti-DPNase) titer was 31. A throat culture taken on September 22, 1953, was reported as positive for beta hemolytic streptococci.

The patient received injections of procaine penicillin, 150,000 units daily for ten days. Throat culture taken on October 8, 1953, was negative for beta hemolytic streptococci. By January 21, 1954, the antistreptolysin-O titer had dropped to less than 50 units, and the other 2 antibody titers remained low. A follow-up on March 8, 1954, when J. S. was 8 months of age, revealed a normal male infant with a negative routine urinalysis and a negative throat culture.

On August 3, 1959, at 6 years of age, he was readmitted with other members of the family for evaluation. History and physical examination were negative. Hemoglobin was 12.9 gm.; white blood count, 15,900; sedimentation rate, 31 mm. per hour; and blood urea nitrogen, 15 mg. per 100 cc. Routine urinalysis was negative.

and a twelve-hour Addis count showed no casts, 65,000 red blood cells, and 65,000 white blood cells. Antistreptolysin-O titer was 625 units; anti-DNAse B, 500; and anti-DPNase, 420.

Case 4. N. S., a 17-month-old white female infant, was well until the day of admission to the hospital—August 23, 1953—when she became irritable and anorexic and developed a diffuse red rash on the abdomen. She had had no other recent illnesses except for a "running ear" two or three months previously, for which she had received no treatment.

On admission, rectal temperature was 103° F. Tongue and mucous membranes were not remarkable. There was diffuse redness of the pharynx, and there were moderately enlarged cervical nodes bilaterally. A scarlatiniform rash was noted over the abdomen, back, and inner aspect of the forearms and thighs. Hemoglobin was 11.3 gm. and white blood count, 9,700, with 77 polymorphonuclear leukocytes, 18 lymphocytes, 2 monocytes, and 3 eosinophils. Urine showed a specific gravity of 1.014, with no albumin and a sediment containing 1 red blood cell and 3 to 5 white blood cells per high power field. The admission throat culture was not interpretable because of plating on bad media, and a repeat throat culture taken after penicillin had been started was negative for beta hemolytic streptococci. N. S. was given an injection of 300,000 units of procaine penicillin, which was repeated on the following day. Within two days, the temperature had returned to normal and the rash had faded. The patient was discharged on the third hospital day.

One month later, on September 21, 1953, she was readmitted, along with other members of the family, for observation and diagnostic work-up. She had not been ill since the previous admission. Admission temperature was normal. Systolic blood pressure was 80; a diastolic pressure was not obtained. There was a mucoid discharge from the nose. Chest roentgenogram was negative. Hemoglobin was 10.2 gm., with 5,850 white blood cells and a differential count of 44 polymorphonuclear leukocytes, 33 lymphocytes, 9 monocytes, and 14 eosinophils. Subsequent differential counts showed from 1 to 7 cosinophils. Sedimentation rate was 54 mm. per hour. The highest blood urea nitrogen recorded was 19 mg. per 100 cc. Throat culture was positive for group A beta hemolytic streptococci. Antistreptolysin-O titer was 50 Todd units. Urine on admission showed a specific gravity of 1.008, with only a trace of albumin and 1 to 2 red blood cells per high power field. Subsequent urinary sediments revealed many red blood cells.

The patient ran an asymptomatic course. She received 300,000 units of procaine penicillin daily for ten days. The sedimentation rate gradually dropped to 15 mm. per hour. She was discharged on November 3, 1953.

On December 11, 1953, she was readmitted for five days because of the finding of 30 to 40 red blood cells in the urine. She was asymptomatic and received no therapy during this stay.

A throat culture on January 21, 1954, was positive for group A beta hemolytic streptococci, and the antistreptolysin-O titer had risen to 400 units. On February 24, 1954, she was treated for croup with penicillin. On March 8, 1954, she was seen in the outpatient clinic for follow-up, at which time she was asymptomatic. The physical examination was negative, and the urine showed only occasional red blood cells.

At 7 years of age, the patient was readmitted on August 3, 1959, for a further follow-up. History and physical examination were negative. Blood pressure was 100/60. Hemoglobin was 13.4 gm.; white blood count, 5,600; sedimentation rate, 19 mm. per hour; and blood urea nitrogen, 17 mg. per 100 cc. A routine urinalysis showed very occasional white blood cells, and a twelve-hour Addis count showed no casts, 230,000 red blood cells, and 2,000,000 white blood cells. Antistreptolysin-O titer was 500 units; anti-DNAse B, 317; and anti-DPNase, 380.

Case 5. J. S., a 2½-year-old white female, was admitted to the hospital on September 18, 1953. One week prior to admission, a sore throat had developed, but no medication was taken. During the week preceding admission, she was irritable and felt warm. For two days before admission, she did not eat well, and the urine was noted to be dark yellow. On the day before admission, she was noted to be puffy about the eyes, and some complaints of aching of the legs were recorded on the day of admission.

Physical examination on admission revealed a rectal temperature of 100.4° F. and a blood pressure of 108/70. The eyes were puffy and the abdomen was distended. The liver edge was 1½ fingerbreadths below the costal margin. There was a heat rash. Chest roentgenograms and electrocardiograms were normal.

Hemoglobin was 9.8 gm.; white blood count, 6,150, with 56 polymorphonuclear leukocytes, 40 lymphocytes, 3 monocytes, and 1 eosinophil; and sedimentation rate, 74 mm. per hour. On admission, urine was cloudy and yellow; specific gravity, 1.015; reaction, acid; albumin, 1+; and sugar, negative. There were 5 to 6 red blood cells, 8 to 10 white blood cells, and occasional granular casts in the sediment. Subsequent urinalyses showed many or packed red blood cells. Blood urea nitrogen was 22 mg. per 100 cc. on admission and rose to a high of 90 on the eleventh hospital day. A throat culture taken just before admission was positive for group A beta hemolytic streptococci. Antistreptolysin-O titer on admission was 1,000 Todd units and continued to rise to 3,170 units during the hospital stay.

On the third hospital day, the patient was vomiting and her temperature rose to 101° F. She became rapidly oliguric and passed only 80 cc. of urine from the third to the eighth hospital day, at which time the temperature spiked to 104° F. and the medial side of the left knee and an area over the adjacent thigh became red and painful. She remained oliguric until October 2, the fifteenth hospital day, when she passed 720 cc. of urine. She received procaine penicillin, 300,000 units daily, for ten days. A transient urticarial rash was noted six days after discontinuation of penicillin. The patient gradually improved and was discharged on December 22, after three months' hospitalization. At the time of discharge, she was asymptomatic, but the urine still showed 14 to 16 red blood cells and a trace of albumin.

One month later, on January 21, 1954, a throat culture was negative and antistreptolysin-O titer was 1,000. At follow-up examination on March 8, 1954, the patient had no complaints, physical examination was negative, and urine examination was negative except for 1 to 2 red blood cells and 1 to 2 white blood cells per high power field.

She was subsequently seen for several bouts of urticaria but was otherwise well. A follow-up hospital admission at 8 years of age, on August 3, 1959, revealed a healthy child with a blood pressure of 102/52. Hemoglobin was 11.8 gm.; white blood count, 7,400; sedimentation rate, 13 mm. per hour; and blood urea nitrogen, 18 mg. per 100 cc. Routine urinalysis was negative. A twelve-hour Addis count showed no casts, 630,000 white

blood cells, and 53,000 red blood cells. Antistreptolysin-O titer was 500 units; anti-DNAse B titer, 400; and anti-DPNase titer, 450.

Case 6. T. S. a 3½-year-old white female, was admitted to the hospital on September 7, 1953. She had had a sore throat two weeks before admission which had lasted for one week. There was no skin rash or fever, and no antibiotics were given. During the week before admission, she had a poor appetite, and for three days, her face had become increasingly swollen. No hematuria or fever was noted during this period.

Physical examination on admission showed a temperature of 98.6° F. and a blood pressure of 126/90. The face was puffy and the swelling was particularly pronounced around the eyes. A nontender, 1½ × ½-cm. node was felt in the anterior neck. The liver was down 5 fingerbreadths and the spleen was barely palpable. There was no edema of the extremities.

Hemoglobin on admission was 8.9 gm.; white blood count, 5,900 with 34 polymorphonuclear leukocytes, 60 lymphocytes, 1 monocyte, and 5 eosinophils; sedimentation rate, 93 mm. per hour; and blood urea nitrogen, 23 mg. per 100 cc. An uncatheterized urine specimen was cloudy, with a specific gravity of 1.022, 1+ albumin, 0 to 1 hyaline casts, occasional granular casts, 4 to 6 red blood cells, and 6 to 8 white blood cells. Subsequent specimens showed up to 70 to 80 red blood cells per high power field in the sediment, and a twelve-hour Addis count on the fifth hospital day showed 133,000 casts, 6,000,000 white blood cells, and 4,160,000 red blood cells. Throat cultures were negative for beta hemolytic streptococci. Antistreptolysin-O titer was 250; anti-DNAse B, 83; and anti-DPNase, 340. A chest roentgenogram showed "pneumonia" in both lower lobes, with fluid in the costophrenic angle. The electrocardiogram was normal.

The patient ran an afebrile hospital course. Blood pressure averaged 110/80, with a period of transient elevation to 120/90. Within four days, T. S. lost 2 lb. and appeared less swollen. Sedimentation rate and blood urea nitrogen gradually fell, and appetite improved. The patient was discharged on October 30, 1953, after seven weeks of hospitalization, at which time the urine showed a very faint trace of albumin and no red blood cells in the sediment.

A twelve-hour Addis count on January 8, 1954, approximately two months after discharge, showed no casts, 2,428,600 white blood cells, and 210,800 red blood cells. An antistreptolysin-O titer on January 21 was 400, and throat culture was negative. A second follow-up on March 8, 1954, revealed a negative routine urinalysis and no history or physical manifestations of continuing disease.

A follow-up admission was obtained when the patient was 9 years of age, on August 3, 1959. The mother said that the child had some nocturia and felt that there was questionable puffiness of the face at times. Hemoglobin was 11.1 gm.; white blood count, 4,800; sedimentation rate, 25 mm. per hour; and blood urea nitrogen, 13 mg. per 100 cc. A routine urinalysis showed occasional white blood cells, and a twelve-hour Addis count showed no casts, 5,900,000 white blood cells, and 450,000 red blood cells. Antistreptolysin-O titer was 500 units; anti-DNAse B, 500; and anti-DPNase, 131.

Case 7. J. S., a 1½-year-old white male, was first seen in the outpatient clinic on August 16, 1953. He had developed a fever of 102° F. the night before and a sore throat on the day of his visit. Temperature was 102.6° F. Physical examination revealed a diffuse reddish rash over the trunk, shoulders, arms, and legs, which blanched with pressure. Tonsils were moderately enlarged, with a follicular exudate. The throat and ear drums were red. Cervical and submaxillary nodes were palpable. A nose and throat culture subsequently revealed numerous colonies of beta hemolytic streptococci. The patient was treated by intramuscular injection of 300,000 units of procaine penicillin daily for ten days.

About one month later, on September 19, 1953, the patient was admitted for observation. He had been well since several days after the preceding episode except for some bilateral swelling of the neck. During the week before admission, he had had some headache, and he had vomited once two days before admission. No gross hematuria had been noted.

On admission, rectal temperature was 99° F. and blood pressure was 170/110. The eyelids were slightly puffy. There were large, nontender, matted nodes at the angle of the jaw bilaterally. A soft systolic murmur was heard over the precordium. No abdominal organs were palpable, but there was some resistance to palpation about 3 fingerbreadths below the right costal margin.

Admission hemoglobin was 9.9 gm. There were 13,300 white blood cells, with 72 polymorphonuclear leukocytes, 21 lymphocytes, 6 monocytes, and 1 eosinophil. Sedimentation rate was 92 mm. per hour and blood urea nitrogen, 7 mg. per 100 cc. The urine showed a trace of albumin and many red blood cells in the sediment. A throat culture was positive for group A beta hemolytic streptococci. Antistreptolysin-O titer was 1,250 units; anti-DNAse B, 3,170; and anti-DPNase, 1,850. The chest roentgenogram revealed increased bronchovascular markings, consistent with patchy bronchopneumonia, at the right base and at the right cardiophrenic angle.

The patient was given magnesium sulfate intramuscularly for hypertension and was placed on a low-salt diet. He also received procaine penicillin intramuscularly, 300,000 units daily for ten days. A twelve-hour Addis count on October 28 showed 4,600 casts, 2,880,000 red blood cells, and 228,000 white blood cells. The patient gradually improved and was discharged on November 17, after two months of hospitalization. Routine urinalysis at that time was negative for albumin and showed occasional red and white blood cells.

The patient was seen at follow-up two months later on January 15, 1954, at which time a twelve-hour Addis count showed no casts, 254,500 red cells, and 40,300 white cells. Throat culture was negative, and the various streptococcal antibody titers had declined. Antistreptolysin-O was 125; anti-DNAse B, 250; and anti-DPNase, 90. At the time of a second follow-up on March 8, 1954, the patient was asymptomatic and physical examination and routine urinalysis were negative.

Two years later, on October 31, 1955, the patient was readmitted because of migrating polyarthralgia and slight fever. There were no objective findings on physical examination, although the sedimentation rate was recorded as 78 mm. per hour. There was a soft systolic murmur over the precordium which was unchanged from previous examinations. The electrocardiogram was normal. A few beta hemolytic streptococci were seen on throat culture, but these were not identified serologically. The sedimentation rate rather rapidly fell to normal, and the patient was discharged on the tenth hospital day.

On August 3, 1959, when the patient was 11 years of age, he was readmitted, along with other members of

the family, for reevaluation of the attack of renal disease which had occurred six years previously. Interval history and physical examination were negative. Blood pressure was 108/64. Hemoglobin was 12.7 gm; sedimentation rate, 23 mm. per hour; and blood urea nitrogen, 12 mg. per 100 cc. A routine urinalysis was negative, and a twelve-hour Addis count showed no casts, 300,000 white blood cells, and no red cells. Antistreptolysin-O titer was 833 units; anti-DNAse B, 400; and anti-DPNase, 550.

DISCUSSION

Clinical observations. Of the 7 members of the family reported here, the father (case 1) and 3 children (cases 5, 6, 7) developed clinical nephritis and 1 additional child showed definite but asymptomatic hematuria (case 4). One of the children with clinical nephritis (case 5) ran a severe course with marked oliguria, and another (case 7) required magnesium sulfate to control hypertension.

It seems likely that the episode of renal disease observed in the father was precipitated by the same agent as that in the children. The epidemiologic and serologic evidence favor this conclusion. However, because of the history of previous costovertebral pain and albuminuria, it is difficult to ascertain whether the father's illness represented an attack of acute nephritis or a streptococcal exacerbation of a pre-existing renal disease.

The difficulty in distinguishing between these two possibilities has been pointed out by Stetson and associates.[6] The difficulty is most acute among adults with nonepidemic nephritis. The latent period of nine days recorded in this patient is suggestive of acute nephritis according to Jennings and Earle,[7] who cite the earlier work of Seegal and associates,[8] which indicates a latent period generally less than five days in exacerbations of chronic glomerulonephritis. Jennings and Earle[7] have recently presented a series of adults without known evidence of preceding renal disease who developed poststreptococcal nephritis and some of whom had not healed at follow-ups of six to forty-two months. Although the father in this family continued to show some evidence of renal disease for two and perhaps more years after his clinical episode, he clearly does not fit with the cases reported by these authors because of the previous urinary findings. The best interpretation here seems to be a superimposition of acute nephritis on preceding renal disease. Therefore, this case does little to clarify the knotty problem of whether a relationship exists between acute and chronic glomerulonephritis and, if so, what determining streptococcal factors are important in this relationship.

As would be anticipated from the experience of most pediatricians,[9] the renal disease among the children reported here appeared to be uniformly self-limited. A six-year follow-up showed no real evidence of continuing kidney disease in any of the children. One child was, by history, apparently having nocturia and questionable occasional puffiness of the face, but objective findings were absent except for slight increase in white blood cells and a high-normal number of red blood cells on Addis count.

Epidemiology. There is a definite history of exposure of this family to scarlet fever, which was occurring in the family of a paternal aunt. Table 2 gives the subsequent pattern of spread through this family. In the latter half of August, 2 of the children (cases 4 and 7) developed illnesses with skin rashes which were diagnosed as scarlet fever. Beta hemolytic streptococci were isolated from 1 of these children at this time. At about the same time, the father (case 1) and 1 other child (case 6) suffered from sore throats; the mother (case 2) had bilateral draining otitis, from which beta hemolytic streptococci were isolated; and the baby (case 3) had a "granuloma" of the umbilicus and was noted to be "fussy." The umbilicus was not cultured, and there was no other clinical evidence of infection in this youngest infant, although a throat culture was subsequently positive for beta hemolytic streptococci. The 1 remaining child (case 5) did not get a sore throat until the middle of September.

Since most of the family demonstrated evidence of streptococcal infection within a short time after the outside exposure to scarlet fever, it seems likely that this was the source of the infection. However, it is also possible that the mother (case 2) introduced the infection to other members of the family by means of the drainage from her ears, the duration of which could not be accurately determined. This possibility is perhaps supported by the very high antistreptolysin-O titer in the baby (case 3), which had dropped to a very low level by 6 months of age. This high titer may be due in part to antibody transmitted via the placenta, and, if so, would suggest that the mother's infection began before the termination of her pregnancy. However, there is no record of ear infection in the mother at the time of confinement, and this elevated antistreptolysin titer in the infant may have resulted from a low-grade infection of the "streptococcosis" type.[10]

In the father (case 1) and 2 of the children (cases 5 and 6), the latent periods between streptococcal infection and onset of nephritis were nine, six, and eleven days, respectively

TABLE 2

CHRONOLOGIC TABULATION OF FAMILY OUTBREAK OF NEPHRITIS

	Case Number						
	1 (Father)	*2 (Mother)*	*3*	*4*	*5*	*6*	*7*
Age	31 years	27 years	2 months	17 months	$2\frac{1}{2}$ years	$3\frac{1}{2}$ years	$4\frac{1}{2}$ years
Sex	Male	Female	Male	Female	Female	Female	Male
Past History	4+ albumin in urine; costovertebral angle pain	draining ears with each pregnancy		running ear at 14 to 15 months; no treatment			
July 18		admitted to hospital for delivery	born				
August 10-16	exposure to scarlet fever	exposure to scarlet fever	exposure to scarlet fever	exposure to scarlet fever	exposure to scarlet fever	exposure to scarlet fever	exposure to scarlet fever
16							
21							seen in clinic with scarlet fever; throat culture positive β strep.; penicillin (10 days)
23	sore throat; no treatment		"granuloma" of umbilicus; "fussy"	admitted to hospital for scarlet fever; penicillin (2 days)			
24		onset of draining ears				sore throat; no treatment	
September 1	swelling of face					swelling of face	
4							
6	admitted to hospital for nephritis						
7				?subclinical relapse of infection		admitted to hospital for nephritis	?subclinical reinfection with same type
11					sore throat; no treatment		headache
15					throat culture positive β strep.		
17					puffy about eyes		
18					admitted to hospital for nephritis; oliguric; penicillin (10 days)		vomiting
19							admitted to hospital for nephritis; throat culture positive β strep.; magnesium sulfate for hypertension
21			Addis count normal; throat culture positive β strep.; penicillin	asymptomatic hematuria			

9 days (cases 1, 2, 3) · *Approximately 1 month* (cases 1, 2, 3, 4) · *2 weeks* (case 4) · *11 days* (case 6) · *6 days* (case 5) · *1 month* (cases 6, 7) · *10 days* (case 7)

1953

1953	*26*		urine negative; ear culture positive β strep.; penicillin (7 days)					
	October 10	sore throat	Pseudomonas and staph. isolated; treatment with variety of antihiotics					
	15	readmitted to hospital for 3 weeks; erythrocyte sedimentation rate, 37 mm. per hour; Addis count, abnormal; throat culture positive β strep.; penicillin (10 days)						
	30						discharged from hospital; urine: very faint trace albumin; no RBC	
	November 17		drainage stopped					discharged from hospital; urine: occasional RBC and WBC
	December 11-16				readmitted because of increase in hematuria			
	22					discharged from hospital; urine: 14-16 RBC; trace of albumin		
1954	*January 21*	throat culture positive β strep.			throat culture positive β strep.			
	March 8			urine negative	urine: occasional RBC	urine: 1-2 RBC; 1-2 WBC	urine negative	urine negative
1955	*October 31*							migrating polyarthralgia
1956	*January 11*	interval history and physical examination negative; urine: 1+ albumin, very occasional RBC and WBC						
1959	*July 15*		urine negative					
	August 3			interval history, physical examination, and Addis count normal	interval history, physical examination, and Addis count normal except for 2,000,000 WBC	interval history, physical examination, and Addis count normal	nocturia; ? occasional puffiness; physical examination negative; Addis count: no casts; 5,900,000 WBC; 450,000 RBC	interval history, physical examination, and Addis count normal

(Table 2). These are well within the expected periods as reported in other studies.[6] It is interesting, however, that, in the 2 children with scarlet fever (cases 4 and 7), both of whom received penicillin, the latent periods were apparently longer, that is, approximately one month. In one of these (case 4), there were no clinical manifestations of nephritis, and it was impossible to know how long the hematuria had been present when it was identified one month later. Also, since she received penicillin for only two days, it is entirely possible that she may have had a bacteriologic or subclinical relapse of infection, in which case the latent period would be more appropriately calculated from the time of the recurrence of infection.

The second child (case 7) received intramuscular penicillin for ten days as treatment for his scarlet fever and developed classical acute nephritis one month later without clinical evidence of a second intervening streptococcal infection. On the basis of experience in other studies,[11] it seems likely that this vigorous treatment would have eradicated the infecting organism. Thus, in this case, either an unusually long latent period, perhaps prolonged by the penicillin therapy, or a second subclinical infection, possibly a reinfection with the same type, must be postulated. Since penicillin therapy inhibits the development of type-specific antibody, reinfection with the same type can occur under these circumstances, and instances of this have been observed in military populations and in family groups in which the reservoir of streptococci is not eliminated from all members of the group. In such instances, reinfection is frequently subclinical.

In this regard, it is of interest that a clinical sore throat did occur in another member of the family (case 5) on or about September 11. On September 18, she was hospitalized with acute nephritis. Shortly thereafter, evidence of clinical or subclinical nephritis appeared in the 2 children who had been treated for scarlet fever one month earlier. On September 19, her brother (case 7) was admitted with classical acute nephritis and on September 21, hematuria was first observed in case 4. It seems reasonable that these last 2 children—the 2 who had received penicillin therapy for scarlet fever one month previously— may have had a recurrence of infection with the same serologic type of streptococcus at the time the clinical sore throat occurred in case 5. Indeed, if the recurrence was actually a relapse of infection, as postulated, in the 1 inadequately treated child (case 4), it is possible that this relapsed infection was the source of infection of the other 2 children (cases 5 and 7).

Thus, it would appear that 2 episodes of streptococcal infections, separated by an interval of approximately three weeks, occurred in this family and that the second episode may in some instances represent relapse or reinfection with the same type (Table 2). It is of interest that the onsets of acute nephritis also span a period of about three weeks as follows: September 1 (case 1), September 4 (case 6), September 17 (case 5), September 17 (case 7), and September 21 (case 4—hematuria only).

An epidemiologic connection between the outbreak of nephritis in this family and a larger outbreak of nephritis that occurred simultaneously on the Red Lake Indian Reservation in northern Minnesota seems probable. Details of this larger epidemic, which involved about 63 cases of acute nephritis, have been reported by Kleinman.[12] There was a simultaneous increase in the number of cases of scarlet fever on the reservation, and a characteristic pyoderma was observed in two-thirds of the patients with acute nephritis. The epidemic began in July 1953 and ran through November, possibly terminated in part by mass penicillin prophylaxis, which was begun in early October, at a time when the number of new cases developing was already decreasing.

As indicated earlier, in August 1953, the family reported here was exposed to scarlet fever, which was occurring in the family of a paternal aunt and among other inhabitants of a crowded multiple-family dwelling in Minneapolis. On further inquiry, it was found that several of the families living in this apartment house were Indians who had recently moved down from the Red Lake Reservation in northern Minnesota. A bacteriologic survey of some of the inhabitants of this building revealed a number who were positive for group A streptococci. In addition to the epidemiologic evidence of a connection between the family reported here and the outbreak at Red Lake, it was subsequently shown that the strains isolated from all of these sources belonged to a common serologic type.

The demonstration by Rammelkamp[1,13] that nephritogenic strains of streptococci are limited to only a few serologic types does much to clarify some of the peculiarities of the epidemiology of acute nephritis after streptococcal infection as contrasted with the remarkably constant attack rate of acute rheumatic fever.[14] The occurrence of nephritogenic types of streptococci also helps to explain the occurrence of family outbreaks.[15] Upon introduction of one of these

strains of streptococci into a family, a high attack rate of acute nephritis, with perhaps several members developing clinical or subclinical manifestations, can be expected within a short period. This type of family pattern, with its short time span from onset to onset, is in sharp contrast to that of acute rheumatic fever, in which members of the family first become affected over wide intervals of time or over several generations.[16] These family outbreaks of acute nephritis should also be carefully distinguished from hereditary nephritis, which is chronic in type and which may show associated defects and a definite genetic pattern.[17–19]

Bacteriology. Beta hemolytic streptococci were isolated at some time from 6 of the 7 members of this family. All of the strains isolated at the time of original infection were readily identified as group A but were not classifiable by any of the available typing antisera.

The finding of a nontypeable strain of group A streptococcus can be explained in several different ways. In some instances, particularly when obtained from chronic carriers, these strains may have lost their M protein, which is the streptococcal substance responsible for type-specificity. The production of M protein can be correlated with virulence of group A streptococci, and strains associated with active infection invariably show M protein production. Since some of the strains isolated here, such as those obtained from the draining ears of the mother, were still causing active infection, it seemed unlikely that loss of M protein had occurred in these strains.

The second possibility was that these strains represented a previously recognized type for which specific typing serum was not currently available. Again, this seemed unlikely, since we were able to test these strains in our laboratory against all of the 36 types of antisera supplied by the Communicable Disease Center (C.D.C.) of the U.S. Public Health Service. Dr. Elaine Updyke[20] of the C.D.C. was also unable to get this strain to react in her laboratory with any of the type-specific antisera produced there. Moreover, Dr. Rebecca Lancefield[21] was unable to get this strain to react in her laboratory with any of an entirely separate set of type-specific antisera produced at the Rockefeller Institute.

The third possibility was that this strain represented a previously unrecognized serologic type. The possibility of a new serologic type was particularly intriguing in view of the demonstrated nephritogenicity of the strain. Therefore, attempts to produce a type-specific antiserum for these strains were made in several different laboratories. The strains proved to be among those against which it is difficult to produce satisfactory antiserum, possibly because of their instability, which seems to be rather characteristic of nephritogenic strains. A satisfactory antiserum was first produced by Updyke and associates[22] at the C.D.C. Satisfactory antisera have subsequently been produced by Dr. Lancefield[21] at the Rockefeller Institute and also in our laboratory. The strain was originally referred to as the Red Lake strain but now has been officially recognized as a new type—type 49—by the Subcommittee on Streptococci and Pneumococci of the International Committee on Bacteriological Nomenclature, International Association of Microbiological Societies.[21]

At follow-up on January 21, 1954, streptococci of a different type, type 43, were isolated from 2 individuals in this family (cases 1 and 4). The possibility that these were carrier strains which were temporarily overrun by infection with the nephritogenic strain or temporarily suppressed by antibiotic treatment must be considered. However, the alternative possibility that this was an indication of intervening infections with a new type appears to be more attractive. An intercurrent sore throat did occur in case 1 four days before his readmission. Unfortunately, the beta hemolytic streptococci which were present in large numbers in the throat culture taken at that time were not available for serologic identification. There was no clinical evidence of an intercurrent infection in case 4, but such an infection might account for the increase in hematuria which led to this patient's third admission to the hospital.

Serology. Elevated streptococcal antibody titers were found in all members of this family. The antistreptolysin-O titer of 250 found in the father (case 1) would be borderline in a child but is probably elevated for an adult. Moreover, this titer was not obtained until four and one-half months after onset of nephritis, by which time his antibody level was likely to be declining. The mother's antistreptolysin-O titer of 317 was also not obtained until several months after clinical healing of her draining otitis.

The antistreptolysin-O titer of 1,585 units found in the baby (case 3) is strikingly elevated for a 2-month-old infant. The possibility of this titer's representing placentally transmitted antibody has already been discussed, but in view of the history and the physical examination at the time of confinement, it does not seem likely that the mother's titer was this high during her pregnancy. If, as it would therefore appear, this represents primarily antibody formed by the

baby, it illustrates the vigor with which some infants can respond to the antigenic challenge of active infection. This observation is in contrast to some generally held views concerning the antibody response in this age group.

In 3 of the children (cases 4, 5, and 6), the antistreptolysin-O titer continued to rise after development of clinical nephritis or hematuria. Indeed, in 1 of them (case 4), the titer rose from a decidedly low level of 50 to a significant level of 400. In view of the short latent period of acute nephritis, low admission titers on some patients should be anticipated, since the antistreptolysin-O titer does not usually reach maximal levels until three to six weeks after a streptococcal infection. It is therefore important to keep in mind, when managing such patients, that it may be necessary to obtain a second titer, and in any case, the demonstration of a definite rise in titer is always more significant than a single high titer, regardless of the degree of elevation.

The demonstration of a different type—type 43—at follow-up in January 1954 on 2 members of the family raises the possibility of an intervening reinfection in these individuals. Such an infection may have contributed to the rising antibody titer in case 4.

Titers for 2 of the more recently described streptococcal antibody tests[23,24] were obtained in several individuals. These antibodies, the anti-DNAse B and the anti-DPNase, are often elevated when the antistreptolysin-O titer is low or borderline and are therefore useful secondary tests.[25] In the 2 children with clinical nephritis on whom these antibody tests were obtained, 1 (case 7) had a high anti-DNAse B titer and both had elevated anti-DPNase titers. In studies reported elsewhere,[26] we have found that the anti-DPNase titer is particularly likely to be high in acute nephritis.

The low titers for anti-DNAse B and anti-DPNase and the high antistreptolysin-O titer found in the baby (case 3) demonstrate the wide differences in antibody response which may occur with different antigens in the same person.

The relatively high streptococcal antibody titers found in most of the children at six-year follow-up suggest that the family has continued to be exposed to streptococcal infections. In spite of this serologic evidence of further streptococcal infection, no evidence of recurrent or continuing renal disease was found in any of these children.

Type-specific antibody develops more slowly than the other streptococcal antibodies,[27] and its formation is more thoroughly inhibited by penicillin therapy.[27,28] Therefore, type-specific antibody may be missed or may not be demonstrable in patients with acute nephritis. Sufficient amounts of satisfactory sera were available for type-specific antibody tests in 3 of the patients reported here. Tests for type 49 antibody were performed by a modification of the Rothbard method, as reported previously.[27] Antibody was demonstrated by the inhibition of growth of 10-fold dilutions of type 49 streptococci by a constant amount of test serum in a phagocytic system. In 1 patient (case 1), a 2-tube inhibition was demonstrated in a convalescent serum taken on January 21, 1954. In another patient (case 6), no inhibition was found in the serum taken at the time of admission (September 9, 1953) and a 4-tube inhibition was observed on the convalescent serum taken on January 21, 1954. In a third patient (case 5), a 1-tube inhibition was found in the serum specimen obtained on admission (September 19, 1953) but insufficient serum was available for this determination at follow-up. Thus, definite evidence of type 49 antibody was found in 2 patients and questionable evidence was found in another.

SUMMARY

In a family of 7, 4 members had clinical acute nephritis and hematuria developed in 1 member within a three-week period. The preceding infections, some of which were accompanied by a scarlatinal rash, were due to a new serologic type of streptococcus—type 49. Streptococci of this new serologic type were isolated from various members of the family, and type-specific antibody was found in several of these patients.

A six-year follow-up of the children revealed no evidence of continuing renal disease. A two-year follow-up of the father showed persistent abnormal urinary findings, but he had originally presented with a history of preexisting albuminuria.

Evidence of an epidemiologic relationship of this family outbreak to an outbreak of acute nephritis at the Red Lake Indian Reservation is presented.

It seems appropriate that this family be reported in connection with a special issue honoring Dr. Irvine McQuarrie. The studies on this family were begun at a time when we were new in the Department of Pediatrics at Minnesota. In his customary fashion of encouraging junior men, which has resulted in such a wealth of Minnesota-trained men in academic pediatrics, Dr. McQuarrie urged that we take advantage of this expanded "experiment of nature." Indeed, at a time when research funds were considerably more difficult to obtain than they are now, he supported, from departmental funds, the initial investigations of this family and of certain aspects of the epidemic at the Red Lake Indian Reservation.

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In many patients with simple postmenopausal and senile osteoporosis, a high-calcium diet relieves pain and prevents fractures. Calcium deficiency rather than defective osteoblastic activity may be the cause of osteoporosis in these patients. While moderate increases in dietary calcium have little effect on calcium metabolism, high concentrations are absorbed and retained for years. This calcium avidity, possibly varying with stage or form of the disease, may suppress hyperparathyroidism caused by calcium deficiency and arrest rapid bone resorption. Osteoporosis in patients with such conditions as anorexia nervosa is not likely to subside when calcium intake is increased.

In 12 patients with postmenopausal and senile osteoporosis, net calcium absorption and urinary excretion appeared normal during medium intake of 0.3 mEq. calcium per kilogram of body weight per day. When calcium intake was increased to 2 mEq., calcium absorption and retention increased abnormally in 8 patients. Of 6 patients examined after ingestion of the high-calcium diets for nine months to three and a half years, 4 maintained a strongly positive calcium balance.

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Spontaneous Complete Closure of a High-Flow, High-Pressure Ventricular Septal Defect

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VENTRICULAR SEPTAL DEFECTS are customarily considered to be permanent abnormalities. This implies that all such lesions which are of hemodynamic significance require surgery at some time. The purpose of this communication is to present the case of a child in whom spontaneous closure of a hemodynamically significant ventricular septal defect was proved by cardiotomy as well as by repeat cardiac catheterization.

CASE REPORT

C.A.L. was the product of a full-term normal pregnancy and delivery and weighed 5 lb., 14 oz. at birth on June 15, 1956. The neonatal period was uneventful, and no feeding difficulties were encountered. A heart murmur was initially detected by the family physician during a routine examination at 2 weeks of age. Tachypnea and tachycardia were observed by the physician when the patient was 3 months of age. After this, upper respiratory infections were frequent, and antibiotics were commonly used.

The patient had 3 bouts of pneumonia before the age of 11 months, 2 of which required hospitalization and oxygen administration. A chest roentgenogram demonstrated cardiac enlargement, and, at the age of 9 months, the infant was digitalized by her own physician. Growth and development progressed satisfactorily; at the age of 11 months, the baby weighed 16 lb. Because of the persistence of the murmur and tachypnea, she was referred for further cardiac evaluation and study.

The initial physical examination of the infant at 11 months of age at the University of Kansas Medical Center was carried out with the aid of chloral hydrate sedation. The respiratory rate was 68 per minute and pulse, 150 per minute and regular. No cyanosis was apparent clinically. The liver was not enlarged. The lungs were clear. The peripheral pulses were all equal and normal in quality. Blood pressure was 90/50 in the right arm and 96/56 in the right leg. A slight precordial bulge and minimal precordial overactivity were observed. Mild cardiomegaly was evident on percussion, and an anterior heave to the precordium was noted on palpation. A grade 1 (1-4) systolic thrill was located at the left sternal border in the fourth intercostal space. The first sound at the apex was slightly accentuated. The second sound at the pulmonic area was split by approximately 0.03 seconds, and the pulmonic component was 2+ (0-4) accentuated. A grade 4 (1-6) harsh, rasping, holosystolic murmur was present at the left sternal border in the fourth interspace. A grade 2 (1-6) mid to late low-pitched apical diastolic rumble was also evident.

The electrocardiogram (figure 1) showed biventricular hypertrophy, with predominant systolic overloading of the right ventricle. A roentgenogram of the chest (figure 2) made seventeen days later demonstrated moderate cardiomegaly, a very prominent main pulmonary artery, and marked increase of the pulmonary blood flow. The aortic arch was noted to be on the left on cardiac fluoroscopy, and the left atrium was slightly enlarged on barium swallow. Ear oximetry gave values of 96 per cent both at rest and with crying.

Cardiac catheterization was carried out on May 29, 1957, when the patient was 12 months of age (table 1). The pulmonary artery could not be entered. There was a 15 to 20 per cent jump in oxygen saturation at the right ventricular level as compared with the right atrium; moderate elevation of the right ventricular pressure (70/0) was found. Peripheral arterial saturation was 91 per cent, with the specimen being secured under the effects of tribromoethanol amylene hydrate basal anesthesia.

The infant was not seen again until the age of 2 years. She had had fewer respiratory infections and only 1

TABLE 1

CARDIAC CATHETERIZATION AT 12 MONTHS OF AGE

Location	*Pressure (mm. Hg)*	*—Per cent oxygen saturation— Specimens obtained late in procedure (Hb. 10.4 gm.; capacity, 14.0 vol. %)*	*Specimens obtained early in procedure (Hb. 11.4 gm.; capacity, 15.4 vol. %)*
Superior vena cava	3.0 (mean)		60.0
Inferior vena cava	1.3 (mean)	59.0	
Right atrium	2.0 (mean)	57.0	69.0
		61.0	71.0
			60.5
Right ventricle	70/0	84.0	80.0
		74.5	
Femoral artery			92.0
			90.5

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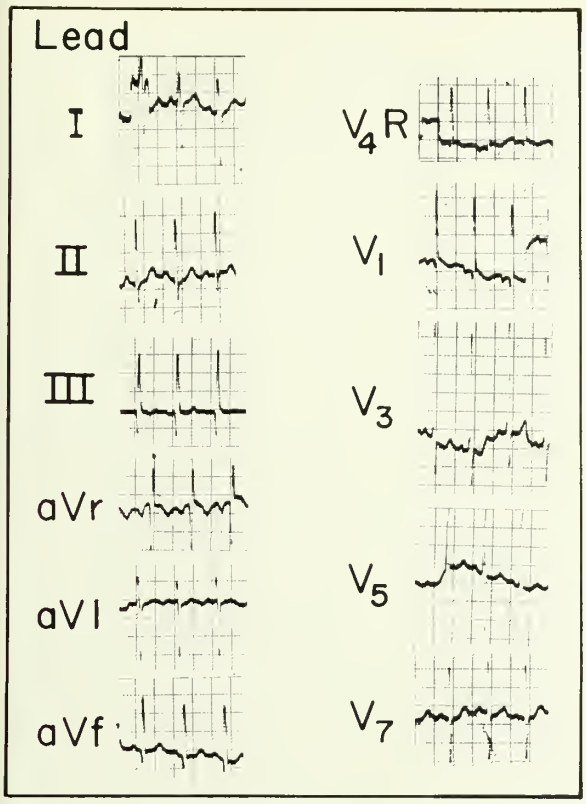

Fig. 1. Electrocardiogram at 11 months of age showing biventricular hypertrophy, with predominant systolic overloading of right ventricle. Note that lead V_4R is recorded at half standard.

more bout of pneumonia. Her appetite continued to be good, and she weighed 25 lb.

Re-examination under sedation showed the respiratory rate to be 28 per minute and the heart rate, 110. There was no overactivity of the precordium, and no thrill was evident. A slight precordial bulge persisted, as did the minimal anterior heave to palpation. The second sound seemed to be narrowly split and the pulmonic component was 1 plus (0-4) accentuated. A grade 3 (0-6) harsh, prolonged systolic murmur was noted at the left sternal border in the fifth interspace. No diastolic murmur was heard. The electrocardiogram (figure 3) showed right ventricular hypertrophy and probable biventricular hypertrophy. Ear oximetry again showed full saturation of 98 per cent.

The child was readmitted in August 1958, at the age of 26 months, for surgical closure of the ventricular septal defect. The physical findings were the same as two months previously. The electrocardiogram preoperatively still showed right ventricular and suggestive biventricular hypertrophy. A prolonged regurgitant systolic murmur was recorded phonocardiographically. The chest roentgenogram (figure 4) continued to show prominence of the pulmonary vascular markings, particularly in the right hilar area, although the heart size was now at the upper limits of normal. The combination of continuing right ventricular hypertrophy electrocardiographically—although in retrospect it was diminishing—and reduction in heart size and pulmonary blood flow gave concern as to the possible presence of progressive increase of pulmonary vascular resistance.

On August 30, 1958, when the patient was 26 months old, the chest was opened through a midline sternal-splitting incision. No thrills were palpable over the surface of the heart and great vessels, although the heart did appear mildly enlarged. The pulmonary artery was slightly larger than the aorta. Direct needle pressure determinations revealed normal left ventricular pressure and 35/0 mm. Hg in the right ventricle. The atrial septum was normal by digital palpation through a right atrial appendage incision. Total cardiopulmonary bypass was then established, and perfusion was carried out with a pump oxygenator. Cardiac arrest was accomplished with potassium citrate after cross-clamping the aorta. A generous right ventriculotomy, extending along the anterior surface of the right ventricle, permitted careful inspection of the ventricular septum. The latter was intact without interventricular communication, and no arteriolized blood came into the field. The mural leaflet of the tricuspid valve appeared slightly thickened, contracted, and adherent against the ventricular septum. The edges of the tricuspid valve seemed to be normal. The atrial septum was also visualized through the tricuspid opening and found intact and normal.

The ventriculotomy was sutured and bypass discontinued. The right ventricular pressure was again measured and found to be normal—30/0 mm. Hg. A lung biopsy from the middle lobe, measuring $3 \times 1.5 \times 1$ cm., showed no microscopic alterations of the pulmonary vessels. Recovery was uneventful after surgery, and no murmur was heard. The patient was discharged on her ninth postoperative day.

Re-evaluation on November 10, 1958, demonstrated a normal physical state. A grade 2 (1-6) short, low-pitched, early, twanging-string, nonorganic murmur was heard at the left sternal border in the third and fourth interspaces. The pulmonic component of the second sound was not abnormal, and no diastolic murmurs were present. Cardiac fluoroscopy was normal as to over-all size, chamber enlargement, and pulmonary blood flow, save for 1+ (0-4) heaviness of the right hilar vascula-

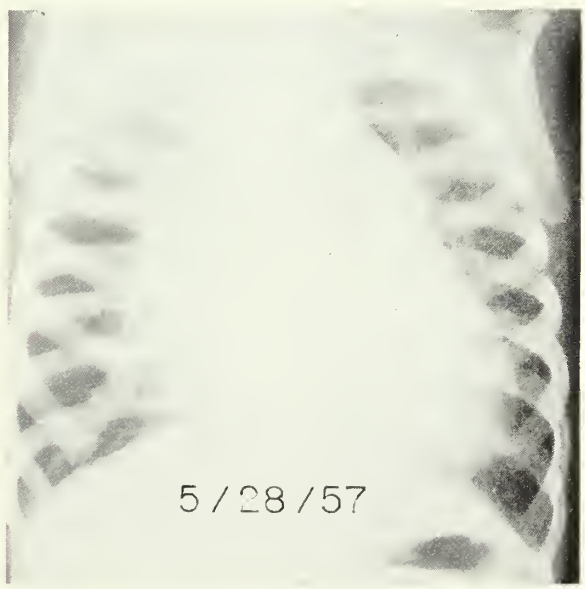

Fig. 2. Chest roentgenogram at 11 months of age demonstrating moderate cardiomegaly, prominence of the main pulmonary artery, and marked increase of pulmonary blood flow, particularly in right hilar area

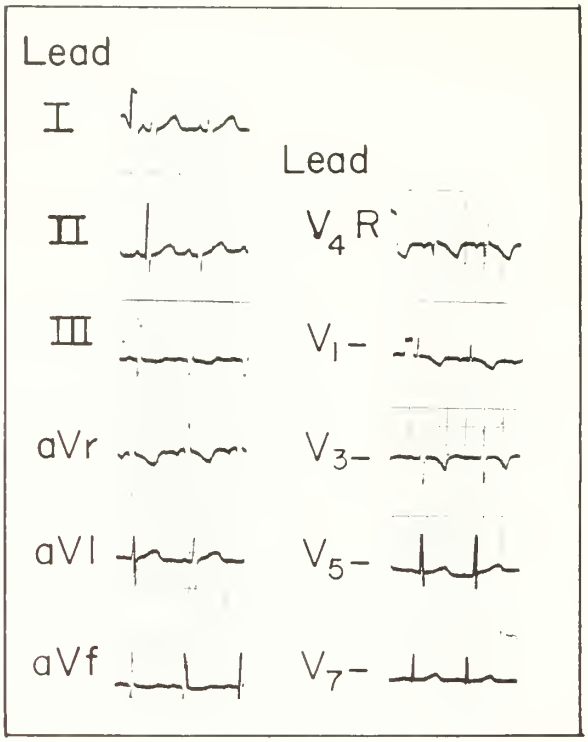

Fig. 3. Electrocardiogram at 24 months of age showing persistence of biventricular hypertrophy and systolic overloading of right ventricle. Note half standard of leads V_1, V_3, V_5, and V_7.

ture without excessive pulsation. A complete right bundle branch block was present electrocardiographically; prominent Q waves persisted in leads III and aVf (figure 5). A chest roentgenogram made ten months postoperatively was normal except for suggestive slight prominence of the right pulmonary artery (figure 6).

Cardiac catheterization was repeated on June 26, 1959, when the patient was 3 years of age (table 2). All chambers and vessels on the right side of the heart were entered, and normal pressures were recorded. No gradient in systolic pressure was present between the main pulmonary artery and right ventricle. A left pulmonary artery mean wedge pressure was 6 mm. Hg; a blood specimen withdrawn from this location was 98 per cent saturated with oxygen. Peripheral arteriolization was normal. Oxygen saturation of the blood specimens from the right side of the heart demonstrated no evidence of a left-to-right shunt. This was confirmed by dye dilution studies.

DISCUSSION

Loud, harsh, systolic murmurs which are suspected, by auscultation, of being caused by ventricular septal defects have been noted by many physicians to disappear. The possibility of this phenomenon's being caused by spontaneous closure of the ventricular septal defect has been suggested by several writers.[1-6] Proof of this speculation has been lacking until recent publications. In 1958, Azevedo and associates[7] presented cardiac catheterization data on a male infant who had had heart failure with clinical findings of a large ventricular septal defect. Two years later, there were no physical signs of a large left-to-right shunt, although the typical murmur persisted. Repeat cardiac catheterization showed resolution of right ventricular hypertension and normal hemodynamics. With the persistence of a characteristic murmur, closure can be questioned, but little doubt exists as to the marked reduction of the size of the defect.

Evans and associates[8] reported 37 patients in whom they had personally observed disappearance of such murmurs. Four of these infants underwent cardiac catheterization, and a left-to-right shunt was demonstrated by oxygen saturations. In 1 infant, there was a 17 per cent jump in oxygen saturation from the right atrium to the right ventricle and a moderate elevation of the right ventricular pressure (55/0 mm. Hg); the other 3 had normal pressures. Cardiac catheterization was done in an additional 9 patients in whom the murmur had not as yet disappeared; 5 of these demonstrated a left-to-right ventricular shunt, but none showed elevated right ventricular pressure. During selective cineangiography from the left ventricle in 1 infant, a left-to-right ventricular shunt was observed. When intracardiac phonocardiography was employed, a systolic murmur within the right ventricle was always recorded. One 6-month-old infant manifested the clinical, radiographic, and electrocardiographic findings of a large ventricular septal defect. Cardiac catheterization confirmed this,

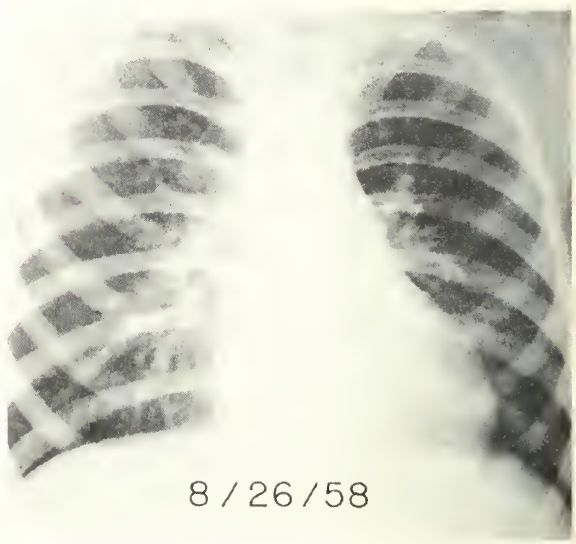

Fig. 4. Chest roentgenogram at 26 months of age continues to show increased pulmonary blood flow, prominence of main pulmonary artery, and mild cardiomegaly, although these are not as evident as at age 11 months.

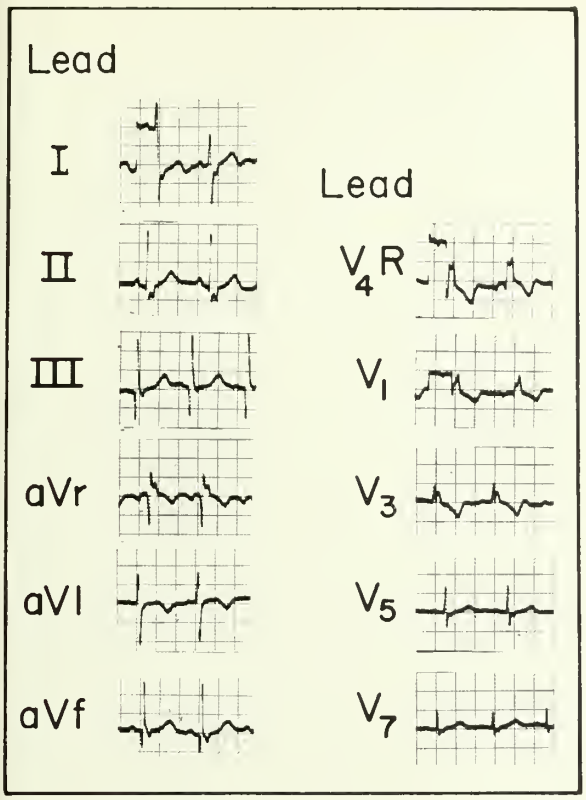

Fig. 5. Electrocardiogram at 29 months of age, two and one-half months after cardiotomy, demonstrating large Q waves in leads III and aVf. Complete right bundle branch block prevents assessment of right ventricular hypertrophy.

as there was a large jump in oxygen saturation at the right ventricular level, with a right ventricular pressure of 60/0 mm. Hg. During the next several years, signs of a large left-to-right shunt disappeared, and, at the age of 7 years, with the systolic murmur being soft and short, recatheterization showed normal hemodynamics on the right side of the heart.

Nadas and associates[9] reported 4 cases of ventricular septal defect in whom either a reduction or elimination of a sizeable left-to-right shunt was observed, with concurrent subsidence of right ventricular hypertension. All 4 infants presented with congestive heart failure and required digitalization. Upon recatheterization two to three years later, the right ventricular pressures were markedly reduced or normal, and the magnitude of the left-to-right shunt was either immeasurable or very small by oxygen saturation technics. Cineangiocardiograms in the 2 children with no demonstrable shunt by specimen oxygen analysis did suggest minimal residual left-to-right shunting.

The infant described in detail in this communication unequivocally demonstrates complete spontaneous closure of a ventricular septal defect. She presented with the classic signs of a ventricular septal defect, with moderate pulmonary hypertension and a large left-to-right shunt. The electrocardiogram and chest roentgenogram were consistent with the clinical diagnosis. Cardiac catheterization at 12 months of age confirmed the alterations in hemodynamics. Cardiotomy fourteen months later proved the absence of a ventricular septal defect. Recatheterization at the age of 3 years showed normal pressure and oximetric data on the right side of the heart. Dye-dilution curves were normal, ruling out a left-to-right shunt greater than 5 per cent of the cardiac output. The murmur at that time was descriptively nonorganic. The chest roentgeno-

TABLE 2
CARDIAC CATHETERIZATION AT 36 MONTHS OF AGE

Location	*Pressure (mm. Hg)*	*Per cent oxygen saturation*
Superior vena cava	2 (mean)	67.3; 65.0
Inferior vena cava	2 (mean)	60.0; 61.5
Right atrium	1 (mean)	61.7; 63.0
		64.0; 61.7
		67.0; 65.5
Coronary sinus		49.0; 50.0
Right ventricle	30/0	64.0; 65.5
		61.5; 64.0
		64.5; 67.0
		64.5; 67.0
Main pulmonary artery	30/5	65.0; 64.5
Left pulmonary artery	25/7	65.0; 64.0
Left pulmonary artery wedge	6 (mean)	98.5; 98.5
Femoral artery	66/42	96.5; 97.0

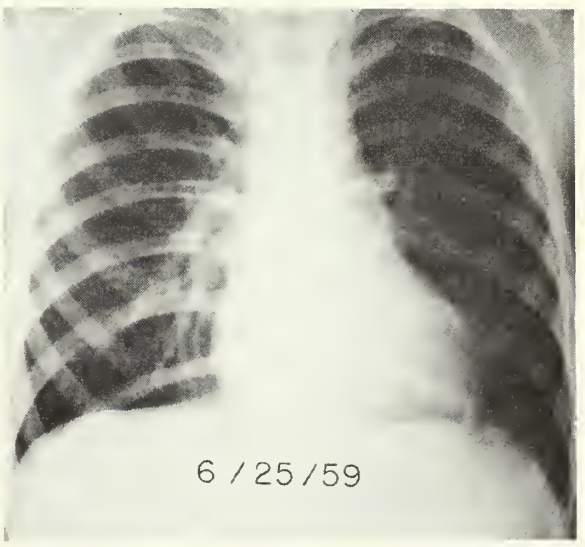

Fig. 6. Normal chest roentgenogram obtained ten months after cardiotomy and at the time of repeat catheterization at age of 3 years

gram returned to normal, and the electrocardiogram demonstrated only a complete right bundle branch block, presumably caused by the ventriculotomy.

The precise mechanism by which spontaneous closure of a ventricular septal defect occurs is speculative. Cineangiocardiographic and intracardiac phonocardiographic evidence presented by Evans and associates[8] suggests that such defects which might undergo closure are in the muscular portion of the ventricular septum. This also has been our impression in those instances in which the left-to-right shunt is small and insignificant pulmonary hypertension exists. Hypertrophy of muscular ventricular septum or of the right ventricular outflow tract might contribute to the encroachment upon the lumen of the ventricular septal defect. The hypothesis that the septal leaflet of the tricuspid valve and its chordae may effectively obliterate some ventricular septal defects is given more credence by the surgical observations in our case.

There is little doubt that ventricular septal defects associated wtih large left-to-right shunts with or without pulmonary hypertension rarely close spontaneously. However, evidence is accumulating that those ventricular septal defects which are hemodynamically insignificant in infancy and present only as a loud, harsh, prolonged systolic murmur are not uncommonly observed to undergo complete closure. In the past year, the authors have appreciated this phenomenon in 11 instances. These infants were evaluated not because they were symptomatic but because their physicians had detected the presence of at least a grade 3 (1–6) harsh, rasping systolic murmur at the left sternal border. Electrocardiograms were invariably normal, and cardiac fluoroscopy showed no chamber enlargement and normal pulmonary blood flow. None had alteration of the second sound or an apical diastolic rumble. Re-examination after six to twenty-eight months showed that no murur was present or else the characteristics of the murmur were markedly changed with reduction in intensity to grade 1 or 2; the pitch was low; the duration was short; and the timing was early in systole.

This communication again emphasizes that not all ventricular septal defects are potentially life-threatening, since spontaneous closure is a reality and may occur even in the presence of a large left-to-right shunt and pulmonary hypertension. When assessing the natural history of ventricular septal defects, it is now apparent that spontaneous closure of the defect may occur, leading to a uniformly favorable prognosis.

SUMMARY

The case history of an infant with a ventricular septal defect in whom there was a large left-to-right shunt and pulmonary hypertension is presented in detail. Radiography, electrocardiography, and cardiac catheterization confirmed the hemodynamics. Spontaneous closure of the ventricular septal defect occurred, over a period of fourteen months, to the point where, at the time of cardiotomy, no interventricular communication was present. Recatheterization demonstrated restoration of normal hemodynamics on the right side of the heart. The phenomenon of spontaneous closure of ventricular septal defects, particularly in those of meager hemodynamic significance, is more common than was formerly appreciated.

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Central Coordinating Agency for Postgraduate Medical Education

CLIFFORD G. GRULEE, JR., M.D.

New Orleans

The need for continuing and continuous medical education after graduation from medical school is universally accepted. Recognizing this, medical faculties constantly are seeking means of better preparing their students for the independent effort necessary in maintaining a lifelong program of study. This is done by continual critical review of both the content and methodology of the undergraduate curriculum. Similar careful surveillance is maintained of graduate programs, whether in basic science or clinical fields; but subsequently, in continuation education, no concerted or well-organized efforts are made to insure that high standards are maintained or that existing facilities are adequately publicized and effectively utilized. The Council on Medical Education and Licensure, working through various interested individuals, and the Committee on Graduate Medicine of the American Association of Medical Colleges have effectively begun to attack the many problems that exist, but much more work remains. The goal in these efforts must be the most efficient utilization possible of existing programs, together with the continual trial of new techniques and methods of education as applied to the progressively more complex and technical fields of medicine.

At the present time, a considerable number of postgraduate programs, including medical school offerings, are rather casually presented and the content of them as much determined by what is opportune as by what is most educational. Some are so planned that they meet the prime consideration of being financially self-supporting. Others are planned primarily to stimulate the interest of alumni and similar groups in supporting particular institutions or are presented primarily as public relations gestures. Whatever the basic motivation for them may be, all are costly, both in terms of actual dollars and in terms of faculty time. In the case of medical schools, these costs are difficult for administrators to justify, particularly if there is reason to believe that programs are reaching a relatively small proportion of the physician population who most need them and if existing opportunities are not being fully exploited. For example, it has become routine to publicize each single program by individual mailings to many thousands of physicians in order to insure an attendance of 50 to 75 men.

There are many reasons for this, but paramount among them is a conspicuous lack of coordination and organization of efforts. Medical faculties, local and national medical societies, voluntary health agencies, drug and other manufacturing concerns, and even governmental agencies are all making contributions, but each is doing its planning more or less independently of the others. The remainder of this presentation will be concerned with certain justifications for and possible functions of a national coordinating agency for postgraduate medical education.

PROGRAM AND NEEDS

Present efforts of the Council on Medical Education of the American Medical Association with the annual listings are not enough and are primarily for the benefit of potential applicants. They are undoubtedly helpful in this connection, but the fact remains that descriptive material for publication must be highly condensed, and no additions or corrections after the one submission deadline can be accepted. As a consequence, most organizations rely on other means of publicizing their courses and, except for the annual course announcement, derive little or no benefit.

There is no mechanism by which a planning group can check particular dates or can be informed, for example, that the proposed subject for a course is being covered by several other institutions at almost the same time. Planning at a national or at least a regional level could eliminate much wasteful overlapping and reduce the danger of inadequate registrations, with associated financial deficits.

CLIFFORD G. GRULEE, JR., *is associate dean, director of graduate medicine, and professor of pediatrics, Tulane University School of Medicine, New Orleans.*

Competition between various organizations presenting postgraduate programs is recognized and to a degree may be desirable. Although it is conceivable that a coordinating agency could be used to increase this competition, far more often it would be used to avoid unfortunate conflicts both as to dates and subject matter. These conflicts with other postgraduate programs, however, are only part of the problem. It is also most difficult to check plans against the schedules of important local, regional, and national medical meetings. By maintaining a current and readily available list of meetings, a central coordinating agency could perform an extremely important service.

Furthermore, it would be most helpful in overall planning by universities if some record of faculty participation in courses of other organizations were available, with the subject discussed, the date, and similar data. Sharing of faculties between universities has obvious advantages and should be encouraged, but it is nevertheless true that some of the best known teachers become so heavily committed to programs being presented elsewhere that they are unable to participate adequately in the postgraduate plans at their own schools. Information of this type would help in planning toward a better distribution of the teaching load. Dollars as well as hours are a part of this problem, since university budgets are not reimbursed for the time that faculty members spend away from their jobs.

There is a need for information concerning the plans and interests of the various drug houses in the postgraduate field. A central clearing house might well channel appropriate help from industry into more effective support of university programs.

In recent years, at least 3 major efforts have been made by professional groups to stimulate continuation education among their members. The first was a revamping of medical meetings, with increased emphasis on seminars and symposia. Secondly, attendance at postgraduate programs was made a condition of membership by the American Academy of General Practice. A third and most promising trend has been the joint planning and sponsorship of postgraduate courses by professional societies.

The proposed organization could be used as a repository of information concerning the requirements and programs of these societies and could be the instrument not only of improving but also of extending these efforts. Possibly a periodic announcement system, on a subscription basis, could be offered listing programs in particular fields. Working relationships with such organizations as the American Association of Physicians, the American Academy of Pediatrics, or the American Fracture Association might be defined. With the channeling of all information through a single office, it should be possible to suggest and make arrangements for a sequence of courses to meet the needs of individual physicians.

For the same reason, it would probably be possible to increase the extramural programs of universities. Contacts between interested local groups, educational institutions, and possible sources of support could be facilitated. A satisfying example of this is a small but most useful grant from a pharmaceutical company which allows us to defray the expenses of groups from our faculty who, at the invitation of outlying medical societies, present one-half- to one-day programs. Suggestions as to program content are solicited and a choice of material agreed upon with the society concerned. A series of interrelated discussions is then planned and ultimately presented by a group from the faculty embracing as many as 4 disciplines. It is also possible that, as television is used increasingly in medical education, video-taped or kinescoped material can be utilized most effectively by central coordination.

We would all agree that there is no better vehicle of education than a well-planned program of professional reading. A coordinating agency might well be the means of bringing expert guidance and greater efficiency to the reading efforts of physicians. This could be done by soliciting the help of experts from various fields in compiling lists of key articles. Further, quiz questions on this reading might be devised for use by the student. The outstanding success of correspondence courses at the University of Southern California has demonstrated the practicability of a similar device.

Finally, through a coordinating agency, directors of graduate education could more easily work together and share ideas. Without question, the planning of formal short courses has become highly competitive and, because of practical considerations, has consumed most of our efforts. At the same time, there is reason to believe that the needs of the practicing medical profession are not being adequately met. Some schools receive appropriations specifically for this type of education and need not be concerned primarily with the revenues received. Some are most interested in serving their own alumni and in contributing to the reputation of their institution or faculty. In this complex of different approaches and motivations, it becomes increasingly clear that there are more meetings and courses than

interested and conscientious physicians can utilize; that to be successful, programs must be widely publicized, well organized, and adequately financed; that many of the most needy among physicians are not touched by current postgraduate educational efforts; and finally, that the "hidden costs"—faculty time, overhead, and the like—are often not realistically met from tuition revenues.

In seeking solutions to these problems, the most pressing task for a central coordinating agency would be the institution of sound fact-finding procedures and the prompt dissemination to all concerned of the information obtained. This might well be the starting point for the type of critical study that the American Association of Medical Colleges has so productively pursued in undergraduate medical education. Only when we have objective data to support our contentions can we command from universities, voluntary health agencies, medical societies, and government the type of support that is needed.

The organization of a national coordination agency for postgraduate medical education should not be too difficult if the potential advantages are appreciated. Cooperative effort and representation should be sought from the Council on Medical Education of the American Medical Association, the American Association of Medical Colleges, the Federation of Specialty Boards, the American Academy of General Practice, the newly formed group of directors of medical educational programs in community hospitals, voluntary health agencies such as the American Heart Association and the American Tuberculosis Association, and, last but not least, no less than 2 directors of postgraduate activities in medical schools. A governing body so defined would direct the operation of a central office and staff and would be responsible for all policy decisions.

Initial support and subsidy for special projects would have to be sought from charitable foundations, from industry, or from government, but probably a scale of reasonable service charges to institutions and individuals could be agreed upon which would meet the basic operational costs after the first two or three formative years.

CONCLUSION

To conclude, may I explain that my purpose was to stimulate thinking and discussion on a most important problem. Certainly, the concept of a central coordinating facility has many controversial aspects, and many important associated questions have ben left unanswered. However, there would seem to be a real need for concerted action in seeking the necessary support not only to stimulate increased interest but also to improve present methods and to evaluate future requirements in the field of postgraduate education. It is hoped that the ideas briefly presented here have stimulated reactions, whether in support or challenge of central coordination in postgraduate education, and that serious consideration can be given to this concept in future planning. The recent paper by Darley and Cain[1] is of particular interest in this connection.

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Mortality with subdural hematoma is extremely high in patients requiring surgical exploration within twenty-four hours after injury, and the term acute subdural hematoma probably should be reserved for these patients. After twenty-four hours, most patients survive surgical intervention. Subdural hematoma apparently is not the primary cause of death, and venous bleeding probably does not produce early symptoms unless accompanied by severe cerebral contusion or laceration.

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R. L. McLaurin and F. T. Tutor: Acute subdural hematoma. J. Neurosurg. 18:61-67, 1961.

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Book Reviews . . .

An Atlas of Acquired Diseases of the Heart and Great Vessels

JESSE E. EDWARDS, M.D., *1961. Philadelphia: W. B. Saunders. Three volumes. 1,897 pages. Illustrated. $70.00.*

Dr. Edwards has recorded, in the 1,400 pages of these 3 magnificent volumes, his extensive personal observations of nearly a decade and a half in his field of cardiovascular pathology. As stated in his preface, this work is a "correlation of functional and clinical manifestations on the one hand, with pathologic anatomy on the other."

Although written by a pathologist, the *Atlas* is clinically oriented in that the anatomic presentations are closely related to the roentgenologic findings, the electrocardiographic pictures, the physiologic derangements, and the clinical symptoms and signs. This being the case, the lessons presented here are readily transferred to and applied at the bedside by the clinician, as well as at the operating table by the cardiovascular surgeon.

Volume 1 covers diseases of the valves, endocardium, and pericardium; volume 2, coronary artery disease, systemic hypertension, myocardiopathies, the heart in systemic disease, and cor pulmonale; and volume 3, diseases of the great vessels—conditions involving the aorta, the pulmonary arteries, the systemic arteries, the veins, and the thoracic duct.

The illustrations are superb, indicating that great care was exercised in the arrangement of the specimens and that the photographic work was expert. The W. B. Saunders Company is to be commended for the part it played in the faithful reproduction of these pictures. Even the electrocardiograms, which generally are difficult to reproduce, are, with but a few exceptions, beautifully done.

These volumes will be almost indispensable to the cardiologist, the internist, the roentgenologist, the pathologist, and the cardiovascular surgeon. The resident in internal medicine will benefit much from them. The medical student and, to a greater degree, the intern will find it a valuable reference book. It is not the sort of book that is likely to be soon put out in a new edition, as it is concerned with basic fundamentals.

Picking up any one of the volumes for casual general reading or for looking up a specific subject for close study is a delightful experience. This work should become a "cardiac classic."

MILTON M. HURWITZ, M.D.
St. Paul

Biology of Pyelonephritis

EDWARD L. QUINN, M.D., *and* EDWARD H. KASS, M.D., *editors, 1960. Boston: Little, Brown & Co. 696 pages. Illustrated. $18.00.*

This book comprises the efforts of 88 contributors, who have attempted to collect all existing knowledge of pyelonephritis. The subject matter is thought-provoking and should stimulate further interest in the investigation of the disorder. Renal anatomy, physiology, biochemistry, immunology, bacteriology, and experimental therapeutics, as well as clinical course and treatment of pyelonephritis, are presented in great detail. The experimental background is emphasized but not at the expense of the clinical applications. As is to be expected because of the large number of contributors, there is some, but still acceptable, overlapping of subject matter. Numerous cross-references are cited. Résumés and discussions are well presented and of great value to the reader. Differences of opinion are advantageously emphasized.

Especially thought-provoking are the discussions by Drs. Davis and Kass as to the dangers of instrumentation of the urinary tract. One can't help but feel that Dr. Kass is overly timid about the danger of instrumentation; one mustn't dig up the whole garden to get rid of the weeds. The limitations of needle biopsy as a diagnostic measure are justifiably emphasized.

The wealth of material will make this a reference text for many years. The illustrations, especially the photomicrographs, are excellent. It is well written, with a few typographic errors. The bibliography is extensive. I recommend this book as a valuable addition to the library of the internist or urologist.

MILTON P. REISER, M.D.
Minneapolis

Social and Medical Problems of the Elderly

KENNETH HAZELL, *1960. Springfield, Ill.: Charles C Thomas. 210 pages. Illustrated. $6.75.*

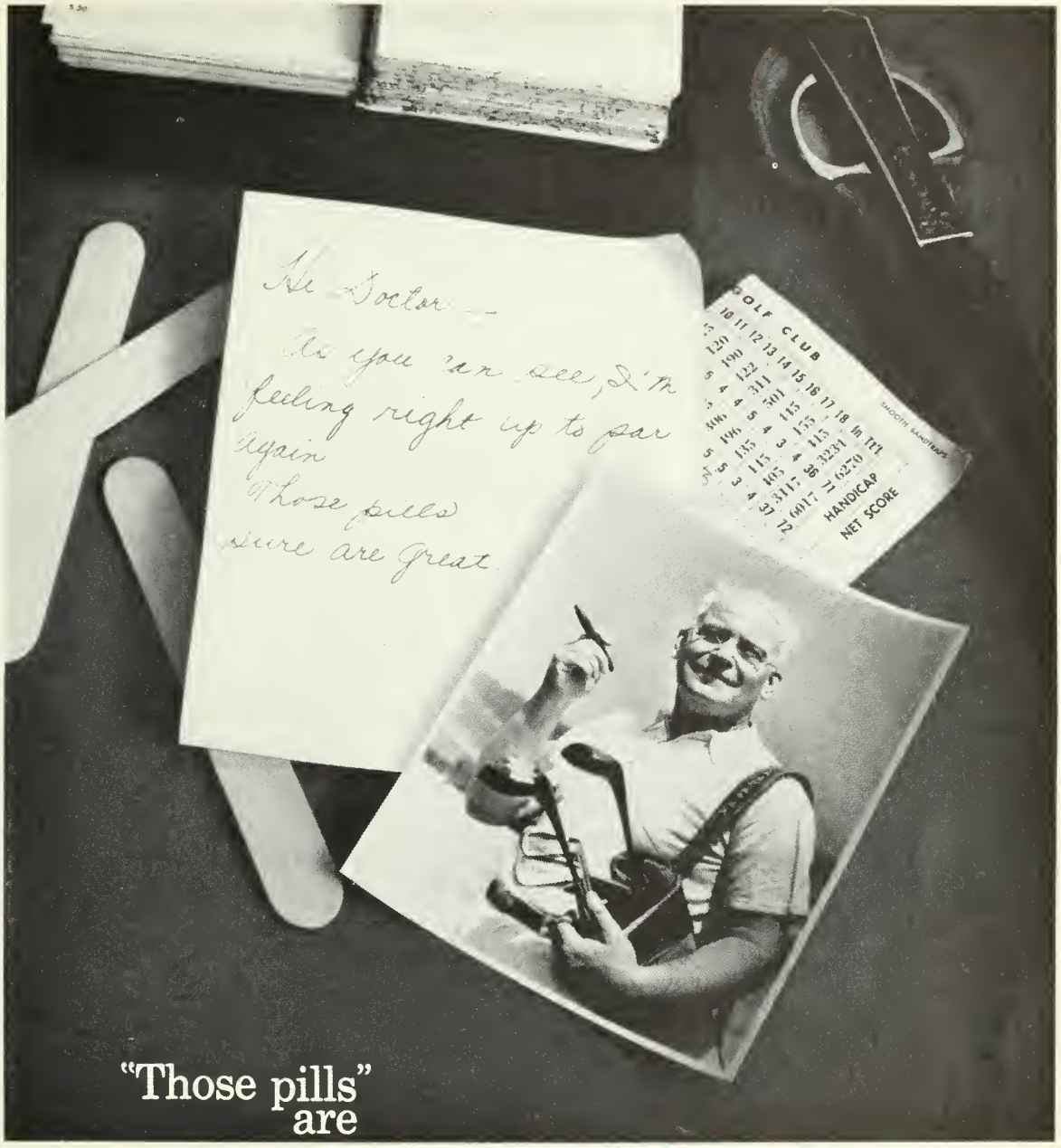
The proper medical care of the chronically ill, aged person is the phenomenon under examination. Written by a doctor primarily for other doctors, the book has as its main emphasis the technical aspects of medical care of the patient at home or in the hospital. Special attention is given to the establishment and operation of a geriatrics unit in a hospital.

An integral part of the book is devoted to a description of the social conditions and problems of elderly ill persons of a working-class background in England. Because the medical and social conditions are so interrelated, these illnesses can be treated properly in the home by medical personnel or the family only with utmost difficulty. The aged in England are moved, therefore, to the short-term hospital under the auspices of the National Health Service, where they are "dealt with rather inadequately and at extreme cost by the hospital medical service."

It is the urgency of the situation of providing proper medical care to the aged today under a system of National Health Service that has prompted this volume by a doctor directly responsible for hospital services to the elderly. The book aims to aid physicians not only on proper medical management of the aged ill person but also on the dire need for additional community services to aid the patient and the physician in England.

The medical section, which comprises over two-thirds of the volume, is written in simple, nontechnical language so that the trained physician, nurse, and/or nurses' aide may find this a ready reference volume. Although English medical terminology is used, these medical sections should make the volume of immediate interest to

(Continued on page 16A)



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(Continued from page 14A)

all persons involved with nursing homes and the elderly ill at home in the United States. The book successfully aims to supplement the advice given by the family physician but in no way to supplement this physician-patient relationship.

The author provides a series of short-term recommendations, such as home-nursing, homemaker, and meals-on-wheels services for the aged, many of which are now being considered by more and more communities in the United States. The author urges the immediate installation of as many services as are practicable, for he believes that, "unless the problem of the aged is properly dealt with, it could reduce the welfare state, full employment and our whole economy into a chaotic muddle."

In the end, the author wonders whether or not the real key to good health is not primarily good social conditions. The use of the National Health Service in England or voluntary health insurance in the United States to ameliorate conditions caused by insufficient income, bad housing, poor diet, and lack of help in the home must be one of the most expensive methods and "one very detrimental to the National Health Service itself." Certainly, this is a book for those struggling with similar problems in the United States.

WALTER POLNER
Madison, Wisconsin

Handbook of Pediatrics

HENRY K. SILVER, M.D., C. HENRY KEMPT, M.D., *and* HENRY B. BRUYN, M.D., *fourth edition, 1961. Los Altos, Calif.: Lange Medical Publications. 574 pages. Illustrated. $3.50.*

This pocket-sized book contains a comprehensive yet concise coverage of the field of pediatrics. It is 574 pages long, with small print and flexible plastic cover. The paper is of good quality.

Wherever possible, the authors list symptoms, diagnosis, treatment, and other factors in outline form, with tables and illustrations. This makes it possible to find any specific point of information in the least possible time.

This book is recommended not only for every pediatric intern and resident but also for pediatricians and general practitioners who might, for example, forget the dosage of Digoxin for a 3-kg. infant with cardiac failure or, possibly, the differential diagnosis of coagulation defects. It will fit easily into the pocket of any office coat and has already proved of definite value to this reviewer.

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Modern Occupational Medicine

A. J. FLEMING, M.D., *and* C. A. D'ALONZO, M.D., *editors, 1960. Philadelphia: Lea & Febiger. 553 pages. Illustrated. $12.00.*

The second edition of this volume, written by 22 contributors, all associated with E. I. du Pont de Nemours & Co., represents an extensive revision of the former text, published in 1954.

The original edition has been criticized as being slanted toward the chemical industry. This has been considerably rectified by the addition of a number of new chapters, such as, "Occupational Chest Diseases," "Men-

tal Illness," "Emotional Factors in Diseases of the Skin," "Lead, Inorganic and Organic," and "Biostatistics in Occupational Medicine."

In considering the scope of the book, one feels that, as a general reference, it could be improved by the addition of more full discussions of the organization and relationships of the small plant medical department, the community industrial clinic, workmen's compensation laws, and the toxicology of some of the more basic materials such as the metals. The dermatologic effects of materials are given in the course of the discussions of the individual materials. One recognizes that it is impossible to present a complete discussion of a subject as large as occupational dermatoses in a book of this type. However, it would be well to include a chapter which would present an impression of the variety of materials producing dermatoses, the general nature of their effects, and the general methods of control.

With a few exceptions, some mentioned above, this is a well-rounded book and contains much authoritative material which should be of value to industrial physicians, students, and other persons concerned with occupational health.

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Epilepsy and Related Disorders

WILLIAM G. LENNOX, M.D., *and* MARGARET LENNOX, *1960. Boston: Little, Brown & Co. 1,168 pages. Two volumes. $13.50.*

This is a monumental work by America's dean of epileptologists. It is based on his enormous experience and wide knowledge of the literature. It is so well written that it can be read with pleasure. Naturally, in so large a treatise, nearly every phase of epilepsy and every one of the several types of the disease are discussed.

There is a fine chapter on treatment which can be of great value to every man who treats epileptic patients. All of the new drugs are discussed, and both their advantages and disadvantages are described.

Naturally, there is much concerning the electroencephalogram in the several types of epilepsy. Dr. and Mrs. Gibbs, who have done so much for electroencephalography, used to work with Dr. Lennox.

As the Lennoxes point out, epilepsy is mainly a disease of the young which often shows up in childhood. Petit mal is a disease of children, and grand mal tends to clear up as the person grows older. This is why the epileptologist should be an optimist. As many physicians do, Dr. Lennox tries not to offend epileptic patients by talking too frankly about their disease. The relatives may be even more touchy than the patient. Perhaps because of this disinclination to offend epileptics and their relatives, Dr. Lennox soft-pedals the subject of heredity and the dangers the epileptic runs in marrying and having children.

Dr. Lennox had a remarkable early tendency to look among only the parents and grandparents for a history of epilepsy, and then to look only for a history of grand mal and not for the many minor equivalents of epilepsy. He admits that if one's statistical study includes all those cases in which grand mal shows up in uncles, aunts, nephews, nieces, cousins, siblings, and children, one will find a high percentage of cases with an obvious hereditary origin. The reviewer wonders why, for years, Dr. Lennox kept publishing his old statistics based ex-

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clusively on the incidence of grand mal in parents and grandparents. He should have known that such figures could have no value. Unfortunately, they are the statistics commonly quoted in the literature.

Unfortunate, also, is the fact that no one studying the heredity of epilepsy has obtained electroencephalograms of all the near relatives. Only when this is done will we have statistics of any value. Dr. Lennox says that if statistics on the hereditary origin of epilepsy were based only on cases in which the patient showed signs of the disease in early childhood, when it almost always is of the "idiopathic variety," the percentage of cases with affected relatives would be large.

Occasionally, as on page 259, Dr. Lennox admits that "We who are 'proponents of the epileptic' would be glad to assign psychotic and unsocial behavior to some condition other than epilepsy . . ." Of course, it is good that an epileptologist feels deeply sympathetic toward his patients, and one admires Dr. and Miss Lennox for their honesty. They admit to feeling so greatly involved personally that they find it difficult to discuss frankly those several phases of epilepsy which are very offensive to most epileptics and their relatives.

One cannot read far in many places in the book without sensing this great reluctance the authors felt to discuss the well-known violent temper of the epileptic and many of his relatives, or the facts that a considerable percentage of epileptics and their relatives have occasional psychotic episodes, that some 60 per cent of delinquent youths have an electroencephalogram that suggests epilepsy, that some investigators have found signs of epilepsy in from 35 to 65 per cent of the relatives of epileptics, that the world is full of epileptics who have never had a seizure of grand mal, that many epileptics become heavy drinkers, or that many should never drive a car. Professor Stanley Cobb of Harvard once said that perhaps only 1 in 25 epileptics ever has a seizure. Dr. Frederic Gibbs has said that certainly only 1 in 10 ever has a seizure.

If a second edition of this invaluable work is ever published, it is to be hoped that all the information in regard to heredity, which now is scattered throughout the two volumes, will be brought into one place. The second edition should be prepared by a scientist who has no personal feelings in regard to epilepsy and hence can write dispassionately about every phase of it. Highly desirable in a second edition would be a well-written chapter on the weird symptoms commonly seen in those innumerable carriers of epilepsy who seldom, if ever, have a seizure.

In another edition, it would help to have a chapter on the great need for more frequent use of electroencephalograms by all physicians and especially by psychiatrists. I recently was consulted by a young woman who had spent $7,500 on psychoanalysis. I uncovered a story of many brief blackout spells—one of them with convulsive movements; I got the typical story of an epileptic personality; I got the story of a bad nervous heredity; and Dr. Gibbs found spikes and seizure discharges in the electroencephalograms.

In closing, the reviewer will say that it would be churlish to complain of the small defects found in so huge a book and one so filled with interesting and valuable information. It is a book which should be in the library of every physician who hopes to be well educated.

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