VOLUME 29 NUMBER 2

ARCHIVES OF NEUROLOGY AND PSYCHIATRY

FEBRUARY, 1933

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, Jan. 7, 1919, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized Jan. 15, 1919.

CONTENTS OF PREVIOUS NUMBER

JANUARY, 1933. NUMBER 1

Archives of Neurology and Psychiatry

VOLUME 29 FEBRUARY, 1933 NUMBER 2

USE OF CARBON DIOXIDE MIXTURES IN STUPORS OCCURRING IN PSYCHOSES

FRANK C. D'ELSEAUX, M.D.
Commonwealth Fund Fellow in Psychiatry
AND
HARRY C. SOLOMON, M.D.
BOSTON

While working with psychotic patients in a study of sodium cyanide as a respiratory stimulant, Loevenhart and Lorenz and their co-workers [1] found evidence of greater cerebration in stuporous patients. They repeated their work,[2] using high percentages of carbon dioxide, and found in stuporous patients, with conditions variously categorized as dementia praecox, manic-depressive psychoses or involutional melancholia, but alike in their relative mutism and noncommunicativeness, a definite, certain and invariable response. Their method of procedure was to use an ordinary nitrous oxide anesthetic machine, and by means of this to regulate the relative percentage of gas as follows: Starting with 10 or 15 per cent of carbon dioxide and the remainder oxygen, they gave this mixture for one minute and then each minute thereafter increased the amount of carbon dioxide at the rate of 5 per cent a minute until between 30 and 40 per cent of carbon dioxide (the remainder being oxygen) was given. The entire administration took from three to ten minutes. The results of this inhalation they described as follows: There are an increase in blood pressure, a decrease in pulse rate, a decrease in rate and an increase in amplitude of respiration, freer muscular movements, an animated facies and a moderately adequate verbal response. They described no loss of consciousness and no convulsions other than a tonic contracture.

Many clinics in this country and abroad repeated this work and agreed in the main with the observations of the original workers.

With the observation checked, the question immediately arises as to the modus operandi of the procedure. Is it a stimulation of the

From the research laboratories of the Boston Psychopathic Hospital.

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 7, 1932.

1. Loevenhart, A. S.; Lorenz, W. F.; Martin, H. G., and Malone, J. Y.: Stimulation of the Respiration by Sodium Cyanide and Its Clinical Applications, Arch. Int. Med. **21**:109 (Jan.) 1918.

2. Loevenhart, A. S.; Lorenz, W. F., and Waters, R. M.: Cerebral Stimulation, J. A. M. A. **92**:880 (March 16) 1929.

higher centers, or is it a blocking or inhibiting of a part of the system which is responsible for the symptoms presented by this type of patient, or is the condition primarily psychologic? Obviously, adequate answers to these questions are likely to contain some indication as to the primary nature of such psychotic manifestations.

The work herein reported was carried out in an attempt to obtain factual evidence which might be of some assistance in answering some of these questions. It was thought that as the greater part of the data on which the statements in this paper are based were so specifically of a physiologic nature and, as such, of greater interest to the physiologist than to the neurologist or psychiatrist, it would be better to interpret the data as they relate particularly to the psychiatric problem and to leave a more detailed account of them to be reported in one of the physiologic journals.

METHODS

Administration of the Gas.—Spirometers of the Tissot variety were used to hold the mixture to be breathed. It was thus possible to give a known, predetermined and uniform mixture. The use of the spirometers served another purpose. By making quarter of a minute readings on the scales of the spirometers, it was possible to ascertain the amount of gas breathed per unit period of time. Further, using one spirometer containing room air and another containing the gaseous mixture to be breathed, the ventilation during rest as well as during inhalation of gas could be observed. The gaseous mixtures were made up from commercial cylinders of oxygen, nitrogen and carbon dioxide.

The mask was of the type used during the World War as a protection against poisonous gases. The two outlets were fitted with flutter valves, which permitted the inflow of the gaseous mixtures through one tube and the overflow of expired air through the other. Under the conditions of the experiment the mask was fitted so tightly as to prevent any leakage on inspiration.

Clinical Observations.—The patient was brought (without breakfast) to the experiment room and encouraged by the physician to talk or to give some other evidence of contact with the environment. Moving pictures were taken. She was then allowed to rest on the bed for half an hour. During this time the rate, quality and regularity of the pulse, the rate, regularity and depth of respiration and the blood pressure were observed by the nurse in as rapid succession as these observations could be made. Detailed notes were made of any activity on the part of the patient or of any one else in the room. If a specimen of blood was to be taken during conditions of rest, it was obtained after this first half hour period, and the patient was permitted to rest under the conditions outlined for another half hour. Following this, the mask was adjusted to the patient's face, and she was permitted to breathe from the tank containing room air for from fifteen to thirty minutes. In addition to the aforementioned observations, the amount of air breathed during each quarter of a minute period was noted. During this period and continuing until the end of the experiment, each member of the group of workers had a single function to perform, and for the most part had this same function throughout all the experiments. It should be noted that the observations as to the patient's mental response to the procedure were always made by one or the other of us (usually by Dr. Solomon). One of the team observed the patient's facies and any change in her general condition; a second observed the pulse; a

third, the rate of respiration; a fourth, the amount of gas breathed, and a fifth, the blood pressure; a sixth took moving pictures of the response. Two others posted themselves one on each side of the patient at the femoral region, each armed with a syringe, one to take arterial and the other to take venous blood. Stenographic notes of all that took place were made on paper divided to indicate the time at which the observation was made. The pulse and respirations were counted for a half minute each minute. With each worker at his post, the patient was allowed to breathe room air as already indicated. Following this, the valve was turned and the patient breathed the desired mixture for a given time (from three to five minutes); the punctures were made, and as soon as the last blood was out the patient was allowed to breathe room air. The aforementioned observations were made until the patient lapsed into the preexperimental state.

Examination of the Blood.—The blood was used to construct carbon dioxide dissociation curves from which could be determined its carbon dioxide capacity, the pressure of the carbon dioxide and the degree of acidity. The amount of lactic acid and the degree of oxygen saturation were observed.

Behavior of Patients.—Thirty patients were observed in their response to inhalation of carbon dioxide. One of the patients was studied in rather great detail, and the data obtained in her case form the chief basis for this paper.

In all the cases the condition was classified as stupor on the basis of a more or less complete lack of contact with the environment, as shown by the overt behavior. Thus the majority of the patients were mute, did not care for their excretory functions in the usual way, had to be induced to eat or be tube fed, sat in a chair, lay in bed, or stood in the place where they were put, showing little spontaneity of activity, were for the most part resistive to attempts to arouse activity in them and either kept the eyes shut or stared ahead with a dull apathetic gaze. While no importance was attached to the formal diagnosis as far as this work is concerned, it may be said that the great majority of cases were classified as cases of catatonic stupor, and only a few fell into the category of depressive or of toxic stupor.

RESULTS

Experiments with Carbon Dioxide.—The gaseous mixtures used in these experiments contained from 5 to 35 per cent of carbon dioxide and 20 or 30 per cent of oxygen, the remainder being nitrogen. When any one of these mixtures was given to a patient to breathe, there were certain observable changes. The nature of some of the changes is shown in figures 1, 2 and 3, representing the results of inhalation of 12, 20 and 25 per cent of carbon dioxide, respectively. Briefly stated, these changes were as follows: There was an immediate increase in depth of respiration with a consequent increase in the rate of ventilation. There was a rise in both diastolic and systolic pressures and in the respiratory rate. The pulse rate either remained the same or dropped slightly at first. Toward the end of the inhalation, and at times following it, the pulse would rise above the level during rest. The quality of the pulse became poorer at first, but later attained a full quality. At times marked cyanosis of the face appeared. A state of acidosis associated with a partial saturation of the tissues with carbon dioxide developed. The oxygen saturation of arterial blood remained

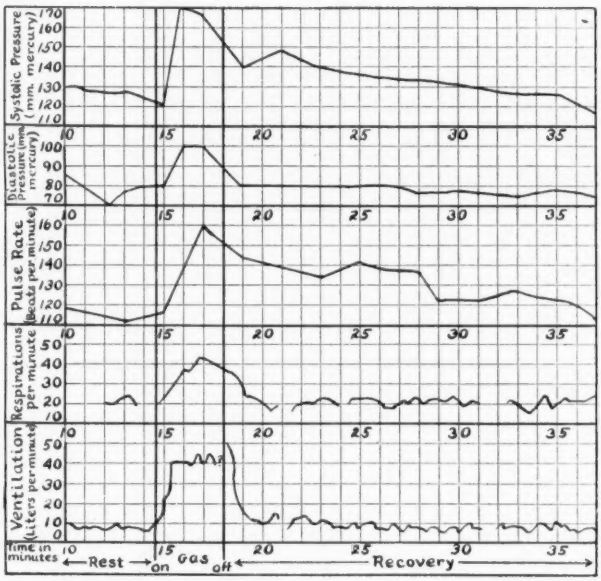

Fig. 1.—Results of experiment with 12 per cent carbon dioxide and 21 per cent oxygen.

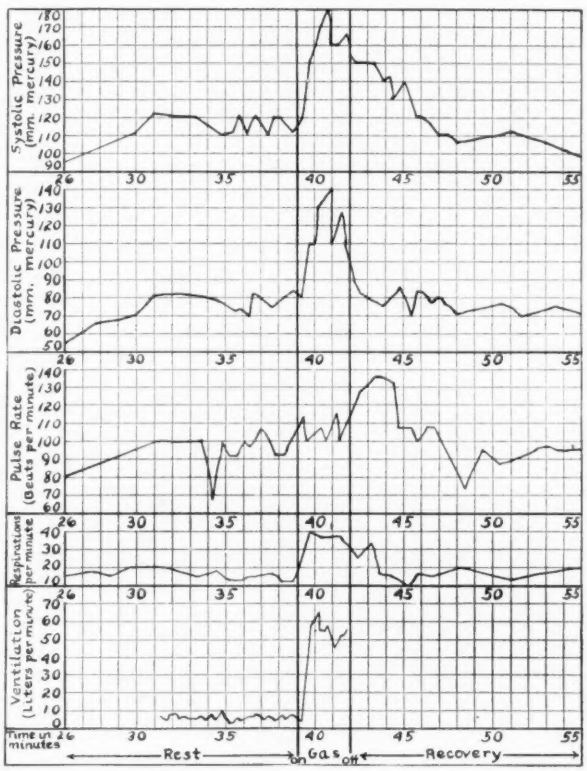

Fig. 2.—Results of experiment with 19.5 per cent carbon dioxide and 20.3 per cent oxygen.

relatively unaltered. The saturation of the venous blood varied greatly, but always dropped below its level during rest, and thus there was a greater difference between arterial and venous blood in this respect during inhalation than during rest.[3] Shortly after these changes set in, the patient appeared more alert; at times she talked spontaneously or in answer to questions, and tried to remove the mask. If the mask was removed at this point, the patient lapsed into her previous state. If the inhalation was continued, she at times became comatose. With

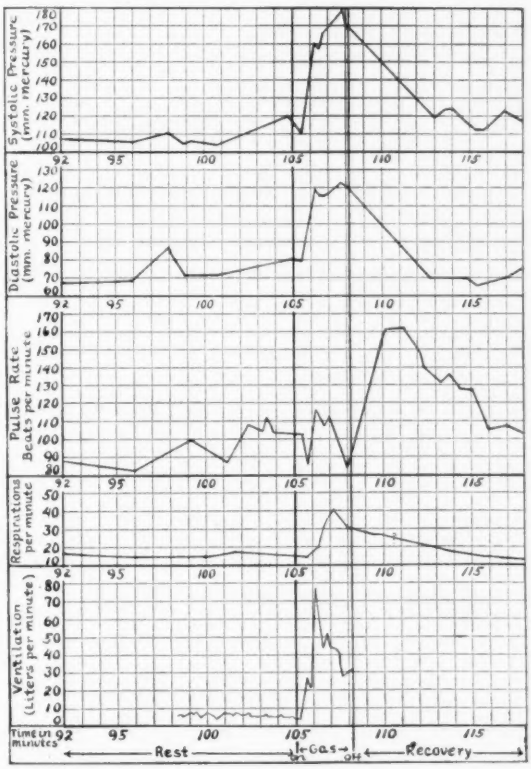

Fig. 3.—Results of experiments with 25.4 per cent carbon dioxide and 21 per cent oxygen.

3. Work being done at present in association with Dr. D. B. Dill of the Harvard Fatigue Laboratory, and to be reported later, indicates that only the metabolic carbon dioxide is stored intracranially, and that this, as well as the inhaled carbon dioxide stored in the tissues of the leg is given off within two or three minutes after cessation of inhalation. It is also indicated that the oxygen saturation of the blood returning from the brain is greatly increased, while that from the leg is decreased, during inhalation, and that immediately following gas both of these bloods resemble arterial blood in degree of oxygenation, gradually returning to their usual state in from fourteen to twenty minutes.

continued inhalation, periocular and perioral tremors presented themselves and were followed by generalized tremors and convulsive movements. Usually the gas was turned off and the mask removed as soon as the patient became comatose. On regaining consciousness, which occurred in a few seconds, the patient smiled, looked alert and spoke spontaneously and in response to commands and questions. Gradually, despite continued efforts to keep her in a communicative state, she faded into the pre-inhalation condition.

Other known effects of this procedure reported by other workers include a marked increase in the pressure of the cerebrospinal fluid (Solomon and Kaufman [4]) and a marked dilatation of the vascular bed of the brain (Wolff and Lennox [5]).

Which, if any, of these changes may be held accountable for the mental response? First, it was found that percentages of carbon dioxide of 20 or less gave rise to little or no particular change in the patient's behavior and that a mixture containing 25 per cent or more did elicit a response. Furthermore, it was observed that percentages higher than 25 did not cause any greater response nor did they insure a response. Concerning the physiologic changes, it may be said that there was a moderately constant relationship between the percentage of carbon dioxide inhaled and most of these conditions. Thus, the degree of acidosis and the carbon dioxide content of the blood, and most probably of the tissues, increased in direct proportion to the increase in the carbon dioxide in the mixture. The increase in blood pressure, respiratory rate and ventilation was in direct proportion to the increase of carbon dioxide inhaled, but did not occur with as great constancy or relative difference from one percentage to another as in the case of acidosis and the carbon dioxide content. Consciousness was not lost when less than 25 per cent of carbon dioxide was inhaled. There was no specific relationship between oxygenation and the percentage of gas breathed. It might well seem from these facts that the degree of acidosis, the carbon dioxide content or the loss of consciousness could be held accountable for the change in the behavior of the patient. However, the fact that the initial indication of a response came immediately after the increase in ventilation and that the ultimate response usually faded as the rate of ventilation returned to the normal level indicated that the response might well be due to the alteration in breathing. Furthermore, the temporal relationship between the gradual fading of response and the gradual change in the oxygen saturation of the venous blood is highly suggestive of a teleologic relationship. Still another factor entered to confuse any attempts at correlation. It was

4. Solomon and Kaufman: Personal communication.

5. Wolff, H. G., and Lennox, W. G.: Cerebral Circulation, Arch. Neurol. & Psychiat. **23**:1097 (June) 1930.

found under certain psychologic or environmental conditions, to be described later, that mixtures ordinarily effective in a given patient, while giving rise to the usual physiologic changes, at times did not produce a response. Furthermore, it was noted that not all patients responded to the usually effective mixtures. It was therefore decided to vary the procedure in an attempt to rule in or out these different variables.

Experiments with a Low Percentage of Oxygen.—It was believed that by using a sufficiently low percentage of oxygen with nitrogen, and in the absence of carbon dioxide, changes could be produced in

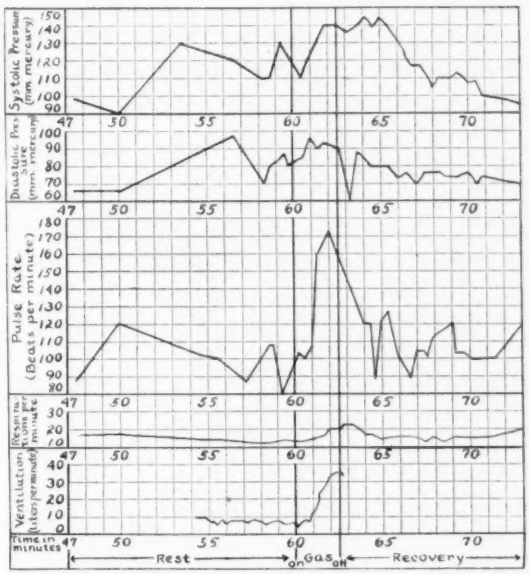

Fig. 4.—Results of experiments with 4.5 per cent oxygen in nitrogen.

the patient which in part would be similar to, and in part different from, those obtained in the experiments with carbon dioxide. Thus, it was thought that the changes in blood pressure, pulse, respiration and rate of ventilation, as well as the psychologic situation, would be of the same nature in both types of experiments, while instead of creating a state of acidosis with partial saturation of the tissues with carbon dioxide, a state of alkalosis associated with a lowered carbon dioxide content of the tissues would be present. The patient was therefore given mixtures to breathe which contained from 4 to 12 per cent of oxygen in nitrogen. The experimental procedure was the same as that used in the experiments with carbon dioxide. (Figure 4 shows the results of breathing a 4 per cent mixture of oxygen in nitrogen.)

Briefly stated, the results of breathing mixtures containing 7 per cent or less of oxygen were as follows: There were a slight increase in systolic pressure, a slight but not constant rise in diastolic pressure, a moderately rapid and marked rise of the pulse rate and no increase in the respiratory rate, but a definite increase in the depth of respiration with a consequent gradual increase in ventilation. At no time was the inhalation of mixtures containing such a low percentage of oxygen carried to a point where consciousness was lost. There was a partial depletion of the tissues of their carbon dioxide, associated with a state of relative alkalosis. There was, in addition, a marked state of anoxemia, the arterial blood being only partially saturated with oxygen. The difference in oxygenation of venous and of arterial blood differed little from that in rest. The change in blood pressure or in ventilation was not as great as in the experiments with carbon dioxide. Shortly after the onset of hyperpnea, the patient usually became restless. This restlessness increased progressively as the experiment was carried on, and became marked—much more so than was ever noted in the experiments with carbon dioxide. Usually, following the onset of the hyperpnea the patient appeared more alert and frequently spoke spontaneously or in answer to questions. Following the removal of the mask, the response usually faded more promptly than in the experiments with carbon dioxide and in general was not as adequate as in some of the better ones of those experiments.

Thus, by the use of a different procedure which produced physiologic changes in part similar to and in part dissimilar from those produced by the inhalation of carbon dioxide, a response was obtained which, while quantitatively not as great as in the latter experiments, was qualitatively the same. In other words, a response was obtained when the patient was made relatively alkalotic instead of acidotic, when the carbon dioxide content was lowered instead of increased, when the patient was in a state of anoxemia and when the difference in the oxygen saturation of the femoral arterial and venous blood was little different than in rest. That the patient did not lose consciousness in these experiments, in which the response was not as great as in the experiments with carbon dioxide in which consciousness was lost, would seem to point with some degree of probability to this factor as being at least a partial determinant of the response obtained. Furthermore, there was the same temporal relationship between the hyperpnea and the mental response. But again it was found that not all patients respond to this procedure nor did the same patient always respond to the usually effective percentage of the gas.

Experiments with Sodium Bicarbonate.—It was desired to saturate the tissues with carbon dioxide to as great an extent as in the experiments with carbon dioxide without creating the state of acidosis present

in the latter. For this purpose the patient was given large amounts of sodium bicarbonate and then allowed to inhale a 10 per cent mixture of carbon dioxide. The bicarbonate was given in 10 Gm. doses in the form of a concentrated aqueous solution, 100 cc. of which was equivalent to 10 Gm. of the drug. A stomach tube of small bore was passed through the nose and left in place during the period the drug was given. Tincture of opium, in 10 minim (0.6 cc.) doses, was administered in order to decrease the chance of vomiting. The method for giving the carbon dioxide was the same as that used in the previous experiments.

The result was an increase in the carbon dioxide content of the arterial blood, and most probably in that of the tissues, to an extent comparable with that obtained in the experiments in which 25 per cent of carbon dioxide was inhaled, while the degree of acidity was increased only to the same degree as when 10 per cent of carbon dioxide was inhaled. The oxygen saturation of the arterial blood remained practically unaltered, while the difference in saturation of arterial and of venous blood increased, as was described in the discussion of the experiments with carbon dioxide. The change in blood pressure and in pulse rate was the same as when 25 per cent of carbon dioxide was breathed, and, except for a slower rise in respiratory rate and ventilation, there was not a great deal of difference between the two types of experiments. Consciousness was not lost. While there was a slight alteration in the patient's activity in this experiment, apparently dependent on the ingestion of alkali, nevertheless the inhalation of gas had no appreciable effect. This alteration will be further considered later.

Thus, in the presence of physiologic changes similar to those obtained in the experiments with carbon dioxide that were successful in arousing the patient—that is, an increase in the carbon dioxide content, blood pressure, ventilation, etc.—except that the acidity was not as greatly increased and consciousness was not lost the patient did not respond.

In regard to the aforementioned alteration in the patient's activity, we may quote the notation made at the time.

> Throughout this hour and a quarter (rest period before gas) the patient lay motionless, offered no resistance and would not respond to questions or commands. At first she kept mumbling under her breath and frequently asked for water indistinctly. Her facial expression was not as vacant as usual, and her eyes seemed to have a more normal gleam, although she did not show any real play of facial expression. . . . Fifteen minutes after the inhalation of the gas she asked for a glass of water, was given it, took it, held it herself as she drank, and returned the glass when through drinking.

This amount of activity was unusual for this patient, and its presence following the ingestion of sodium bicarbonate led us to repeat this

torm of medication without supplementing it with inhalation of carbon dioxide, with the following results.

Briefly, when the patient was given large amounts of sodium bicarbonate, there was little or no alteration in blood pressure, pulse, respiratory rate or ventilation. There was no loss of consciousness, and in all probability the spinal fluid pressure was decreased. There were a gradual loss of water and an increased urinary output, and if water was given to replace that lost there was no particular change in the patient's mental status. However, if at the same time that the loss of water was going on the fluid intake was limited, there were gradual dehydration and an increase in temperature; the patient became thirsty and rather restless, then began to make more and more purposive movements, such as trying to get out of bed and when restrained trying to undo the restraints, and finally spoke spontaneously. At first she asked for water, then to get out of bed and then to go home, and following this she had a long (five pages of notes) conversation with the physician touching on varied subjects. We wish to stress that this was a conversation. The patient had a more normal gleam in her eyes and showed proper and adequate change of facial expression and considerable spontaneity in expressive movements of the hands and facies and in expressed thoughts. Throughout she asked constantly for fluids, specifying various drinks which she liked, such as orange juice. With the quenching of thirst, the activity of the patient decreased. The change in activity was not temporally correlated with the change in temperature. In these experiments the patient was relatively alkalotic, while the carbon dioxide content of arterial and venous blood, and probably of the tissues, was similar to that which obtained when she breathed from 15 to 20 per cent carbon dioxide. The oxygen saturation of arterial blood was unaltered from the usual level during rest, and the difference between arterial and venous oxygen saturation was within the limits of values obtained in rest.

Thus, of the known changes in the experiments with either carbon dioxide or sodium bicarbonate, the only one common to both is the relatively high carbon dioxide content. However, during the experiments with sodium bicarbonate this resembled the state present during the inhalation of relatively ineffective percentages of carbon dioxide, and, furthermore, in the first described experiment with sodium bicarbonate (with supplemental inhalation of carbon dioxide) there was a carbon dioxide content which was comparable to that present when effective percentages of carbon dioxide are inhaled, without there being any response. But we have introduced two other variables—increased temperature and dehydration. It has been stated that there was no temporal correlation between the height of the temperature and the

response, but in order to have further data in regard to this variable, we employed two other types of experiments, namely, diathermy and protein shock.

Experiment with Diathermy.—A patient was exposed to an ordinary diathermy machine, and the temperature was raised to 100.6, 104 and 102.6 F. on three separate occasions during the same experiment, the temperature being allowed to drop twice by removal of the coverings. Shortly after the current was turned on, the patient began to tremble and to become restless, but did not talk, except in an inaudible mumble. Restraints became necessary. Shortly after this she appeared to the physician to be in pain, her facies appeared pinched, and she had an anxious expression. The electrodes were removed, and the patient was examined, but no burn was noted. The electrodes were replaced, and the experiment was continued. From this point on the patient became restless and talked whenever the current was on, but not when it was off. There was no temporal correlation between the temperature and the patient's activity. At the end, when the temperature and dehydration, owing to loss by perspiration, were greatest, the patient did not respond when the current was off. On the other hand, when the temperature was only slightly raised and the current was on she did talk. Her response to this procedure was entirely different from that to any other procedure. She was like a cornered animal, fighting to be released, asking repeatedly in an urgent and at times demanding voice that she be allowed to get up, and saying she was burning to death. Answers to questions irrelevant to her being released were given in a hurry and followed by pleas to be allowed to get up, and at times these questions were not answered at all. The explanation of this response, we believe, rests in the fact, noted when the electrodes were finally removed, that the patient had sustained a deep burn, the size of a nickel, which apparently had been overlooked at the first examination. While we regret that the patient was unwittingly made to suffer, the experiment served to show that an increase in temperature per se was not adequate to arouse the patient and, furthermore, that patients of this type, renowned for their ability to withstand painful or unpleasant conditions imposed on them, do have a threshold at which they respond to such conditions. One might compare this patient's response to that of an apparently normal person attempting not to respond to an unpleasant or painful procedure and doing so with a good amount of success, when finally the unpleasantness overpowers him and he breaks down in an urgent, forceful plea to be relieved—a plea that carries all the emotion dammed up during the period when he was refraining from responding.

Other than the determination of the pulse and respiratory rates, none of the observations, such as examination of the blood and deter-

mination of ventilation and blood pressure, made in the other experiments were made. However, despite the physiologic changes that may have been induced by the increased temperature, it is obvious that these will be dependent on the temperature and not on whether or not the current is on. Since it has been seen that the temporal correlation of the mental response exists in relation to the presence or absence of the current, and not to the degree of temperature, it is evident that the mental response is not correlated primarily with the physiologic changes induced by the change in temperature.

Experiment with Protein Shock.—The patient was given inoculations with typhoid vaccine on several different occasions, with the result that the temperature was raised to the same and to a greater extent than in the experiments with sodium bicarbonate, though not to the same degree as in the experiments with diathermy. Despite the rise in temperature, with its accompanying physiologic changes, there was no alteration in the patient's mental status.

Experiment with Nitrous Oxide.—It has already been stated that in cases in which a good response was obtained when carbon dioxide was inhaled the patient lost consciousness, and it was suggested that this factor alone might bear some etiologic relationship to the arousal from stupor. With a view to seeing whether or not the patient would respond if made unconscious by some means other than carbon dioxide, she was given nitrous oxide anesthesia on two occasions, but failed to change particularly as a result of this procedure. The changes in blood pressure, pulse and respiratory rate were comparable to those obtained in the experiment with carbon dioxide. The ventilation was not observed, nor was the blood examined.

COMMENT

The essential purpose of this work has been to determine the cause or causes instrumental in arousing patients from their stuporous condition when they are given carbon dioxide to inhale. This arousal has been called the mental response, and on the evaluation of it depend the judgment as to the relative efficacy of the various procedures used and the judgment as to what are the factors causative in bringing it about. It seems desirable to make some comment as to the method of evaluation.

One is forced to rely on the overt behavior of the patient for making this estimation. This includes muscular movement of both the voluntary and the involuntary sort, verbal utterances and such elusive yet real factors as the gleam in the eye and modulation of the voice. Furthermore, there are a number of attributes of each of these forms of activity which are used in estimating the mental activity of a person.

Some are the degree of spontaneity of the act, or, on the other hand, the amount of stimulation needed to produce it; the relative complexity of the movement or verbal utterance and of the stimulus calling it out; the speed of initiation and of performance, and the completeness of performance; the purposiveness, adequacy and degree of relevancy of the act to the stimulus and to the total situation. These are the criteria and their special attributes, by use and evaluation of which we ascribe to a person a certain quantitative and qualitative degree of emotional and intellectual activity, i. e., describe him as normal or abnormal. In evaluating the mental response obtained with various procedures, these were used to determine the degree of normality of the patient's activity. It would be excellent if one could assign mathematical values to each of the details involved, and thereby grade exactly the normality of the response. Since this is impossible, we have depended on our intuitive and empathic appreciation of the various details for the rather rough estimation that results.

Besides the degree of normality, two other factors must be considered: (1) the amount of response obtained or, in other words, the increase in overt behavior over that present in rest, and (2) the duration of the response, that is, the length of time during which the change in overt behavior is present. In the final grading of the mental response, the first of these factors, i. e., the normality of the response, was given greatest weight. The amount of response was considered of next importance, and the duration of the response of least importance.

It has already been stated, on the basis only of the observations in the experiments with carbon dioxide, that several physiologic changes are induced by the inhalation which might be held accountable for the arousal. These were: the degree of acidosis, the high carbon dioxide content, the loss of consciousness, the increase in ventilation and the temporal relationship between the duration of the mental response and the high oxygenation of venous blood. A review of these factors in the case of the other procedures used indicates that no one factor or group of factors is essential to the occurrence of the arousal. Thus, in regard to the degree of acidosis, we find that, despite the relative alkalosis that one obtains in the experiments with oxygen and in those in which sodium bicarbonate was ingested, there was in the former as good a response as, and in the latter a much better response than, is obtained with carbon dioxide in any concentration. Furthermore, despite the fact that in some of the experiments with carbon dioxide the degree of acidity was that of the successful experiments, the patient did not respond. Concerning the high carbon dioxide content, virtually the same holds true. Despite the low content in the experiments with oxygen (and most probably in those with diathermy), a response was obtained, while in the experiments with sodium bicarbonate with sup-

plemental inhalation of carbon dioxide the content was as high as in the effective experiments with carbon dioxide, and yet the patient did not respond. Furthermore, in some of the experiments with carbon dioxide in which the content was as high as in the usually effective experiments the patient did not respond. In regard to the loss of consciousness, this was absent in the experiments with oxygen, sodium bicarbonate and diathermy, and yet the patient responded; on the other hand, in some experiments with carbon dioxide in which consciousness was lost and in the experiment with nitrous oxide there was no response.

In summary, one may say that of the physiologic changes observed, no one change or group of changes is essential to the arousal from stupor; i. e., the patient may respond without the indicated changes being present, and the changes may be present without the patient responding. The multiplicity of the methods used in various clinics to arouse patients in stupors—administration of sodium amytal, increase of atmospheric pressure, oxygen therapy, etc., as well as those reported herein—would seem to indicate almost a priori that there is no one physiologic factor responsible in all cases of arousal. The procedures used by us which were successful had, so far as can be said, but one thing in common, namely, a shock to the body economy of one sort or another. Just how this may have influenced the patient cannot be said exactly, but two observations may throw some light on this. First, it will be noted that there is a qualitative specificity of response to the various procedures. In the case of the experiments with carbon dioxide, the patient usually regains consciousness suddenly, smiles and looks about in an easy manner, free from the usual restraints to movement, as though caught unawares and being more active than was intended. At the same time there is an element of relief, as though the patient is glad to have done with the experience she had just been through. There is no push to activity, but rather a bubbling over of activity. The fact that patients who have recovered invariably describe the experience as if the sole idea in relationship to it were a sense of suffocation, and the fact that the fading of the response goes hand in hand with the diminishing ventilation lend support to this concept of the response being an outgrowth of relief from an unpleasant experience. In regard to the experiments with sodium bicarbonate, there is an ever present physiologic demand, an urge to quench thirst. This is sufficiently stimulating to maintain the patient in her responsive state as long as the thirst lasts, but not so urgent as to cause her not to be able to think of anything else. Lastly, in the case of the experiment with diathermy, an exceedingly urgent physiologic need, one that touches on the urge of self-preservation, dominates the picture. The patient was like an animal, and virtually refused to talk of anything or to do

anything but to ask and try to get up. Responses to other questions were few and were given hurriedly, and were immediately followed by a request to get up, as though to say: "I'll answer your questions and do what you want if you will only let me get away from this instrument that is burning me and may kill me."

The second observation is that on several occasions the patient expressed a desire not to die. Thus, just before being given carbon dioxide to breathe, as well as during the inhalation of carbon dioxide and also of a mixture low in oxygen, the patient said; "Doctor, I don't want to die." On two separate occasions when the patient was markedly dehydrated following the ingestion of sodium bicarbonate the same statement was made. In the experiment with diathermy the statement "I don't want to burn to death" was repeated several times in association with requests to get up. Did these various methods of procedure act as a death threat to this particular patient? Is the concept of a stupor being a flight from reality and a feigning of death adequate in this case? Detailed knowledge of the background of the patient's mental life prohibits us from answering either of these questions with any degree of certainty, but we think that they must be borne in mind.

There are certain other psychologic or environmental factors to be considered. Before turning to them, however, it may be said that the mere influence of the procedure from the purely impressive effect of having so much attention, etc., is not adequate to cause a response. In too many instances in which the setting was the same as when a response was obtained there was a lack of response. Yet these environmental factors were not without effect. Thus, on one hand, on occasions when ordinarily effective procedures were used and when the physiologic response to these procedures was exactly similar to that obtained at times when the patient responded, the patient did not respond. On one occasion when there was a large number of strange physicians in the room, the patient responded only slightly to the inhalation of a mixture of carbon dioxide to which she ordinarily responded well. Furthermore, it was noted that on those occasions when blood was taken the response was not as great, or was even absent, despite the fact that the patient had been exposed to an ordinarily effective procedure. On the other hand, it was noted that when effective procedures were used, the patient responded less with one physician in attendance than with another. Thus, for a certain period of time during the course of a long series of experiments on one patient, she misidentified the physician as a man of whom she had been enamored before she became ill. The responses during this period had a distinct erotic coloring and were much better when the physician in question spoke with the patient than when he was replaced by another. During several of this same series of experiments the responses given when the afore-

mentioned physician officiated were poor as compared with the responses when another (female) physician carried on the questioning. The response was also determined by the attitude of the physician. This was more easily observed in the case of the experiments with sodium bicarbonate, in which the duration of the response was longer than in the other procedures. Thus, in a single sitting when the physician asked questions in a manner that lacked interest as to whether or not he received an answer, answers were not forthcoming. However, as soon as he assumed a more insistent attitude and really showed an interest in the responses answers were far more frequent, adequate and rapid.

SUMMARY

No one or no combination of the observed physiologic changes induced by these procedures can be considered as essential to the obtaining of the response; the multiplicity of methods used with success hardly admits of a single and common physiologic factor being responsible; the only known similarity between these procedures which may be responsible for the effect is some sort of shock to the body economy; yet other such shocks are not effective, nor are these always effective. There are various psychologic factors which alter the response, at times increasing it or insuring it and at other times decreasing or even negating it. The various a priori hypotheses that have been advanced to explain the effect obtained, such as stimulation of the nerve structures by carbon dioxide or by a difference in the supply or utilization of oxygen, or a change in the metabolic and functional activity of the nerve cells as a result of changes in acidity, lack factual evidence for their support; they are neither proved nor disproved, but it can be said definitely that none of them is adequate to explain the phenomena in question.

CONCLUSIONS

1. Several different means of arousing patients from stupors and the changes induced by them have been described.

2. None of the physiologic changes studied is essential to the arousal.

3. The change in the mental activity of the patient appears to depend on the nature of the shock to the body economy caused by each procedure used.

4. Certain psychologic factors have been shown to alter the response.

5. It is believed that none of the hypotheses known to us and advanced in explanation of the phenomena is adequate.

6. The work indicates that the physiologic and mental factors complement each other.

ABSTRACT OF DISCUSSION

DR. WALTER FREEMAN, Washington, D. C.: Dr. Solomon and Dr. d'Elseaux have added another method of producing this peculiar stimulating effect on catatonic patients. There must be some underlying physiologic mechanism that is common to all these methods, although it has not yet been found. It is of interest that high temperature, as brought out by salt fever, or by diathermy, can do this. The results may be similar to the beneficial effects of the intravenous injection of various fever-producing substances.

DR. F. FREMONT-SMITH, Boston: One factor that possibly is common to two or three of these procedures is the effect on the cerebral circulation.

In a paper by Dr. Cobb and myself (ARCH. NEUROL. & PSYCHIAT. **26**:731 [Oct.] 1931) we showed that breathing mixtures of oxygen and carbon dioxide causes dilatation of the retinal and cerebral vessels, resulting in an increased blood flow. In experiments on cats Dr. J. E. Finesinger has shown that sodium amytal also causes a dilatation of the cerebral vessels (unpublished data).

There is some suggestive evidence, at least, that fever (both diathermy and typhoid vaccine fever) produces similar dilatation.

Does Dr. d'Elseaux believe that the temporary influence of these various procedures on the mental picture presented by the patient could be due to a temporary increase in cerebral circulation? This question raises another: Could any of the symptoms of catatonia be dependent on disturbance of cerebral circulation?

DR. H. G. WOLFF, New York: In attempting to evaluate the relative weight of the various factors implicated in the alteration produced in stuporous patients by carbon dioxide, it is important, as Dr. d'Elseaux has mentioned, to stress the rôle of the psychobiologic factors associated with the administration of the gas. I am sure, however, that he would not have one infer from what he has said, that these psychobiologic factors are in themselves sufficient to account for the major part of the effects that follow the administration of carbon dioxide and (as he suggested) sodium amytal.

It is difficult to lose sight of the fact that through the administration of sodium amytal in dogs, for example, alterations in the highest integrative functions, closely resembling those in man after like administrations, have been produced.

In brief, it seems inexpedient to assume an "either—or" attitude and infer that simply because carbon dioxide changes in the blood will not account for the difference in performance, "transference," "death threat" or the influence of the presence of visitors will explain all. It seems sounder to take an "and—and" standpoint. In experimental animals the effects of the complex factors of experience (positive and negative conditioned responses) summate with those produced by simpler chemical measures in a combined influence on the threshold of the highest integrative functions. There is no reason why they should not also so summate in man to produce the effects which Dr. d'Elseaux has so carefully studied.

DR. D'ELSEAUX: Concerning Dr. Freeman's remarks: I apparently did not make clear the fact that in the experiment with diathermy there was absolutely no correlation between the temperature and the response. The response was present only when the current was on; that is, we believe, when the patient was being burned.

Likewise in the experiments with sodium bicarbonate there was no direct or strict correlation between the increased temperature and the response. The correlation was between the sense of thirst, as indicated by the patient's continually asking for water, and the response.

Concerning Dr. Fremont-Smith's question (and Dr. Wolff's remarks might well be partially considered here), in experiments with carbon dioxide we found that jugular blood resembled arterial blood in degree of oxygenation by the end of the inhalation and thus corroborated Dr. Cobb's and Dr. Fremont-Smith's aforementioned work. Following the inhalation the degree of oxygenation falls to the level obtaining in rest within a period of fifteen minutes. Femoral venous blood decreases in oxygenation during inhalation and immediately after the latter is ended becomes oxygenated to the same degree as arterial blood. Thereafter it falls parallel to the fall in jugular blood oxygenation.

These changes indicate that there are different responses in the leg as compared with those in the intracranial cavity. Whether they are dependent on a difference in oxygen utilization or on a difference of blood flow cannot be said definitely. The latter seems more likely.

Furthermore, some experiments in the utilization of oxygen by the body as a whole show that there is an increase in utilization of oxygen during the inhalation of gas to about two to four times that existing in rest.

There are certain other factors. The intracranial tissues do not absorb any carbon dioxide that is inhaled. If any carbon dioxide is retained intracranially, it is that produced metabolically. We do not know and we cannot say just what the metabolism of different portions of the body is.

But in conditions in which the blood flow is the same, and apparently the oxygen utilization and the storage of carbon dioxide are the same, there may be a response on one occasion while on another occasion there is none. Thus no one, or group, of these factors may be considered as solely responsible for the arousal.

Concerning the psychologic factors referred to by Dr. Wolff, we are not bringing in new factors. Animal experimentation, in my opinion, is chiefly supportive of investigations on human beings and one has in human beings these factors to begin with. It is unfortunate that in animal experimentation one should have to rule them out. That they are important was shown from our experiments, which indicate that there are certain psychologic factors which influence the response.

This leads us to the final conclusion that any hypothesis purporting to explain human behavior at all adequately must have an adequate description of both the physiologic and the mental phenomena. We cannot exclude either set of phenomena in the present state of our knowledge. I believe that these experiments more or less bear out that attitude.

ACTION OF SCOPOLAMINE AND CARBON DIOXIDE ON CATALEPSY PRODUCED BY BULBOCAPNINE

ARTHUR S. PATERSON, M.D.
Rockefeller Fellow from the University of Edinburgh; now at the Maudsley Hospital, London
LONDON, ENGLAND
AND
CURT P. RICHTER, PH.D.
BALTIMORE

One of the most characteristic features in the behavior of monkeys under the influence of bulbocapnine is their tendency to hold on to any object placed within their grasp (Richter and Paterson[1]). A normal monkey with three limbs tied will cling to a horizontal bar brought within reach of the free hand but will drop from it and attempt to escape as soon as he is left hanging by the experimenter. A monkey similarly bound but given an injection of bulbocapnine will not only grasp the bar but will hang from it for several minutes. This hanging response, probably closely related to the grasp reflex of the new-born infant, is doubtless a part of the catalepsy produced by the drug, in that the animal continues to grasp the bar once it has obtained a hold, just as it tends to maintain any other posture in which it is placed. In these animals given bulbocapnine, the hanging response appears, together with the catalepsy, about ten minutes after the drug is injected, and disappears again about an hour later, when the catalepsy disappears. As the grasping response can be measured by the length of time the animals hang before they fall, it may be used to estimate the degree of catalepsy, for which hitherto no adequate criterion has been available. From a study of the duration and magnitude of the effect produced by varying doses of bulbocapnine, curves have been obtained of the types shown in charts 1 *A* and 2 *A*, with the hanging time in seconds represented on the ordinates and the duration of the experiment in minutes on the abscissas.

It can readily be seen that, with such curves as a basis, it is now possible to determine to some extent how the catalepsy produced by

From the Psychobiological Laboratory, Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital.

1. Richter, C. P., and Paterson, A. S.: J. Pharmacol. & Exper. Therap. **43**: 677 (Dec.) 1931.

bulbocapnine can be modified by various experimental procedures. The present paper is concerned with the modification and possible elimination of the cataleptic symptoms by two pharmacologic agents, scopolamine and carbon dioxide. Scopolamine has been studied because of its well known relaxing effect in cases of paralysis agitans, the muscular rigidity of which is supposed to be similar to that found in the condition produced by bulbocapnine. Carbon dioxide has been studied because of

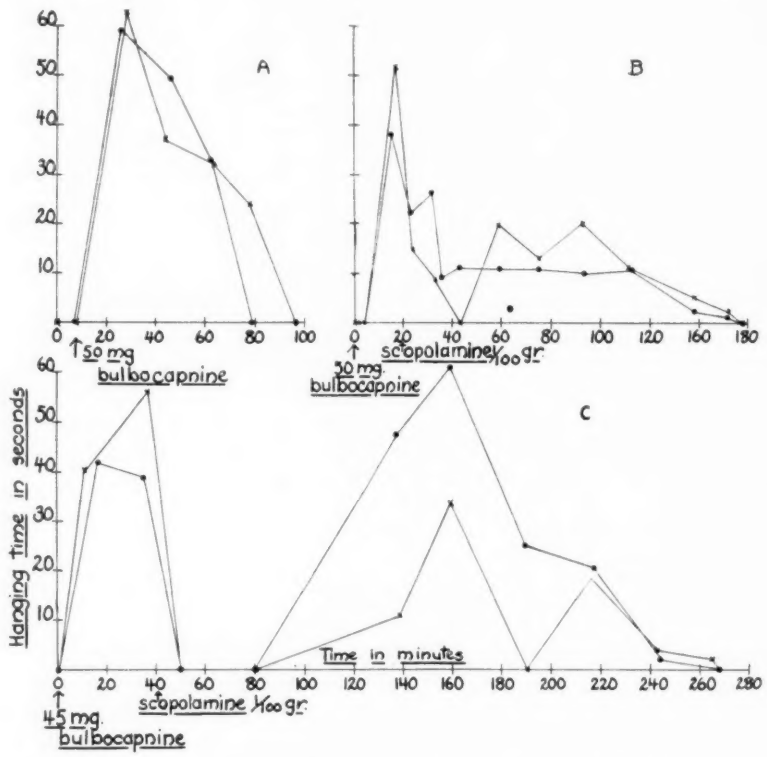

Chart 1.—*A*, curve for a monkey showing the effect of bulbocapnine on the hanging response. The hanging time in seconds is given on the ordinates, the duration of the experiment in minutes on the abscissas. *B*, curve for the same monkey showing the effect produced on the hanging response obtained by bulbocapnine by the injection of scopolamine (1/100 grain). *C*, curve for another monkey showing the effect produced on the hanging response obtained by bulbocapnine by injection of scopolamine (1/100 grain).

the symptomatic respite it frequently produces in the catalepsy of man (Loevenhart, Lorenz and Waters). The action of various other chemical agents will be discussed in later papers.

METHODS

The technic for these experiments has been described in detail (Richter [2] and Richter and Paterson [1]). The animals were bound so that both legs and one arm were confined in a single muslin bandage. Bulbocapnine was injected, and the animal was lifted immediately thereafter by its head and placed in such a position that the palm of the free hand came into contact with a horizontal bar. As soon as the monkey obtained a grip on the bar, it was released. When it fell, it was caught in a net suspended below. After the animals had hung several times, scopolamine was injected or carbon dioxide administered and the tests were continued at frequent intervals until the hanging response had entirely disappeared.

The bulbocapnine was injected intramuscularly into the hindleg in moderate doses of about 17 mg. per kilogram of body weight. Scopolamine was given likewise by intramuscular injection in doses varying from $\frac{1}{1.000}$ to $\frac{1}{100}$ grain. (0.000065 to 0.00065 Gm.). Nearly all of the animals received the larger dose, which was found to produce a high degree of relaxation. The carbon dioxide was given with a nitrous oxide mask in concentrations varying from 15 to 50 per cent over periods of from one to ten minutes.

Several curves with moderate doses of bulbocapnine alone were obtained on each animal before bulbocapnine in combination with either scopolamine or carbon dioxide was administered. For the most part, the carbon dioxide and the scopolamine were given a short time after the peak of the effect produced by bulbocapnine was reached, usually about fifteen minutes after injection of the latter drug.

The hanging time was measured for both the right and the left hand at intervals of from five to ten minutes from the time the bulbocapnine was injected until the hanging response had entirely disappeared. Observations were made at the same time on changes produced by carbon dioxide and scopolamine in the general behavior of the animal, with special attention to the changes produced in its responsiveness, as an index of any modification in the degree of catalepsy.

RESULTS

Bulbocapnine and Scopolamine.—A. Effect on the Hanging Response: The action of scopolamine on the hanging response can be seen in chart 1, with the hanging time in seconds for the right and the left hand given on the ordinates, and the duration of the experiment in minutes on the abscissas. The first curve (*A*), obtained from an animal which had received 50 mg. of bulbocapnine alone, is fairly typical. The peak was reached about twenty minutes after the injection, and from then on there was a gradual drop until the response disappeared completely. The total duration of the effect on the right and the left hand was seventy and eighty-eight minutes, respectively.

In another experiment on the same animal, represented in the curve *B*, 50 mg. of bulbocapnine, injected as before, produced a similar rise in the hanging response. Scopolamine (1/100 grain), given twenty minutes after the bulbocapnine, caused an immediate, relatively sharp fall in the response. For one test it actually was absent, but the drop

2. Richter, C. P.: The Grasping Reflex of the New-Born Monkey, Arch. Neurol. & Psychiat. **26**:784 (Oct.) 1931.

cannot be regarded as uniformly progressive, since a low level of ten seconds was maintained for over eighty minutes. When the decline began again it was slow, so that the reflex did not disappear finally until one hundred and eighty minutes after the initial injection of bulbocapnine. Scopolamine then produced a marked prolongation of the effect of bulbocapnine, in this instance to more than twice the average of eighty minutes for bulbocapnine alone.

An even more striking result is presented in the third curve (*C*) in chart 1. In this animal, 45 mg. of bulbocapnine produced the usual curve. Forty-one minutes after the bulbocapnine was given, 1/100 grain of scopolamine was administered. This second drug caused a complete disappearance of the hanging response for over half an hour. A test one hundred and thirty-six minutes after the first injection, however, found the hanging response definitely present again and twenty minutes later it had increased even more, so that one hand actually showed a much stronger reaction than before the scopolamine was given. From then on, the reflex decreased in magnitude until it finally disappeared two hundred and sixty-eight minutes after the first injection. The total duration of the effect was over four times as long as with bulbocapnine alone.

Similar results were obtained in twelve other experiments with scopolamine, in which doses of from 1/200 to 1/100 grain (0.00032 to 0.00065 Gm.) were given. No effects were obtained from doses of 1/1,000 grain.

B. Effect on Muscle Tone and General Behavior: Scopolamine produces a marked degree of muscular relaxation or ataxia in the animals given bulbocapnine. In spite of this relaxation they are still able, for the most part, to maintain their usual squatting postures and to hang from the horizontal bar. The limpness of the fingers, however, changes the nature of the grasping response. Following the injection of bulbocapnine alone, the monkeys grasp the rod as soon as it comes into contact with the palm of the hand. Under the additional influence of scopolamine, the fingers must be held over the bar and the animal lifted quickly a few times. By this process they gradually take hold and can be released to maintain their own weight. They do not grasp the bar with the palm of the hand, however, but tend to hang by the fingers alone, the bar being under the first joint. It is interesting that, in spite of this awkward grip, they are able to hang as long or even longer than they do during simple narcosis produced by bulbocapnine.

Scopolamine in no way relieves the stuporous condition of the animals. They continue to sit in whatever position they are placed and seem to be entirely unresponsive. Furthermore, both the catalepsy and the unresponsiveness are prolonged by the scopolamine, persisting as long as the hanging response.

It is clear from these results that scopolamine and bulbocapnine cannot be counteracting drugs; on the contrary, they act in the same direction, one augmenting the effects of the other.

Bulbocapnine and Carbon Dioxide.—A. Effect on the Hanging Response: Carbon dioxide was administered in ninety experiments on twelve monkeys under the influence of bulbocapnine. The effects produced by this gas can be seen in the curves presented in chart 2. The first curve (*A*), obtained with bulbocapnine alone, is similar to that shown in chart 1 *A*. The animals received 50 mg. of bulbocapnine, and the hanging response was present for seventy-two minutes after the injection.

The second curve (*B*) shows the effect produced by a comparatively small dose of carbon dioxide, 25 per cent given for one minute. The hanging response had appeared after an injection of 50 mg. of bulbocapnine, but reached a peak, and had started a gradual decline. The carbon dioxide, given forty-one minutes after this dose of bulbocapnine, caused a temporary increase in the hanging time, from eleven to seventeen seconds. Then the curve resumed its original course and the response disappeared completely sixty-four minutes after the initial injection.

Another experiment, represented by the third curve (*C*) employed a larger dose of carbon dioxide, 25 per cent for nine minutes. A peak in the hanging response had been reached six minutes after the usual injection of bulbocapnine. Administration of carbon dioxide, started a few minutes later, eliminated the hanging response for one reading. After that it returned and remained present, at a low level of nearly ten seconds, until eighty-two minutes after the injection of bulbocapnine. This is similar to the curve with scopolamine.

The animal whose curve is shown in chart 2 *D* received a higher concentration of carbon dioxide, 35 per cent for four minutes, twenty-eight minutes after the initial injection of bulbocapnine. It will be noted that this caused an instantaneous disappearance of the hanging response. It returned at once, however, reached a level almost as high as that present before and persisted for some time, so that the total duration of the effect of bulbocapnine was markedly prolonged beyond its average length (one hundred and thirty-eight minutes, as compared with seventy-three minutes).

Similar curves obtained from experiments on other animals all show that small doses of carbon dioxide (25 per cent for one minute) cause a slight increase in the hanging time, rather than a decrease as might be expected. Larger doses cause a decrease followed by a small increase, and still larger doses, a sharp decrease followed by a large and much prolonged increase. However, the total duration of the effect produced

by carbon dioxide is still considerably shorter than that found after injection of scopolamine.

B. Effect on General Behavior: In marked contrast to scopolamine, carbon dioxide produces a profound change in the behavior of the animals. Even before the mask is removed they begin to struggle and screech. For a few seconds afterward, they sit still and look as though dazed. Then, quite suddenly, they seem to come into full contact with their surroundings, leap from the table and attempt to escape. It is only a few minutes, however, before they begin to slow up, become less

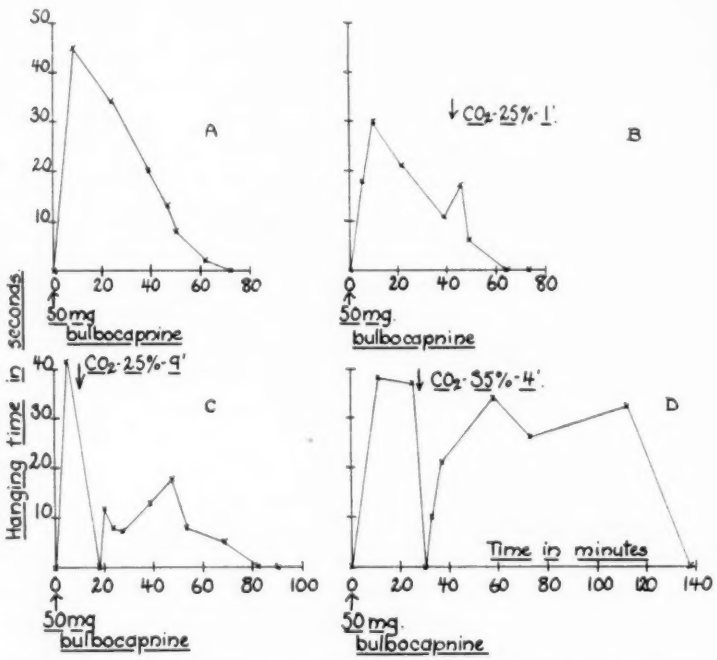

Chart 2.—*A*, curve for another monkey showing the effect produced by bulbocapnine on the hanging response of a monkey. *B*, curve for the same monkey showing the effect produced on the hanging response obtained by bulbocapnine by inhalation of carbon dioxide, 25 per cent for one minute. *C*, curve for the same monkey showing the effect of carbon dioxide, 25 per cent for nine minutes. *D*, curve for the same monkey showing the effect of carbon dioxide, 35 per cent for four minutes.

responsive, and finally sink back into the original stuporous state. Kaufman and Spiegel [3] have made similar observations on the effect of carbon dioxide on cats under the influence of bulbocapnine. The effect

3. Kaufman, M. R., and Spiegel, E. A.: Ztschr. f. d. ges. Neurol. u. Psychiat. **127**:312, 1930.

produced in the cats, however, is less striking and less constant. This must be due, at least in part, to the lack of overt behavior in the cat as compared with the monkey. The effect produced by this gas in the monkeys is practically identical with that produced in catatonic stupors in man, as reported by Loevenhart, Lorenz and Waters.

The full respite from the stuporous condition is obtained only when high concentrations of carbon dioxide (35 per cent or more) are administered over a sufficiently long period of time. A 15 per cent mixture has no noticeable effect.

The hanging response follows closely the changes in the cataleptic condition of the animal, disappearing completely only when the animal is entirely free from catalepsy and in full contact, and it gives a much better picture of the effects produced by the carbon dioxide than could be obtained by simple observation.

EFFECT OF SCOPOLAMINE AND CARBON DIOXIDE ALONE

It has already been shown that the effect of bulbocapnine, as measured by the hanging response, is prolonged by both carbon dioxide and scopolamine. This result may be explained in at least two ways: these drugs may themselves produce the hanging response, quite independently of the bulbocapnine, or they may have no such direct effect but may act only indirectly through some modification of the catalepsy produced by bulbocapnine.

In order to throw more light on these considerations, we have investigated whether or not the hanging response can be brought out by scopolamine or carbon dioxide without bulbocapnine.

Scopolamine Alone.—A. Effect on the Hanging Response: The hanging reflex was brought out by scopolamine alone (1/100 grain) in three animals, but the magnitude of the response was much smaller than with bulbocapnine. In ten animals the response was not elicited by the scopolamine.

B. Effect on Behavior: Scopolamine (1/100 grain) produced no noticeable change in the behavior of the animals. The great relaxation present when the drug was given with bulbocapnine was lacking, and there were no symptoms of stupor.

It is difficult to explain the great prolongation of the effect of bulbocapnine produced by scopolamine in view of the fact that scopolamine alone causes no stuporous or catatonic symptoms. It must be that the action of scopolamine is dependent on the presence of the bulbocapnine.

Carbon Dioxide Alone.—A. Effect on the Hanging Response: The experiments in which carbon dioxide was given alone were striking (chart 3). It was found that carbon dioxide in concentrations of from 25 to 50 per cent brings out the hanging reflex consistently. The magni-

tude of the response is about the same as that obtained in animals under the influence of bulbocapnine; the duration of the effect, however, is usually much shorter, from two to ten minutes as compared with from eighty to one hundred minutes. This short duration is due undoubtedly to the fact that the gas is quickly expelled from the lungs.

B. Effect on Behavior: The animals seem to be dazed while hanging under the influence of the carbon dioxide, but their behavior is different from that produced by bulbocapnine. They are more active, look about blankly and bite at the bandages securing their legs; considerable activity of the mouth and throat muscles is expressed in screeching and grinding of the teeth.

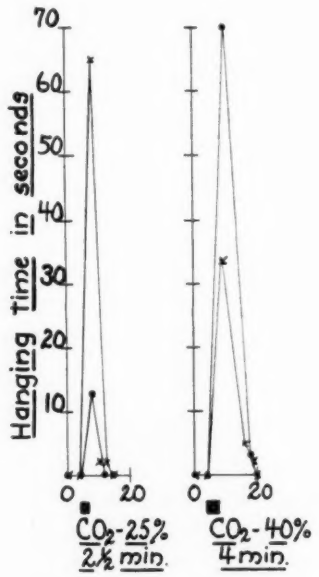

Chart 3.—Curves demonstrating the production of the hanging response by inhalation of carbon dioxide gas in high concentrations.

The results of these experiments indicate, then, that the effect produced by carbon dioxide on the hanging time of animals given bulbocapnine is due, at least in part, to an effect of carbon dioxide independent of the bulbocapnine. Since both carbon dioxide and bulbocapnine elicit the hanging response, they must act on the same mechanism in the brain; but since bulbocapnine produces a cataleptic picture in addition, it must be assumed that it has a more general effect and acts on other parts of the brain.

As the hanging response is one of the characteristic features of catalepsy produced by bulbocapnine, it would not be expected that any agent capable of bringing out the response when given alone would

have a counteracting effect on this type of catalepsy. Scopolamine definitely is not a counteracting agent, since it has the opposite effect of prolonging the symptoms produced by bulbocapnine. Nor is carbon dioxide a consistent counteracting agent. It may be that in some concentrations it will be found to counteract, and in others to intensify, the effect produced by bulbocapnine. Experiments are now in progress to study any changes produced on the hanging response by the administration of various concentrations of carbon dioxide for varying lengths of time.

The object of the research at the present time is to find agents that give a longer and longer respite from the symptoms produced by bulbocapnine, and cause the hanging response to remain absent for longer and longer intervals until it finally disappears permanently.

COMMENT

The extent to which the results recorded may be applied in a consideration of the catatonic condition in man depends to a great extent on how closely the catalepsy produced by bulbocapnine and catatonic catalepsy are thought to be related. As carbon dioxide has practically the same effect on the experimental stupor as it has on the clinical stupor, it is possible that a close relationship may exist between these two phenomena, and this possibility in turn suggests that the prolongation of cataleptic symptoms observed in the experimental animals after inhalation of carbon dioxide may occur in man under similar conditions. For this reason, great caution should be observed in the use of carbon dioxide as a therapeutic agent in cases of catatonia.

If it is assumed that catalepsy produced by bulbocapnine and catatonic catalepsy are fundamentally closely related phenomena, then it becomes obvious from the experiments with scopolamine that catatonia and paralysis agitans are widely dissimilar in origin and nature. The effects of bulbocapnine are actively prolonged by injections of scopolamine, whereas the muscular disturbances in paralysis agitans are almost uniformly relieved by it.

With the present status of knowledge, it seems futile to make any attempt to relate the condition produced by bulbocapnine to either human catalepsy or paralysis agitans. However, further study of this interesting experimental phenomenon, entirely on its own merits and quite apart from all possible relationships, may eventually lead to a greater understanding of similar conditions in man.

SUMMARY

1. One of the characteristic features of catalepsy produced by bulbocapnine is the presence of the grasp reflex. The strength of the reflex can be determined by measuring how long the animal will hang from

a horizontal bar. By testing the animal at regular intervals after the injection of bulbocapnine, a curve can be obtained of the effect and its intensity at various times following the injection.

2. With these curves as a basis, a study was made of the effect of carbon dioxide and scopolamine on catalepsy produced by bulbocapnine.

3. Scopolamine caused a marked prolongation of the effects of bulbocapnine from sixty or eighty minutes to three hundred minutes or more, despite the high degree of muscular relaxation present. The animals showed no sign of recovery from the stupor.

4. Carbon dioxide had different effects, depending on the dosage. In lower concentrations, from 15 to 25 per cent, administered for from one to two minutes, it caused an increase in the length of time that the animal hung immediately after administration of the gas was discontinued. In higher concentrations, from 35 to 50 per cent, with the appearance of anesthesia, it caused a decrease in the hanging response with a subsequent increase, the total duration of the effect of bulbocapnine often being increased, as it was with scopolamine.

5. In marked contrast to scopolamine, however, carbon dioxide given in a higher concentration caused a transient disappearance of the hanging response for a few minutes following the administration of the gas, and a complete respite from the stuporous symptoms. The effect was practically identical with that produced by the gas on catatonic symptoms in man.

6. The fact that carbon dioxide and scopolamine produced an increase in the hanging time suggested that these agents have a positive action on the response and that they might produce it when given without bulbocapnine. It was found that both carbon dioxide and scopolamine, when given alone, elicit the grasp reflex and the hanging response.

7. To this extent they are not counteracting agents. However, it was pointed out that carbon dioxide might have either an augmenting or a counteracting effect, depending on the concentration of the gas.

8. On the basis of these observations, the relationship of catalepsy produced by bulbocapnine to human catalepsy and paralysis agitans was discussed.

SYPHILITIC AMYOTROPHY

R. P. MACKAY, M.D.
AND
GEORGE W. HALL, M.D.
CHICAGO

That syphilis may be a cause of spinal muscular atrophy is probably not sufficiently realized. Yet long before the original work of Aran and Duchenne on progressive muscular atrophy, Graves [1] described a case in which syphilis seemed to be the etiologic factor. In time, many other contributions [2] appeared to attest the fact and to increase knowledge of syphilitic amyotrophy.

Just how frequently this condition occurs has not been definitely shown. In 1902, Bramwell [3] analyzed 155 cases of tabes dorsalis and found definite localized muscular atrophy in about 4 per cent. Four years before, Whiting,[4] in a survey of 200 cases of tabes dorsalis at the National Hospital for the Paralyzed and Epileptic, found obvious atrophy in 8 per cent, and stated that this was the percentage given by Duchenne. Whiting's study is instructive and demonstrates that almost any voluntary muscle in the body is a possible site of atrophy from syphilis. Dejerine,[2c] in 1889, had found atrophy in 19 of 93 "tabetic" cases studied. This is about 20 per cent, and is by far the highest proportion reported, but Dejerine's criteria for the diagnosis of syphilis were rather vague; this renders his figures unreliable, and makes an otherwise instructive and exhaustive article of doubtful value. Con-

---

Read before the Section on Nervous and Mental Diseases at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 12, 1932.

1. Graves, Robert J.: Clinical Lectures on the Practice of Medicine, Dublin, Fannin & Co., 1848, vol. 1, p. 509.

2. (*a*) Gowers, W. R.: Diseases of the Nervous System, ed. 2, London, J. & A. Churchill, 1892, vol. 1. (*b*) Raymond, F.: Sur quelques cas d'atrophie musculaire à marche progressive chez des syphilitiques. Rélations eventuelles de la syphilis avec l'évolution de la maladie. Meningo-myélite vasculaire diffuse, constatée à l'autopsie dans un cas, Bull. et mém. Soc. méd. d. hôp. de Paris **101**:55, 1893. (*c*) Dejerine, M. J.: Étude clinique et anatomo-pathologique sur l'atrophie musculaire des ataxiques, Rev. de méd. **9**:81, 208 and 294, 1889. (*d*) Collins, J. A.: Case of Progressive Muscular Atrophy and Tabes, with Autopsy, J. Nerv. & Ment. Dis. **28**:564 (Oct.) 1901.

3. Bramwell, B.: Analysis of 155 Cases of Tabes, Brain **25**:19, 1902.

4. Whiting, A. J.: On Paralysis and Muscular Atrophy in Tabes Dorsalis, with Observations on the Relation of Afferent Impulses to Movement and Muscular Nutrition, Brain **21**:494, 1898.

versely, Charles L. Dana,[5] in 1906, analyzed 72 cases of progressive muscular atrophy and found that 19 of the patients, or over 26 per cent, had a history of syphilis and that 4, or 5.5 per cent, had an associated tabes dorsalis. It is highly desirable that modern diagnostic methods be utilized in making careful surveys of large series of neurosyphilitic patients, in order to establish what percentage show spinal muscular atrophy. It is possible that through early treatment with the newer specific antisyphilitic drugs, a smaller proportion of syphilitic patients show atrophy than in the days of Dejerine. There seems little doubt, however, as was pointed out recently by Kino and Strauss,[6] that the frequency of atrophy among syphilitic patients is much higher than mere coincidence can explain. According to his argument, if atrophy is only a coincidence among tabetic patients, it should occur just as frequently in other neurologic diseases. But 4 per cent of tabetic patients show atrophy, according to Bramwell, who gave the lowest figures available. To say that atrophy of spinal origin occurs among 4 per cent of all neurologic patients would be untenable, and consequently there must be more than an accidental relationship between syphilis and the atrophy in these cases.

American contributions [7] to this subject have been few as compared with the extensive European literature. It is our purpose in this article to redirect attention to syphilis as a cause of muscular atrophy, and to emphasize a therapeutic possibility. A complete review of the literature will not be attempted, since excellent bibliographies have been compiled recently by Kino and Strauss,[6] Martin [8] and Margulis.[9] The following case reports from patients actually seen by us within the past three years will serve as a text for a further discussion of this interesting subject.

REPORT OF CASES

CASE 1.—*Clinical History.*—A. P., a white man, aged 38, an operator of an electric crane, was first seen in consultation on Sept. 29, 1930. The family history was not significant, but the patient had been married and divorced twice without any pregnancy having occurred. He was in the United States Army in 1918 and

5. Dana, C. L.: Progressive Muscular Atrophy; a Study of the Causes and Classifications, with the Report of an Autopsy, J. Nerv. & Ment. Dis. **33**:81, 1906.

6. Kino, F., and Strauss, A.: Metaluetische Muskelatrophie zur Pathogenese der Muskelatrophie bei Tabes, Deutsche Ztschr. f. Nervenh. **89**:221, 1926.

7. (*a*) Leopold, S.: A Case of Progressive Muscular Atrophy with Necropsy, Probably Syphilitic in Origin, J. Nerv. & Ment. Dis. **39**:606, 1912. (*b*) Spiller, William G.: Syphilis a Possible Cause of Systemic Degeneration of the Motor Tract, ibid. **39**:584, 1912. (*c*) Stone, Theodore, T.: Amyotrophic Syphilitic Meningomyelitis: Report of Two Cases with Argyll Robertson Pupils, ibid. **66**: 595, 1927.

8. Martin, J. P.: Amyotrophic Meningo-Myelitis (Spinal Progressive Muscular Atrophy of Syphilitic Origin), Brain **48**:153, 1925.

9. Margulis, M. S.: Amyotrophische spinale Syphilis, Deutsche Ztschr. f. Nervenh. **86**:1, 1925.

1919, during which time he had influenza and two or three attacks of gonorrhea, but no chancre. In 1928, a Wassermann test of the blood was positive during treatment for acute prostatitis. Treatment was instituted with arsenicals, bismuth and mercury, but in April, 1929, the cerebrospinal fluid revealed a strongly positive (4 plus) Wassermann reaction, positive Noguchi and Ross-Jones tests and a colloidal gold curve of 0011100000. In spite of vigorous intravenous, intramuscular and inunction treatment, the spinal fluid in March, 1930, was still strongly positive, and the colloidal gold curve was 0122210000.

In June, 1930, the patient noticed "jerking" of the right arm when he was lying down to sleep. He was able to feel the muscles of the right arm and left shoulder twitching. A few aching pains occurred between the scapulae. By August, 1930, atrophy had become obvious to the patient in the right hand, which had become awkward and clumsy in all finer movements, such as buttoning his shirt.

Examination.—In September, 1930, there was moderate palpebral ptosis on the right, which was related possibly to an old injury. There were no other cranial nerve abnormalities, but a definite spastic weakness, with moderate atrophy, appeared in both arms; this was more marked on the right side. Fibrillary tremors, both large and small, were seen in the whole of both upper extremities; they were exceedingly frequent and numerous. Tremors were also seen in the supraspinati and infraspinati and other muscles of the neck and the upper part of the back. There was a partially developed *main en griffe* on the right.

The tendon reflexes were markedly increased throughout, with a strongly positive Hoffmann sign on both sides. The abdominal reflexes were diminished on the right, and the Babinski response was present on both sides. There was no jaw jerk or sucking reflex.

All forms of sensation, as well as gait, station and coordination, were normal.

Course.—In spite of treatment with large doses of mercury and potassium iodide, and the induction of fever by typhoid vaccine, the patient became steadily worse, more definitely spastic and weak, and showed fibrillation of the tongue and lips. The spinal fluid in January, 1931, showed a Wassermann reaction that was only 10 per cent positive, a negative Kahn test and a gold curve of 0122210000, though the Wassermann and Kahn tests of the blood were still strongly positive. In January, 1932, he began to have definite dysphagia. He died on March 24, 1932 (in the Veterans' Hospital, Danville, Ill.). Permission for necropsy, unfortunately, was not obtained.

This patient's condition illustrates a rapidly progressive and ultimately fatal disease involving both upper and lower motor neurons. The onset was in the cervical region, but the disease spread to involve the legs in spasticity, and to bring about death from bulbar paralysis. If it is assumed that the patient contracted syphilis when he was infected with gonorrhea, the onset of the amyotrophy took place twelve years after the original infection. Less than two years later he was dead, the whole process of the disease of the spinal cord beginning and progressing during intensive antisyphilitic treatment.

The next case illustrates a more favorable therapeutic result.

CASE 2.—*Clinical History.*—E. N., a white man, aged 43, a chauffeur, was married at the age of 30, and became the father of two healthy children. His wife remained in good health, and suffered no miscarriages. The family history was without significance. The patient had a penile chancre at the age of 22, and

immediately received one injection of arsphenamine, which was followed by oral medication for four years. In 1927, however, the Wassermann reaction of the blood was still strongly positive (100 per cent).

At the age of 40, he began to notice weakness in first the left and then the right arm, followed soon by wasting of the muscles. A few vague pains were present in the arms, but gave him little concern.

Examination.—In 1929, there were bilateral palpebral ptosis, anisocoria, and pupillary irregularity and extreme sluggishness to light, with a good reaction in accommodation. The cranial nerves were otherwise normal, but the speech was lisping. Marked weakness was present in the left arm, and definite but less marked weakness in the right arm. Atrophy was advanced in both upper extremities, including the pectoral and deltoid muscles, and a *main en griffe* with thenar and hypothenar wasting was present on both sides. Buttoning the clothes and driving a car became difficult, and the patient could not lift his arms above the horizontal. All these changes were more marked on the left side. Fibrillary tremors were seen in the right arm.

The tendon reflexes were sluggish in both arms, were absent in the right knee and ankle and were markedly reduced in the left knee and ankle. The plantar response was normal on both sides, as were the abdominal reflexes. Sensation, gait, station and coordination were normal.

Course.—Improvement in strength and even some restoration of muscle bulk began on the institution of treatment with mercury and potassium iodide. The patient was able to return to work as a chauffeur, although he still had difficulty in finer hand movements and in activity involving the shoulder muscles.

The onset in this patient was eighteen years after the chancre, and followed inadequate treatment. After progressing with fair rapidity for some months, the process ceased on the administration of adequate amounts of mercury and iodides. At present, though still exhibiting considerable atrophy, the patient is functionally much improved. It should be noted that the diagnosis of syphilis in this patient is independent of the positive Wassermann reaction of the blood. The ptosis, pupillary signs and reflex changes of tabes dorsalis would make syphilis an almost obligatory diagnosis even without the serologic findings.

Case 3.—*Clinical History.*—P. R., a white man, aged 46, an iceman, who was married and had three healthy children, and whose family history was without significance, had had a penile sore at the age of 22; it was excised by a physician who said that it was "poisonous." There were no secondary manifestations. When 28 years of age, he had a severe attack of vertigo which lasted for several weeks. At the age of 38, the Wassermann reaction of the blood was positive at the Cook County Hospital, and the patient was given intensive intravenous and intramuscular treatment for two years.

At the age of 45, he noted, after heavy exercise, weakness and heaviness of the left arm and shoulder, followed by weakness in the left hand. Since then the weakness in the left hand had become worse, and awkwardness of the hand had developed. In addition, a sense of coldness of the whole left side of the body developed.

General Examination.—There were: cyanosis, chronic bronchitis, marked emphysema, cardiac hypertrophy and an enlarged liver. There was a small scar on the glans penis.

Neurologic Examination.—There was definite weakness of the whole left upper extremity, with atrophy of moderate degree, especially in the interosseous spaces. Fibrillary tremors were observed in both hands, forearms and arms, usually rather large, but occasionally fine and typical.

The tendon reflexes were all absent in the arms, while the knee jerks were obtainable only on reenforcement, and the ankle jerks were absent. The Babinski sign was positive on both sides. Sensation was entirely normal.

Serology: The Wassermann reaction of the blood was negative on June 17, 1931; the spinal fluid was entirely normal except for 7 cells on the same date.

Course.—In spite of vigorous treatment with mercury, bismuth and arsenical preparations, progress has since been slowly downward, with an increase of the atrophy and spasticity.

The onset of the weakness and atrophy in this patient came twenty-three years after the chancre. The diagnosis of syphilis was made entirely on the history, including the history of a positive Wassermann test of the blood at the Cook County Hospital. This case illustrates that in syphilitic amyotrophy the Wassermann test may be negative at the time of examination, a situation not infrequent also in tabes dorsalis.

CASE 4.—*Clinical History.*—I. J. W., a white woman, aged 39, who had been married for fifteen years, and whose husband had died of pneumonia six years before the present report, had had one stillbirth. The family and past histories were without significance. At the age of 37, the patient began to have "neuritic" pains in the shoulders and weakness in the right thumb; this spread at once to the rest of the hand and was followed closely by wasting. A Wassermann reaction of the blood was negative at that time. Six months later, weakness and atrophy appeared in the left shoulder, arm, forearm and hand, and progressed for one year, after which it remained stationary.

General Examination.—There was a small, nontoxic thyroid adenoma.

Neurologic Examination.—There were small, irregular Argyll Robertson pupils, with bilateral ptosis. The cranial nerves were otherwise normal except for a small patch of hypalgesia above the left orbit. There was complete paralysis with extreme atrophy in the left hand, forearm, triceps, pectoralis major, infraspinati and serratus magnus. The left biceps and deltoid were very weak and atrophic.

The right grip was almost completely paralyzed except for some flexion in the fourth finger; there were marked weakness and atrophy in the forearm, and less in the right arm. A few scattered fibrillary tremors were seen.

The tendon reflexes were all exaggerated except the left triceps, which was absent. The Hoffmann reflex was absent on both sides; the abdominal reflexes were present on both sides, and the plantar response was normal. There was hypalgesia from the second to the tenth thoracic segments, including the medial half of both arms. Vibration sense was slightly diminished at both ankles.

Serology: The Wassermann test of the blood was graded as 25 per cent positive, the Kahn test as 3 plus. The spinal fluid was completely normal.

Course.—The condition has been apparently stationary for about one year.

It is impossible to state when this patient contracted syphilis, but even without the serologic data it is difficult to deny that she has had syphilis. The diagnosis is securely founded on the pupillary changes, bilateral ptosis and sensory changes that are typical of neurosyphilis.

CLINICAL COMMENTS

André Léri [10] stated that syphilis is responsible for almost all (*presque la totalité*) of the cases of progressive spinal muscular atrophy. There is no doubt in our minds, however, that the majority of such cases seem to have a nonsyphilitic cause. Little reason can be found in many cases for considering syphilis as the etiologic factor. But the cases reported here, as well as a large number available in published reports, illustrate well that syphilis is sometimes responsible. Such cases often differ in their clinical manifestations from those of the more common (Aran-Duchenne) type to such an extent that usually a purely clinical differentiation can be made.

Other objective signs of syphilis of the central nervous system often assist in the diagnosis. Martin [8] stated that "the generally accepted clinical signs of nervous syphilis usually fail us," but this has not been our experience. True, in case 1 it would not be possible without the serologic data to make a diagnosis of syphilis, and in case 3 the history of infection, a positive Wassermann reaction of the blood and subsequent antisyphilitic treatment in a reliable institution are essential to the diagnosis. In cases 2 and 4, however, a clinical diagnosis of syphilis is inescapable, even without the history, serologic findings or atrophy. Thus, in half of our cases a correct idea as to the cause of the condition can readily be obtained from a careful neurologic examination. This is also in accord with the opinion of Kaiser.[11]

The serologic findings, if positive, offer a valuable aid in arriving at a diagnosis, but if negative may be misleading. The Wassermann reactions of the blood or the spinal fluid were positive in 3 of our 4 cases and in case 3, while negative at the time of examination, had formerly been positive. That this form of amyotrophy may develop in the presence of entirely negative serologic findings is illustrated in case 3, in which the atrophy was actively advancing in the face of such findings. The patient in case 1 also, though exhibiting a strongly positive reaction of the blood and spinal fluid before treatment, showed marked improvement in the spinal fluid while clinically growing worse. Syphilitic amyotrophy, thus, like tabes dorsalis, may present no serologic evidence of syphilis at the time of examination, especially when treatment has been given before. Case 4 illustrates that, though never having had antisyphilitic treatment, the patient may have an entirely normal spinal fluid and a weakly positive reaction of the blood.

It is our opinion, therefore, that with a careful history, complete general and neurologic examination and serologic studies a correct

10. Léri, André, in discussion on Claude and Schaeffer, Rev. neurol. **27**:644, 1920.

11. Kaiser, Herbert: Lues spinalis unter dem Bilde der amyotrophischen Lateralsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:798, 1931.

diagnosis can usually be made. There are, however, other rather suggestive diagnostic aids. Pain was present in or near the site of the atrophy at the time of its onset in 3 of our 4 cases; this point is frequently emphasized in the literature. Martin [8] reported pain as occurring in 23 per cent of the cases, and the symptom is also recorded by Falkiewicz,[12] Claude and Schaeffer,[13] Head and Fearnsides [14] and others. Since pain rarely occurs in nonsyphilitic types of spinal atrophy, its presence should always render the physician suspicious. The reason for the pain will be pointed out later.

Atrophy in the nonsyphilitic forms of spinal amyotrophy almost always begins in the small muscles of the hand. In 3 of our 4 cases it began simultaneously in the shoulder, arm, forearm and hand, and in the fourth case the muscles of the shoulder were involved soon after those of the hand. This is a variation from the usual sequence in the nonsyphilitic forms, in which the shoulders are involved late or not at all. Other differences are seen in the frequent tendency of syphilitic amyotrophy to "skip" certain muscles and to involve others in a very patchy manner. These differences, while not invariable or characteristic, may often be of suggestive value in diagnosis. These points have been made before by Falkiewicz [12] and others. Martin [8] has pointed out that the syphilitic amyotrophies may begin in the hands (60 per cent), shoulders (22 per cent) or dorsiflexors of the feet (10 per cent), but in many cases with an onset in the hands the shoulders were soon involved while the biceps and triceps often escaped or were involved much later.

In cases 1, 3 and 4 there was definite clinical evidence that the pyramidal tracts were involved, but in case 2 tabes dorsalis was present and no such evidence was found. This is contrary to the opinion of Martin,[8] who said that the atrophy is usually of the atonic type. It would seem that the presence or absence of involvement of the pyramidal tract has no great diagnostic significance, but this point can be discussed more profitably with the pathologic phenomena.

Sensory changes are seldom reported in this condition; they occurred in only 1 of our 4 cases. Fibrillary tremors were present in all patients, but were numerous only in case 1. We obtained the impression that these twitches were often large and fascicular rather than truly fibrillary, but whether this is characteristic we are not prepared to say. Sphincter

---

12. Falkiewicz, Tadeusz: Zur Kenntnis der amyotrophischen Spinallues, Deutsche Ztschr. f. Nervenh. **89**:232, 1921.

13. Claude, Henri, and Schaeffer, H.: L'atrophie musculaire progressive syphilitique avec sclérose combinée, Rev. neurol. **27**:642, 1920.

14. Head, Henry, and Fearnsides, E. G.: The Clinical Aspects of Syphilis of the Central Nervous System, in the Light of the Wassermann Reaction and Treatment with Neosalvarsan, Brain **37**:65 and 109, 1914.

disturbances were not present in any of our patients, and this fact is consistent with the observations of many others.

Summary of Clinical Findings.—We are thus able to draw a clinical picture of syphilitic amyotrophy as being, in most cases, associated with other clinical or serologic evidences of syphilis, in the history, chronology or examination, but often presenting a negative serologic status after treatment. The onset is frequently associated with pain; the atrophy is most often found in the upper extremities, where it often involves the shoulders as early and as extensively as the hands, and often assumes an irregular or patchy distribution. The pyramidal tracts may or may not be involved; sensory changes are few; fibrillary tremors, when present, are apt to be large, and sphincter disturbances and involvement of the medulla are rare.

PATHOLOGY AND PATHOGENESIS

Three locations suggest themselves as possible sites for the pathologic changes responsible for syphilitic amyotrophy, and for each a theory has been advanced. Although others [15] supported him vigorously, Dejerine [2c] was the chief defendant of the hypothesis that a syphilitic peripheral neuritis constituted the pathologic basis for the atrophy. In 1889, he published an extensive article with histologic studies in 9 cases, describing in them all a peripheral neuritis which was most marked distally and decreased in severity as one approached the cord. Several objections have been made to this theory and few investigators support it now. Steiner [16] found that careful search showed degenerative and inflammatory changes in most cases of so-called "metasyphilis," whether atrophy was present or not. Such findings throw doubt on the significance of peripheral neuritis in cases with atrophy. On the other hand, the objection has been made that the distribution of atrophy is often such as could not be explained by a peripheral nerve lesion. Whiting [4] pointed out that in some of his patients a single nerve often supplied atrophic and normal muscles. This condition occurred in our case 4, in which there was almost complete flexor paralysis of the whole right hand except for the fourth finger. Furthermore, were peripheral neuritis the basis for the atrophy, one would expect sensory changes which usually do not occur, and which, when they do occur, do not necessarily correspond to the peripheral nerves that innervate the atrophic muscles.

The second theory explains certain cases of syphilitic amyotrophy as being due to a toxic lesion of the ventral horn cells, a truly parenchymatous lesion, independent of any meningeal, vascular or inflamma-

15. Collins.[2d] Remak, E.: Ueber neuritische Muskelatrophie bei Tabes dorsalis, Berl. klin. Wchnschr. **24**:462, 1887.

16. Steiner, Gabriel: Beiträge zur pathologische Anatomie der peripheren Nerven bei den metasyphilitischen Erkrankungen, Arch. f. Psychiat. **49**:667, 1912.

tory processes. Those who defend such a theory usually have in mind a lesion that is "parasyphilitic" in the old sense, or else they conceive the process to be a syphilitic toxic anterior poliomyelitis. English neurologists, from Gowers [2a] to Holmes [17] and Wilson [18] have upheld such a theory, and while not contending that every case is so caused, they reserve a group, usually associated with tabes dorsalis, as being so produced. Wilson described 2 cases in which a tremendous disappearance of ventral horn cells corresponded to the atrophic muscles, and in which the meningeal process was, to him, insufficient to explain the process. He called the condition in these cases a "primary atrophic affection of the cornual cells."

Others supporting such a theory were Tooth and Howell,[19] who also thought that there are many cases due to peripheral neuritis, Head and Fearnsides,[14] Claude and H. Schaeffer,[13] C. Schaffer,[20] and more recently, Kino and Strauss [6] and Kaiser.[11] Several objections may be made to such a theory. The most important is that practically all such cases cited in its support show a meningovascular inflammatory process in addition to the ventral horn cell lesion. This is true to a varying degree in the cases reported by Tooth and Howell, Head and Fearnsides and Claude and Schaeffer. In some cases no mention is made as to whether the meninges and vessels are normal or not. It is thus difficult to say that such ventral horn cell disease as is present in these cases is not due to a meningovascular inflammatory process.

The theory that the muscular atrophy of syphilis is most often due to a meningovascular type of inflammation involving the ventral roots is now widely held, leaving the question as to the existence of a parenchymatous syphilitic anterior poliomyelitis open to debate. Such a meningitis is consistent with the frequent occurrence of pain in these cases, and is almost always found at necropsy.

Léri,[10] prominent among the modern authorities on this question, doubts the existence of such primary ventral horn cell disease due to syphilis. He thinks that in cases in which no meningeal reaction is found, it is because such a reaction has previously existed but subsequently subsided, leaving only the ventral horn cell atrophy to catch the pathologist's eye. Others ascribing the atrophy to a syphilitic meningo-

---

17. Holmes, Gordon: A Case of Combined Degeneration of the Cord with Amyotrophy, Rev. Neurol. & Psychiat. **11**:76, 1913.

18. Wilson, S. A. K.: The Pathology of Two Cases of Tabetic Amyotrophy, Rev. Neurol. & Psychiat. **9**:401, 1911.

19. Tooth, H. H., and Howell, C. M.: Progressive Myatrophy in Tabes Dorsalis, Proc. Roy. Soc. Med. (Sect. Neurol.) **52**:81, 1911-1912.

20. Schaffer, C.: Sur l'origine de l'amyotrophie tabétique, Rev. neurol. **4**:97, 1896.

myelitis are Raymond,[2b] Raymond and Cestan,[21] Falkiewicz,[12] Martin,[8] Kino and Strauss,[6] Stone,[7c] Margulis,[9] Kaiser[11] and Claude and Schaeffer.[13]

The pathologic description of two cases by Martin forms a good discussion of the pathology of syphilitic meningomyelitis. In both of his cases he found leptomeningitis, marginal degeneration of the white matter of the cord, severe destruction of the ventral horn cells and arteritis and perivascular infiltration of the meningeal and intraspinal vessels. In one of his cases there were a diffuse degeneration of ventrolateral white matter of the cord and ependymitis of the aqueduct of Sylvius and of the fourth ventricle, with proliferative outgrowths on the ependymal surfaces and on the meninges like those seen in dementia paralytica. Martin concluded from his pathologic and clinical studies that the process begins in the spinal meninges and affects the cord by direct extension into the subpial marginal regions of the spinal cord. He thought that the lymph channels served as the pathway for this advance, and this is the conception held by Margulis[9] and by Léri.[10] The former divided the clinical course into two stages, the first being the "latent" stage, with meningoradiculitis as its pathologic basis, and characterized by pareses of single muscles and groups of muscles, with a remittent course, and the second being a stage of progressive, unremittent and more generalized atrophy, with alteration of the ventral horn cells as its pathologic foundation. The illustrations in the article by Ostheimer, Wilson and Winkelman[22] show the marginal cord degeneration mentioned by Martin, though the authors made no reference to it. This marginal degeneration extends from the pia into the cord for varying distances in different cases. It would appear that whether or not a patient will exhibit signs of involvement of the pyramidal tracts will depend on whether or not this degeneration goes deeply enough to injure the corticospinal tracts. This being true, clinical signs of involvement of the pyramidal tracts have but little significance so far as pathogenesis is concerned.

This conception of a meningoradiculomyelitis as the pathologic starting point of syphilitic amyotrophy is strikingly in accord with the work of Sachs,[23] Nageotte[24] and Hassin,[25] which demonstrates that tabes

21. Raymond, F., and Cestan, R.: Méningo-myélite marginale progressive, Encéphale **4**:1, 1909.

22. Ostheimer, Alfred J.; Wilson, George, and Winkelman, N. W.: Syphilis as the Cause of Muscular Atrophy of Spinal Origin, Am. J. M. Sc. **167**:835, 1924.

23. Sachs, B.: Syphilis and Tabes Dorsalis, New York M. J. **59**:1, 1894.

24. Nageotte, I.: La lésion primitive du tabes, Bull. Soc. anat. de Paris **69**: 808, 1894; Compt. rend. Soc. de biol. **52**:352, 1900.

25. Hassin, G. B.: Beiträge zur Histopathologie der Tabes dorsalis, Neurol. Centralbl. **33**:1138, 1914; J. Nerv. & Ment. Dis. **42**:699, 1915; Tabes Dorsalis: Pathology and Pathogenesis; A Preliminary Report, Arch. Neurol. & Psychiat. **21**:311 (Feb.) 1929.

dorsalis itself is not a truly parenchymatous disease, but is due to the preceding meningitis, and the burden of proof would seem to rest on those who contend that syphilitic amyotrophy is not also due to similar, although perhaps not identical, meningitis. It is indeed difficult to see why the ventral roots are not more frequently involved in tabes by the same process which involves the dorsal roots, and one must fall back on the theory that in some way the lower motor neuron is less vulnerable.

A valid objection to this line of argument was brought forward by Kino and Strauss,[6] who pointed out that if similar processes were responsible for the atrophy and the tabes, the atrophy, like the tabes, should occur most frequently in the lower half of the body. Since this is not the case, one must admit that the whole germ of the matter has probably not been revealed, and one must await further work for a final answer. As intimated by Kinnier Wilson, the pathology of the syphilitic amyotrophies is a vexed problem, and one not capable of a simple and categorical explanation at this time.

THERAPEUTIC CONSIDERATIONS

The cases that we have reported illustrate the perils which await one who attempts to draw conclusions as to treatment. The first is the case of a man who, during vigorous antisyphilitic treatment, developed syphilitic amyotrophy and in spite of continued therapy grew slowly and steadily worse until death. The second is the case of a man who, having begun to exhibit a progressive amyotrophy while being inadequately treated, promptly improved under moderate but consistent treatment with mercury by inunction and potassium iodide. The third represents a man whose condition was not visibly affected by active therapeutic effort, while the fourth is the case of a woman whose amyotrophy began, progressed and ceased without a diagnosis having been made or treatment instituted. Gowers [2a] stated that the atrophy of syphilis might begin or increase during treatment, but that some patients were benefited. Head and Fearnsides [14] thought that the types based on meningovascular changes were amenable to treatment, while the parenchymatous types, based on a disease of the anterior horn cells, were not.

We wish to emphasize our belief, however, that vigorous and adequate antisyphilitic treatment in syphilitic amyotrophy can do no harm and may in many cases do much good. When a reasonable suspicion exists as to a syphilitic etiology, we believe that active treatment should be instituted with a judicious combination of arsphenamine, tryparsamide, bismuth and mercury, and the administration of artificial fever.

SUMMARY AND CONCLUSIONS

1. Four cases are reported as representing a form of progressive muscular atrophy due to syphilis.

2. As a group, these cases exhibit historical, physical and serologic evidences of syphilis; the atrophy often begins with pain, most frequently involves the upper extremities and not uncommonly occurs first in the shoulders and simultaneously or later in the hands, and may be very patchy in its distribution; the pyramidal tracts may or may not be involved.

3. A review of knowledge of the pathology of the group reveals much confusion, but seems to indicate a syphilitic meningoradiculomyelitis as the basis for most cases, with the question of a truly parenchymatous and selective syphilitic disease of the anterior horn cells as yet unsettled.

4. Antisyphilitic measures, vigorously and actively adopted, offer therapeutic hope in an otherwise hopeless neurologic field.

ABSTRACT OF DISCUSSION

Dr. Henry Daspit, Jr., New Orleans: Dr. Mackay and Dr. Hall have done a good thing in calling attention to these atrophies of syphilitic etiology. It seems to be the habit of a great many neurologists to cling rather tenaciously to ideas about classic syndromes.

In a previous paper commenting on the case of amyotrophic lateral sclerosis with combined columnar disease, if I remember correctly, Dr. Hassin said that he did not think that the total picture and the gastric analysis showed a marked general relationship. As many of us are in the habit of seeing classic pictures of muscular atrophy, we take things for granted and do not complete our laboratory survey, and in all probability miss early involvements from syphilis, which I think, as does Dr. Hall, is a real factor in many of these atrophies.

A man whom I saw at least fifteen years ago showed none of the ordinary signs of neurosyphilis. He had been treated elsewhere by every conceivable method, other than antisyphilitic, from Christian science to psychotherapy, and was found to have a positvie Wassermann reaction of the spinal fluid. He was given active treatment with arsphenamine and potassium iodide, and he made a complete recovery with restoration of muscle bulk. He is living at present and is active.

This also brings up for consideration that even in progressive atrophies there may be, as in other syphilitic involvements of the nervous system, none of the ordinary somatic criteria.

I have nothing further to point out other than the extreme desirability, in any picture presenting amyotrophy, of checking all the sources of information, particularly the spinal fluid, in cases in which—contrary to precedent in meningovascular conditions—the blood findings may dominate. We had one or two cases that showed positive tests of the spinal fluid and normal blood.

As to response to treatment, I cannot say much because I have not seen a sufficient number of cases. In two instances, however, in which the syndrome was typically that of amyotrophic lateral sclerosis, neither patient did well and both cases terminated rather typically.

Dr. George B. Hassin, Chicago: The paper by Drs. Mackay and Hall is the best presentation and discussion of so-called syphilitic atrophies that I have ever come across.

It is known that atrophies occur in tabes or syphilis without tabes, and that amyotrophic lateral sclerosis has nothing to do with syphilis in the majority of cases. Again, there are amyotrophies that are due to syphilis as such, and the

majority of progressive muscular atrophies are probably of syphilitic origin. More common are the atrophies that occur in tabes and that are known as tabetic. I wish to call attention to this phase of syphilitic amyotrophy, the tabetic type, although Dr. Hall described it very well.

We all know that the meningeal theories of tabes explain the sensory involvement, but do not explain the apparent absence of motor phenomena. The common objection to the meningeal theories of tabes is that a tabetic patient does not show involvement of the anterior roots if the meninges of the central nervous system are affected; that is, if meningitis is responsible for the lesion of the posterior roots, then why should it not also produce changes in the anterior roots? As a matter of fact, there is a motor involvement, and in some cases it is extensive, appearing as a widespread amyotrophy. In such patients there may be little involvement of the sensory nerve fibers, and then a typical picture of progressive muscular atrophy is seen.

The meningeal theories of Obersteiner, Nageotte and Richter cannot explain satisfactorily the phenomena of atrophy. However, if the lesion of tabes is assumed to be outside, in the epidural space around the spinal ganglia, where the posterior and anterior roots emerge to form a peripheral nerve, the lesion in this area, whether due to syphilis or another infection, may attack the motor component of the nerve and produce an atrophy, or, as is usually the case, may affect the sensory part, producing sensory signs and symptoms typical of tabes. The theory of the peripheral origin of tabes and the atrophies, long ago advocated by Dejerine, thus seems to be absolutely correct.

Dr. Theodore T. Stone, Chicago: Syphilitic amyotrophy is not a rare clinical syndrome. Many times a causative factor of spinal cord lesions showing amyotrophic signs and symptoms is not appreciated as such. For instance, in a case showing signs of a lower motor neuron lesion, which may happen to be in the cervical dorsal region, a spastic paraplegia below the level of the lesion, which is known as amyotrophic lateral sclerosis, may occur in persons who have a syphilitic infection and who, on vigorous antisyphilitic therapy, show considerable improvement.

These patients also may have, in conjunction with the spinal cord symptoms, signs of cranial nerve involvement, such as ptosis, Argyll Robertson pupil and other cranial nerve abnormalities.

There are three theories advanced as to the production of this type of spinal cord amyotrophy. One is that the meninges and roots are generally and diffusely involved around the entire spinal cord, with the pia and arachnoid becoming adherent and matted together. As a result of pure pressure or compression the marginal aspects of the spinal cord degenerate. In that way, symptoms of the posterior and lateral columns and direct and indirect signs and symptoms of the cerebellar tract may be found.

The second theory is that these infective agents or toxins reach the spinal cord through the lymph channels. In many instances of syphilitic amyotrophy there is involvement of the entire spinal cord, with the exception of the posterior columns.

The third theory is that the changes may be associated with involvement of the vascular system; this, in all probability, is correct.

The pathology in these types of cases is widespread. There may be involvement of the margin of the cord, the blood vessels of the anterior and posterior median fissures, the anterior horns and the posterior horns and roots, with a pathologic process so diffuse that one must certainly consider it not as a disease of a specific tract but as a condition that can be produced by a disease like syphilis.

I believe that syphilis is a common cause of spinal muscular atrophy of the progressive type, showing lower motor neuron signs and symptoms. In this type of spinal cord atrophy one rarely, if at all, sees bulbar paralysis, which one often sees in amyotrophic lateral sclerosis.

Finally, in this type of spinal cord atrophy one rarely sees sphincter difficulty, such as is often seen in amyotrophic lateral sclerosis.

DR. CARROL TURNER, Memphis, Tenn.: This interesting presentation of Drs. Mackay and Hall calls to mind a case that was definitely one of syphilitic poliomyelitis. A child, 3 years old, presented all the symptoms and clinical findings of an acute epidemic poliomyelitis. We considered this as the diagnosis until a report of the serology revealed a four plus Wassermann reaction and a syphilitic curve of the spinal fluid. She made a rapid recovery following spinal drainage and the institution of antisyphilitic treatment. There were no neurologic sequelae in this patient as is usual following poliomyelitis. At the time of the last examination, about two years following the syphilitic condition, the patient was entirely normal.

The ventral portions of the cord, particularly the ventral gray matter are more vascular than the posterior portions of the cord. Therefore, it seems logical to expect more involvement of the ventral gray matter in the presence of a vascular disease, such as syphilis, than there seems to be.

ACTION CURRENTS IN THE CENTRAL NERVOUS SYSTEM

LEON J. SAUL, M.D.
Commonwealth Fund Fellow in Psychiatry, Boston Psychopathic Hospital and Harvard Medical School
AND
HALLOWELL DAVIS, M.D.
Assistant Professor of Physiology, Harvard Medical School
BOSTON

This paper is a report of work begun over a year ago as part of a study of action currents in the central nervous system. A great stimulus was derived from the striking experiment of Wever and Bray [1] and its highly suggestive relationship to hallucinations.

The central nervous system may be thought of as an organization of tracts and centers which transmit and integrate nerve impulses. Nervous and mental diseases may be considered as disorders of such transmission and interplay. A method for detecting and studying the nerve impulses in the functioning nerve tissue might therefore illumine the workings of the nervous system in health and in disease.

We believe such a method to be available in the form of an adaptation of the modern neurophysiologic technic for the study of action currents in peripheral nerves.[2] It consists simply of a sensitive electrical device for detecting and recording action currents. Such application to the central nervous system was exhaustively studied by Gotch and Horsley [3] and has been reported frequently from this laboratory.[4]

Nerve impulses are invariably associated with electrical disturbances called action currents. One is never found without the other. Although complete identity is not established, the relationship is so intimate that, if the distinction is recognized, they may be spoken of interchangeably. The action current travels at a speed of about from 50 to 100 meters a second, and derives its energy from the nerve itself, something like the

---

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, June 6, 1932, at Atlantic City, N. J.

1. Wever, E. G., and Bray, C. W.: Science **71**:215, 1930.

2. Adrian, E. D.: The Basis of Sensation, New York, W. W. Norton & Company, 1928.

3. Gotch, F., and Horsley, V.: Phil. Tr., Roy. Soc. **182**:267, 1891.

4. (*a*) Forbes, A., and Miller, R. H.: Am. J. Physiol. **52**:113, 1922. (*b*) Forbes, A.; Miller, R. H., and O'Connor, J.: Am. J. Physiol. **80**:363, 1927.

burning of a long narrow trail of gunpowder. It must not be confused with the conduction by nervous or any other body tissue of ordinary electric currents. These may arise locally, as from a contracting muscle, or externally, as from a stimulating coil. They travel through all electrically conducting tissues at an enormous speed, deriving their energy from the stimulus and not from the tissue, which merely serves as a conductor.

TECHNIC

We use cats almost exclusively. They are either decerebrate or anesthetized with ether, diallyl barbituric acid or that which is most satisfactory, avertin plus occasionally a little ether. The operation, depending on the experiment, is usually a clear exposure of the auditory nerve and subarcuate fossa of the petrous bone, through a dorsilateral subtentorial approach, plus an exposure of one or both hemispheres. The preparation may then be stimulated in a variety of ways: light to the eyes, sounds to the ears, odors to the nose, and so on, and the action currents generated are then picked up from the appropriate tracts in the central nervous system. This is done by using electrodes made of straight silver wire, insulated except at the very tip, or else those of the Adrian-Bronk type.[5] This type consists of a hypodermic needle which serves as a shield to the fine, insulated wire down its center. The needles pick up disturbances only at the very tip, so that they must be accurately placed on the particular pathway in order to detect the highly localized electrical phenomena the pathway transmits. For example, if a sound is applied to the cat's ear, in order to detect the resulting action currents going up the auditory tracts, such electrodes must be placed exactly on one of these tracts. At a distance of a half millimeter the effect is lost. A micromanipulator is, therefore, frequently used.

The action currents are led through these electrodes into an amplifier. A selector switch makes it possible to have several electrodes in place at a time and to shift easily from one to another. The amplifier, designed and built by Mr. Lovett Garceau, gives us an effective amplification of up to ten million, for the operation of a cathode ray oscillograph and a loud speaker. A sweep circuit makes the responses appear on the oscillograph as standing waves. The action currents may thereby be detected by eye and ear simultaneously. For exploring parts of the brain, locating tracts and similar purposes, head phones may be used at the same time. Records are made from the oscillograph by tracings, or by photographs with moving films, giving pictures of the same type as the electrocardiogram.[6]

After the experiment the brains are removed, fixed and sectioned to verify the placements of the electrodes. In this we are assisted by Dr. Rioch of the anatomy department.

To recapitulate: A stimulus is applied to a sense organ as a light to the eye. This results in a localized flow of nerve impulses along the appropriate tracts of the central nervous system. Electrodes placed on the proper tract, in this example, the optic tract, detect the action currents. The disturbance thus detected is amplified by electron tubes sufficiently to operate a recording device. These action currents may then be seen and heard and permanently recorded for later study. The brains are sectioned for anatomic correlation.

---

5. Adrian, E. D., and Bronk, D. W.: J. Physiol. **67**:119, 1929.

6. The construction of this apparatus was made possible by grants from the DeLamar Mobile Research Fund and from the Josiah Macy, Jr., Foundation.

EXPERIMENTS AND RESULTS

The brief descriptions which follow are intended to give the types of experiment performed and the kinds of results obtained.

In the original experiments we stimulated a branch of the sciatic nerve with an ordinary inductorium, and explored the medulla. The largest and most constant responses were obtained from the ipsolateral dorsal columns. Further statements are unwarranted, because this work was left incomplete, owing to the fact that we accidentally struck an auditory tract; this occurrence deflected our interest to the acoustic phenomena.

Our observations indicate that there are two distinct electrical phenomena involved in hearing: true action currents and "spread." This "spread" is an electric current which seems to originate in the cochlea, and which is conducted throughout all the tissues (like any electric current) at the usual speed of electricity. It is probably involved in the transformation by the cochlea of sound into nerve impulses, and is almost certainly in no way concerned with the transmission of impulses from the ear to the brain.[7]

The auditory action currents are highly localized in the auditory pathways, and follow their contralateral relationships. They are reversibly deleted by anesthetics and disappear immediately on the death of the animal. Musical tones applied to the cat's ear are reproduced in the loud speaker only up to 1,000 double vibrations per second. Words come back blurred, probably because frequencies higher than 1,000 double vibrations are not reproduced. This probably means that the fibers of the eighth nerve do not transmit more than 1,000 impulses a second as a maximum figure; i. e., the auditory nerve behaves like other peripheral nerves. This may be taken to support the frequency theory of pitch discrimination up to 1,000 double vibrations and to be evidence against it for higher frequencies.

The "spread," in contrast to the action currents, is not localized, but broadcasts throughout all the tissues of the head. The point of maximum intensity (so far found) is in the posterior groove of the subarcuate fossa where the bone is thin.[8] The spread is extremely resistant to anesthetics and may persist for as much as twenty minutes after the heart stops, or after the eighth nerve and cochlear artery are cut. It gives back frequencies of up to at least 4,000 double vibrations and reproduces words accurately. It is distinguished from the action currents by the different shapes of the waves on the cathode ray oscillograph, by the differential suppression by anesthetics (action currents

7. Saul, L. J., and Davis, H.: Tr. Am. Otol. Soc., 1932, to be published.

8. Subsequent experiments show that the "spread" recorded from the round window is still stronger than that from the subarcuate fossa.

are much more vulnerable), by its size in relation to strength of stimulus varying in more of a straight line than a logarithmic curve relationship (as with action currents) and by its almost instantaneous transmission through tissues (as electricity) in contrast to the relatively slow speed of action currents in tracts.[7]

Electrodes may be placed on the optic tract, between chiasm and lateral geniculate body. This preparation is so sensitive that in a diffuse light, a foot from the cat's eyes, the amount of movement necessary to pinch a small forceps stimulates the retina to produce action currents enough in the optic tract to give a definite response on the oscillograph and in the loud speaker. This response is mostly contralateral. If in a dark room a light is flashed on, there is a sudden loud discharge, which settles down to a disturbed background (fatigue or adaptation). When the light is covered again, there is again a loud burst, settling down to a background much quieter than when the light was on. The sudden dark seem to stimulate.[9]

If an electrode can, by good luck, be placed on the nucleus supra-opticus, a powerful discharge is observed. A light flashed into the contralateral eye greatly reduces this disturbance. The pupil, of course, constricts when the light is applied.

Our olfactory experiments are not sufficiently conclusive to warrant more than mention.

As to touch, pinching the cat's hind foot gives action currents only in the well demarcated hind leg area of the cortex. Stretching or hyperflexing gives responses in the proprioceptive tracts.

In addition to these electrical nervous responses to stimulation of sense organs, many points in the brain yield definite "spontaneous" discharges, for example, the supra-optic nucleus already mentioned. In addition to its loud tonic background, it shows a strong rhythmic disturbance, a little slower in frequency than the heart beat (probably sympathetic).[10] In the region of the hippocampus is a point giving huge discharges (500 microvolts, peak voltage), about five times a second, which are very regular and have waves of very constant and definite shape.

The clinical trials of this technic in the form of direct stimulation of the auditory nerve or of the round window by a voice frequency stimulator have thus far proved inconclusive. In the operating room,

---

9. (*a*) Einthoven, W., and Jolly, W. A.: Quart. J. Exper. Physiol. **1**:373, 1908. (*b*) Bovie, W. T.; Chaffee, E. L., and Hampson, A.: J. Am. Optical Soc. **7**:1, 1923. (*c*) Adrian, E. D., and Matthews, R.: J. Physiol. **63**:378, 1927. (*d*) Hartline, H. K., and Graham, C. H.: J. Cell. and Comp. Physiol. **1**:277, 1932.

10. Adrian, E. D.; Bronk, D. W., and Phillips, G.: J. Physiol. **74**:115, 1932.

through the cooperation of Dr. Harvey Cushing and of Dr. Tracy Putnam, action currents have been observed in human beings, but this work is at present too incomplete to report.

SUMMARY

1. A method is described for the study of nerve impulses in the central nervous system. It is an adaptation of the standard neurophysiologic technic for the study of action currents in peripheral nerves. A stimulus is applied to a sense organ, and the resulting action currents are detected in the appropriate tracts and studied.

2. Responses have thus been obtained from the proprioceptive, tactile, auditory and optic pathways. "Spontaneously" discharging points in the brain have been observed.

3. Two electrical effects are distinguished in the acoustic mechanism, true action currents and "spread." The latter is an electrical disturbance spreading in all directions, probably originating in the cochlea.

4. Preliminary clinical experiments are mentioned. In the neurologic operating room observations have been made of the transmission of nerve impulses in the central nervous system of man.

DISCUSSION

DR. LEWIS J. POLLOCK, Chicago: Were the responses to stimulation in the sciatic nerve obtained ipsolaterally, bilaterally or contralaterally?

DR. L. J. SAUL: They were predominantly ipsolateral. There were some contralateral responses.

HYSTERICAL ANESTHESIA, ANALGESIA AND ASTEREOGNOSIS

EXPERIMENTAL STUDY

ROBERT R. SEARS, PH.D.
Blossom Fellow in Neuro-Anatomy, 1931-1932
AND
LOUIS H. COHEN, PH.D., M.D.
Sterling Fellow in Psychology, 1930-1931
NEW HAVEN, CONN.

It is unfortunate that with the realization of the psychic causation of hysterical symptoms there has been a widespread neglect of the study of these phenomena from the physiologic standpoint. Psychoanalysts, in their elaborations of the psychologic mechanisms involved in the production of conversion symptoms, have not questioned seriously the means by which the nervous system is able to build these sudden physiologic manifestations of psychopathologic processes. The existence of the question has not been entirely ignored,[1] but with the exception of Hurst,[2] who reported a number of excellent experiments on the frequency and extent of special sense disorders in the war neuroses, there is an astonishing paucity of experimental data bearing on the problem. That this paucity has been a result of a lack of adequate methodologic approach seems possible.

However, within the last decade technics have been developed which should prove fruitful if employed in this connection. One need mention but a few to indicate the possibilities. The study of chronaxia in functional anesthesias and paralyses, the application of Hull's [3] technics for the quantitative analysis of amnesias, the pharmacologic study of vascular changes, globus hystericus and conditions of sleep disturbance

From the Department of Psychology and the Department of Psychiatry, Yale University.

1. Ferenczi (Theory and Technique of Psychoanalysis, New York, Boni & Liveright, Inc., 1927), in a discussion of this topic, suggests that, ". . . in spite of all our satisfaction with what has been achieved, it is more to the purpose to indicate the lacunae in our knowledge of these matters. The 'mysterious leap from mental to bodily' (Freud), for instance, in the symptoms of hysteria is still a problem" (p. 90).

2. Hurst, A. F.: Croonian Lectures: The Psychology of the Special Senses and Their Functional Disorders, New York, Oxford University Press, 1920.

3. Hull, C. L.: Quantitative Methods of Investigating Hypnotic Suggestion, J. Abnorm. & Social Psychol. **25**:200 and 390, 1930.

should all yield valuable experimental data. Indeed, the majority of technics and methods suggested by Hull for a study of hypnosis should be applicable with profit to hysterical phenomena.

The difficulty of securing adequate experimental controls in pathologic conditions is especially great in the case of hysterical reactions. No observation can be considered valid, however, unless comparable observations have been made on normal persons or on the patient himself either under controlled conditions or after disappearance of the phenomenon under investigation. Hurst and Symns,[4] among others, have demonstrated the danger of neglecting this type of "normal control." For decades, pharyngeal anesthesia had been accepted by clinicians and textbooks as an unquestioned stigma of hysteria. A seven point rating scale was devised by these investigators and the excitability of the pharyngeal reflexes examined in three groups of subjects: 170 persons who were normal; 64 who had hysteria, and 34 who had hysterical mutism and aphonia. The excitability of the pharyngeal reflexes proved to be as great in the two hysterical groups as in the normal group, and in all three the distribution conformed to that of the normal probability curve. The writers drew the obvious conclusion that pharyngeal anesthesia is not an hysterical stigma.

Present knowledge of the physiology of hysterical symptoms is derived mainly from the results of the work of Hurst and his collaborators and the experiments of Levine.[5] Hurst limited himself to a study of hysterical anesthesia and areflexia. His theoretical conclusion was that functional anesthesias are a result of inattention to the sensory input from the anesthetic area. This inattention, it is suggested, may consist of "a throwing out of dendrites, or it may depend on some biochemical change in the material which occupies the space between the dendritic terminations of adjacent neurones. Whatever it may be, the increased resistance which is present when attention is very deficient results in anesthesia, and at the same time a block is produced in the reflex arc which results in diminution or abolition of the reflex."

Rosanoff,[6] on the other hand, believed that hysterical symptoms are similar to those manifested in deliberate malingering, and are thus on a purely verbal and conscious level of behavior. It might be noted in support of this conception that Levine obtained the galvanic skin reaction to pain in two cases of hysterical analgesia and in two cases of hypnotically induced analgesia. The reaction was not measured quanti-

4. Hurst, A. F., and Symns, J. L. M.: Scale Hayne Neurol. Studies **1**:43, 1918.

5. Levine, M.: Psychogalvanic Reaction to Painful Stimuli in Hypnotic and Hysterical Anesthesia, Bull. Johns Hopkins Hosp. **46**:331, 1930.

6. Rosanoff, A. J.: Manual of Psychiatry. New York, John Wiley & Sons, 1920.

tatively, however, and one of us (Dr. Sears) [7] showed recently that, though the galvanic skin reaction to pain is indubitably present in cases of hypnotic analgesia, it is considerably reduced in strength. Possibly this same reaction, though present, may also be reduced under hysterical analgesia in comparison to normal reactions. Technical difficulties with the galvanometer have prevented a study of this problem in the present case.

The purpose of the present study has been to determine, in three types of sensory dysfunction, the extent to which the normal reactions to stimuli affecting these modalities are modified by the functional sensory losses. More specifically, the problem has been to investigate some of the fundamental physiologic reactions concomitant with such phenomena.

It is unfortunate that only one patient has been immediately available for this study, but it is believed that the relatively large number of observations and their comparison with control experiments under normal conditions may compensate to some extent for the lack of a larger number of subjects.

Mrs. I. B., aged 45, whose complete case history, physical and mental examinations are not relevant for present purposes, developed symptoms eight months before admission to the psychiatric clinic.

The left hand was completely anesthetic to superficial touch as produced with cotton-wool and by brushing of the hairs; it was analgesic to superficial pain and to deep pain except that produced by flexion of the fingers, which were partially paralyzed (probably a functional paralysis). Thermal sensitivity was normal. There was complete astereognosis. The right hand was entirely normal except that the thumb was "numb."

The following diagnosis was made: psychopathic personality, with hysterical anesthesia to superficial touch, analgesia to superficial and deep pain and astereognosis.

ANALGESIA

In a recent study,[7] it was shown that when normal persons are hypnotized and by the process of suggestion are rendered anesthetic or analgesic in one leg, painful stimulation of that member will not produce the normal respiratory reaction to pain evoked by stimulation of the normal or control leg. In an attempt to determine whether hysterical analgesia modifies this reaction in a similar way, the technic used in the former study was applied to an investigation of the present case.

Two types of painful stimuli were utilized: (1) that produced by an algesimeter, and (2) that produced by electric shock from a high frequency induction coil.

---

7. Sears, R. R.: An Experimental Study of Hypnotic Anesthesia, J. Exper. Psychol. **15**:1, 1932.

Technic.—The algesimeter [8] consists of a sharp steel point inserted at an angle of 45 degrees in the end of a small metal rod. The rod slides easily within a sleeve and rests against a small coil spring held in place by a transverse pin at the upper end of the sleeve. The sharp steel point, which presses against the skin at an angle of 45 degrees, exerts a pressure of 20 ounces against the skin surface when the coil spring is completely depressed. Depression of the spring produces an increased air pressure in a tube leading from the upper end of the sleeve to a recording tambour on the kymograph. Incidence of the stimulus is thus recorded automatically. Comparable areas, 5 cm. square, on the dorsum of each hand were used for stimulation. Respiration was recorded by a Sumner pneumograph placed over the region of the eighth rib.

The patient was blindfolded during each of the four experimental periods, the first three of which were devoted to stimulation with the algesimeter and the last with electric shock. Stimuli were presented in the *A B B A* order, beginning with the anesthetic arm, and were from fifty to eighty seconds apart. A definite rhythm was avoided in order that temporal conditioning might not be a source of error.

Measurement of the respiratory records was made with the Hull oscillometer,[9] an instrument which summates the vertical oscillation of a wavy line. One inch of vertical tracing is equivalent to 39 oscillometer units. Periods of twenty seconds' duration were marked off before and after each stimulus. The total amount of oscillation in each of these two periods was measured and the algebraic difference (increase, +; decrease, —) in amount of breathing following stimulation noted. Normally the total oscillation is markedly increased following stimulation. The reliability of this method of measuring the respiratory reaction to pain has been amply demonstrated in the studies of one of us (Dr. Sears)[7] and of Garvey.[10]

Results.—Table 1 shows the number of stimuli presented to each arm, the normal and anesthetic, and the mean amount of oscillation in the respiratory tracing both before and after the stimulus. These values are in terms of oscillometer units. The normal reaction to pain produced by the algesimeter is an increase of 10.73 units over the prestimulus amount of respiration. The probable error of this mean is 1.56. The reaction to pain presented to the anesthetic area, however, is an increase of only 2.85 units, with a probable error of 1.5. The difference between the sensitivity of the two arms, as measured by respiratory response, is 7.88 units. This difference is 3.63 times as great as its probable

8. For a more comprehensive description of the apparatus, methods of measurement and technic, see footnote 7, p. 2.

9. Hull, C. L.: An Instrument for Summating the Oscillations of a Line, J. Exper. Psychol. **12**:259, 1929.

10. One exception may be noted. One of us (Dr. Sears), in collaboration with Mrs. Helen Hope Dibbell, attempted to apply the foregoing technic to a patient at Bellevue Hospital, New York, who suffered from a complete hemilateral functional analgesia. Although a hundred stimuli were presented on each leg, measurement of records shows that no reaction to pain was obtained from either the normal or the anesthetic side. Whether the cause lay in faulty recording or in the patient has not been discovered. It is possible that a complete bilateral analgesia was spontaneously developed during experimental periods as a defense against the pain. Garvey, G. R.: J. Exper. Psychol., to be published.

error. The difference between the sensitivity of the two arms as measured by reaction to shock is 2.87 times its probable error.

In the earlier experiments on hypnotic analgesia, a control series was run in which six subjects were instructed to pretend that they felt no pain when the left leg was stimulated but to react normally when the right was stimulated. No difference was found between the respiratory reactions to pain on the respective legs. In other words, voluntary inhibition, the verbal level of behavior described by Rosanoff, does not produce the same type of modification of this reaction to pain that is produced by true hypnotic analgesia. The present data indicate that hysterical analgesia modifies the normal reaction to pain in substantially the same way as hypnotic analgesia. It seems probable, therefore, that the loss of sensitivity is on a lower level of physiologic activity than that implied by Rosanoff.

TABLE 1.—*Stimuli Presented to the Normal and Anesthetic Hand and the Mean Amount of Respiratory Oscillation* *

	Cutaneous Pain (Algesimeter)				Electric Shock			
Hand Stimulated	Number of Stimuli	Mean Before Stimulus	Mean After Stimulus	Mean Difference	Number of Stimuli	Mean Before Stimulus	Mean After Stimulus	Mean Difference
Normal....	49	81.73	92.46	+10.73 ± 1.56	25	67.04	69.04	2.00 ± 0.86
Anesthetic.	47	86.76	89.61	+ 2.85 ± 1.50	23	70.65	69.13	−1.52 ± 0.89
Difference between normal and anesthetic.....			7.88 ± 2.17				3.25 ± 1.22	
D / P. E. D.			3.63				2.87	

* The differences between the two arms in this respect, with the probable error of difference and the critical ratio, are given at the foot of the table.

This abolition of the normal respiratory response to pain is consonant with the results of tests made by Schilder [11] on a patient with a hemilateral functional analgesia. Application of pin pricks to the normal arm raised the blood pressure to 140 mm. from its normal level of 130 mm., but similar stimulation of the analgesic arm failed to elicit any change in pressure. Schilder referred to some experiments of Lowenstein, which gave results that conflict with these findings, however; in these, no modification of pain responses by the analgesia was demonstrated. Unfortunately, the original reports of Lowenstein's work have not been available to us.

The point in the nervous system at which this modification occurs cannot yet be ascertained. In consideration of Levine's results, one must surmise that it is neither in the sense organ proper nor in the afferent pathway to the thalamus.

11. Schilder, P.: Notes on the Psychopathology of Pain in Neuroses and Psychoses, Psychoanalyt. Rev. **18**:1, 1931.

It may be concluded, then, that hysterical analgesia consists of a blocking of at least two of the normal reactions to pain, viz., verbal report and increased respiration. This blocking is not simply a voluntary inhibition of verbal report (simulation), but its position in the nervous system can be defined only in a negative fashion; i. e., it lies neither in the sense organs nor in the afferent pathways to the thalamus.

ASTEREOGNOSIS

Stereognosis, unlike pain, pressure, touch and temperature, is not a simple cutaneous sense. It belongs to that class of psychologic acts termed perceptions rather than sensations. It is an act mediated by the fundamental senses and is, essentially, a correlation of the data derived through those senses. The question arises in a study of the hysterical loss of stereognosis as to whether the loss is confined to the perceptual level or whether there is a concomitant loss of the fundamental sense modalities underlying the perceptual act.

Campora,[12] from an analysis of a large number of cases of astereognosis in which the organic foundations were subsequently verified by autopsy, concludes that the sense data which are of primary significance in the stereognostic act are those of two point discrimination. Deep sensibility was often but not uniformly impaired, and superficial touch was occasionally destroyed in this series of cases, but the two point limen was invariably raised no matter what the other sensory losses were.

An examination of the efficiency of two point discrimination was therefore made in this case of hysterical astereognosis. Since the right hand, except for the thumb, was perfectly normal, it was used as a control for the measurements obtained from the left hand (astereognostic).

Technic.—Twelve separate areas were chosen on the left hand at which to determine the two point threshold, and exactly comparable positions were marked on the right hand. In this way differences in the thresholds of the left hand were made immediately discernible by reference to the values obtained from the comparable positions of the right, or normal, hand.

The twelve positions chosen for the examination were: (1) the tip of the thumb; (2) the tip of the first finger; (3) the tip of the second finger; (4) the tip of the third finger; (5) the tip of the fourth finger; (6) a line drawn horizontally across the center of the palm; (7) a line drawn vertically across the center of the palm; (8) the inner phalangeal margin of the thumb; (9) the ball of the thumb (palmar surface of the distal phalanx); (10) the palmar surface of the second phalanx of the first finger; (11) the palmar surface of the second phalanx of the second finger, and (12) the palmar surface of the second phalanx of the third finger.

12. Campora, G.: Astereognosis: Its Causes and Mechanisms, Brain **48**:65, 1925.

The thresholds were obtained in the usual manner. The determination by descending order was made first; the limen was found and passed, and the determination by ascending order followed promptly. This process was repeated three or four times and the lowest reading obtained for each order of stimulation recorded on the chart, as indicated in table 2. The values are in terms of sixty-fourths of an inch. Thus, on the tip of the index finger of the right hand the distance necessary between two points simultaneously presented, if they were to be discriminated as two separate points, was found on ascending order to be $\frac{6}{64}$ inch, and on descending order, $\frac{5}{64}$ inch. The threshold values obtained by ascending and descending order have been averaged for each area, and the means thus derived are considered to be the "true" threshold of discrimination.

TABLE 2.—*Thresholds for Two Point Discrimination Determined by Ascending and Descending Order at Twelve Comparable Positions on the Normal (Right) and Astereognostic (Left) Hands* *

Position	Right (Normal)			Left (Astereognostic)			Per Cent Increase
	Ascending	Descending	Mean	Ascending	Descending	Mean	
Thumb tip	9 (9)	7 (8)	8.0	10 (9)	8 (6)	9.0	12.5
First finger tip	6	5	5.5	10	8	9.0	63.6
Second finger tip	6 (8)	4 (6)	5.0	10 (10)	8 (10)	9.0	80.0
Third finger tip	7	4	5.5	11	10	10.5	90.9
Fourth finger tip	9 (7)	7 (8)	8.0	10 (7)	10 (6)	10.0	25.0
Palm: horizontal	22	21	21.5	23	23	23.0	7.0
Palm: vertical	32	28	30.0	29	27	28.0	−6.7
Thumb: phalanx	18	15	16.5	30	20	25.0	51.5
Thumb: ball	27	27	27.0	54	32	43.0	59.2
First finger: phalanx	14	13	13.5	48	44	46.0	240.8
Second finger: phalanx	13	11	12.0	22	22	22.0	83.3
Third finger: phalanx	14	14	14.0	40	18	29.0	107.7
Mean			13.834			21.950	+67.9
Difference between hands				8.116 ± 1.772			
Critical ratio				4.58			

* Values in parentheses are for retests. All values are in terms of sixty-fourths of an inch.

Results.—Table 2, giving comparable measurements on the two hands, indicates that in all but one of the twelve positions the threshold was higher on the astereognostic hand. However, the tip of the thumb and the tip of the fourth finger were given retests, since the patient reported that the thumb on the right (normal) hand was in a condition similar to that of the left hand; i. e., it was "no good, feels numb and is stiff," and the little finger on the left (astereognostic) hand was normal.

Little difference between the thumbs was found originally, and on the retest (values in the brackets) the ascending order gave the same value for each hand while the descending order seems to have demonstrated a lower threshold for the left hand. The patient's uncertainty during stimulation of this area renders doubtful the reliability of all values obtained for the thumb tips.

This ambiguity is not present in the retest results for the fourth finger. The criteria were quickly and easily satisfied, and the outcome was a reversal, again in favor of the astereognostic hand.

A retest on the two second fingers, done as a control because of the equivocal results obtained from the other two retests, showed that here, where there was no question as to the relative conditions of the fingers, there was no reversal of the limens, although the actual values have changed. This is not an unusual phenomenon. The two point threshold, like other physiologic processes, varies somewhat from day to day, although the limens obtained within any one hour may be considered fairly reliable.

TABLE 3.—*Two Point Thresholds at Twelve Comparable Positions on the Right and Left Hands After the Spontaneous Disappearance of the Astereognosis in the Left Hand*

Position	Right			Left (Formerly Astereognostic)			Per Cent Increase
	Ascending	Descending	Mean	Ascending	Descending	Mean	
Thumb tip	6	6	6.0	5	4	4.5	−25.0
First finger tip	6	5	5.5	6	3	4.5	−18.1
Second finger tip	6	6	6.0	5	5	5.0	−16.7
Third finger tip	6	5	5.5	6	5	5.5	0
Fourth finger tip	6	6	6.0	6	5	5.5	− 8.3
Palm: horizontal	11	10	10.5	14	10	12.0	+14.3
Palm: vertical	16	15	15.5	18	16	17.0	+ 9.0
Thumb: phalanx	14	12	13.0	20	8	14.0	+ 7.8
Thumb: ball	8	7	7.5	7	6	6.5	−13.3
First finger: phalanx	15	15	15.0	13	12	12.5	−16.7
Second finger: phalanx	15	13	14.0	18	18	18.0	+28.5
Third finger: phalanx	14	13	13.5	17	17	17.0	+20.6
Mean			9.78			10.12	− 1.5
Difference between hands				0.34 ± 0.38			
Critical ratio				0.89			

The means of the twelve values for each hand have been calculated. The difference between the two is 8.116, and the probable error of that difference [13] is 1.772. There is little question as to the reliability of the difference, the critical ratio being 4.58.

Six weeks after this series of determinations, an examination showed that there had been a spontaneous recovery of the stereognostic ability. This fact presented an opportunity to discover whether the loss of two point discrimination had been directly correlated with the astereognosis. The former procedure was repeated in every detail, and the results of this second series of determinations are given in table 3.

It will be seen that there is now practically no difference between the thresholds of the two hands. The left hand (formerly astereog-

13. The two columns of means were correlated and the r used in the following formula for determining the probable error of the difference between the means:

$$\sqrt{P.E._{A}^{2} + P.E._{B}^{2} - 2\,r\,P.E._{A}\,P.E._{B}}$$

nostic) has a slightly higher mean threshold value, but the difference is only 0.89 of the probable error of the difference. This indicates no more than a normal variation. The difference between the thresholds of the normal hand on the two series of determinations is not of significance in the present study; it may be accounted for by normal daily variability and the fact that a different pair of compasses was used in the second series.

It may be concluded that if Campora is correct in his assumption that two point discrimination is fundamental to cutaneous spatial perception, there is, in functional astereognosis, a dropping out of the fundamental processes concerned with this activity. The astereognosis is not, as might be expected a priori, simply a loss of discrimination between common sense objects such as knives and keys or velvet and wood, but involves the deeper and more fundamental physiologic mechanisms that are involved in this type of perception. With return of the higher function, moreover, we find a concomitant return to normal of the underlying discriminatory ability.

ANESTHESIA

Although, as was demonstrated in the experiment on analgesia, the innate unconditioned reaction to a stimulus acting on a functionally anesthetic sense may be greatly modified, the question arises as to how effective the sensory block is if the anesthetic sense is used as the medium for the conditioned stimulus in the process of establishing a conditioned reaction. As early as 1912, this method suggested itself to von Bechterew [14] as a technic for differentiating organic from functional anesthesias. He said, in part (p. 188):

> While in organic lesions of cutaneous sensibility the associative-motor-reflex method clearly shows the presence or absence of an anesthesia, it cannot be employed with security in the case of hysterical anesthesia. In a case of hysteria with anesthesia and paralysis of the lower extremities, we were unable to set up an associative-motor-reflex, although Kunjajew (1911) succeeded in establishing an a.-m.-r. in a patient with total hysterical anesthesia but retention of voluntary movement. The stimulation was associated with a bell-active finger retraction serving as the response.

More recently, Myasishchev,[15] in an extensive study of hysterical and hypnotic symptoms, was able to repeat Kunjajew's reported success.

An attempt was made in the present instance to establish a conditioned reaction to cotton-wool stimulation of the dorsum of the left

14. von Bechterew, W.: Die Anwendung der Methode der motorischen Assoziationsreflexe zur Aufdeckung der Simulation, Ztschr. f. d. ges. Neurol. u. Psychiat. **13**:183, 1912.

15. Myasishchev, V.: Experimental Evidence on the Problem of Objective Indices in Sensory Disorders, Nov. refl. fiziol. nerv. sist. **3**:458, 1929; Psychol. Abst. **4**:4349, 1930.

hand; this, it will be remembered, is an area anesthetic to superficial touch. The unconditioned stimulus was an electric shock applied to the normal (right) hand, the reaction being a quick withdrawal movement. Although a severe shock was used, this withdrawal was not, initially, great enough to be accurately observed.[16] The patient was therefore requested to withdraw her hand voluntarily as quickly as possible each time she felt the shock. In conditioned reflex terminology this verbal instruction amounts to an externally induced but internally maintained constant facilitation of the unconditioned reaction.

Experiment 1.—The hands were placed palm down on a table before the patient, the right resting on a simple electric grid. A bandage was placed across the eyes, and every effort was made to eliminate slight sounds of movement as the stimulations were given. No attempt was made to record the reactions mechanically. The conditioned stimulus consisted of a quick brush of a wisp of cotton across the back of the left hand (anesthetic). Preliminary examination proved this to be an entirely insensible stimulus. The unconditioned stimulus (shock) acting on the right (normal) hand followed the cotton stimulus by approximately one second.

Fifty reenforcements of the cotton stimulus were given with the shock, but no conditioned reaction was evoked.

Experiment 2.—The fingers of the right hand were placed on the electrodes of a delicate recording apparatus[17] and the procedure of experiment 1 repeated for ten further reenforcements. The graphic record showed clearly the failure of the cotton stimulus to evoke even a minimal reaction.

In the belief that the phenomenon of irradiation, as described by Anrep,[18] might be invoked to elicit a conditioned reaction, the conditioned stimulus was transferred to the right (normal) hand. A conditioned reaction appeared after two reenforcements. In consideration of some preliminary work carried out by Mr. Shipley, we believe this to be fewer reenforcements than are necessary in the average normal subject with this technic. It seems not improbable that some type of association had already been established between the cotton stimulation and the finger reaction by the previous stimulation of the anesthetic hand; even if this is true, the reaction tendency had not yet reached the threshold at which an overt reaction would appear.

Ten further reenforcements were given to the cotton stimulus acting on the right hand. A return of the stimulus to the anesthetic hand did not evoke a response. In the course of the experiment, six more cotton stimuli were presented to the left hand interspersed in a series of twenty-five cotton stimuli presented to the right. No conditioned response was established in the left hand, however, although the normal hand provided consistent reactions.

---

16. This restriction of defense behavior to a relatively small portion of the available reactive mechanism is in accordance with the observations of Schilder[11] and Bender and Schilder (Am. J. Psychiat. **10**:365, 1930) on the pain reactions of hysterical and catatonic patients.

17. Designed and constructed by Walter C. Shipley, who assisted in this experiment.

18. Anrep, G. V.: The Irradiation of Conditioned Reflexes, Proc. Roy. Soc. London, s. B. **94**:404, 1923.

Experiment 3.—Although there was no irradiation from one part of the body to another within the same sense modality, it seemed possible that there might be an irradiation from one sense modality to another within the same part of the body. In order to test this hypothesis, a sharp rap with a pencil was used as the conditioned stimulus, the pressure sense being normal in the otherwise anesthetic hand.

The conditioned response appeared after one reenforcement on the left hand and remained strong through ten trials. On the twelfth reenforcement the cotton stimulus was substituted for the pencil rap and evoked a similarly strong response. The cotton was repeated, but no reaction occurred. Six further reenforcements were given to the pencil rap stimulus and again the cotton was interspersed in the series. The result was the same positive response as before. Another series of six reenforcements of the pencil rap was given, and a third time the cotton was presented. Reactions this time appeared to two successive stimulations before extinction of the response.

Experiment 4.—Forty-eight hours later the patient was brought to the laboratory and tested for retention of the conditioned response to the tap of the pencil and the cotton. Both responses had suffered spontaneous extinction. After one reenforcement, however, the response to the cotton stimulus reappeared.

The patient was asked why she withdrew her hand before receiving a shock. She replied that she "didn't know" and, to questioning, denied that she felt the cotton on this day or at the session two days previously. The two succeeding stimuli were not felt and failed to evoke reactions, but the third evoked not only a finger withdrawal but an exclamation of surprise. The patient reported that she had felt the cotton. Twenty further stimulations were given, and fifteen of these were felt by the patient and reacted to by withdrawal of the hand. The cotton stimulus had become frankly sensible to her and thereafter served as an easily perceptible warning signal. It is worthy of note that the anesthesia disappeared completely at this time and that there was no evidence of its return six months later.

In conclusion, it may be said that although neither simple reenforcement nor the ordinary process of irradiation (within the same sense, but from one anatomic area to another) was adequate to develop a conditioned response to a stimulus affecting a functionally anesthetic sense modality, irradiation from a normal sense to the anesthetic sense within the same anatomic area was shown to be a usable mechanism. This conclusion is valid, however, only on the supposition that the pencil rap actually affected the deep pressure sense and did not bring about its conditioned response simply by supraliminal stimulation of the superficial touch sense. This possibility must not be ignored; the problem is one which can be settled only by further experiment.

SUMMARY

1. Hysterical analgesia modifies the normal reaction to pain in much the same way as hypnotic anesthesia if the reduced respiratory response to pain found in these two conditions be accepted as the criterion.

2. Hysterical astereognosis presents a concomitant heightening of the two point threshold; spontaneous recovery of the astereognosis is

concomitant with a return to the normal two point discrimination threshold.

3. A conditioned response to a stimulus affecting an hysterically anesthetic sense modality can be established by utilizing the principle of irradiation from one sense modality (normal) to another (anesthetic) within the same area of the body, but cannot be established either by simple reenforcement or by irradiation within the same sense modality from one part of the body (normal) to another part (anesthetic).

With the modern development of psychologic and physiologic methods, a few of which are illustrated, the subjection of the physical manifestations of functional nervous disease to rigorously controlled investigation and measurement becomes feasible. The value of such study lies not only in the clinical realm but in the information it may give to an understanding of certain principles of endogenic control of nervous activity. Hysterical reactions may be considered as limiting cases of the action of these principles and, as such, should provide valuable laboratory material for their discovery and examination.

ELECTRIC ACTION POTENTIALS IN MUSCLES DURING RECORDING OF MECHANICAL TONUS TRACINGS

J. CHARNLEY McKINLEY, M.D., PH.D.
AND
NATHANIEL J. BERKWITZ, M.D., PH.D.
MINNEAPOLIS

In our former attempts to obtain a measure of human muscle tonus in quantitative terms,[1] we found that the resistance of apparently resting muscles to stretching forces was extremely variable from time to time in many of the persons tested. This variability occurred in numerous subjects in whom no reasonable doubt could be entertained as to their desire to cooperate in releasing their muscles from conscious control during the testing. We deduced, therefore, that mechanisms other than simple tissue elasticity or relatively unvarying innervations of muscles were often at play. One's thoughts naturally turn to the possibility of demonstrating the presence of voluntary or reflex activities in muscles being stretched in a search for an explanation of these fluctuations. Few comments are required to dispose of the literature as far as pertinence to our present problem is concerned.

Wertheim Salomonson [2] has made the following statement:

> We may observe strong muscle spasms and also notable changes of the muscle tension without any electric action current. All changes in muscle tonus occur in this way and do not seem to cause any change in the electric state of the muscle. If the triceps brachii be connected to the galvanometer terminals and the arms passively extended or bent, the string does not move, yet the passive movement of extension is accompanied by a shortening of the muscle, the tonus contraction. Similarly, a tonus-relaxation does not act upon the string.

From the Division of Nervous and Mental Diseases, University of Minnesota Medical School.

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, Atlantic City, June 6, 1932.

1. McKinley, J. C., and Berkwitz, N. J.: Quantitative Studies on Human Muscle Tonus: I. Description of Methods, Arch. Neurol. & Psychiat. **19**:1036 (June) 1928. Berkwitz, N. J.: Quantitative Studies on Human Muscle Tonus: II. An Analysis of Eighty-Two Normal and Pathological Cases, Arch. Neurol. & Psychiat. **28**:603 (Sept.) 1932.

2. Salomonson, J. K. A. W.: Tonus and the Reflexes, Brain **43**:369, 1920.

Wachholder [3] and Wachholder and Altenburger [4] have studied in some detail the presence of action currents in muscles undergoing passive movement. Wachholder stated that under certain conditions (exclusion of gravity, the attempt psychically to relax as completely as possible, sufficient time, a moderate arc of movement of the joint) it is possible for one to adapt oneself to passive motions so that each position given to the joint can be maintained without the presence of action currents in the muscles. He stated that not every one can make such an adaptation without action currents. He presented some figures during passive motion of the wrist joint with needle electrode leads from the proper agonistic and antagonistic muscles which show no action currents whatsoever during the movement. Wachholder and Altenburger are the only investigators whose reports we have encountered who have approached the problem in such a way as to isolate the action currents from individual muscles. Other writers have reported the use of surface electrodes, usually in such fashion that they have been obtaining the composite action currents from both groups of muscles, agonists and antagonists. According to Weigeldt,[5] who studied the action currents in cases of rigidity (encephalitis, Wilson's disease, hemiplegia), there were times during which the rigidity was sufficient to support an extremity against gravity, and yet during which it was not possible for him to demonstrate the presence of action currents. He concluded that muscle tonus is certainly not to be considered as due to a uniform mechanism either clinically or electromyographically and believed that the muscle of warm-blooded animals can be entirely without action currents even in the case of increased tonus and even during tonic rigidity. He did not imply that action currents are always absent in such muscles. Hansen and Hoffman [6] and Preisendörfer [7] have busied themselves with studies of the action currents of the proprioceptive reflexes, but their studies had to do with stimulation by such means as percussion hammer strokes and vibrating rods, so that, important as these observations undoubtedly are, the type of stimulation used and the skin electrode method of detection of action currents without separation of the opposing muscles cause their work to have only indirect bearing on the present study.

3. Wachholder, K.: Willkürliche Haltung und Bewegung insbesondere im Lichte elektrophysiologischer Untersuchungen, Munich, J. F. Bergmann, 1928.

4. Wachholder, K., and Altenburger, H.: Haben unsere Glieder nur eine Ruhelage? Arch. f. d. ges. Physiol. **215**:627, 1927.

5. Weigeldt, W.: Elektromyographische Untersuchungen über den Muskeltonus, Deutsche Ztschr. f. Nervenh. **74**:129, 1922.

6. Hansen, K., and Hoffman, P.: Die Bedeutung der Sehnenreflexe für die Erhaltung einer Gelenkstellung, Ztschr. f. Biol. **71**:99, 1920.

7. Preisendörfer, F.: Versuche über die Anpassung der willkürlichen Innervation an die Bewegung, Ztschr. f. Biol. **70**:505, 1920.

With the foregoing comments in mind, we believe that further objective data on the action potentials in muscles during the recording of tonus tracings in human beings may throw additional light on the mechanism of muscle tonus. At least it will show graphically some of the variations of muscle contraction that may prove to exist during the application of stretch to muscles. In order to avoid confusion, it should be understood that in this paper we are using the word "tonus" in the ordinary clinical sense, namely, the sum of the resistances and pulls about a joint in an intact person which aid or hinder a passive movement at a time when the musculature of the joint is apparently resting or relaxed.

MATERIAL, METHODS AND CRUDE DATA

The details of construction of the apparatus used in this study are being reported separately by Hathaway and McKinley.[8] As stated in their paper, the apparatus consists essentially of a Westinghouse six element type oscillograph fitted with a mechanical device for recording photographically extension or flexion of the forearm on the elbow, a timing device and two supersensitive oscillographic galvanometers. Each galvanometer is connected to the output of its respective three-stage resistance-coupled amplifier. Amplification is adjusted so that at a frequency of 100 cycles per second an input of 200 microvolts from a low frequency oscillator produces a deflection of 1 cm. on the photographic film for each galvanometer unit. One needle with its active and grounded electrodes is plunged into the middle of the long head of the biceps brachii, local anesthesia having first been produced by the use of the ethyl chloride spray; the other needle, into the distal third of the long head of the triceps brachii just proximal to the tendon. The forearm is placed on the arm rest, which rotates horizontally, with the axis of the elbow in line with the axis of the machine. The needles are prevented from slipping out by adhesive tape over the wire from the active electrode, and the electrodes are attached to their respective amplifier-galvanometer units.

Muscle tonus tracings are recorded, following essentially the technic described by us in an earlier paper,[1] except that here the records are made on the photographic film instead of on kymograph paper. Muscle action potentials are thus detected simultaneously with the movement of the forearm. Passive movement of the forearm is obtained by turning the arm rest in or out by means of weights and suitable pulleys. The subject knows neither the amount of weight to be applied nor the direction in which his forearm is turned until the mechanism is tipped so as to release the weight. The reader is referred to our former paper and to that of Hathaway and McKinley for a more detailed understanding of our technic.

The material studied consisted of fourteen persons from the staff and student body at the University of Minnesota. The age range was from 17 to 40. Persons of both sexes were tested. The accompanying figures illustrate the major points of interest that were observed during the studies.

Each illustration represents tracings from a single person studied. Figures 5 and 6 are from the same person. All the experiments were performed on the right elbow. The figures all read from left to right. At the beginning of each tracing

8. Hathaway, S. R., and McKinley, J. C.: Article in preparation on the multi-element oscillograph with amplification for use in physiologic experiments.

the upper line represents the biceps lead and the next lower line the triceps lead; immediately below that is time marked off in quarter seconds, and the lowest line represents the mechanical movement of the forearm. The time marker indicates half seconds with almost absolute accuracy; quarter seconds, however, with an appreciable error. Deflection of the lowest line upward signifies movement of the elbow in extension; deflection downward, movement in flexion. The amount of weight hung on the apparatus in order to make a given movement as shown in the figures is indicated at the beginning of each mechanical tracing.

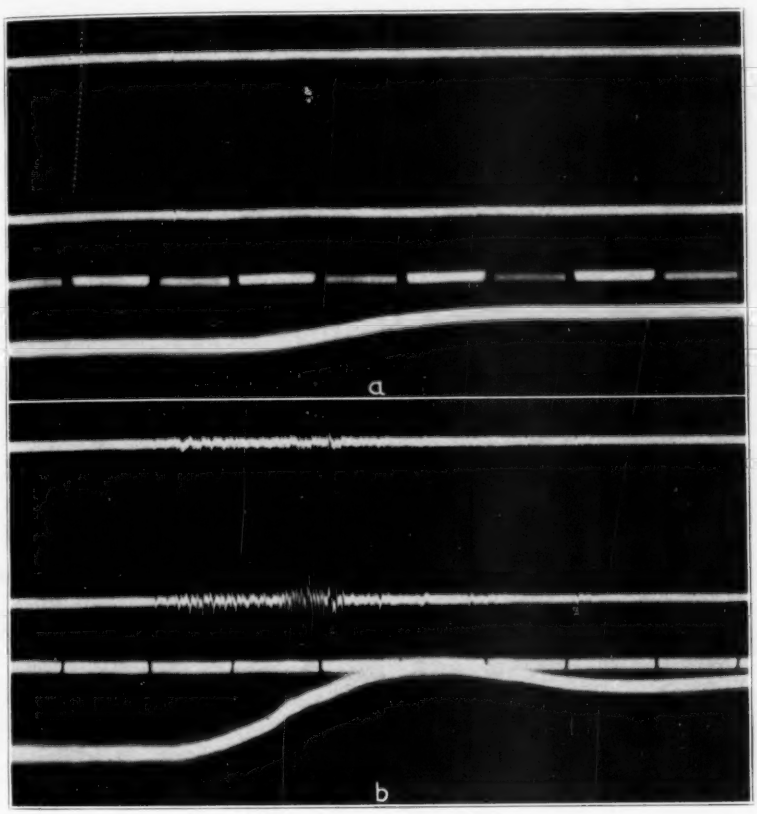

Fig. 1.—Tracings from a psychologist, aged 34.

The tracing shown in figure 1 was obtained from a psychologist, 34 years of age, a man who has had years of training in psychologic experiments. In figure 1*a* his forearm was moved into extension 14.4 degrees from the resting point by a weight of 500 Gm. hung on the apparatus. One can see that the galvanometers recording the action potentials from the biceps and triceps remain practically steady throughout the experiments. The very slight unrest may be due to action currents, but more likely is extraneous in origin. Very few curves of this type have been obtained from persons whom we have tested. It is interesting to note that the subject who gave the most constant tonus readings in our previous work during the present work produced curves regularly free from action currents. She

is one of the persons whom one infrequently encounters who is really able to relax. Figure 1*b* likewise shows an extension on this same psychologist, excepting that his forearm was extended by a weight of 1,000 Gm. The forearm turned outward 45 degrees. Almost simultaneously with the release of the weight, action currents begin to appear, particularly in the triceps but also in the biceps. By the time the forearm has moved about half of its excursion, the triceps developed rather lively action currents, as judged by amplitude and frequency. This corresponds with the fact that the forearm has turned out with double the weight, not twice 14.4 degrees, which would be 28.8, but almost four times as far as one would expect from a purely mechanical point of view. Rather obviously, the tetanus in the

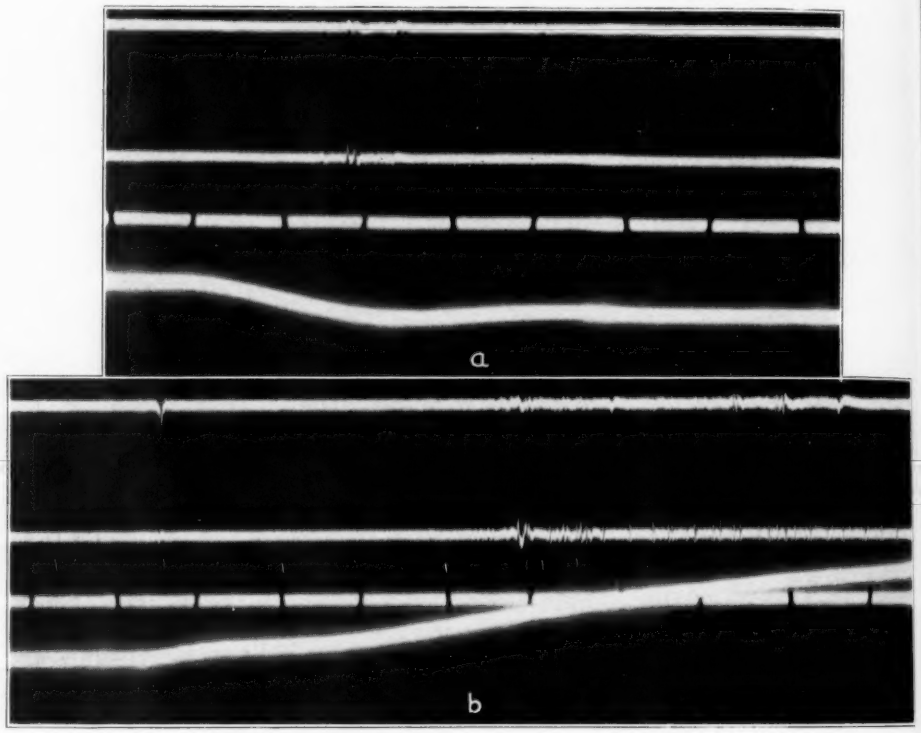

Fig. 2.—Tracings from a medical student, aged 23.

triceps has caused the forearm to extend farther than would be the case if no action currents had occurred. It may be noted that a certain synchronism of larger responses, at least at the beginning of the action potentials, appears to be present in the biceps and triceps. On the other hand, when the triceps curves reach a rather high amplitude, there is practically no synchronism visible in the biceps leads. When the motion is completed, the action currents practically disappear.

Figure 2 was obtained from a medical student, 23 years of age, whose muscular development is extraordinarily good. Figure 2*a* shows a flexion of the elbow through an arc of 14.4 degrees produced by a weight of 1,000 Gm. No action potentials make their appearance until the movement is nearly completed. At this

time only a slight unsteadiness of the galvanometer and two rather large impulses occur. The arm has behaved largely as though it were resisting the weight by elastic forces only. Tetanic contraction currents in this case do not appear to have interfered with the passive motion of the elbow. In figure *2b*, on the other hand, which is an extension through an arc of 49.2 degrees due to a weight of 500 Gm., the first portion of the motion has been accomplished almost without action currents, but the last half, as far as can be seen in this tracing, shows moderately active potentials throughout the whole time interval. The forearm has not stopped as usual after beginning to decelerate, but has reaccelerated to extend further than it probably would have moved had there been no activity in the muscle. Action currents have obviously occurred both in the biceps and in the triceps; the predominance is certainly in the triceps, though the frequency is not high. There is little correspondence of the currents in the one muscle with those in the other. The time interval during which the forearm is extended to the fullest degree, as shown on the tracing, is at least two or three times longer than would be the case had this arm been resisting by elasticity alone (compare with fig. 1*a*). At the beginning of the movement of the forearm an isolated, fairly strong action potential has developed in the biceps, and in correspondence with this the forearm has decelerated for a short time.

Figure 3 was taken from a member of the psychology staff of the University of Minnesota, a man, 39 years of age. As in the case of the other psychologist, this man has had long training in psychologic technic. One would think that he could relax his muscles more cooperatively than is the case with average persons. Figure *3a* shows a flexion of the elbow through an arc of 25.8 degrees in response to a weight of 500 Gm. In this case, very slight unsteadiness of the biceps galvanometer is noted, while the triceps galvanometer shows moderate unsteadiness during the last third of the movement of the forearm. Both before and after the movement there is no evidence of action potentials. In figure *3b* the forearm moved with a 500 Gm. weight through 6.8 degrees of extension. During the movement a few potential waves are seen in both biceps and triceps tracings. They appear to be absolutely synchronous. This synchronism is not easily explainable on physiologic grounds, as far as we can determine. Figure *3c* is particularly interesting in comparison with figures *3a* and *3b*. In this case the forearm was passively extended by a weight of 1,000 Gm. Here, too, as in the case of figure 1*b*, the forearm has passed through an arc which is much greater than one would expect from the measurements made of the angle in figure *3a*. That is, instead of passing through an angle twice 25.8 degrees, it actually goes about four times as far, namely, 103.6 degrees. In this case, after the first fifth of the motion has been completed, lively action currents appear, first in the biceps and then in the triceps. Even after the arm has come to rest, very active potentials are developed in both muscles.

The subject from whom the tracings in figure 4 were made was an intern, 24 years of age. This man was obviously the least able to relax of any of our subjects. It seemed impossible for him to let his muscles go so that there would be little or no voluntary interference when his forearm was being passively moved. Figure *4a* shows 51.8 degrees flexion of the elbow due to the release of a weight of 500 Gm. Even before the movement started, it is obvious that this man had a small number of action currents in his triceps muscles. Shortly after the movement was initiated volleys of impulses developed both in the biceps and in the triceps. After the movement was completed, however, he seemed to be relatively at rest. In figure *4b* his arm was moved 80.2 degrees in extension by a weight of 500 Gm. Immediately on initiation of the movement, action potentials appeared, predominantly in the triceps, but likewise, and with synchronism, in the biceps.

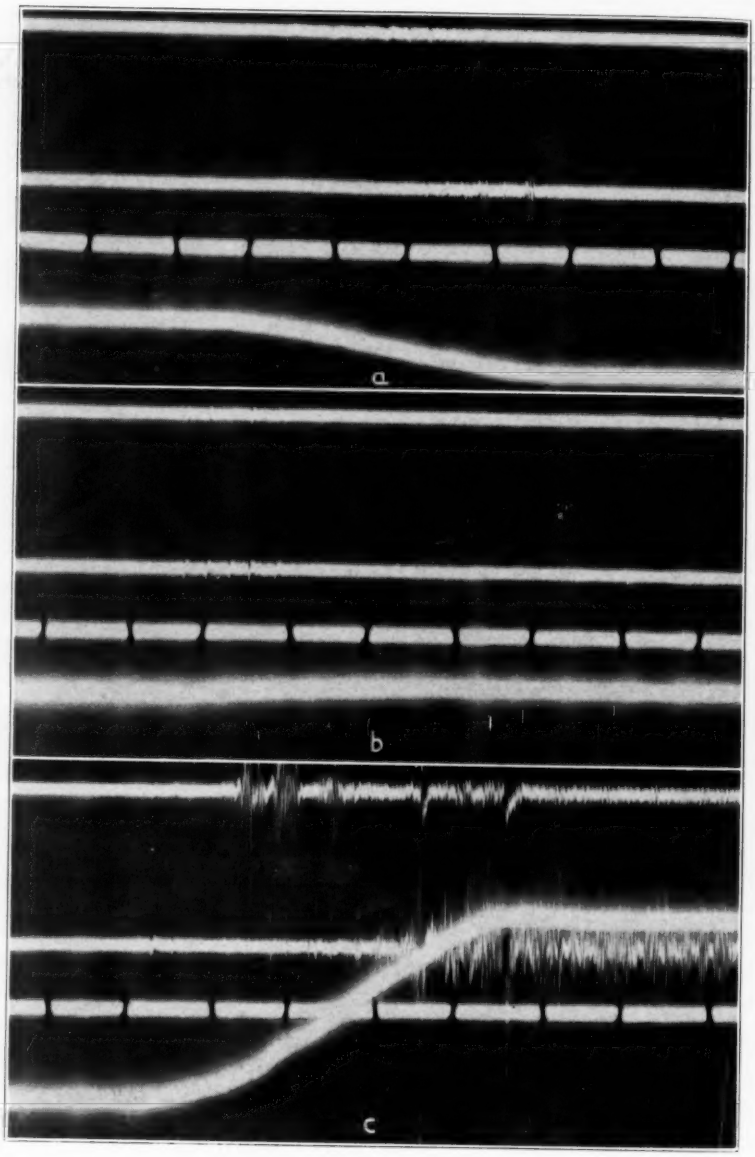

Fig. 3.—Tracings from a psychologist, aged 39.

About a third of the way through the movement he began to have very active potentials in the triceps and less active ones in the biceps. Synchronism is not nearly so apparent from this point on. After the motion had come nearly to rest, the muscles were still contracting tetanically, and it can be seen that the arm began to extend still further after a period when it seems that it should have come to rest. It is likewise obvious in this curve that the movement was relatively slow, at least two and one-quarter seconds being consumed before it came to completion.

Figure 5 was obtained from one of the teaching staff in nervous and mental diseases. He is a man, 33 years of age. He is well muscled, but not of the

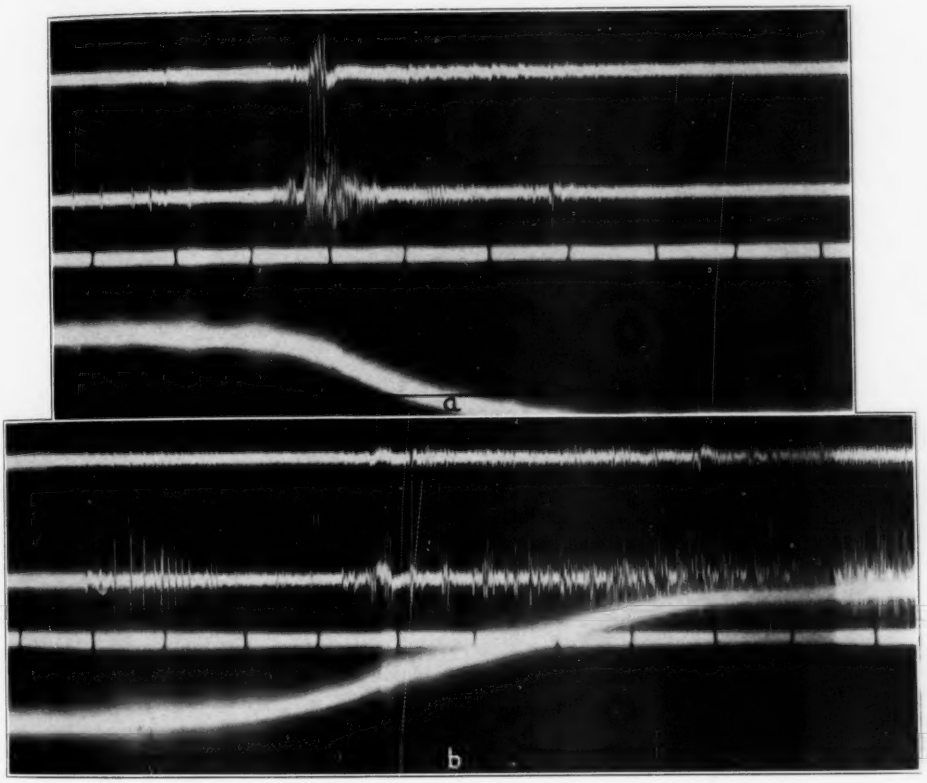

Fig. 4.—Tracings from an intern, aged 24.

extremely athletic type. Figures 5*a* and *b* are rather difficult to interpret. In both cases the arm was moved into extension by a weight of 500 Gm. through an arc of 24.5 degrees. In figure 5*a* it is obvious that very active potentials were present in the biceps during the last quarter of the movement of the forearm and continued until after the elastic swing-back had been completed. In 5*b* there are only a few twitches in the biceps. In neither case are there appreciable action potentials in the triceps. The discrepancy existing between the tracings shown in figures 5*a* and 5*b* prompted another set of observations. Electrodes were placed in the triceps of this same subject so that one pair was inserted into the triceps approximately half way between the shoulder and the elbow joints. Another pair of electrodes

was placed 5.3 cm. distally and laterally to the first pair. We thus had simultaneous leads from different parts of the same muscle in taking our tonus tracings. Some of the results of this experiment are shown in figure 6. In figure 6*a*, with the

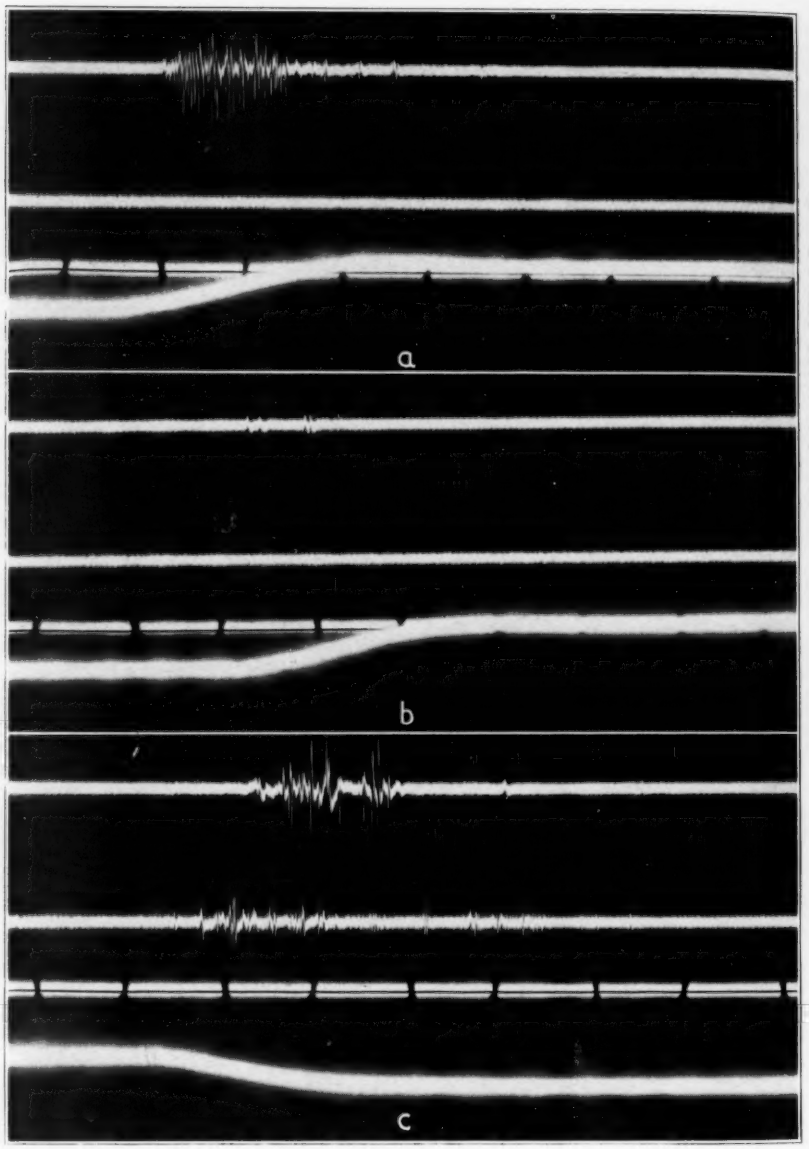

Fig. 5.—Tracings from an instructor in nervous and mental diseases, aged 33.

electrodes in place as described, the arm was passively moved into flexion by a weight of 500 Gm. It is seen that action potentials develop in both electrodes but that the frequency is different in the two and no synchronism is observable in the

occurrence of the two sets. (In the first portion of figure 6*a* two tracings were accidentally superimposed for a short distance which shows in the timing and in the mechanical recorder lines.) Figure 6*b* shows a similar experiment except that

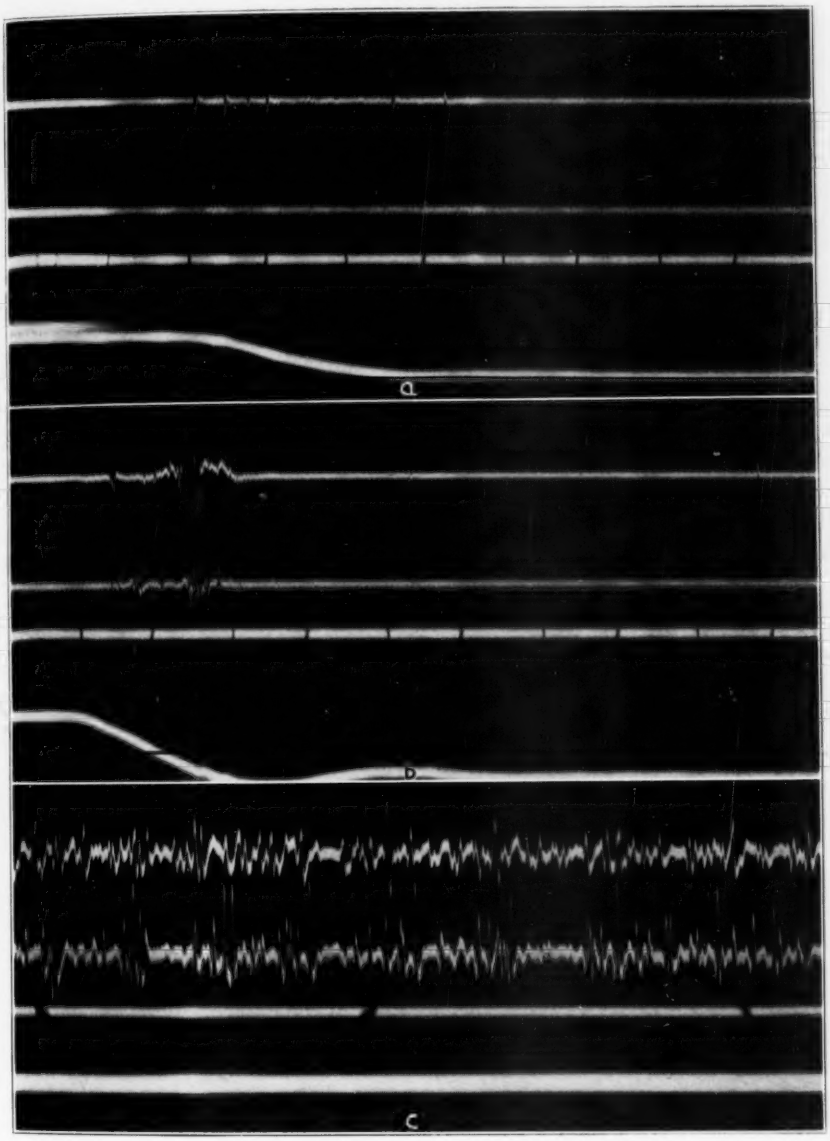

Fig. 6.—Tracings from the same subject as in figure 5.

the arm is thrown into flexion by means of a weight of 1,000 Gm. Again there is no correspondence of the individual potentials developed, but a large series of discharges occurs almost at the same time in the two parts of the muscle. Small

action potentials occur in the proximal electrodes during the elastic swing-back of the muscle and are practically absent in the distal electrode during this same period. As a further check, the experiment which is illustrated by figure 6*c* was performed. With the same electrodes in the triceps, the subject was directed to press lightly in extension against the finger of one of the examiners. The film was speeded up so that it had a velocity of 33 cm. per second. Simple inspection of this tracing (fig. 6*c*) shows that there is no correspondence of action currents, either large or small, in the two parts of the muscle. Figure 6 merely demonstrates what has already been discussed by others;[9] namely, that an electromyogram cannot portray in any complete sense the activities that may be going on in any muscle made up of a composite of many muscle fibers. Wachholder and Altenburger stated that multiple leads from a single muscle always show the whole muscle in contraction (except the biceps brachii). This may well hold for larger volleys, but figure 6 shows that this is not wholly true for smaller ones. It may well be, therefore, that the muscle can be in slight activity without detection by leads such as we used. This would explain such a discrepancy as we have just discussed.

Figure 5*c* portrays the condition when the forearm is passively flexed with a weight of 500 Gm. It passed through an angle of 13.6 degrees. Immediately on the beginning of movement, action currents appeared in the triceps, became more marked and then died away on completion of the movement. In the biceps, after about half the movement had been completed, very lively action potentials appeared.

COMMENT

A description, point by point, like the foregoing, is necessary for an understanding of the tracings, but gives no easily grasped insight into their possible significance. The following two classifications of the data are therefore presented, though we are aware of the possibility of serious disagreement existing between our interpretation of such terms as "minimal," "moderate" and "marked" action potentials, and the interpretation of others who might be interested enough to scrutinize the tracings in some detail. The classifications are presented by figure number, for convenience of comparison with the tracings, but it should be remembered that each of the figures numbered 1 to 5 refers to an individual subject. Thus we can write figure 5*a*, 5*b* and 5*c*, and yet it is clear that we are referring to a single subject by each of these designations.

Let us first assemble the data according to the preponderance of location of the action potentials in one or the other muscle, during and after the movement, so as to estimate whether or not the tetanic contractions so detected are:

1. Absent or minimal in both muscles (ordinary reflex or voluntary mechanisms excluded). This result is shown in figures 1*a*, 2*a* (1,000 Gm.), 3*a*, 3*b* and 5*b*.

---

9. Fulton, J. F.: Muscular Contraction and the Reflex Control of Movement, Baltimore, Williams & Wilkins Company, 1926, chap. 19, p. 474.

2. Moderate to marked in the muscle being stretched, and minimal or absent in the muscle being passively relaxed (the usual concept of the myotatic or proprioceptive reflex). This result is shown in figure 5*a*. Figure 4*a* may also belong here.

3. Moderate to marked in the muscle being relaxed, and minimal or absent in the muscle being stretched (complicated mechanisms at play). This result is shown in figure 1*b* (1,000 Gm.), 2*b* (resulting change in the mechanical curve is apparent) and 4*c* (resulting change in the mechanical curve also apparent). Figure 5*c* may also belong here.

4. Moderate to marked action potentials in both muscles (complicated mechanisms at play). This result is shown in figures 3*c* (1,000 Gm.), 4*a* (probably preponderant in the muscle being stretched) and 5*c* (probably preponderant in the muscle being relaxed).

This grouping has served only to complicate matters. It may be that only the first part of the tonus curves will show any uniformity of behavior of the muscles around a joint during passive motion. Leaving aside the cases in which minimal or no action currents appeared in either muscle, let us locate the initial preponderant action potentials after the passive motion has started:

1. Initial action currents more marked in the muscle being stretched. This is shown in figures 2*a* (1,000 Gm., interpretation questionable), 2*b*, 3*c* (1,000 Gm.), 4*a* (action currents are present preceding the motion in this case), 5*a* and 5*c*.

2. Initial action currents more marked in the muscle being relaxed. This is shown in figures 1*b* and 4*b*.

It is apparent from the two groupings of our data that no uniformity of behavior of the muscles has occurred in our series of tonus tracings. There is a tendency for the initial action potentials during the passive motion to be located in the muscle being stretched, but the two exceptions in our small series of measurements seriously vitiate any conclusions which one might hazard on this point.

As far as orderly conclusions are concerned, from a study of normal persons, we are forced to the position that muscle tonus, as it is usually tested clinically, is obviously a very complicated mechanism neurally, and therefore mechanically. One may be permitted some speculation as to what some of the mechanisms of resistance are in a stretched muscle in an intact animal or human being. In the first place, the elasticity of the muscle offers a resistance to stretch. This has been demonstrated in rabbits by McKinley and Wachholder,[10] and has been

10. McKinley, J. C., and Wachholder, K.: Ueber das sogenannte Bremsungsphänomen in Muskeldehnungskurven, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**: 24, 1929.

demonstrated by Wachholder and Altenburger by means of curves similar to some of ours (fig. 6*b*, for example), in which there is an elastic rebound at the end of the tonus tracing without action currents in the muscle being stretched. The curves in which no action potentials are developed may be interpreted as resisting by elasticity alone. But Weigeldt's demonstration of varying resistance in muscles in pathologic states, without the presence of action currents, makes one cautious even on this point. The proprioceptive reflexes have received a large share of attention in discussions on the behavior of the muscle. Such reflexes cannot be used to explain all of our results, because in two of the tracings during the passive motion the first action potentials appeared in the muscle undergoing relaxation during the movement (figures 1*b* and 4*b*) rather than in the muscle being stretched. In several other tracings the initial action potentials were in the muscle undergoing stretch, so that in these cases one could make a partial explanation of tonus resistance on the basis of the myotatic reflex. Even in these cases there are several examples in which, immediately after the "myotatic reflex," action potentials appear likewise in the relaxing muscle.

The rôle of voluntary or higher reflex mechanisms in producing fluctuations in muscle tonus, therefore, cannot be discarded. Voluntary holding or relaxation, in any ordinary sense of the term, seems to us not to be a very large factor. There is every reason to believe that each subject in our series attempted to let the muscles be relaxed most cooperatively during the experiments. Relaxation with the arm at rest was readily attained in practically every experiment, but relaxation during the movement in the arm was evidently a matter not so much of volition as of the general physiologic make-up of the subject at the moment. A possible view is that the afferent impulses entering the nervous system during the movement tended to set up a series of reflexes. Volitional inhibition of this type of response, in an attempt to keep the arm relaxed, resulted in irregular nervous overflows and motor discharges which have been recorded by our oscillograph. It remains for future work to clarify this matter, if, indeed, it can be clarified.

CONCLUSIONS

The term muscle tonus is used in this paper in the following sense: the sum of the resistances and pulls about a joint in an intact subject which aid or hinder a passive movement at a time when the musculature of the joint is apparently resting or relaxed.

Muscle action potentials, detected synchronously with mechanical tonus measurements, show that only in certain of the tracings are the muscles not reacting tetanically.

These potentials may occur in the muscle group being relaxed, in the group being stretched or in both.

Neither simple muscle elasticity nor proprioceptive reflexes can be called on for a complete explanation of the findings. More likely, along with these mechanisms, more complicated neural set-ups, not necessarily volitional, are at play in producing the variabilities observed.

ABSTRACT OF DISCUSSION

DR. LEWIS J. POLLOCK, Chicago: Dr. McKinley and Dr. Berkwitz should be commended for their studies and for their sustained effort in attempting to determine some methods for the measurement of tonus, which is so poorly definable and deals with so many elements that it is no surprise to find that there is considerable difficulty in evaluating the factors necessary in its measurement. When we consider that it is exceedingly difficult to measure even the simple qualities of a completely denervated muscle in relation to the terms of its hardness, extensibility, plasticity, ductility, or viscosity, we can readily see why, if we add to these numerous neural mechanisms which cannot be isolated, the reasons for the absence, presence or dissonance of certain action currents may not readily be determined.

Not only are these neural mechanisms involved, but the attention of the individual and other mental factors dealing with the emotional reactions and feelings undoubtedly play a large part too in that combination of qualities, which we designate as tonus. For example, one may refer to the work of Paskind who, during laughter, found that there is a very marked diminution of the total work done in a muscle being stretched as measured by one of Dr. McKinley's apparatuses that records extension.

Another difficulty in evaluation of the measurement of tonus is in the time element, which is used in the extension of a passive muscle in that viscosity is related directly to the factor of time. Unless we obtain definite standards of the time necessary to extend a passive muscle, we will be dealing with different physical qualities in the muscle, and if rapidly extended will be producing tremendous internal friction that may give rise to some phenomenon difficult to explain clearly.

DR. H. DAVIS, Boston: I would like to point out from our personal experience at Harvard one or two features in the situation and set-up such as Dr. McKinley has used with such success in this case.

One is that, in using an electrode of this type, we have not been getting a record of the total activity of the whole muscle that is involved; it is merely a random sample of the activity of relatively a small number of the muscle units of which the muscle is composed. The presence or absence of action currents taken in this way will not correlate very accurately in our experience with the degree of tension which is exerted by the muscle at the moment. Very slight movements of the electrodes may bring in or get out of the range of action of actively contracting muscle fibers.

Another point that we have been led to suspect, although we cannot prove it definitely, is that movement of the needle in the muscle may serve in some cases to inhibit activity in that particular region; it is possible to stimulate muscle fibers mechanically if any movement of the electrode in the musculature is allowed.

I should, therefore, be interested to know what Dr. McKinley's experience has been in these connections, whether he has any further light to throw on these particular difficulties which surround the use of the action current technic in quantitative measurements of this sort.

I would add my appreciation of the work he is doing on the subject, and for the further light which I believe will be thrown by careful investigation in this direction on the tonic activity of muscles.

DR. J. F. FULTON, New Haven, Conn.: I greatly admire the approach that Dr. McKinley has made to the subject, and I share Dr. Davis' views as to interpretation; but I do feel that the term "tonus" is an unfortunate misnomer. At the session at Bern last year an entire morning was devoted to a consideration of the subject, and it seems to me that Professor Sherrington's summing up of the situation should be heeded: at the end of this long program of twenty-three papers, Professor Sherrington said very calmly that as a result of the discussion he felt that the word "tonus" should be abolished forever; and I share this view.

Dr. McKinley has pointed out that when muscles are stretched they show action currents in response to the stretch. The reflex response of a stretched muscle is well known. It plays an important part in the development of reflex posture, and my feeling is that we should speak in terms of known reflexes, stretch reflexes, and in this instance of their modification by higher levels of nervous activity, e. g., by labyrinthine reflexes, and dismiss this term which has caused so much mystification.

Dr. Pollock, for example, mentioned that qualities such as viscosity modify the picture. Viscosity does indeed modify the tension record, but it does not produce action currents, and I think in Dr. McKinley's experiments one should recognize that he is dealing with a well recognized reflex, i. e., the response to stretch, and that if we use the term "tonus" to describe these phenomena it introduces an element of mystery which is unfortunate. I would urge therefore that both in clinical and in physiological literature we avoid the use of this confusing term.

DR. MCKINLEY, in closing: In regard to Dr. Davis' remarks about our needle sampling only a small part of the muscle being recorded, that was really just the point of the last three tracings that we showed. As to the movements of electrodes producing action currents, no doubt that happens, and yet we have been able to place our electrodes in the muscles and then massage those muscles in rather lively fashion without any action potentials being developed whatsoever.

GLIOMAS ARISING FROM THE REGION OF THE CAUDA EQUINA

CLINICAL, SURGICAL AND HISTOLOGIC CONSIDERATIONS

JAMES W. KERNOHAN, M.D.

HENRY W. WOLTMAN, M.D.

AND

ALFRED W. ADSON, M.D.

ROCHESTER, MINN.

In a recent study,[1] we investigated the primary tumors of the spinal cord, paying particular attention to their histologic structure. Since the cellular elements of the spinal cord are similar to those of the brain, we found, as had been anticipated, that the types of tumors were analogous. The present study is an attempt to classify, histologically, gliomas occurring in the region of the cauda equina and also to consider their clinical manifestations and the surgical procedures instituted for their relief. We did not study any tumors arising from the extradural filum terminale, known as the coccygeal ligament, but only those found within the dural sheath and arising from the region of the cauda equina.

Most of the gliomas which occurred in the region of the cauda equina arose either from the conus medullaris or from the intradural filum terminale, although it is possible that some at least could have arisen from glial or ependymal heterotopic masses attached to the nerve fibers of the cauda equina. We shall consider most of them as having arisen from the conus medullaris or filum terminale.

The subdivision of the tumors into those arising from the conus medullaris and those arising from the filum terminale is not justified from the histologic point of view, or from the clinical data, but the operative procedure, as well as the results obtained, supports the theoretical division. Several of the tumors involved both the conus medullaris and the filum terminale, whereas others involved the filum terminale alone. Most of them had surrounded one or more nerve roots which in several cases had to be sacrificed in an endeavor to remove the tumor completely.

Read at the Fifty-Eighth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 6, 1932.

From the section on pathologic anatomy, neurology and neurologic surgery, the Mayo Clinic.

1. Kernohan, J. W.; Woltman, H. W., and Adson, A. W.: Intramedullary Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **25**:679 (April) 1931.

The development of the conus medullaris and the filum terminale is understood from such works as those of Streeter [2] (1919) and Kunitoma,[3] but it is difficult to find accurate histologic descriptions. The conus medullaris is the tapering, caudal end of the spinal medulla, containing in its lower portion the ventriculus terminalis. It has elements similar to those found in the spinal cord. The ventriculus terminalis is the boundary between the conus medullaris and the filum terminale. In our study of the conus medullaris, the same elements were present as in the spinal cord except that ganglion cells were less numerous and less well organized. Axis cylinders were also present but were less numerous than in the spinal cord, whereas there was a considerable diminution in the number of myelin sheaths. These rapidly diminished as the filum terminale was approached. The lower end of the central canal of the spinal cord dilates to form the ventriculus terminalis so that there is an excessive number of ependymal cells in this region of the central nervous system. There were some astrocytes present, but oligodendroglia cells were sparse. Numerous corpora amylacea were present, especially underneath the pia mater, where in places they had collected in large groups.

During a study of the ventriculus terminalis,[4] it was noted that ependymal cells extended from its lower end in small masses downward into the filum terminale. In a study of several fila terminalia and from the observations of Harmier [5] it is seen that the filum is not the rudiment that most authors suppose it to be. It is made up of all the elements that are present in the spinal cord. There were glia cells, especially astrocytes and some oligodendroglia cells, but no microglia cells were seen in any of the normal tissue examined. Ganglion cells were common, but none of these was normal. An excess of pigment granules was present in most cells. Nissl granules were fewer than is normal, and other signs of premature degeneration were noted. In addition to the ganglion cells present, there were many neuroblasts or immature forms of ganglion cells. These were in different stages of differentiation, and varied from rounded cells without processes to more mature forms. Many axis cylinders were also present, and myelin was demonstrated in considerable amounts in some cases and was almost absent in others. The most interesting histologic feature of the filum terminale was the masses of ependymal cells distributed throughout its entire length.

2. Streeter, G. L.: Factors Involved in the Formation of the Filum Terminale. Am. J. Anat. **25**:1 (Jan.) 1919.

3. Kunitoma, Kuane: The Development and Reduction of the Tail and of the Caudal End of the Spinal Cord. Contrib. Embryol. **8**:161, 1919.

4. Kernohan, J. W.: The Ventriculus Terminalis: Its Growth and Development, J. Comp. Neurol. **38**:107 (Dec.) 1924.

5. Harmier, J. W.: The Normal Histology of the Intradural Filum Terminale. Arch. Neurol. & Psychiat., this issue, p. 308.

These cells were not arranged in any definite manner, but formed irregular islands of cells with no characteristic cellular arrangement, sometimes as small tubules or cavities, but usually as clusters with no cavity and not demarcated from the surrounding tissue. Frequently the ependymal cells lining such cavities were ciliated. Another outstanding feature was the presence of numerous corpora amylacea. These were often collected in masses beneath the pial covering of the filum terminale; they were also scattered diffusely throughout the tissue. Blood vessels were not more prominent than in the spinal cord, and the central vein occupied a very small portion of the normal filum terminale when examined histologically.

CLINICAL CONSIDERATIONS

As in cases of tumors situated elsewhere in the spinal canal, pain was the initial complaint in more than 80 per cent of the cases (fig. 1). The behavior of the pain was such as to suggest the possibility of a tumor in twelve of the twenty-five cases; it suggested sciatic neuritis in four,

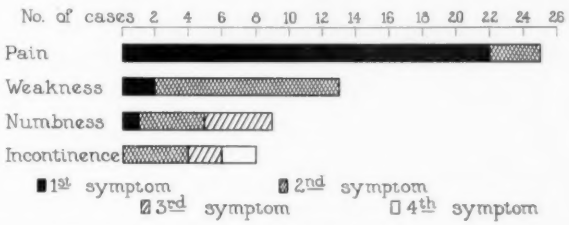

Fig. 1.—Incidence and sequence of onset of four cardinal symptoms in a series of twenty-five cases.

and was atypical for either a tumor or neuritis in eight. The pain was limited entirely to the spinal region in two cases; it was limited entirely to the sciatic distribution in two; it was in the back and in the sciatic distribution on one or both sides in twenty-one cases, and it presented the superficial appearance of bilateral sciatica in sixteen cases.

It will be seen that weakness was the initial disturbance in about 8 per cent of the cases. Sphincteric disorders, present in 32 per cent of the cases, were not the first complaint in any.

As one might anticipate from this group of symptoms, early diagnosis is often elusive and may be impossible. The history of the treatment these patients had received indicates this. Foci had been removed in ten cases; abdominal operations had been resorted to in three; sounds had been passed, a cast had been applied on the assumption of Pott's disease, and the coccyx had been removed in one case each.

The character of the objective findings is indicated in figure 2, which is self-explanatory. The only comments we wish to make with reference to this figure are that both the patellar and the achilles tendon reflexes

were normal in eight cases. The roentgenograms were helpful in making the diagnosis of tumor in seven cases. Camp and Adson [6] recently called attention to a more careful study of the pedicles, which are often eroded in cases of tumor. A study of the roentgenograms with this in mind will probably increase the helpfulness of this examination. The most diagnostic data were obtained on spinal puncture; the fluid removed was yellow in eighteen cases, and the needle entered the tumor in eight. Naturally the question arises as to how many cases in which spinal

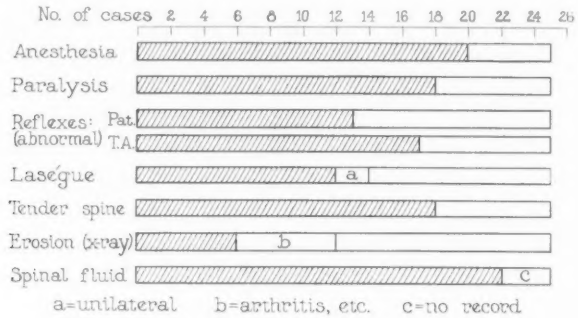

Fig. 2.—Principal objective observations in twenty-five cases.

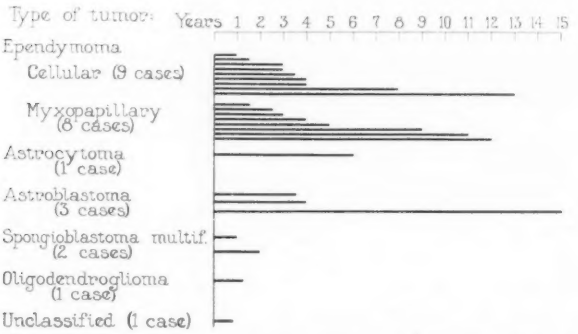

Fig. 3.—Frequency and duration of twenty-five gliomas arising in the caudal region. Various types are shown.

puncture was not done we have diagnosed wrongly as instances of sciatic neuritis when spinal puncture would have led us to make a diagnosis of tumor. We know that this was so in at least two cases. Perhaps a spinal puncture should be done as part of the general examination in more cases in which we suspect sciatic neuritis; however, one dislikes to institute such an arbitrary procedure in every case. Roentgenologically, opaque oils were of no diagnostic value in this particular group.

6. Camp, J. D., and Adson, A. W.: Roentgenologic Findings Associated with Tumors in the Spinal Canal, Proc. Staff Meet., Mayo Clin. **6**:726 (Dec. 9) 1931.

The relationship between the duration of symptoms before operation and the type of tumor found is interesting, but the series is too small for any definite conclusions to be drawn (fig. 3). The longest duration in any case in this series was fifteen years; this was a case of astroblastoma. The average duration of symptoms in this group of three cases, however, was seven and a half years. A larger series of cases probably would lower this average considerably. There was one case of astrocytoma which lasted six years. Of the ependymal tumors, the average duration of the myxopapillary type was six years and of the cellular type four and six-tenths years. The average duration before operation in the entire group was four and eight-tenths years. This corresponds closely with the duration in a group of intramedullary tumors, mostly gliomas, previously studied, which was four and nine-tenths years.

It is impossible in many instances to determine whether a given tumor originated in the conus medullaris and extended downward into the caudal region, or whether it originated in the filum terminale and extended upward to invade the conus. In any event, the cases in which the conus was invaded, those in which a tongue of tumor overlay the conus and those in which the growth was exclusively in the caudal region were similar as to symptoms, kind of tumor and duration; that is, a preoperative differentiation, while of interest, was often wrong.

A number of cases with unusual clinical features will be mentioned briefly. In one case, after a prodromal period of pain, there was an apoplectiform onset of weakness, numbness and incontinence; at operation a large cyst was found in the conus medullaris, possibly the result of hemorrhage; the tumor was situated below the tip of the conus. Another patient, aged 61, had had bilateral pes cavus since childhood. The Wassermann reaction of the spinal fluid was strongly positive in one case. Another patient had severe diabetes. Six patients gave a history of injury to the lumbar portion of the spine, usually the result of falls shortly preceding or coincident with the onset of the symptoms.

SURGICAL CONSIDERATIONS

Of this group of spinal tumors situated in the region of the cauda equina it was observed that eighteen arose from the filum terminale and that seven involved the conus medullaris and the filum terminale. The growth of the tumors extended in all directions but naturally followed the lines of least resistance, which explains the finger-like projections which extended upward over the lower portion of the cord and downward toward the sacral canal. Usually, these tumors originate from a single area in the filum terminale (fig. 4), but occasionally they appear to have originated in several areas and to have coalesced as the growth developed. They are soft in consistence, and are usually very vascular and capable of producing erosions of the

laminae, the pedicles and the bodies of the vertebrae. They produce a thinning of the meninges, but rarely break through them to invade the adjacent tissues, and we have never seen them invade nerve trunks. They grow between the roots of the cauda equina and extend along the roots into the intravertebral spaces, thus making extirpation tedious (fig. 5). The tumors are usually very large and extensive when the patients present themselves for surgical relief; many of them extend down from the eleventh dorsal vertebra to the sacrum.

In reviewing the results, it was observed that fifteen of the eighteen tumors of the filum terminale were completely removed and three were

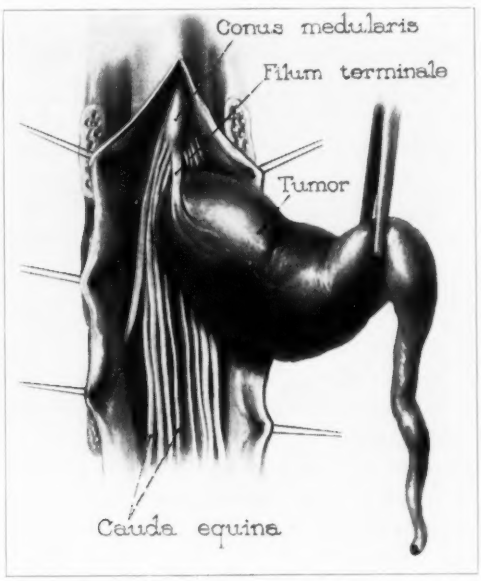

Fig. 4.—The tumor is partly removed with its attachment to the filum terminale below the conus medullaris. The nerve roots of the cauda equina are free from the neoplasm.

only partially removed. Recovery for periods up to thirteen years without recurrence has been obtained with the removal of the tumor and wide resection of the filum terminale. Only partial and temporary relief was obtained by partial resection, decompression and roentgenotherapy. The degree of recovery depends more on the compression of the conus medullaris than on pressure of the roots, since the symptoms from root pressure disappear satisfactorily on removal of the tumors. There was one postoperative death of a senile patient on the seventh day from coronary occlusion, and the three patients with partial removal of the tumor died at three and four year intervals following operation, presumably from pyelonephritis, except one patient in whom ependymoma of the medulla developed which caused death.

Complete resection of the tumors was done in one case and partial resections in six cases in which the lesion involved the conus medullaris and the filum terminale. The conus was resected as high as the lower border of the eleventh dorsal vertebra, which failed to include all of the tumor in six cases. Prolonged partial relief was obtained in two cases. These two patients recovered to the extent that they were able to carry on their regular vocations for three years. The remaining patients did not improve appreciably.

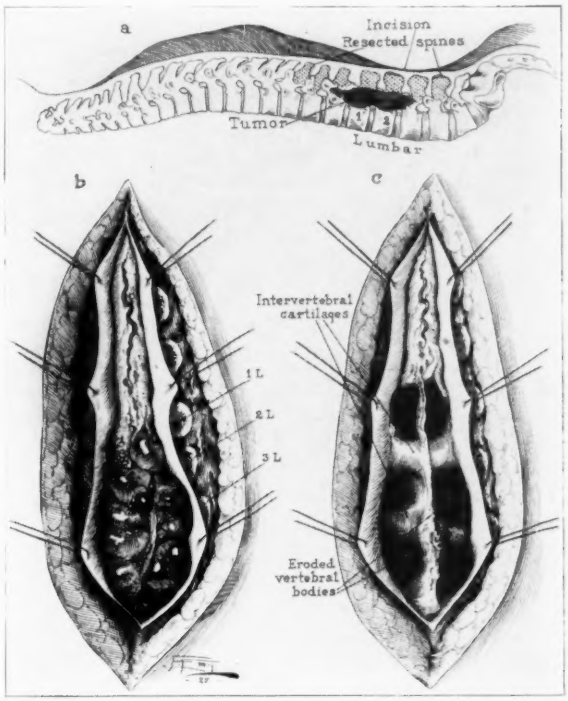

Fig. 5.—At the top is shown the level of the tumor in the lumbar region; at the left, the tumor filling the lower part of the dural sac and surrounding the conus medullaris above, and, at the right the erosion of the vertebral bodies after the tumor was removed. The nerve roots, etc., are not included, in order to give a clearer view of the vertebrae.

It is, therefore, apparent that early diagnosis is essential to effect complete removal of tumors of the filum terminale. Complete removal produces better results than partial resection, although the procedure is tedious and time-consuming and one must avoid too great a surgical shock, even though the surgeon is compelled to divide the operation into stages.

The resection of the conus medullaris containing the tumor is justifiable if there is a fair prospect of including all visible growth.

HISTOLOGIC CONSIDERATIONS

Since the elements found in the conus medullaris and the filum terminale are similar to those present in the spinal cord and brain, neoplasms arising from them should be similar, and this was found to be the case. Twenty-five neoplasms were available for histologic study. Seven of these arose from the conus medullaris, and the remaining eighteen arose from the filum terminale. Since the groups contain histologically similar types of neoplasms, they will be considered

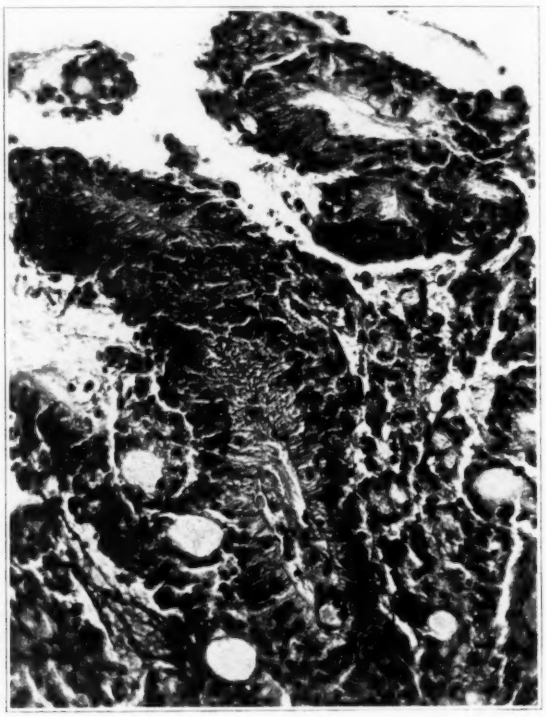

Fig. 6.—Ependymoma, showing the perivascular arrangement of the cells. The majority of this tumor belonged to the cellular type, but this area simulated a myxopapillary ependymoma. No mucus was present in this neoplasm. Mallory's phosphotungstic acid hematoxylin stain; × 100.

together. As in the primary tumors of the spinal cord, there were more ependymomas than any other type of neoplasm, which is in marked contrast to tumors of the brain among which, according to our experience and to that of Bailey and Cushing,[7] ependymomas are relatively

7. Bailey, Percival, and Cushing, Harvey: A Classification of the Tumors of the Glioma Group, Philadelphia, J. B. Lippincott Company, 1926.

uncommon. Ependymomas are common among the Mitteldorf tumors arising from the hollow of the sacrum. There were seventeen ependymomas in the region of the cauda equina, but only two types were demonstrated, in contrast to those arising from the spinal cord in which three definite types of cellular arrangement were present. However, it was unusual to encounter a growth in which the structure was limited to one type of cell arrangement. Nine of the neoplasms examined were characterized by a solid arrangement of the cells, and there was little attempt to form canals or tubules. Occasionally small canals were present, such as may be seen in a normal spinal cord during the process of obliteration of the central canal, in which numerous ependymal cells lay free in the adjacent tissue without assuming any characteristic arrangement. Some of the cells had a tendency to arrange themselves around blood vessels (fig. 6). When stained by differential methods, some of these cells were shown to have vascular processes such as may be seen in astroblastomas, and in the latter type of tumor they would be called astroblasts. There was an absence of the large multinucleated cells with excessive cytoplasm, which are so common in the astroblastomas, and the universal perivascular arrangement was not so abundant or so constant as in the latter tumors. The nuclei were oval; the cytoplasm was abundant and usually formed one and sometimes two heavy processes. One process often ended around a perivascular space, whereas the other, equally heavy, passed into the surrounding tissue where it tapered off gradually or ended with a frayed termination like a fish tail. The processes appeared to be fibrous rather than protoplasmic; yet neuroglial fibrillae were not demonstrable with Mallory's phosphotungstic acid hematoxylin stain. Occasionally a similar arrangement of the cells was noted, except that a blood vessel was not present in the center. The cells were arranged in a roset with the processes pointing toward the center, where they intermingled and terminated without any attachment to a blood vessel (fig. 7). Tubules were not present in the center of these rosets. Such a cellular arrangement has been termed *ballon*. In one case there was no tendency toward interlacing of the processes. Blepharoplasten were present in many of the cells, especially in those that participated in the formation of tubules, but there were no cilia. Mitotic figures were not seen in any of these neoplasms. There were tubules in most of this group of tumors, which was the one type of ependymoma with the major portion composed of a fairly uniform cellular arrangement. The blood vessels were well formed, and endothelial proliferation or hyperplasia was not present in the intima. Areas of necrosis and degeneration were not present, and there were no collections of mucus. In one tumor there were several tubules and several large cavities lined with ependymal cells simulating the arrangement of

the cells in tumors of the epithelial type, but the greater portion of the neoplasm belonged to the cellular type.

The group of tumors designated as myxopapillary ependymomas was most difficult to classify. This term has been adopted because these ependymomas in places have a tendency to grow in papillomatous formation, and the centers of the papillae contain mucus (fig. 8). In some ways the tumors of this group simulated neuro-epitheliomas, which have been claimed by Penfield [8] to be of ependymal origin. These tumors,

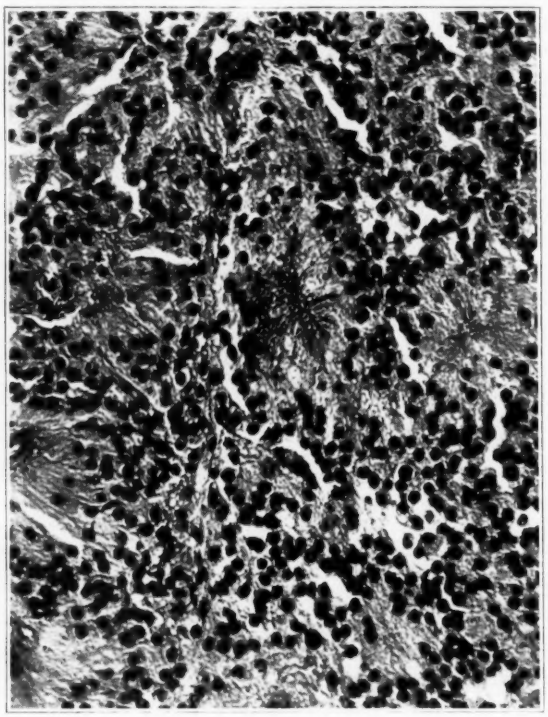

Fig. 7.—Cellular ependymoma, showing at the lower left margin the perivascular arrangement of some cells and fibrils. There are several examples of the *ballon* arrangement of the fibrils without blood vessels in the center. Hematoxylin and eosin; × 200.

like those of the cellular group, were not limited to one type of cellular arrangement, as some areas were cellular and groups of cells simulating supportive spongioblasts were present. The characteristic arrangement (fig. 8) simulates a portion of thyroid gland. The homogeneous colloid-

8. Penfield, Wilder: Principles of the Pathology of Neurosurgery, in Nelson: Loose-Leaf Living Surgery, New York, Thomas Nelson and Sons, 1927, vol. 2, chap. 6, p. 303.

like material in the acini stained specifically for mucus, some portions showing greater quantities than others. The cells were arranged around the walls of the acinus-like spaces, but were separated from the mucus by a basement membrane. The cells contained blepharoplasten, but cilia were rarely present. The amount of mucus varied in different parts of the tumor; some of the papillae contained only a slight amount, which seemed to arise from degeneration of the connective tissue stroma; consequently, it was not a secretion. In no case was it possible to dem-

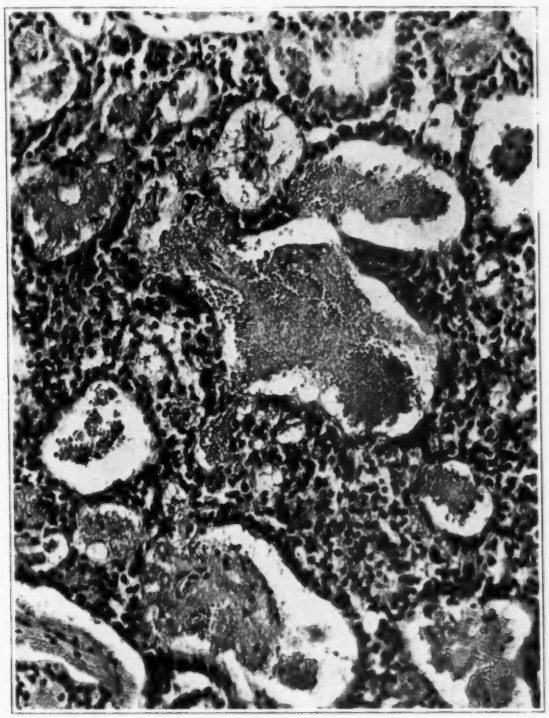

Fig. 8.—An example of the myxomatous appearance of part of a myxopapillary ependymoma. The cells are growing around the myxomatous stroma and are separated from it by a basement membrane. Hematoxylin and eosin; × 135.

onstrate mucus droplets in any of the neoplastic ependyma cells; this further supports the opinion that the mucus is the result of degeneration of the connective tissue stroma. The blood vessels were well formed, and proliferative changes of the lining endothelial cells were not visible. These tumors grew slowly, and mitotic figures were not present.

In the group of tumors arising from the conus medullaris and the filum terminale, no tumor of the epithelial type of ependymoma was present. Several of those belonging to the two types of ependymomas

already described contained areas in which the arrangement of cells simulated the epithelial ependymomas but the greater part of the tumor was typical of one of the other types, and as the dominant cell arrangement was used in classifying the tumor, they have been classified accordingly.

Only one neoplasm that belonged to the astrocytoma group of tumors was found in this series. It belonged to the protoplasmic type of astrocytoma, and, in spite of the fact that the patient had had symptoms for

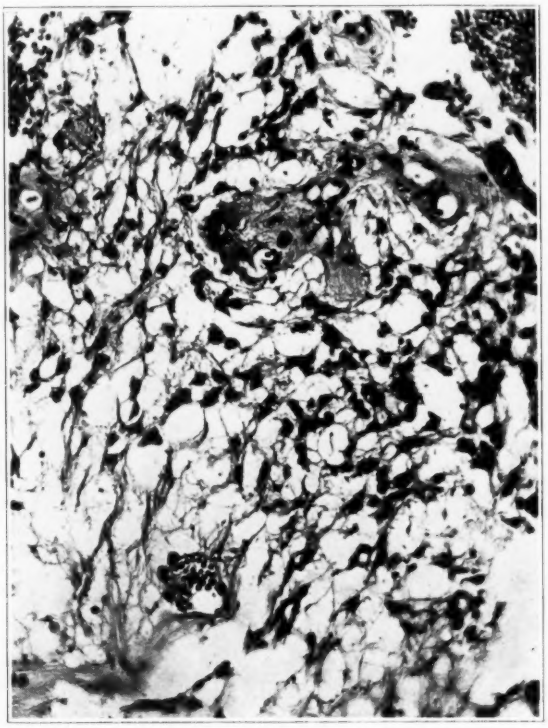

Fig. 9.—Astrocytoma with protoplasmic astrocytes dominating. The neoplasm has an edematous appearance. The numerous processes arising from the cell bodies can be seen with some attached to the perivascular space. Mallory's stains revealed very few neuroglial fibrils. Hematoxylin and eosin; × 225.

six years, the tumor was soft in consistence, simulating the more rapidly growing tumors. Histologically, it was characteristic of the protoplasmic astrocytomas (fig. 9). Many of the cells had perivascular processes and numerous long, tortuous, nonfibrous processes streaming off into the surrounding tissue. Some of the cells had fibrous processes, as demonstrated by Cajal's gold chloride and sublimate method and Mallory's phosphotungstic acid hematoxylin stain, but the majority were free from neuroglial fibrils. Occasional astroblasts were also present, but these

were few. The cells varied much in size and were larger than those seen in the fibrous type of astrocytoma of the spinal cord. In spite of its soft consistence, it was a comparatively acellular tumor, and there were many apparently empty spaces between the cells. The blood vessels were well formed with no endothelial hyperplasia, but some of the vessel walls were thickened, showing hyaline changes. Some areas of degeneration containing blood pigment which reacted to the iron stain were also present. Superimposed on this tumor there was a chronic

Fig. 10.—Astroblastoma with long vascular processes. The cell bodies are small, and lateral processes are rare. Binucleated cells were not present. Hematoxylin and eosin; × 200.

inflammatory process evidenced by the presence of a considerable number of lymphocytes. The patient gave a history of trauma to the lower portion of the back one year previously, and this had accentuated his symptoms. Probably the injury had caused a hemorrhage into the tumor, with subsequent degeneration and fibroplastic change and deposition of blood pigment. The tumor was well differentiated with no mitotic figures; although some fibrous astrocytes and a few astroblasts were present, the majority of the cells were protoplasmic astrocytes, and consequently the tumor was designated protoplasmic astrocytoma.

The three tumors designated as astroblastomas were characterized by perivascular processes (fig. 10). The cell bodies were no larger than those of astrocytes. Binucleated cells were not encountered. All these tumors simulated to a marked degree polar spongioblastomas, except that interlacing fibrils were uncommon and vascular processes were the rule. The cells differed from astroblasts found in astroblastomas of the brain, as most of the cells were bipolar with one process ending on a perivascular space and the other streaming off into the surrounding tissue. The latter stained with Mallory's phosphotungstic acid hematoxylin stain as a wirelike process, but fibrils could not be detected in the cell body or in the process, which was solid and rarely divided. Lateral processes from the cell bodies were uncommon. Little difficulty was encountered in distinguishing these tumors from cellular ependymomas, in spite of the fact that in the latter tumor there was a tendency to perivascular arrangement. Tubules were not present; the nuclei were smaller and more oval, and the processes did not have frayed terminations. Occasionally, more characteristic astroblasts and astrocytes were rendered visible by Cajal's gold chloride and sublimate impregnation method. The cell bodies were smaller than those seen in typical astroblastomas, but the body stained deeply with eosin, and the nuclei were eccentrically situated. The blood vessels were generally well formed with an absence of endothelial activity of the intima; yet occasional areas of degeneration were seen containing blood pigment which reacted for iron with the Turnbull blue stain. There was no excess of chromatin in the nuclei, and mitotic figures were not present in any of these tumors, which were essentially slowly growing neoplasms.

Considerable technical difficulty is encountered in proving conclusively that a tumor belongs to the group recognized as oligodendrogliomas. It is necessary to obtain the tissue fresh and to fix it in a formaldehyde-bromine solution. It is difficult to obtain satisfactory results even with normal brain tissue, and the difficulties are increased considerably when one is dealing with neoplasms. Certain criteria are laid down by Bailey and Bucy,[9] and it is on this basis that we classify the following tumor as an oligodendroglioma. It was a soft cellular mass, with little reticulum and thin-walled dilated blood vessels. Several types of cells were encountered. The majority of them when stained by routine methods had the appearance of typical, acutely swollen adult oligodendroglia cells described by Penfield and Cone.[10] In other areas

9. Bailey, Percival, and Bucy, P. C.: Oligodendrogliomas of the Brain, J. Path. & Bact. **32**:735, 1929.

10. Penfield, Wilder, and Cone, William: Acute Swelling of Oligodendroglia, Arch. Neurol. & Psychiat. **16**:131 (Aug.) 1926; The Acute Regressive Changes of Neuroglia (Ameboid Glia and Acute Swelling of Oligodendroglia), J. f. Psychol. u. Neurol. **34**:204 (Oct.) 1926.

the cytoplasm in the cells was stainable and not represented by a vacuole, and there was a gradation between these types of cells. The nuclei stained deeply with hematoxylin and were invariably round. In the vacuolated cells frequently more than one nucleus was encountered, but in those with stainable cytoplasm usually only one nucleus was visible. The tumor had a honeycombed appearance (fig. 11). On account of the tissue having been fixed for a long time in a diluted solution of formaldehyde, U. S. P. (1:10), it was impossible to use Hortega's specific

Fig. 11.—Oligodendroglioma with small nuclei and the cytoplasm of the cells failing to take the stain. The cell outlines are definite, and occasionally two or more nuclei are present within what appears to be one cell outline. Calcium is not present. Hematoxylin and eosin; × 315.

silver carbonate impregnation method for oligodendroglia. One part of the tumor contained many mitotic figures and all the signs of rapidity of growth, including endothelial reaction in the blood vessels. After partial removal, the tumor recurred and invaded the striated muscle at the site of operation. The mesodermal tissue reacted to this tumor as it would to the presence of a foreign body, namely, by the formation of foreign body giant cells. These were not neoplastic giant cells. This tumor was different from those usually found in the brain, as no calcium

salts were precipitated, and it contained several types of cells. However, the general and cellular appearance strongly suggested an oligodendroglioma, especially when comparison is made with the oligodendrogliomas reported by Bailey and Bucy, or with those arising in the brain in our series of cerebral gliomas. This tumor was probably an oligodendroglioma composed in part of well differentiated oligodendroglia cells and in part of more embryonic oligodendroglia cells, or, as one might call them, oligodendroblasts.

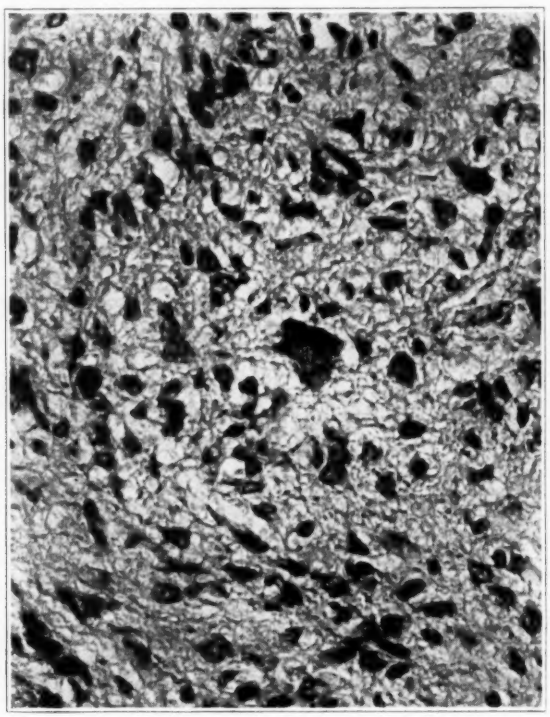

Fig. 12.—Spongioblastoma multiforme. The variation in the size of the nuclei is visible, and a multinucleated tumor giant cell is present. The stroma is visible, and occasional cell bodies are seen. This type of tumor has been referred to as the giant cell glioma of Ströbe. Hematoxylin and eosin; × 400.

When we were considering the classification of the intramedullary tumors of the spinal cord, and later the classification in the cytology of the primary tumors of the spinal cord and the intradural filum terminale,[11] the two tumors which we are including in the spongioblastoma

11. Kernohan, J. W.: Primary Tumors of the Spinal Cord and Intradural Filum Terminale, in Penfield, Wilder: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 991.

multiforme group were considered. One of the tumors of the spinal cord was a classic example of spongioblastoma multiforme, judged by the criteria of Globus and Strauss.[12] The other tumors were somewhat different, but we suggested that they be included in this group. The two tumors arising from the region of the cauda equina did not belong to the classic group so frequently found in the brain, but rather to that group which sometimes has been referred to as "giant cell glioma of Ströbe." The cells were spongioblasts, and the bodies were demonstrated with difficulty by Mallory's phosphotungstic acid hematoxylin stain and by Cajal's gold chloride and sublimate method. However, frequently neuroglia fibrils could be seen even with hematoxylin and eosin (fig. 9). We hesitate to accept the idea that the numerous nuclei were those of a syncytial mass and that no cell bodies were present. There was marked variation in the size of the nuclei, and many giant nuclei were present as well as multinucleated giant cells (fig. 12). The tumors differed from the classic ones of the brain in that the blood vessels were better formed and there was less endothelial hyperplasia of the intima, and in consequence areas of necrosis were not common. However, in one of these two tumors several necrotic areas were present; also blood pigment, which gave a positive reaction for iron with the Turnbull blue stain. Only occasional mitotic figures were present in these tumors, and in this respect they were different from typical spongioblastoma multiforme found in the brain. It seemed that these tumors belonged to the spongioblastoma multiforme group, although they grew somewhat slowly.

COMMENT

The histologic structure of the spinal cord is similar to that of the brain, and in our study of intramedullary tumors we found them to correspond in type with tumors arising from the substance of the brain. There was considerable difference in the distribution of the numbers of tumors in the various types of glioma, and there was a slight variation in the characteristics of the individual tumors in some of the subgroups, but for the most part they corresponded closely. Our study of the normal conus medullaris and filum terminale and the observations of Harmier have shown that they contain all the elements that are present in the spinal cord. There were relatively more ependymal cells, sometimes growing as tubules but usually without any definite cell arrangement except in the ventriculus terminalis, than any other type of cell, and consequently we should expect that ependymomas would be relatively more common than in the spinal cord. This proved to be true, as 68 per cent of tumors arising from the region of the cauda equina were ependymomas. In the spinal cord the ependymomas were divided

12. Globus, J. H., and Strauss, Israel: Spongioblastoma Multiforme, Arch. Neurol. & Psychiat. **14**:139 (Aug.) 1925.

histologically into three types according to the cellular arrangement; this classification was not justified clinically or surgically, but nevertheless, the types were different in histologic structure, and this differentiation may ultimately prove to be of benefit to the patient. In the ependymomas arising from the region of the cauda equina, only two types were distinguished, namely, the cellular and the myxopapillary. The cellular type was more numerous, and there was some variation even in this one group. The stroma in some tended to undergo myxomatous degeneration, but there was no papillomatous arrangement of the cells. Sometimes the cells grew in small groups with their processes projecting toward the center, giving the *ballon* arrangement. In the other type, the myxopapillary, the structure was papillomatous with a tendency for connective tissue stroma to undergo myxomatous degeneration. In no instance could mucus be demonstrated in the cytoplasm of the tumor cells. The amount of mucus in the stroma varied from scarcely demonstrable amounts to large masses which were surrounded by the ependymal cells, which were separated from the mucus by a basement membrane. In these tumors there was a variety of tumor cells, and at times cells similar to the supportive types of spongioblasts were present. In the cellular ependymomas the cell type in the perivascular arrangement was not definitely settled. The cells had many of the appearances of astroblasts, but we hesitate to accept completely the idea that most of these neoplasms contained both ependymal cells and astroblasts.

The protoplasmic astrocytoma was similar to those described in the spinal cord and to those we have examined in the brain. In this tumor the inflammatory reaction, the blood pigment and the small areas of necrosis might possibly be explained by the injury which this patient suffered one year previously and which aggravated the symptoms. This type of tumor is frequently found to have spongioblasts or other primitive cells, but no such activity was present in this case. No fibrous astrocytomas were present in this group of tumors, but there were three astroblastomas which were readily distinguished from ependymomas. They simulated polar spongioblastomas, from which they were distinguished by the absence of interlacing fibrils and of well formed vascular processes. The cells were different from those of astroblastomas of the brain; this difference was probably the result of environment.

There was only one oligodendroglioma arising from the filum terminale, and this contained many typical cells, according to the criteria laid down by Bailey and Bucy. It was very cellular, but all the cells were not completely differentiated, and mitotic figures and other signs of activity of growth were present. After removal it recurred and invaded the operative site, and produced an unusual reaction on the part of the mesodermal tissue. Giant cells were formed which were not neo-

plastic, but foreign body giant cells. They were in close proximity to the tumor cells, and there were no other foreign bodies present, such as suture material. In the spinal cord we examined two oligodendrogliomas, one of which invaded the subarachnoid space. It is interesting that of all the tumors arising from the spinal cord, conus medullaris and filum terminale only three invaded the subarachnoid space, and two of these belonged to the oligodendroglioma group. This tumor arising from the filum terminale contained many cells more primitive than oligodendrocytes, which should probably be called oligodendroblasts. There were no classic examples of the spongioblastoma multiforme type of tumor, such as is frequently seen in the brain, but there were two tumors which have frequently been described as "giant-cell glioma of Ströbe." We have suggested that these should be classified under the heading spongioblastoma multiforme until more is known about them. They were less rapidly growing, but nevertheless were made up of spongioblasts with many giant nuclei but few giant cells; mitotic figures were not common, and degeneration was rare.

We have frequently encountered heterotopic masses of glial tissue in the subarachnoid space of the spinal cord, and in the filum terminale we have seen islands of ependymal cells beneath the pia mater and separated from the main mass which is situated in the middle of the filum terminale in its upper half. After histologic examination of the normal filum terminale it is easy to understand why ependymomas are the most common tumors arising from this structure. Most of the neoplasms arising from the filum terminale are slow growing and enucleable, with only a slight tendency to recur. One notable exception was the oligodendroglioma.

ABSTRACT OF DISCUSSION

DR. PETER BASSOE, Chicago: I believe it is true that not only the spinal fluid below the tumor but also the fluid from above is apt to be albuminous. Were these fluids obtained below and above the tumor and to what extent? Were fluids from both sources examined as to the protein contents?

DR. A. W. ADSON: I cannot give the exact percentage. Often we have done punctures above and below the tumor. It is quite true that a large percentage of these patients do present an increase in protein in the spinal fluid above the tumor.

DR. ISRAEL STRAUSS, New York: The last sentence of Dr. Adson's remarks is the most pertinent one. He states that if a patient has a sciatic syndrome, and after prolonged observation and treatment is not cured, one should think of an intraspinal condition as the cause.

Probably many of the cases of long duration which Dr. Adson described were not observed by neurologists. The differentiation that Dr. Adson makes in the pain from which these patients suffer is not a differentiation that can be applied as between the sciatic syndrome and caudal disease. Patients with so-called sciatica have a pain which is increased on defecation, on laughing and on sneezing, just as do these patients.

Furthermore, it is well known that patients having a sciatic syndome of, say, two, three or four weeks', or two months', duration not infrequently show the loss of an achilles reflex. Why the achilles reflex is lost I have never been able to determine, but it frequently is absent.

Furthermore, in many of the patients suffering from a sciatic syndrome the condition is due to spondylitis, and pressure on the lumbar spine not infrequently brings out pain and tenderness. In other words, it is impossible to differentiate these cases from those of the sciatic syndrome by the clinical manifestations I have mentioned. However, when a case of so-called sciatica lasts for a considerable length of time, and sensory disturbances other than hyperesthesia in the distribution of the first sacral segment appear, every neurologist is aware of the fact that he may be dealing with some condition other than spondylitis or symptomatic sciatica, and if the condition has lasted long enough the changes in the spinal fluid give him the clue, as Dr. Adson has pointed out.

I recently had a case that showed the difficulty in this diagnosis; the patient had suffered considerable pain in the sciatic distribution for about two years and had received all sorts of treatment. Roentgenograms had been normal. When he came to me he was suffering from jaundice due to cinchophen taken over a long period of time. The achilles reflex was absent. The only disturbance of sensation was a diminution in the fourth or fifth sacral segments, so slight in fact that many of my staff could not find the diminution of sensation which I thought was there. There was no weakness and no atrophy. Lumbar puncture revealed xanthochromic fluid. In every case of sciatic syndrome of long duration I examine the spinal fluid. Operation revealed an irremovable growth coursing along all the roots of the cauda equina. The symptoms had been present for only two years.

Dr. Byron Stookey, New York: Radicular neuritis is equally difficult to differentiate from cauda equina tumors and sciatica. This condition produces atrophy, and shows a pain syndrome comparable to and almost impossible to differentiate from that of a true tumor of the cauda equina. The only means that I know which permits a differential diagnosis is a careful manometric study of the spinal fluid, which demonstrates an open subarachnoid space. The condition may also show increased total protein.

In attempting to make a more accurate localization I have made use of a procedure which I am sure Dr. Adson has frequently used, namely, multiple puncture. I often make the puncture below the twelfth thoracic vertebra, following the puncture downward until a block is reached, and then often the needle, as Dr. Adson said, is in the tumor. In those instances I have always attempted to aspirate and obtain some of the tissue for pathologic examination.

Dr. W. G. Spiller, Philadelphia: In approximately how many cases was exaggeration of the achilles tendon reflex, and particularly of the patellar tendon reflex, obtained when the lesion was below their reflex arcs, and when it did not involve the roots contained in the reflex arcs? Lesions below the reflex arcs may cause exaggerated tendon reflexes.

Dr. Strauss is right in mentioning the importance of the absence of the achilles tendon reflex in sciatica. It is a sign that I regard as almost necessary for the diagnosis of pronounced sciatica.

Dr. Stookey spoke of radicular neuritis, which is difficult to distinguish from tumor of the cauda equina. Dr. Frazier will remember a case in which he operated, in which the patient was believed to have a tumor of the cauda equina. The roots of the cauda equina were greatly swollen, so that they entirely filled the dural canal, and the diagnosis was by no means easy before the operation.

DR. FOSTER KENNEDY, New York: Dr. Strauss gave his clinical insight less than justice when he stressed and seemed to agree with Dr. Adson on the difficulty in the diagnosis of these cases.

Most neurologists have been familiar with the syndrome for a good many years; the picture, however, would be a little clearer if one learned the type of paralysis in the particular situation, the loss of motor control, which in such cases is definite, the loss of sexual power and the type of sensory loss, instead of speaking of all of these complexes in a mass manner. It did not seem possible to obtain this information from the diagrams.

DR. S. P. GOODHART, New York: I believe that Dr. Adson has occasionally misinterpreted his findings in that the sensory level has appeared clinically much higher than he would anticipate or expect if the lesion were in the cauda. However, the clinical findings indicating a pathologic process at a higher level were made clear at operation. Dilatation of veins with corresponding pressure on the cord above the tumor caused the symptoms pointing to a higher level. The relation of these varicosities to the lesion in the cauda is worthy of investigation.

DR. A. W. ADSON: In reply to Dr. Kennedy, I regret that the time was not sufficient to permit me to go into all of the details of the paper during the discussion. I feel confident that the questions he has asked are answered in the manuscript, and further I can assure Dr. Stookey that manometric readings were made whenever it was possible. In reply to Dr. Spiller on the situation of the reflexes, these were reduced when the lesions produced pressure on the roots below the conus medullaris. When they were increased we explained it on the basis of a finger-like projection which had grown cephalad and had produced pressure on the cord above the conus medullaris.

In summarizing the results I have tried to stress the fact that tumors arising from the filum terminale are removable even though they may be very extensive and have filled the lumbar canal and surrounded the roots of the cauda equina.

THE NORMAL HISTOLOGY OF THE INTRADURAL FILUM TERMINALE

JOHN WATSON HARMEIER, M.D.
Fellow in Medicine, the Mayo Foundation
ROCHESTER, MINN.

The gross anatomy and embryology of the intradural filum terminale have been fully considered, but it is difficult to find accurate data on the normal histology. The importance of an understanding of this structure is apparent because of the formation of tumors in this region.

The filum terminale, the slender glistening thread which is prolonged downward within the vertebral canal from the end of the conus medullaris, finally anchoring the spinal medulla to the back of the first piece of the coccyx, is described as being about 6 inches (15 cm.) long. Down to the level of the second sacral vertebra it is enclosed with the surrounding nerve roots within the dura mater. This portion is called the filum terminale internum, in contrast to the portion distal to it to which the dura mater is directly applied, and which is called the filum terminale externum. It receives its supply of blood from the lateral sacral artery, which sends spinal offsets into the sacral canal, and these in turn supply the filum terminale.

The embryology of the filum terminale has been well known since the work of Kunitomo,[1] in 1918, and that of Streeter,[2] in 1919. Kunitomo made a careful study of the region of the tail in a large number of human embryos representing the period of greatest development of the caudal appendage and also of the later period of its gradual reduction. He demonstrated that in very young specimens the spinal cord reaches the extreme tip of the tail and is uniform in structure throughout its length. Somewhat later (11 to 15 mm. stage) it can be divided at about the level of the thirty-second vertebra into two parts, a cranial or main part, having a wide central canal and thick walls in which can be recognized well developed mantle and marginal zones, and a caudal

---

Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Medicine, March, 1932.

1. Kunitomo, K.: The Development and Reduction of the Tail and of the Caudal End of the Spinal Cord, Contrib. Embryol. **8**:161, 1918.

2. Streeter, G. L.: Factors Involved in the Formation of the Filum Terminale, Am. J. Anat. **25**:1 (Jan.) 1919.

slender part, having a narrow canal with walls consisting only of an ependymal zone. Kunitomo demonstrated that this caudal atrophic portion eventually forms the filum terminale. The main part lying cranial to the thirty-second vertebra undergoes uninterrupted and progressive differentiation, whereas the portion caudal to this undergoes regressive changes and, with the exception of the extreme tip, finally becomes converted into a fibrous strand, the tip forming the coccygeal medullary vestige. The part played by retrogressive differentiation in the caudal region of the spinal cord is more apparent in the earlier stages of development. It is also known that the so-called absorption of the tail is completed before the embryo reaches a length of 30 mm. In the formation of the filum terminale, in addition to the retrogressive differentiation of the caudal end of the medullary tube, there is mechanical disproportion between the growth of the medullary tube and that of the vertebral column. The part played by each of these two factors in the further development of the filum terminale was not determined by Kunitomo, but by Streeter, who thought that the answer could be found by the determination of the elongation of the nerve roots. In the early embryos the spinal cord and the vertebral column lie side by side in a metameric manner, corresponding in position segment for segment, but, owing to the disproportion in growth, there occurs a relative displacement of their segmental levels, so that, for instance, the thirtieth segment of the cord comes to lie opposite the twentieth segment of the vertebral column.

The segmental levels in the spinal cord are marked by the attachment of nerve roots, which are attached before movement begins. The spinal ganglion, which is held in the intervertebral foramen, registers the original position of the segment. It was by measuring the distance between these points in various embryos that Streeter arrived at the index of the relative displacement of the spinal cord as regards the vertebral column. Any alteration not explained by mechanical displacement was attributed to retrogressive changes. Streeter found that there is no further differentiation of the sacral region after the embryo has reached a length of 30 mm. The cephalic migration that is subsequently experienced by the ventriculus terminalis and points of attachment of the sacral nerve roots relative to the bodies of the vertebrae is clearly a result of the fact that the vertebral column gradually extends farther caudalward than the spinal cord, and since the nerve roots and filum terminale are attached at both ends they are correspondingly elongated. The latter process is not a simple stretching, for as these structures lengthen they actually become thicker, a sort of compensatory interstitial growth.

Streeter also studied the dura mater and its relations and found that the caudal tip of the dural sac maintains its relation to the vertebrae rather than to the spinal cord and remains attached to the filum terminale in the sacral region at a more or less fixed point.

Accurate data concerning the filum terminale and its structure are difficult to find. The filum terminale has been considered a rudiment or merely an extension of the dura mater by certain observers, whereas others assume that it consists of delicate vessels that originate in the pia mater.

The earliest of the few references available is that by Rauber.[3] He described the filum terminale as consisting of two parts, the external and the internal, and pointed out their relations to the dural sac. He gave the length of the internal filum as about 16 cm. and that of the external filum as 8 cm. To Rauber is given the credit for not only the foregoing anatomic description but also the fact that the filum terminale internum is composed largely of pia mater. In the superior half it encloses the terminal part of the central canal, and around this a variable amount of gray substance is prolonged downward into the filum. On transverse section through the superior part of the filum some bundles of medullated nerve fibers are observed clinging to the sides, and Rauber supposed that these bundles represented rudimentary or aborted caudal nerves.

Tourneux,[4] in 1892, reported his observations on the structure of the filum terminale in the fetus and in two adults. In the fetus he found that at the level of the medullary conus the central canal of the cord enlarged to form the terminal ventricle. Lower it became flattened, while at the same time the medullary cells diminished in number, and there was a gradual transition from the lower extremity of the cord to the filum terminale. The canal of the cord extended into the filum as far as the vicinity of the dural culdesac. At a distance of 1 mm. from the external segment the few epithelial and nerve cells found above this point were absent. The regular cylindric form of the filum terminale was lost at the interior of the coccygeal ligament, and at the lower part of this ligament it was almost impossible to recognize the tissues which represented the continuation of the internal segment of the filum terminale.

In the study of the filum terminale of adults, the measurements of the internal and external parts were taken. In one case, that of an adult aged 45, the measurements were 14.5 cm. for the internal segment

3. Rauber, A. A.: Lehrbuch der Anatomie des Menschen, Leipzig, G. Thieme, 1907.

4. Tourneux, F.: Sur la structure et sur le développement du fil terminal de la moelle chez l'homme, Compt. rend. Soc. de biol. **44**:340, 1892.

and 7 cm. for the external segment, and in the other, that of an adult aged 50 years, the measurements were 17 and 5 cm., respectively. These segments were described as being composed chiefly of lamellar bundles surrounding the arteries and a large spinal vein. The nerve cells diminished in number from above downward and seemed to collect at the surface of the filum. In a recent report (1930) by Sachs, Rose and Kaplan [5] on two tumors of the filum terminale, the central canal was described as being surrounded by a layer of nerve substance in which nerve cells are usually present.

In 1924, Kernohan,[6] in a study of the ventriculus terminalis, noted that there were ependyma-lined cavities below its lower end. In 1931, after a study of the filum terminale internum, he concluded that all the elements present in the spinal cord were present also in the filum terminale. He noted that the ganglion cells contained an excessive amount of pigment and showed signs of premature degeneration. In addition to the ganglion cells there were many neuroblasts or immature forms of neurogenic elements. There was also an excessive number of corpora amylacea scattered throughout the tissue, large collections of ependymal cells, some of which lined cavities and were ciliated.

MATERIAL AND METHODS

The material on which this study is based was collected at necropsy while I was on duty in the Section on Pathologic Anatomy, the Mayo Clinic. The material was collected from thirty-four consecutive cases when opportunity permitted, irrespective of age, sex or cause of death.

The specimens were removed intra-abdominally. The lower lumbar vertebral bodies were cut through and removed on one side to expose the spinal canal. The dural sac was opened, and the filum terminale internum was identified by its bluish-white, glistening appearance and by its accompanying vessels, which were usually distended with blood. For safety, the lower end of the cord was removed, and the filum was followed down within the sac to its termination and cut. In several instances the entire internal filum was not obtained, owing to difficulty in proper exposure. The following stains were used: Weigert myelin sheath, Mallory phosphotungstic acid and Mallory-Heidenhain; hematoxylin and eosin, Orlandi, thionine and van Gieson.

The method of embedding and cutting presented a problem because of the tendency for the small filum to curl. In order to get longitudinal sections, the filum was curled and sectioned parallel to the long axis. A sufficient number was cut in this manner, and those remaining were cut in cross-section. In this latter method the filum terminale was cut at distances of 1 cm., and the pieces were embedded side by side in rotation, with the proximal end uppermost.

---

5. Sachs, E.; Rose, D. K., and Kaplan, A.: Tumor of the Filum Terminale, with Cytometric Studies; Report of Two Cases, Arch. Neurol. & Psychiat. **24:** 1133 (Dec.) 1930.

6. Kernohan, J. W.: The Ventriculus Terminalis: Its Growth and Development, J. Comp. Neurol. **38:**107 (Dec.) 1924.

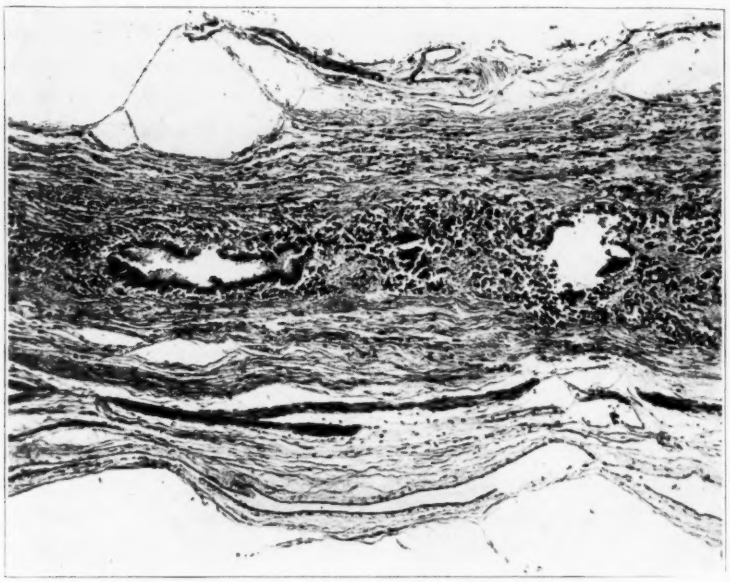

Fig. 1.—Longitudinal section showing ependyma-lined cavities; × 60. Hematoxylin and eosin stain.

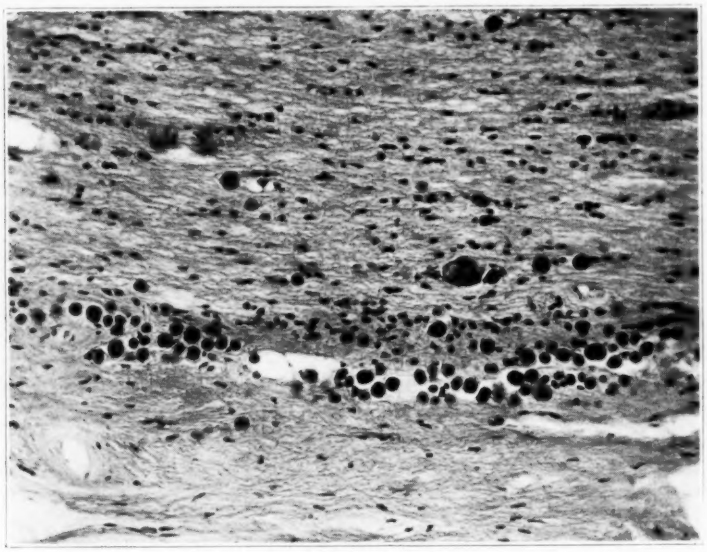

Fig. 2.—Collections of corpora amylacea beneath the pia mater; × 125. Hematoxylin and eosin stain.

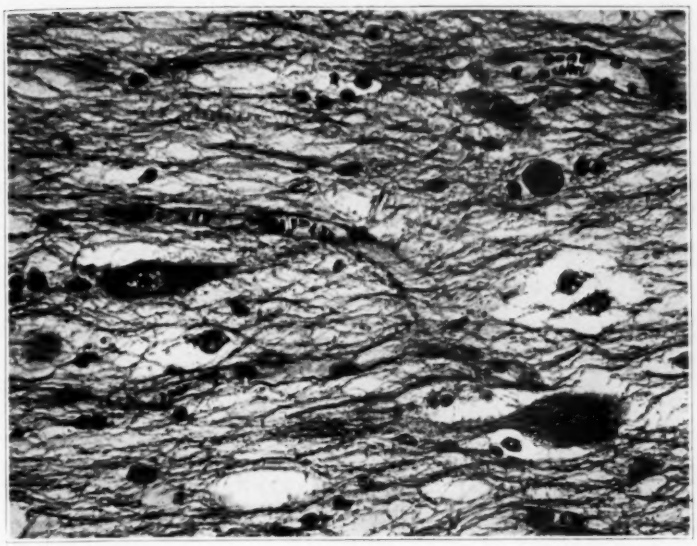

Fig. 3.—Ganglion cells, containing excessive pigment; × 325. Hematoxylin and eosin stain.

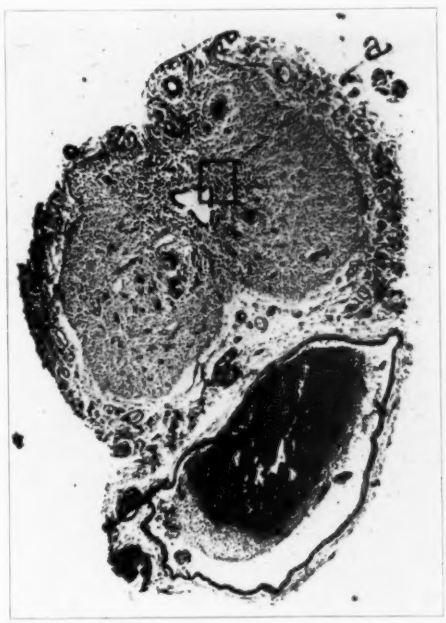

Fig. 4.—Cross-section of filum terminale, approximately 1 cm. distal to the ventriculus, showing structure of neurogenic tissue and relation to the vessels; × 35. Van Gieson's stain. At *a* is indicated neurogenic tissue shown under high power in figure 5.

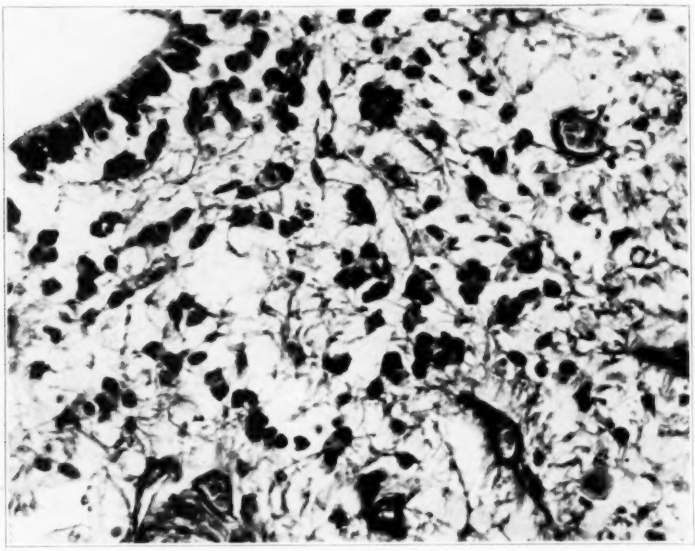

Fig. 5.—High power magnification of section of area marked *a* in figure 4, showing structure of neurogenic tissue adjacent to the ependyma-lined cavity; × 350. Van Gieson's stain.

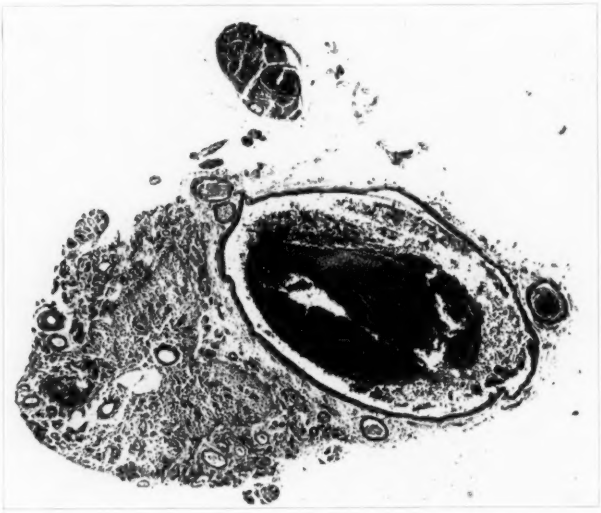

Fig. 6.—Cross-section of filum terminale, approximately 3 cm. from the ventriculus, showing decrease in amount of neurogenic tissue; × 35. Van Gieson's stain.

RESULTS

Microscopic study of the material described has disclosed much of interest. In the longitudinal sections large collections of ependymal cells were seen, in certain places without definite arrangement and in other places lining small irregular cavities. The ependymal cells lining the cavities were occasionally ciliated. Beneath the pia matter, but also collected in masses and scattered throughout the tissue, there were excessive numbers of corpora amylacea. Ganglion cells were seen in the sections, but they did not penetrate deeply, being confined principally to the proximal half. These ganglon cells were not all polygonal like the anterior horn cells, but were seen to be of all types, unipolar, bipolar and polygonal. The cells contained Nissl's granules and excessive pigment; others seemed to be undergoing degeneration. Some neuroblasts were scattered throughout the tissue.

Axis cylinders extended all the way down the filum terminale. They were not abundant or normal, as compared with those seen in the lateral columns of the spinal cord. They were irregular, especially in the distal portions, with a tendency to be beaded, and they seemed to be undergoing degeneration. With the Weigert stain the myelin could be seen in large amounts in the proximal half of the filum, but it decreased gradually as it progressed distally. Figures 1 to 3 show the structures and elements described. On cross-section the structure was studied further, and the relation of the accompanying vessels to the neurogenic tissue was observed. The ependyma-lined cavities also were identified. In one of these cavities a mass of glial tissue was noted. The surrounding connective tissue structure was seen in abundance in most sections. A large vein and two small arteries accompanied the neurogenic tissue. These vessels occupied considerable space, but the neurogenic structure was also present, disproving the contention that it was composed entirely of blood spaces. There were many small vessels in the substance of the neurogenic tissue. However, it was interesting to note that as one progressed distally the amount of nerve tissue decreased and became more superficial, until finally there remained only a fine layer of cells along one side of the section. Tourneux also made this observation in his study. Figures 4 to 6 show the structure in cross-section.

The measurements of the filum terminale internum vary and are not related to the length of the body. The variations in the length of the filum terminale internum in children and adults can be easily understood. Sex and associated pathologic conditions did not play a part in variations.

SUMMARY

The filum terminale internum contains all of the elements found in the spinal cord.

A large vein and two small arteries are found in association with the neurogenic tissue.

The more distal the segment examined, the less neurogenic tissue is found.

The more distal the segment examined, the greater is the decrease in the component parts of the neurogenic tissue.

Tumors of the filum terminale internum should be similar in type to those found in the spinal cord.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

A STUDY OF THE UNDERLYING PATHOLOGIC PROCESS

N. W. WINKELMAN, M.D.
PHILADELPHIA
AND
CHARLES DAVISON, M.D.
NEW YORK

Basically, tissue changes may be considered in the following general divisions: (1) inflammatory, (2) degenerative, (3) neoplastic, (4) regenerative, (5) hyperplastic or hypertrophic, (6) those which begin as an inflammatory process and develop or remain as a degenerative process and (7) those which begin as a degenerative process with resulting secondary or symptomatic inflammatory changes. The character of the basic changes in the tissues serves as an index of the underlying pathologic process and thus may give a clue to the etiology.

No one today doubts the type of changes present in many of the common neurologic conditions. No one will deny that poliomyelitis and epidemic encephalitis are inflammatory diseases, even though degeneration takes place in the final stages. There can also be no question as to the type of changes in cerebral softening due to vascular occlusion, even though in the study of the end-result one may find perivascular collaring with round cells in the immediate vicinity.

In certain diseases there may still be doubt as to the nature of the process. Pernicious anemia falls in this group. A study of the pathologic changes may help in elucidating the etiology.

Pernicious anemia is at present thought to be due to one of three possible factors: a toxin, an infection or a dietary deficiency.

In the involvement of the nervous system, the adherents to the toxic theory are divided into two groups: One group is headed by Nonne,[1]

From the Laboratory of Neuropathology, Montefiore Hospital, New York, and the Laboratory of Neuropathology, Philadelphia General Hospital.

1. Nonne, M.: Beiträge zur Kenntnis der im Verlaufe der perniziösen Anämie beobachteten Spinalerkrankungen, Arch. f. Psychiat. **25**:421, 1893; Beiträge zur Kenntnis der im Verlaufe letaler Anämien beobachteten Spinalerkrankungen, Deutsche Ztschr. f. Nervenh. **6**:313, 1895.

Wohlwill,[2] Shimazono[3] and Spielmeyer,[4] who claim that the toxic agents of pernicious anemia reach the spinal cord by way of the blood stream; the long-standing action of the toxin on the blood vessel damages its wall, and secondarily injures the nerve parenchyma by acting on the myelin sheaths, axis cylinders and glia. The second group, headed by Henneberg,[5] maintains that the blood vessels play an unimportant part. The hypothetic toxin attacks the nerve tissue directly by a primary disease of the myelin sheaths, the destruction of which produces secondary swelling and fragmentation of the axis cylinders with ensuing phenomena of destruction. As regards the pathologic changes in the spinal cord, the manner in which the toxin attacks the nerve tissue is of little significance. In either case, the pathologic process should not show the typical picture seen in inflammatory conditions.

Macht[6] and his followers claim that the disease is due to an intoxication, and by phototoxic experiments Macht showed that the blood serum in pernicious anemia is toxic.

Seyderhelm[7] performed autopsies on eighty-one horses suffering from a type of anemia simulating pernicious anemia in human beings. He found in their stomachs the larvae of several varieties of flies belonging to the Ostidiae group. From the bodies of these he extracted a toxic agent. By injecting subcutaneously an extract of four of the larvae in one case, the horse was killed in twelve minutes. The administration of minute quantities of this substance to horses produced the picture typical of pernicious anemia.

Finnish investigators maintain that pernicious anemia is induced by the liberation of an endotoxin on the death of the worm, Bothriocephalus latus. This toxin apparently consists of the cholesterol ester

2. Wohlwill, F.: Zum Kapitel der pathologisch-anatomischen Veränderungen des Gehirn und Rueckenmarks bei perniziöser Anämie und verwandten Affektionen, Deutsche Ztschr. f. Nervenh. **68**:69, 438, 1921.

3. Shimazono, J.: Ueber das Verhalten der zentralen und der peripheren Nervensubstanz bei verschiedener Vergiftungen und Ernährungstörungen, Arch. f. Psychiat. **53**:972 (March) 1914.

4. Spielmeyer, W.: Pseudosystemerkrankungen des Rueckenmarks nach Stovain-anaesthesia, Neurol. Centralbl. **28**:69, 1909.

5. Henneberg, R.: Die funikuläre Myelitis und die anämische fokale Leukomyelitis, in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1911, vol. 2, pp. 694 and 769.

6. Macht, D. I.: A Phyto-Pharmacological Study of Pernicious Anemia, J. Pharmacol. & Exper. Therap. **29**:461, 1926. Macht, D. I., and Anderson, W. T., Jr.: Clinical and Experimental Studies on Photo-Therapy in Pernicious Anemia, ibid. **34**:365, 1928.

7. Seyderhelm, R.: Ueber die perniziöse Anämie der Pferde, Beitr. z. path. Anat. u. z. allg. Path. **58**:285, 1914. Seyderhelm, K. R., and Seyderhelm, R.: Die Ursache der perniziösen Anämie der Pferde, Arch. f. exper. Path. u. Pharmakol. **76**:149, 1914.

of oleic acid. Faust and Talquist [8] experimented with it and induced a slight reduction in the number of red blood cells without actually inducing pernicious anemia.

Nonne and Eisenlohr [9] described a blood picture, resembling Addison's anemia, in patients suffering from infestation with Taenia saginata. Effective vermifugal treatment resulted in a return of the blood picture to normal.

Infection as the etiologic factor in Addison's anemia is chiefly advocated by the English investigators, Hunter,[10] Hurst [11] and others, who claim that the anemia is due to oral sepsis. They regard the infection of the mouth as streptococcal, and the general intoxication as due to a streptococcus toxin. The loss of the bactericidal hydrochloric acid barrier permits the streptococci of oral origin to pass through the stomach unaffected. The achylia gastrica explains the occurrence of streptococci in the duodenum and the inflammatory foci in the gastrointestinal mucosa.

The intestinal flora have been incriminated in pernicious anemia as in many other conditions the etiology of which is unknown. The suspected organisms include Bacillus coli,[12] B. welchii,[13] Monilia psilosis and other fungi. Nye [13c] found that the number of Bacillus welchii spores are increased in the stools in cases of pernicious anemia. This same increase in Bacillus welchii is also present in stools from cases of

8. Faust and Talquist: Ueber die Ursachen der Bothriocephalus Anämie: Ein Beitrag zur Pathogenese der perniziösen Anämie auf physiologisch-chemischer Grundlag, Arch. f. exper. Path. u. Pharmakol. **57**:367, 1907.

9. Nonne and Eisenlohr, cited by Morowitz, P., and Denecke, G.: Blut und Blutkrankheiten, in Bergmann, G., and Staehelin, R.: Handbuch der inneren Medizin, Berlin, Julius Springer, 1926, vol. 4, pt. 1, p. 91.

10. Hunter, W.: Severest Anæmias: Their Infective Nature, Diagnosis, and Treatment, New York, The Macmillan Company, 1909, p. 110; Pernicious Anæmia: Its Pathology, Septic Origin, Symptoms, Diagnosis, and Treatment, London, C. Griffin & Company, 1901.

11. Hurst, A. F.: The Pathogenesis of Subacute Combined Degeneration of the Spinal Cord with Special Reference to Its Connection with Addison's (Pernicious) Anæmia, Achlorhydria and Intestinal Infection, Brain **48**:218 (June) 1925; Addison's Anæmia and Subacute Combined Degeneration of the Spinal Cord, Lancet **1**:1212 (June 6) 1925.

12. Draper, G., and Barach, A. L.: Studies in Experimental Anemia: Effect on Rabbits of Injection of Stool Extracts of Patients with Pernicious Anemia and Normal Individuals, J. Clin. Investigation **4**:529, 1927.

13. (*a*) Herter, C. A.: On Bacterial Processes in the Intestinal Tract in Some Cases of Advanced Anemia, with Especial Reference to Infection with B. Aerogenes Capsulatus (B. Welchii), Tr. A. Am. Physicians **21**:725, 1906. (*b*) van der Reis: Ueber die bakterien Flora des Darms, Ztschr. f. d. ges. exper. Med. **30**:296, 1923. (*c*) Nye, R. N.: Investigations Relative to B. Welchii Infection of the Intestinal Tract as the Etiological Factor in Pernicious Anemia, J. Clin. Investigation **4**:71, 1927.

gastric achylia without pernicious anemia. Nye [13e] considered that the pernicious anemia is due to the increase in spores rather than to the chronic intestinal infection with Bacillus coli.

A third school, West,[14] Gildea [15] and others, believes that pernicious anemia is a deficiency disease and places it in the same category with pellagra and beriberi.

It was thought that a study of the histopathology of the spinal cord in cases of pernicious anemia might be of value in determining which of these various theories is correct. We were interested in the significance of round cell infiltration, especially in view of the fact that the

Laboratory Findings in Cases Reported

				Blood Picture								
No.	Sex	Age	Duration of Illness	Hemoglobin, per Cent	Red Blood Cells	Color Index	White Blood Cells	Differential	Free Hydrochloric Acid	Clinical Neurologic Findings	Spinal Cord Changes	Apparent Inflammatory Evidences
1	F	50	4 yrs.	68	2,610,000	1.30	7,300	Typical picture of pernicious anemia	Absent	Typical	Present	Present
2	F	42	5 yrs.	30	1,112,000	1.34	12,500	Typical picture of pernicious anemia	Absent	Typical	Present	Present
3	M	41	7 yrs.	30	700,000	2.14	7,000	Typical picture of pernicious anemia	Absent	Typical	Present	Present
4	M	42	5 yrs.	48	2,100,000	1.14	7,200	Typical picture of pernicious anemia	Absent	Typical	Present	Present
5	M	57	9 mo.	66	2,680,000	1.30	6,500	Typical picture of pernicious anemia	Absent	Typical	Present	Present

condition found in the cord has been considered as entirely degenerative. In the selection of the material we were careful not to include cases of pernicious anemia that were complicated by syphilis.

MATERIAL

Of a group of twenty-five cases of pernicious anemia, the cords of which showed a picture of subacute combined degeneration, five were found that showed apparent signs of an inflammatory reaction in the form of perivascular infiltration. There was a question as to whether these were true inflammatory cells or cells belonging to the group of compound granular corpuscles. In order to determine this definitely, the sections were stained with the myelin sheath (Weil modifica-

14. West, R.: Pernicious Anemia as a Deficiency Disease, Ann. Int. Med. **3:** 122 (Aug.) 1929.

15. Gildea, E. F.; Kattwinkel, E. E., and Castle, W. B.: Experimental Combined System Disease, New England J. Med. **202:**523 (March 13) 1930.

tion), cresyl violet, hematoxylin-eosin, Unna-Pappenheim, polychrome methylene blue (methylthionine chloride, U. S. P.), Giemsa and sudan IV stains.

The duration of the illness in these cases was from four to seven years (table 1). One case, of eight months' duration, an unusually early case, was studied carefully but did not show signs of inflammatory or apparent inflammatory changes.

REPORT OF CASES

CASE 1.—*History.*—F. M., a woman, aged 50, was admitted to the Montefiore Hospital on Dec. 13, 1924, with pernicious anemia and neurologic signs and symptoms that had been first noticed in November, 1920. General and neurologic examinations revealed a picture of pernicious anemia and subacute combined degeneration. For the laboratory findings in this and the succeeding cases, the reader is directed to the accompanying table.

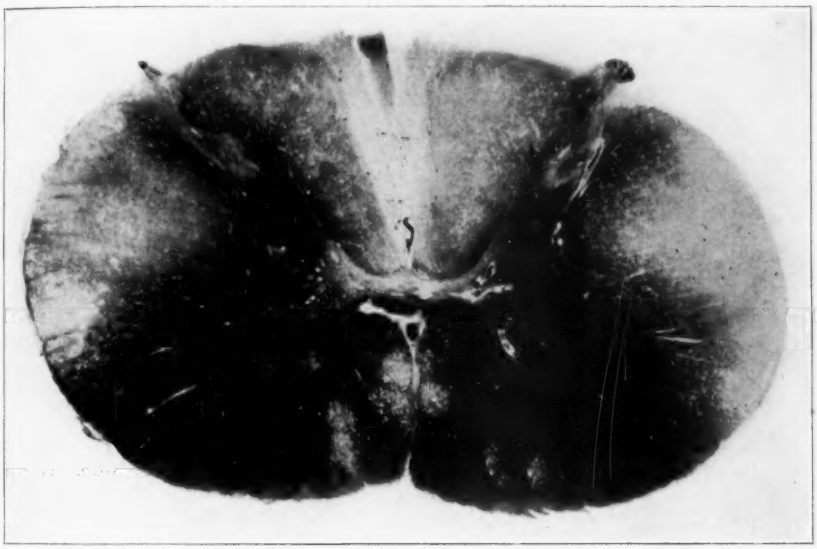

Fig. 1.—Transverse section of the cervical spinal cord, showing demyelinization of the posterior columns and the crossed and direct pyramidal tracts. Myelin sheath stain (Weil modification); × 30.

Pathologic Data.—Gross Examination: The brain and cord were normal.

Microscopic Examination: The spinal cord presented the histopathologic picture usually seen in subacute combined degeneration. There was demyelinization of the posterior columns and the lateral and anterior pyramidal tracts (fig. 1). A detailed description of the pathologic changes of the myelin sheaths, axis cylinders and glia has been given before, and, as they do not concern us in this presentation, will be omitted. In the areas of demyelinization, many of the blood vessels were collared by apparent round cells (fig. 2). The same sections stained by the fat stains showed these cells to be definitely compound granular corpuscles (fig. 3). With the Unna-Pappenheim stain, a differential stain for plasma cells, the adventitial spaces were free from round cells (fig. 4). The apparent cellular infiltration was most marked where the destructive process appeared more recent. With higher

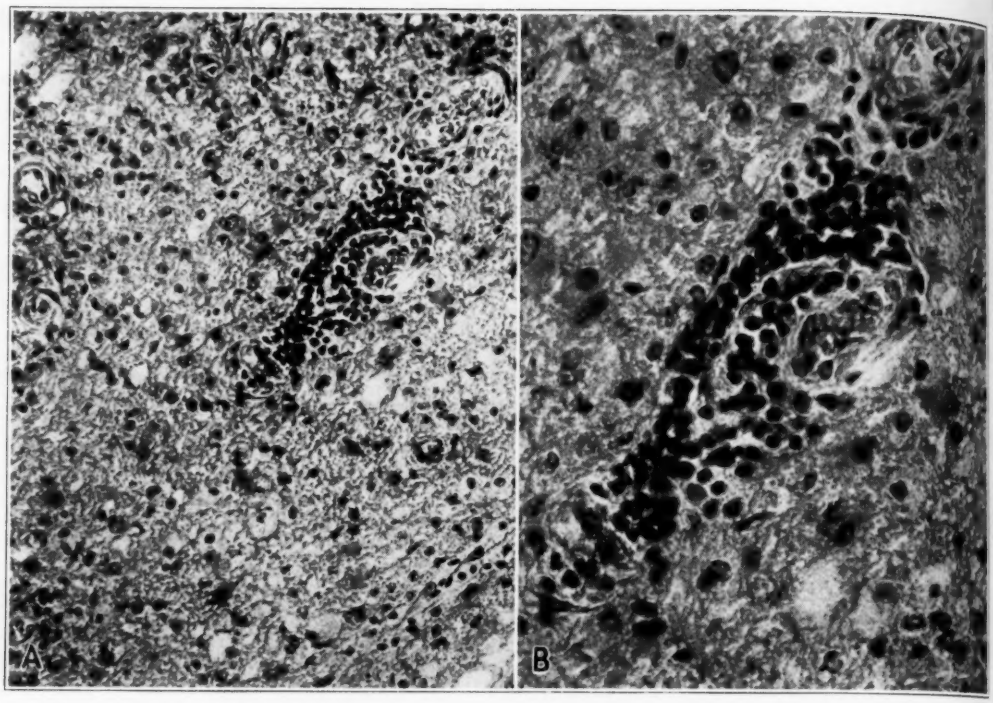

Fig. 2.—Accumulation of apparently round cell infiltration in the adventitial spaces. Hematoxylin-eosin stain; *A*, reduced from × 300; *B*, reduced from × 800.

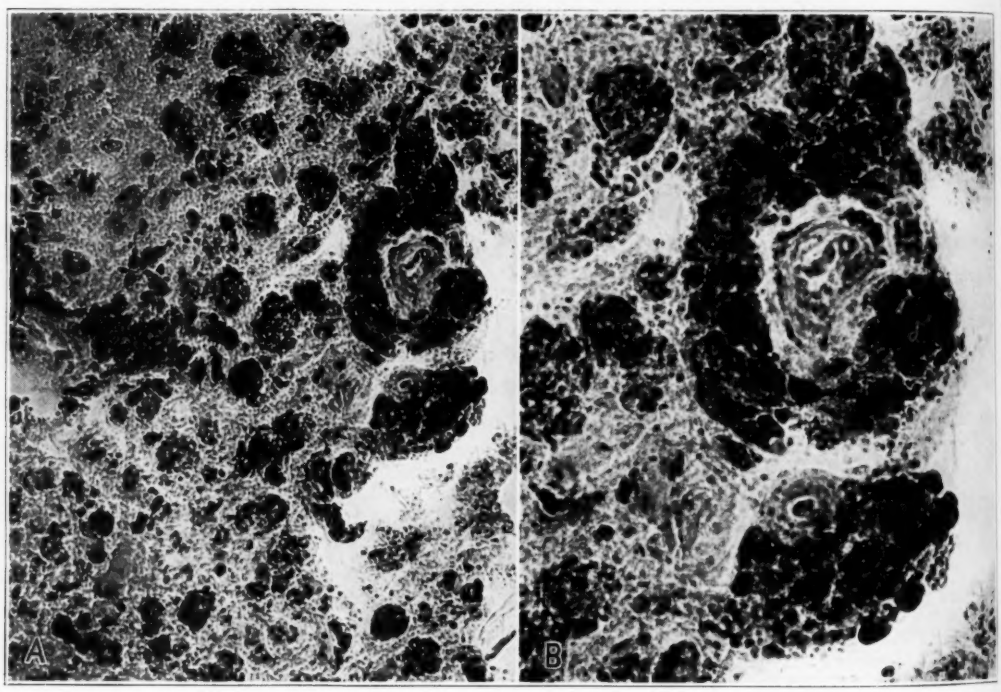

Fig. 3.—Same as figure 2, showing the adventitial spaces filled with fat-laden compound granular cells. *A*, reduced from × 300; *B*, reduced from × 800.

magnification the apparent round cells (fig. 3*B*) were either round or oval, and contained chromatin material arranged in small, uniformly distributed, spherical particles (fig. 5). These cells attained the size of large mononuclears, though smaller individual cells were also encountered. With the fat stains, the same cells formed one conglomerate mass; the outlines of these cells could barely be made out (fig. 6). As will be shown later, none of these cells resembled the typical lymphocyte.

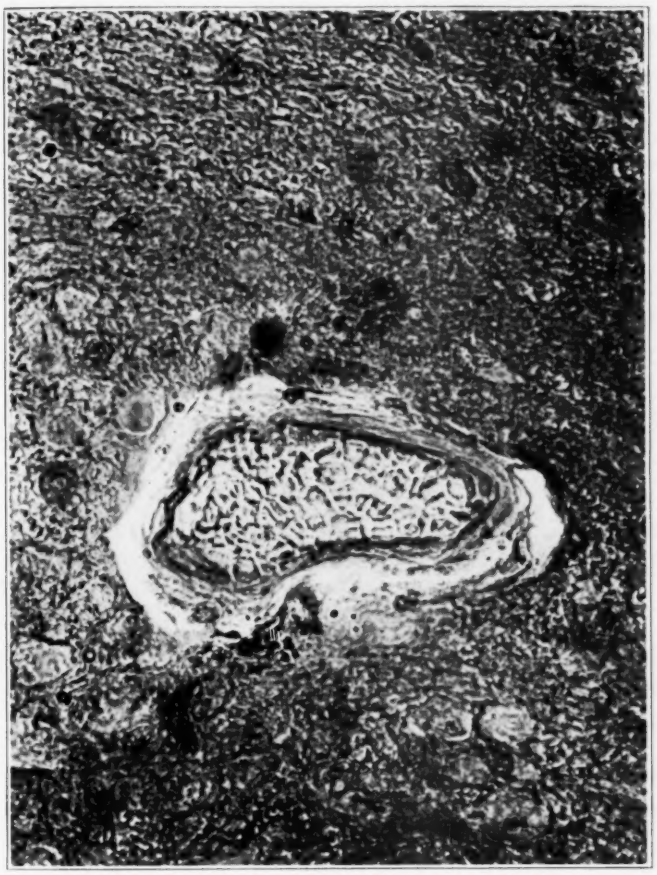

Fig. 4.—Same as figure 2*B*, showing thickening of the adventitia and absence of plasma cells. Unna-Pappenheim stain; × 800.

Case 2.—*History.*—G. P., a woman, aged 42, was admitted to the Montefiore Hospital in August, 1920, with a history of pernicious anemia. The general and neurologic findings were those of pernicious anemia and subacute combined degeneration.

Pathologic Data.—Gross Examination: The brain and spinal cord showed no abnormalities.

Microscopic Examination: The cervical and thoracic spinal cord presented the histopathologic picture of subacute combined degeneration. The apparent cellular

reaction in these sections was limited to the posterior columns and resembled those in case 1.

CASE 3.—*History.*—N. G., a man, aged 41, was admitted to the Montefiore Hospital in July, 1922, with pernicious anemia that had first been noticed in April, 1916. The neurologic complications appeared in December, 1921. General and neurologic examinations showed signs of pernicious anemia and subacute combined degeneration.

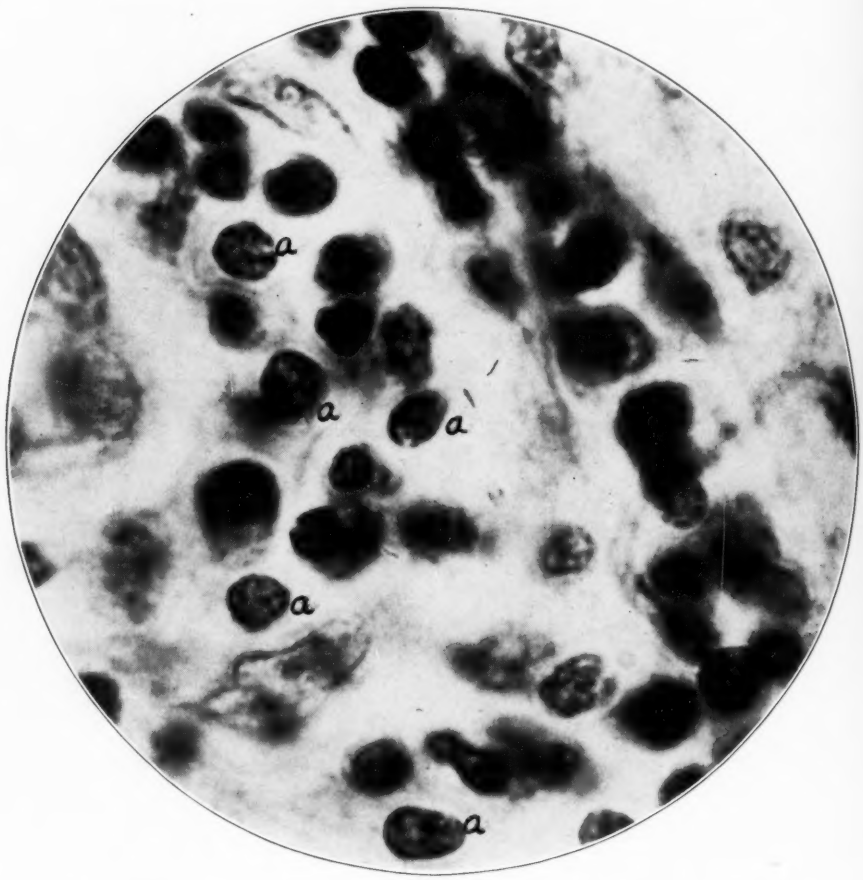

Fig. 5.—Apparent round cell infiltration from the adventitial spaces, showing the non-uniformly distributed spherical particles (*a*). Hematoxylin-eosin stain; × 1,500.

Pathologic Data.—Gross Examination: The spinal cord, on sectioning, presented a translucency of the posterior and lateral columns.

Microscopic Examination: In addition to the usual histopathologic findings of subacute combined degeneration, there was also an apparent round cell perivascular infiltration in the posterolateral columns of the cervical region.

CASE 4.—*History.*—I. S., a man, aged 42, was admitted to the Montefiore Hospital on July 25, 1924, with anemia that was first observed in July, 1919. The neurologic signs appeared in February, 1923. General and neurologic examinations revealed pernicious anemia and subacute combined degeneration.

Pathologic Data.—Gross Examination: The spinal cord, on sectioning, showed a translucency of the posterior columns.

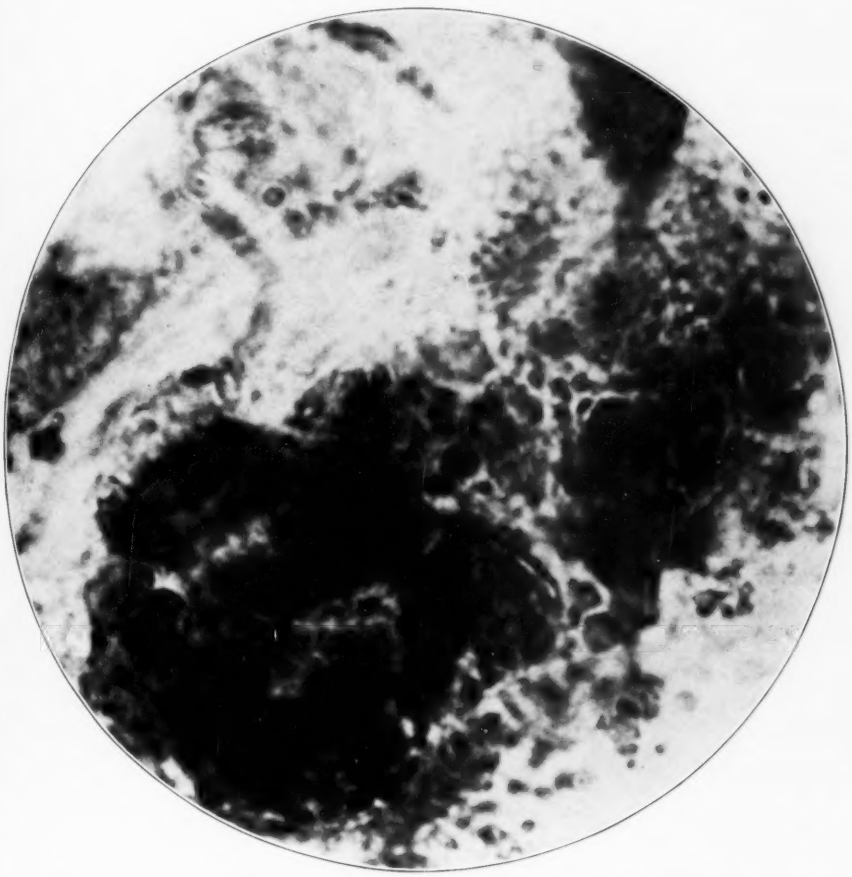

Fig. 6.—Same as figure 5, showing conglomeration of fat in the adventitial spaces. Sudan IV stain; × 1,500.

Microscopic Examination: The same apparent round cell infiltration was noted, and was best seen in the thoracic segments.

CASE 5.—*History.*—A colored man, aged 57, was admitted to the service of Dr. Potts at the Philadelphia General Hospital on Dec. 21, 1927. He presented the usual neurologic signs of a posterolateral sclerosis of the anemic type. There was an absence of free hydrochloric acid in the gastric contents, and the blood findings were typical in every way. The serologic findings were entirely negative for syphilis. The patient died on May 3, 1928.

Pathologic Data.—Microscopic Examination: The changes typical of posterolateral sclerosis of the anemic type were present, as shown by the myelin sheath preparations. The cellular preparations showed the same type of perivascular collaring seen in our other cases. Differential staining methods showed the cellular make-up to consist almost entirely of compound granular cells rather than lymphocytes and plasma cells.

COMMENT

As can be seen from the photomicrographs, the myelin sheath stains give results that are characteristic of the changes in the spinal cord in

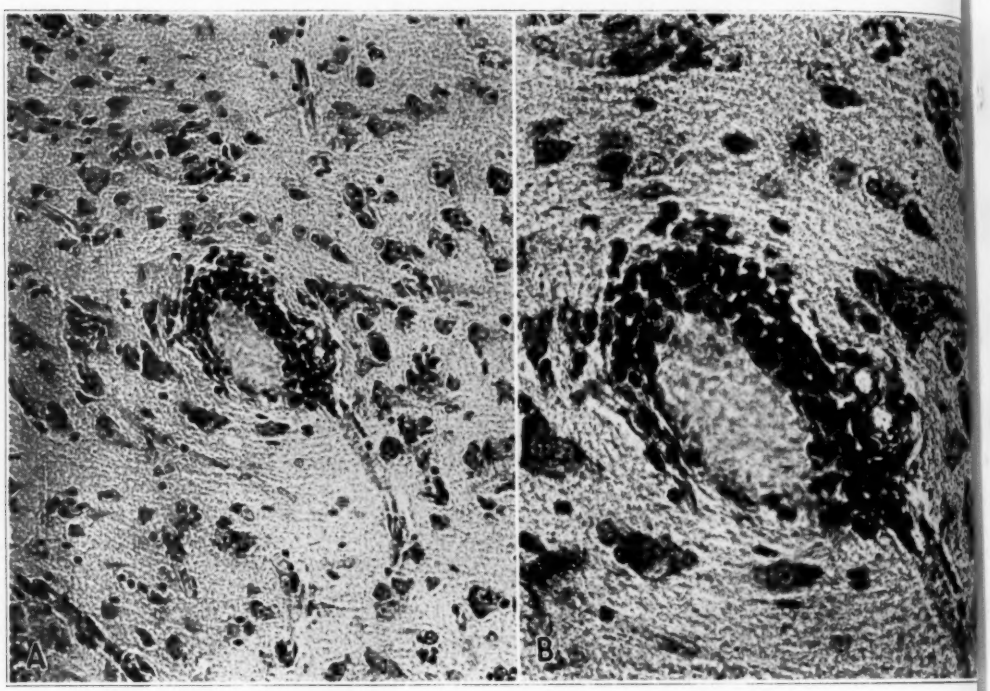

Fig. 7.—Blood vessel in a case of dementia paralytica, showing round cell infiltration in the adventitial spaces. Unna-Pappenheim stain; *A*, reduced from × 300; *B*, reduced from × 800.

pernicious anemia. With the routine stains, such as hematoxylin-eosin and toluidine blue, there is, in some cases of pernicious anemia, a perivascular infiltration with what appear to be round cells (figs. 2 and 7). If perivascular infiltration with small round cells indicates inflammation, one cannot escape the conclusion that pernicious anemia, in some cases at least, is an inflammatory disease. The literature contains numerous reports of cases in which a small round cell collaring of the vessels is the only evidence of inflammation. Schilder himself, in the description

of what is now a well recognized pathologic, and at times a clinical, entity, chose the title of "encephalitis" solely because of this finding.

It was this feature that led us to a study of this group of cases. While there is no specific stain for the small lymphocyte, it was thought that the presence of plasma cells would be significant, and a stain for

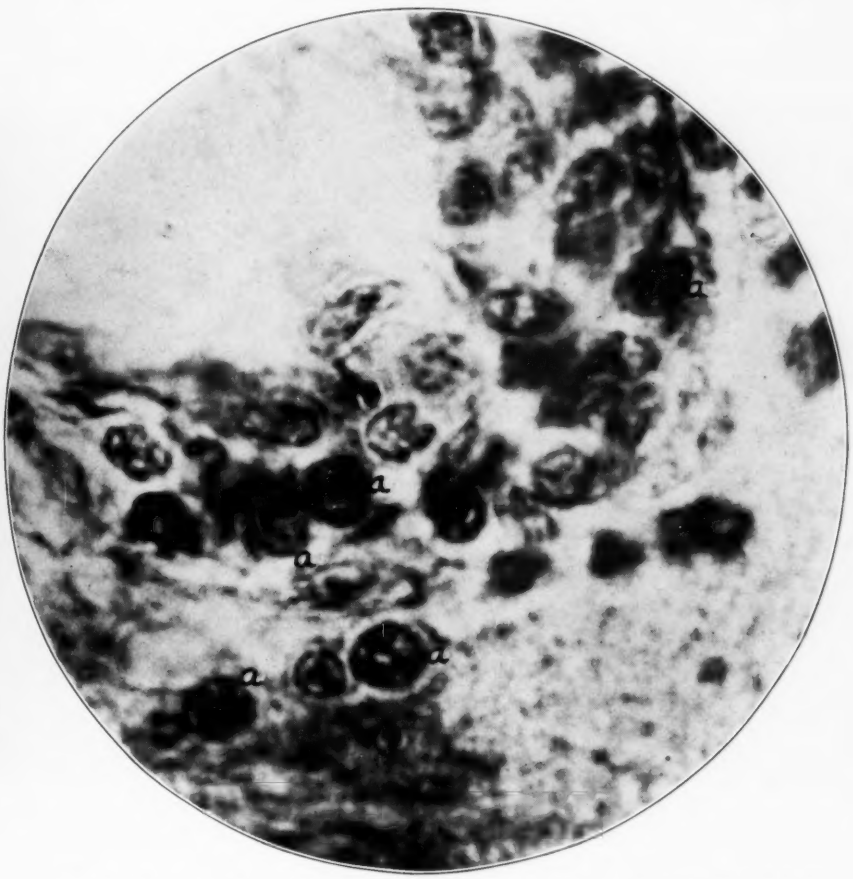

Fig. 8.—Same as figure 7, showing abundance of chromatin material (*a*) in the round cells. Unna-Pappenheim stain; × 1,500.

the plasma cell is available that is sufficiently differential. It is well known that in most chronic inflammatory conditions the plasma cells occur in association with small lymphocytes. These cells are found in syphilis and tuberculosis, and we have even seen them in long drawn-out suppurative meningitis. The cell with which the lymphocyte is confused is the compound granular cell. It is now admitted that the compound granular cell is derived mainly from microglia and possibly, also,

according to Hortega, from the large mononuclears and adventitia. We have seen active mitosis of the compound granular cells. These cells are migratory, and, on ingesting the lipoid and other forms of pigment, active migration occurs toward the adventitial space of a nearby vessel. In long-standing degenerative lesions, one notes a progressive decrease in the size of the cytoplasmic mass, until finally a round nucleus, not at all unlike the small lymphocyte, is to be seen with a faint narrow cytoplasmic ring around it. We agree with Penfield that with the

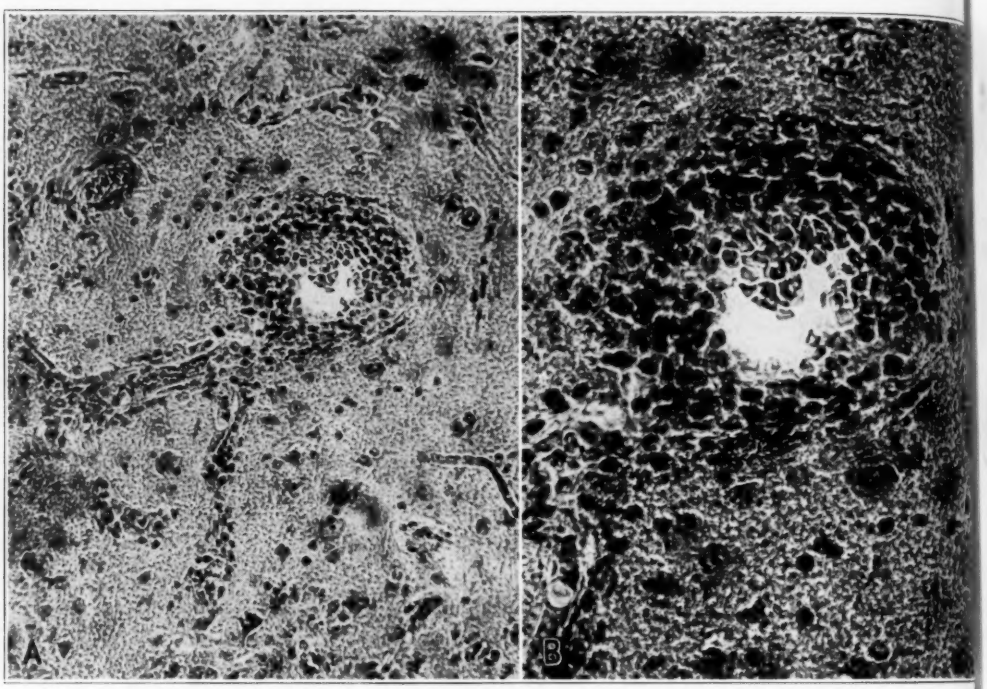

Fig. 9.—Blood vessel in a case of dementia paralytica, showing round cell infiltration. Sudan IV stain; *A*, reduced from × 300; *B*, reduced from × 800.

ejection of the pigment into the perivascular space there can occur a migration of the cells back to the area of degeneration, the cells thus acting like small transports, going back and forth.

For the compound granular cells, also, there is a specific stain because of the fat they contain, unless the cells have completely discharged their contained lipoid, a process which often requires years. Every one has seen typical compound granular cells in and about degenerated areas, years after the onset of the condition. Therefore, in a perivascular infiltration the occurrence of fat in most of the cells would point to the conclusion that the compound granular cell was predominant.

With the foregoing thoughts in mind, differential stains were made in our cases of pernicious anemia, and, as a contrast, sections from known cases of dementia paralytica were also used. As a result of our comparative study, we found that in the cases of pernicious anemia in which perivascular collections of round cells occurred, the Unna-

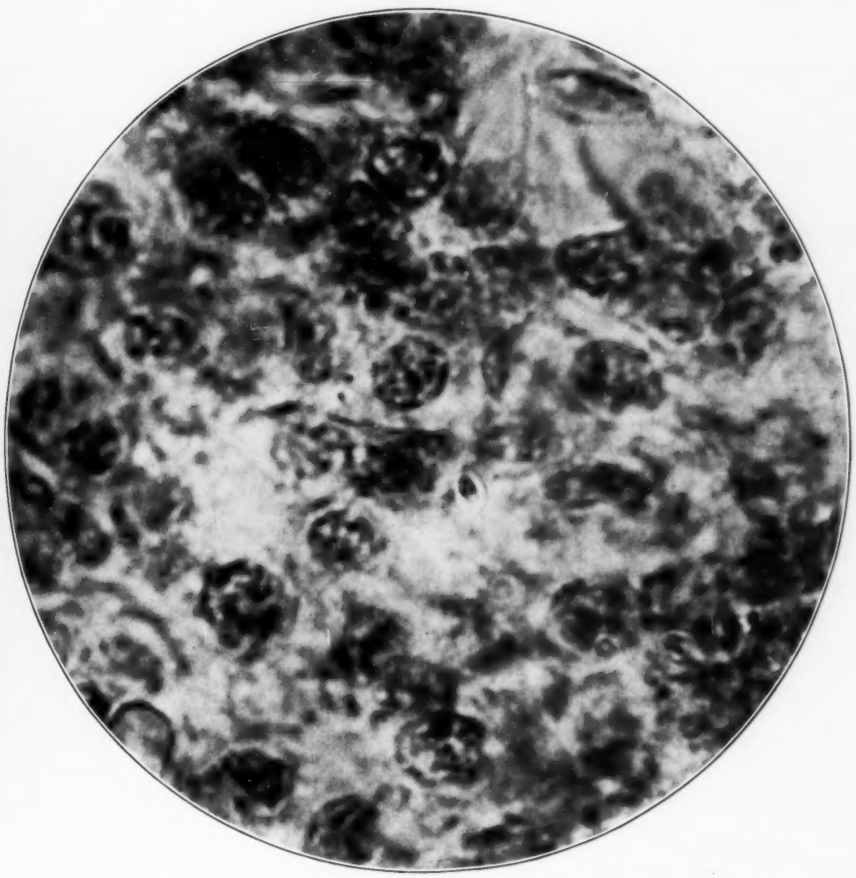

Fig. 10.—Same as figure 9, showing abundant chromatin material in the round cells, the meshes of which show angular block formations. (Compare with fig. 6.) Sudan IV stain; × 1,500.

Pappenheim preparation of adjacent sections showed no trace of plasma cells, while the sudan IV and Scharlach red gave a beautiful picture of compound granular cells (figs. 3 and 6). As shown, the perivascular space was almost filled with lipoid substance.

Our contrast preparations from cases of dementia paralytica showed excellent pictures of plasma cells with the Unna-Pappenheim method,

especially when applied to alcohol-fixed material. The lymphocytes can also be made out with this staining method (figs. 7 and 8) and can easily be differentiated from the plasma cells in that the latter have a pinkish or reddish cytoplasm and are usually somewhat larger. With the fat stains, however, especially when counterstained to bring out all the nuclear structures, one can see clearly that the perivascular infiltration is made up of both inflammatory and degenerative elements; that is, it contains numerous lymphocytes and plasma cells, as well as fat-laden compound granular cells. We know from studies of dementia paralytica that it is both an inflammatory and a degenerative disease, and both elements can be recognized in the perivascular lymph spaces. With a high magnification, the lymphocytes can be further differentiated from the compound granular corpuscles with the sudan IV and other stains. In the sudan IV sections from a case of dementia paralytica, the lymphocytes (figs. 9 and 10) do not appear as a conglomerate mass (compare with figs. 3 and 6). Furthermore, with the same and other cell stains they are more uniform, contain abundant chromatin material and show block formations (figs. 8 and 10). The compound granular corpuscles are less uniform, do not contain as much chromatin, do not show angular block formations (fig. 5) and in the fat preparations, with a higher magnification, often lose their outline and form a conglomerate mass (fig. 6).

A similar examination in cases of acute poliomyelitis showed complete absence of fat and pigment carrying compound granular cells. This disease, therefore, is purely inflammatory in the beginning.

The principles herein expressed may seem only of theoretical interest. They are, however, practical in pointing the way to a proper understanding of the basic changes in various conditions. This may serve as a clue to the etiology. It is known that acute epidemic encephalitis is an infectious disease, even though the organism has thus far escaped isolation. On the other hand, as a result of studies of its underlying pathology, Schilder's disease is recognized as degenerative.

Although one can sometimes dispense with them, the differential staining methods are much the safest guides in determining the type of cells present in the perivascular spaces.

SUMMARY AND CONCLUSIONS

1. In a study of twenty-five cases clinically and pathologically diagnosed as pernicious anemia with changes in the spinal cord twenty presented nothing unusual in the histologic pictures. These showed the typical funicular myelopathy that is characteristic of this disease.

2. In five cases there was, in addition, a perivascular round cell infiltration, mainly in the posterior and lateral portions of the spinal cord.

3. In an effort to determine whether the condition was inflammatory or degenerative, differential staining methods were used. In the cases of pernicious anemia, the majority of the perivascular cells proved to be of the compound granular cell type. In contrast to this, dementia paralytica was studied by the same methods, and the plasma cell and lymphocyte were found to be the predominating round cells. The term "small round cell infiltration" is therefore a noncommittal description of cells lying in the perivascular spaces. An effort should be made to determine the type of cell in the exudate, because it gives a clue as to the nature of the pathologic process that is going on. While it is true that degeneration is part and parcel of an inflammatory process, inflammation is not usually part of a degenerative condition.

4. We think that it is worth while to make a distinction between inflammation and degeneration; only by this distinction will it be possible to arrive at a knowledge of the basic type of change that is going on.

MYELITIC AND MYELOPATHIC LESIONS (A CLINICOPATHOLOGIC STUDY)

I. MYELITIS

CHARLES DAVISON, M.D.
AND
MOSES KESCHNER, M.D.
NEW YORK

The term "myelitis" is too frequently loosely employed to designate cases of diffuse nonsystemic disease of the spinal cord in which the pathologic process bears no relation to infection but is due to toxins, avitaminosis, vascular disease, trauma, compression and similar causes. This naturally gives rise to great confusion in regard to the classification and diagnosis of these conditions. In order to clarify this subject we reviewed the clinical histories and studied histopathologically forty-three cases of nonsystemic disease of the spinal cord (excepting multiple sclerosis) in which the cases came to necropsy. The chief aim of this study was an attempt to establish definite pathologic criteria for the classification of these cases according to the pathologic observations and to correlate them with the clinical picture and the etiologic factor at the basis of each case.

As a result of this investigation we were enabled to classify our material as follows:

Myelitis—Infection
Myelopathy
- I. Toxic
- II. Circulatory interference
  1. Vascular (arteriosclerosis, arteritis)
  2. Compression (trauma and expanding lesions)

METHOD OF PROCEDURE AND MATERIAL

Transverse sections of the spinal cord from these patients were embedded in celloidin, cut and stained by the myelin sheath (Weil modification), Mallory phosphotungstic, van Gieson, hematoxylin-eosin, Nissl and cresyl violet methods. Longitudinal frozen sections were stained by the myelin sheath (Weil modification), sudan IV, Cajal silver impregnation, Bielschowsky and victoria blue methods. In some cases sections from the brain were also studied by these methods.

In the myelitic group are included cases of myelitis in which the lesion is a true inflammatory process of the substance of the cord. Many

From the Neuropathologic Laboratory, Montefiore Hospital, New York.

Read before the Fifty-Eighth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 7, 1932.

cases of so-called "infectious myelitis" are not cases of myelitis at all, but represent a primary condition of the meninges or vessels with secondary changes in the cord which may ultimately lead to myelomalacia—a myelopathic process.

In our entire series we could find only two cases of true infectious myelitis. This is not surprising when one bears in mind that in most acute myelitides recovery occurs.

REPORT OF CASES

CASE 1. *History.*—E. B., a woman, aged 52, was admitted to the hospital on Nov. 9, 1924, with the history that in February, 1924, there developed a productive and tenacious cough, associated with general malaise, loss of appetite, occasional severe headache and nausea. In July, 1924, she complained of constant sharp pain in the left arm and weakness which gradually progressed to almost complete paralysis; in August, 1924, she noticed that her face was "screwed up" to the right.

Except for some impairment in breathing over the base of the left lung, medical examination gave negative results.

Neurologic Examination.—The left pupil was smaller than the right; both reacted well to light and in accommodation. There was a left peripheral facial palsy. There was atrophy of the left half of the tongue with deviation to the left. The uvula and the posterior pharyngeal wall were pulled over to the right. The voice was dyspneic. Laryngoscopic examination revealed paralysis of the left abductor and adductor muscles. The left trapezius and sternocleidomastoid muscles appeared wasted, and there was flaccid paralysis with atrophy of the left upper extremity. The reflexes of the right upper extremity were exaggerated, and those of the left diminished. The abdominal reflexes were not elicited. Tactile, pain and vibratory sense were diminished in the left upper extremity. There was tenderness over the upper part of the cervical spine and in the left retroparotid region.

Laboratory Data.—All laboratory examinations, including roentgen examinations, gave negative results.

Clinical Course and Diagnosis.—The patient's condition remained stationary; an acute respiratory infection developed, and she died on Nov. 18, 1924.

A clinical diagnosis of sarcoma of the base of the brain, involving the cerebral meninges, with extension to the spinal cord and syphilitic pachymeningitis was made. Anatomically, the diagnosis was that of infectious myelitis, atelectasis of the lower lobe of the left lung, bilateral pleural pericardial and diaphragmatic adhesions, chronic cholecystitis and cholelithiasis.

Necropsy.—Gross Examination: The brain showed no changes. The cervical region of the spinal cord appeared more prominent than normally. The dura and the anterior and posterior nerve roots were markedly thickened. On cutting the cervical portion of the cord, the left side was found to be large, soft and reddish. The dorsal and lumbar segments were normal.

Microscopic Examination: The brain showed perivascular infiltrations consisting of lymphocytes and plasma cells in sections through the left posterior horn of the lateral ventricle. Numerous amyloid bodies and a slight increase in glia fibers were also observed near the ependyma. Near the cornu ammonis there were collections of round cells, as well as a slight proliferating endarteritis.

In the pons, sections from the region of the fifth motor nucleus, medial and lateral lemniscus and left brachium pontis showed perivascular infiltrations. The nerve cells in this area presented degenerative changes manifested chiefly by a dense accumulation of pigment and disappearance of the Nissl substance. The pia-arachnoid in the lower portion of the pons showed a slight leptomeningitis.

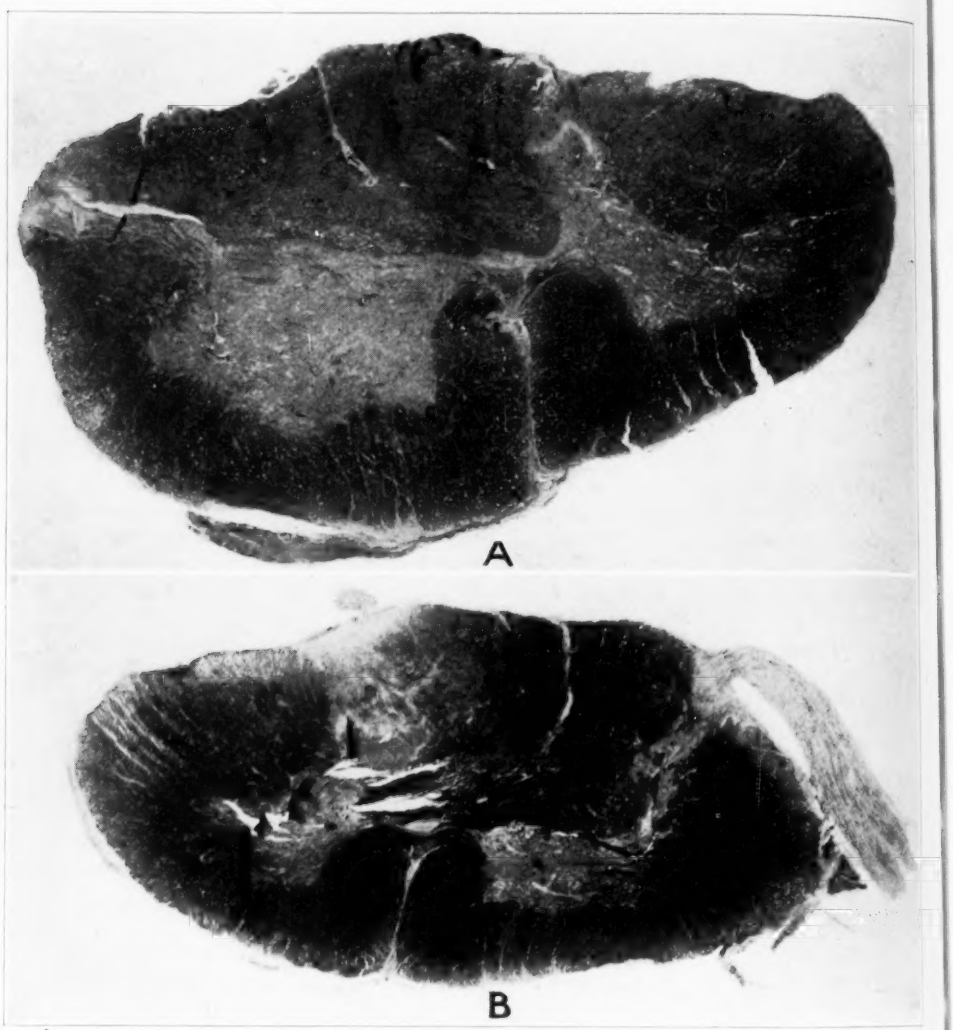

Fig. 1.—*A*, transverse section of the cervical cord, showing swelling of the entire left side and demyelinization of the left posterolateral columns. Compare the gray matter of the left side with that of the right. *B*, transverse section of the cervical cord below *A* showing a slight distortion of the contour of the cord and demyelinization of the left posterior root. Myelin sheath stain (Weil modification); × 25.

The changes in the medulla oblongata were similar to those in the pons.

Examination of the spinal cord with the myelin sheath stain showed that the left posterior and lateral columns and the left anterior horn of the cervical part of the cord were markedly distorted (fig. 1 *A*); there was partial demyelinization

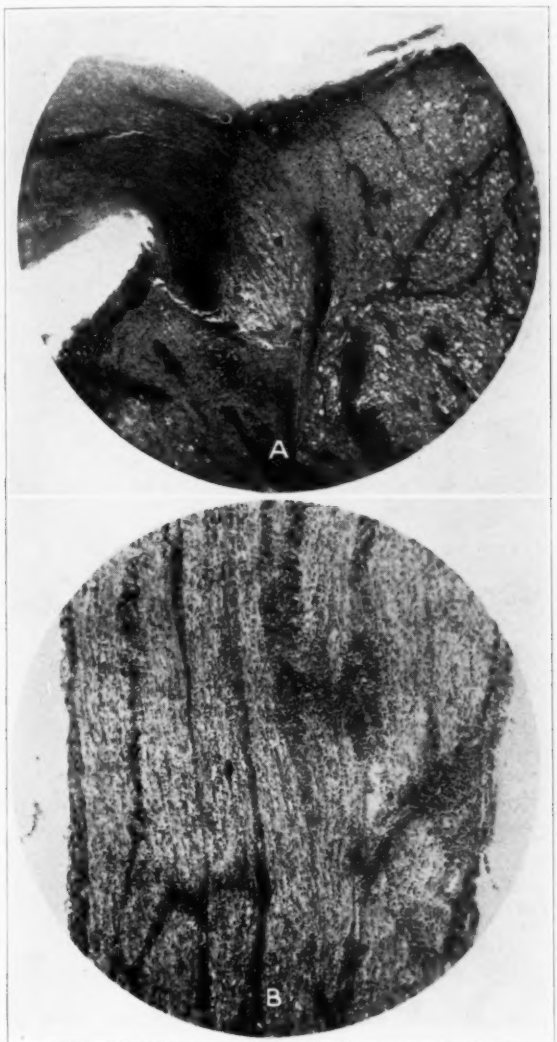

Fig. 2.—*A*, shows the posterior root, which is the seat of an inflammatory process. The infection is seen to invade the posterior horns and columns. Hematoxylin-eosin stain; reduced from × 50. *B*, mass of inflammatory cells in the posterior root. Hematoxylin-eosin stain; reduced from × 100.

of the right crossed pyramidal tract. Under a higher magnification, the myelin sheaths throughout the whole cord appeared swollen, especially in the posterior and lateral columns. Numerous areas of degeneration were found in the left

anterior horn, left posterior column and the left crossed pyramidal tract. The upper posterior nerve roots on the left side were also demyelinated (fig. 1 *B*). With the hematoxylin-eosin stain, the pia-arachnoid appeared somewhat thickened and infiltrated by round and plasma cells. The left posterior nerve roots consisted of a mass of inflammatory cells (fig. 2 *A* and *B*), which invaded the left posterior

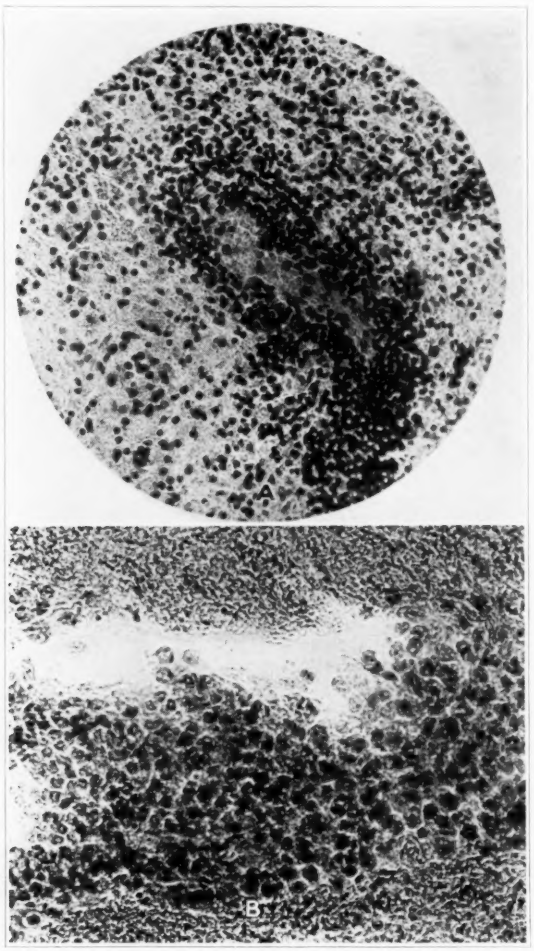

Fig. 3.—*A*, shows the perivascular infiltration consisting of lymphocytes, plasma and endothelial cells. Hematoxylin-eosin stain; reduced from × 240. In *B* it is noted that the round cells in the perivascular spaces do not contain fat as seen in compound granular corpuscles when stained with sudan IV stain; reduced from × 480.

horns and, to a lesser extent, the posterior columns and crossed the pyramidal tract on the left side (fig. 2 *A*). These cellular masses were clustered chiefly around the vessels and consisted of lymphocytes, plasma and endothelial cells, and a few glial elements (fig. 3 *A*). With the sudan IV stain, it was evident that the peri-

vascular infiltration did not consist of compound granular corpuscles but of round cells (fig. 3 *B*). The right side of the cord showed slight evidences of inflammation. With the Nissl and cresyl violet stains the left anterior horn cells were markedly swollen, with eccentrically situated nuclei; the tigroid bodies were replaced by fine granules and pigment (fig. 4 *A* and *B*). With the Cajal and Bielschowsky stains (fig. 5 *A*) longitudinal sections in the involved area showed disintegration of most of the axis cylinders, the few remaining ones having a corkscrew appearance. With the Mallory phosphotungstic stain there was seen a poor glial response (fig. 5 *B*) in the inflammatory areas.

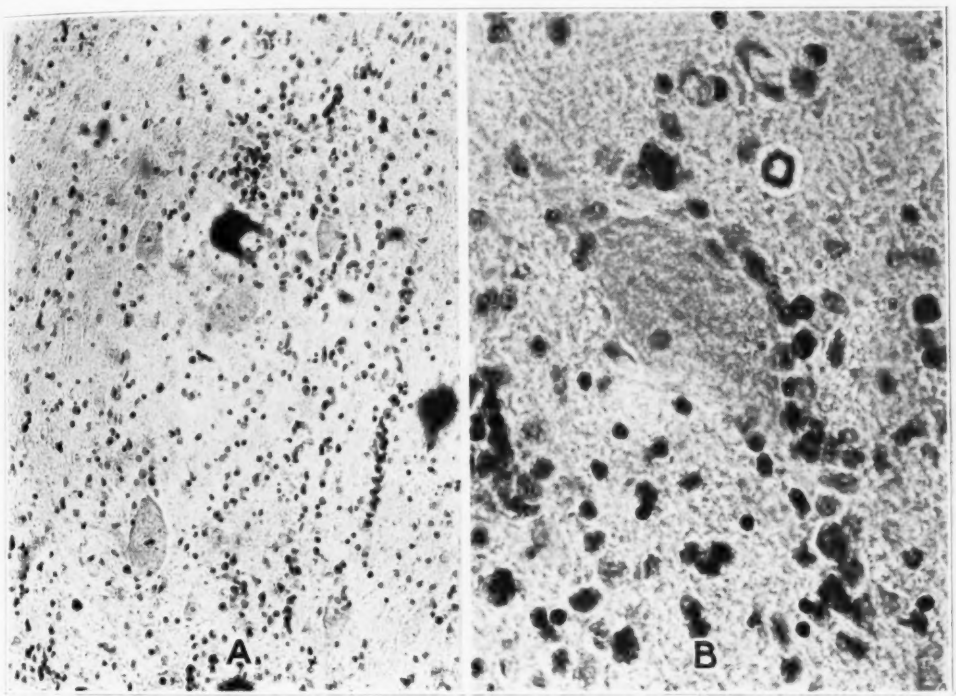

Fig. 4.—*A*, anterior horn cells from the left gray matter in the stage of acute swelling. Cresyl violet stain; × 120. In *B*, notice complete loss of Nissl substance, loss of nuclear membrane and eccentrically placed nucleus (same as fig. 4 *A*); × 600.

Comment.—This case is one of a disseminated inflammation of the neuraxis. The presence of lymphocytes and of plasma and endothelial cells points definitely to an inflammatory process. The histopathologic changes in the posterior nerve roots together with the inflammatory reaction in the posterior column and gray matter are in favor of an infection traveling along the posterior nerve roots, which finally invaded the spinal cord.

The microscopic diagnosis was encephalomyelitis disseminata of unknown etiology.

CASE 2.—*History.*—A. C., a man, aged 41, was admitted to the hospital on Aug. 17, 1929, with the history that in January, 1929, pulmonary tuberculosis had developed. In July, 1929, his legs became weak, and shortly thereafter complete paraplegia and loss of sphincteric control occurred; two weeks before admission there appeared paresthesias and pains in the lower extremities.

Examination.—Medical examination on admission revealed marked emaciation, with physical signs of bilateral fibrocaseous pulmonary tuberculosis and cavitation.

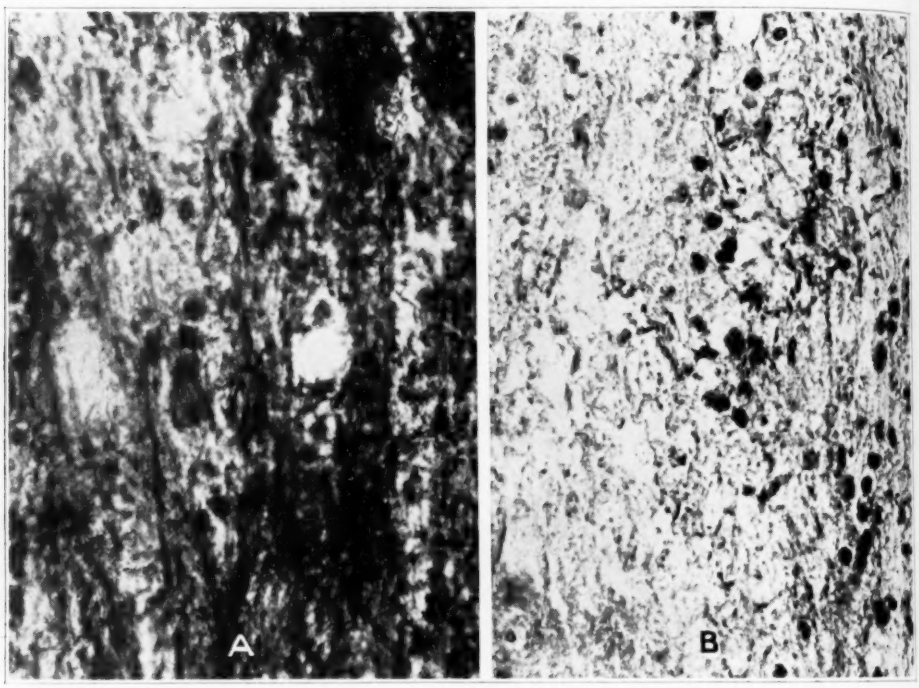

Fig. 5.—*A*, longitudinal section from the inflammatory area showing marked destruction of the axis cylinders. Bielschowsky stain; reduced from × 400. *B*, longitudinal section from the inflammatory area, showing poor glial response. Mallory phosphotungstic stain; reduced from × 400.

Neurologic examination showed: flaccid paraplegia with bilateral pyramidal tract signs in both lower extremities; analgesia and marked hypesthesia below the twelfth dorsal segment, more so on the right, and thermhypesthesia, more marked on the left; loss of vibration from the toes to the hips, with marked impairment of the postural sense in the toes, ankles and knees; tenderness over the upper dorsal spinous processes; loss of sphincteric control.

Laboratory Data.—Except for the presence of tubercle bacilli in the sputum and secondary anemia, all laboratory observations were negative. Spinal puncture revealed no block.

Clinical Course and Diagnosis.—Cystopyelitis developed and the patient died on September 23.

A clinical diagnosis of chronic bilateral pulmonary tuberculosis, tuberculous cervical adenitis, compression myelitis in the lower thoracic region and chronic cytopyelitis was made. Anatomically, the diagnosis was that of multiple tuberculomas of the spleen, kidneys, right suprarenal, cervical and mesenteric lymph nodes and the spinal cord.

Necropsy.—Gross Examination: At about the ninth thoracic segment of the spinal cord, on the anterior surface, there was a firm oval nodule, 2.5 by 1 cm., freely movable in the subarachnoid space for a distance of about 5 cm. On section, this nodule was found to be yellowish green. Below the ninth dorsal segment the pia-arachnoid was adherent to the cord; from this area down to the lumbar region the cord appeared mushy.

Microscopic Examination: Sections of the spinal cord from the tenth dorsal segment to the second lumbar segment with the myelin sheath stain showed complete destruction of the anterolateral columns which were replaced by a typical tuberculoma (fig. 6 *A*). Remnants of the posterior columns, consisting of some destroyed myelin and accumulations of numerous compound granular corpuscles and tubercles (fig. 6 *B*), were observed on the posterolateral surface of the tuberculoma. Conglomerations of round and plasma cells were also found in the vicinity of the blood vessels and the tubercles. The changes on the inferior surface of the tuberculoma were similar to those on the posterolateral surface, though less marked. The posterior surface of the cord was distorted and under a higher magnification showed a definite honeycombed appearance. The myelin sheaths had undergone various degrees of destruction. Most of the gray matter was destroyed, and the few remaining nerve cells were slightly swollen. It is striking that these few anterior horn cells were so well preserved. Sections immediately above the tuberculoma showed unusual distortion of the cord, markedly thickened meninges, demyelinated nerve roots and ascending degeneration of the posterior columns. Longitudinal sections stained by the victoria blue and Bielschowsky methods revealed a poor glial response and destruction of the axis cylinders similar to that in case 1.

A microscopic diagnosis of transverse myelitis and tuberculoma was made.

Comment.—Histologically, this case was one of a tuberculoma in the cord proper and an inflammatory process on its posterolateral surface. The case could also perhaps be included in the group of cases of compression of the cord, but is discussed here because the mode of infection was definitely hematogenous. That the tuberculoma was part of the spinal cord proper is evidenced by: (1) its destruction of the anterior half of the cord; (2) the freedom with which it could be moved in the subarachnoid space, and (3) its confluence with the posterolateral surface of the cord (fig. 6). We are inclined to believe that the inflammatory process was due to tubercle bacilli which invaded the spinal cord at its lower dorsal level, probably through the anterior spinal artery. The presence of tuberculomas in other organs of the body is additional evidence that the pathologic process in the spinal cord was hematogenous in origin. For these reasons the case is designated as infectious trans-

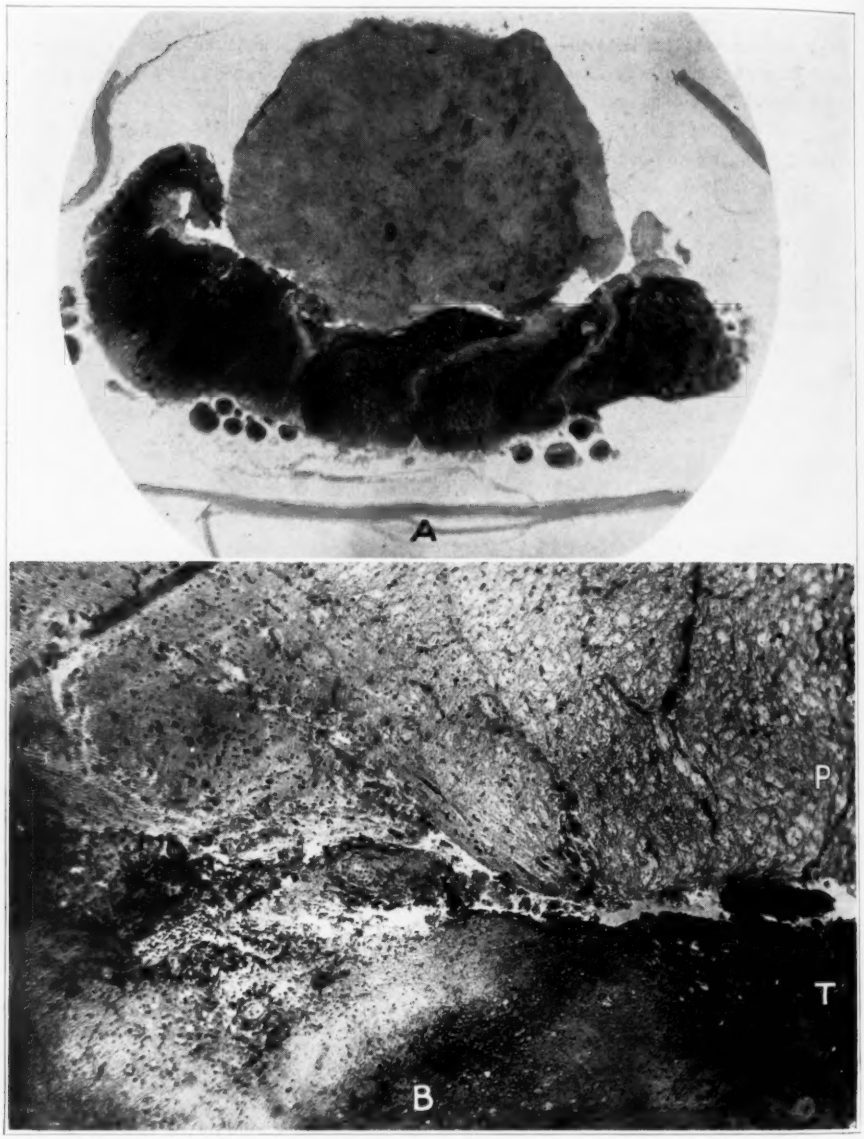

Fig. 6.—*A*, transverse section of the cord showing complete destruction of the anterolateral columns by the tuberculoma. Myelin sheath stain (Weil modification); × 30. *B*, posterolateral surface of cord (*P*) invaded by the inflammatory process, a tuberculoma (*T*). Hematoxylin-eosin stain; reduced from × 70.

verse myelitis and a tuberculoma. Several observers, recently Doerr [1] and Bassoe,[2] have emphasized that tuberculomas of the cord are usually due to infection by way of the blood stream.

Undoubtedly, some secondary changes in the cord occurred as a result of compression by the tuberculoma, but the effects of this were minimal as compared with those of the inflammatory lesion in the posterolateral surface of the cord.

GENERAL COMMENT

The literature contains reports of cases of myelitis which are said to have been due to: chickenpox, smallpox, measles, whooping cough, diphtheria, malaria, scarlet fever, various forms of streptococcic or staphylococcic infection, gonorrhea, syphilis, poliomyelitis and Landry's paralysis. The clinical observations in these cases, however, do not always conform to the pathologic observations. In many of them the etiologic factor may have been an infective organism which attacks mesodermal structures (blood vessels and meninges) but rarely the cord proper.

In myelitis, the changes in the cord are definitely inflammatory; that is, a response on the part of the polymorphonuclear leukocytes, plasma and endothelial cells. Later the process changes to an infiltration of round and plasma cells. According to Pette [3] and others, plasma cells are indicative of an inflammatory process; in their absence the infiltrative foci should be investigated with special stains, such as sudan IV or Unna-Pappenheim stain, in order to determine the character of the round and plasma cells. For this differentiation, the reader is referred to another communication by one of us (Davison).[4]

Infectious micro-organisms may produce lesions of the cord indirectly by invading the vessel walls and producing vascular obstruction and circulatory interference, with ultimate destruction of the substance of the cord. This process is similar to that seen in infarctions; that is, the lesion in the cord is not inflammatory in nature, a myelitis, but is a destructive process, a myelopathy.

So far as we know, except in tuberculosis and syphilis, bacteria have not been demonstrated in most of the cases diagnosed clinically

1. Doerr, C.: Zur Kenntnis der Tuberkulose des Rückenmarks, Arch. f. Psychiat. **49**:406, 1912.

2. Bassoe, P.: Conglomerate and Combined Degeneration of the Cord as Complication of Viscerol Tuberculosis, Arch. Int. Med. **21**:519 (April) 1918.

3. Pette, H.: Infection und Nervensystem, Zentralbl. f. d. ges. Neurol. u. Psychiat. **54**:111, 1929.

4. Winkelman, N. W., and Davison, C.: Subacute Combined Degeneration of the Spinal Cord, A Study of the Underlying Pathologic Process, Arch. Neurol. & Psychiat., this issue, p. 517.

as infectious myelitis. The occasional finding of micro-organisms has been reported by many observers, but a survey of these reports shows that the micro-organism recovered from the cord was not the same as that found in the spinal fluid or in the blood stream.

Several observers have attempted to produce myelitis in animals by injecting micro-organisms into the spinal cord. A careful study of the reports of these experiments shows that most of the changes consisted of diffuse softenings of the white and gray matter, with alterations in the ganglion cells; in very few instances was there a semblance of an inflammatory reaction. The trauma to the cord and the technical difficulties, especially as to asepsis, must be taken into consideration in the evaluation of these experiments. The hyperemia and hemorrhages found in these cords may also have been due to trauma, for it is well known that any traumatized tissue may react by the production of inflammatory cells. It is also noteworthy that very few of the animals showed the infective organism in the cord. This may have been due perhaps to the fact that in most of them the organisms did not invade the cord proper, or, if they did invade it, they were immediately destroyed, so that the lesions found were due to the effects of the toxins of these organisms on the blood vessels. Another factor to be taken into consideration is that in most cases of myelitis decubitus and cystitis sooner or later develop, with resulting secondary infection of a previously diseased cord. For these reasons, reports of streptococcic and staphylococcic infections of the spinal cord must be carefully scrutinized if not wholly disregarded. Furthermore, great caution is necessary in evaluating the results obtained from experimental work on animals and applying them to man, unless the experiments are carried out in higher apes.

Most observers believe that when direct infection of the spinal cord does occur, the pathologic process is a disseminated one. Occasionally, such a process may produce a level lesion as the outstanding clinical feature in the case. This was true in one of our cases (case 1), in which there was some clinical evidence of dissemination of the inflammatory process, although the brunt of the lesion was found in the cervical region.

It is conceivable that a considerable number of cases of transverse or of disseminated forms of true myelitis end in recovery, so that there is no opportunity to determine pathologically the nature of the process. When the latter is not too far advanced and the infective organism does not remain in contact with the spinal cord for too long a period, the chances for recovery are favorable. When the infective organism, however, remains in contact with the cord for a longer period, the pathologic changes are more permanent, and the chances for recovery are correspondingly less favorable.

True myelitis may, in some cases, be due to an ascending process in which the infection travels from the periphery by way of the nerves and roots (as in one of our cases, case 1) to the cord. This has been substantiated experimentally in rabies and poliomyelitis, in which the noxious agents responsible for these diseases were injected along the peripheral nerves and were found to reach the cord. In rabies the affected segments of the cord corresponded to the nerve roots into which injections had been made.

So-called "myelitis" during the puerperium or following abortions has been attributed by many observers to an infection which reached the cord by way of the blood stream; in most of these cases the lesions were embolic.

It would seem, therefore, that a true "myelitis" due to bacterial invasion of the cord proper is a relatively rare condition. Confusion in both nomenclature and classification can readily be avoided by adhering closely to the pathologic criteria of inflammation and limiting the term "myelitis" to cases in which the pathologic process is in the cord proper and predominatingly inflammatory and not degenerative.

SUMMARY

1. Two cases of acute disease of the spinal cord illustrating inflammatory reactions of the cord are reported.

2. The condition in case 1 was a disseminated infectious process of unknown etiology, and that in case 2 an inflammatory process due to a tuberculous infection of the cord proper.

3. A critical review of the literature would seem to show that acute "myelitis" due to bacterial invasion of the cord is a relatively rare condition.

4. The term "myelitis" should be limited to cases in which the pathologic process is in the cord and predominatingly inflammatory and not degenerative.

NERVE DEGENERATION IN POLIOMYELITIS

VI. CHANGES IN THE MOTOR NERVE ENDINGS

HERMAN CHOR, M.D.
ST. LOUIS

The special predilection of the virus of poliomyelitis for the large anterior horn cells of the spinal cord is a well established and generally accepted feature of this disease. The cytopathologic changes occurring in these cells have been reviewed frequently. In the earlier papers of this series by O'Leary, Heinbecker and Bishop,[1] the changes in nerve fibers resulting from the action of the poliomyelitis virus have been described from both the histologic and the physiologic point of view. The lesions in the muscles have frequently been investigated, and the results have been reviewed by Kopits.[2] The status of the motor nerve endings received passing comment by him to the effect that in the specimens of paralyzed muscles studied no endings were demonstrable. Whether or not such findings imply their absence or a failure of the staining technic to reveal them, Kopits was unable to determine. It was the purpose in this study to investigate the changes in these motor nerve end-organs—the most peripheral portions of the lower motor neuron involved in poliomyelitis—and to ascertain if possible whether they are primary, being caused directly by the local action of the virus, or secondary to injury of the cells originating in the cord.

MATERIAL

The material used was obtained through the courtesy of Dr. E. V. Cowdry. Young Macacus rhesus monkeys served as the source. The muscles selected were principally the biceps and triceps brachii, the interossei and lumbricales of the hand and the gastrocnemius, soleus, tibialis anticus, quadriceps femoris, biceps femoris and small muscles of the foot. For the study of the normal motor nerve endings, specimens of muscles were obtained from healthy animals.

For an experimental control, studies on the degeneration of motor end-plates were carried out through nerve section experiments. These were performed in

---

From the Anatomical Laboratories, Washington University School of Medicine.

This study was conducted with the aid of a grant from the Milbank Fund for the Study of Infantile Paralysis and the Rockefeller Foundation to Washington University for Research in Science.

1. O'Leary, J. L.; Heinbecker, P., and Bishop, G. H.: Nerve Degeneration in Poliomyelitis: IV. Physiologic and Histologic Studies on the Roots and Nerves Supplying Paralyzed Extremities of Monkeys During Acute Poliomyelitis, Arch. Neurol. & Psychiat. **28**:272 (Aug.) 1932.

2. Kopits, I.: Beiträge zur Muskelpathologie, Arch. f. Orthop. u. Unfall-Chir. **27**:277, 1929.

such a manner that a series of specimens demonstrating different stages of the degeneration was obtained. Thus, the sciatic and femoral nerves in the lower extremities and the three primary cords of the brachial plexus of the upper extremities were severed. This procedure was carried out so that an interval of twelve hours or so was allowed between the operations, each animal accordingly being operated on four times under light ether anesthesia. In this manner a series of muscle specimens was obtained with nerve endings in stages of degeneration of forty, fifty, seventy-two, eighty-four and one hundred hours.

For the study of the changes in the nerve endings in poliomyelitis material was plentiful. Thus, when a standardized virus originally obtained from Dr. Simon Flexner was used, the animals were found to become ill regularly, the condition starting with tremors and incoordination on the sixth or seventh day following intracerebral inoculation. On the following day paralysis was usually present. A series of specimens of muscles was obtained so as to include the following stages:

1. Tremor stage (incoordination, no true paralysis)
2. Paralysis (one day)
3. Paralysis (two to three days)
4. Paralysis (three to four days)
5. Paralysis (four to five days)
6. Paralysis (five to six days)
7. Paralysis (six to seven days)
8. Paralysis (two months)
9. Paralysis (five months)

To discover whether the virus could be made to act locally on the nerve endings, four monkeys were inoculated intramuscularly, massive doses of a 5 per cent virus emulsion being used so as literally to saturate the muscle fibers with their motor end-plates. The inoculations were performed in such a way that 15 cc. of the virus was distributed throughout the muscles of the left foot, followed after twenty-four hours by 15 cc. more distributed throughout the muscles of the leg, and twenty-four hours later by a third injection saturating the muscles of the thigh. Multiple punctures were used, and the needle was moved about in order to traumatize some of the muscle tissue. An emulsion of normal monkey brain distributed in a similar manner was employed as a control. The virus was tested by intracerebral inoculation of two monkeys as controls; at the same time two other monkeys were inoculated intraneurally in the sciatic nerve.

Twenty-four hours after the third intramuscular inoculation, one of the animals was killed, and specimens of muscle were obtained from the left foot, leg and thigh. These contained motor nerve endings which had been in contact with virus seventy-two, forty-eight and twenty-four hours, respectively. The left sciatic nerve was removed under sterile precautions at this time and ground into an emulsion with saline solution. This emulsion was injected intracerebrally into another monkey in order to determine the presence or absence of active virus.

Seven days after the last of the intramuscular inoculations another monkey treated in the same way was killed, its sciatic nerve was employed as a test virus and its muscles were obtained for the examination of nerve endings in a manner similar to the procedure just described. The factor of incubation period was allowed for in the second animal. The remainder of the monkeys inoculated intramuscularly were kept under observation for four weeks.

All virus used in these experiments was tested by intracerebral inoculation and found potent in every instance.

METHOD OF OBTAINING SPECIMENS AND TECHNIC OF STAINING

In obtaining specimens the following procedure was used: The animal to be killed was etherized and bled from the heart. The skin was reflected from the muscles selected, and as much fascia as could be hurriedly removed was stripped from them. Too much time, however, was not consumed in this step, because postmortem changes occur rapidly, and the presence of fascia does not interfere with the staining. The muscles were removed from their attachments and immediately cut transversely into pieces about 1 cm. in length. A modified Ranson's silver-pyridine procedure was employed, the specimens being treated as follows:

1. Placed in a fixing solution consisting of ammonia water (28 per cent, Merck), 1 cc., and alcohol (95 per cent), 99 cc., for twenty-four hours.

2. Washed for one-half hour in distilled water.

3. Placed in full strength pyridine for forty-eight hours.

4. Washed thoroughly in eight changes of distilled water over a period of twenty-four hours.

5. Placed in silver nitrate solution (2 per cent) for seventy-two hours and kept in a dark place at room temperature.

6. Reduced in pyrogallic acid solution:

Pyrogallic acid	4 Gm.
Distilled water	95 cc.
Solution of formaldehyde	5 cc.

This reduction was carried on for from six to eight hours or overnight.

7. Dipped in water, and then immediately in 95 per cent alcohol. After being in the alcohol for a few seconds, each specimen was placed on a glass slide so that the longitudinal markings of the muscle fibers were visible. Another slide was placed on this surface, and the specimen was squeezed between the slides. Only moderate pressure was necessary. Irregular edges were cut off with a sharp knife, and neat, trim, flat blocks were secured. These blocks were placed in 95 per cent alcohol for thirty minutes.

8. Placed in absolute alcohol—two changes—and left overnight for thorough dehydration.

9. Placed in xylol for from ten to twelve hours until the blocks are clear.

10. Embedded in paraffin for eight hours, with repeated changes every hour for the first five hours.

11. Cut in serial sections, 10 microns thick.

12. Mounted in neutral balsam.

By this method the nerves were colored a dark brown or black, with the muscle and connective tissue yellow, which gave a contrast satisfactory for study and photography. Supravital staining with methylene blue (Hines and Tower [3]) and also with neutral red (Forkner [4]) was attempted by perfusion through the femoral artery. Gold chloride methods were used as recommended by Miller,[5] with fair

3. Hines, M., and Tower, S. S.: Studies on the Innervation of Skeletal Muscles of Muscle Spindles in Certain Muscles of Kittens, Bull. Johns Hopkins Hosp. **15**:269, 1928.

4. Forkner, E. C.: Supra-Vital Staining with Neutral Red, J. Exper. Med. **52**:379, 1930.

5. Miller, Charles: Note on Demonstration of Motor and Sensory Nerve Endings, Anat. Rec. **25**:77, 1923.

results, as was also a combined silver-gold method recommended by Rogers, Pappenheimer and Goettsch.[6] Although these procedures occasionally gave brilliant results, they were not constant enough for detailed study of so large a series of specimens.

OBSERVATIONS

Structure of Normal Motor End-Plates in Macacus Rhesus.—In the study of the intramuscular portion of the somatic motor innervation, the presence of medullated nerve fibers is striking. Coursing along in the interfascicular connective tissue these nerves show an elaborate branching as the muscle fibers are approached. One sees a nerve fiber giving off terminal branches to three or more end-plates which may be situated on the same muscle fiber or on adjacent muscle fibers (fig. 3). The terminal nerve elements which eventually enter the muscle fiber are single nerve fibers consisting of axon and medullary sheath with their finer components. The entrance usually is made at the tapering end or pole of the muscle fiber, although occasionally one sees a termination at the middle of the fiber (fig. 1). On entrance the medullary sheath fuses with the sarcolemma, allowing the naked axis cylinder to enter the muscle fiber substance. In doing so this axon ramifies, giving rise to the telodendrion, or end-brush, so characteristic of the motor nerve endings (fig. 2). This ramification may be elaborate, with the participation of numerous neurofibrils with their finer twigs, or it may be very simple, with the formation of a "clawlike" structure.

On closer examination of this ramification the presence of varicose or knoblike expansions can be made out at the extreme terminals. In many instances the finest neurofibrils are seen to form end-loops or ringlets, which are striking in appearance. This so-called end-brush, with the aforementioned terminal buds and loops, lies embedded in a layer of granular protoplasm which is collected in a small mass at the place of the nerve ending. In this protoplasm are numerous vesicular nuclei. This structure, the "sole," forms a more or less distinct elevation on the side of the muscle fiber, described many years ago by Doyere and hence called Doyere's elevation (fig. 1). Thus the so-called motor end-plate is composed of two main parts: (1) the ramification of the axis cylinder, and (2) the granular sole plate with its nuclei.

On high magnification one may see, in sections especially well stained, a very fine and more or less granular reticulum extending from the finest twigs of the neurofibrils. That this fine structure is the "periterminal network of Boeke"[7] is highly probable, although the exact relationship to the myofibrils was difficult to ascertain.

Degeneration of Motor Endings Following Nerve Section.—The changes that occur in the motor endings are characteristic. Thus, until the end of the first day practically all the endings present a normal structure, and the muscle responds to an electrical stimulation of the nerve. During the second day, however, noticeable structural changes are seen (fig. 8). These are ushered in with the appearance of irregular round or oval thickenings which appear on the arborization of the axon. After forty hours, these knob-shaped enlargements are evident and seem to stain more deeply than the more central portion of the fiber. The latter, however, begins to exhibit some irregularity, with swellings and narrowings along its course and a lack of uniformity in staining characteristics.

---

6. Rogers, W. M.; Pappenheimer, A. M., and Goettsch, M.: Nerve Endings in Nutritional Muscular Dystrophy in Guinea Pigs, J. Exper. Med. **65**:167, 1931.

7. Boeke, J.: The Innervation of Striped Muscle, Brain **44**:1, 1921.

After fifty hours, pathologic changes are much more obvious (fig. 9). The neurofibrils of the telodendrion begin to fragment, and the swollen reticulated terminals and loops lose their identity. In their place are numerous irregularly staining particles. The axon shows advancing irregularity in contour, with further lack of uniformity in staining properties. Its medullary sheath also begins to show alterations in the form of tortuous swellings, giving an appearance of

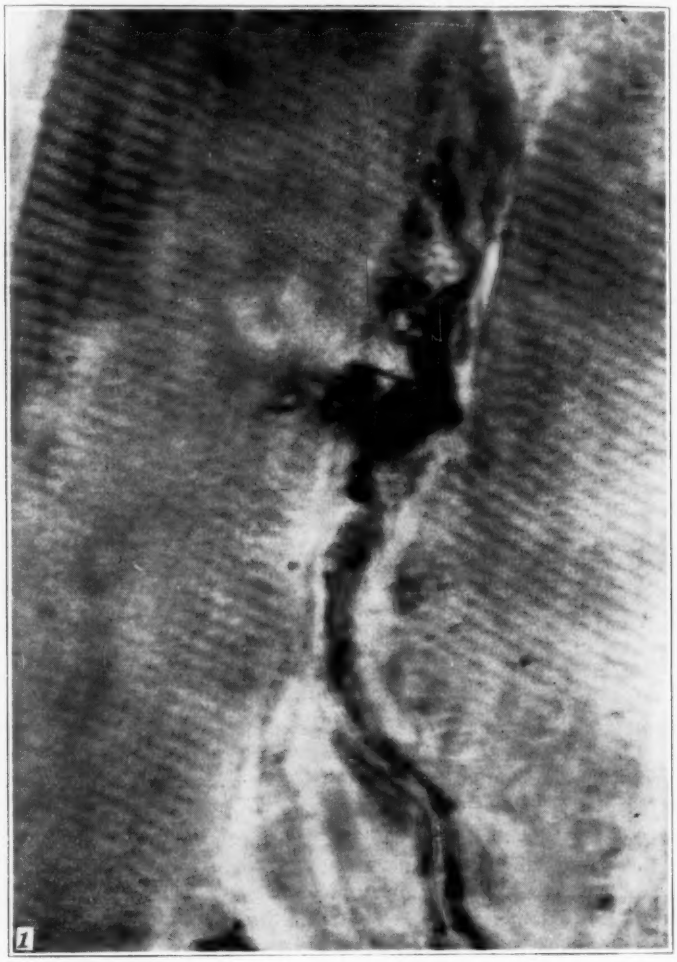

Fig. 1.—Lateral view of motor end-plate, showing a single nerve filament entering the striated muscle fiber and forming an elaborate end-brush, or telodendrion. This lies embedded in a layer of granular protoplasm containing numerous vesicular nuclei—the "sole"—which forms an elevation on the side of the muscle fiber called Doyere's elevation. Magnification, × 1,800.

segmentation. This change is much more pronounced at the extreme distal portion than in the larger nerve trunk, although minor irregularities can be observed all along the motor nerve fiber.

At seventy-two hours, the hypolemmal portion of the ending is broken up into a granular strand. The neurofibrils are no longer recognizable as such. The button-like endings and the characteristic loops or ringlets have disappeared, their places being taken by particles, some of which stain deeply. Eventually they all lose their staining properties, as the granules break down further and absorption begins. In this stage the more central parts of the axis cylinders show an elaborate

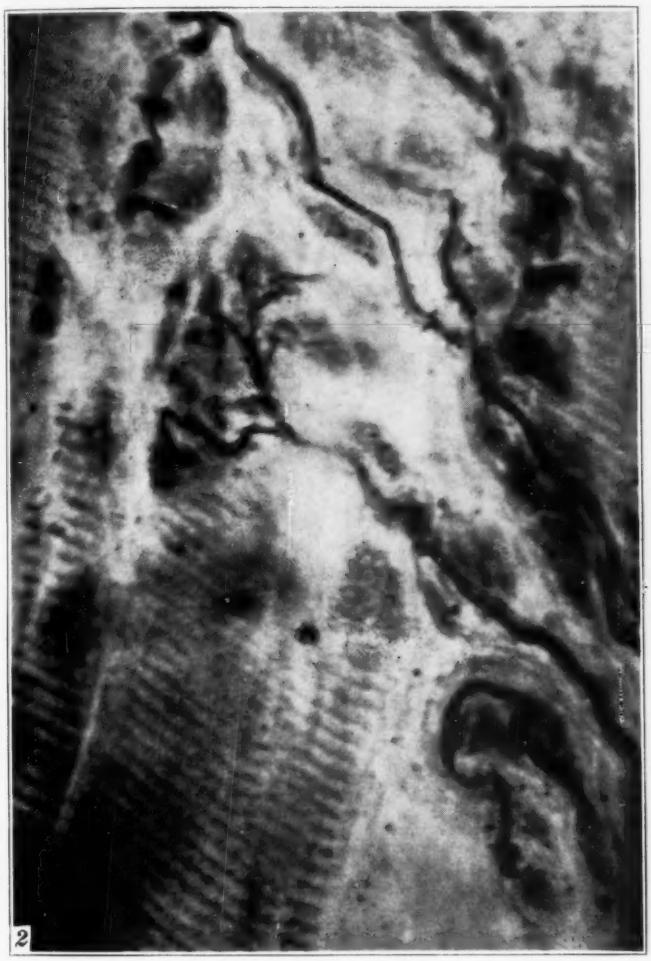

Fig. 2.—Ramification of axon on the sole plate of the muscle fiber. The neurofibrillar twigs end in knoblike expansions or end-loops. Vesicular nuclei of the sole can be seen under the neurofibrillar twigs. Magnification, × 1,800.

fragmentation, with a corresponding mosaic of gradations in staining. The medullary sheaths of such fibers seem to have lost their individual membranes and to have coalesced with adjacent fiber sheaths so that in the cross-section of a nerve bundle a characteristic picture is presented with irregularly shaped and variously

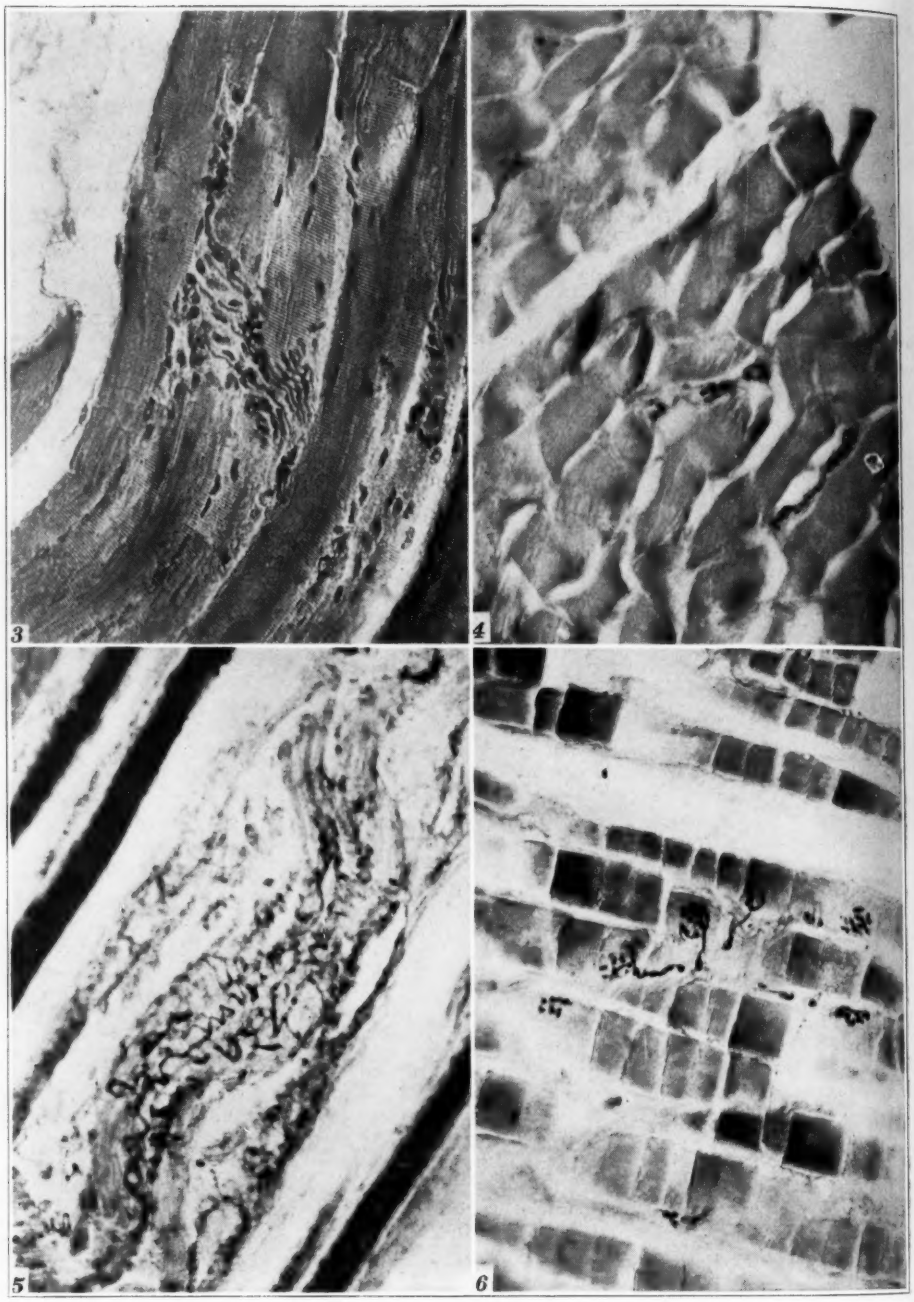

Fig. 3.—Nerve giving off branches to three adjacent muscle fibers. The sole plate nuclei are very prominent on the middle fiber. Magnification, × 280.

Fig. 4.—Cross-section of muscle bundle showing hypolemmal position of nerve endings. Magnification, × 280.

Fig. 5.—Muscle spindle showing elaborate sensory innervation—the spiral organ of Ruffini—in contrast to motor end-organ. Magnification, × 280.

Fig. 6.—Group of motor endings on adjacent muscle fibers showing characteristic branching of telodendrion. Magnification, × 280.

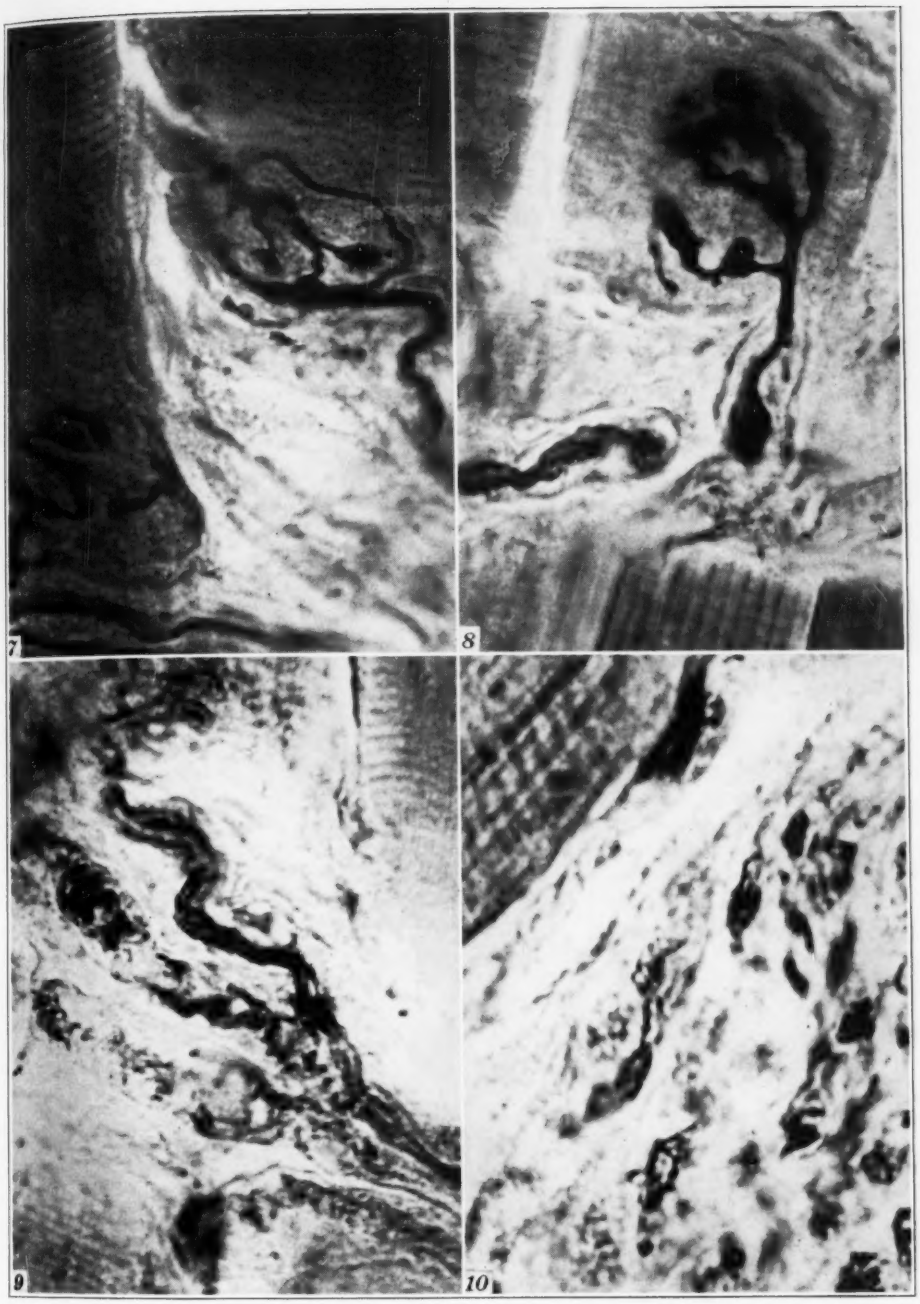

Fig. 7.—Normal motor endings showing distinct and regular outline of axon filament with knoblike terminal expansions. The outline of the granular sole plate and its nuclei forms the background. Magnification, × 1,800.

Fig. 8.—Earliest evidence of degeneration of the motor nerve ending (first day paralysis). Note deeply staining, irregular, oval thickenings on the arborization of the axon, with beginning swelling of the axon proper. Magnification, × 1,800.

Fig. 9.—Later stage in degeneration—fragmentation of the neurofibrils. End-knobs and ringlets are no longer present. The axon is breaking up to form granular strand (second to third day). Magnification, × 1,800.

Fig. 10.—Remnants of motor nerve endings—irregularly staining particles and granular débris replacing the axon terminals (third to fourth day). Magnification, × 1,800.

stained axon fragments embedded in a more or less homogeneous mass of degenerated myelin.

At eighty-four hours, only remnants of motor endings are visible as granular débris (fig. 10). Shells of the fibers, consisting essentially of connective tissue elements, can be distinguished. Here and there occasional structures are seen which retain their staining properties and suggest persistence of some nerve endings. These are to be noted even after one hundred hours, when there is practically no trace of endings on the majority of the muscle fibers.

As to the status of the sole plate following nerve section, a careful study has failed to reveal much information; the same is true of the periterminal network of Boeke. With the fragmentation of the neurofibrils, the granular débris interferes with the picture presented by these finer structures.

Pathologic Changes in Motor Nerve Endings in Experimental Poliomyelitis.—With the earliest appearance of tremors and incoordination (usually from six to seven days following intracerebral inoculation), examination of the motor nerve endings fails to reveal perceptible changes. On the following day, however, when definite paralysis is present, alterations are evident. The terminal twigs and their loops and knoblike endings appear swollen and stain darkly. Their finer characteristics, so clearcut in the normal state, can no longer be detected. This condition, however, is not present in all the end-plates, for scattered abundantly throughout the sections are entirely normal looking terminals, while some endings show changes indicating severe damage. This disparity will be discussed later.

After two days of paralysis, the irregularity of the terminals with their swollen knobs and buttons becomes more pronounced, and the nerve fiber begins to show some alteration in its margins, with evidence of irregular swelling of myelin and axon. In these specimens also one sees well preserved endings as well as the earliest changes corresponding to a one day paralytic stage.

The three day picture shows a decided alteration in the appearance and in the staining properties of the endings. The telodendrion has started to fragment, with irregularly staining particles replacing the terminal twigs, loops and buttons. Boeke's periterminal network can no longer be differentiated. The formation of a hypolemmal granular strand is already under way, and the fibers show an increase in the degree of swelling and irregularity, which is especially marked in the axon. The myelin, too, is swollen, and segmentation can be observed.

By the fourth day, the hypolemmal portion of the ending has become entirely granular and stains poorly. The process of fragmentation has advanced centrally, and the medullated fibers appear broken throughout the axon (figs. 11 and 12). The medullary sheaths are irregular and swollen, and there seems to be destruction of their limiting membranes with resulting coalescence of adjacent fibers.

After five days, remnants of end-plates can be recognized through the presence of granular débris, although by this time absorption of the most severely damaged endings has already taken place (fig. 13).

Two month and five month paralytic specimens exhibited occasional elaborate regeneration forms (fig. 14). These consisted of fine, deeply staining filaments, irregularly disposed along the muscle fibers, eventually terminating in the persisting sole plates. These newly formed elements later take on the structure of the specific motor end-organ.

Results of Experiments on Direct Action of Virus on Motor Endings.—Of the four monkeys inoculated intramuscularly, typical poliomyelitis developed in one, M 365. On the tenth day following the last injection of virus, tremors were noted in the left lower extremity where the inoculations had been received, with sluggishness and incoordination. By the twelfth day, paralysis of this extremity

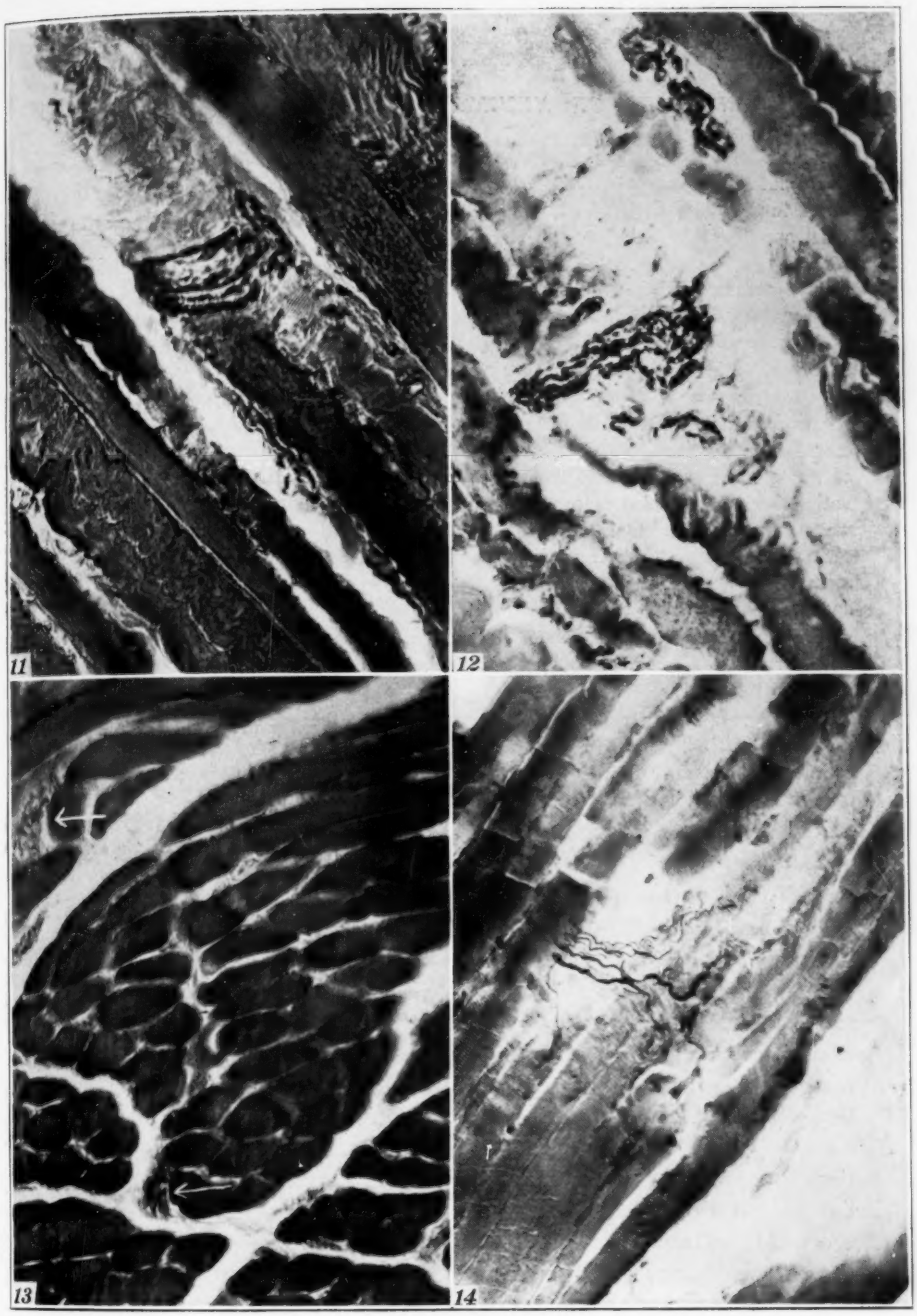

Fig. 11.—Fragmentation of motor nerve terminals following nerve section (fifty hours). Magnification, × 280.

Fig. 12.—Intramuscular nerve fibers showing fragmentation. The changes in these more proximal portions of the nerves are not so severe as those in the distal segment (nerve section, seventy-two hours). Magnification, × 280.

Fig. 13.—Cross-section of paralyzed muscle showing nerve terminals in advanced stages of degeneration—only remnants are seen (poliomyelitis, third to fourth day). Magnification, × 280.

Fig. 14.—Regeneration form of motor nerve ending. Note the fine filaments traversing the muscle fibers and ending in delicate branches which eventually will take on the structural characteristics of specific end-organs. Magnification, × 280.

occurred. On the following day, the right leg was involved, and twenty-four hours later the upper extremities, the monkey becoming prostrate. It was then killed for examination. M 312 was killed seven days after the last inoculation, in what appeared to be the preparalytic stage, in order to obtain specimens of muscle showing nerve endings which had been in direct contact with the virus, before the cell bodies to which such endings belonged were involved. M 369 had severe diarrhea and died from general weakness within two weeks following inoculation, without having shown evidence of paralysis. M 364 showed evident muscular weakness with a rise in temperature and some general reaction, but did not present a true picture of poliomyelitis within four weeks following inoculation.

Examination of the motor nerve endings of M 312, following intramuscular inoculation, revealed poorly staining nerve terminals, but no characteristic alteration of the specific structure—no fragmentation of neurofibrils or axons. Such observations were noted also in control specimens which had been in contact with normal brain emulsion. Only occasionally was a damaged ending to be seen, probably owing to trauma at the time of inoculation. It was not until there was evident injury to the anterior horn cells, as shown in M 365, that degenerative changes appeared in the nerve endings.

Nerves taken from the extremities which had been inoculated intramuscularly with virus failed to induce poliomyelitis when injected as emulsion intracerebrally into two monkeys.

In the two monkeys inoculated intraneurally in the sciatic nerve poliomyelitis failed to develop. Specimens of muscle obtained at biopsy (muscles innervated by the sciatic nerve) failed to show histologic evidence of primary action of virus on the nerve endings, indicating centrifugal transmission.

COMMENT

In poliomyelitis, the changes observed in the motor nerve endings were found to be histologically similar in many respects to those following section of the nerves, with this significant difference: After section, all the end-plates suffer alike with the single exception that occasionally some endings seem to retain elements of their original structure even after several days. In poliomyelitis, on the other hand, a striking feature is the lack of such uniformity. Apparently normal endings can be seen in the same group of muscle fibers with severely degenerated ones. Scattered throughout the muscle are numerous end-plates in various stages of destruction. Such observations are probably explained by the variation in degree of damage to the anterior horn cells which represent the trophic centers of the endings. Histologic examination of the anterior horns at a given level showed cells in various stages of degeneration—some completely destroyed and represented by mere shadows and others apparently little involved, with intermediate stages of degeneration shown by still others.

In addition to this factor of unequal involvement of anterior horn cells as a possible explanation of the differences in the reactions of the endings following section and the action of the poliomyelitis virus, there is the physiologic factor of plurisegmental innervation of musculature of the limbs. This feature was recognized very early in studies of the

motor nerve endings by Agduhr,[8] who corrected the old idea of segmental representation of muscle fibers and the notion that each muscle fiber was innervated by but one motor ending. Floresco and Cavalie demonstrated the multiplicity of motor endings on striated muscle fibers. More recently, Aycock,[9] in a study of the relation of plurisegmental innervation to recovery in infantile paralysis, remarked: "Although the muscular areas involved in the paralytic process have been more or less closely associated with the lesions in corresponding segments of the cord, this cannot be said to have been worked out in sufficient detail to permit an accurate correlation between the varying degrees of cell injury and the several grades of severity which are observed in the paralysis which results."

It has been noted that the alterations in the nerve cells in the early phases of the disease are sufficient to explain the paralysis resulting in the musculature of the limbs (Covell[10]). Oscillographic studies of the nerve trunks at this time reveal increased irritability (O'Leary and his associates), although clinically the muscles are paralyzed. The changes in the nerve endings reported in this paper support Covell's observations. It is true, however, that even during the first two or three days of paralysis electrical stimulation of the proper nerve roots and peripheral nerves produces some response in the group of muscles innervated. This response becomes weaker and absent in later stages (from four to ten days).

The motor nerve ending is known to be the site of primary attack in several diseases, as for instance, tetanus,[11] botulism[12] and beriberi.[13] In tetanus[14] and beriberi[13] this is supported by histologic evidence, with changes noted as being characteristic of primary involvement of this structure in contradistinction to those observed following section of the motor nerves. As already described, the termination of the motor

8. Agduhr, E.: Morphologischer Beweis der doppelten (segmentalen) motorischer Innervation des einzelnen quergestreiften Muskelfasern bei den Saügetieren, Anat. Anz. **49**:1, 1916.

9. Aycock, W. L.: The Relation of Plurisegmental Innervation to Recovery in Infantile Paralysis, Science **60**:85, 1924.

10. Covell, W. P.: Nerve Degeneration in Poliomyelitis: V. Correlation in Fiber Changes in Nerves with Cellular Changes in the Spinal Cord, Arch. Neurol. & Psychiat. **28**:1056 (Nov.) 1932.

11. Meyer, H., and Ransom, F.: Researches on Tetanus—Preliminary Communication, Proc. Roy. Soc., London **72**:26, 1903.

12. Cowdry, E. V., and Nicholson, F. M.: An Histological Study of the Central Nervous System in Experimental Botulinus Poisoning, J. Exper. Med. **39**:827, 1924.

13. Woolard, H. H.: The Nature of the Structural Changes in Nerve Endings in Starvation and in Beri-Beri, J. Anat. **61**:498, 1927.

14. Kura, N., and Kamesawa, S.: Changes in Nerve Endings Due to Tetanus Toxin, Tr. Jap. Path. Soc. **18**:330, 1928.

nerve fiber in the sole plate of the muscle fiber is in the nature of a naked axon. Theoretically, this should offer a special opportunity for the entry of poliomyelitis virus, as the myelin, supposed to be an insulator against virus, stops at the sarcolemma.

The fact that in one of four monkeys inoculated intramuscularly typical poliomyelitis developed (verified by histologic examination of the lumbar region of the cord) implies that in the peripheral tissues is available some avenue favorable for invasion by the virus. Just what constituent of the musculature serves as the site of entry, however, is difficult to establish. Histologic examination of the motor nerve endings in the "preparalytic" stage does not reveal evidence of primary damage here. When paralysis occurs, changes can be observed. But by this time there is destruction of the anterior horn cells, which is always associated with demonstrable alteration in the structure of their terminals, in accordance with the wallerian doctrine. A careful study of many specimens failed to yield any structural evidence to support a hypothesis of primary action of the virus on the motor end-organs.

CONCLUSIONS

1. The motor nerve endings of Macacus rhesus monkeys have structural characteristics common to other mammals, with slight variations in finer details, such as an elaborate terminal branching and abundance of neurofibrillar end-loops and buds.

2. Following nerve section, degenerative changes occur which are evident by the end of twenty-four hours. These are ushered in by irregular swelling and staining of the fine terminal twigs of the neurofibrillar end-brush. By the second day, fragmentation of the neurofibrils appears, and the axon and myelin sheath outside the muscle fiber show irregularities in contour and in staining qualities. After the third day, the ending is replaced by a granular strand which goes on to complete absorption, and the more proximal portions of the motor nerves show advanced fragmentation of axons and segmentation of myelin. Subsequently, only remnants of nerve endings can be made out, although occasional persisting neurofibrils are encountered.

3. In poliomyelitis in the preparalytic stage the motor nerve endings appear normal, but with the onset of paralysis perceptible changes occur. These changes, associated with the appearance of muscle weakness and advancing through the various stages of paralysis, are identical in most respects with those observed after section of the nerves. The distinguishing feature, however, is the lack of uniformity in the degree of damage displayed by the endings at any given time in contrast to the uniformity found following section. This may perhaps be explained by the unequal involvement of the anterior horn cells in poliomyelitis and also by the plurisegmental innervation characteristic of striated muscle.

4. Direct contact of motor nerve endings with the virus of poliomyelitis (as implied by saturation of muscles with the virus) failed to produce perceptible histologic changes sufficient to indicate primary involvement.

5. These findings lead to the conclusion that the changes in the motor endings observed in experimental poliomyelitis are secondary to primary damage of the anterior horn cells.

DISCUSSION

DR. W. LLOYD AYCOCK, Boston: Dr. Chor presents a minute study of the various steps in the essential lesion of poliomyelitis.

In his experiments in which the nerve trunk was cut, if he used botanical terms he would have a good description of what happens to the leaves when a limb is cut from a tree, even though the "lesion" is far removed from the leaves. In his experiments on poliomyelitis he similarly pictures the changes that take place in the leaves and the limb of a tree when it is partially broken down by ice, for example. Even though some of the earliest changes may be seen in what one might call the more tender nerve endings, as he points out, it does not necessarily follow that the nerve ending is the seat of the primary damage.

It is to be hoped, in view of the recent demonstration of the selective vulnerability of certain nerve cells to certain chemicals, such as orthotricresol phosphate in jamaica ginger poisoning, that a continuation of studies such as Dr. Chor's will shed some light on the selective vulnerability of nerve cells to the virus of poliomyelitis.

DR. WILLIAM H. HARRIS, New Orleans: Since receiving Dr. Chor's manuscript and excellent illustrations about two weeks ago, I have read it two or three times, and have studied the photomicrographs carefully. In general, discussions consist of a series of compliments, of exceptions or of constructive criticisms. I am pleased to agree with my predecessor, Dr. Aycock, that in the instance of Dr. Chor's work there seems little to add except compliments.

Dr. Chor's work is carefully carried out and properly controlled. The only feature concerned is the number of animals employed. Although the series is small, it seems apparent that a more extensive survey will elaborate on his findings and aid in the minute differentiation of very virulent invasions as compared with those in which there has been lesser injury. His results, therefore, appear convincing.

In the local inoculations of the virus in which Dr. Chor has saturated the muscle structure and has permitted various periods to elapse before taking specimens for study, including the period of incubation of seven days, one must, of course, appreciate that the virus is not remaining in situ, and that much of it is being absorbed in the lymphatic and blood routes. Nevertheless it is reasonable to suppose that, because of his massive injections, if there was any local activity of the virus, it would be likely to occur in such an area.

Dr. Chor apparently sees no changes in the sensory nerve endings of the local areas of injection. One wonders, in connection with poliomyelitis, whether the sensory nerve fibers might form to a considerable extent the route of infection of the virus. In the intranasal inoculations, there occur a large number of positive results. In this instance, the olfactory bulb or special sense organ forms the intake. In the intracerebral injections sensory nerve fibrils are also involved.

It is interesting to compare involvement of the nerve endings with that seen in the spinal cord. In the spinal cord there is cellular infiltration throughout both the motor and the sensory tracts, and, on the other hand, only the motor nerve cells are injured; similarly, in the terminal area, Dr. Chor reports marked involvement of the motor endings without apparently any involvement of the sensory nerves after the disease has been induced and the primary site involved.

It is plausible that there might occur a centrifugal invasion of the virus without demonstrable injury of the conveying factors, and the morbidity and mortality of the anterior horn cells might produce a process of wallerian retrogression of the nerve with extensive injury to the motor nerve terminal organs. My only experience in this field has been the transmission of the disease from animal to animal, with observations on the possible cultivation of the virus together, of course, with the routine histopathologic study.

I should like Dr. Chor to discuss the matter of regeneration of the motor nerve termini, and if possible to bring out their relationship to convalescence and function. I think this is an important point. In other words, at times these areas are sick but not dead.

Dr. George B. Hassin, Chicago: I have had no special experience with the normal histology or pathology of nerve endings, and for this reason I cannot add much to what Dr. Chor has said.

I was interested in one phase of the problem. In discussing degeneration it is imperative to point out also the accompanying degenerative phenomena. Some authorities, such as Spatz, claim that even in degeneration of the central nerves there is an attempt at regeneration, and I was glad to hear Dr. Chor point out that in the degeneration of the endings of nerve fibers there is also some regeneration in evidence. I should like to ask him how one is to differentiate between a young regenerated nerve and an ordinary terminal nerve fiber. In a degenerated peripheral nerve stem it is difficult to differentiate between the two types of fibers, a regenerated one and a normal thin fibril. How did Dr. Chor make such differentiation in his work?

Another point that I should like to ask about is, what is the reaction, if any, of the tissues surrounding the degenerated nerve endings?

Dr. Walter Freeman, Washington, D. C.: The correlation that Dr. Chor presents of the unequal involvement of the muscle end-plates with the unequal involvement of the anterior horn cells is excellent. However, the segmental innervation of muscles seems to have been pretty well worked out, emphasizing the relation to the segments of the spinal cord rather than that to the spinal roots. A certain myelomere innervates the corresponding myomere by way of an indefinite number of roots. The cells in the anterior horns of the spinal cord are in definite relationship to the muscle fibers involved, but the roots are variable and unimportant factors in the architecture.

Dr. Herman Chor, St. Louis: Regarding the regeneration form of motor nerve endings, the studies of Boeke, Huber and Langley have been the basis for my recognition of such new forms. Their appearance "as an exuberance of delicate nerve fibrillae" in contrast to the typical normal nerve ending picture is striking. Furthermore, it was only in the muscles of animals paralyzed for from two to five months that such forms were seen. It is difficult to interpret them to mean anything but the regeneration form.

As to the question of plurisegmental innervation of striated muscle, a survey of the literature reveals the fact that it is extremely difficult to correlate studies of nerve endings with anterior horn cell representation of peripheral musculature. I am unable to offer any further assistance in this problem.

Clinical Notes

ABSCESS AND THROMBOSIS OF THE SUPERIOR LONGITUDINAL SINUS

Clinicopathologic Report of a Case

GEORGE B. HASSIN, M.D., CHICAGO

Professor of Neurology, College of Medicine, University of Illinois; Attending Neurologist Cook County Hospital

The longitudinal (sagittal) sinus is the most conspicuous of the dural venous channels which gather the blood from the cerebral veins for final elimination through the internal jugular vein. Being only a part of the vast system of venous sinuses, its obstruction may not affect intracranial circulation as a whole but, depending on the fundamental cause, may indirectly involve the brain tissues. These phases, namely, the possible involvement of the cerebral parenchyma by an obstruction of a sagittal sinus and the histologic changes in the sinus itself, are the subject of the present paper.

REPORT OF CASE

History and Course.—A colored man, aged 51, entered the ear, nose and throat service of the Research Hospital of the University of Illinois on July 1, 1929, because of severe pain in the occiput and a mastoid infection, to which he succumbed on Nov. 11, 1930. During the sixteen months of illness, the patient was under constant medical care in the hospital and as a dispensary patient, and from the voluminous record only the most important features will be noted.

In May, 1929, after a "cold," pain developed in the "right side of the head." On July 1, 1929, a right linear mastoidectomy was performed, after which a soft fluctuating swelling developed over the right mastoid process, which was very tender.

In September, 1929, optic neuritis was found, and a week later another mastoidectomy was performed. Pus was located, from which Streptococcus mucosus was isolated.

On Nov. 23, 1929, an abscess cavity was discovered in the right temporal region. The original incision was opened, and the patient was discharged.

On Dec. 5, 1929, 300 cc. of pus was removed from a bulging scalp.

On Dec. 17, 1929, "nearly the entire scalp over the occipital region was loosened."

On Jan. 3, 1930, an incision was made into a fluctuating area in the right side of the neck, and drainage was established.

On Sept. 5, 1930, there were "fluctuating masses and swellings" over the right mastoid; the temperature was elevated; there was pain in the joints and in the

---

From the neuropathology laboratories of the College of Medicine, University of Illinois.

Read by title at the fifty-eighth annual meeting of the American Neurological Association, Atlantic City, N. J., June 8, 1932.

occipital and temporal regions; loss of 30 pounds (13.6 Kg.) in weight had occurred in three months.

On Nov. 8, 1930, two incisions were made in the scalp, and a considerable amount of pus was expressed. Three days later, a subaponeurotic abscess was detected and the patient was prepared for the drainage of the abscess, but he died on the table just after administration of an anesthetic had been started.

At no time did neurologic examination reveal any changes; the speech, cranial nerves, coordination and sensibility showed nothing abnormal. There were no hemianopia and no signs of meningeal involvement; the fundi showed an optic neuritis, which probably was due to a general infection and not to an abscess. Against the latter was also the marked leukocytosis. No change was present in

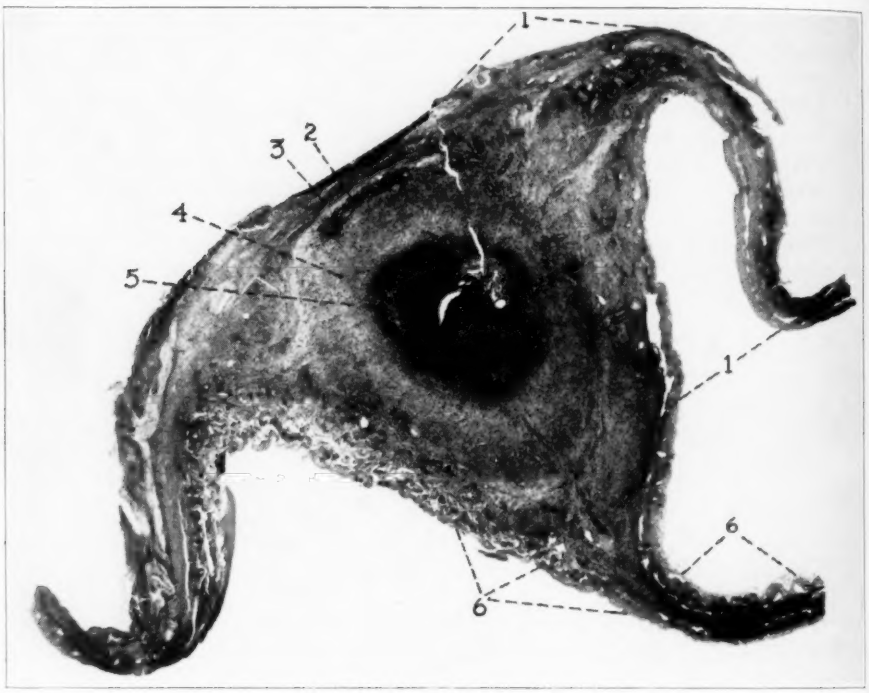

Fig. 1.—Transverse section of the sagittal sinus: (1) the outer surface of the dura; (2) an island of the abscess (the large, black, oval mass in the center is the main abscess); (3) elastic fibers, separating the dura from (4) the connective tissue ring below; (5) a dense, dark ring of plasma cells investing the abscess; (6) arachnoid under which (to the left) the dura is folded. Van Gieson stain.

the visceral organs. The temperature usually ranged between 100 and 102 F.; the pulse rate was between 99 and 100.

Laboratory Data.—The average count of the red cells was 4,750,000, and of the white cells, 16,950; on Dec. 5, 1930, the white cells numbered 21,400, and once the count was 34,750. A differential count revealed: lymphocytes, 10 per cent; polymorphonuclears, 84 per cent, and large mononuclears, 6 per cent. Chemical examination of the blood showed: sugar, 82 mg. per hundred cubic centimeters of blood, and carbon dioxide, 62 cc. per hundred cubic centimeters of plasma.

Bacteriologic examination revealed nonhemolytic, gram-positive streptococci, single and arranged in short chains. Cultures showed Streptococcus mucosus.

The spinal fluid was clear, contained 8 cells per cubic millimeter and no albumin or globulin and gave a negative Wassermann reaction.

Necropsy (Dr. Milles).—There were: thrombosis of the sagittal and lateral dural sinuses, which drained externally through the mastoid wound; abscess of the scalp; focal areas of osteoporosis in the skull, and concentric hypertrophy and brown atrophy of the heart, with moderate fibrosis.

The clinical and gross changes may be summarized as follows: invasion of the lateral and sagittal sinuses of the dura by a streptococcus infection from the right

Fig. 2.—Organized thrombus of the sagittal sinus. At *1* is seen the outer layer of the dura with numerous lacunae (light vacuoles); at *2*, an elastic fiber separating the thrombus from the thickened dura (better seen with a magnifying lens); at *3*, villi of the arachnoid and the subarachnoid space below.

mastoid process, with formation of abscesses and a subsequent thrombosis of the frontal end of the sagittal sinus.

Microscopic observations: Further studies of the dura and brain after delivery to the laboratory showed that the external surface of the dura was fairly smooth and clean; the inner surface facing the arachnoid was folded in some places (fig. 1), and over the falx cerebri it was thickened. In the thrombosed area the dura was covered by pacchionian bodies which could be traced almost to the thrombus, from which the dura was separated by a thin band (fig. 2).

A section through the sagittal sinus showed its triangular shape and the abscess by which it was obliterated. It consisted of polymorphonuclear cells which were mixed with histiocytes and, as figure 3 shows, contained immense masses of blood vessels (*V.V.* in fig. 3). These were mostly patent, were often obliterated by enormously hyperplastic and thickened walls (*B.V.* in fig. 3) and were always surrounded by large masses of plasma cells and fibroblasts. The former often appeared as dark nests in specimens stained with the method of van Gieson, and the latter, the fibroblasts, as huge cell bodies (fig. 4). Large histiocytes are indi-

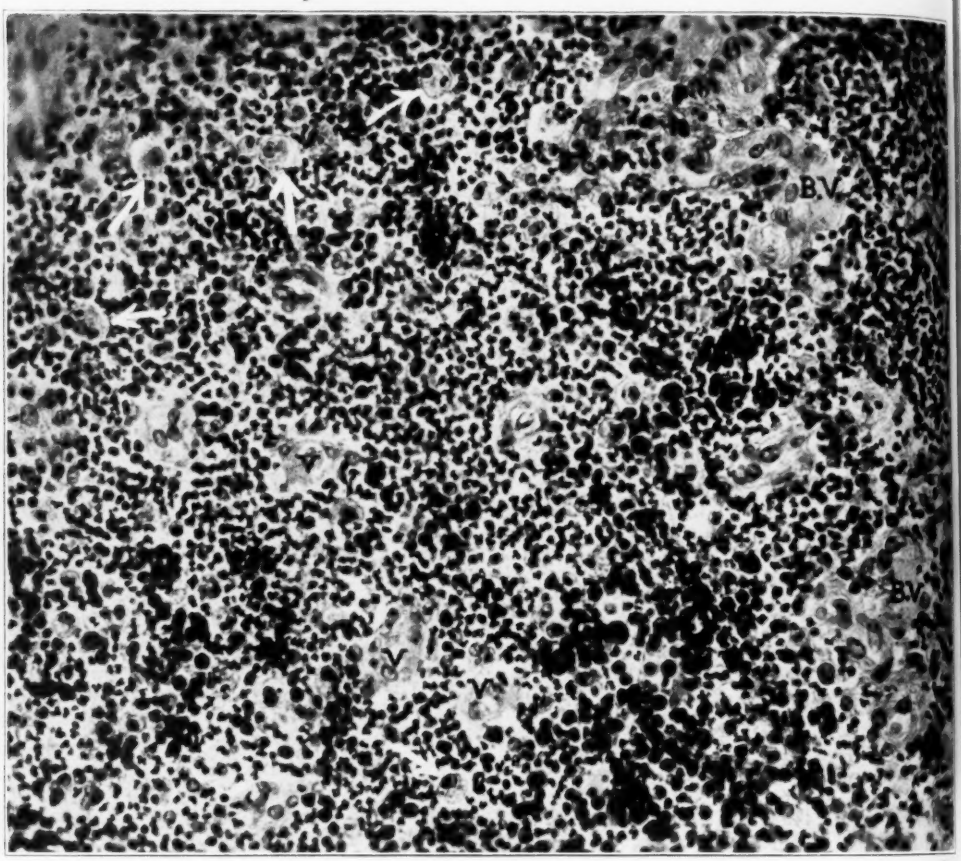

Fig. 3.— *V.V.V.*, indicates blood vessels; *B.V.*, blood vessels with thick, hyperplastic walls. The arrows indicate histiocytes; the black masses are plasma cells. Scattered among the foregoing structures are numerous polymorphonuclears. Van Gieson stain; × 240.

cated in figure 3 by arrows; they show as honey-combed bodies, some containing large vacuoles harboring dead lymphocytes, broken up polymorphonuclear cells or an amorphous substance. The nearer to the periphery of the abscess, the less numerous became the polymorphonuclears, and the more numerous became the histiocytes and plasma cells. At the extreme periphery of the abscess the plasma cells formed a dense, dark ring (fig. 1). Between this and the hyperplastic dura

or falx was another, much broader and lighter ring, which in the picture is indicated by *4*. It was sharply limited and consisted of plasma cells, histiocytes and fibroblasts, scattered among numerous collagen fibers of connective tissue. The same elements were in evidence throughout in the adjacent dura, where they filled the interspaces among the fibers. When stained with scarlet red, numerous fat granule bodies (gitter cells) were seen in the abscess, the surrounding ring and the dural interspaces (fig. 5), as if streaming from the former toward the dura.

In figure 1, at the top, indicated by *2*, a small, dark, longitudinal island is present. It possesses a structure somewhat similar to that of the abscess and is reproduced under a higher magnification in figure 6. It is somewhat better organ-

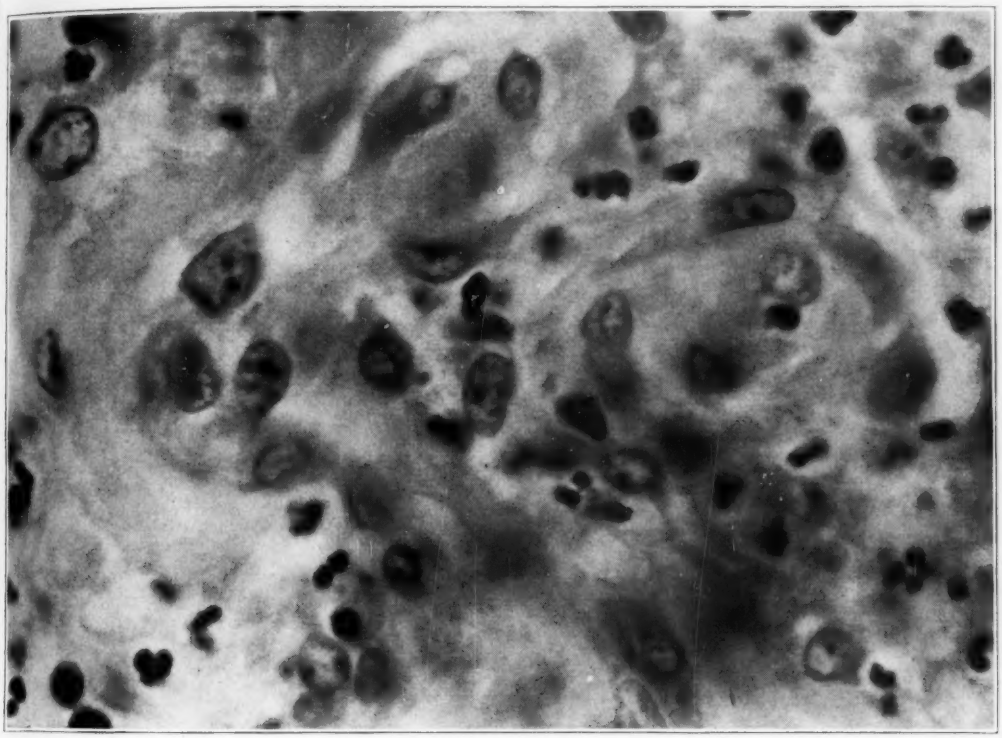

Fig. 4.—Huge fibroblasts and collagen fibers among which are scattered single polymorphonuclears. Van Gieson stain; reduced from × 1,100.

ized, representing a more advanced stage than that seen in the abscess. One may assume that the abscess of the longitudinal (sagittal) sinus originally extended to the borders of the outer ring and included the island, from which the abscess became separated when it grew progressively smaller. It shrank from the activity of the plasma cells, histiocytes, fibroblasts and collagen fibers. All these structures can be seen in figure 3, in which the dark masses mentioned before are those of plasma cells and are also pictured in figure 6. To the right (fig. 6) is a blood vessel which exhibits hyperplastic walls, also similar to those pictured in figure 3 (*B.V.*), while the huge fibroblasts can be seen in figure 4 and the bundles of connective tissue fibers formed by them can be seen encroaching on the island which

they gradually transform into what is seen in figure 2, that is, an organized, connective tissue thrombus.

The thrombus occupied the frontal portion of the sagittal sinus. The larger portion of it was adherent to the dura (fig. 2), and with the help of a magnifying lens one can see a thick, elastic fiber dividing the dura from the thrombus. The upper part of the thrombus contained a few empty spaces resembling similar vacuoles in the dura, where they are known as lacunae (fig. 2, *1*). In the thrombus, they were bordered by fibroblasts and were probably tissue spaces that did not become sufficiently contracted as did the rest of the thrombus and thus remained open. Some of the empty spaces harbored minute blood vessels; some contained

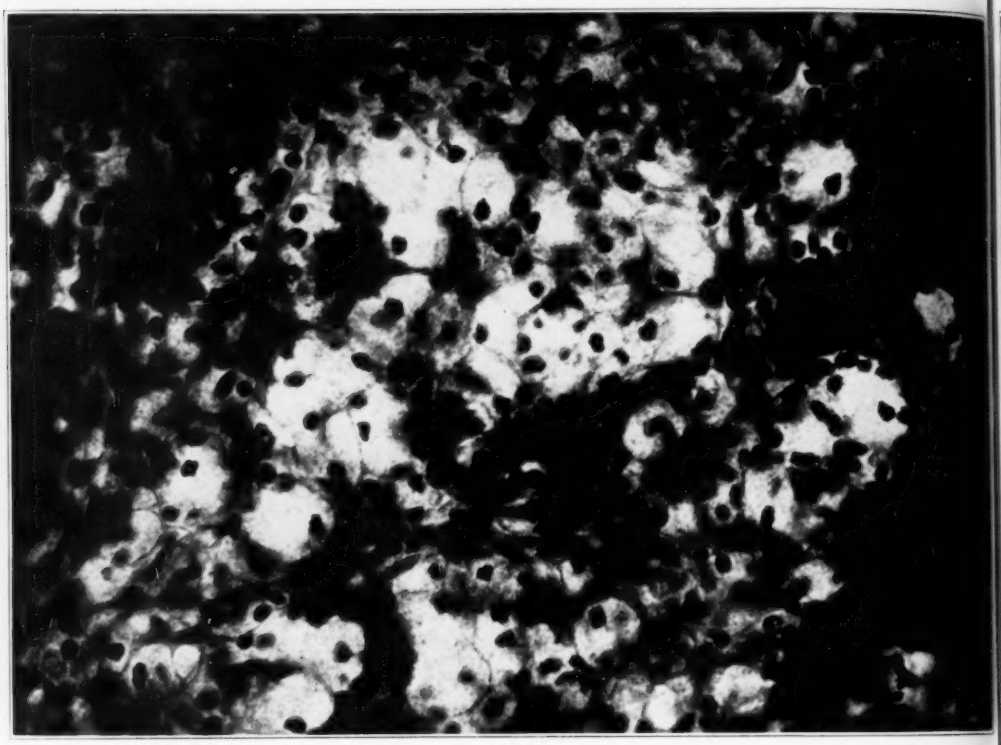

Fig. 5.—Gitter cells in the interspaces of the dura. Van Gieson stain; reduced from × 500.

hemorrhages, but the majority were filled with fibroblasts, plasma cells and gitter cells which were laden with fatlike substances. In general the entire structure resembled that of the dura.

The outer layers of the dura showed nothing abnormal. There were no plasma cells, lymphocytes or fibroblasts. They contained the usual empty lacunae and stained much brighter than the connective tissue of the underlying thrombus. Though the dura, the hyperplastic tissue around the thrombus and the latter itself were in some areas fused into one mass, it was possible to differentiate them by their staining qualities. The dividing line between the dura and the neoplastic tissue underneath was a group of elastic fibers, which is marked by *2* in figure 2

and can be seen even without a magnifying lens. The tissue below the elastic line was the thrombus which, with the method of van Gieson, stained less densely than the dura above, the fibers being more slender and forming dense longitudinal bundles; their interspaces were wide and harbored plasma cells, fibroblasts and gitter cells filled with neutral lipoids (stained with scarlet red). The thrombus also was richer in blood vessels, the walls of which were thickened and surrounded by numerous large fibroblasts.

The lateral sinus contained no thrombi, but the abscess exhibited various stages of healing—phenomena of transformation into connective tissue. It contained large masses of gitter cells and was traversed by bundles of connective tissue

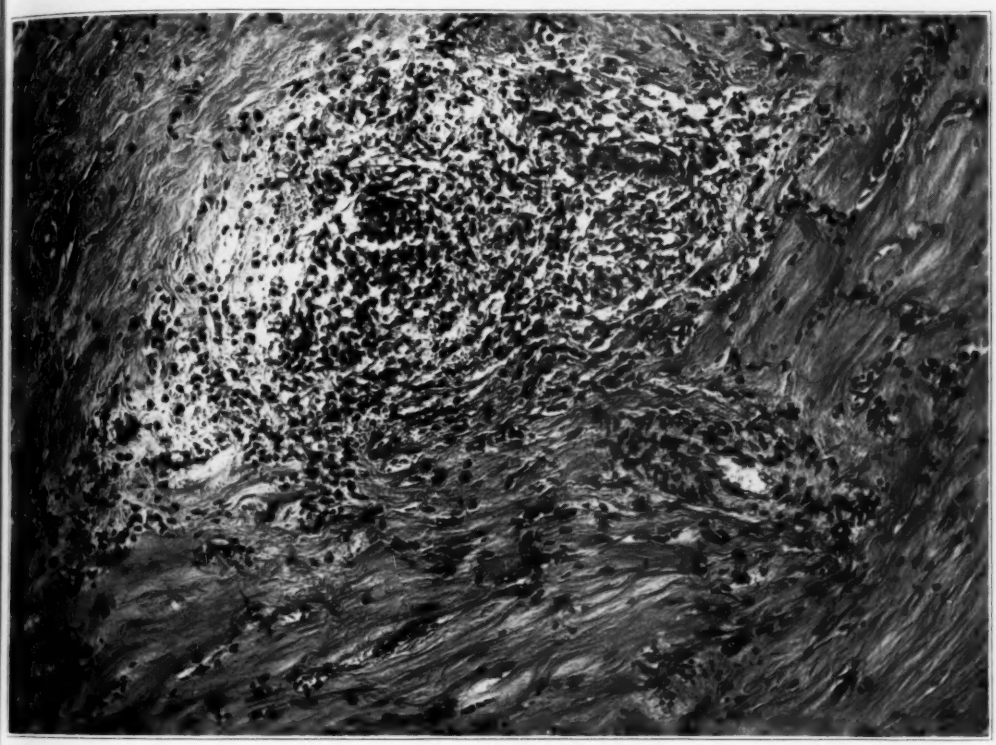

Fig. 6.—Abscess in the process of organization. Explanation in text. Van Gieson stain; reduced from × 150.

which broke up the abscess into smaller parts. However, the abscess was not confined to the sinus as in the longitudinal sinus, but invaded the dura, which was studded with small abscesses. The phenomena of suppuration were here more marked, probably because they were nearer to the place of infection.

No particular changes were present in the pia, while the arachnoid in some places showed immense masses of mesothelial cells.

No inflammatory phenomena were present anywhere in the tissues of the brain. There were some rarefied areas, with slightly dilated glial interspaces, but the ganglion cells exhibited marked phenomena of satellitosis and neuronophagia, especially in the frontoparietal region. There were also pale areas with profoundly

changed ganglion cells and so-called swollen oligodendroglia scattered throughout the white substance. The changes in the brain were decidedly pathologic, and I should classify them as toxic encephalitis. No reticular or areolar foci indicating a hydropic state of the brain tissues were present, and the subarachnoid space appeared to be of normal size. In short, signs of hydrocephalus were absent.

COMMENT

The thrombus in the case here recorded was of organized connective tissue. It was sharply limited from the normal dural tissue and resulted from an infected sinus. There were therefore two phases: one pathologic, destruction and replacement of the contents of the longitudinal sinus by an abscess, and the other physiologic, repair or transformation of the latter into a connective tissue scar. The elements active in both phases were exclusively mesodermal. The histiocytes invaded the abscess, removed its decomposed elements (broken down or dead cells) and were replaced by powerful fibroblasts and connective tissue fibers. These elements could come only from the adjacent dura which supplied, as it were, the affected area with construction material.

A noteworthy feature was the gitter cells. They possessed the same morphologic and physicochemical properties as when encountered in pathologic conditions of the central nervous system. Commonly occurring in nerve degenerations, they are associated with the process of glial scar formation, which they precede; in the formation of a connective tissue thrombus they are associated with a mesodermal scar formation. In the case under discussion they were unquestionably of mesodermal origin, and originated most likely from the resting wandering cells—polyblasts or clasmatocytes—of the walls of the longitudinal sinus. Some of these cells became transformed first into fibroblasts and subsequently into connective tissue fibers, and some into gitter cells, all these elements, including the gitter cells, being instrumental in the formation of a connective tissue scar. In broken up nerve fibers, the process of healing with ultimate glial cicatrization is, as has been said, accomplished by the glia (fibrous glia), but the preceding process, that of removal of the débris of broken-up myelin and axon is supposed to be accomplished, according to some, by microglia (considered to be mesodermal elements by the majority of writers).

Without discussing nerve degeneration and regeneration, I wish to state that in rendering the damaged nerve tissue harmless and replacing it by a scar tissue both processes are, at least in the human spinal cord and experiments, carried out by the glial elements, just as in mesodermal lesions, such as are described in this paper, they are carried out by connective tissue.

Another interesting feature in the case here recorded was the absence of an external or internal hydrocephalus, in the presence of a complete obliteration of the longitudinal and both transverse sinuses. It is generally assumed that the spinal fluid is drained by the longitudinal sinuses after it is passed or filtered through the pacchionian bodies. The complete occlusion of the former in this case should have, according to this theory, interfered with the escape of the spinal fluid from the subarachnoid space, where it should have accumulated and produced an internal hydrocephalus with hydrops of the brain and other changes seen in hydrocephalus and described elsewhere.[1] The absence of such changes speaks decidedly

1. Hassin, George B.: Hydrocephalus: Studies of the Pathology and Pathogenesis with Remarks on the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **24**: 1164 (Dec.) 1930; Hydrocephalus: Report of a Case in an Infant with Vestiges of a Choroid Plexus in the Fourth Ventricle Only, ibid. **27**:406 (Feb.) 1932.

against a view that the longitudinal sinus and the pacchionian bodies serve for the purpose of absorption of the cerebrospinal fluid. The few changes in the brain noted, such as marked neuronophagia, were rather accidental complications, which were probably caused by the septic state of the patient. Through the formation of an organized thrombus and the checking of the inflammation the process was localized, but the general septic state could be only partly prevented.

CONCLUSIONS

1. An infection from the mastoid process may result in the formation of dural sinus abscesses.

2. Like a foreign body, an abscess provokes a reaction in the form of proliferation of histiocytes and fibroblasts and becomes transformed into a solid scar or an organized connective tissue thrombus.

3. The histiocytes remove the cells of the abscess, transformed into lipoids, to the dural tissue spaces.

4. The brain substance, which is affected only slightly or indirectly, exhibits changes of so-called toxic encephalitis.

5. The obstruction of the longitudinal (sagittal) sinus, partly by an abscess, partly by a thrombus, even when complete and associated with that of the lateral sinuses, has no effect on the absorption of the spinal fluid from the subarachnoid space.

SPECIAL ARTICLE

TRAINING OF THE NEUROLOGIST

F. M. R. WALSHE, M.D., F.R.C.P.
LONDON, ENGLAND

In a recent edition of an American textbook of neurology, the distinguished authors, in giving a reference to a paper written by me on certain reflex phenomena, were at pains to warn their readers that the paper in question "should be read with caution as not free from insular prejudices."

Perhaps I may be allowed to preface my remarks on the training of the neurologist by expressing the hope that they will be found to bristle with these same prejudices; that is, with views which, although they may not command general approval, represent the fruits of my experience and express my personal convictions. That there are limitations inherent in such a method of approach is clear, but it has the merit that by it discussion is more likely to be stimulated than by a series of colorless generalizations, or counsels of perfection.

Nevertheless, in the endeavor to take as broad a view as possible, I have taken down from the shelf Flexner's well known monograph on "Medical Education." From this, it would appear that in this country it is our business to learn rather than to teach; an impression that gains some strength from critical accounts of our neurologic methods and achievement appearing in American and German neurologic journals from the facile pens of returned visitors to this country. These articles seem to convey their writers' conviction that we no longer have anything to teach save only the old-fashioned discipline of bedside observation and study which, it appears, no one now desires or needs to acquire, so ingenious are the numerous technical devices and experimental studies widely thought to have replaced it.

None the less, I regard this discipline as the basis of a neurologic training, and its ancient banner I propose to raise. It has been said that while new mechanical contrivances and chemical processes have transformed military tactics, they have not and cannot displace the infantryman from his primacy of peril and importance in the wars of the future. So I believe that while technical methods of investigation and experimental studies have now to be included in the essentials of a complete neurologic training, clinical observation remains the founda-

tion of neurologic medicine, and on it all else must be built. Only the adequately trained clinical observer can evaluate the relationship of the results of laboratory and other technical methods of investigation to the symptoms of disease presented by the individual patient, for it is the individual that is the material of our study, be it remembered, and not an abstract thing called disease.

This belief, then, is the "insular prejudice" which will color most deeply what is to follow.

I propose to deal with my subject under the two headings of (1) the neurologic aspirant and (2) his neurologic training.

THE NEUROLOGIC ASPIRANT

None will dispute that a neurologic training can be no more than a superstructure on a sound general medical education, and for this reason the practice of some schools of permitting the student to substitute some part of his general clinical training by special courses in a particular branch of medicine in which he proposes later to specialize seems to me an unsound one.

From time to time, undergraduate students arrive in this country with a view to devoting some weeks or months exclusively to neurologic studies, and this at the expense of the all-too-scanty time allotted to them in their curriculum for the acquisition of a broad elementary knowledge of clinical medicine. It is difficult to conceive of a more short-sighted policy. Such students prove to be so ignorant of elementary clinical medicine and of the technic of clinical observation that one cannot teach them neurology. At almost every turn they are held up by some hiatus in their knowledge, by some inability to appreciate the reciprocal relationships between the nervous system and the rest of the organism.

By the time he is ready to take his medical degree, the student should be able to find his way about any ordinary clinical problem, to elicit the signs of disease and to discuss their significance. The full time at the undergraduate's disposal is already barely adequate for this, and any attempt to cut into it for special studies imperils the whole course of study.

Further, even the student who has avoided the peril of precocious specialization may yet succumb to it after graduation if he does not make it his first business to serve a term of duty as a house physician or intern to a general physician or to a general medical unit. In this way he amplifies and reenforces his preliminary training, becomes familiar with the handling and care of patients and learns something of the natural history of disease. Six months is the minimum time after graduation that should be spent in this way, and not more than a year.

Since morbid processes remote from the nervous system are capable of producing disorders of function in that system, disorders that may dominate the clinical picture, the neurologist must be competent to deal with a much wider range of problems than are comprised by primary disorders of the nervous system, a statement that is amply borne out by the example of cardiovascular diseases and their influence on the nervous system.

No one of experience will dispute that there are specialists in different branches of medicine and surgery whose work clearly betrays the defects of judgment and limitation of outlook that come from a premature concentration on some small field of medical knowledge.

If one accepts the requirements thus outlined as necessary and reasonable, one may proceed to ask whether there are any additional preliminary studies that the future neurologist may fruitfully make. One of the most disquieting features of the modern medical curriculum is the high pressure under which the student is forced to work. So large is the quantity of bare information that he has to acquire, that he has no time for reflection.

In some universities in this country, the medical student having completed his routine courses in anatomy and physiology may, before passing to his final and clinical studies, spend an additional year in the study of physiology, a year mainly devoted to experimental work designed to introduce him to scientific method and modes of thought. At Oxford, for example, this year is known as the Final Honours School in Physiology, and from the fact that Sir Charles Sherrington directs its labors it follows that the physiology of the nervous system takes a prominent place in the curriculum. While this fact gives the course a special interest, its essential value—like that of comparable courses elsewhere—is that it teaches the student to observe and to measure, trains his critical faculty and "habituates his mind to method."

Therefore, the devoting of an extra year to biologic studies is an excellent preparation for the student who desires later to become a neurologist. There are, of course, dangers in taking such a course, for not a few students, fascinated by physiologic work, linger too long in the laboratory and on emerging are found to display a strange incapacity to adapt themselves to the very different discipline of clinical study. Others, again, imagine that in some incomprehensible way laboratory studies fit them to step full-armed into clinical work without serving any apprenticeship. This is a fallacious idea, for even though the student has given his whole time to the study of the nervous system, he still remains ignorant of the technic of clinical work, and even of the nature of clinical problems.

In conclusion, it is essential that the future neurologist should approach the threshold of his subject adequately equipped to do justice to it and to himself.

THE NEUROLOGIC TRAINING

While the education of the neurologist may be said never to end, it is not precisely in this philosophical sense that I am here using the word. I am concerned rather with the apprenticeship that the beginner has to serve to fit him to become a neurologist. Even on a matter apparently so simple, opinions may differ widely. Thus one is often consulted by postgraduates who have a few weeks or months at their disposal and imagine that such a period is adequate to the production of a neurologist. Alas! One cannot become a neurologist in a summer vacation, not even if one takes a postgraduate course of lectures and demonstrations, and what follows is based on the assumption that the student has two or three years entirely free to devote to neurologic studies. In a shorter period he cannot expect to acquire the necessary experience and judgment to fit him to practice neurology.

The aspects of neurology to be studied may be tabulated as follows: (1) anatomy and physiology, (2) psychology, (3) clinical study and (4) pathology. This perhaps is the logical sequence in which to consider the matter. The central nervous system, enclosed within the bony framework of the skull and vertebral column, is not accessible to direct observation. One cannot study it by methods of inspection, palpation and the like that are employed in the case of the viscera, and the recognition and localization of disease in the nervous system is largely a matter of applied anatomy and physiology. These studies, therefore, must be undertaken at the outset of a neurologic training. Similarly, a knowledge of mental processes, which is not to be obtained by an uncritical adhesion to any particular psychologic school of thought, is also essential. Nevertheless, for practical reasons, I propose to deal first with the purely clinical aspect of the subject.

The Clinical Study of Nervous Disease.—To familiarize himself with the common nervous diseases, to gain a rough idea of their behavior and of their variations from case to case will require not less than a year's whole time study in a neurologic clinic. Since nervous diseases of every kind have to be studied, it is clear that the neurosurgical clinic is not a place wherein a complete and balanced survey of the field of neurologic medicine can be obtained. A reasoned justification of this opinion, for those to whom its cogency is not already clear, will be given in its proper place.

Having gained his footing in the clinic or hospital, there are various methods by which the student may seek to obtain the requisite knowledge and experience. Unquestionably, the most important of these

is the careful routine examination of patients at the bedside, and also the systematic and detailed recording on paper of what is found at this examination. I am prepared to plead guilty to insular prejudice in the conviction which I have that the work of a house physician at the National Hospital, Queen Square (and to a less extent, that of a clinical clerk) provides an incomparable clinical training in neurology precisely in respect of his duty in making and recording complete routine examinations of all the patients who come under his care. It is my belief that this scrupulously careful recording of his observations and their criticism and correction by his chief are a vital part of his training. By this means, the facts are impressed on his memory, and by the careful arranging of them in his notes the observer is forced to think clearly of his problem and to make precise and unequivocal statements.

The first step in this education is the acquisition of *a habit of systematic examination.* The student should learn to go over every case in an orderly fashion from head to foot, and he can then go more deeply into any particularly significant feature it may present.

At the risk of seeming to labor the point, I should like to go into it still further. In writing clinical papers for publication, it is often necessary to embody case notes in the text, and most of us have at times groaned in spirit as we have struggled through the paper in which the case notes display no consistency of arrangement, nomenclature or phraseology, but read as though the examiner—like a butterfly—had flitted airily around his patient, jotting down at random whatever chanced to catch his roving eye. Few defects detract more from the effectiveness of a paper than this, for it is the hallmark of an ill trained and disorderly mind.

Finally, there are good and bad methods of case note-taking, and from the first the student should be trained in a good method. An eminently bad one is that in which a physical sign is not recorded in plain terms, but by giving the name of the writer who first described it, followed by a plus or minus sign. Sometimes, indeed, a long list of such names, each with its mathematical sign, takes the place of a straightforward statement. This method tends to make the student regard physical signs as mysterious phenomena sent down by a beneficent Providence to aid him to a diagnosis, and prevents him from regarding them as manifestations of disordered function, each of which has a significance. In short, the practice degrades clinical recording to the level of a rule-of-thumb ritual.

Still another modern evil is the reckless coining and employment of new words of classic derivation in place of terse descriptive terms. A patient no longer "moves slowly," but he "presents bradykinesis." A scientific nomenclature is a necessity, but the extravagant use of these

cacophonies is fast rendering neurologic writings wholly unintelligible to workers in other branches of medicine—surely a result that has nothing to commend it.

In short, the student must be taught that the careful and intelligible recording of his observations is one of the most potent influences in his training.

Further, the student's progress may be facilitated if, in earlier stages of his work, he is given selected cases to examine and record: cases which exemplify the main types of disorder of nervous function. Thus, to have worked out thoroughly a case of spastic residual hemiplegia is in itself a liberal education in the features of one of the chief types of motor disorder. Comparable examples will readily occur to the mind of the neurologist.

In seeking clinical material, the outpatient clinic is an essential complement to the ward, for in the former are to be seen minor and ambulant disorders such as are seldom seen in patients admitted to a ward, and also the preliminary sorting out of the mass of unselected clinical material. Furthermore, there are persons with "acute" diseases and disorders of the nervous system—infections, vascular lesions, injuries, convulsions and coma arising from various non-nervous factors—that find their way rather into the general wards of a hospital than into a neurologic clinic. These patients provide some of the most difficult and anxious problems of neurologic practice, and they must be sought out and studied where they are to be found.

Attendance at lectures and demonstrations and—as a spectator—at clinics can take only a second place in the training of the neurologist, and the chief value of these lies, not in the facts of information acquired, but in the insight which the student gains into the method of approach and into the sequence of observation and inference of the experienced neurologist.

Unfortunately for this end, the student is apt to prefer the histrionic style of clinical teacher in whose hands diagnosis becomes a mysterious affair of signs and wonders only to be interpreted by the inimitable flashes of the teacher's genius, while the "spot diagnosis" becomes the acme of cleverness. These are meretricious attractions that do not teach the student how to work out clinical problems for himself, for they serve but to hide the intellectual processes that it is the teacher's first duty to reveal.

No specific reference has so far been made to laboratory and other technical methods of investigation, but it is clear that a knowledge of when to employ them and of how to interpret their results is an integral part of a neurologic training. Many of these methods should be within the competence of the clinician himself, though some few of them are

of value only when carried out with the special skill and experience of the clinical pathologist. In this connection, it is necessary to emphasize the importance of training the student to make a thorough clinical examination at the bedside and, with his teacher, *to come to as definite a diagnosis as the facts allow before having recourse to accessory methods of diagnosis*, such as examinations of the blood and cerebrospinal fluid, roentgenography and the like. Except on these terms, it is impossible to become a sound and reliable clinician, and unless he is this, the student cannot evaluate the results of these accessory methods. On the contrary, his opinions will always be led captive by this or that device of the laboratory.

Here, a quotation from Flexner's monograph [1] may not be inappropriate:

> There is a widespread impression that the scientific quality of medical education and practice is in some fashion dependent upon the part played by the laboratory. This is not the case. Science is essentially a matter of observation, inference, verification and generalization. . . . Not only is the part played by the active senses the essential criterion of science; one may go further—the vast and complicated paraphernalia of science are merely means of extending their scope.

In brief, there is no mechanical substitute for the use of a trained intelligence.

The study of modern neurologic writings and some personal experience with postgraduate students from abroad lead me to think that this "impression," as Flexner puts it, has in some minds become an ineradicable obsession. There is a waning of trust in the results of straightforward clinical observation, and what is at times an almost pathetic reliance on some fragment of equivocal information revealed by microscope or roentgenogram. Thus, one may see some cogent piece of information derived from simple observation lightly discarded on the strength of a vague shadow in the roentgenogram of a skull, which common sense suggests—and the event proves—to have no more to do with the problem under consideration than "the flowers that bloom in the spring."

The truth is that it is the clinician's business to be the master of all available weapons, and to know the use and the proper occasions of each, but not to be the slave of any one of them. Unhappily, as I believe, there is an influential and growing body of opinion that is turning the mind of the student of medicine away from the clinical study of the patient at the bedside to investigation by methods depending on roentgenology, bacteriology, biochemistry and the like. An example familiar to readers of neurologic writings will be the view expressed by more

1. Flexner, A.: Medical Education, New York, The Macmillan Company, 1925, p. 5.

than one authority to the effect that in the recognition and localization of intracranial tumors ventriculography is now an adequate substitute for neurologic investigation.

The outlook implicit here is the antithesis of that which I have been primarily concerned to sustain in this article, and I may, therefore, be allowed to subject it to some further examination.

Arising out of this question are two others intimately involved in it; namely, the place of the neurosurgical clinic in a neurologic training and the relation of the neurosurgeon to the neurologist.

The Neurosurgeon and the Neurosurgical Clinic.—The suggestion that routine neurologic investigation is no longer necessary leads us to consider the nature of the clinical material reaching the neurosurgical clinic. Clearly this represents an extremely restricted part of the field of neurologic medicine. A case is referred to such a clinic not because it is one of nervous disease, but because some one—often of doubtful competence in the matter—believes it to belong to the relatively small category of cases amenable to and in need of surgical treatment.

But this preliminary process of selection may be very unreliable, and in practice cases may be referred that are wholly unsuitable for surgical therapy. In these circumstances—which the experienced neurologist knows full well are not merely hypothetical—how is a satisfactory differential diagnosis to be achieved? By neurologic investigation, or by ventriculography? Neurosurgeons have not been lacking who suggest that the former is superfluous and unreliable, and one may therefore assume that ventriculography will be the chief instrument of diagnosis in not a few neurosurgical clinics. If this is so, then a large number of fruitless and hazardous ventriculographies will have to be performed, and if no tumor is revealed nothing that can rightly be called a diagnosis will have been made, and some futile negative label such as that of "unverified tumor" will be all that the patient obtains for what he has suffered at the hands of his surgical adviser.

It can scarcely be too plainly stated that this "hit or miss" travesty of diagnosis is neither surgery nor neurology. It certainly has nothing to do with scientific method, and is rather in the direct line of descent from the naive procedure of Ho-ti who, as readers of Charles Lamb will recall, burned down his house to roast a pig.

The situation would, of course, be the same were exploratory craniectomy in question and not ventriculography.

That this picture is not remote from reality is demonstrated by the frequency with which in some neurosurgical clinics ventriculography, with or without subsequent craniectomy, is performed as a diagnostic measure in cases which prove ultimately not to be cases of intracranial tumor, but examples of the familiar organic nervous diseases, or even of

the psychoneuroses. There is something radically unsound in this state of affairs, and its existence affords the strongest argument for the routine use of the most exhaustive neurologic studies. Surely one of the first duties to patients is not to inflict on them more radical remedies or diagnostic procedures than their situation warrants and requires. The point is too obvious to need elaboration, but it will be well to remind oneself of it from time to time. There can be few diagnostic problems more difficult than that involved in the recognition and localization of an intracranial tumor, and few cases in which a precise diagnosis is more essential. It is a problem calling for every resource of clinical experience. It will be generally agreed, therefore, that clinical investigation affords the first line of attack on intracranial tumors, as on every other disease that flesh is heir to; indeed, it would be a situation without precedent in the whole range of medicine and surgery were it otherwise.

From what has been said, it would appear that the neurosurgical clinic is not the place in which the neurologic experience essential to the recognition of even those maladies which reach the clinic is obtainable. Certainly a comprehensive knowledge of nervous diseases cannot be obtained within its walls. How, then, are the vitally necessary neurologic studies to be made, and by whom?

This brings one to the question of the training of the neurosurgeon. It would seem that the latter has two alternatives before him. He may regard himself primarily as a surgeon, not concerned with the niceties of neurologic diagnosis, but only with the acquisition and practice of the special surgical technic demanded by the nervous system. In this case he must of necessity work in collaboration with a neurologist.

Alternatively, he may regard himself as a neurologist capable of making his own diagnoses and of prescribing treatment, and possessing the additional accomplishment of being able to carry out this treatment himself when it chances to be surgical.

As I understand the present trend of neurosurgical opinion, this latter conception of his powers and functions is the one favored by the young neurosurgeon. It carries with it the obvious corollary that his clinical training must be what has been outlined as essential for the neurologic physician. It does not always appear, however, that the neurosurgeon carries his conviction in this matter to a logical conclusion. Experience shows that many young men now seeking a training in neurosurgery pass to the neurosurgical clinic unhampered by any previous training or experience in clinical neurology. Within the clinic they cannot, as has been pointed out, obtain the necessary training, but having acquired a surgical technic they can rarely be induced to go to a neurologic clinic to gain the experience essential to its judicious use. On the contrary, by a familiar process of rationalization, they speedily come to

the consoling conclusion that ventriculography—or some other short cut to knowledge—has rendered neurologic studies no longer necessary. This naive conclusion represents the final triumph of technic over reason, for by it the young neurosurgeon is able easily to satisfy himself that he is indeed a neurologist, and at the same time to persuade himself that a neurologic training is superfluous.

It may be thought that these are hard words, but the working hypothesis they indict is fraught with danger for the future of neurology, and its illogical and unwise character cannot be too clearly exposed. Indeed, the shadow of the neuro-robot which, switched on to the electric supply or working on a couple of accumulators, will be able to carry out the mechanical processes now thought by some to be all-sufficient for universal diagnosis, lies heavy over the neurologic scene, and only the chill wind of criticism can dispel it.

To hold these views is not to belittle the many valuable contributions to neurology that have flowed in a rich stream from neurosurgical clinics during the past twenty years. It is simply to recognize that logically—if the neurosurgeon is to make his own diagnoses—there can be but a single adequate school for the neurologist, whether he proposes to practice neurosurgery or not. Physician or surgeon, he must go through the same mill: the neurologic clinic.

The Psychoneuroses.—No special reference has been made to the study of the psychoneuroses, and indeed I have deliberately refrained from discussing the controversial theoretical issues involved. None but the boldest would venture to offer advice as to which of the "seven and twenty jarring sects" of the new psychology the neurologist should offer that intellectual submission they appear to require of him. To choose between them is to invoke the wrath of the remaining claimants to pontifical status, while to advise the student to use his reason and take from each school of thought what it has of truth is to call down thunder from them all.

It may not, however, be superfluous to remark that a primary function of the neurologist is to recognize a psychoneurosis when he meets it, and to be able to differentiate it from the syndromes of structural disease. Unless he can do this, the profoundest erudition and the most enlightened views on the genesis and treatment of the psychoneuroses are but a barren academic attainment.

It would be unnecessary to make this trite observation were it not that many enthusiastic psychotherapists ignore the truth that underlies it. Yet clearly, the discipline of a sound clinical training is as essential to the rational practice of psychotherapy as to that of neurosurgery. In this respect, the two are in one category. On the other hand, it is not to be supposed that in acquiring the skill to recognize the psycho-

neuroses, the neurologist has done all they demand of him. They provide one of the most exacting aspects of neurologic practice, calling for every resource of psychologic knowledge, for common sense and insight, and for clinical acumen. In the past neurologists have been too cavalier in their treatment of this problem, and it is perhaps the function of the trained neurologist in the future to import reason and the scientific outlook into a field that has for too long been the happy hunting ground of the half-trained enthusiast.

Pathology.—That the neurologist should have a sound working knowledge of the morbid anatomy and histology of the nervous system needs no statement. Familiarity with histologic methods and appearances is best acquired in the course of working at some special pathologic problem.

While histologic studies still continue to yield fruit, as for example in the case of gliomas of the brain and in that of the demyelinating diseases, it is clear that they can never be final. At most they can but provide clues as to the paths along which further investigations can be pursued. In the future it is reasonably certain that biochemical methods will play an increasingly important rôle in the investigation of nervous diseases, particularly in the matter of their causation. It would be unreasonable to expect the neurologist to be an expert biochemist, but an informed interest in certain aspects of the subject is a necessity for the study of many etiologic problems. How important the biochemistry of nutrition may be for the neurologist has been demonstrated in the case of subacute combined degeneration of the cord, and it is not unlikely that disseminated sclerosis, multiple neuritis and other maladies may have to be approached along similar lines. Hitherto neurologists have shared too deeply in the medical preoccupation with infection and have been content to regard histologic studies with some rather perfunctory bacteriologic investigations as an adequate scheme of research into etiologic problems. The story of disseminated sclerosis research affords a case in point, and shows on what fruitless excursions one may be led by an obsession with the notion of infection, and this despite the fact that there has never been any conclusive indication that the malady in question is infective in origin. The real evil of this narrow outlook on neuropathologic problems is not that it is barren of results, but that it prevents the seeing of any other possibilities.

If neurologists are to keep pace with the general tide of advance in medicine, their outlook will have to be broader than in the past, and their knowledge wider. They cannot hope to be experts in every branch of scientific endeavor, but will need to be sufficiently in touch with other branches to know when to invoke the aid of the biochemist, the physicist and so on.

Here again, though the iteration be wearisome, it is necessary to repeat that one does not become a neurologist in the laboratory. Whatever time it may be decided to spend in the laboratory, and in whatever mode of investigation, must not be at the expense of clinical training. It would be an unhappy day for the future of neurology if the notion got abroad that the path of academic advancement lay through the laboratory and not also—and imperatively—through the clinic.

Anatomy and Physiology.—The undergraduate receives some elementary instruction by lecture, demonstration and by gross dissection in the anatomy of the nervous system, central and peripheral, and it is probable that he receives as much as he is capable of assimilating at this stage of his education. It is germane to the problem, however, that in some medical schools special courses in neuro-anatomy are given. From these the student is expected to attain a fairly high level of information, by comparative anatomic studies, by the making of models and other means. This ambition is rarely achieved, for like the overfed infant, the student quietly rejects what he cannot assimilate, and after graduation a few barely recognizable fragments of this forced feeding are all that he retains, and these seldom the most useful. How exacting may be the demands of the professor of neuro-anatomy is illustrated by the textbooks on the subject that are produced for the undergraduate student. In one recently published and describing "the principal nervous pathways," there are set out in diagrams and charts those facts of anatomy "which will be most directly used in the future." When I say that prominent among them are two diagrams of the pathways of the rhinencephalon, with over fifty names apiece and as many complicated pathways, it is clear that opinions may differ widely as to what is and what is not of practical value. For the student of neurology, the use of textbooks and diagrams can be no more than an aid to the study of anatomy by dissection and the examination of serial sections by the microscope. The exclusive study of diagrams and atlases leads to a highly artificial and conventionalized conception of structure, and still more of function. Thus, in the analysis of such disorders of function as athetosis, tremor and the like, there is a widespread tendency to "invent" physiologic pathways in the nervous system by the mere stringing together in a list of contiguous tracts, as they are displayed in diagrams. In this easy fashion, hypothetical nervous impulses are sent on circuitous journeys along tracts that may or may not act as the links in a physiologic chain, and this often for no better reason than that in diagrams such linkages appear possible.

In other words, the correlation of the facts of anatomy with the symptoms of lesions is not the simple matter it may appear and requires considerable insight into the physiology of the nervous system as well as a knowledge of its minute structure.

This brings me to the question of physiology. An essential primer for every neurologic student is Sherrington's classic work, "The Integrative Action of the Nervous System." This book is of that small class which Bacon advises must be "chewed and digested." The neurologist should read and reread it until his thought is saturated in the principles of neural function therein so brilliantly expounded. This done, he may be safely let loose on physiologic literature for he will have acquired a sound standard of values. The more recent work of the Sherrington school has been embodied in a short volume entitled "The Reflex Activity of the Spinal Cord," and with its predecessor it provides a liberal education in the physiology of the nervous system.

Although they are wholly based on clinical observation, Hughlings Jackson's lectures, recently collected and reprinted, may be appropriately referred to here in that they exemplify the highest form of scientific observation and generalization carried out in the field of neurology.

There will also occur to the mind of the neurologist other contributions to neurology, in which the material has been clinical and the methods in line with the high traditions of physiologic research. Thus, for example, there are papers on the sensory system of Head and Holmes and of Trotter and Davies. The two papers by the last-named authors are far too little known. They form a beautiful example of scientifically conducted clinical investigation admirably recorded and of penetrating scientific imagination.

Thus trained on the classics of neurophysiology, the neurologist will be able to steer clear of the false analogies and misapplications of physiologic knowledge that are still seen so frequently in the literature on neurology. Certainly every neurologist should have some degree of first hand acquaintance with the phenomena revealed by decerebration, spinal transection and the like in the lower mammals. Without it he cannot hope to apply the facts revealed by experimental physiology to the study of clinically observed phenomena.

In the Golden Age of neurology in this country, the clinician was also the experimental physiologist, though Hughlings Jackson, the master of all neurologists in his time, never combined these two rôles, and I may be allowed to quote from some remarks on this subject that I have made elsewhere,[2] thus:

> If we look back upon the past fifty years of neurology in this country we see that the period opened with a close and brilliant association between clinical and experimental investigation, an association maintained for many years and depending upon the fact that clinical and experimental methods were often pursued by the same investigator. Ferrier, Horsley, Beevor, Page May and Risien Russell were

2. Walshe, F. M. R.: Oliver-Sharpey Lectures on Physiological Analysis of Some Clinically Observed Disorders of Movement, Lancet **1**:963, 1929.

among the outstanding examples of this fruitful combination. Within recent years the collaboration between these two methods has been less close. The hewing out of the main features of neurophysiology by relatively simple methods has given place to the minute analysis of fundamental nervous processes by methods of great complexity. Clinical and pathological problems have become correspondingly difficult and exacting, and a single individual can no longer easily pursue knowledge by all these paths.

Nevertheless, we must admit that the divorce has been most unfavourable to advance by the two latter methods, clinical and pathological, in so far as the interpretation of symptoms is concerned. This is illustrated by the barrenness of nearly twenty years of intensive study of the functions of the basal ganglia by these unaided methods. Even in the case of the sensory system, it required the experimental method before the chief factors in cutaneous sensibility could be elucidated. We may say, then, that whatever success has attended clinical studies in the interpretation of the symptoms of nervous disease has been proportional to the degree in which these studies have been inspired by physiological principles, and to the extent to which—within the narrow limits possible in clinical medicine—the precise methods of experimental physiology have been applied.

Neurology makes a strong appeal to men of many interests and diverse temperaments. The man with a flair for clinical medicine will find no branch of the subject that offers him more fascinating exercises; for the pathologist, the nervous system is a rich mine of problems awaiting discovery and solution; for the biochemist, it offers a new world scarcely yet explored, while for the experimental physiologist, it has been the scene of some of his greatest triumphs. Perhaps it is the clinical neurologist who can partake most fully of the intellectual opportunities and satisfactions that the study of the nervous system in health and disease affords, and this in addition to the gratification he may obtain in the right exercise of his vocation as a physician and servant of the community. But if he is to rise to the height of his opportunity and to attain to the summit of these satisfactions, he must serve a hard and long apprenticeship.

This brings me back to the proposition with which I started; namely, that a sound training in clinical neurology is the foundation of a neurologic education. This is as true for the neurologist who proposes to devote himself mainly to the surgical treatment of such nervous maladies as require it, as for the pure physician. However wide and deep may be the individual's knowledge of the anatomy, physiology or pathology of the nervous system, however cunning his hand and judgment in surgical technic, he is not and cannot become a neurologist in the full sense of this word until he is conversant with the phenomena and natural history of diseases of the nervous system and is the master of the clinical method.

Abstracts from Current Literature

DIPLOPIA AND OTHER DISORDERS OF BINOCULAR PROJECTION. ALEXANDER DUANE, Arch. Ophth. **7**:187 (Feb.) 1932.

This is the third of a series of posthumous articles written by Dr. Alexander Duane, who died on June 10, 1926. As the editor of the ARCHIVES OF OPHTHALMOLOGY states in a footnote to the article, these articles, published through the courtesy of Mrs. Duane, are chapters from Dr. Duane's book on "Ocular Muscles," on which he was working at the time of his death, and they represent the views of an authority who devoted his life to scientific research in a field to which he had so ably contributed.

Disorders of binocular fixation are regularly accompanied by corresponding disorders of projection. Of these, the most common is double vision or diplopia.

Pathologic diplopia, due to derangement of binocular coordination, is to be distinguished from physiologic diplopia, which is the regular accompaniment of normal vision and which is a potent factor in the production of stereoscopic vision. The differentiation of the two follows:

Physiologic Diplopia	*Pathologic Diplopia*
The object of fixation appears single and is distinct.	The object of fixation appears double, one image being distinct, the other indistinct.
The only objects seen double are those that are obviously further or nearer than the object of fixation. The nearer the objects are to the latter, the less double they appear, and those that are alongside it appear single.	Most of the objects in the field of view appear double, but particularly those that are close to the object of fixation and are alongside it.
The diplopia is hardly ever recognized spontaneously and rarely causes confusion.	Diplopia often obtrudes itself on the notice, and often causes confusion and discomfort.
If an object is seen double, both images are indistinct, and are also shadowy or ghostlike, so that if one is in direct line with the object of fixation, the latter can be seen through it.	When an object is seen double, one image has the natural appearance of the object itself; the other is more or less indistinct and shadowy.
The diplopia is not affected by shifting the gaze laterally or vertically, provided the convergence is unaltered.	The diplopia is often increased or diminished by shifting the gaze sideways, or up and down.
The diplopia can be made to disappear at once by changing the convergence, so as to fix an object nearer or more remote, as the case may be.	Frequently the diplopia remains when the convergence is altered.

Both types of diplopia are distinguished from monocular diplopia by the fact that in the former one of the double images at once disappears when either eye

is shut. The various types of diplopia are then described in detail. Dr. Duane's table illustrating them are given *in toto:*

Diplopia, Its Causes and Correction

	Caused by		Corrected by		
Kind of Diplopia	A Deviation of	A Prism Placed with Apex	A Double Movement of Eyes (Vergence + Version)	A Prism with Apex	Head Movement
Homonymous	Either eye in	Out before either eye	Movement of divergence combined with a parallel movement of both eyes, to right or left	In before either eye	Turning of head in direction in which diplopia increases
Crossed	Either eye out	In before either eye	Movement of convergence combined with a parallel movement of both eyes, to right or left	Out before either eye	Turning of head in direction in which diplopia increases
Right	Right eye up or left eye down	Down before right eye; up before left eye	Movement of left supervergence combined with parallel movement of both eyes up or down	Up before right eye; down before left eye	Turning of head in direction in which diplopia increases, or more often tilting of head to one shoulder
Left	Left eye up or right eye down	Up before right eye; down before left eye	Movement of right supervergence combined with parallel movement of both eyes up or down	Down before right eye; up before left eye	Turning of head in direction in which diplopia increases, or more often tilting of head to one shoulder
Intorsional	Turning of either or both vertical meridians in	.....	Movement of divergence of vertical meridians (distorsion)		
Extorsional	Turning of either or both vertical meridians out	.....	Movement of convergence of vertical meridians (contorsion)		

The discussion of the cause of diplopia is highly satisfactory. It must be noted that binocular diplopia, whether physiologic or pathologic, is always the result of a false projection. In monocular vision the eye almost invariably projects correctly; the combination of visual and postural impressions enables it to do this. In binocular vision the two eyes, if acting in a normal way, project correctly the object looked at with even more accuracy than in monocular vision. They also project correctly a few outlying objects, which form images on corresponding points, or which at any rate occupy the horopter. But all other objects are projected out of their true place, and the same is true of all objects seen by a deviating eye. The false projection in both cases is due to the preponderance of the postural impressions, derived from convergence over those derived from conjugate movement; i. e., it is due to the fact that when one looks with both eyes one locates objects with reference to the midline instead of with reference to the visual axes of the eyes themselves.

As Duane stated before in an article previously abstracted, "Binocular Vision and Projection," the explanation of diplopia occasioned by a deviation of the eyes is like that of physiologic diplopia. One must recall that the dominance of convergence sensations makes each eye project as if from the midline binoculus.

Diplopia is instinctively avoided, because to most persons it is very disagreeable, causing confusion and sometimes vertigo, so that those in whom it occurs make constant instinctive efforts to avoid it. The most natural method of doing this is to place the eyes in the right position by muscular effort, thus overcoming the diplopia. This, however, is usually impossible. Such attempts may even cause considerable strain and may actually augment the symptoms. Espe-

cially disagreeable are conditions in which transient correction is obtained so that the patient at one time has single vision and at other times diplopia. Particularly annoying are the sudden variations in the diplopia of paralysis when the eyes are turned in different directions. The patient may overcome the diplopia by closing one eye. He may learn to suppress one of the two images and thus get over the disagreeable results of diplopia. The patient often helps by increasing the deviation, so as to separate the images widely and thus render them less confusing. It is known that the closer the diplopia images are brought, the more troublesome does the diplopia become. The patient may diminish the diplopia not only by turning the eyes, but also by turning the head.

If there is either a simple lateral diplopia or a combined vertical and lateral diplopia to start with, tilting the head to the right shoulder always depresses the right-hand image, no matter whether the image belongs to the right eye or to the left; tilting the head to the left shoulder has the reverse effect. In this way a vertical diplopia is developed if it does not already exist, and a vertical diplopia originally present is made to increase or decrease. The lateral diplopia, originally present, decreases when a vertical diplopia is developed by tilting the head, or when by the same means it is made to increase. On the other hand, it increases when by tilting the head a vertical diplopia originally present is made to decrease. If there is a simple vertical diplopia to start with, tilting the head to either shoulder diminishes it and produces an associated lateral diplopia, which is crossed or homonymous according to circumstances.

This statement would mean that a patient with a combined crossed and right diplopia or with a combined homonymous and left diplopia would tilt the head to the right in order to diminish the vertical diplopia and deviation, while one with a combined homonymous and right diplopia or a combined crossed and left diplopia would tilt the head to the left. The patient would tilt the head in precisely the opposite way, if he altogether ignored the information afforded by postural projection and were governed simply by visual guides. As a fact, many patients do thus diminish a vertical deviation and diplopia by habitually tilting the head, and in such patients the diplopia shows a considerable increase as soon as the head is set straight. In many of these cases a purely postural projection evidently obtains; i. e., the patients follow the rules given. In other cases, the head is tilted in the opposite fashion, as if visual projection predominated. This seems to happen especially in congenital paralyses. The explanation of these cases is difficult, as in other regards the projection does not seem different from the usual.

The article is continued by a rather extensive discussion of the suppression which the patient may practice in diplopia just mentioned. This not only occurs in squint, including the alternating type, but may also be produced artificially in any eye, especially by conditions that for the time render the sight of one eye different from that of the other, such as continuous microscopic study with one eye. Furthermore, if permanent suppression has once been produced in a case of squint, it regularly, although not invariably, persists after the squint has been relieved and the two eyes once more fix normally together. The relationship of suppression to visual acuity is considered in detail. Continuous uniocular suppression tends to produce amblyopia in the deviating eye.

Suppression does not generally occur in noncomitant squint, no matter how long it has lasted. True suppression is rarely seen in congenital paralysis, in which one would most expect to find it. In any condition that would naturally give rise to diplopia, suppression does not usually occur so long as the position of the diplopia images, with relation to each other, varies noticeably either when the eyes are carried in one direction or the other, or when they are convergent or divergent.

The article closes with an explanation of suppression and incongruous diplopia. Incongruous diplopia is that type in which the deviation found by the objective tests (screen, etc.) differs in amount from that shown by the diplopia or other subjective tests. One must regard cases incongruous only when the discrepancy between objective and subjective tests is not only marked but is found repeatedly.

The author reviewed a series of forty-two cases of incongruity. This included twenty with esotropia, four with esotropia with vertical deviation, nine with exotropia, five with exotropia with vertical deviation and four with a deviation mainly vertical.

Incongruity may even occur when there is no deviation, but this apparently happens only in cases in which there has been a squint that has been relieved by operation.

A special type are the cases in which, owing to a large central scotoma, the patient fixes more or less uncertainly with an eccentric portion of the retina. In incongruity of this type there may be little or no deviation shown by the subjective tests, but a considerable one may be shown objectively. Regularly, in all types of incongruity, the subjective deviation is less than the objective, but is of the same kind. Duane speaks of this as negative incongruity. He also states, however, that there are a number of exceptions to this rule wherein the diplopia may be even greater than the objective, or may be of an opposite kind, being homonymous when there is an exotropia or crossed when there is an esotropia. Duane states that, in his experience, both of these latter (positive incongruity) are not really different from negative incongruity, but are simply a result of operation.

The abstractor thinks that this article should be read in full for more reasons than one. It presents clearly Dr. Duane's experiences in the study of this rather interesting and definitely important attribute of disturbed ocular motility.

SPAETH, Philadelphia.

REMARKS ON THE PATHOLOGY OF DEMENTIA PARALYTICA TREATED BY INFECTION. EUGEN POLLAK, Jahrb. f. Psychiat. u. Neurol. **48**:339, 1932.

It is generally admitted that in dementia paralytica there occurs a complete transformation of the brain as a result of spirochetal activity. Normally, the connective tissue plays a subordinate rôle in the central nervous system. The blood vessels, conveying the substances essential for life, run in a more or less dense network through the brain and parallel to a similar network of glia; these are entirely shut off from the ectoderm. The same is true of the second great mesodermal system—the meningeal—which stands in close relationship to the vascular system. This complete shutting off of the nerve parenchyma from the connective tissue structures is a striking phenomenon and accounts for the transformation of the entire parenchymatous structure of the brain whenever there occurs a disturbance in the relationship between these two tissues. The histopathologic process of the brain in cases of dementia paralytica may therefore be said to be due to a change in the connective tissue reaction, manifested by a dilatation and increase in the blood channels so that there results an increase in the surface of the connective tissue and vascular system at the expense of the nerve parenchyma. The spirochete is a mesodermal parasite, which through direct irritation or other factors increases its radius of activity and looks for its nutrition in other tissues. As long as the spirochete must struggle against the defensive mechanism of the mesoderm only, it produces local and occasionally also generalized irritative reactions of the type observed in typical forms of infiltrative cerebrospinal syphilis. At this stage then, there is only a nonspecific type of mesodermal reaction, which is not specially characteristic of a syphilitic process. Should the spirochete, however, succeed in gaining a stronger foothold, there results, under conditions as yet not understood, a more specific mesodermal connective tissue reaction—the gummatous connective tissue proliferation. Even at this stage the process is still strictly limited to the mesoderm, without any participation of the parenchyma. Between these two processes, i. e., the infiltrative and the gummatous, there may occur other types of tissue reaction such as, for instance, the productive proliferation of the blood vessels, which, as it increases, facilitates the spirochetal invasion of the parenchyma. This is actually the first indication that the defensive mechanism of the mesoderm is becoming feeble and unable to prevent the invasion of the parenchyma by the spirochete. In this stage

the earliest evidences of ectodermal involvement become manifest by a reaction in the glia that must be regarded morphologically as the defensive mechanism of the ectoderm. As the process advances, the glial hyperplasia becomes so marked that it interferes with the nutrition of the parenchyma, resulting finally in its destruction, first in localized areas, and later more diffusely.

Histologic examination of the cerebral cortex in dementia paralytica following malarial therapy shows that the most prominent substratum at the basis of the improvement is the disappearance of the inflammatory infiltrates from the cortex, a condition corresponding to what Alzheimer has designated as "stationary paralysis." At the same time the spirochetes also disappear. In this connection it is noteworthy that Jakob and his school showed by a most comprehensive study of a large number of serial sections that after a certain interval following malarial therapy a new paralytic process may develop in the cerebral cortex. This raises the question as to the nature of the beneficial effects following malarial therapy. The answer to this question may perhaps be found in a study of the malarial changes in the brain. Italian investigators have shown that malarial infection in general is not infrequently associated with a severe serous meningitis, that is, that the plasmodia may produce an inflammatory reactive process in the meninges. Other observations would also seem to show that the malarial organism may affect the reactions of the mesoderm. As a matter of fact, Dürck showed that the plasmodium may produce diffuse or localized glial hyperplasias that may go on to the formation of nodules. Similar processes have been demonstrated recently by Hoeppli and Regendanz in experimental trypanosome infections. These facts by themselves, however, are not sufficient to explain the effects of malaria in dementia paralytica. In the first place, there is a great difference between genuine endemic malaria and malaria induced by inoculation. Secondly, in dementia paralytica one is dealing with a constellative cross-section of two differently acting influences on the same apparatus. The vascular-meningeal tissue, the breeding place for the spirochetes, is invaded by another organism (plasmodium), which produces a functional change, in the course of which the spirochetes are severely damaged because the functional capacity of the connective tissue has apparently become reduced. The disappearance of the cortical changes is due either to a destruction of the spirochetes or to an attenuation of their vitality by the plasmodium. The possibility of a change in the primary reactivity of the connective tissue may also be a factor. In favor of this possibility is the fact that the typical plasma cell infiltration observed in untreated patients with dementia paralytica becomes converted into a lymphocytic infiltration following treatment by malaria. This transformation may possibly be due either to direct mesodermal inactivity or to a loss of the proliferating capacity of the connective tissue following the destruction of the spirochetes. Whether the spirochetes are actually destroyed or whether they migrate to other regions (bone marrow or spleen), though of great practical significance in the problem of recidivation, is of no importance as far as the local anatomic process is concerned. This phase of reconstruction during treatment with malaria does not occur without significant changes in the functional capacity of the brain, for it has been observed in most cases that during treatment the psychic symptoms are definitely increased. While there may be several reasons for this phenomenon, the most plausible is that the destruction of the spirochetes is associated with a liberation of endotoxins which affect the surrounding nerve substance, producing new defects which may be the basis for the aggravation of the mental symptoms.

Recent observations would seem to show that there occur a considerable number of cases in which in spite of the change in the pathologic process following malarial inoculation there results no improvement in the clinical picture of the disease. This, according to Pollak, does not speak against the therapeutic effects of malaria but is due to the unfortunate fact that in these cases the diagnosis of dementia paralytica has been delayed too long. No restoration of function can be hoped for when the pathologic process has been allowed to progress beyond the possibility of repair. This was recognized and emphasized long ago by von Jauregg.

It would thus seem that the destruction of the spirochetes is followed by a "purification" of the inflammatory process in the cerebral cortex and that this is the essential factor in the production of the remissions; whatever else may happen in the cortex following malarial therapy is of only secondary importance. One other factor, however, is worthy of discussion. As is well known, there is no disease in which the iron content in the cerebral cortex is as high as in dementia paralytica. Unusually large quantities of iron are found in the cells, especially in the Hortega cells, and also freely in the lymph sheaths. In cases of dementia paralytica in which the patient is treated with malaria there occurs simultaneously with the disappearance of the infiltrate also a disappearance of the accumulated iron. This would seem to indicate that the normal relation between glia and mesoderm has also been reestablished in this respect. With the reestablishment of this normal relationship there occurs a return of normal mesoderm-ectoderm reactivity, which goes hand in hand with a return of the defensive mechanism of the ectoderm. The renewed defensive activity of this tissue is also manifested by a progressive hyperplasia of the glia which, although quantitatively not so marked as before treatment, is nevertheless considerable. It is sufficiently extensive to indicate an increase in the immunizing capacity of the cerebral "connective tissue" as manifested by the development of gummas (Sträussler). It is noteworthy that in patients with dementia paralytica or tabes who have been subjected to malarial therapy gummas develop not only in the brain but also in remote parts of the body. These observations would seem to indicate that the cerebral alterations following malarial treatment are also of great significance for spirochetal reactions throughout the entire body. The changes in the reactions of the spirochetes of the brain in cases of dementia paralytica also induce a tertiary spirochetal reaction in the skin, mucous membranes, liver, spleen, lungs, pleurae and other organs. Whatever the fundamental cause for these phenomena may be, there is no doubt that malarial therapy has some effect on the functions of all organs and that the type of reaction of the individual organ depends to a great extent on the individual variations of the particular organ.

KESCHNER, New York.

CEREBRAL LOCALIZATIONS IN NEURO-OPHTHALMOLOGY: I. AUGUSTE TOURNAY, Rev. d'oto-neuro-opht. **10**:81 (Feb.) 1932.

Before studying localizations in the ophthalmic zone, cerebral localizations in general are considered. Localizations are not limited to motor acts but embrace also functions and faculties. All points in an organ like the brain are not of the same order, and it may be asked whether areas of a certain topography do not correspond to certain possibilities of action—certain determined functions.

After tracing the evolution of the nervous system from its fundamental form (primary) through the synaptic type, with its association of effectors, receptors and connectors, to the development in man of the highly complex superstructures for coordination and integration of the synaptic system and to the eventual development of the brain and of the special senses in the forepart of the system, reference is made to the idea of Hughlings Jackson and Head, namely, that the parts of the nervous system are not simply superposed one on another, but that the inferior parts are in subjection to the superior; and that when the influence of the superior part is abolished, the phenomenon of liberation appears in the inferior part. It is necessary to bear this notion in mind in order to comprehend the significance of localizations in the cerebral cortex. The various discoveries relating to the cerebral motor areas (area precentralis) are enumerated, and attention is called to the fact that the area in the cortex for the control of a segment is not of a size proportionate to the segment. Thus the area which governs movements of the thumb and index finger is as large as that which controls the entire leg. Adjoining the area precentralis in front is the area frontalis agranularis, where are located centers that command certain coordinated

motor acts, such as conjugate deviation of the head and eyes, movements of mastication and deglutition, and maintenance of the erect posture and locomotion. Still farther forward are the areas which govern the act of lying in wait.

When a cortical motor area is stimulated, an integrated movement results; but this movement is not identical with a similar voluntary movement, since it is not correlated with other attitudes and movements of the body and limbs. Again, repeated stimuli do not produce identical results. First, succeeding stimuli produce the movement more easily (this is called facilitation); second, in consequence of fatigue, a reversal of the reaction results, and, finally, a veritable inhibition may occur.

The motor area on the front lip of the rolandic fissure is matched by the sensory area on its opposite side. The difficulties of determining these sensory areas are great, but work done so far attempts to locate with precision the areas where the elementary sensations, for which the cortex is directly receptive, first arrive. The sensory centers lie on the same level as the motor centers and correspond with the same body segments. Whereas the various qualities of general sensibility, such as touch, temperature and pain, are not yet localized precisely, it appears established that the elementary center for touch is found in the anterior part of the area. It is from the correlation of elementary receptions that the synthesis of perceptions and representations is made. Thus position, movement, form and volume of objects, weight, the site of tactile or painful sensations and the difference between two points of excitations are appreciated.

Leaving the sensory sphere, the intellectual domain is approached. Analogous to the praxias, adapted to one purpose, found in the frontal margin of the prerolandic area, are the corresponding areas adapted to recognition (gnosias) that are found on the parietal margins. Below the praxias, in the third frontal convolution, and especially in the field of Broca, lies the praxia of articulated language. The praxia for writing is near the second ascending frontal convolution and near the motor centers for the hand. The gnosias for language that is heard and read and those that are concerned with the recognition and evocation of symbolic expressions are located in the gyrus supramarginalis and the area angularis of the parietal region.

Two methods of studying the brain structure have been devised: the myeloarchitectonic of Flechsig, and the cyto-architectonic of Meynert. In the latter, the cells of the cerebral cortex are of three types: pyramidal, granular and fusiform. In most parts of the cortex, according to the section, they may be grouped in six layers: (1) a molecular layer; (2) a layer composed of grains; (3) a layer of pyramidal cells, large, medium, small and giant; (4) a layer of grains; (5) a layer of large and medium-sized pyramidal cells, and (6) a layer of fusiform cells. In certain regions variations in the proportion of the elements occur. Two extreme variations are: one in which layers of pyramidal cells are substituted for layers of granular cells (this variation is found in the so-called electromotor area) and a second in which there is disappearance of the pyramidal cells (this arrangement occurs in regions where the areas of sensitivo-sensorial receptions appear to lie, the koniocortex of von Economo). Between these extremes are: a frontal type, which is mostly pyramidal, with the addition of grains; a parietal type, mostly granular, with the addition of pyramidal cells, and a polar type, containing cells of all kinds, with the peculiarity that the cortex is compressed, which causes a greater concentration of the elements. This type is found in the occipital pole.

DENNIS, Colorado Springs, Colo.

SEX AND SOCIETY. FRITZ KUNKEL; translated by W. BÉRAN WOLFE, J. Abnorm. & Social Psychol. **27**:1 (April-June) 1932.

The author, by an intensive application of logic and psychologic laws, postulates the interrelation of sexual with social adjustment. Sexual love is conditioned by the love of humanity, the love of an individual human being necessitating the capacity "to feel with" mankind or society, and difficulties of sexual function are

symptoms of disorders in the social and human sense. Success in sexual life, therefore, is to be found only where there is a general harmonious adjustment to mankind. In postulating a law of this interrelationship, many apparent discrepancies will be met, and it is the purpose of the author in this article to refute them. Cases that appear superficially as glaring exceptions are classified under two general headings: (1) an apparent success in personal and sexual love on the basis of deficient humanitarianism and (2) the reverse of this, namely, an apparently well marked humanitarianism associated with inadequate sexual adjustment.

The author presents four typical cases, two for each of the classifications, but here will be cited only one example of each. In each case there was a psychologic mechanism operating to mask the fundamental emotional trends which objectively had been parading as its contrary emotion. Under the bombardment of analysis, the exceptions were dissolved, and the author's hypothesis stood unchallenged.

Representing the first group is the case of an army officer who denied in word and deed the existence of humanitarianism, yet he was reputed to be an irresistible conqueror of women's hearts. It can be shown, however, that this conquest was not in the spirit of a genuine desire to possess a love object and become united with that object in biologic fulfilment, but conquest remained always a game in which the subjugation of the opposite sex was the chief end in view. The sexual organ and the sex act served to gratify the ego rather than the id. In this case it is shown that the sex life as well as the general attitude toward humanity were of like polarity. Both were deficient.

A case illustrating the second class, namely, the sexually maladjusted person with apparently a well marked feeling for humanity, is: A teacher of the history of arts, a man, aged 28, was reputed to be a great benefactor of humanity, a veritable St. Francis of Assisi; not only mortals but even animals were his brothers, yet sexually he was frigid with his wife. In his erotic imagination he was stimulated sexually by other and less noble women than his wife. This situation dissolved itself on analysis into Freud's Madonna and harlot situation. In the patient's neurotic conception, coitus was synonymous with subjugation. The male imposes his will on the female, thereby gaining security. When he imagined a threatening defeat in a contest with the Madonna type (his wife), he rationalized his fear of humiliation by impotency. But this fear of humiliation can be seen on analysis to ramify into his relationship with mankind as a whole. He felt well only when helping others, because in that manner he could hide his egoism. He demanded little of society even as he demanded little of his wife, because he never wished to appear deficient. Again the failure to adjust with an individual indicates the failure to adjust with mankind at large. Even as he was unable to merge his own goal into the goal of society, he was unable to arrive at an individually higher biologic level. The courage to grow and evolve was lost. Such persons rather than admit defeat in the game of life prefer to act as if there were no game at all. All friendship and sexual happiness become unreal.

The author visualizes "the social attitude" on a graduated scale, one pole of which extends high in social sympathy and rests on a feeling of human solidarity. There is represented the willingness to subordinate the self to the solution of life's problems. The other and lower pole lies low in the mire of eccentricity, discouragement and evasiveness, and is barnacled with a sense of inadequacy and inferiority, and usually results in a striving to overcompensate for these deficiencies in order to establish validity of personality. Those who occupy the lower pole in this scale are likely to believe in an autonomous sexual instinct. As this concept seemingly lightens the individual's many problems but in reality leads only to the circumvention of life's problems, which must eventually be faced, it leads to stasis of development, to insecurity, isolation and pain.

As a correction for this faulty and dangerous attitude toward sex and life, namely, as "libido" isolated from a general social function, the author admonishes those who are faltering to cease evading reality and to adopt a policy of courage. The first step in this scheme is for one to adjust his behavior as though his attitude on life were broadening and evolving. Courage is contagious, and if

resistance or hatred is not too strongly rooted, the concept of life will eventually change and catch step with the more highly evolved policy. In other words, the only chasm that exists between man and wife is the chasm that exists if they behave as if there were a chasm.

WISE, Howard, R. I.

A MENTAL HYGIENE STUDY OF JUVENILE DELINQUENCY. JOHN LEVY, Am. J. Psychiat. **12**:73 (July) 1932.

This paper represents impressions (not, strictly speaking, conclusions) drawn from observations at a small guidance clinic during the last two years. About half of the children at this clinic were delinquents; the other half were used as controls, in spite of the fact that they were all problem children. Levy opens the paper by warning psychiatrists against unscientific procedure as represented by an insufficient number of case studies or an inadequacy of control groups; this report is itself characterized by both of these defects, a fault which is presumably to be excused because of the author's recognition of it.

Heredity of such qualities as "social stigmas" and "neurotic taints" is reported as being a factor. How much of a factor it is is not stated; the terms are not defined, and case records on which this conclusion is reached are not tabulated or even summarized statistically. The author finds that children of inferior intelligence are more likely to engage in plundering and heterosexual delinquencies, whereas children with superior intelligence commit such relatively complicated offenses as forgery or homosexuality. It is further reported that parents of delinquent children employ different disciplinary measures from parents of nondelinquents. This sweeping statement, important if true, is unsubstantiated by any reported data in this paper. In any event disciplinary irregularities can be found in the delinquent group, ranging from overprotection to neglect. Physical status is also correlated with social misbehavior, the virile boys being the leaders, the effeminate the followers in juvenile gangs. This finding is suspiciously similar to one's a priori conclusions, and it is unfortunate that Levy failed to cite the enumeration of cases by which it was reached. Not only were physical defects found, but mental examinations often gave positive results, the commonest diagnosis being constitutional psychopathic inferiority.

While attaching proper importance to intrapsychic conflict, the author believes that external forces, e. g., bad conditions in the neighborhood, play significant rôles; there is, furthermore, a group of delinquent children whose problems are due to absence of conflict. Of the various personality relationships which break down in these children, relationships to other members of the family are the most important. Second in importance is a distortion in relationships between children themselves. Sex conflicts are also stressed, as in some instances a child falls back on a delinquency such as stealing as an escape from sexual misbehavior. Importance is also attached to cultural conflicts between parents and children.

For purposes of prognostic classification, the author groups offenses as mild and serious according to the depth of their rooting. In the latter class of patients are sexual perverts, those with uninhibited psychopathic tendencies, encephalitic, epileptic, feebleminded, emotionally unstable and neurotic persons and those with sociologic deviations. In the milder group are placed those with cultural deviations, nonresistant and dissatisfied children and those who suffer from sex conflicts apart from constitutional bias. This diagnosis is important for therapeutic purposes. For example, a recreation program would vary with the type of child: The expansive, "bossy" child joins a club where he can be an officer; the sexual invert is invited to take part in artistic activities (dancing, painting, etc.); when cultural conflicts loom large, settlement houses, boy scouts and "Y's" may bridge the gap. The unsatisfied child is assigned to activities where he receives approbation and an outlet for self-expression.

For a therapeutic program, Levy's first recommendation is making a complete change in surroundings, such as may be afforded by a camp, hospital, boarding school or foster-home. If this is impossible, vigorous effort is made to improve

the home, both by elevating its material standards and by explaining the mechanisms of the delinquent member's behavior. A recreational regimen is then instituted (as already described). Scholastic conditions are changed if necessary, a trade school, a special tutor, a new teacher or even a new school being prescribed as the case may demand.

The paper is closed by the presentation of a guide to be used by social workers in guidance clinics. It is over 3,600 words in length and is a complete but highly formidable document. The history is divided into ten sections: (1) identifying data, (2) a description of the delinquencies, (3) the developmental history, (4) the child's present make-up, (5) the family history, (6) the history of the siblings, (7) a report of disciplinary methods, (8) the sociologic and environmental background, (9) information about the informant and (10) summary. A briefer outline for an initial psychiatric interview is appended.

The paper is lengthy, and occupies over seventy pages without the presentation of a single statistical summary in support of any of its conclusions.

DAVIDSON, Newark, N. J.

PERIPHERAL AND CENTRAL NEUROFIBROMATOSIS. HENRI ROGER AND ALBERT CREMIEUX, Rev. d'oto-neuro-opht. **10**:17 (Jan.) 1932.

In the case reported, the initial localization was parasellar, causing the syndrome of the apex of the orbit. The terminal localization was at the level of the two acoustic nerves. The evolution in several stages, separated by long intervals, indicated multiple lesions. The patient was a woman, aged 28, who entered the clinic complaining of difficulty in walking during the preceding six months, and of deafness, which had begun three years before presentation and which was practically complete. She had lost 18 Kg. within two years; menstruation had always been normal; she had had three children and no miscarriages. The previous history revealed that at the age of 3 years there appeared paralysis and ptosis of the left eyelid, which had persisted unchanged; at 18 years of age subcutaneous nodosities were noticed on several areas; during the development of the deafness, which started in the left ear, the patient suffered with severe facial neuralgia on the right side, of about fifteen days' duration.

An examination was made. In the left eye, there were marked exophthalmos and ptosis, deviation outward and immobility of the globe, dilated and stationary pupil and papillary atrophy. In the right eye the intrinsic and extrinsic motility was normal, and there was papillary atrophy, though some vision was preserved. There were anosmia, anesthesia of the supra-orbital region on the left and corneal anesthesia on both sides. Deafness was of the nerve type. Marked dysmetria for prehension, in the finger-to-nose test, and marked adiadokokinesis were present on the left side. The left arm deviated to the left in the pointing test. The patient stood with a wide base of support; in the Romberg test she tended to fall backward, and closure of the eyes did not accentuate the disequilibrium. In walking, the left leg made unequal steps, and there was marked dysmetria in the heel-to-knee test on the left side. The Bordet-Wassermann test of the blood and spinal fluid gave negative results; the blood urea was 0.36 mg., and the urine was normal. The spinal fluid contained 3 Gm. of albumin and 7 lymphocytes. A roentgenogram showed an opaque shadow behind and in the left orbit, masking the sphenoidal fissure and the sphenoidal sinus, enlargement of the sella turcica and absence of the posterior clinoid processes. Biopsy of one of the subcutaneous nodules revealed microscopically neurofibromatosis (Recklinghausen).

The symptoms are grouped into three syndromes: subcutaneous nodular, occulopalpebral and neurologic, with cerebellar and acoustic predominance. The first can be only Recklinghausen's disease. The second is undoubtedly a parasellar tumor, extending into the orbit. This process began in infancy and its evolution has long since been completed. As to the nature of the tumor, true hypophyseal

neoplasm may be eliminated on account of the lack of its characteristic manifestations, and meningioma of the lesser wing of the sphenoid or craniopharyngioma would not have remained stationary for such a long period. It is more logical to conclude that the condition was a neurofibromatosis. During the last twenty years numerous observers have reported palpebro-orbital localizations of Recklinghausen's disease and also Recklinghausen's disease with tumor in the hypophyseal or sellar region.

To the cerebello-acoustic syndrome was added the syndrome of intracranial hypertension: increased pressure of the spinal fluid (36, Claude) without blockage, albuminocytologic dissociation and bilateral atrophy. On account of the complete bilateral deafness, the existence of a tumor in both cerebellopontile angles must be assumed. The co-existence of tumors of several cranial nerves is not rare. Of twenty-three known cases of central neurofibromatosis, affecting the acoustic nerves, bilateral deafness was found in sixteen and unilateral deafness in four. In 1930, Gardiner and Frazier stressed the association of bilateral tumor of the acoustic nerves with Recklinghausen's disease. The case reported belongs to the evolutive form of Recklinghausen's disease, described by Schulmann and Terris in 1927.

While recognizing the tremendous operative risk and the gloomy prognosis, surgical intervention was advised in this case, but it was refused, and the patient disappeared from observation before the alternative treatment, deep roentgen therapy, could be instituted.

DENNIS, Colorado Springs, Colo.

LARYNGEAL VERTIGO: ITS RELATION TO CATAPLEXY. J. GORDON WILSON, Arch. Otolaryng. **15**:534 (April) 1932.

Laryngeal vertigo, first described by Charcot in 1876, still remains obscure to most physicians. It is not a real vertigo, nor is it a disease, but it is a sequence of abnormal symptoms or responses in the larynx, associated with coughing, laughing, emotional excitement and, in Wilson's case, swallowing, preceded by a sense of constriction, burning or tickling. It is characterized by: (1) a cough, severe or slight, preceded in three of the cases by a tickling of the larynx; (2) a fall to the ground, with or without loss of consciousness and without convulsive movements, and (3) rapid recovery, with no after-effects. Wilson excludes the laryngeal crises in tabetic patients. Real laryngeal vertigo is not due to syphilis. Other names for this disease are: spasm of the glottis, laryngeal epilepsy and laryngeal ictus. Six chronic cases of laryngeal vertigo are noted from the literature. In the author's case the attack came on with an attempt to drink water; after drinking about half a glass, the patient fainted and fell to the floor. He recovered immediately, with no after-effects. The experience was repeated at intervals of from six to ten years.

Cataplexy is described as a transient condition of physical powerlessness under the influence of emotion—excitement, laughter, rage—so that the patient's knees give way and he may sink to the ground without any loss of consciousness. Narcolepsy (a definite brief sleep interrupting a normal state) is not unusually associated with cataplexy. The sudden fall, the brevity of the attack and the immediate recovery are similar in both diseases. In laryngeal vertigo, however, there is said to be loss of consciousness, but on analyzing the case histories one finds that a number of patients did not lose consciousness. Wilson calls attention to the fact that these two diseases may be the same. The question of the similarity between epilepsy and cataplexy has been raised, but the best evidence is that they are not the same. Other theories are that laryngeal vertigo is due to disturbance of the pulmonary circulation, causing syncope or passive cerebral congestion from paroxysms of coughing. Other writers think that it is due to a reflex through the vagus. It is well known that a reflex from the larynx through the superior laryngeal nerve can slow the respiration. Coughing requires a sudden contraction of the glottis, with forced expiratory efforts. Laughter, which commonly accom-

panies both conditions, also is associated with closure of the glottis, as are drinking, deglutition and surprise. The fall to the ground may possibly be due to primitive functions of the larynx, causing reflexes through the taste buds, and in startled animals to primitive protective actions from the center for kinesthetic postural reflexes.

Wilson concludes: 1. Laryngeal vertigo is a sequence of abnormal motor responses produced reflexly from the larynx and its associated respiratory mechanism by closure of the larynx under conditions not yet understood. 2. The essential phenomena are a sudden fall to the ground and a speedy and complete recovery, with or without loss of consciousness. 3. Frequently superadded clinical phenomena are observed, traceable to a more prolonged closure of the larynx, with increase of intrapulmonary pressure. 4. Neither those cases in which consciousness is retained nor those in which syncope occurs are to be regarded as distinct, as they are due to the same laryngeal closure and reflex. 5. Reasons are given why laryngeal vertigo and cataplexy are to be regarded as related clinical entities presenting at times characteristics that differentiate one from the other. 6. The pathogenesis is not known. Reflex inhibition of tonus, from laryngeal closure and arrest of respiration, is suggested.

HUNTER, Philadelphia.

DETERMINING MENTAL INSTABILITY. J. W. BARTON and D. J. INGLE, J. Abnorm. & Social Psychol. **27**:52 (April-June) 1932.

Just how many mentally unstable persons are to be found in colleges and universities has never been definitely determined. Smiley Blanton found, in a study of more than 1,000 unselected college students, juniors and seniors, that fully one-half have emotional difficulties which will prevent them from realizing their highest possibilities, while 10 per cent have maladjustments serious enough to warp their lives and in some cases to cause mental breakdown unless they are properly treated. It was observed by Barton and Ingle that the correlation between the results of mental tests given at the University of Idaho and the academic success that the student subsequently attained did not exceed 0.42. It was therefore obvious that other factors were responsible for the lack of success. This factor must determine what use will be made of a latent intelligence. Obviously, this other element is emotion. Since it is desirable to be able more completely to prognosticate success or failure, the degree and direction of the emotional state must be known. Therefore an attempt was made to discover a means of ascertaining stability in the students. The questionnaire given to the students included one hundred and fifty questions, divided into three groups. The first group concerned the student's attitude toward his present life; the second concerned his life as a child, and the third requested the student's opinion as to his mental health. Furthermore, a frank answer was requested as to what the questionee thought of the questionnaire, and it was sought to learn whether or not he or she desired to accept expert advice on mental hygiene.

In establishing a norm, each question that was construed to have psychopathologic significance was given a rating of a unit (1). The highest possible score that could be made was 84. The mean score of those who were considered neurotic was placed at 26.26. The mean score for those who were considered normal was placed at 13.24. The returns revealed no significant difference in the ratings of the four undergraduate year groups. Females were found to be more unstable than males, a score of 15.94 for the former as against 12.44 of the latter. Premedical students were found to be more unstable than law students, 15.6 as compared with 13.55. This perhaps shows the influence of temperament on the selection of careers.

As evidence of the truthfulness in the answers was the unusually favorable comparison of scores made on the questionnaires by those who were requested to sign their names and those who were permitted to hand the papers in anonymously —13.52 scored for those signed as compared with 15.38 scored for those unsigned.

Some of the interesting statistics were: Ninety-two per cent of the students claimed that they were able to answer the questions truthfully; 12 per cent admitted that they had some problem of mental health about which they were concerned; 42 per cent were willing to discuss a mental problem should they have one and were willing to go to any faculty member for advice; of the remaining 48 per cent the great majority were willing to talk over their problems but only with the head of the psychology department; 41 per cent stated that their college course had created for them many problems which they had not previously had.

The authors are checking their scores against clinical findings such as blood pressure readings, pulse rates, fluctuations in galvanic deflection and rate and depth of respirations, but so far there seems to be little agreement.

WISE, Howard, R. I.

THE CYTO-ARCHITECTONIC AREAS OF THE GYRUS RECTUS. G. NGOWYANG, Jahrb. f. Psychol. u. Neurol. **44**:475, 1932.

Cyto-architectonically, the gyrus rectus can be clearly distinguished from adjacent areas. It differs from the frontal lobe, which is directly in front of it, chiefly by the fact that the total cerebral cortex of area 1 (O. Vogt) is much wider and contains larger cells than the area recta anterior tenuipyramidalis. On the orbital surface the following difference is noted: In area 5 (O. Vogt) the cortex is considerably wider than in the area recta tenuipyramidalis and in the area recta profunda tenuilaminaris. In area 8, although the entire cortex is only a little wider than in the area recta anterior tenuipyramidalis, the area recta posterior densoganglionaris and the area recta posterior euganglionaris, there is present a relatively wide layer III. On the mesial cerebral surface the areas in the gyrus rostralis (areas 10, 11 and 12 Vogt) all have quite a dense layer V, although this type of layer is already found in area recta densoganglionaris. Posteriorly, in the gyrus parolfactorius, the cells in the various layers are smaller and their form as well as arrangement distinguishes them definitely from the cells in the gyrus rectus.

In 1910, Vogt described on myelo-architectonic grounds the individual areas in the gyrus rectus as follows: In area 4, there are more ground fibers in layers II to VI and thinner individual fibers in layers III to VI than in area 3; in area 6, layers II to VI are poorer in fibers than in area 4, and in area 7, in contrast to areas 4 and 6, there are fewer and more delicate fibers in layers II to VI. Ngowyang's cyto-architectonic studies of these areas also show definite characteristics. Some of them are: The area recta anterior tenuipyramidalis (4) is distinguished from the other areas in the gyrus rectus chiefly by the fact that the cells in layer III are larger and more pyramidal than those in layer V of the area and also than those in layer III of the other areas. Another characteristic is found in area recta profunda densoganglionaris (6) in the form of a nestlike arrangement of the cells in layer V.

In area recta posterior euganglionaris, the cells in layer III are not so well developed as those in area recta anterior tenuipyramidalis, but the cells in layer V resemble in size and form more closely those of the same layer in area recta profunda tenuilaminaris, which again can be differentiated from the other areas by the dwarfing of the cells in layers III and V. The small size of the cells in layers III, V, VI and VII of the area pretrigonalis parvocellularis is a peculiarity of this area which is observed nowhere else than in the gyrus rectus.

From this investigation it is obvious that wherever there exists in the previously described areas of the gyrus rectus a myelo-architectonic peculiarity, there is also found a cyto-architectonic peculiarity. It would also seem that structural differences always affect all cellular layers ("omnilaminar structural differences"), so that by studying these differences the various individual areas in the gyrus rectus can be definitely outlined.

KESCHNER, New York.

THE OPERATIVE TREATMENT OF FACIAL PALSY. CHARLES BALLANCE and ARTHUR B. DUEL, Arch. Otolaryng. **15**:1 (Jan.) 1932.

This is one of those rare articles that cover the entire field from beginning to end in the light of the authors' personal experience, which in this case has been extremely wide. It is possibly better not to abstract the whole article but to give the important findings. These give an entirely new outlook on facial palsy due to injury during operations on the mastoid.

To indicate the scope of the work an outline may be given of the various topics discussed: The history of the operation of nerve anastomosis. The early history of the operative treatment for facial palsy. The choice of the nerve to be grafted to the facial nerve: (1) the hypoglossal nerve, (2) the descendens noni nerve, and (3) the glossopharyngeal nerve. Stages in recovery from facial palsy and the reassumption of control of the facial muscles by the nerve cells of the rolandic cortex. Experimental investigations: (*a*) Experiments since the World War and (*b*) experiments carried out at Laurelwood since July, 1930: (1) anastomosis experiments, (2) division of the nerve in the fallopian canal and decompression and (3) the introduction of nerve grafts into the fallopian canal. The history of intratemporal operations in man: (1) decompression of the facial nerve, (2) direct suture or apposition of the ends of the divided nerve without displacement from the canal and (3) displacement of the nerve from the canal and removal of the damaged portion and suture. Comments and conclusions: The operation of choice — the introduction of a nerve graft into the fallopian canal.

The work is beautifully illustrated with numerous colored plates.

After thirty-five years of experience with all of the various methods of treatment, Sir Charles Ballance has concluded that anastomosis operations for the cure of facial paralysis should not be done except in cases in which the destruction has involved such a long portion of the nerve that no other operation is possible.

The ideal operation is to locate the source of injury and to bring together the healthy ends of the facial nerve. If this cannot be done, the authors advise an autoplastic graft. This is their new and important contribution. The nerve that they have selected, on account of its size, which is similar to that of the facial nerve, is the external respiratory nerve of Bell; thus they use Bell's nerve of respiration to cure Bell's palpsy of the face. The operation on the mastoid, the aqueduct of Fallopius, the introduction of the nerve graft, the dressing and the after-treatment are described at length. It has been discovered that the nerve graft may be put in place regardless of the direction in which impulses were carried in the nerve from which it came. Eleven cases are cited from the literature, and thirty-nine experiments are quoted in full. The authors state that a completed report cannot be made at present. They believe that this new plan is better than any other for the cure of facial palsy in man.

HUNTER, Philadelphia.

SUBDURAL HEMATOMA IN INFANTS. M. M. PEET and E. A. KAHN, J. A. M. A. **98**:1851 (May 28) 1932.

The authors have observed nine infants with subdural hematoma. Since these cases are usually diagnosed as idiopathic hydrocephalus, the authors report the series to stress the ease of differential diagnosis. The importance of making this distinction lies in the fact that idiopathic hydrocephalus is hopeless, while subdural hematoma is amenable to surgical treatment. The symptom first noted in subdural hematoma is a gradual enlargement of the head, usually associated with convulsions. This is seldom observed before the age of 4 months. Though the shape of the head resembles that of hydrocephalus, the expression of the face is different. This is a most important point. Instead of a dull, apathetic face, one sees a bright, alert expression, even though the eyeballs are displaced downward. In the far advanced cases this may not be true. On percussion over the parietal region a dull note is obtained, while in hydrocephalus the note is tympanitic

(McEwen's sign). On examination of the fundus, retinal hemorrhages and various degrees of optic atrophy may be seen and, occasionally, choked disk. The diagnosis is established on puncture of the fontanel. If true hydrocephalus exists, the ventricle is usually entered at a depth of from 1 to 2 cm., colorless ventricular fluid being readily obtained. In subdural hematoma the fluid appears just after the click of piercing the membranous fontanel. It varies from slightly straw-colored to almost pure blood and gushes from the needle with each cry. One should not be confused here by subarachnoid fluid which might be increased by cortical atrophy and slightly colored by the trauma of the puncture. Immediate centrifugation will show in the latter condition a clear colorless supernatant fluid. The authors' operative procedure in subdural hematoma is now as follows: If the case is bilateral, the subdural space opposite the side to be operated on is first tapped. This is to avoid subsequent pushing over of the brain with pressure on the brain stem by the fluid on the nonoperative side after operation, when the intracranial pressure commences to reach the normal. One should not wait until the operation has been completed before tapping the nonoperative side, since the pressure then may be so low that very little fluid would be obtained. A moderate sized osteoplastic flap is then turned down over the frontoparietal region. The dura is opened, leaving the base toward the occipital region. The middle meningeal vessels are clipped. The blue black gelatinous membrane is removed without an attempt being made to go too far beneath the dural incision. Following this, the depressed brain covered by a tough transparent or milky white membrane is seen. This is removed from the arachnoid as widely as possible, there being but slight danger from hemorrhage in this procedure. The dura is then closed and the bone flap replaced without making a decompressive opening. The scalp is sutured in two layers with silk. Facilities for immediate transfusion should be available.

EDITOR'S ABSTRACT.

BLASTOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM. H. DEMME and C. MUMME, Deutsche Ztschr. f. Nervenh. **127**:1, 1932.

The authors describe a rather typical case of infection of the nervous system by Torula in which the pathway of invasion was peculiar and led originally to a mistaken diagnosis. The patient, a quarry man, aged 60, complained of pain in the chest, and though physical findings were minimal, a roentgenogram showed a large, rounded tumor eroding the tenth and eleventh ribs. When meningeal signs with psychotic symptoms appeared and many cells were found in the spinal fluid, invasion of the meninges by tumor cells was diagnosed. Later, however, the presence of yeasts was recognized in the spinal fluid, and biopsy on the tumor presenting in the paravertebral space revealed many organisms in a delicate reticulum of connective tissue. At the end of life, some ten months after the onset of the illness, cultures were obtained from the wound, fluid and urine, four different organisms being differentiated. During spinal puncture, pressure on the tumor would increase the pressure and the cell count, indicating a direct communication between the tumor and the spinal canal.

At necropsy the mass in the thorax was the size of a child's head, soft and gelatinous, consisting mostly of yeast cells. No other somatic foci were recognized. The brain presented a low grade meningitis with many giant cells and no leukocytes. The perivascular spaces were dilated and flask-shaped, and the membrane of the pia-glia was stretched and then broken by huge numbers of organisms with their gelatinous capsules. The authors found the Mallory stain best for demonstrating the torulae. No foci were found in the white matter or basal ganglia; a few small lesions occurred beneath the ependyma; nodules of cherry size were found in two locations; the meningitis and cortical invasion were observed in the cerebellum, but nothing important was detected in the brainstem or spinal cord. Serologic studies gave negative results. Inoculations into animals were unsuccessful after four months (too short a time for some strains).

The authors remark on the minimal reaction of the cerebral tissue to the presence of the organisms and believe that the cysts form by direct internal expansion from the proliferating organisms and that invasion of the brain takes place along the perivascular spaces, but they are puzzled by the occurrence of nodules, resembling erosions, beneath the ependyma and in the cerebellar cortex.

FREEMAN, Washington, D. C.

CLINICAL FINDINGS IN "RECOVERED" CASES OF SCHIZOPHRENIA. NOLAN D. LEWIS and ELSIE BLANCHARD, Am. J. Psychiat. **11**:481 (Nov.) 1931.

With the intention of finding the factors responsible for the occasional instance of "recovery" from an attack of dementia praecox, the authors have investigated the clinical data in one hundred instances. Their failure to provide the parallel data in a control group of unimproved patients, however, seriously reduces the value of the interpretations. Eleven per cent of the patients were the children of psychotic parents or grandparents. In thirty more instances, cases of syphilis, alcoholism or epilepsy were found in the family. The authors combine these figures to reach the misleading conclusion that in 41 per cent of the cases a reliable family history of significant mental disorder was obtained. Thirty-seven of the patients in this group were high school graduates, and seventy-six had had no previous hospitalizations. The average duration of the psychotic attack was one year or less in 94 per cent of the cases. Physical and laboratory examinations gave negative results in forty-nine and positive results in fifty-one cases. The latter group (of fifty-one "positive" cases) included such findings as "mild nervous system disturbances" in fifteen patients, tachycardia and varicocele; six patients had organic heart disease and four had testicular hypoplasia; thirty-six were extroverts, sixty-four, introverts; seventy-four had failed to make a satisfactory economic adjustment before the onset of the psychosis; fifty-three had been in the Navy, twenty-seven of whom rendered unsatisfactory, irregular service. Of the one hundred patients, only twenty-seven lived in pleasant homes free from undue conflict. How many nonpsychotic or nonrecovered persons live in such homes is not stated. Seventeen of the patients were overtly homosexual; fifty-six had had heterosexual experiences, forty-five of whom contracted venereal disease. The assigned exciting causes were overwork (seventeen), alcohol (thirteen), sexual difficulties (fourteen), unhappy family situations (fourteen), physical disorders (fourteen) and various less frequent factors, such as nostalgia, blow on the head and religious conflict. The outstanding mental symptoms were no different from those noted in nonrecovered patients, with confusion, auditory hallucinations, mannerisms, hypochondriasis, autistic thinking and negativism, each appearing in more than one third of the group. The paper is closed with a plea for a more careful study of each patient.

DAVIDSON, Newark, N. J.

ACUTE PYOGENIC INFECTION OF SPINAL EPIDURAL SPACE. S. S. ALLEN and E. A. KAHN, J. A. M. A. **98**:875 (March 12) 1932.

Three cases of acute pyogenic infection of the spinal epidural space are reported. The conditions most likely to be confused with epidural infection are poliomyelitis, leptomeningitis, abscess of the spinal cord and tumor of the spinal cord. Poliomyelitis may be ruled out by the presence of a sensory level and of a subarachnoid block. Lumbar puncture, with examination of the fluid, is usually sufficient to eliminate the second possibility. As to abscess of the spinal cord, the simultaneous appearance of the sensory and motor symptoms certainly suggests the presence of an intramedullary lesion, while pain, appearing several days before the onset of the paralysis, is in favor of extradural involvement. A spastic and not a flaccid type of paralysis would be expected in the case of tumor of the spinal cord. The severe febrile state would also be absent. Of course, these points of differentiation are merely generalities, as the diagnosis of the localization and nature of

lesions of the spinal cord is often extremely difficult. Aside from an academic standpoint, a mistaken diagnosis of abscess or tumor of the cord is of no great import, as immediate laminectomy, on the sudden appearance of paralysis, is certainly indicated. From the onset, the disease assumes the character of a profound toxemia. The only method of combating the infection is, perhaps, operation with adequate drainage of all the tissue involved. As the process is always extensive, it requires the removal of many laminae. The greatest involvement is in the midthoracic region, posterior to the spinal nerve roots. Following operation, the treatment of the wound depends entirely on the method most favored by the surgeon. The prognosis is poor, regardless of how early a diagnosis is made and how soon thereafter a laminectomy is done. Very few recoveries have been reported. The cord changes lead one to believe that unless operation is employed early in the course of the disease, the damage to the cord will be irreparable.

EDITOR'S ABSTRACT.

TRAUMATIC INJURY OF THE EXTRAPYRAMIDAL APPARATUS. ROBERT BING, Schweiz. Arch. f. Neurol. u. Psychiat. **27**:193, 1931.

Bing expresses the opinion that parkinsonism of traumatic origin is rare, because the centers involved in such cases are deeply seated and therefore well protected. A concussion sufficiently severe to injure the basal ganglia, furthermore, is liable to produce lesions in surrounding parts, with the result that the ensuing parkinsonism is atypical, being accompanied by signs and symptoms of lesions of the thalamus and pyramidal tracts. Four cases are reported in which Bing was asked to render an expert opinion relative to the part played by trauma in the genesis of the symptoms. The first case was included in an earlier contribution by the author (*Schweiz. med. Wchnschr.* **59**:717, 1929) and also in one by Hans W. Maier (*Klin. Wchnschr.* **5**:1827, 1926). In this, as well as in the second case, the patients had been struck on the face in such a manner that the force was applied in an anteroposterior direction, parallel to the base of the skull. Bing agrees with Maier that injuries of this type are peculiarly liable to produce lesions of the basal ganglia. The patient in the second case, unlike the one in the first, was not rendered unconscious by the blow, but a roentgenogram of the skull revealed a probable fracture of an anterior clinoid process. Signs of parkinsonism developed in both patients a few weeks after the injury, and both suffered from pain attributed to a lesion of the thalamus. The second patient also presented some evidence of involvement of the pyramidal tracts. Bing reserves judgment as to the part played by trauma in the etiology of parkinsonism in the third case, because the patient had been struck over the top of the head rather than over the face and the clinical features suggested a postencephalitic state, although a history of acute encephalitis was lacking. In the fourth case, the author's opinion that the patient did not have parkinsonism was confirmed later by an anatomic study of the brain.

DANIELS, Rochester, Minn.

CAPSULAR HEMIPLEGIA IN RELATION TO PYRAMIDO-EXTRAPYRAMIDAL LESIONS: FIVE CASES. AUSTREGESILO, JR., An. assist. a psicop., 1931, p. 189.

Austregesilo, Jr., recalls that the ordinary classic conceptions of capsular hemiplegia consider the appearance of extrapyramidal symptoms as exceptional, whereas the pyramidal syndrome is constant. The author had an opportunity to study the anatomopathologic aspects of five cases of hemiplegia, and he gives detailed histories of all five cases. In case 1, the putamen, in the focus of degeneration, was found to be slightly involved in the surface adjacent to the internal capsule. The second focus did not have the extent of the first; it was found to be located chiefly in the external portion of Brissaud's globus medialis. In case 2, the degeneration involved the caudate nucleus; the putamen presented in its superior and posterior portion a small lacuna of triangular shape. In case 3, in the right hemi-

sphere there was a hemorrhagic degeneration of the external capsule, including in its extent the putamen and the upper part of the internal capsule. This aspect is seen in a section that passed directly through the optic chiasm. The degenerative area was 4 cm. long, and had its beginning in the frontal lobe, just at the point where the head of the caudate nucleus begins. The degeneration involved the caudate nucleus, the anterior portion of the internal capsule. There were no other degenerative foci. There was, however, a lesion of the pyramidal tracts and the extrapyramidal centers. In case 5, there was an old focus of degeneration that involved the internal capsule, the caudate nucleus and the globus pallidus. In the left hemisphere no macroscopic changes were found. In the anterior portion of the lenticular nucleus, at the junction of the corpus striatum and the globus pallidus, there appeared to be a minute lacuna, about 2 or 3 mm. wide at its largest diameter. This section passed directly through the commissura anterior.

EDITOR'S ABSTRACT.

INTRADURAL TERATOID TUMORS OF THE SPINAL CORD. KIYOSHI HOSOI, Arch. Path. **11**:875 (June) 1931.

Bidermal, or teratoid, tumors of the spinal cord are exceedingly rare. Hosoi has not been able to find a single case of genuine tridermal or teratomatous new growth of the spinal cord recorded in the literature. Teratoid tumors are obviously congenital. They are often associated with other congenital abnormalities or defects. One of the cases of Kubie and Fulton and the case reported showed spina bifida occulta and a pilonidal cyst. Hansmann's case was a vertitable potpourri of congenital defects. There was an associated syringomyelia in the cases of Gerlach, André-Thomas and Quercy and Bielschowsky and Unger.

Since these complex tumors are benign and grow slowly over a period of many years, the acute symptoms of pressure on the spinal cord may not arise until adult life. In the case reported, it is to be noted that this young man gave a vague history of not being able to walk for a short time when a child, although previously he had been able to do so.

Histologically, only the derivatives of the mesodermal elements were present in the cases of Gowers, Gerlach and Forbes. Frick described a teratoid tumor containing bone with myeloid reaction in the marrow spaces. It is difficult to say just what is the nature of the cysts or glands lined by ciliated and nonciliated, tall columnar cells. In two of the reported cases there were an associated glioma and an endothelioma or alveolar sarcoma. Endodermal elements were uniformly lacking, so that all of the collected complex tumors of the spinal cord are bidermal. Intradural tridermal tumors or genuine teratomas are perhaps yet to be described.

WINKELMAN, Philadelphia.

PSYCHOTHERAPY IN THE SCHIZOPHRENIAS. WILLIAM MALAMUD and WILBUR MILLER, Am. J. Psychiat. **11**:457 (Nov.) 1931.

In reviewing the importance of psychotherapy in dementia praecox, Malamud and Miller introduce for analysis three problems: (1) How much success can reasonably be expected from this or from any treatment? (2) What is the relative weight of the organic and functional factors in the etiology of this psychosis? and (3) What limitations must be placed on the concept of schizophrenia? In discussing the first problem the authors compare psychiatry with general medicine and ask why perfect cures should be expected in the former when physical diseases so often leave permanent scars. In analyzing the second question the authors emphasize the absence of evidence of organicity in dementia praecox, and are inclined to assign superior weight to functional factors. The definitions of schizophrenia are reviewed with the suggestion that Bleuler's concept is a highly impractical one and that the necessity of resorting to obscure organic mechanisms to explain some of the psychotic symptoms is a serious flaw in the hypothesis.

Psychoanalysis, in the orthodox fashion, is, in the opinion of the authors, more suited for reaching an understanding of these patients than for effecting a cure. They outline a psychotherapeutic regimen, which consists in appreciating the mechanisms underlying the content of the psychosis, in gaining a rapport with the patient and in reconstructing for him a logical evaluation of the external world. Four cases are detailed in which the patients obtained relief from psychotic symptoms following a demonstration to their own satisfaction of the mechanisms underlying their conditions. The best results were obtained with intelligent patients early in the course of the psychosis.

DAVIDSON, Newark, N. J.

EFFECTS OF SPINAL ANESTHETICS ON THE SPINAL CORD AND ITS MEMBRANES. LOYAL DAVIS, HALE HAVEN, J. H. GIVENS and JOHN EMMETT, J. A. M. A. **97**:1781 (Dec. 12) 1931.

The facts that the spinal anesthetic solutions in common use today are hemolytic as well as myelolytic and would seem to act on the myelin of the nerve fibers as they do on the lipoids of the red blood cell membrane causing its dissolution are emphasized. After the injection of the spinal anesthetics in most prevalent use today into the spinal dural sacs of dogs, the following changes have been observed: (1) a varying degree of inflammatory reaction in the leptomeninges; (2) passive changes in the ganglion cells of the gray matter of the cord similar to those seen in retrograde or so-called wallerian degeneration; (3) swelling and fragmentation of the axis cylinders; (4) signs of degenerative changes in the fiber tracts of the cord. The fact that the last three of these changes were not pronounced in the cords of animals which were allowed to live ninety days speaks against their permanent nature. This is also suggested by the incomplete picture of degeneration in the ganglion cells and by the absence of Marchi evidence of degeneration in the cervical and dorsal segments. However, the inflammatory changes in the leptomeninges were so constantly present that they cannot be overlooked. The authors hope to extend their studies to the spinal cords of human beings and to incorporate their results with the clinical observations that have been made in a careful neurologic examination of patients who have been operated on under spinal anesthesia. In many instances, neurologic complications have been present for as long as a year after the injection of the spinal anesthetic.

EDITOR'S ABSTRACT.

OBSERVATIONS ON EMBRYONIC AND FETAL MOVEMENTS OF THE CAT. W. F. WINDLE and A. M. GRIFFIN, J. Comp. Neurol. **52**:149 (Feb.) 1931.

Pregnant cats were placed under a light ether anesthesia; the carotid arteries were ligated; a cannula was inserted into the trachea, and the animal was decerebrated. The animal was then allowed from one to four hours to recover from the effects of the ether, after which the fetuses were delivered from the uterus and were observed within the amnion, with the circulation intact. Methods of studying the fetuses varied according to their size. Movements of the smallest embryos were visible only at the moment of delivery. Large embryos could be transferred to warm physiologic solution of sodium chloride and studied there. Movements persisted longest when the fetus and placenta were transferred to the solution. By this method the development of motility has been followed from its earliest manifestation as a slight ventrolateral flexion in the 16 mm. cat embryo to a time shortly before birth. The movements are to a large degree massive and generalized with a gradual evolution of the more discrete reflexes from the total pattern. In other cases the reflexes appear with no apparent relation to the primitive behavioral background. Functional motor differentiation proceeds cephalocaudally and proximodistally. Postural and locomotor reactions seem to appear in the fourth fetal quarter, feeding response appearing later. No conclusions are drawn as to the mechanisms in the behavior movements.

ADDISON, Philadelphia.

THE TREATMENT OF NEUROSYPHILIS. A. BENSON CANNON, Am. J. Syph. **15**:517 (Oct.) 1931.

The popular idea that arsenical therapy is responsible for an increase in the incidence of neurosyphilis is doubted by Cannon, who is inclined to emphasize interrupted, inadequate or infrequent treatment as the significant factor. His practice is to suspect neurosyphilis when the Wassermann reaction is persistently positive in spite of ordinary treatment or when there are irregular, unequal or sluggish pupils, asymmetrical reflexes, occipital headache, facial or oculomotor palsy, fainting spells or muscle pains or twitchings. The author recommends the Swift-Ellis treatment in all cases of serologically demonstrable neurosyphilis. The technic of the preparation of the serum and administration of the treatment is detailed. Cannon believes that this treatment is most likely to give a normal serologic picture, a shorter convalescence and ultimately a relief of symptoms. The author believes that no physician who withholds the Swift-Ellis treatment from syphilitic patients who fail to respond to intensive intravenous therapy is doing his duty.

DAVIDSON, Newark, N. J.

RECOVERY IN DEMENTIA PRAECOX. H. L. LEVIN, Psychiatric Quart. **5**:475 (July) 1931.

A report is made concerning thirty-five patients with dementia praecox who were discharged as recovered during a period of four years. Recovery indicated the condition of a patient who has regained his normal health so that he may be considered as having practically the same mental status as previous to the onset of the illness. Of the thirty-five patients, in nineteen the condition was of the paranoid type, in ten of the catatonic and in five of the hebephrenic. In twenty of the thirty-five cases the author was able to ascribe some physical or mental stress prior to the development of the psychosis. Seventeen gave no record of any discrepancy between thought content and emotional expression; twenty-one had delusions, and nine had a severe regression. At the time of discharge, eight had no insight; eight had limited insight, three partial insight, four fair insight and eleven good insight. A year following discharge, twenty-six had continued to maintain a satisfactory social adjustment; four had been readmitted, and one was psychotic, but was being cared for at home. Four were unaccounted for. No general conclusions were drawn.

HOWARD, Milwaukee.

MOTOR LOCALIZATION ON THE CEREBRAL CORTEX OF THE GUINEA-PIG. C. PING, T. H. CHANG and L. T. CHENG, J. Comp. Neurol. **52**:247 (April) 1931.

This is the first study of the distribution of motor areas of the guinea-pig. Electrical stimulations, histologic investigations and ablations are employed. The distribution is comparatively indefinite, and there is great individual variation. Since on the average the motor points of the head and arm are situated anterior to those of the leg, it suggests that the cerebrum is not so much developed and differentiated as in dogs, lemurs, anthropoid apes and other higher forms, and probably has retained the primary segmental feature.

The Betz cells appear much scattered between the anterior frontal lobe and the occipital lobe. The larger Betz cells are distributed in areas responsible for the limb and trunk movements.

After ablation of a portion of the cortex the animals recovered in a day, which indicated to the authors that in the case of a less differentiated brain the motor centers are more readily shifted to the other hemisphere or to some lower center.

ADDISON, Philadelphia.

INTERVERTEBRAL DISK EXTENSIONS INTO THE VERTEBRAL BODIES AND THE SPINAL CANAL. DAVID SASHIN, Arch. Surg. **22**: 527 (April) 1931.

The first case of extension of an intervertebral disk into the spinal canal was reported in 1929. The cause is usually trauma, often mild repeated injuries;

arthritic changes may be a factor. When these disks project into the spinal canal they may cause displacement of the cord with symptoms of pressure. A case of Dandy's is quoted in which this condition resulted in diplegia that cleared up following an operation. The disk extensions are roentgenologically discernible only when lateral roentgen views are taken. Sashin presents nine cases of extension of the disk, usually only into the spinal column; in at least one case, however, there was extension into the spinal canal, as a tentative diagnosis of tumor of the cord had been made. The patient was a girl, aged 15, who complained of backache and pain in the legs following a fall; she had atrophy of one thigh and leg. Treatment in some cases is operative, but more often firm immobilization is required, especially when pain is severe.

DAVIDSON, Newark, N. J.

A STUDY OF THE NEUROFIBRIL STRUCTURE OF THE NERVE CELL. O. W. TIEGS, J. Comp. Neurol. **52**:189 (Feb.) 1931.

The author has described neurofibrils in the cells of the spinal cord, spinal and cranial ganglia, cerebral cortex, sympathetic ganglion, tangential nucleus, trapezoid nucleus, and the Mauthner and Purkinje cells in a large series of animals, using Cajal and Bielschowsky preparations. He states that neurofibrils are not fixation artefacts, but that they can be seen in the living cell in favorable preparations. He attributes a conducting function to them because of their mechanical properties and arrangement. He describes in the spinal cord and cerebral cortex collaterals ending by "end-feet" the fibrils of which are in direct continuity with those of the receptive cell, and in other cases by directly merging with the fine branches of the dendrites. He claims neurofibril continuity for the termination of fibers on Mauthner's cells and the cells of the tangential nucleus in the trout and on the trapezoid nucleus in the cat.

ADDISON, Philadelphia.

EXPERIMENTAL CATATONIA. GEORGE W. HENRY, Psychiatric Quart. **5**:441 (July) 1931.

Experiments were made on birds and small animals in which catatonic motor phenomena were provoked by the use of toxic substances. The substances used were bulbocapnine, veronal, sulphonmethane, a barbituric acid derivative (somnifen), harmin, cannabis indica, mezcaline and epinephrine. Bulbocapnine was the most successful. As the state of intoxication induced in animals by these substances was increased there seemed to be a loss of function of the most recent phylogenetic acquisitions of the nervous system. The author deduces that there is an interference with the function of the cerebral cortex and a dominant action of the extrapyramidal system, particularly of the basal ganglia. There is therefore a regression at the physiologic level of integration, and in man it is probable that this regression is concomitant with the regression at the psychologic level.

HOWARD, Milwaukee.

THE CAUSE OF EXOPHTHALMIC GOITER. WILLIAM S. REVENO, Arch. Int. Med. **48**:592 (Oct.) 1931.

The loss of weight, diarrhea and tachycardia that accompany hyperthyroidism are ascribed to the production of thyroxine, while the exophthalmos, tremor and hypertension are presumably due to the influence of epinephrine. Both of these agents are derived from tyrosine. When the intestinal medium is alkaline and deficient in carbohydrate, there is an alteration in the biochemical constituents, resulting in the elaboration of histamine and tyramine and in the overproduction of thyroxine and epinephrine. Together, these four drugs can produce all the symptoms of exophthalmic goiter. On this basis, Reveno advances the hypothesis that hyperthyroidism is primarily a disturbance resulting from long-continued toxic processes in the intestinal tract.

DAVIDSON, Newark, N. J.

"Pseudo-Kernig Symptom" as a Symptom of Tumor of the Frontal Lobe. H. Hoff, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:522, 1931.

Hoff found what he called a "pseudo-Kernig sign" in a patient with a tumor of the frontal lobe. This sign is elicited like the Kernig sign, but is unaccompanied by signs of meningeal involvement, and the distribution of the pain is in the muscles of the leg like that of a swimming cramp. He examined twelve other frontal lobe lesions, seven of which were tumors (five endotheliomas and two gliomas). There were one frontal lobe abscess and five cases of injury of the frontal lobes. The sign was absent in only two cases. It has no definite localizing value as regards the frontal area, because it is found in lesions anywhere in the frontal lobe. The sign is found also in cerebellar tumors, but here it is usually bilateral.

Alpers, Philadelphia.

Cisternal Puncture in Infants: Observations in One Hunlred Cases. G. W. Kutscher, Jr., Am. J. Dis. Child. **42**:1428 (Dec.) 1931.

Kutscher reports his observations in 100 cases of cisternal puncture in infants, dealing in tabular form and in a concise manner in each case with the indications, the history, the diagnosis made and the results obtained. He described in detail his technic, which may be of considerable help to those who contemplate performing this type of puncture. The study revealed thirty-one cases of intracranial hemorrhage, seven of meningism, two of encephalitis and three of meningitis. Of the hundred patients treated, eleven died, but in no instance did death or demonstrable injury result from the cisternal puncture. He concludes that in competent hands cisternal puncture on infants is a much safer and better diagnostic procedure than lumbar puncture.

Leavitt, Philadelphia.

Spasmus Nutans (Head Nodding) as Associated with Defective Lighting in the Home. Donald Paterson and R. W. B. Ellis, Lancet **2**:737 (Oct. 3) 1931.

Four brief records of infants who had spasmus nutans are presented. The outstanding feature in each case was that the child had been kept in a dim light for a considerable time before the onset of the symptoms. Three of the children occupied basement rooms, and the fourth occupied a top back room, dimly lighted and requiring artificial light in the daytime. In each case there was associated rickets, and recovery took place as the rickets improved. Since the illness itself is self-limited, much importance cannot be attached to antirachitic treatment.

Beck, Buffalo.

The Metabolism of the Choroid Plexus. H. A. Krebs and H. Rosenhagen, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:643, 1931.

Krebs and Rosenhagen found that the respiration of the choroid plexus was twice as great as that of the gray substance in the brain and four times as great as that of the white matter. The production of lactic acid is somewhat less than that in the gray matter and slightly greater than that in the white substance. The metabolism of the choroid plexus is therefore of the same order as that of the gray substance of the brain and of the glandular organs such as the liver and the kidneys. The demonstration of a large energy metabolism in the choroid plexus leads to the assumption that the formation of spinal fluid is not a physical process (dialysis), but is also a product of secretion from the plexus cells.

Alpers, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 4, 1932

HENRY ALSOP RILEY, M.D., *President, in the Chair*

FORCED DRAINAGE OF THE CEREBROSPINAL FLUID IN THE TREATMENT OF DISEASES OF THE CENTRAL NERVOUS SYSTEM: THE THEORETICAL AND EXPERIMENTAL BACKGROUND. DR. LAWRENCE S. KUBIE.

Under conditions of forced drainage (i. e., the reduction of intracranial pressure to atmospheric pressure, and the lowering of the osmotic pressure of the blood), the chief point of origin of cerebrospinal fluid shifts from the choroid plexus to the capillary bed of the central nervous system as a whole. The theoretical and practical distinction between simple drainage alone and forced drainage may be emphasized, with particular stress on the point that it is only under the special conditions of forced drainage that the formation of cerebrospinal fluid in large amounts throughout all of the parenchymatous tissue of the central nervous system can occur; pure drainage alone, on the other hand, draws only the surface fluid of the preexisting lake of cerebrospinal fluid, and obstructs the formation of any new fluid and also drainage from the depths by allowing the collapse of the leptomeninges. Under conditions of forced drainage, fluid courses along the perivascular channels from the depths of the central nervous system to the surface, carrying with it the products of any inflammatory reaction. Under these conditions there are no increase in intracranial pressure and no hydration of the parenchyma.

Extensive use of this method in experimental work on dogs, cats and rabbits reveals no ill effects from repeated forced drainages in either normal or sick animals. It places no strain on the cardiovascular apparatus. With the application of the method, the cellular picture of the cerebrospinal fluid usually shifts to a predominantly lymphocytic reaction, and forced drainage probably increases the transfer of immune bodies from the blood to the spinal fluid. Preliminary tests of the safety of the method were made on patients in Boston during the summer of 1927. No other method of administration of fluid can be as effective in reducing the osmotic pressure of the blood as the direct introduction of hypotonic saline solution into the veins.

SOME CLINICAL APPLICATIONS OF FORCED DRAINAGE TO VARIOUS INFECTIONS IN INFLAMMATORY CONDITIONS IN THE CENTRAL NERVOUS SYSTEM. DR. GEORGE M. RETAN, Syracuse, N. Y. (by invitation).

Forty patients have been treated on more than 100 occasions with forced drainage for from a few hours to a few days. The forty cases have been distributed among different types of acute and chronic infections and inflammations of the central nervous system. There are not enough cases in any one group to make statistical treatment possible, but the clear-cut symptomatic and clinical changes in these patients in response to forced drainage show that the therapy affects the course of these diseases of the central nervous system, even though it is still premature to make any claims as to the ultimate value of the procedure. Since the various groups are small, it seems better to report a few cases in detail rather than to attempt any generalizations. In some cases the ultimate outcome was favorable; in others the results were unfavorable; but in no case was there a failure to observe profound symptomatic alteration in response to the treatment. Surprisingly enough,

this change occurred even in symptoms that had existed for many years, in cases in which it was difficult to postulate some purely transient pathologic basis, such as edema or cellular exudate. It would seem necessary, therefore, to assume that there is some form of tissue change which can cause a symptom to persist for many years without becoming permanently "structuralized," and that this pathologic condition responds, at least temporarily, to forced drainage.

There were ten cases of different types of syphilis of the central nervous system, three of multiple sclerosis, two of acute epidemic encephalitis in children, four of chronic progressive encephalitis with parkinsonism, three of chorea (two of them acute and one a chronic recurrent chorea of five years' duration), two of proved tuberculous meningitis and one of presumptive tuberculous meningitis, two of acute anterior poliomyelitis and several different kinds of pyogenic meningitis.

Some of the most surprising results occurred in chronic cases of syphilis. Alterations were observed in reflexes, changes in the pupillary responses, with a disappearance of the Argyll Robertson reaction, disappearance of chronic and intractable pain and marked fluctuations in, and improvements of, sphincteric control. It is too early to discuss the question of cures; but it is safe to say that individual symptoms which had obstinately resisted the most intensive antisyphilitic treatment responded to a surprising degree to forced drainage. Patients themselves have been so enthusiastic over the results of therapy that they eagerly seek repetition of it.

The remission of symptoms in cases of multiple sclerosis is something that one naturally expects because of the inherent nature of the disease. Prompt diminution of objective signs, however, such as the disappearance of ankle or patellar clonus and Babinski reflexes, the sudden relief of severe amblyopia during the course of the forced drainage itself, when this amblyopia had existed continuously for the preceding nineteen months, and many similar experiences show beyond question that the procedure has a profound influence on lesions in the neuraxis which produced these symptoms and signs.

The response in acute encephalitis was dramatic. In the cases of chronic progressive encephalitis of three, six, and seven years' duration, respectively, one would naturally expect little change. Limited experience, however, with conservative use of the method suggests that even here under certain conditions there may be improvement.

The results in the cases of chorea were particularly striking. All three cases showed a prompt disappearance of all choreiform movement after one, or at most two, treatments. The improvement was striking on the morning after the treatment, and even more marked by the second day. A reel of moving pictures demonstrated the condition of one of the patients before treatment, the actual application of the method and the condition on the following day.

The presentation of some of the results in cases of proved and probable tuberculous meningitis and in cases of pyogenic meningitis led to a general discussion of technic. Technically, the main problem is the maintenance of a free pathway for drainage. Repeated lumbar puncture or tendencies for the needle to become loose in the tissue probably lead to ascending infections. For this reason a very large needle has been devised to fit over the usual needle. Because of its size, this larger needle is firmly held in the tissues of the back. It is used in any drainage lasting for twenty-four or forty-eight hours. For shorter periods the ordinary needle for lumbar puncture is used. In cases of pyogenic or tuberculous meningitis it is sometimes necessary to perform a laminectomy on a single lumbar vertebra, in order to drain through a rubber tube or cigaret drain. While definite curative value cannot be attributed to the treatment in these cases, clinical experience has proved that the patient shows improvement as long as free drainage is maintained. The problem would seem to be primarily one of securing adequate and uninterrupted forced drainage.

Experience has shown also that the profession has been too conservative in the administration of hypotonic solution of sodium chloride. While this conservatism was necessary in the beginning, it is now evident that the patient feels far less discomfort when the injection is given promptly after the initial puncture, without

a long preliminary drainage, when larger amounts of fluid are given, and when fluid is administered freely by mouth or by rectum after the treatment is over. At the beginning, the injection was limited to 1 liter of 0.45 per cent saline solution; now my associates and I administer larger amounts, up to 2 and 3 liters. It is also possible that, with increasing experience, we may find it safe to use solutions of even lower concentration without producing hemolysis.

The contraindication is the presence of any lesion in the central nervous system into which fluid may be poured and from which it cannot escape, as an internal or obstructive hydrocephalus, a cyst or a tumor or an area of fresh hemorrhage with destruction of tissue and engorgement. Such conditions must be carefully ruled out by accurate differential diagnosis.

In conclusion, one is justified only in emphasizing the safety of the method and the highly encouraging nature of the results so far achieved. No untoward results have occurred so far. The earlier treatments were sometimes accompanied by a moderate amount of headache, nausea and vomiting. These symptoms occurred either before or after the injection. By shortening the initial period of drainage, increasing the amount of fluid injected, interrupting the drainage from time to time by replacing the stylet, and by administering fluids liberally after the treatment is over, these symptoms have been practically eliminated.

DISCUSSION

DR. OSCAR M. SCHLOSS (by invitation): I find it difficult to discuss a subject concerning which I have had no personal experience, particularly when it involves a therapeutic procedure. This presentation is interesting, because it was conceived on purely physiologic grounds and has been demonstrated to have clinical application. I wish to ask whether there is a definite relationship between the amount of spinal fluid secreted and the rate at which the hypotonic solution is being given. In regard to the use of a more dilute solution, which Dr. Retan has considered, I am sure that it can be used safely, because in infants I found that I could give as low as 0.3 per cent of salt solution without producing hemolysis, provided the solution was given very slowly.

I can say little about the results obtained in this group of diverse cases. If one chooses to speculate as to how they might be brought about, two possibilities suggest themselves: first, the one made by Dr. Kubie, namely, the increased permeability of antibodies; the other, the profound circulatory changes induced by the forced secretion of spinal fluid. It seems that the latter may be the more probable way, particularly in view of the rather diverse group of cases in which the procedure was of apparent benefit.

Two dangers suggest themselves to me, both of which were considered in Dr. Retan's paper; first, that this might prove a hazardous procedure in cases in which there is an obstruction of any degree to the flow of cerebrospinal fluid from the ventricles, and second, the danger of inducing infection through a needle kept for a long time in the spinal subarachnoid space. I think that this is an important question, because I have not infrequently seen secondary infections with organisms other than those inducing the primary meningitis in cases in which repeated lumbar punctures were done. This condition seems to me to be due to injury to the tissues, with resultant lowered resistance to infection, rather than to the mere mechanical introduction of micro-organisms by the needle. These are, however, purely hypothetic questions which the continued use of the method will or will not substantiate.

DR. JOSEPHINE B. NEAL (by invitation): I am much impressed with the keen thought by which Dr. Kubie has evolved this theory and the careful work which he has done in laying the scientific foundations for it. My experience with its clinical application has been limited to two or three cases of purulent meningitis following infection of the sinuses or mastoid; these cases resulted fatally. Of course it often happens that the meningitis is simply the terminal state of a long series of infections and not much can be hoped for by treatment unless the focus of infection is removed. In regard to the treatment by forced drainage in the other

diseases with which I have worked (poliomyelitis and encephalitis), one must safeguard oneself with controls; otherwise the physician will be carried away by too much enthusiasm for a new method. No doubt all of us have in mind the wave of enthusiasm that was caused by the use of convalescent serum in the treatment of poliomyelitis. It swept all over the world and was believed generally to be of great value until a large group of patients was studied in comparison with an equally large group of patients whose condition was diagnosed in the pre-paralytic stage and who received no serum. This experiment showed that the serum was of no value, at least so far as could be demonstrated in that particular group, consisting of about 1,000 patients, both treated and untreated. Those who have worked with poliomyelitis and acute encephalitis must have seen instances of marked improvement following single or repeated lumbar punctures. In cases of poliomyelitis I have seen children who were very unhappy and irritable fall quietly to sleep after a single lumbar puncture, and not infrequently that was all that was necessary to stop restlessness and discomfort. While I think that this method of treatment may have great possibilities, I earnestly hope that sufficient controls may be used in order that unjustifiable conclusions will not be drawn.

DR. HAROLD G. WOLFF, Baltimore (by invitation): Dr. Kubie's closely reasoned and adequate summary concerning the production and resorption of spinal fluid needs no supplementary comment, except, perhaps on one issue. Dr. Kubie indicated that the cerebrospinal fluid arises primarily from the choroid plexus, that it is unnecessary to assume any special secretory function for cells of the choroid plexus, and that eventually, according to the Starling postulates, it is resorbed into venous channels. In reference to choroid plexus cells, however, he postulates a special quality, for, he says, "The evidence in hand would suggest rather that their main function is to stand as barrier against this very reabsorption at the venous end of the vessels which Starling showed to be operative in the rest of the body."

Unfortunately, the experimental evidence on this barrier function does not justify more than tentative conclusions. That the cells of the choroid plexus do not inevitably act as a barrier, and may, in fact, act contrariwise, was shown by several of us (Forbes, H. S.; Fremont-Smith, F., and Wolff, H. G.: ARCH. NEUROL. & PSYCHIAT. **19**:73 [Jan.] 1928) in the Harvard laboratories, in 1928. For when hypertonic solutions were injected into the blood stream, at least some of the smaller molecules in solution in the subarachnoid space were found to have made their way through the cells of the choroid plexus into the venous capillaries of the plexus. To what extent such resorption occurs in nature is unknown, but that it may do so impressed itself on some of us. This equivocal issue, however, does not in any way weaken the case for forced drainage.

The issue concerning forced drainage may be resolved into the following questions: 1. As a result of lumbar tap and the intravenous injection of hypotonic solutions, does more fluid pass through the perineuronal and perivascular spaces of the central nervous system? The conclusion that this does occur seems to be justified by the observations of Kubie (*J. Exper. Med.* **46**:615 [Oct.] 1927) and Kubie and Shults (*Bull. Johns Hopkins Hosp.* **37**:91 [Aug.] 1925) in experimental animals. In a more recent report, Kubie and Retan (*Bull. Neurol. Inst., New York* **1**:419 [Nov.] 1931) describe their results on a patient following the injection of hypotonic solution. They found that the amount of cerebrospinal fluid drained off during six hours exceeded by nine times the drainage of the preceding six hours when no hypotonic intravenous fluid had been administered.

2. Does forced drainage sweep out the cells contained in the perineuronal and perivascular spaces? Here again the evidence from the animal experiments of Kubie seems conclusively positive. Furthermore, it seems probable from the report of Kubie and Retan that in man also deep lying cells are swept out.

3. Does the increased amount of fluid thus passing through and the clearing out of cells in the spaces mean an increase of immune and other protective agents in these spaces? On this question no direct evidence is, as far as I am aware, available. The speakers were obliged to rely on an inference. In animals, Kubie and Shults, and in man, Spurling (references from, *Kentucky M. J.* **26**:242 [May]

1928) and the workers in the Harvard Neuropathological Laboratory (Forbes, H. S.; Fremont-Smith, F., and Wolff, H. G.: ARCH. NEUROL. & PSYCHIAT. **19**:73 [Jan.] 1928) have shown that large molecules, even molecules of protein, are found in greater amount in the cerebrospinal fluid after drainage. The inference is that if such large molecules are found in the fluid, similar large molecules of a protective nature may also occur. To complete the argument, direct evidence on this important point must ultimately be forthcoming.

4. What evidence is available that forced drainage is of therapeutic value? From a review of the literature to September, 1932, I was able to collect evidence that forty-six patients had been treated by forced drainage.

Dr. Retan has tonight added nineteen additional cases. Unfortunately, only the more interesting of these were presented, so that analysis of the entire group was impossible.

Cases in which Forced Drainage Was Used and Results

Physician	Case	Results
Casten, V.: New England J. Med. **202**: 676 (April 3) 1930	1 case, tryparsamide amblyopia	Recovery
Fremont-Smith, F.: Putnam, T., and Cobb, S.: Arch. Neurol. & Psychiat. **23**: 219 (Feb.) 1930	16 cases	No satisfactory conclusions; 22 instances; 16 patients with nonsuppurative disease, 13 with disseminated sclerosis
Spurling, R. G.: Kentucky M. J. **26**: 242 (May) 1928 (references from)	8 cases with laminectomy and forced fluids by mouth	4 septic meningitis (3 recovered), 2 brain abscesses (1 recovered), 1 poliomyelitis (1 recovered)
Retan, G.: J. A. M. A. **99**: 826 (Sept. 3) 1932	21 cases:	
	2 preparalytic poliomyelitis..	2 recovered (1 with serum)
	2 acute encephalitis.....	2 recovered
	3 chronic encephalitis.....	1 improved; in 2 no improvement
	1 Sydenham's chorea.....	1 recovered
	1 syphilitic meningitis hydrocephalus	1 recovered
	4 tabetic form of dementia paralytica	4 improved (1 case striking)
	1 tuberculous meningitis, proved	1 died
	1 tuberculous meningitis (?)	1 recovered
	5 septic meningitis	5 died
	1 cerebrospinal meningitis..	1 died

Total number of cases, 46

	Per Cent
Recovery	13 (29)
Improvement	5 (11)
Inconclusive	16 (35.6)
No improvement...	2 (4.4)
Death	9 (20)

From the results in this heterogeneous group of cases it is impossible to draw any certain conclusions. Spontaneous recovery and remissions are not uncommon in a good percentage of cases, presumably as a result of forced drainage. It must be appreciated, however, that certain of the cases, notably those with suppurative infections, have, in the absence of forced drainage therapy, a high mortality. By this method at least three patients in nine reported cases of septic meningitis have recovered. Hence, judgment must be suspended pending the accumulation of more data.

5. Is there any danger in the method? I could find no instance in the literature of an animal or a patient made worse by the procedure of forced drainage. Except for transitory discomfort, I have heard of no such reports. I see no reason to anticipate difficulties if Dr. Retan's precautions and contraindications are kept in mind. The danger from infection, though present, seems to be small. This was startlingly demonstrated in one of Dr. Retan's cases in which drainage was maintained practically continuously for eighteen days and nights.

In brief, then, it may be said that forced drainage is a reasonable procedure, that it is desirable to further its experimental use, and that it may ultimately prove

to be one of the more useful adjuncts in the treatment of infections and intoxications of the central nervous system.

DR. B. H. BALSER, Syracuse, N. Y. (by invitation): I have been priviledged to work with Dr. Retan in many of these cases, and have therefore seen the various changes he described in his paper. What impressed me most was the sudden change in symptoms and signs following the treatment. I wish to discuss some points not referred to in the paper. One case of syphilis, on examination before treatment, showed a right positive Hoffmann sign, so marked as to produce a wrist clonus, and at the same time motor aphasia. On the day following treatment, the Hoffmann reflex and wrist clonus were gone; the patient was able to enunciate clearly several sentences before becoming fatigued. It seemed as though I were examining an entirely different patient. This patient has asked for further treatment. Another patient, with tabes, had severe pain in both arms and both legs, with spasticity of the right arm. I saw him at the County Hospital two weeks previous to presentation (about one month after the second drainage), when he was able to swing his right arm about freely.

In the course of the treatment, headache followed by nausea and then vomiting will often, but not always, occur. It is interesting to observe how readily these symptoms can be controlled by replacing the stylet in the needle. I have seen several patients who had no headache, nausea or vomiting during the drainage, although the treatment often lasted as long as twelve hours. I have observed but one case in which the patient complained of a persistent headache following the treatment. This was a case of chorea in which the headache persisted for four days following drainage. This patient was then given a second forced drainage. Both the rate of administration and the amount of hypotonic solution were increased, and no headache developed.

DR. GEORGE H. HYSLOP: There is one academic question which I think has received the attention of workers in this field, that is, the change, if any, in the function of the kidneys during the period of administration of the hypotonic solution. It is a little difficult to insert in human beings ureteral catheters during forced drainage, but at least a careful study of the specific gravity and the solutes in the urine is important in determining how much of this fluid administered by mouth or vein is eliminated through the kidneys. For its practical bearing, the only experience I have had with the use of this procedure is worth mentioning. The patient had a persistent bloody spinal fluid throughout the drainage, which lasted three hours. He had unquestioned multiple sclerosis, of six years' duration, and after the procedure was completed complained of a persistent headache for ten days. In addition to causing an uncomfortable sequel, the forced drainage also produced in this patient an accentuation of disability. Before drainage there were slight signs of a lesion in the lower thoracic portion of the spinal cord. After drainage, level symptoms were more prominent, and examination showed an increase of ataxia and sensory impairment of the posterior column.

DR. BERNARD SACHS: I am much impressed by the way the subject was presented, but I think that the entire procedure calls for most careful collaboration between the experienced neurologist and the experienced internist. Above all, one has to be extremely critical and careful in the study and appraisal of any new therapeutic procedure. I am sure that this care is going to be exercised; otherwise it would lead to unwarranted conclusions. I believe, if this matter is carefully studied, that there is promise of a new therapeutic procedure applicable in definite types of cases.

DR. FOSTER KENNEDY: Will Dr. Retan say how long improvement was maintained after each procedure? The improvement in some cases was marked; the disappearance of the Argyll Robertson pupil is especially important. One sees this occasionally in cases of encephalitis, but practically never in syphilis, and I should like to know if these improvements were continued for a definite time, and if so, for how long.

DR. KUBIE (in closing): The assurance which Dr. Schloss gives that it is safe to use hypotonic solutions of much lower concentration than those employed

in the past is going to be helpful. It will be possible to lower the osmotic pressure of the blood rapidly and repeatedly with smaller volumes of the fluid injected. This will have many advantages.

The two dangers to which Dr. Schloss refers are, of course, those which must be kept constantly in mind in the application of the method. Dr. Retan discussed at some length the problem of secondary ascending infection along the drainage tract, and his experience suggests that this danger arises chiefly from the necessity of moving and readjusting the needle. This point, however, must of course be carefully checked. If this is true, it would explain why repeated lumbar punctures are more likely to introduce secondary infection than the presence of a needle retained permanently in place and held in such a way that it cannot move in relation to the surrounding tissues. The second danger is that of trapping fluid in the intracranial cavity behind a fixed obstruction. Against this danger one can guard best, first, by great care in the initial differential diagnosis; secondly, by testing the pressure response in the lumbar sac to compression of the jugular vein, and thirdly, by making the initial injection cautiously and slowly until one has established the freedom of outflow in the lumbar fluid. Certainly one must bear in mind that the chief contraindication to the use of the method is the presence of a lesion into which fluid can be poured and from which it cannot escape. Such a lesion might be a tumor mass, a cyst, an obstructive hydrocephalus or an area of fresh hemorrhage with necrosis and engorgement.

As Dr. Schloss suggests, the problem of the relationship of the rate of formation of cerebrospinal fluid to the rate and volume of the injection is one of great interest. At various times in the course of the experimental work we have made preliminary observations on this problem; but it is difficult, for several reasons, to put it on a quantitative basis. First, the state of hydration or dehydration of the tissues will vary from one animal to another, with different anesthetics, in different diseases and with different temperature levels. Such factors vary the amount of fluid which is free to appear through the draining needle. In addition, there are great variations in the response of the kidney to the injection. Some efforts have been made to control this by the administration of drugs which inhibit kidney activity, but this inhibition is only relative and therefore still leaves matters on a variable basis. Nevertheless, the observations that we have made on this point would indicate that in general the fluid tends to leave the blood stream for the tissue spaces first, and that after a period of elimination in this direction, during which there is an active flow from the needle in the subarachnoid space, there is a secondary response on the part of the kidneys, with an increasing urinary output and a decreasing output of cerebrospinal fluid. Furthermore, both in the experimental and clinical work, we have a definite impression that increasing the volume and rate of the injection, and thereby increasing the steepness of the curve at which the osmotic pressure of the blood stream is dropping, markedly enhances the rate of production of cerebrospinal fluid.

With regard to Dr. Neal's comments, we must agree that there can be a dramatic cessation of symptoms in some cases of acute infection of the central nervous system from a single lumbar puncture. In general, however, this is true particularly where there is a rather marked increase in intracranial pressure or a good deal of meningeal irritation. It must be kept in mind, however, that such a drainage reaches only the superficial fluid from the surface of the neuraxis. With the withdrawal of this surface fluid the leptomeninges tend to collapse around the neuraxis, thus obstructing further drainage. This is one reason why it is so essential to maintain the constant fresh formation of fluid by the intravenous injection of the hypotonic solution. Otherwise one has drained only the surface and left the depths obstructed, very much as though one allowed a superficial drainage tract of an abscess to collapse, leaving deep pockets of infection without any pathway of egress.

My own digression touching on the problem of the function of the choroid plexus led to Dr. Wolff's comment on the capacity of the cells of the choroid plexus to absorb from the ventricles. The experimental work to which he refers is undoubtedly sound, and indicates, as he said, that with the production of marked

negative pressures within the head these cells can absorb certain constituents at least from the fluid in the ventricles. Such negative pressures as these, however, are never found in nature, although a slightly negative pressure can occur in the head when a "long" animal, like a human being, is in a vertical position. This does not hold true for the quadrupedal position, nor for the recumbent posture. I believe, therefore, that despite these experimental observations on special conditions it will be possible to prove that the main function of the cells of the choroid plexus is to block reabsorption of fluid at the venous end of the capillaries of the plexus.

Another important question raised was the possibility of demonstrating an increased transudation of immune bodies from the blood stream to the cerebrospinal fluid under the conditions of forced drainage. This presents great experimental difficulties, because it must be remembered that one is increasing not only the transfer of the immune bodies, perhaps, but also the transudation of fluid. Therefore, unless the immune bodies are carried over in greater concentration than the fluid itself, the final concentration will not be increased. Indeed, it is likely that even with a material increase in the amount of immune body transferred, the measurable concentration will be lower. A similar problem presents itself when one attempts to demonstrate by cell counts the cellular extrusion from the depths.

Finally, as to the mechanism of the headache, nausea and vomiting that occasionally occur. The most striking thing about these disturbances is that they never occur at the period when one would expect the intracranial pressure to be most raised, if it is raised at all; that is, they never occur at the height of the injection of hypotonic solution. On the contrary, these disturbances tend to appear either before the injection is given, if the preliminary drainage is unduly prolonged, or long after the injection is given, again if the drainage is unduly prolonged and when the rate of flow of the lumbar fluid has decreased materially. Therefore it would seem safe to conclude that these symptoms are not due to increased intracranial pressure. It would seem more likely that the dislocation of the meninges, with the resultant stress and tension on the meningeal blood vessels, must be the basis of these unpleasant, though not alarming, symptomatic disturbances. If this explanation is true, it is easy to understand why these symptoms are relieved by replacing the stylet in the needle for a few minutes, by renewing the intravenous injection of fluid or by the administration of fluid by mouth when possible or by proctoclysis.

DR. RETAN: I was asked to state how often these treatments should be given. That is a rather difficult question to answer, because one is dealing with different diseases and in various stages. My associates and I tend of late to use larger quantities of hypotonic salt solution and to inject it more rapidly. We use about 3,000 cc. of hypotonic solution, and I think that our results are better. Our patients are much more comfortable with these larger injections, and have very little headache, and there is practically no vomiting during this period. In the beginning we drained for a time after the first injection; we now cut that period down to very short intervals. The patients with syphilis of the central nervous system are given repeated treatments, being treated about once a week. In one or two instances we have given a treatment on one day, and repeated it on the third day. The patients made no objecion.

In the instances in which treatments are repeated after twenty-four hour periods, there is no danger of secondary infection. I think that the latter is due to the fact that the needle is pushed back as it slips out; that does not occur during the first twenty-four hours. It loosens up on the second day and then has to be pushed back several times; in this lies the danger of infection.

Concerning the work of Fremont-Smith, in his report on forced spinal drainage, I do not think that it is strictly comparable to ours, because of the difference in technic. Fremont-Smith used a continuous drainage in which he blocked the kidney with injections of pitressin or solution of pituitary and gave quantities of water by mouth. Such a procedure changes the osmotic pressure to some extent, but I do not think sufficiently to make the two series of cases comparable.

In reply to Dr. Kennedy's question as to how long the improvement was shown in the case of syphilis with the Romberg sign and the cellular changes, this patient was free from the Romberg sign on the next morning. He has had three treatments and no antisyphilitic therapy in the intervals; he has remained free from the Romberg sign and other signs during five months. He has been driving a truck, and reports that he is feeling well. We have checked up on this case often, expecting that the patient would show changes in the wrong direction, but he has not as yet. Another man, observed three months after the first treatment, has also lost the Romberg sign. His gait has improved remarkably, and he has continued to show improvement for a period of three months. The Wassermann test was negative. In a case of syphilis of thirty-eight years' duration, the patient had been free from pain for two weeks when it recurred. He had one treatment, but the pain was severe. He asked for another treatment, but circumstances prevented it from being given. The patients with chorea have been free from choreiform movements, and have been apparently perfectly well. The first patient has been well for six or eight months, and the patient with recurrent chorea has remained well for four months.

CEREBRAL ATROPHY WITH HOMOLATERAL HEMIHYPERTROPHY OF THE SKULL AND SINUSES. DR. CORNELIUS G. DYKE, DR. LEO M. DAVIDOFF and DR. CLEMENT B. MASSON.

A number of conditions, such as race and custom, affect the shape and size of the skull. The fact that trauma or infection of the brain early in life may affect the development of the skull is not generally appreciated, as is evidenced by the scanty literature on this subject. During the latter half of the nineteenth century, a few papers were written describing thickening of the skull associated with infantile hemiplegia. One author called attention also to an enlargement of the frontal sinus on the side of a cerebral lesion in postmortem material.

In a review of four hundred encephalograms we have frequently noted asymmetry of the skull associated with certain types of hemiplegia. The present report concerns itself with ten patients who show this condition to a marked degree.

The clinical picture is that of so-called typical infantile hemiplegia. The etiology may be trauma at or shortly after birth or infection of the brain in infancy. These patients have hemiplegia of varying degree, with underdevelopment of the hemiplegic side, more or less mental deficiency, and usually convulsive seizures.

In the roentgenograms there is a varying increase in the thickness of the cranial vault on the homolateral side. In addition, there is an overdevelopment of the frontal sinus and the ethmoid cells, and pneumatization of the petrous ridge on the same side. The degree of overdevelopment and thickening varies as a rule with the age of the patient, the duration of the disease and the severity of the cerebral lesion.

In the encephalograms there is enlargement of the lateral ventricle on the diseased side of the brain. The entire ventricular system, including the third ventricle, is shifted toward the side of the lesion. This displacement must not be confused with that produced by a tumor; from a roentgenographic point of view the differentiation can be made only by noting the changes in the cranial vault and sinuses already described.

A study of these ten cases has made it possible to predict in advance from the roentgenogram, without resorting to encephalography, that the patient has unilateral cerebral atrophy.

DISCUSSION

DR. L. BEVERLEY CHANEY: The first impression one might gather from this paper is that an additional observation is contributed to a group of cases that have a clearcut clinical picture. All of the cases show definite objective organic signs of a cerebral lesion. I must admit that it is disappointing to know that in all cases the roentgen findings are the same, regardless of whether the lesion is inflammatory, traumatic or agenetic. In other words, it appears that any process which causes atrophy of the brain or retarded development of the brain will

manifest itself in the roentgen examination by homolateral hypertrophy of the skull and sinuses and a dilated ventricle on the side of the lesion.

So far as I know, attention has never before been called to hypertrophy of the bone overlying an area of atrophy of the brain. Encephalography is rather new, and I doubt if a sufficient number of encephalograms have been made on normal persons, especially normal children, to allow a correct interpretation of the findings in all cases. After a wider experience with encephalography, and an extension of such a study to include other varieties of obscure cases, I think that much additional knowledge and diagnostic assistance may be afforded, especially in a great many cases of birth trauma and other infantile intracranial disorders.

DR. CHARLES WADSWORTH SCHWARTZ (by invitation): I shall mention a few points that may even strengthen the theory presented. First, hypertrophy of the calvarium may be due to a variety of causes. It has been my conception that as long as the cerebrospinal fluid pathways are open the laws of hydrostatic pressure will not permit of much, if any, difference of pressure between the two sides, even if the brain substance is less on one side than on the other, so that I can hardly conceive of production of bone from any difference in pressure. A type of hypertrophy of the inner table of the frontal bone in the female skull is seen frequently after middle life. I do not believe that this bony overgrowth is due to atrophy of the frontal lobe in women. Yet writers have presented a type of bone hypertrophy somewhat comparable. In looking at skulls I have noticed that not infrequently there is a slight difference in the thickness of the calvarium on the two sides. It has occurred to me that possibly investigation of such cases with respect to right or left handedness may be of interest.

The development of the sinuses seems to be an essential part of the findings, but, on the other hand, sinuses are individual. They offer perhaps a better means of identification than fingerprints, so that when one tries to evaluate sinus development, one must be careful. I have never seen development of a sinus equal on the two sides. Supra-orbital ethmoid cells are not particularly uncommon, except when they have grown to such an extent as in these films. In overdevelopment of sinuses in other diseases, as in acromegaly, the development is purely external, a bulging forward, not at the expense of the cranial cavity.

DR. BERNARD SACHS: It is well known that in most of the older cases the contents of half of the skull are distinctly less than the contents of the other half; for this reason I think that the unilateral hypertrophy is largely compensatory; but one can make all sorts of speculations as to the immediate cause of the hypertrophy. The facts that have been shown are of extreme interest. I wish to ask what the explanation is of the rather unusual involvement of the sphenoidal and ethmoidal sinuses, and whether there is any connection between them and the original pathologic process.

DR. LEON T. LE WALD: I wish to support Dr. Schwartz' comments in regard to right and left handedness. The roentgenologist has not as yet been able to make that distinction, but I know that Dr. Elliott Smith, of the University of London, stated definitely that he could examine a skull and say whether it was from a right-handed or a left-handed person. At the present time the refinements of roentgen diagnosis are not sufficient to make that distinction roentgenographically, but in the future it may be possible.

DR. GEORGE VAN N. DEARBORN: It is possible that one or more of these interesting cases has come to necropsy. If so, I wish to know the results of any observations on the pathologic conditions.

DR. RUBIN A. GERBER: What were the findings as to the subarachnoid space on the involved side of the skull?

DR. LAWRENCE S. KUBIE: Is there any evidence that changes in vascularity might play a rôle in these cases?

DR. DAVIDOFF: In answer to Dr. Sachs, the sinus development is, in his own words, probably a compensatory reaction. I think that it occurs simply to fill up space. By pushing their inner wall toward the defective brain, the sinuses occupy a great deal of the space that might have been occupied by the brain substance.

In answer to Dr. Kubie as to whether this may not be on a vascular basis, I have no way of checking that point. I assume that the vascularity of the skull depends to a certain extent on an independent vascular supply. Whether that is affected I cannot say. I concluded that it was due to a difference in pressure.

In answer to Dr. Dearborn's question concerning histologic studies, we have had no autopsies. We have had occasion to do biopsies at the time of operation, and histologic study of the brain taken from these degenerative sites showed a marked sclerosis, with few normal ganglion cells. This is not an uncommon condition, and autopsies have been done by others; the postmortem findings were similar to ours. In one operative case, Dr. Masson found the skull at least 1.5 cm. in thickness, which increased the difficulty of the operation. From a practical point of view we believe that we may have learned from the combination of the clinical picture, encephalography and the plain films of the skull that we may be able in the future to diagnose these cases from examination of the films of the skull alone, with the thickening of the calvarium and dilatation of the sphenoidal, ethmoidal and mastoid cells on one side. Such findings would indicate a cerebral degeneration and avoid the need of an encephalogram.

In regard to Dr. Gerber's question about the subarachnoid space I may say that it varies in different persons. In the last case there was a marked filling of the subarachnoid space with air, so that presumably the space was patent. In the operative cases, the subarachnoid spaces were found obliterated, owing to the many fine adhesions of the pia to the under surface of the dura.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 28, 1932

A. M. Ornsteen, M.D., *President, in the Chair*

Mechanical Factors Governing the Trömner Reflex. Dr. Melbourne J. Cooper.

The patient whom I am presenting has a spastic paralysis of all four limbs, due probably to a tumor compressing the spinal cord in the upper cervical region. Although the digital reflex of Trömner was readily elicited by flicking or snapping the terminal phalanx of any of the digits of the right hand, or of the thumb or the index, ring or little finger of the left hand, no response could be obtained by such manipulation of the left middle finger. Many years ago the patient sustained an injury, which evidently did serious damage to the tendon of the flexor digitorum profundus muscle just proximal to the last phalangeal joint of the left middle finger, making voluntary flexion at that joint impossible, though it did not interfere with passive flexion. It was inferred from these circumstances that the failure to obtain a Trömner reflex through the agency of the left middle finger was due to inability to stimulate the flexor muscle through the inoperative tendon.

A reflex flexor response, apparently identical with the usual Trömner response, could be obtained, however, by suddenly stretching the tendon of the flexor digitorum sublimis attached to the base of the second phalanx of the left middle finger. This was accomplished by holding the finger in hyperextension at the metacarpophalangeal joint and in strong passive flexion at the proximal phalangeal joint, and then suddenly slipping the restraining hold from the dorsum of the intermediate segment so as to permit an elastic rebound into extension at the proximal phalangeal joint. A typical Trömner response was elicited also by simple percussion of the volar surface of the terminal segment of any of the digits other than the left middle finger, a procedure which accomplished sudden stretching of the intact tendons of the flexor digitorum profundus or the flexor pollicis longus. No such reflex was obtained by percussion of the dorsal aspect of any digit, a procedure that causes a comparable stretching of the tendons of the extensors.

The conclusion is that, at least in this case, the Trömner reflex response seems to require a sudden stretching of the muscles acting as flexors of the fingers or thumb, and that such a reflex can be elicited by any of several methods which mechanically produce such a stretching effect.

DISCUSSION

DR. W. G. SPILLER: The finding made by Dr. Cooper shows the necessity of careful examination. In eliciting the Trömner reflex it is customary to snap the end phalanx of the middle finger, and other fingers may not be examined. The end phalanx of the middle finger in the patient presented has been injured, and the afferent tract for the reflex is impaired, but the reflex may be obtained from the ring finger. It might have been supposed that the reflex was present only on one side, and that both pyramidal tracts were not equally involved.

A COMPLETE POSTOPERATIVE RECOVERY FROM COMPRESSION OF THE SPINAL CORD. DR. ALFRED GORDON.

Compression within the vertebral canal should create a sensorimotor disorder, the localization of which would depend only on the level involved. Clinical experience, however, disputes this apparently logical contention, and examples have been reported in which sensorimotor manifestations appeared in the extremities and were attributed to other conditions. In the last analysis, the clinical signs are more important than all the other data that may be gathered. This is illustrated in the following case:

Sarah P., aged 10 years, began to experience difficulty in walking in December, 1930. The condition grew gradually worse. The trunk was held rigid in walking. There was no pain and no rigidity of the limbs. This continued until March, 1931, when the child became bedridden, and there was complete loss of locomotion.

Examination revealed that the patient was unable to sit up, and when she was held in a sitting position and then released the trunk fell either forward or backward. The paralysis of the lower extremities was complete and flaccid. In spite of the long standing paralysis, there was no atrophy of the muscles. The patellar reflexes were greatly increased; on the right there was leg clonus on the least tap of the patella. Ankle clonus was present on both sides. There was a bilateral extensor plantar reflex. The abdominal reflexes were abolished. There was unusual irritability of the lower extremities. Objective sensory disturbances were pronounced: There was complete anesthesia from the toes up to two finger-breadths above the umbilical line on both surfaces of the limbs and abdominal wall. There was incontinence of urine and feces. Examination of the vertebrae revealed no abnormalities. At no time since the onset of the disease has there been pain either in the extremities or along the spine. A high subarachnoid injection of iodized oil was made, which gave indefinite results: A goblet was seen at the lumbosacral articulation, and two goblets were seen at the level of the seventh, eighth and tenth thoracic vertebrae, apparently outside the spinal canal and posterior to it, as if there were a herniation of the spinal meninges. Roentgenograms of the spine revealed no anomalies. The Wassermann reaction of the blood and spinal fluid was negative. Red blood cells numbered 5,041,000, and white cells, 10,000, the distribution of which was: mononuclears, 9 per cent, small lymphocytes, 24 per cent, polymorphonuclears, 65 per cent, and eosinophils, 2 per cent; the hemoglobin was 65 per cent. The urine was normal.

The gradual development of the paralysis suggested a slow, progressive compression of the spinal cord, but the absence of pain made one hesitate to accept this view. The gradual development of weakness of the limbs, which finally developed into flaccid paralysis, and the total loss of all forms of objective sensibility led to the assumption of a gradual compression of the cord. The sensory level was at the twelfth thoracic vertebra.

An operation was performed, with removal of the spinous processes of the eighth, ninth and tenth vertebrae. The spinal cord was constricted by an excrescence of bone. The dura over the constricted portion of the cord was intact, and the cord

at this level was reduced to one third of its normal size. The tissue above and below was congested, but normal in thickness, contrasting strikingly with the constricted area. The bony excrescence was removed.

On the sixth day after the operation, slight voluntary movements appeared in some toes. The anesthesia remained unaltered. On the twentieth day, a slight return of objective sensibility was noticeable. The patient was then able to move the legs slightly from side to side. The condition of the sphincters began to improve. Gradually, movements and sensation in the lower extremities and trunk became normal. At the end of the fourth month the patient was able to sit unsupported. The sphincters became completely normal. At the present time, eight months after operation, the patient is able to take a few steps without assistance. Sensation is normal to touch, pain and temperature. In a sitting position, she is able to move the legs in all directions. The knee jerks are still increased, but the leg clonus can no longer be elicited. The plantar reflexes are still in extension.

Two Cases of Distal Atrophy. Dr. Samuel J. Sperling.

Case 1.—S. T., a single, white man, aged 71, was readmitted to the Philadelphia General Hospital in the service of Dr. F. W. Sinkler, on Sept. 27, 1932, his first admission to the hospital having been on July 27, 1899, at the age of 37, when he entered the surgical service because of ulcers of the leg. According to the records made at that time, he had noted discoloration and subsequent ulceration, which was occasionally painful, in the left thigh about two years before. The chief interest in the case, however, lay in certain deformities of the hands and feet. Dr. Dercum presented the patient before this society on Jan. 22, 1900 (*J. Nerv. & Ment. Dis.* **27**:324, 1900) and stated that several years prior to admission, pains had begun in both thighs, and somewhat later in the legs and feet; the pains were at times shooting and at others dull, but never burning, and they lasted for from one to two hours, when they disappeared, but recurred after several hours. For the previous three or four months pains had been present in the arms, especially on motion, and the patient said that the muscles would "catch." Two years before, he had noted that the right ankle was becoming weak, so that it turned under at times; and six months later the same condition occurred in the left foot. He had to raise the feet higher from the ground in walking so as to avoid dragging his toes. There were no other symptoms of importance. Bowel and bladder control was good. The patient had been a bartender, but drank moderately. The family history was significant in that an older brother suffered from a similar condition of the extremities.

Examination, in 1899, revealed atrophy of the hands and lower third of the forearms, with associated weakness of the hand grips and coldness and lividness of the hands. There were bilateral footdrop, with the feet in an equinovarus position, and marked wasting of the muscles of the legs, chiefly of those of the peroneal group, more noticeably on the right side. The thighs appeared normal. The patient was unable to dorsiflex the foot at the ankle or to extend the toes, but there was slight power of flexion in the toes despite some flexion contraction of them. The gait was of steppage type. All sensation was preserved. The patellar reflexes were exaggerated, and the pupils normal.

Dr. Dercum diagnosed the case as one of primary neuritic atrophy, although the condition simulated peripheral neuritis. He did not believe that alcohol was an etiologic factor.

The patient received treatment with iodides and mercury for several months, presumably because of a history of a chancre; the ulcer of the leg healed, and the patient was discharged to the hospital employment service. Since then he has worked mainly at the hospital, having had charge of the clothes room for a number of years and later having served food in the dining room. He has been hospitalized on several occasions during the past thirty years, e. g., in 1907 (for three days), for weakness following absence from the hospital for six weeks. In 1913, he was admitted to the neurologic service for a month, presumably for a "bilious" attack.

The distal deformities and atrophy, exaggeration of the knee jerks and the presence of normal sensation were again noted. In 1930, he was in a medical ward for treatment for acute bronchitis; the Wassermann reaction then was negative.

He has returned to the hospital now, after having lived outside for fourteen months, because of bladder symptoms and increased weakness of the legs, which caused him to fall when the ankle "turned" on several occasions during the past few months. The history given now is essentially the same as before, except that he says that the pains in the limbs began in childhood; this feature is mentioned in the hospital records of 1899 and 1913 as "rheumatic." The pains, usually a dull aching in the thighs, have continued, but are less severe now and recur about once a month; they last only a day, although the occasional pains of shooting type are of momentary duration. He likewise says that the weakness of the feet began before the age of 20, when he noticed, while working, occasional "turning under" of the right foot. Otherwise there has been a slow progression of the atrophy and weakness. Other symptoms complained of are: occasional headaches, dizzy spells, tinnitus for the past twenty years, occasional "spots" before the eyes, a nonproductive cough, and for the past five years polyuria and dysuria.

The patient had two brothers; one died at 5 years of age from an unknown cause; the other, William, four years older than the patient, died at 69 years of pneumonia; he had had deformed legs and hands similar to those of the patient, but was never under a physician's care. A maternal uncle probably had a similar condition, for the patient recalls that his mother stated that William "got his clawhands from his uncle."

The patient had a chancre and a bubo at the age of 24, and gonorrhea two or three times, the first time at the age of 21. Because of its etiologic significance I have inquired deeply into the amount of alcohol that he drank and his occupation. He began drinking beer at the age of 10, and whisky when he first started to work at a shipbuilding company as a fireman at the age of 18. He would then drink about from 2 to 4 ounces of whisky after work; he never became drunk. At 22, he took charge of a saloon and drank much beer and some whisky, but rarely drank as much as a pint a day or became drunk. He worked in saloons for about eight or ten years.

The significant features revealed by physical examination are: slight arcus senilis, cardiac enlargement, with distant heart sounds except for accentuation of the second sound at the aortic and mitral valves, sclerotic radial arteries and hypertension, the blood pressure ranging from 205 to 100 systolic and from 150 to 85 diastolic. There are enormous bilateral hernias, which commenced twenty-five years ago. The prostate is enlarged, firm and smooth. Over the middle and upper anterior surface of the left leg there are several thin, atrophic scars, with pigmented circinate borders, remains of the old ulcers, which are suggestive of an old syphilitic lesion. There are no prominent varicose veins in the legs, and the dorsalis pedis pulses are palpable. The patient has had slight fever, the temperature ranging from 98 to 100 F., for the past few weeks, owing to an associated pyuria.

Neurologic examination revealed: The pupils are equal, although slightly irregular, and react slightly sluggishly to light and in accommodation. External ocular movements are full, and there is no nystagmus. There is a slight diminution of sense of vibration in the legs and of position of the toes, but touch, pain, heat and cold sensibilities are normal.

Examination of the extremities showed: In the upper limbs there is distinct atrophy of the hands, with main-en-griffe and wasting of the lower third of the forearms, which gives a distinct spindle shape to the forearms. More specifically, the atrophy is marked in the thenar eminence, lumbricales and interossei muscles, those between the thumb and index fingers, and somewhat less in the hypothenar group. In the forearm the atrophy of the lower third is somewhat more marked in the flexor than in the extensor group. Fibrillations have been noted occasionally in the extensor muscles of the forearms. There is good power of flexion and extension at the elbows and wrists, in contrast to the marked weakness of the finger movements. There are diminished power of abduction and adduction of the fingers and thumb and incomplete apposition of the thumb to the fingers. Flexion

of the distal phalanges is fairly well performed, but that of the proximal phalanges is poor. Both hand grips are weak, registering from 6 to 10 on the dynamometer as compared with a normal reading of from 80 to 100. The biceps and triceps reflexes are somewhat hyperactive and equal; there is no Hoffmann sign. There are slight coldness and cyanosis of the finger tips, and the patient states that during cold weather he cannot move the fingers.

In the lower extremities, wasting is marked in the legs and feet and slight in the lower third of the thighs, the atrophy being more pronounced in the plantar aspect of the feet and in the peroneal and extensor muscles of the leg. There is bilateral foot-drop, the feet being in an equinovarus position, with slight contracture of the tendo achillis and marked flexion contracture of the toes at the distal joints but slight hyperextension at the metatarsophalangeal joints. No fibrillations are noted in the legs. They are hypotonic, particularly in the distal portions. There is no movement of the toes or extensor power at the ankles, and there is little ability to perform plantar flexion with the feet, more marked on the right. There are some weakness in flexing and extending the leg on the thigh and slight weakness of abduction and adduction. The patellar reflexes are hyperactive, but the achilles jerks cannot be obtained. There is no response to plantar stimulation and no patellar or ankle clonus. There are marked cyanosis and coldness of the feet, with glossy skin.

There is no wasting of the proximal portions of the limbs or of the trunk, neck or face. The abdominal reflexes can scarcely be elicited.

Electrical reactions showed diminished response in the muscles of the forearms and no response in the intrinsic muscles of the hands, except in the left adductor pollicis, but there was no reaction of degeneration. In the lower limbs there was no response in the peroneal group or tibialis anticus muscles, with quantitative reduction in the intrinsic muscles of the foot but no reaction of degeneration.

Examination of the eyegrounds showed marked arteriosclerosis, the disks being normal. The urine was of low specific gravity and showed few leukocytes. Blood counts and the results of chemical examination of the blood were essentially normal. The Wassermann reaction of the blood was negative, but the Kahn reaction was + 3. The basal metabolic rate was — 5.

X-ray films showed distinct osteo-arthritis of the lumbar vertebrae. There was a small calcified mass, probably a fecolith, in the intestines, entrapped in the scrotal hernias. There was no evidence of arteriosclerotic vessels in the lower limbs. There were an old fractured patella and possibly an old fracture of the external malleolus on the right. On the left there was evidence of an old ununited bimalleolar fracture.

Case. 2.—M. W., a white man, aged 76, was admitted to the Philadelphia General Hospital to the service of Dr. F. W. Sinkler on Sept. 27, 1932, with a noticeable footdrop. He attributed this to an injury on Jan. 6, 1888, when a stallion, which he was leading from the stable, kicked him and trampled on him. He does not know exactly where he was struck, as he was unconscious for a day and awakened in his own home completely paralyzed except for some movement of the neck. However, he had good control of the bowels and bladder and good sensation throughout the body, for he recalls being able to feel everywhere the physician stuck him with a pin. There were no visual or aural disturbances and no convulsions, and the physician told him that no bones were broken, and that the spine was not permanently injured.

About three weeks after the injury, he noted wasting of the legs and had cramplike pains in the thighs, which lasted for several months. The feet were clammy and perspired freely. About a week or two later, power began to return in the upper limbs, but he was still unable to change his position in bed without aid. About a week later, pulleys were put on the ceiling to facilitate movement in bed, but he recalls being unable to pull himself up to a sitting posture or to move his legs. In the last week of February, 1888, he was removed to a private hospital because he could not move his legs; there he was treated with massage and electricity, which caused the legs to rise up. He was seen on several occasions by Dr. S. Weir Mitchell, who told him that time would bring him around. He

gradually regained power in the lower, and greater power in the upper, limbs, so that he could move about in bed, although with difficulty. At the end of seven weeks in the hospital, he could walk downstairs with aid, although he had marked footdrop, and was able to help himself. For the next six months he used crutches.

About five weeks after the accident his ankles became swollen and remained so for two months. There was no pain, tenderness or feeling of warmth in the ankles, and the patient had no fever. There was considerable loss of weight for several months following the injury, which he regained subsequently. At no time were there sphincteric or sexual disturbances or sensory involvement. The footdrop has remained practically unchanged, but he has noticed some wasting of the hands in the past few years. A year after the accident he was able to resume his occupation as manager of a stock horse farm, and he worked about horses until one year ago. He has no other significant symptoms than occasional nocturia and nonproductive cough.

The significant features revealed by physical examination were: a small epithelioma on the right cheek, which has since been removed; arcus senilis; complete adentia; large, injected tonsils; distant heart sounds, with slightly sclerotic radial arteries and a blood pressure of 150 systolic and 80 diastolic; slightly relaxed rectal sphincter; a small lipoma in the right deltoid region; a partially ankylosed forefinger and middle finger of the right hand; no varicose veins, and palpable dorsalis pedis pulses.

Neurologic examination revealed that the pupils were slightly irregular but equal and reacted well to light and in accommodation.

Examination of the extremities showed: In the upper extremities, there is slight atrophy of the muscles of the hands, which is distinct in the muscle mass between the thumb and the forefinger but is present also in the thenar and hypothenar eminences. There is no apparent wasting of the forearms, arms, face or trunk. There is weakness of abduction and adduction of the thumb and all fingers, although he can appose the thumb to all fingers. There is fairly good power of flexion of the distal phalanges, but some weakness of flexion and extension of the proximal phalanges. The power of flexion and extension at the wrist and elbow is good. Fibrillations are occasionally noticed in the extensors of the forearm. The biceps and triceps reflexes are slightly hyperactive and equal, and there is no Hoffmann sign.

In the lower extremities there is general wasting, chiefly in the legs. There is distinct footdrop, the feet being in an equinovarus position. There is slight contracture of the tendo achillis, although the ankle joint is loose. No fibrillations are noted in the legs. There is fairly good power of flexion, extension, adduction and abduction of the thighs on the body, but diminished power of flexion and extension of the legs on the thighs and no movement of the toes or ankles.

The patellar jerks are active and equal, but the achilles reflexes are absent, and there is no response to plantar stroking. The feet are cold, clammy and reddish blue, and there is slight edema about the feet and ankles. The gait is typically steppage type. The abdominal reflexes are present. There is no dysmetria in the finger-to-nose or heel-to-knee tests, and no adiadokokinesis. There are no palpable or tender peripheral nerves. The patient appears clearly oriented, with good memory and intellect for a man of his age, and speech is clear. The eyegrounds showed normal disks and marked arteriosclerosis. The electrical reactions showed slightly diminished quantitative responses in the hands. In the legs there were no contractions of the peroneal group, extensors of the feet and intrinsic foot muscles, and there was diminished response in the flexors of the feet.

X-ray examination showed hypertrophic osteo-arthritic changes in the spine, which were more marked in the twelfth dorsal and first and second lumbar vertebrae. The joint spaces were normal. Slight calcification of the vessels in the thighs was noticed in the x-ray pictures.

The urine was normal; the excretion of creatinine was 0.229 Gm., and that of creatine 0.079 Gm. in twenty-four hours. A blood count was normal; the Kahn test was negative. Examination of the spinal fluid was not permitted. The blood sugar was 87 mg., and the urea 10 mg. per hundred cubic centimeters. The basal metabolic rate was plus 13.

Comment.—These cases are of interest from the standpoint of diagnosis and etiology. In case 1, the subsequent course of the disease has, I believe, confirmed Dr. Dercum's diagnosis of primary neuritic atrophy, which is more commonly known as the peroneal form of progressive muscular atrophy of Charcot-Marie-Tooth. The characteristic feature of the disease is the symmetrical, distal distribution of the atrophy, usually beginning in the legs, without involvement of the proximal muscles. There are frequently slight fibrillations and diminished electrical reactions in the affected muscles (occasionally reactions of degeneration), diminished or absent tendon reflexes, preservation of cutaneous reflexes, no pronounced contractures and distinct vasomotor disturbance in the regions involved. Sensation is usually intact, but may be impaired distally, and pains and paresthesias may occur. Clubfeet and clawhands may be present. The disease is very slowly progressive, without remissions, and patients may live to old age with ability to perform moderate tasks.

Case 1 fits this symptom picture well, except for the presence of pain and increased reflexes. Exaggerated tendon reflexes have been reported in this case by Dercum and in a large family by the Longs. Intermittent lancinating pains are not rare and have been recorded by Charcot and Marie (*Rev. de méd., Paris* **6**:97, 1886), Marinesco (*Arch. de méd. exper.* **6**:921, 1894), Bernhardt (*Virchows Arch. f. path. Anat.* **133**:259, 1893) and Dawidenkow (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **107**:259, 1927; **108**:344, 1927); the latter found pains reported in 39 of 193 cases. Paralysis of the hands when cold, with recovery when warm, was likewise recorded by Dawidenkow, who found similar cases reported.

As regards etiology, three factors are of significance in case 1, namely, alcohol, syphilis and heredity. As far as can be judged from the patient's present and past history, he had never drunk alcohol in excessive quantities, although he was a bartender. Moreover, it is likely that the onset of the condition occurred before he entered this trade; there is an indirect check on this point in that the man was never a patient in the alcoholic wards, although he had been almost continuously about the hospital for the past thirty-three years.

A diagnosis of syphilis is based on the history of a chancre, the presence of a 3 plus Kahn reaction, despite a negative Wassermann reaction, and the suggestive character of the old ulcers of the legs. The latter are certainly not varicose in origin, as this condition is not present now and the ulcers are usually lower on the leg. Oppenheim (Textbook of Nervous Diseases, ed. 5, translated by A. Bruce, Edinburgh, O. Schulze and Company, 1911, p. 253) has seen neuritic atrophy with a perforating ulcer in the diseased extremity. Syphilitic amyotrophy has been discussed by a number of observers, among them Dana (*J. Nerv. & Ment. Dis.* **33**:81, 1906), Leri and Lerouge (*Gaz. d. hôp.* **86**:885, 1913), Burr (*Therap. Gaz.* **38**:90, 1914) and recently Kaiser (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **136**:798, 1931). It usually affects the upper extremities and upper part of the trunk, rarely the lower extremities. It is apt to be asymmetrical. It is extremely rare for it to affect the distal portions of all four extremities, as it usually progresses anatomically from one portion of the body to adjacent muscles. There are usually associated involvement of the pyramidal tract and urinary disturbances, but rarely sensory disturbances. The condition occurs in middle life (an average of eleven years after the initial infection) and runs a more rapid course. Bulbar symptoms, Argyll Robertson pupils and other evidences of syphilis may be present. It is interesting that Sainton reported a case of Charcot-Marie-Tooth atrophy in a man who had a chancre; I am inclined to believe that the syphilis was coincidental in this case also.

Familial hypertrophic neuritis of Dejerine-Sottas presents an almost similar symptomatic picture to that of Charcot-Marie-Tooth atrophy, except that the peripheral nerves are thickened and palpable. In fact, Marinesco, Tkatschew (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **137**:244, 1931) and Dawidenkow considered it not a nosologic entity but rather a variety of Charcot-Marie-Tooth atrophy. This does not hold for the Marie-Boveri or the Gombault variety, in which tabetic or cerebellar symptoms are present.

Progressive spinal muscular atrophy may occasionally offer difficulty in differentiation, but usually occurs at a more advanced age, and a hereditary factor is uncommon; there are fibrillations, electrical changes and contractures, and the condition affects the upper extremities and the trunk early, spreading anatomically from this focus and frequently terminating in bulbar paralysis.

In the discussion of this case in 1900, the question of vascular disease in the extremities was raised. Dr. Dercum did not believe that this was a factor in the case, and the subsequent course, the patient having good dorsalis pedis pulsations, has borne this out.

In case 2, the diagnosis and the rôle of trauma are not clear. One cannot explain easily the presence of paralysis of the entire body without sphincteric or sensory disturbances from a lesion of the cord. Yet repeated questioning of the patient does not raise a doubt concerning the story of the illness, and the mentality appears good for a man of his age. The symptomatic picture resembles closely that in the first patient, although the history is totally different.

A number of cases of progressive atrophy following injury have been recorded in the literature. William Gull (*Guy's Hosp. Rep.*, 1858, p. 195) reported, in 1858, a case following a blow on the neck with a fist. Mann (*Alienist & Neurologist* **7**:430, 1886) reported, in 1886, the case of a patient whom Gull had seen about twelve years before, in which generalized atrophy followed a fall on a ship in which some injury to the base of the brain occurred. Dana recorded a similar case associated with syphilis. Bailey (Diseases of the Nervous System Resulting from Accident and Injury, New York, D. Appleton and Company, 1906) stated that to prove an etiologic relationship it is necessary to show that the patient had progressive atrophy which he did not have before some severe injury. Most of the recorded cases show involvement of the upper limbs, usually on one side at the onset, frequently with associated pain; the atrophy progresses anatomically and may eventually involve the entire body, and there are occasional associated pyramidal tract signs.

A Case of Cerebral Neoplasm Showing the Difficulty in Differentiating Between Cerebellar and Frontal Lobe Hemiparesis. Dr. Ross H. Thompson.

According to Luciani (1915), all symptoms of cerebellar dysfunction are ascribed to the classic triad of asthenia, atonia and astasia. There must be an anatomic explanation of how a tumor involving the frontal lobe can produce symptoms of such nature as to direct attention to the opposite cerebellar hemisphere. It is held by some that the frontopontocerebellar conduction system, with its various connections acts as an intermediary. By way of this pathway the cerebrum may utilize the cerebellum to provide more delicate tonic and postural adjustments on centers of the brain stem and cord. Holmes (1918) stated that the cerebellum seems to exert an influence on the nervous mechanisms, most probably on the spinal, immediately concerned in the execution of voluntary muscular contraction, by virtue of which these react promptly on cerebral impressions.

A woman, aged 39, a patient of Dr. William G. Spiller, who was admitted to the University Hospital on Oct. 5, 1932, for six months had complained of persistent headache, extending from the forehead backward over the vertex to the occiput. Two months before admission, her husband noticed that she could not raise a fork properly in the right hand. She seemed to be childishly playing with the food. Soon afterward, staggering was noticed, always to the right and backward. In the two weeks before admission she fell in her house a number of times. Mental deficiency was marked. On admission, there was a little weakness of the lower part of the right side of the face, but the difference between the two sides was not more than might be found normally. The right upper limb seemed a little weaker than the left, but not strikingly so. The right hand grasp was good. The tendon reflexes of both upper extremities were increased, possibly a little more so on the right. Trömner's sign was pronounced in both hands, possibly a little more in the right. All attempts at sensory examination were unsatisfactory because of the mental impairment. In testing stereognostic perception, scissors, a large

key and a spoon were used; the patient was unable to name correctly any of these objects in either hand. Power in the right lower limb was good; it was doubtful whether this limb was weaker than the left. The patellar and achilles tendon reflexes were exaggerated on both sides, probably a little more on the right; persistent ankle clonus was present on the right but not on the left. The Babinski reflex on the right side was suggestive but not typical; it was not present on the left. When placed on her feet, the patient immediately fell to the right and backward, never to the left. It seemed impossible to explain this falling by the moderate weakness of the right side of the body. It was regarded as an evidence of hypotonia and incoordination of the right limbs.

Ophthalmologic examination showed choking of 4 diopters in both disks. The visual fields could not be charted because of the mental condition.

Roentgen examinations revealed complete destruction of the dorsum sellae and posterior clinoid processes. The pituitary fossa was enlarged, with some encroachment on the lumen of the sphenoid sinus. Accurate measurements were not obtained. It was thought that the deformity of the sella was due probably to increased intracranial pressure, the result of a block of the ventricular system, and, while there were no localizing signs, that the lesion was in the posterior fossa.

A ventriculographic examination was made on Oct. 12, 1932, and the results were interpreted by Dr. Henry K. Pancoast as follows: "The ventricular system is visible throughout its entirety. The right lateral ventricle is fully outlined but the left is only partly visible. The anterior horn and body, the posterior horn and part of the descending horn are obliterated. The ventricles are displaced toward the right; the lateral ventricles, the third ventricle and aqueduct. The visible portions of the left lateral ventricle are somewhat dilated. This displacement and deformation are due to a large cerebral tumor in the left parieto-occipital region; it is supratentorial."

Operation, performed by Dr. Francis C. Grant, revealed a large subcortical tumor. It lay behind the left motor cortex at a depth of 2.5 or 3 cm. and measured 5 by 5 by 5 cm.

The pathologic diagnosis made by Dr. B. J. Alpers was fibroblastoma.

The differential diagnosis in this case lay between a cerebral tumor on the left side, with hemiparesis of the pyramidal tract, and a cerebellar tumor on the right side, with cerebellar weakness, hypotonia and falling. The ventriculogram indicated a large cerebral tumor in the left parieto-occipital region. The displacement of the lateral ventricles to the right gave evidence that the growth extended pretty well forward into the left frontal lobe. A bilateral involvement of the frontal lobes was thus indicated, and with it possibly interference with the frontopontocerebellar pathways of each side.

Hare (1931), reviewing the records of fifty patients with tumors of the frontal lobe, found that of five who had marked cerebellar dysfunction, four exhibited bilateral lesions. The occurrence of cerebellar disturbances in only those with bilateral involvement of the frontal lobes was considered significant.

DISCUSSION

DR. W. G. SPILLER: Cerebellar symptoms, especially rapid falling to the right and backward when the patient rose to her feet, suggested a cerebellar tumor. Symptoms of involvement of the parietal lobes were unreliable, because of the mental impairment of the patient. A ventriculogram was necessary, and the findings obtained permitted Dr. Grant to cut deeply into the cerebral hemisphere and to remove the tumor, although there was no indication on the surface of the brain of a tumor.

DR. F. C. GRANT: When I first saw this patient with Dr. Spiller, she presented right-sided ataxia and fell backward when she tried to stand erect. During the time between her transfer to the neurosurgical service and the operation, the weakness of the right side of the face became definite. This made me favor a diagnosis of a cerebral rather than of a cerebellar lesion, although even with the development of this symptom I was not sufficiently sure of the localization of the tumor to operate without a ventriculographic study. It was fortunate that an

injection of air was made, because the cortex on exposure was so normal in appearance that I should have hesitated to cut through it without positive evidence that the tumor was there. An exploratory plunge with a brain cannula revealed a solid mass at a depth of 3 cm. from the surface.

When I first exposed the surface of the tumor, it was firm, red and granular, separating readily from the surface of the brain. In size it was roughly 4 by 5 by 8 cm. and weighed about 90 Gm. At its base it appeared to be attached to the choroid plexus and invaded the left lateral ventricle. The center of the mass was scooped out with an electrosurgical knife and the tumor thus reduced in size until I could draw it out through the cortical incision. There was a little bleeding from a vein at the base; otherwise the extirpation was bloodless. Forty-eight hours after the operation, hyperthermia developed which could not be controlled. The manipulations attendant on the removal of the tumor may have damaged structures about the third ventricle and caused vasomotor collage.

DR. J. C. YASKIN: It has been mentioned that this patient had sensory disturbances. If so, is it not possible that some of the incoordination that was so striking in this case might have been due to disturbances of proprioceptive sensibility? Sensory disturbances were observed in a large perceptage of a series of cases of flaccid hemiplegia, and it was thought that the sensory disturbances accounted for the changes in tonus. It occurred to me that the combination of tonus disturbances and incoordination in this case may have been due to a lesion of the parietal lobe.

DR. R. H. THOMPSON: It is not possible in this case definitely to explain symptoms resembling those of cerebellar dysfunction. Necropsy was not performed, and no anatomic evidence can be produced that the connecting pathways between the cerebral cortex and the cerebellum were involved.

A SPECIMEN WITH BILATERAL SUBCORTICAL HEMORRHAGE CAUSING PARAPLEGIA. KENNETH FOWLER.

The specimen that I am presenting was removed from a white man, aged 69, who was brought to the hospital with a history of suddenly having been seized with convulsions two days previously. The convulsions were generalized, lasted for one-half hour and were followed by an unconscious state and paralysis of both lower extremities. These conditions remained unchanged until death, which occurred six days after the seizure. The past history and physical examination disclosed nothing of note other than evidences of advancing arterial degeneration. The presence of neurosyphilis was suspected but was not substantiated by serologic tests.

At autopsy the most noteworthy change was the advanced arteriosclerosis of the visceral vessels. The same change was present in the vertebral and internal carotid arteries. Horizontal sections of the brain disclosed, in the paracentral regions, small, bilateral, subcortical hemorrhages of nearly symmetrical distribution in the centrum semi-ovale. I am assuming, on the basis of the gross lesion, that the hemorrhages are the result of breaks in medullary branches of the anterior cerebral artery. From the clinical findings and from the locations of the hemorrhages it seems fair to conclude that the lesions affected exclusively the pathways for the cortical areas for the legs. I present this specimen as being unusual: first, because of the relatively small size of the hemorrhages; second, because of their bilaterality, and third, because of their symmetrical distribution.

DISCUSSION

DR. W. B. CADWALADER: The specimen is of particular interest because it shows two fairly small symmetrical spontaneous hemorrhages, which probably developed simultaneously, so situated that only the fibers that supply the lower limbs were implicated. The patient was paralyzed only in the legs; the upper limbs were not affected. Crural paraplegia caused by spontaneous cerebral hemorrhage is exceedingly uncommon. During the World War, I observed cases of

gunshot injury of the brain in which only the paracentral lobules were injured, resulting in crural paraplegia. Dr. Spiller (in Osler Memorial Volume, Contributions to Medical and Biological Research, New York, Paul B. Hoeber, Inc., 1920) called particular attention to paralysis of only segments of limbs from cerebral vascular lesions. I know of no other case, however, exactly like the one that Dr. Fowler has just presented.

FREQUENCY WITH WHICH TUMORS IN VARIOUS PARTS OF THE BRAIN PRODUCE CERTAIN SYMPTOMS. DR. FREDERICK A. GIBBS.

This paper was published in full in the November, 1932, number of the ARCHIVES.

News and Comment

AWARDS

The New England Society of Psychiatry, at its next spring meeting, will make two awards, one of $100 and one of $50, to the writer (or writers) of the best papers completed or published during the calendar year of 1932 embodying research in psychiatry by a younger worker (or workers). Physicians, psychologists, social workers and others are eligible. Membership in the society is not a requisite.

Writers who have once received an award are not again eligible. Seasoned writers, senior physicians or heads of departments in which there are junior workers, while not inevitably excluded, will not generally be regarded as eligible for the awards.

The work on which the papers are based should preferably have been done in New England or by workers now living in New England.

The papers will be examined by a committee of three members who are accustomed to reviewing papers, and by the executive committee of the society. They will be judged on the basis of their scientific quality.

Copies of articles or marked copies of journals in which the articles appeared should be sent without delay to the secretary of the society.

Superintendents of institutions, public or private, for the care of mental patients in New England are requested to post this notice and to send to the secretary a list of those papers published by members of their staffs that they think are entitled to be considered for the awards.

HARLAN L. PAINE, M.D., *Secretary*.
North Grafton, Mass.

AMERICAN NEUROLOGICAL ASSOCIATION

The fifty-ninth annual meeting will be held on May 9, 10 and 11, 1933, in Washington, D. C. The headquarters of the association will be at the Hotel Washington, where the meeting will be held.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The tenth annual meeting of the American Orthopsychiatric Association will be held at the Hotel Pennsylvania, New York, Feb. 23 to 25, 1933.

Book Reviews

Zur Ausdruckslehre und Charakterkunde. By Ludwig Klages. Price, 9.80 marks. Pp. 388. Heidelberg, Germany: Niels Kampmann, 1926.

Persönlichkeit. By Ludwig Klages. Price, 4.80 marks. Pp. 13. Pottsdam, Germany: Müller & Kiepenhauer, 1927.

L. Klages, who is known and exerts a wide influence in German cultural life and in psychiatry because of his works on characterology, graphology and philosophy, presents in the first volume a collection of brief publications from 1897 to 1927. The various papers give the reader an excellent understanding of the development of his ideas and interests. In 1897, he wrote a brief discussion on tuism and egoism, describing two fundamental types of personality which would correspond to some extent to the syntropic and egotropic types of A. Meyer. Some of his most important concepts appear clearly in contributions published in 1899, when he emphatically maintained that soul and body form a unit, and that therefore gestures and bodily expressions offer a possible key to the understanding of a personality. Every personality feature has a double aspect, and for its evaluation the whole setting and the interrelations have to be considered. He illustrates this with an analysis of cruelty and the feelings that form the basis for one's contact with others. A discussion of the German philosopher Bahnsen (1899) offers an opportunity to stress the importance of a psychologic analysis of language. One needs to study the formation of new names and the change in their meaning and to compare the various languages. Bahnsen's theory of temperament and his physiognomic teaching are critically reviewed. These topics have interested Klages all his life. His later points of view were already defined in 1901, when he presented the fundamental principles of Lavater. Physiognomy (or pathognomy, as it ought to be called correctly) tries to understand the meaning of movements of the body. On this basis, Klages analyzes the causes of Lavater's success in arriving at correct interpretations. Physiognomically important features derive from lasting interests and strivings. Physiognomic judgment is based on an understanding of harmonious and disharmonious strivings. All features have to be considered in the setting of the whole personality and ought not to be taken as definite signs. (All these contemplations reach their maturity in his later work on characterology.)

Graphology, which Klages has developed on a scientific basis, is mentioned in an early contribution (1898), when he points out that attention exerts an inhibiting and disturbing influence on writing. When the content interests the writer fully, the form of the handwriting is genuine and his mood reaction can be recognized in it. The pressure of the handwriting (1902) corresponds to the degree of inner tension, which is the result of the present constellation and the constitutional make-up. A graphology that is based on such an interpretation cannot accept Michon's teaching that each sign has a definite meaning. The double aspect of all personality features (polarity), their interrelations and the whole setting have to be considered. This is also quite different from Saudek's procedure. The latter tries to avoid depending too much on the general impression of the writing, which Klages uses as his basic principle, and to replace this subjective factor by an analysis of the formative factors of writing. Saudek's studies have advanced the knowledge of writing, but do not offer the possibility of analyzing a personality as Klages does in his later books on handwriting. In 1904, Klages discussed the signs which indicate dissimulation and allow identification of handwritings. This has now been developed into a special science and ought not to be confused with the characterologic interpretation of handwriting. Interesting is the graphological study of Nietzsche and Wagner (1904). It allows Klages to develop his concept of the hysterical character, of which he considers Wagner a representative, and which is characterized by being shallow and calculating, exaggerating and always

playing for effect. The importance of the individual impression of space, which is constantly and invariably seen in expression and which plays an important rôle in graphological expression, was mentioned in 1908. This symbolism of space has preoccupied Klages for many years and led to another discussion with special regard to religion in 1927. Writing as a means of expression through signs and with a definite direction is essentially different from drawing, in which one composes in figures and is free with respect to direction. Handwriting has less freedom and latitude of fluctuation. The full development depends on the degree with which the writer can devote himself to the content that he desires to communicate (1912). A collection of specimens of Schopenhauer's handwriting (1926), from the age of 23 to his death, shows well the change which the human personality—and therefore the handwriting—undergoes during life. A critical study of Nietzsche's handwriting (1927) proves the objective value of Klages' graphology. He and two associates analyzed the same specimens of handwriting independently and arrived at surprisingly similar conclusions. (I might add that several years ago I sent Klages the handwriting of a patient. His interpretations were practically the same as mine and tallied fully with our knowledge of the patient's personality. The personality change, which was caused by epilepsy, was clearly expressed in his handwriting. This contradicts also Saudek's criticism that Klages' graphology applies only to German writing.)

In 1905, a publication dealt with the problem of expressive movements. (This was later fully developed in his book on expressive movements and formative endowment.) He proposes here the theory that all the dynamics of the soul life have a corresponding bodily movement. Expressive movements are the symbol of action.

Fine characterologic studies, which also show the working method of Klages, were presented in 1906 (Ahasver) and 1912 (a criminologic study). They led to the philosophical conception of the opposition of Geist and Seele (thinking and more instinctive life), which has recently found its thorough presentation in Klages' philosophical work. As early as 1910, and again in 1918, he discussed it, stressing the irreconcilable contrast between "conceive" and "perceive" and the harm that is done to man by exalting "cogitare" over life.

His conception of consciousness (as intermittent and not continuous and rhythmic like a life process) is found in his introductory chapter to Palágyi's philosophic work (1925). Both had arrived at a similar formulation independently. Klages offers here a fine analysis of imagination and perception. In the same year appeared a paper on Carus, by whom he has been greatly influenced. It is striking to see how, in the middle of the last century, this romantic physician attempted to formulate the human personality from a psychobiologic and genetic-dynamic point of view.

In the small and easily read book, "Personality," Klages gives a brief presentation of his characterologic theories, which have gained an increasing influence on the thinking of the younger German psychiatrists. He also discusses the philosophical foundation for his personality concept.

The personality is a whole, which cannot be divided into parts, and the features found have therefore to be considered in the setting of the whole and in interrelation to other tendencies. People change constantly, and later features will never be the same as the present ones. From a theoretical and practical point of view, Klages offers the following division: (1) material (intellectual capacity and talents as well as endowment for emotional life and volitional capacity); (2) structure (parts of it are temperament, basic mood and energy and their display); (3) strivings (they are grouped according to the drive for surrender or self-preservation; the latter is of an active, the former of a passive, nature); (4) tectonic (from the interrelation of material, structure and strivings a harmonious or disharmonious, loose or too rigid personality results); (5) behavior aspects (the characteristic behavior with regard to others).

According to the temperament, a person reacts more or less slowly or quickly and with different durations, and is more or less active or passive, superficial or

exact. The essential factor is in the proportion of drive to resistance. Volitional and affective responsiveness depend on similar relations. Strivings are characterized by the feature of having a direction. They are closely related to underlying feelings. Through the influence of the ego they are divided into active (self-preservation) and passive (surrender of the ego to the "id," the latter term used in a vitalistic sense) feelings. Active feelings are the fundamentals for the act of volition. In persons who have more of the surrender strivings, emotions and feelings direct the strivings. The features that stand out in these personalities are the capacity for passion and enthusiasm. The aggressive "will type" is lacking in sympathy. Reason and egotism rule him. Pure types do not exist. A difference in the mixture of the two basic strivings leads to individual differences in personalities.

La syringobulbie: Contribution à la physiopathologie du tronc cérébrale. By N. Jonesco-Sisesti. Price, 70 francs. Pp. 391, with 28 figures. Paris: Masson & Cie, 1932.

The brain stem is a region of peculiar interest to the anatomist, physiologist and pathologist on account of its sharply defined nuclei and tracts, its varied physiologic functions and the striking disorders produced by lesions within its restricted area. In syringobulbia the lesions are essentially chronic, well demarcated and quite varied in location and extent. The author presents detailed records in eleven cases, with four anatomic studies by serial sections, and has drawn on over a hundred cases reported in the literature. The work is evidently a labor of several years, and Professor Guillain rightly states that the views advanced are worthy of serious consideration.

Especially noteworthy points made by the author are the paucity of symptomatology in the presence of extensive lesions, the frequency of unilateral signs in bilateral lesions, the preponderance of vegetative symptoms in certain cases and the almost uniform disturbances in facial sensibility and vestibular function. Other points worth noting are the absence of crossed hemiplegia and of nerve deafness; the occurrence of severe spontaneous pains, hiccup and pharyngeal, laryngeal and respiratory paralyses, and the dissociation of taste, of caloric nystagmus and of facial sensibility. Bulbar lesions give rise to rotatory nystagmus toward the side of the lesion; pontomedullary ones cause horizontal nystagmus in the opposite direction, and lesions higher up provoke vertical nystagmus. Diplopia is attributed to tonic innervation of certain ocular muscles, conjugate movements being disturbed by damage to the fibers entering the longitudinal bundle from the vestibular nuclei.

Pain in the face would seem to indicate an irritative lesion of the spinal trigeminal root, since this gives way to anesthesia as the lesion progresses. Moreover, symptoms referable to the sympathetic system seem to take place particularly in patients who suffer the most. Thermal sensation seems to disappear first in the face, and tactile sensibility only much later. The ophthalmic and maxillary divisions are affected long before the mandibular division. This is believed to be due to the peculiar localization of the fibers in the descending tract. In view of the marked trophic disturbances in the face, often accompanied by anesthesia and sometimes by hemiatrophy, the author believes that the trigeminal nerve carries trophic fibers. (This view will be objected to by those who have studied cases of retrogasserian neurectomy.—Abstractor.) The Horner syndrome is occasionally observed, as is also the Argyll Robertson phenomenon, which the author cannot explain. The section on trophic disorders is particularly illuminating as a whole. Psychic disturbances are sometimes merely incidental, but the author believes that some may be due to sympathetic disturbances acting through the vascular system.

The onset of syringobulbia may be apoplectiform, and it is by no means always preceded by indications of cavitation in the spinal cord. From a review of the cases, Jonesco-Sisesti comes to the conclusion that indications of extension of the process from the spinal cord are of graver moment than the primary bulbar onset. The course is often of remitting type, while changes in the symptomatology are

attributed to progressive destruction of the brain stem as well as to circulatory disturbances with edema in the neighborhood of the growing lesions. The prognosis depends on the condition of the respiratory centers. Painful forms are apt to progress rapidly; those associated with spinal deformity are usually prolonged. Death is usually rather sudden. Some cases, anatomically proved, have shown no indications during life.

The "anatomic synthesis" is particularly valuable, the conclusions being as follows: 1. There is marked disproportion between the extent of the lesions and the severity of the symptomatology. Structures may be thrust aside and continue to function. 2. Cavities are apt to be dorsolateral, less frequently central, and the former are often bilateral fissures of the formatio reticularis cutting across the internal arcuate, vestibular and olivocerebellar fibers. Around these fissures there is apt to be little proliferation, but the central lesions tend to develop tumor-like characteristics. The simple fissure and the true tumor are linked by all gradations. 3. Sudden aggravation of the symptoms is usually due to circulatory disturbances. 4. Involvement of the vegetative nuclei is always present. These do not threaten life unless the lesions are located bilaterally. 5. Dissociation in disturbances of a particular nerve would seem to be due to disease of one of its component nuclei, and by a study of many cases, these nuclei may be mapped with greater precision. 6. Cavities may be single or multiple, unilateral or bilateral, central or dorsolateral, accompanied by much or little destruction or tumor infiltration, which may be extensive or *minuscule*. They are most common about the sensory decussation and seldom extend rostrad as far as the pons.

The author has combed the literature, like Schlesinger, with whose classic work on syringomyelia this book may well be compared; 460 references are given. The illustrations are not particularly clear, but give a good idea of the location of the lesions. On the whole, this work is one that will interest greatly the neurologist and the anatomist interested in the finer anatomy of the brain stem.

Psychology and Psychiatry in Pediatrics: The Problem. Report of the Subcommittee on Psychology and Psychiatry of the White House Conference on Child Health and Protection. Bronson Crothers, M.D., Chairman. Price, $1.50. Pp. 146. New York: Century Company, 1932.

This book is the report of the Subcommittee on Psychology and Psychiatry of the White House Conference on Child health and Protection. It consists of two parts: first, the report itself on the relation of psychology and psychiatry to pediatrics, and second, the discussion of that report and a presentation of typical programs of organizations, such as the Merrill-Palmer School, Institute for Child Guidance, Essex County Juvenile Clinic, training centers for psychiatric social workers and the visitors and teacher groups, which are dealing with and training people to deal with children's problems. The Committee concludes that adequate medical care of the child cannot be given without intelligent attention to the intellectual and emotional difficulties which may be present. However, the fields of psychology and psychiatry are broad and rather ill defined, and physicians in general are not urged to attempt to become expert in these subjects. There is, however, such a thing as psychiatric intelligence which can be achieved by most physicians.

When signs of difficulty arise, the psychiatrically intelligent physician is not bewildered by bizarre behavior or depressed by evidence of sin, but is curious as to motives. He recognizes that the motives can be discovered only by discussion with the child and by study of the human environment. For an effective study of personality the psychiatrist needs two assets: First, he must have an adequate attitude. Patience, curiosity, tolerance and almost invincible optimism are essential. To this attitude technical resources of a more or less elaborate, but by no means standardized, sort are added. The general practitioner must decide whether he regards the maintenance of the attitude as practicable. If he feels that his time table allows patient and often prolonged conversations he can begin to acquire technical resources. These technical resources should be derived from

those of psychiatrists. If physicians in large numbers acquire psychiatric intelligence and become sensitive to the educational implications of the situations that arise in their practice, a new and effective service can be rendered. There is no uniform program which will be suitable. The medical profession cannot dictate to home or school, which do most of the work. Psychologists have established a strong position as directors of education, and physicians have no particular authority in this side of child guidance. When trouble arises and the individual child is in distress, a well informed and alert physician is the obvious adviser. Unwillingness of physicians at large to acquire the ability to deal wisely with problems involving the personality of the child may lead to transfer of this field to formal organizations or to persons without medical experience. Such a solution will inevitably diminish both the prestige of the private practitioner of medicine and the interest of his job.

With these conclusions the reviewer is in hearty accord. There is every reason why the private practitioner of medicine should be competent to understand the behavior problems of children and to treat them if he has the time and inclination so to do or to refer them to a psychiatrist if he deems that most advantageous. The report falls short in one most vital respect. It states that first the physician must be psychiatrically intelligent—that he must have an adequate attitude—but it does not make any statement as to how he may acquire this attitude. This is most important because it cannot be obtained alone through study and reading, no matter how extensive or intensive, but comes mostly either through the fact that he has met and solved his own problems in a complete and adequate way, or through a real understanding of his own personality and an awareness of his own blindspots. It is the reviewer's opinion that a personal psychoanalysis is the most effective technic available at present to gain such an understanding. It seems to the reviewer, therefore, that the problem is not whether the psychiatrist can make any contribution to other fields of medicine, or vice versa, or whether the field of child behavior should be restricted to the pediatrician, the psychologist or the psychiatrist, but how the average medical student can be led to appreciate, first, the dynamics of the psychology of the human beings with whom he comes in contact, and second, the fact that his own personality difficulties do produce blindspots which will hinder his ability to help his patients solve their problems; for the therapeutist must solve his own personality difficulties before he can help others solve theirs. Also, greater opportunities for the recognition and solution of their own personality problems can be made available to medical students. Fortunately a beginning along these lines has already been made in several metropolitan centers—New York, Chicago and Boston.

Hypnoanalyse. By S. Lifschitz. Price, 10 marks. Pp. 122. Stuttgart: Ferdinand Enke, 1930.

The author discusses first the various theories and experimental investigations of sleep, paying particular attention to the experiments of Pavlov. Hypnosis as well as sleep is considered a state of inhibition of the cerebral cortex. Deep hypnosis is characterized by a temporary inhibition of the entire cortex with the exception of the center of hearing.

On the ground of his own investigations of hypnosis by determination of the threshold of hearing in waking suggestion and various depths of hypnosis the author arrives at the following conclusions: First, the susceptibility to hypnosis is an ordinary, normal property of man. In the normal waking condition the author attributes to this susceptibility the value 1.60. In the hypnotic state it increases and reaches a value of 3.2 for the first stage of hypnosis, 4.4 for the second and 8.4 for the third. Second, the hypnotic condition is characterized chiefly by the degree of inhibition of the motor centers and the displacement of consciousness. The susceptibility to hypnotic suggestion may vary within certain limits from case to case and in one and the same hypnotic state. Third, fatigue and the sense of organic malaise and restless condition reduce the susceptibility to hypnosis.

The author distinguishes three types of subjects: (1) the emotionally lazy, who fall rapidly into deep hypnosis but react slowly to suggestions and in a clumsy and dull fashion; (2) the emotionally excitable, in whom it is difficult to attain deep hypnosis and who assume an unusually wary and suspicious attitude (many of these begin to hallucinate even in the first phase); (3) the refractory, who show no reaction to suggestion, neither hypnogenic nor hypnotic, and who are evidently dominated by a strong unconscious resistance.

As hypno-analysis the author designates a more or less deepened cathartic method in which numerous valuable elements of freudian technic find frequent use. It is pushed to what he calls the "sensitive point," in which memories of the past arise especially readily and favorably. This "sensitive point" lies somewhere between the lightest and the deepest hypnosis. The author claims to succeed in finding this point in every patient, but unfortunately he does not show how this sensitive point can be found—that which would be the most interesting point of the whole book for the practical therapeutist.

A long chapter deals with the dreams and with partly unclear and by no means thoroughly convincing attempts to get square with psychoanalytic concepts. The infantile trauma, which receives a further chapter, is, according to the author, not a consequence of a psychic conflict, as Freud claims, but always the consequence of a collision with external crude violence (seduction and overpowering by an adult). In opposition to psychoanalysis the author tends to "physiologic" explanations in contrast to psychologic ones without, however, escaping the danger of losing himself in mythologic speculations on the brain. The book has the undoubted merit of pointing to the importance of a well recognized cathartic method. The author does not, however, state that such treatment is suitable only for certain cases and that as a matter of fact his material consists only of hysterias. With proper consideration of indications the method deserves, without question, its place beside the psychoanalytic one, but is hardly superior to it generally and in all cases, as the author seems to assume.

Behind the Door of Delusion. By Inmate Ward 8. Price, $2. Pp. 324. New York: The Macmillan Company, 1932.

This book is "dedicated to a better understanding of those on the inside by those who are not yet locked in." The author declares himself to be a newspaper editor and writer, noted for his campaigns for civic betterment, who came to grief through alcoholism. He gives an extraordinarily vivid picture of the inside of a well run state hospital, his terse reportorial style being well adapted to the vignettes, the "human interest" stories, the progress in science. The editor breaks out in his attacks on sterilization and on the evils of commitment as at present practiced. The man himself comes to light here and again, as indeed he admits, through his egotism, as a high-strung intellectual worker, keenly humiliated by the droves of curious visitors, some of whom recognize him, constantly embarrassed by the unswerving devotion of a "party girl" who brought him through the acute stages, to whom he owes his life and in whom he cannot merge his identity. He gives an inadequate picture of the cravings of the periodic drinker, since his interests are much more in those about him than in the workings of his own mind. The medical reader of detective stories will be interested in determining the location of the hospital. It is evidently a progressive one, of 2,000 beds, 3 miles from a midwestern town in a state that begins with I and has recently passed a sterilization law. The malaria treatment for dementia paralytica is established, and other pyretogenic treatments are being investigated; encephalitic sequelae are being treated actively. From the author's craving for companionship with the opposite sex, one would judge that women nurses and psychiatric aides are not employed in the men's department. "Inmate" is a little too credulous here and there concerning proceedings in mental hospitals, but, as a good reporter should, he gives his authority for almost every statement. The value of the work to the psychiatrist is in the attitude of the patients toward those in charge, their genuine respect for a good attendant, their hatred of a bad one and their desire to aid

one another, but their contempt for the "quirks" of their fellows, the everpresent desire to get out, which would, if gratified, result in an overpowering desire, for most patients, to get in again. There is little said about the physicians.

One cannot help comparing this book with "A Mind that Found Itself." The two are so completely different. Beers, interested in his own mental processes, viewed the hospital as a prison from which he finally escaped by a subterfuge; Inmate, the extrovert, utilized a unique opportunity of semivoluntary confinement to portray his less fortunate associates. One wonders, and so does he, what will happen when he and Constance, the Light o' Love, start life anew in wild New Mexico. "Place your bets, Ladies and Gentlemen. Fate, the croupier, is about to spin the wheel."

Endocrine Medicine. Volume I. General Considerations. Volume II. The Infantile Endocrinopathies: The Juvenile Endocrinopathies. Volume III. The Adolescent Endocrinopathies: The Adult Endocrinopathies. By William Engelbach, M.D. Price, $35. Pp. 1795. Springfield, Ill.: Charles C. Thomas, 1932.

The presentation of a summary of knowledge of any particular branch of medicine is of great value, provided it is well done. It can be of great scientific value if the author has the analytic knowledge and the ability to present all of the pertinent material. In fact, such summaries may be milestones in scientific progress, and in many instances their value is greater than that of original research, unless the latter is of outstanding value. Such a compilation in three volumes is presented by William Engelbach in "Endocrine Medicine." The scheme of presentation is to present the endocrine glands as individual functional units, as related to each other through the interhormonic action and the interrelation of their incretions on the nonendocrine system. The individual glands are discussed in order of the period of life in which they are most active.

The first volume, of 460 pages, presents the fundamentals—etiology, diagnostic procedure, endocrine reactions and relation of endocrinopathies to general medicine and to the specialties. The second volume, of 473 pages, discusses the infantile and the juvenile endocrinopathies. The third and largest volume, of 862 pages, discusses the adolescent and the adult endocrinopathies. This method of presentation, of course, has its advantages in that it gives a logical presentation of the subject. Nevertheless, there are some disadvantages in that, for example, the history of the thyroid is not presented in compact form, but in several volumes. From the clinical standpoint, however, the arrangement hereby used is of great value.

It would be impossible to review such a compilation as this. It is a pleasure, however, to say that the material is well presented in a critical and presentable manner, so that the reader has all the facts before him. The book is abundantly illustrated, there being altogether 933 illustrations. An unusual but valuable feature is that each particular section, as for example, the infantile endocrinopathies, has its own introduction and presentation of material. Each section has a final chapter on public health, the plan being to discuss the relation of disorders of the glands and the resulting reaction of the nonendocrine system. The publisher has done his work well, the type, the illustrations and the paper being of presentable quality.

A fourth volume containing the bibliography and index is to appear shortly. It will add greatly to the value of the volumes reviewed.

Lectures on Psychiatry. By E. D. Wiersma, M.D. Price, 25 shillings net. Pp. 610. London: H. K. Lewis & Co., Ltd., 1932.

This is a particularly timely book, for it gives the lifelong experience of a psychiatrist who has taught this branch in the University of Groningen from 1896 to 1930. During this period the author has lectured on both psychiatry and neurology, and the lectures which are hereby published, while they do not offer

a complete survey of general psychiatry, for etiology, prognosis and therapeutics are not touched on at all or only incidentally, nevertheless furnish an exceedingly comprehensive view of general psychopathology. To modern neuropsychiatrists they are particularly interesting, for the author believes that for both neurologists and psychiatrists an intimate knowledge of both branches is necessary. "The intimate connection between material and psychical processes . . . gives the firm conviction that the material and the psychical worlds differ only in external form, not in essence, from each other. Both spheres are governed by similar laws." He also believes that a knowledge of psychology is necessary as much for the neurologist as for the psychiatrist; in fact, it is evident that the author has an equal knowledge of psychiatry, neurology and psychology. This is an interesting point of view, for particularly in this country there are those who believe that for a knowledge of psychiatry, neurologic knowledge is very little or not at all necessary, and there are many neurologists who believe that a knowledge of psychiatry and psychology is not essential.

The contents of this volume are divided into twenty-two chapters. As already stated, it is not a book on psychiatry, but takes up only the theoretical aspects, such as consciousness, to which five chapters are devoted, disturbance of perception, memory, thinking, emotionality, manifestations of will and an excellent chapter on aphasia.

Altogether this is a stimulating book, for it shows that after all it is impossible to divorce psychiatry from neurology and that the best psychiatrist is he who knows not only mental medicine but psychology and neurology as well.

Classic Descriptions of Disease. By Ralph H. Major, M.D. Price, $4.50. Pp. 630. Springfield, Ill.: Charles C. Thomas, 1932.

The increasing interest of medical men in the historical aspects of medicine is particularly heartening, for there is nothing so stimulating as a wide knowledge of the traditions of medicine. After all, medicine is an art, and the discoverers of disease have contributed more than their share in the development and the welfare of the race. Physicians are too prone to belittle their profession, and nothing will give them a better perspective of their craft than a knowledge of the great names of medical history. This particular volume deals with the classic descriptions of disease from the medical standpoint as contrasted, for example, with the neurologic aspect. With an introduction that naturally deals with Hippocrates, the author discusses the infectious diseases, diseases of metabolism, lead poisoning, diseases of the circulatory system, diseases of the blood, kidney diseases, respiratory diseases, deficiency diseases, allergic diseases and, finally, diseases of the digestive tract, so that there are presented 376 selections from the original. In each instance, where available, a brief summary of the author is given. The exact references to the original sources are given. There are 130 illustrations of unusual portraits, facsimiles of title and text pages and reproductions of apparatuses and drawings. The volume is beautifully bound and is the sort of book that should be in the library of every physician.

Lectures on Endocrinology. By Walter Timme, M.D. Second edition. Price, $2.50. Pp. 204, with 38 illustrations. New York: Paul B. Hoeber, Inc., 1932.

This little book is already so well known that it needs no extended discussion here. The second edition shows few changes from the first other than the correction of some errors and the addition of two new chapters. The first, of twenty-nine pages, deals with the parathyroid glands. The second, of ten pages, with the caption "Compensatory States," describes the occurrence of pituitary hypertrophy as a physiologic effort of the organism to compensate for the deficiencies inherent in the status thymicolymphaticus. The book retains its dogmatic style and compendial condensation; nothing is offered or suggested in the direction of criticism or possible controversy.