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CEREBRAL LOCALIZATION OF EPILEPTIC MANIFESTATIONS

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A study of the localization of epileptic manifestations is a study of the localization of cerebral function. The movement, the sensation or the disturbance of consciousness observed may seem only a crude caricature of the function normally discharged by the area of brain in question, but from the caricature one may learn to discern the true features of normal cerebral activity.

In this study we have analyzed seventy-five cases of focal epilepsy, after eliminating the cases of generalized epilepsy in which careful study revealed no local sign. In nearly all cases cerebral pneumography was carried out and the patient was operated on under local anesthesia. The seizures which we studied were either spontaneous or induced by hyperpnea, by hydration or by direct cortical stimulation.

This is intended to be a study of human physiology. No effort will be made, therefore, to indicate, except incidentally the reasons for operation, the nature of treatment or the results obtained. A clinical analysis of these cases will be made when the results have been tested by a sufficient lapse of time. For the present, the results seem to justify the means.

Epilepsy is not a disease. It is, as Hughlings Jackson [1] expressed it, "an experiment made upon the brain by disease." In order to avail ourselves of this experimental material, as Jackson did, the following hypotheses must be accepted:

1. A focal pathologic lesion has an effect on adjacent gray matter which renders it liable to recurring, abnormal, violent neuronal discharges. For convenience, the continued effect of this pathologic lesion may be called *"irritation."*

2. The physiologic response of the nerve tissue is an unbridled discharge of neuron units. This discharge may be localized for some time

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1. Jackson, J. H.: Selected Writings of John Hughlings Jackson, edited by James Taylor, London, Hodder & Stoughton, Ltd., 1931, vol. 1.

near its site of origin or it may spread to adjacent areas of gray matter, in which case the spread takes place topographically over the cerebral cortex or from one area of the brain to an adjacent center. Therefore local epilepsy is due to a spread of the discharge by contiguity.

3. An epileptiform convulsion is the external expression of this neuronal discharge when the motor area is involved in it. But an epileptiform seizure (local epilepsy) must be given a much broader definition so as to include all manifestations of the neuronal discharge whether objective or subjective.

An epileptiform seizure includes, therefore, all such positive manifestations, whether they result from activity of the somatic motor area, the so-called sensory area, the cortical, the visual, the auditory, the olfactory or the gustatory area, the cerebral centers for autonomic activity and visceral sensation, or even the sensorimotor areas the activity of which is the physical basis of thought and consciousness.

In this conception there is no difference in significance between a spasm and a sensory aura. Thus, under the heading of epileptiform seizures or fits, the following may be marshaled: (1) clonic and tonic spasm; (2) paresthesias of the limbs or of the body; (3) hallucinations of sight, sound, smell and taste; (4) certain disturbances of consciousness and dream states; (5) visceral sensations (epigastric and thoracic), and (6) autonomic phenomena (such as disturbances of respiration, heart beat, tear secretion, perspiration and flushing).

We do not include, however, postepileptic paralysis or the paralysis which sometimes appears without any evident positive phenomenon, as we believe that, instead of being due to positive inhibition, this paralysis results from an associated vasomotor phenomenon. It is not, therefore, a direct manifestation of epileptic discharge.[2] Further, we do not include postepileptic automatic states and postepileptic psychoses, believing, as Jackson did, that these are negative states due to temporary paralysis of the highest cerebral centers.

LOCALIZATION OF EPILEPTIFORM DISCHARGE[3]

The most frequent characteristic of any unilateral epileptiform seizure is deviation of the head and eyes to the side opposite to the

2. Discussion of this question, though interesting to us, would lead too far afield from the present study.

3. Frequent reference will be made to the observations of Foerster, who verified the type of seizure and its point of origin by electrical stimulation of the cortex in conscious patients on the operating table, just as we have done. His conclusions as to localization are summarized in the paper by Foerster and Penfield (Der Narbenzug am und in Gehirn bei traumatischer Epilepsie in seiner Bedeutung für das Zustandekommen der Anfälle und für die therapeutische Bekämpfung derselben, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:475, 1930). It will be seen that our conclusions substantiate those of Foerster, and we hope, amplify them.

hemisphere involved. Such deviation is obtained easily from the frontal adversive field (area *6aβ* of Vogt, fig. 1), from the upper posterior portion of the parietal lobe (area *5b*), the posterior portion of the temporal lobe (area *22*), and probably also from the occipital pole.

The turning of the head and eyes to the opposite side is doubtless a part of the reaction which should normally direct the patient's gaze toward the source of any external stimulus coming from the opposite side. One automatically turns one's head and eyes to the proper side, whether the stimulus is visual, auditory, tactual or painful. As these sensations have their "arrival platforms" more or less completely in the

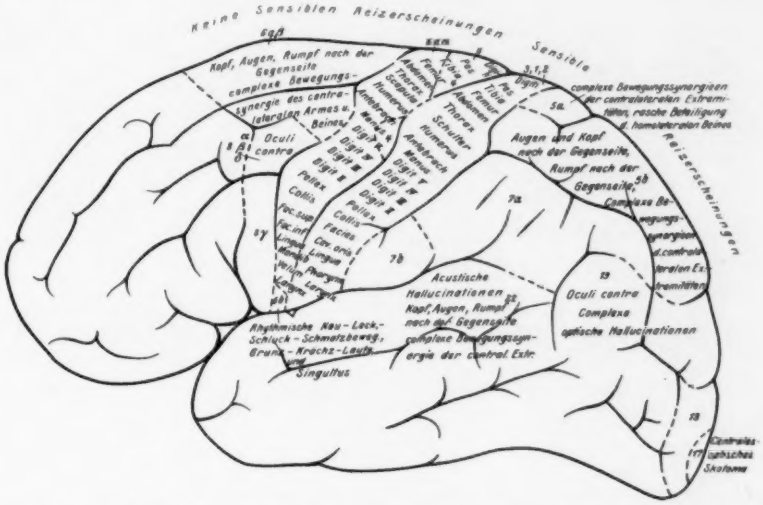

Fig. 1.—Histologic areas of the human cortex worked out according to the architectonic studies of O. Vogt. The results of stimulation of the human cortex are filled in by Foerster (after Foerster and Penfield [3]). *6a β*, frontal adversive field (cytologically it belongs to the regio frontalis agranularis unistriata). *6a α*, secondary field for isolated movements (cytologically it resembles *6a β* but has its own characteristics). *4*, primary field for isolated movements, source of the pyramidal tract; area giganto pyramidalis astriata (most of this area is in the fissure itself). *3, 1, 2*, postcentral cortical termination of the sensory pathway.

hemisphere of the opposite side, it is to be anticipated that direct stimulation of these areas, if sufficiently strong, might result in turning the direction of gaze to the opposite side as though the subject were watching the source of the stimulus.[4]

4. The reverse of the phenomenon is seen in a complete hemiplegia. The head and eyes then deviate to the side of the lesion, as first described by Vulpian and Prevost. Jackson [1] pointed out that this was ordinarily the first characteristic of complete hemiplegia to disappear in the course of recovery.

Deviation of the eyes alone, without turning of the head results, according to Foerster, from stimulation of the frontal ocular field (area *8aβδ*, fig. 1) just below the frontal adversive field and also from stimulation of the occipital ocular field (area *19*).

Frontal Lobe.—Epileptiform seizures which arise far forward in the frontal lobe begin without any sensory aura. The patient looks over the opposite shoulder and gradually turns his whole trunk about in that direction. If he is erect he may turn several times before falling.

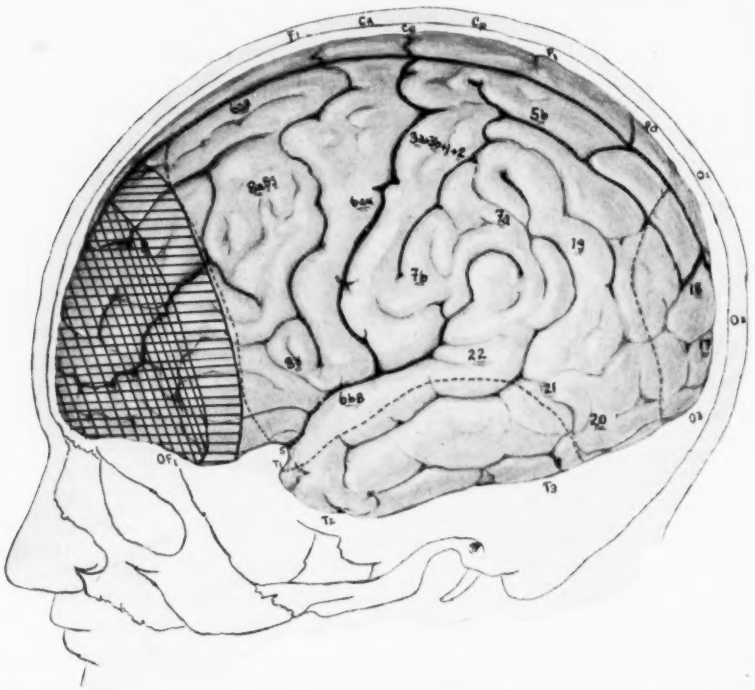

Fig. 2 (case 1).—Destruction of the left frontal lobe. The cross-hatching indicates the dense area of the scar. The shading indicates the transition to normal. Removal was carried out 1 cm. into the normal portion of the brain.

Case 1.—W. B., observed at the Royal Victoria Hospital, gave a history of a fall at the age of 16, when he suffered a depressed fracture of the left frontal bone and was unconscious for several weeks. At the age of 22, epileptiform seizures appeared. At 24 years of age, encephalography showed the left frontal pole to be largely destroyed and cystic, while the rest of the brain appeared normal. We carried out a left frontal osteoplastic craniotomy and found the left frontal pole to be converted into a brownish, gelatinoid tissue (fig. 2). Posterior to this was a zone of leather-like cerebral cortex. The area of abnormal cerebral tissue is indicated in figure 2 by cross-hatching. Radical lobectomy resulted in cessation of attacks.

In this case the seizures were consistently of the same type and were observed on several occasions to be as follows: The patient stared and then rotated his head and eyes to the right. The body then turned to the right. If standing, he might turn about three times before falling. This was followed by tonic spasm of the right arm and leg, which became clonic. At times the attack spread until convulsive movements of the opposite limbs occurred.

This we consider typical of an attack arising far forward in the frontal lobe. There was no warning, and the patient had no memory of the seizures. The initial blank expression doubtless means that consciousness was disturbed or lost at the start, but the lower centers were intact as he did not fall at once. The deviation of the head and eyes to the right and the turning to the right may have meant that the zone of discharge had reached the frontal adversive field (*6aβ* of fig. 1).

The fact that spasm began almost simultaneously in the arm and leg of the opposite side is characteristic of cases in which the focus is removed some distance from the motor area. This suggests that the expanding zone of discharge meets the motor convolution on a wide front.

In general, *turning without aura* points to a localization in the part of the opposite hemisphere in front of the precentral convolution, and *turning with aura* points to a situation behind the central sulcus or below the fissure of Sylvius.

It sometimes happens, however, that postcentral seizures are associated with inability to speak and with a retrograde amnesia, so that no account can be obtained of an aura even though it seems probable that there was some warning. The patient's conduct may indicate clearly that he has a premonition or an unusual sensation, but he is unable to describe it later.

CASE 2.—The case of P. F., a woman, aged 20, observed at the Royal Victoria Hospital, will serve as an example of a seizure beginning farther posterior in the frontal lobe. She had suffered a depressed fracture in the right frontal region at the age of 6 years. At operation it was found that the right frontal lobe and its anterior pole were full of cysts. This abnormal tissue shaded off into normal-appearing convolutions 1 or 2 cm. in front of the central gyrus. This gyrus was localized by galvanic stimulation (fig. 3, 4). Faradic stimulation at points *S* in figure 3 between the cystic area and the frontal adversive field produced an epileptiform seizure which was in all respects typical of those from which she suffered chronically. Before its onset she said, "I'm going to have an attack." What the warning was it is impossible to state.

A typical attack may be described as follows: She turned the head and eyes steadily toward the left. She then fell. The fingers of the left hand were clinched. Stiffness traveled up the left arm until the whole limb was involved; the left leg also became stiff. This was sometimes followed by clonic movements in the left arm and leg. Occasionally the attack became generalized, with involuntary micturition and biting of the tongue. When consciousness was retained she reported tingling and weakness of the left hand followed by twitching of the left side of the mouth.

As indicated by the arrows in figure 3, the discharge passed back into or perhaps arose in the frontal adversive field. There was contralateral deviation of the head and eyes which was not followed by simultaneous movements of the contralateral extremities as seen in the case in which discharge seemed to originate farther forward but by movements beginning locally in the hand and spreading into other regions controlled by the motor gyrus.

From an anatomic point of view, the frontal lobe in man is a very large unit, even though we have excluded from it the precentral convolution and the specialized speech areas.

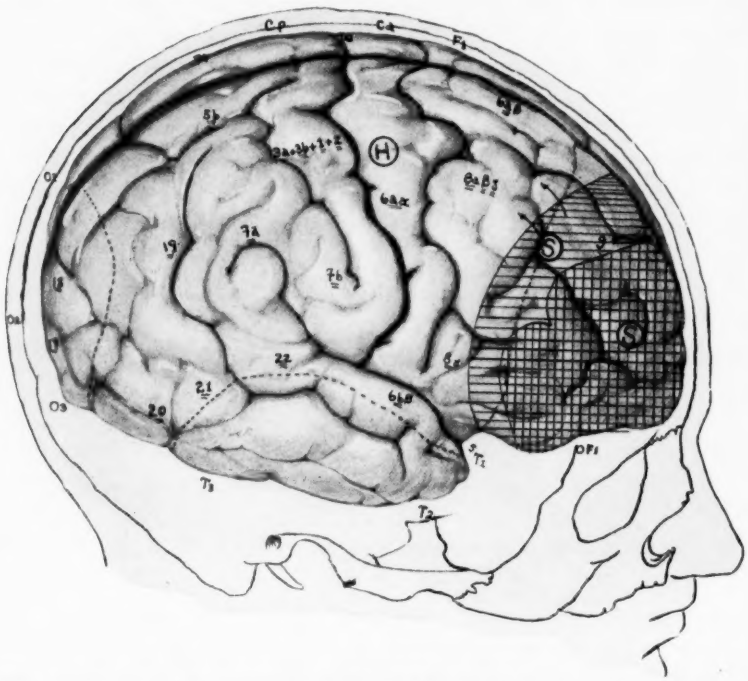

Fig. 3 (case 2).—Destruction of the right frontal lobe. The cross-hatching indicates the dense area of the scar. The shading indicates the less dense area of the scar. The line of removal in normal cerebral tissue is shown. *H* indicates the site of stimulation producing movements of the hand (galvanic); *S*, the sites of stimulations producing seizure (faradic). The arrows indicate the direction of spread of the stimuli.

The lowest centers are represented in the motor region and must be represented [5] in other regions, such as the frontal lobes, where one

5. Jackson [1] (p. 349) spoke of three levels in the central nervous system: (1) the lowest level, in the spinal cord and brain stem; (2) the middle level, or the rerepresentation of all parts of the body about the central sulcus; (3) the highest level or rerepresentation, which he surmised might be in the frontal, prefrontal and occipital lobes.

would expect complex associative processes to take place. Such complex processes must require multiplicity of neurons and a large volume of cerebral tissue, such as are present in the frontal lobe.

But in attempting to examine the function of a *terra incognita* such as the frontal lobe by means of the manifestations of epileptic discharge, it must be realized that silence of a part during discharge is evidence that it lies high in the scale of evolution. During a local discharge in the motor area the arm moves, but voluntary movement of the arm is impossible. When the discharge occurs at a higher level, in the speech area, voluntary speech ceases and the center may find no outward expression. As a further proof of this, we cite the following experiment: While asking a patient to count we stimulated a portion of the speech area strongly as she reached the number eleven. The counting stopped suddenly at that number, but there was no outward indication of the strong discharge that must have been occurring in the neighborhood of the stimulation.

Consequently the arrest of consciousness which may occur when the frontal lobe alone is discharging is suggestive. This silence may indicate that the mental processes which go on there are of a higher order than those of the temporal lobe, which expresses itself to some extent during discharge. In the frontal lobe the processes may well approach more nearly the final associative nervous activity which is the indispensable accompaniment of conscious thought. But this must be left in the realm of conjecture.

Although epileptiform discharge usually leaves the frontal lobe silent, we mention the following puzzling case in which the silence seemed to be broken. We shall not attempt analysis until we are able to study other similar cases.

CASE 3.—M. R., observed at the Royal Victoria Hospital, had a small depressed fracture of several years' standing in the right frontal adversive field. A convolution of the frontal lobe just below the frontal adversive field was stimulated galvanically. The patient instantly wept and ground his teeth. Five minutes later we stimulated the same area again, without either the patient or the assistants anticipating it. The patient wept aloud and gnashed his teeth as before, and this was followed by wild and apparently unconscious struggling, which required four people in addition to the operating team to hold him in position on the table. The movements did not resemble a convulsion but were identical with those in the recurring violent state of which the patient complained when he came to the hospital and which we had considered to be an example of postepileptic automatism. This second stimulation was associated with the vasomotor and arterial changes of the cortex which we have learned to consider an accompaniment or a sequel to most epileptic seizures (Penfield[6]).

6. Penfield, W.: The Evidence for a Cerebral Vascular Mechanism in Epilepsy, Ann. Int. Med. **7**:3 (Sept.) 1933.

Precentral Convolution.—Epileptiform seizures arising in the precentral convolution (areas *4*, *6a α* and *6b* fig. 1) result in local clonic spasm in the part represented; this is such common knowledge that we shall add no examples. As Jackson [1] pointed out, consciousness is lost late in these discharges at his "middle level" of nervous integration.

The peripheral parts most frequently involved are those with movements which are the "most specialized and least automatic." It may be pointed out also that it is these same movements which have the largest topographic representation in the cortex and therefore are most exposed to pathologic influence on the theory of chance. According to Jackson, in order of frequency, initiation of the seizure occurs most often in the hand (the thumb and index finger); next often in the face (the side of the cheek); and next in the foot (almost invariably beginning in the great toe).

In our electrical explorations we verified the cortical localization ordinarily accepted, but found regularly that swallowing or masticatory movements may be obtained from the region just above the fissure of Sylvius in an area considerably larger than that represented by area *6b* in figure 1.

Local seizures may arise in this region without deviation of the head and eyes. As Jackson pointed out, the beginning of this deviation in such cases seems to coincide with loss of consciousness. The deviation therefore probably occurs only when the discharge spreads beyond the motor area and produces the turning by activity of the frontal adversive field (or possibly by activity of some postcentral adversive area). Electrical stimulation of areas *6a α* and *6b* produces the results expected from area *4*. Area *4* is the giant pyramidal cell area, which in man is largely submerged in the central fissure itself. From the point of view of localization of epileptic discharge the whole prefrontal lobe may be considered together without subdivision into the two cytologic areas.

Postcentral Convolution.—Epileptiform seizures arising in the postcentral convolution (areas *3*, *1* and *2* of Vogt) have been called sensory. The sensation is a simple, crude one usually described as "a tingling, numbness, a shock," or even as "a loss of sensation." Sense of movement of a part without the occurrence of movement is rare, according to Holmes,[7] although it has been fairly common in our cases and we have frequently encountered it as the result of stimulation.

Lesions either in the "sensory" area or posterior to it may give rise to such sensory phenomena, and, curiously, we have several times found that an aura of tingling of the part preceded its convulsion when the gross lesion lay close to but in front of the precentral gyrus. But, of course, the "firing point" is not necessarily adjacent to the pathologic

7. Holmes, G.: Local Epilepsy, Lancet **1**:957 (May 7) 1927.

focus, and Gowers [8] made the observation that the postcentral sensory convolution seemed to offer less resistance to the course of the discharging disturbance than the motor centers. This brings up a further observation which we have made.

In two cases, an infiltrating glioma which surrounded or displaced the middle cerebral artery gave rise to epileptiform sensory seizures beginning at a distance from the neoplasm but in the distribution of the artery. In one case, when the neoplasm was removed it was found to extend deep into the temporal lobe, passing beneath the fissure of Sylvius. For several years there had been attacks of tingling and numbness in the arm, occasionally spreading to the leg and the face. At times, later in the progress of the condition, there were other forms of aura probably due to a local effect of the tumor beneath the temporal lobe, such as a bitter taste and a burning sensation in the epigastrium.

Thalamus.—That there are cases of "autonomic epilepsy" arising from centers as high as the anterior portions of the thalamus seems clear, as indicated by a case of tumor of the third ventricle reported by Penfield.[9]

It is ordinarily considered that pain is not represented in the cerebral cortex, but that its highest level is found in the thalamus; and it is of interest in this regard to note that patients sometimes complain of pain as an aura preceding a major seizure or as a warning without sequel. Sometimes, moreover, the aura of tingling becomes severe in a part and is followed by pain (Gowers [8]). Holmes [7] described a case of sensory seizure in which tingling spread gradually through one side of the body, sometimes becoming so severe as to be painful. This was followed by postepileptic hemianesthesia that was complete for all types of sensation, even pain.

This suggests that at least the postseizure paralysis may extend into the gray matter of the thalamus even if the original discharge does not take place there. Holmes stated that during the return of normal sensation in the case cited he made an observation which he had made in other cases and which may throw some light on the finer details of cerebral sensory representation. Following the complete hemianesthesia, sensation first returned to the trunk and gradually passed out to both limbs and down to the hands and the feet. During this recovery there was a glove and stocking type of anesthesia, the upper limit of which was represented roughly by a circular line around the limb. This bears a strange resemblance to some so-called hysterical manifestations!

8. Gowers, W. R.: Epilepsy and Other Chronic Convulsive Diseases, London, J. & A. Churchill, 1901.

9. Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.

The following operative observations suggest a relationship between certain forms of pain and the cerebral cortex.

Case 4.—C. M., a woman, aged 20, observed at the Royal Victoria Hospital, suffered from epileptic seizures heralded by a sharp pain or an "aggravating sensation" in the right lower quadrant of the abdomen. The pain was followed immediately by apparent loss of consciousness, with turning of the head partly to the right and convulsive movements which were more marked on the right.

At operation, performed under local anesthesia, there was found comparative atrophy of a small convolution just posterior to the postcentral convolution and

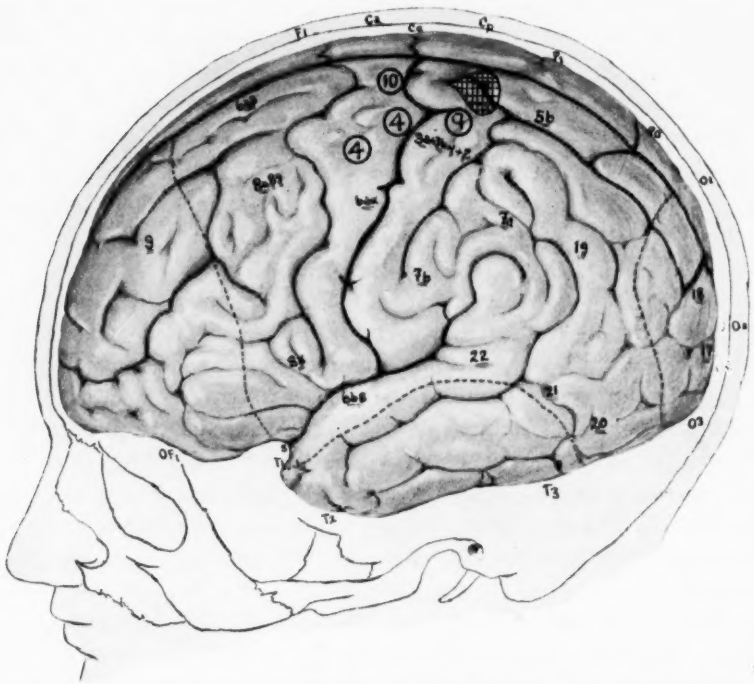

Fig. 4 (case 4).—The cross-hatching indicates the area of cortical atrophy; *9*, the site of stimulation causing a "prickly" feeling in right arm; *4*, the site of stimulation producing a typical seizure, and *10*, the site of stimulation causing flexion of the right thigh and ankle.

near the midline (fig. 4), corresponding to area *5a* in figure 1. Galvanic stimulation of this area produced a "prickly sensation" down the right side. Stimulation was repeated, and she reported pain in the right side like that experienced before an attack. Faradic stimulation just in front of this area reproduced what was for her a typical seizure.

Case 5.—In another case of posttraumatic epilepsy (that of R. M., observed at the Royal Victoria Hospital), during general exploration of the normal cortex with galvanic stimuli the patient reported pain in the hand of the opposite side when the same area as in case 4 was stimulated, i. e., area *5a* in figure 1.

These cases suggest that seizures beginning in this region may be initiated by pain or discomfort in the opposite side of the body and without direct reference to the thalamus.

CASE 6.—*Epigastric sensation.*—N. B., a man, aged 18, observed at the Royal Victoria Hospital, suffered from postepileptic automatic states following small focal seizures in the right arm. Preceding the automatic state there was an aura of epigastric sensation that filled him "with disgust." If the sensation rose as high as the midsternum he always had an attack. He would get on his feet and while doing so might froth at the mouth and become cyanotic. He continued then with unconscious automatic actions and if opposed became dangerously violent.

Exploration of the left hemisphere was carried out under local anesthesia. That portion of the postcentral convolution where sensation in the hand could be produced was found. Posterior to this, probably in the anterior portion of area *7a* in figure 1, an area was found where bipolar faradic stimulation produced a sensation in the right side of the chest. Stimulation of a neighboring point reproduced a sensation in the chest which the patient asserted was like the aura to which he was accustomed. A third stimulation caused a typical aura, with twitching of the fourth and fifth fingers of the contralateral hand. This was a bodily sensation which the patient considered analogous to, or the same as, the epigastric warning produced by posterior parietal stimulation.

We have thought that representation of visceral sensation, when further information was obtained, would eventually be localized somewhere near the temporal lobe because of the frequent association of epigastric sensation with "uncinate fits," as in case 14 to be described, but we believe that bodily sensations may also be represented in this portion of the cortex as well as in the postcentral convolution.

Occipital Lobe.—Epileptiform seizures arising in the occipital lobe are characterized by a crude, simple aura of light in the contralateral visual field. Jackson [1] pointed out that when the light is colored it is usually red, and Holmes [7] cited a case of epileptiform discharge in the occipital pole which he studied under Gowers in which the sensation was that of red light with a blue circle about it.

CASE 7.—L. P., aged 14, observed at the Royal Victoria Hospital, had a calcified, sterile abscess in the left occipital lobe. For four and a half years he had suffered from epileptic seizures which were considered by those who first saw him to be idiopathic. There was a quadrantic homonymous defect in the right visual field.

The attacks at first were minor seizures. He saw stars, which he described as of all colors, on the right side. At another time he described the sensation as seeing color. This was followed by shaking of the right hand. As the light disappeared, "blindness" on the right side followed and persisted for about two minutes.

CASE 8.—In the case of B. W., observed at the Royal Victoria Hospital, epileptiform seizures began in the left occipital visual cortex, as indicated by an aura consisting of a formless red and white ball of light with a blue ring around it in the right field (compare with the case already cited from Holmes). After an interval of about a minute the patient felt a sensation of shaking in

the hand (although there was actually no movement), associated with a feeling of "pins and needles" in that hand. Following this sensation the convulsive seizure made its appearance rather suddenly, as follows: The right hand raised and quivered; the whole body turned to the right and the head and eyes deviated strongly to the right; the mouth pulled to the right, and both legs were "convulsed" strongly at about the same time.

The progress of the slowly spreading discharge can be followed easily through the sensory areas to the motor zone which explodes throughout its length almost simultaneously. This excitation spreading outward like a wave sometimes invaded

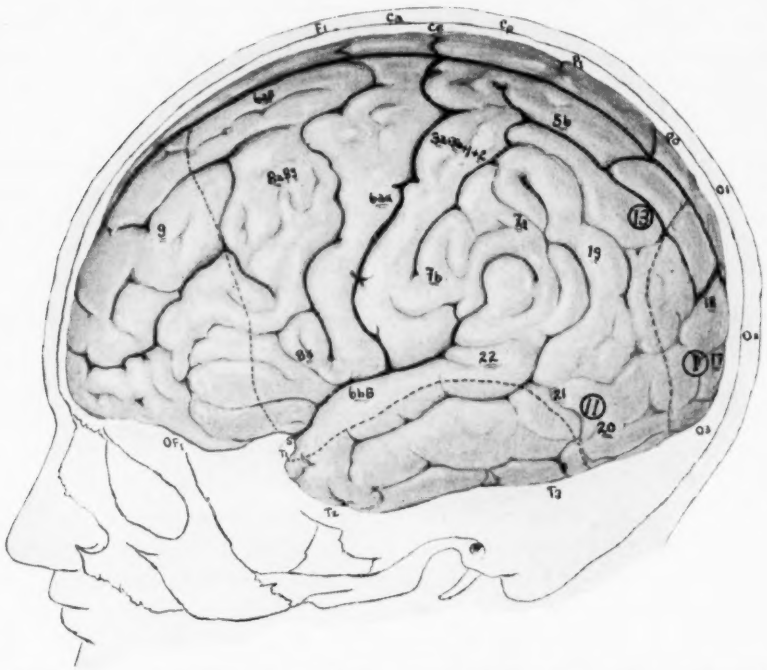

Fig. 5 (case 8).—Site of stimulation which produced at (*1*) a sensation of colored light starting in the middle of the forehead and migrating to the right (galvanic), at (*11*) a flash of yellow light in the right eye and at (*13*), nystagmoid deviation of the eyes to the right.

the temporal lobe as indicated by the fact that after the ball of light she might hear a buzzing, chiefly referred to the right ear, and occasionally she became dizzy.

Galvanic stimulation of the occipital pole at *1*, figure 5, 2 cm. above the horizontal sinus (area *17* or *18*, fig. 1) produced a sensation of red and blue light which came to be "mixed." This light started in the middle of the forehead and passed over to the right. Stimulation of a point 4 cm. anterior to this (fig. 5, *11*) produced a flash of what the patient said was yellow light in the right eye.

Above this, at *13*, faradic stimulation caused the patient's eyes to deviate, with nystagmoid jerking to the right, and the eyelids flickered. She cried out that everything was moving and on inquiry stated that things moved from the

left to right. The condition persisted for about a minute after cessation of the stimulus and she volunteered that it felt like an attack except that she could see. We had produced a local epileptiform seizure including what might be called the middle portion of the habitual attack but without the usual preliminary discharge and paralysis of the visual area of the occipital lobe.

The fact that temporary complete blindness may be produced during a discharge in only one occipital lobe was demonstrated in another case, and Holmes also mentioned it. This may be due to the effect of the unbridled discharge on the contralateral centers, or it may perhaps be due to an effect on the higher sensorimotor complex which one may suppose intervenes between the occipital lobes and consciousness.

The sensation of light may arise from areas of the cortex well removed from the calcarine region, as is indicated by cases 9 and 10:

CASE 9.—L. K., who was under the care of one of us at the Presbyterian Hospital, New York, was reported on in further detail in a paper on cerebral lobectomy.[10] It is sufficient to say that she suffered from epileptiform seizures which we considered to arise in the left occipital lobe because of the fact that there was an aura of two small colorless stars seen about a foot from the right eye. After a long experience of these stars, or "prickles," she said that she lost vision in the right eye. The left occipital lobe, which was abnormal in appearance, was amputated up to a line 7 cm. anterior to the posterior tip of the pole and including the posterior end of the ventricle.

At the present time, six years later, the major seizures have recurred, being ushered in by a sensation in the right hand, and she still experiences minor attacks of what she calls "prickles." By this she means the stars of light (no color) already described. They do not change position, but they twinkle or "prickle" like a real star. She has a right homonymous hemianopia, which is complete except for preservation of macular vision. She has seen the "prickles" in the blind field occasionally for the six years since operation and she is clear that they are identical with the "prickles" which she saw frequently before operation.

Holmes pointed out that patients sometimes "see something" in a blind hemianoptic field, which he likens to the hallucinations not uncommonly experienced by the blind. But the evidence in the case we have just reported would indicate that stars may be seen as the result of supracalcarine neuronal activity.

Another case bears this out.

CASE 10.—E. B., a man, aged 24, observed at the Royal Victoria Hospital, suffered a depressed fracture caused by the blow of a hammer, without losing consciousness. The location and extent of the resultant cerebral scar are indicated by the cross-hatching in figure 6. The generalized seizures, which began six months later, were ushered in by flashes of light to the left side. There was no color or form to the flash. Occasionally also he noted blurring of vision on the left, which gave him the impression that "hot air" was rising before him so

10. Read at the same meeting of the Association for Research in Nervous and Mental Diseases.

that what he saw was indistinct and moving. The cicatrix was excised by our associate, Dr. Cone, who made the following interesting observations: Faradic stimulation at various points about the cicatrix produced contralateral colorless dancing lights (fig. 6), and at *6* stimulation produced "quivering" before both eyes with lights to the left. It seems unlikely that the current could have escaped from this area all the way to the calcarine cortex or that the optic radiations could have been affected. The sensations of light appear to have been produced by the local cortical stimulation, just as the aura probably arose there.

These two last cases lead one to the conclusion that neuronal discharge in the region of the supramarginal gyrus (area *7a,* fig. 1), and possibly

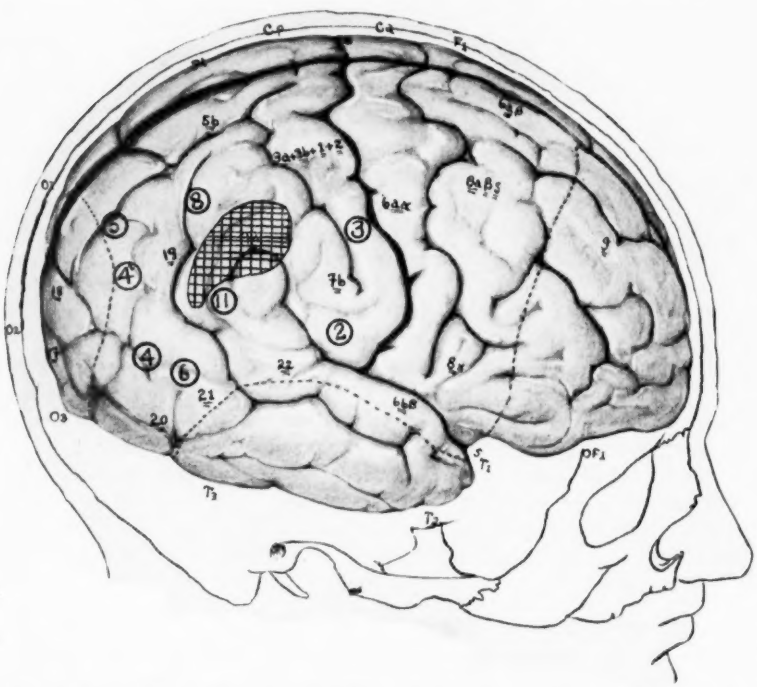

Fig. 6 (case 10).—The cross-hatching shows the location and extent of the cortical scar. The site of stimulation which produced at (*2*) sensation and movement in the tongue, at (*3*) movement and sensation in the left thumb, at (*4*) a flash of light (white) in both eyes, at (*4'*) the same type of flash, but not so bright, and at (*8*) and (*11*) dancing lights resembling an aura in front of the left eye.

extending into areas *19* and *22,* may produce a sensation of light in the absence of the area striata. Foerster and Penfield [3] stated that Foerster had never obtained results from stimulation of areas *7a* and *7b*; so this may supplement those results to that extent.

It is our impression that positive stimulation may be obtained when an area has been subjected to recurring epileptic discharge, whereas the

same area may seem inexcitable in the normal brain. In other words, the habitual local epileptic discharge may leave behind a sort of facilitating influence.

Thus if the sensation of twinkling light is possible in the absence of the so-called visual cortex may it not be due to the activity and the existence of a higher associative visual area?

Temporal Lobe.—Epileptiform seizures arising in the temporal lobe are characterized by certain peculiar auras and complex mental states, some of which are associated with manifestations arising from activity of the region beneath it, particularly the neighborhood of the uncinate

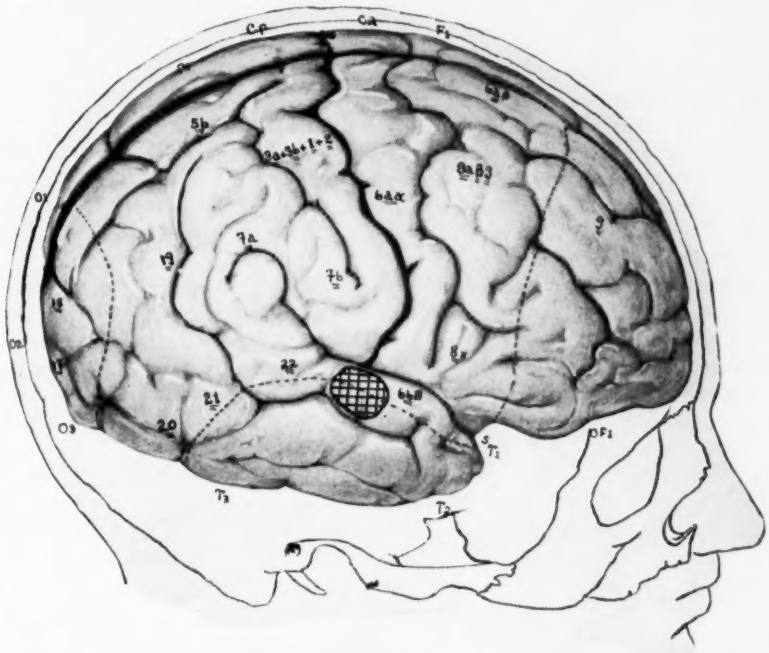

Fig. 7 (case 11).—The cross-hatching shows the cortical presentation of a small, discrete, calcified, sterile abscess beneath the surface.

gyrus. So-called uncinate fits have been elaborately studied (Jackson,[1] Holmes,[7] Wilson,[11] Horrax[12]). We shall not go into this syndrome extensively at present, but shall confine our observations chiefly to the lateral aspect of the temporal lobe.

CASE 11.—F. B., observed at the Royal Victoria Hospital, a rather stupid woman, aged 29, had a small, discrete, calcified, sterile abscess within the superior

11. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood and Compnay, 1929.

12. Horrax, G.: Visual Hallucinations as a Cerebral Localizing Phenomenon, Arch. Neurol. & Psychiat. **10**:532 (Nov.) 1923.

temporal convolution of the right temporal lobe (fig. 7). At the time of excision the surrounding portion of the brain appeared grossly normal, and only a small cuplike area of atrophy indicated its position. Encephalography had shown the area of calcification to be above the inferior horn.

The major seizures came on suddenly, beginning with a cry and immediate loss of consciousness. Generalized convulsive movements apparently appeared at once, although we were never able to observe or to induce an attack, and unfortunately the patient insisted on receiving a general anesthetic at the time of operation.

In the eight or nine years during which she had the major seizures she also had recurring attacks of "giddiness." By this she meant buzzing or ringing in the ears associated with a feeling of which she said: "Things seem to go around. My head swims." She would sit down for from three to five minutes until the feeling passed off, and would at times place her hands over the eyes and ears in an effort to stop the unpleasant sensations.

Case 12.—P. L., observed at the Royal Victoria Hospital, had an infiltrating astrocytoma in the right temporal lobe. The seizures developed as follows: Everything seemed to grow large, and noises became very loud.[13] He then had an acid taste in the mouth, felt nauseated and was dizzy. He stated that at times when he was dizzy things seemed to turn around him; at other times they did not. After that the whole left side might become very weak, but this did not always occur. Occasionally, consciousness was lost. At times there were attacks of deafness associated with the sound of music like the "beginning of a melody." This might last several minutes.

One night the patient suddenly became deranged. Whether or not he had a preliminary seizure is an open question. None was observed by the patients or nurses who were with him in the ward. During this derangement he had both visual and auditory hallucinations and was completely disoriented, although he continued to obey commands to a limited extent. This state disappeared only gradually several weeks after operative removal of the tumor, and it necessitated the use of a general anesthetic at the operation.

Case 13.—A. B., observed at the Royal Victoria Hospital, had a glioma of the right temporal lobe (an oligodendroglioma) which extended beneath the fissure of Sylvius. The attack was inaugurated by a bitter taste, followed by a "pins and needles" sensation in the left arm and side. The macropsia and hyperacusis accompanied the paresthesias.

Case 14.—E. W., observed at the Royal Victoria Hospital, was an intelligent and cooperative woman, aged 37, whose attacks had begun at the age of 20 not long after a moderately severe injury to the head. She described the attacks as follows: There was first a feeling as though the heart was bursting or being squeezed. She then had a "silly grin" (not one-sided) and at the same time seemed to see a picture which she could usually not quite comprehend. Sometimes, at least, it was associated with her own past life. Sometimes she saw a picture of herself as she felt at childbirth, and there might follow a picture of the child. Just when the patient felt that she had comprehended the picture it disappeared. She did not hear any one speak to her, but she might say, "Oh, my heart." Although conscious in some degree during the attack, she could not hear what was going on about her. Attempted concentration, she said, seemed to stop short the attacks to some extent.

The major seizures developed somewhat like those just described, but often without the "silly grin" and "pictures." Stiffness appeared on the right side,

13. We encountered another example of this simultaneous magnification of things seen and things heard.

including the face, and the head was turned to the right. There had been no clonic seizures, so far as she knew, although movements of the right leg had been reported.

Under local anesthesia the motor and sensory areas were mapped out with bipolar galvanic stimuli, the current being varied from 2 to 11 milliamperes. The numbers shown on the photograph of the brain (fig. 8) indicate the responses to this preliminary stimulation and are described in the legend. Faradic current was then used, and the exposed frontal and parietal lobes, except the motor region, were explored without eliciting any response suggestive of an epileptic seizure.

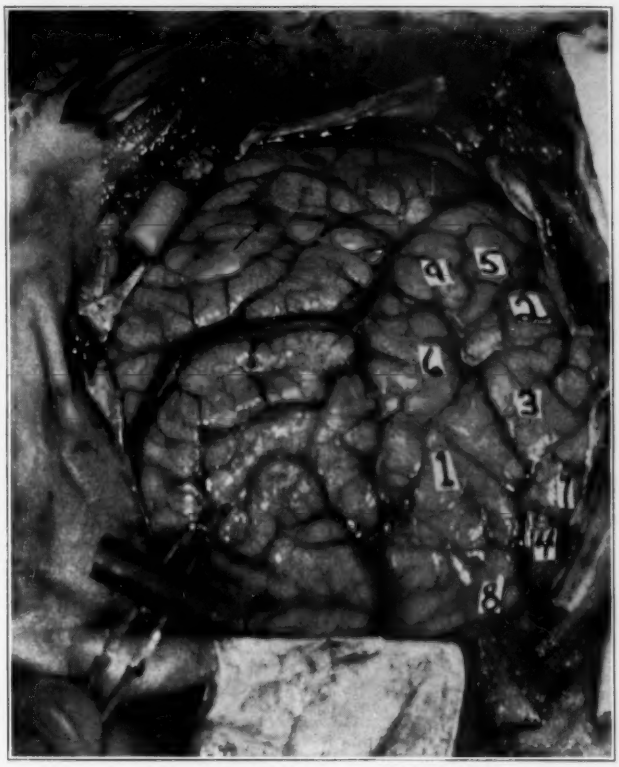

Fig. 8 (case 14).—Photograph of the left hemisphere at operation, the temporal lobe above. The numbers on either side of the fissure of Rolando indicate sites of stimulation and the results as follows: *1,* sleepy feeling in the right arm; *2,* drawing down of the right side of the mouth; *3,* a prickling sensation in the right side of the face; *4,* twitching of the toes of the right foot; *5,* movement of the jaw; *6,* tingling of the right arm; *7,* twitching of the right thigh; *8,* a sleepy feeling in the whole right leg; *9,* numbness of the right side of the face. The arrow points to the hollow from which an aura and a slight attack were produced.

In the second temporal convolution was a small, slightly cupped area (figs. 8 and 9), 7 mm. in diameter. Below this, in the third convolution at the edge of the floor of the middle fossa, stimulation at point *1,* indicated in figure 9, produced a definite sensation of hearing a drum. The stimulation was repeated twice without warning the patient. Each time she stated that she heard the "vibration of a

drum." Stimulation at point *III* caused her to say that she heard a "buzzy sound" in her head. On being questioned carefully she was certain that it was a definite sound.

Finally the small cup-shaped hollow was stimulated for a brief period. She immediately complained of a feeling about her heart. The hollow was stimulated again, and she complained of the sensation about the heart and of a "dizzy feeling." The area was stimulated a third time, for a longer period. She said that she had a dizzy feeling and a feeling about the heart which was "exactly like" the one which preceded her attacks. She said also that things seemed to be going away.

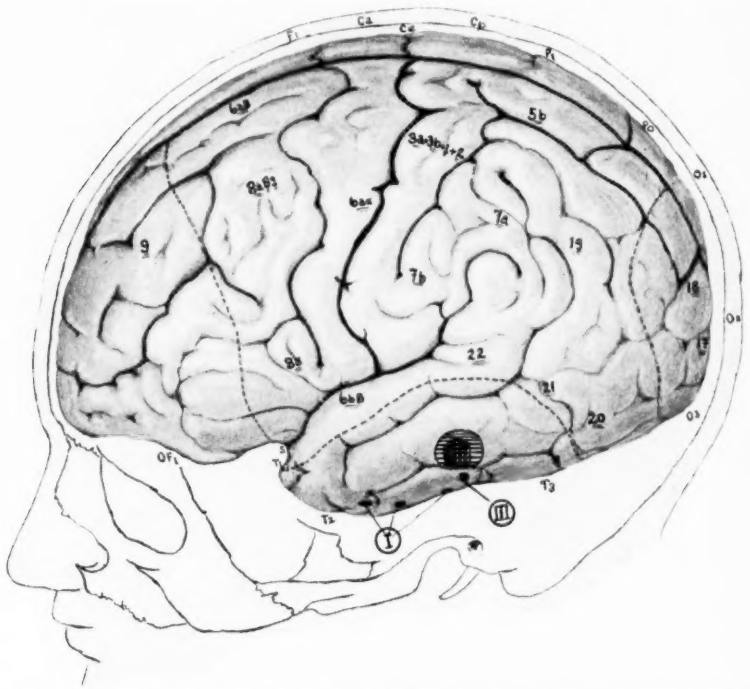

Fig. 9 (case 14).—The cross-hatching indicates the small cupped area (indicated by an arrow in figure 8) from which a seizure was produced by faradic stimulation. Faradic stimulation caused the patient to hear at (*I*) the sound of a drum (repeated at each site) and at (*III*) a "buzzy sound."

The next stimulation was continued still longer. It caused her to say she was going to have an attack; she had all the feelings of it; she had a light feeling in the head and hands.

Those who were observing her stated that her face became slightly cyanosed; there was slight twitching of the mouth, and the eyelids twitched. During this small seizure there was cessation of pulsation in a small artery nearby, and other vasomotor phenomena which we have learned to associate with epileptic seizures were present.

SUMMARY

A complete summary will not be attempted. The reader must refer to the descriptions under the foregoing headings. At a later time it will

doubtless be possible to amplify these descriptions and to localize some manifestations the origin of which we now only surmise.

The most frequent lateralizing sign is deviation of the head and eyes to the side opposite the hemisphere involved. Seizures which have their origin in the frontal lobe are usually characterized by loss of consciousness (without aura) and turning of the eyes, head and body to the opposite side, followed by nearly simultaneous convulsion of the opposite extremities, falling and generalization of the attack. In seizures which arise in the precentral or postcentral gyrus consciousness is usually lost late. A "tingling sensation" may follow a jacksonian "march," just as movement follows in seizures arising in the frontal lobe. Consciousness is likewise apt to be lost late in seizures arising anywhere behind the central sulcus, and such seizures are, of course, ushered in by auras. It must be remembered, however, that a major attack may leave retrograde amnesia, so that the aura is forgotten. In such circumstances the aura may be remembered only in slight seizures which do not progress to generalization.

Certain epileptiform patterns have often been described, such as so-called temporosphenoidal fits and attacks arising in the occipital lobe beginning with lights or darkness in the opposite visual field. But we have pointed out that seizures originating in the supramarginal gyrus in area *7a*, possibly extending to areas *19* and *22*, are characterized by a discontinuous twinkling of lights seen in the contralateral field without any involvement of the calcarine zone.

An aura of pain or of epigastric distress may arise from activity of the cerebral cortex, and cortical stimulation reproduces such sensory phenomena. The buzzing sounds and the dizziness which are characteristic of unilateral temporal lobe seizures have been reproduced by electrical stimulation, but the more complicated dream states and odors have never been reproduced, perhaps because of the limitation of surgical approach.

It should be noted further that involvement of a large artery, such as occurs when a glioma surrounds the origin of the artery, may give rise to an epileptiform seizure beginning at a distance from the primary lesion but within the distribution of the artery.

Finally, cerebral localization of epileptic manifestations is necessary for the interpretation of convulsive seizures and is of obvious importance in cases in which radical therapeutic measures are indicated. Electrical exploration of the cortex in conscious patients during craniotomy has given us unusual opportunity to study cerebral physiology, both normal and abnormal. Although some of our observations are of necessity incomplete, we have nevertheless recorded them in the expectation that they may be as useful to others as they have been to us in the study of cerebral localization.

HYPOTHALAMUS AND TEMPERATURE CONTROL

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AND

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PHILADELPHIA

The modern literature dealing with temperature control appears to become more and more concordant in ascribing the main function of this control to the hypothalamus. Thus, Hasama [1] found that electrical, mechanical or thermal stimulation of the base of the brain between the corpora mamillaria and a point slightly cephalic to the tuber cinereum gives changes in body temperature accompanied by sweating; cooling of this area induces a rise of rectal temperature, warming a fall. The most sensitive area lies from 1 to 3 mm. lateral to the midline according to this author. Keller and Hare [2] reported that removal of the hypothalamus alone destroys the capacity of cats to control their own temperature.

Ott,[3] in 1884, showed that the thermal control centers were situated in the neighborhood of the corpus striatum and later, in 1891, placed the reactions of polypnea and other thermolytic reactions to heat more precisely in the tuber cinereum. Emphasis was placed on the importance of the corpus striatum by Aronsohn and Sachs,[4] Barbour [5] and Hashimoto; [6] the functional importance of the tuber cinereum area was supported by the work of Isenschmidt, Krehl and Schnitzler.[7] The probable importance of centers situated very close to the third ventricle and readily affected by damage to the ventricle has been emphasized by Jacobi and Roemer,[8] and by Gordon.[9] The polypneic response to heat

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1. Hasama, B.: Arch. f. exper. Path. u. Pharmakol. **146**:129, 1929.
2. Keller and Hare: Proc. Soc. Exper. Biol. & Med. **29**:1067 and 1069, 1931.
3. Ott: J. Nerv. & Ment. Dis. **11**:141, 1884; **16**:431 and 433, 1891.
4. Aronsohn, E., and Sachs, J.: Arch. f. d. ges. Physiol. **37**:233, 1885.
5. Barbour: Arch. f. exper. Path. u. Pharmakol. **70**:1, 1912.
6. Hashimoto: Arch. f. exper. Path. u. Pharmakol. **78**:394, 1915.
7. Isenschmidt and Krehl: Arch. f. exper. Path. u. Pharmakol. **70**:109, 1912. Isenschmidt and Schnitzler: ibid. **76**:202, 1914.
8. Jacobi and Roemer: Arch. f. exper. Path. u. Pharmakol. **70**:149, 1912.
9. Gordon, Alfred: The Relation of Withdrawal of Cerebrospinal Fluid to the Body Temperature: Consideration of a Thermoregulatory Center, Arch. Int. Med. **44**:263 (Aug.) 1929.

has been observed not to be affected seriously by removal of the corpus striatum or by the so-called cold puncture (passing dorsoventrally between the diencephalon and mesencephalon to the substantia perforata) according to Nemoto and Sato.[10] On the other hand, it is prevented by decerebration at the collicular level (Bazett and Penfield,[11] Sherrington,[12] de Almeida and Xavier[13] and Keller and Hare.[2] Bruman[14] found that puncture injuries in the thalamus, hypothalamus, corpus striatum and septum pellucidum might all cause derangements of temperature control, and that no exact localization by the puncture method was to be anticipated. The presence of centers in the hypothalamus affecting the secretion of sweat has been demonstrated by Karplus and Kreidl,[15] and by Hasama.[1] The existence of fibers which arise in the hypothalamus in the neighborhood of the corpora mamillaria, which can be traced down the spinal cord to the lateral horns in the thoracic region and which affect sympathetic activity has been excellently demonstrated by Beattie, Brow and Long.[16]

Other evidence is accumulating that centers affecting temperature also occur in the medulla, but there is little evidence that these centers are capable of exercising a fully coordinated control. This evidence will be discussed later.

The evidence here advanced supports the hypothesis of the importance of the hypothalamic area. It consists of a histologic study of the brain stem in a small series of cats in which the presence of temperature control to a greater or lesser extent was demonstrated after decerebration at a somewhat anterior level.

METHODS

Operative Technic.—The operative procedure followed closely that described by Bazett and Penfield.[11] Wax was usually used to fill the cranial cavity after removal of the brain; occasionally a larger amount of bone was removed and the temporal muscles were employed to fill the cavity as far as possible. The main difference has been the use of pentobarbital sodium, or a mixture of dial and pentobarbital sodium, given intraperitoneally, as an anesthetic. Pentobarbital sodium so injected proves satisfactory, but the dose required bears no simple relationship to body weight; the curved relationship observed is described elsewhere (Bazett and Erb[17]). With a dosage of this drug adequate to cause a deep

10. Nemoto, M., and Sato, H.: Tohoku J. Exper. Med. **14**:109 and 135, 1929.

11. Bazett, H. C., and Penfield, W. G.: Brain **45**:185, 1922. Bazett, H. C.: Am. J. Physiol. **101**:6, 1932.

12. Sherrington, C. S.: J. Physiol. **58**:405, 1924.

13. de Almeida and Xavier: Compt. rend. Soc. de biol. **104**:677, 1930.

14. Bruman, F.: Arch. f. d. ges. Physiol. **222**:142, 1929.

15. Karplus, J. P., and Kreidl, A.: Arch. f. d. ges. Physiol. **129**:138, 1909.

16. Beattie, J.; Brow, G. R., nad Long, C. N. H.: Proc. Roy. Soc., London, s.B, **106**:253, 1930.

17. Bazett, H. C., and Erb, W. H.: J. Pharmacol. & Exper. Therap., to be published.

anesthesia, hemorrhage during operation is relatively slight, but the animals recover brisk reflexes in about twelve hours, and later reactionary hemorrhage is sometimes seen. Dial has also been used as an anesthetic, and is equally good from the standpoint of hemorrhages; its effects, however, last much longer, and if a deep anesthesia is used respiratory complications, exaggerated by a long period of depressed respiratory reflexes, are apt to cause trouble. For this type of operation a combination of a two-thirds anesthetic dose of dial, supplemented for the period of operation by pentobarbital sodium, may prove to be most satisfactory. For this purpose an intraperitoneal injection of dial solution to the amount of 50 per cent of the dose indicated in the graph (Bazett and Erb,[17] 1933) for pentobarbital sodium, supplemented by one third of the dose of pentobarbital sodium is suggested, but this combination has so far been given no extended trial. The longer depression of reflexes by the light dial anesthesia appears to reduce the risk of reactionary hemorrhage.

Postoperative Care.—When the brain stem was divided in the immediate neighborhood of centers controlling temperature, temperature control was not regained for several days. Consequently it was essential to have mechanical control of the temperature of the animal following operation. Therefore, the animal was kept in a warm moist room and received additional heat from a lamp beneath it. The room was kept at from 25 to 27 C., dry bulb, and had a humidity of 80 per cent or more. The air was humidified by covering the walls with gauze and keeping a constant stream of water flowing over them. The room was heated electrically, and the temperature was controlled by a toluene regulator. It was found necessary to have a humid atmosphere, owing to the dehydration that occurs when animals are artificially warmed in dry air. The additional heat supplied by the lamp was regulated by a control system operated by the animal's rectal temperature. A resistance thermometer was inserted deep in the rectum and was fixed to the tail to prevent extrusion. It connected with a Leeds and Northrup recorder (a recording Wheatstone bridge), so that a continuous record of the rectal temperature was obtained. The recorder can also be used as a thermoregulator, and it was therefore adjusted so that additional heat was supplied only when the rectal temperature was below a definite level; usually this level was set at from 38.65 to 38.75 C.

Usually a series of animals (up to six) was kept in the room at one time, and the regulator was modified by selective switches, which sampled the rectal temperature of each animal, once every ten minutes, and adjusted the heat according to whether the rectal temperature at this time was, or was not, above the control setting.

Cats with anterior decerebrations make violent active movements of the pseudoaffective character described by Woodworth and Sherrington,[18] and by Bard.[19] They were consequently kept on smooth metal tables, free from any objects on which the cats could obtain a grip. They were bound to the table by cloth bands.

Nursing and feeding were conducted as described by Bazett and Penfield[11]; the animals were turned twice a day. Each morning the thermometers were removed, the animals were cleaned, and the room was aired.

Level of Transection.—The brain was transected with a blunt spatula from the level of the superior or inferior colliculi in an oblique plane to the level of the optic chiasm. Usually the plane has been somewhat concave. After removal of all brain anterior to the cut there has been some additional trimming of the

18. Woodworth and Sherrington: J. Physiol. **31**:234, 1904.
19. Bard: Am. J. Physiol. **84**:490, 1928.

brain stem. Such animals have usually shown a capacity to control their own temperature, but this has often not been in evidence for several days after operation. Control animals have had a second transection passing from the colliculi to the anterior border of the pons, and these animals have consistently shown no capacity to control their temperature, with a single exception in which the second transection was not quite complete and which is consequently also described here in detail.

Histologic Examination.—All of the brains were fixed in 80 per cent alcohol as soon as possible after death; a few brains have had to be discarded owing to the postmortem changes when the animals happened to die and to be incubated for some hours before autopsy. The brains were embedded in celloidin and were stained with toluidine blue. It was thought that studies of the cells were the more valuable, since the experiments were relatively acute and none of the animals with temperature control survived long enough to show Marchi degeneration. Serial sections were cut from the most cephalic portion of the brain stem to the caudal limit of the lesion. Control animals of the usual decerebrate type (with the double section described by Bazett and Penfield) were studied with both toluidine blue and Marchi methods. Every fourth or sixth section was studied. The specimens were cut without separating the blood clot or disintegrated nerve tissue from surviving tissue, so as to avoid any injury during preparation; the photomicrographs illustrate the normal tissue surrounded by a considerable mass of nonfunctional tissue. The terminology used by Rioch [20] has been used in describing the changes observed.

RESULTS

Attention will be directed mainly to four cats in which a greater or lesser degree of temperature control was observed, to the single cat which showed some temperature control in spite of an incomplete second more caudal transection, and to the contrasts observed in control animals. Observations were made on a number of other animals and support the general contentions advanced; little attention will be paid to them, since for one reason or another a complete study of these animals was not possible.

CAT 1.—Operation was performed on the morning of April 12, 1932. The cat showed brisk reflexes (including righting) on the following morning and made violent, fairly well coordinated running and jumping movements. Artificial heat was discontinued at 9 a. m. during the first day on the chart. In the evening, at the commencement of the third twenty-four hour period, records were discontinued, and the animal was moved to a cage where it showed very active climbing movements. It died during that night from strangulation, after forcing its head between the cage and the door. The cat was kept throughout in the warm room at a temperature of from 25 to 26 C. (dry bulb) and with a humidity of 80 per cent or more. Autopsy demonstrated slight bronchopneumonia; there was an epidemic of "distemper" among the animals at this time. The rectal temperatures recorded are shown in figure 1.

In the gross specimen the transection could be seen severing the brain at the level of the inferior colliculi and sweeping forward, leaving a portion of the inferior surface of the base of the brain intact. Study of the most anterior of

20. Rioch, D. M.: J. Comp. Neurol. **49**:1 and 129, 1929; **53**:319, 1931.

the serial sections, which passed through the diencephalon and optic chiasm, showed that here the third ventricle and the tissue surrounding it remained intact, including the hypothalamic nuclei and the supra-optic ganglia. The nucleus amygdalae was destroyed on the right and was intact on the left. The tissue immediately dorsal to the third ventricle in the midline was destroyed. On either side the basal portions of the tissue of the brain were destroyed and the distribution was uneven.

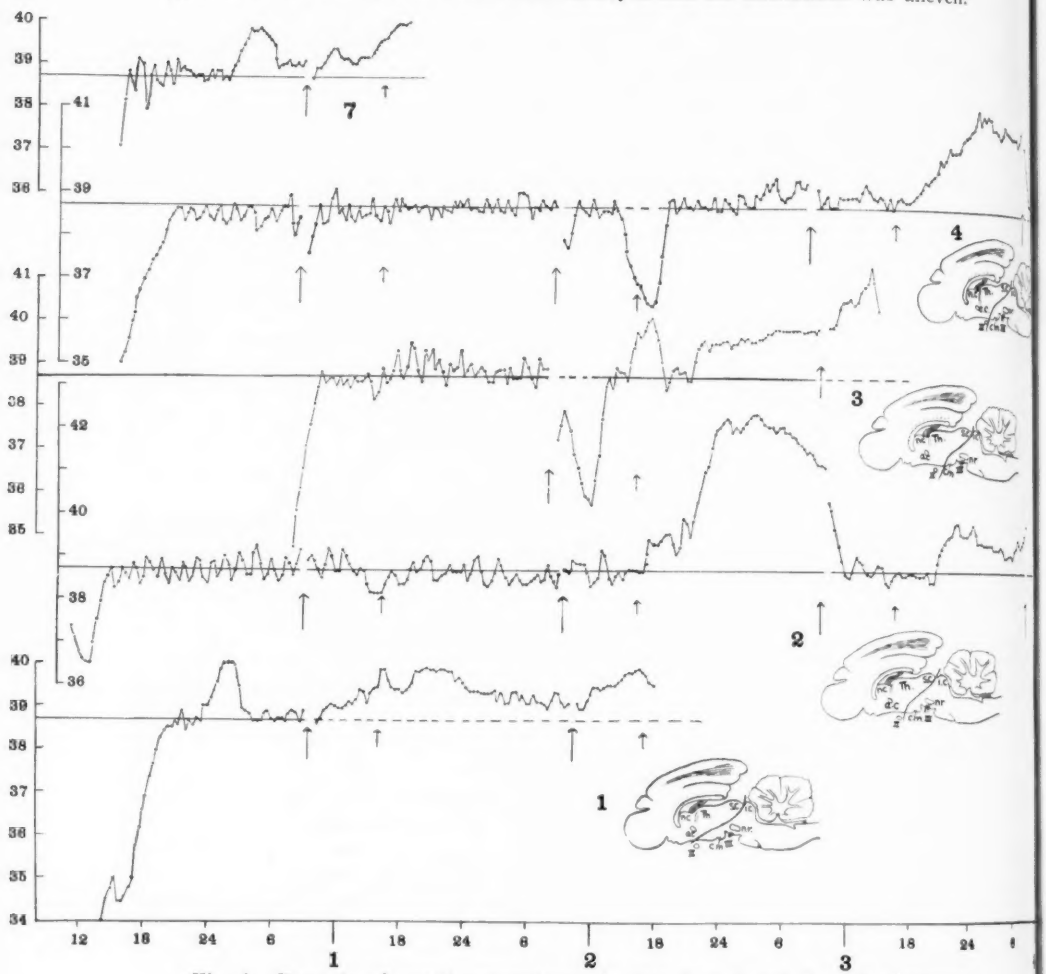

Fig. 1.—Records of rectal temperatures in cats 1 to 4 and 7, with diagrams of the position of the lesion in cats 1 to 4. The abscissas represent time; the larger numbers indicate the number of days from the end of the operation, which for convenience is assumed to have ended exactly at midday. The smaller numbers indicate the time of day; midday is indicated by *12*, midnight by *24*. The large arrows and breaks in the temperature record indicate the times when the cats were fed and cleaned, and when the thermometers were removed; the smaller arrows indicate the times when the cats were merely fed. The horizontal lines through the records indicate the level of the artificial thermal control; the line is interrupted when artificial control was discontinued.

On the left the anterior and lateral thalamic nuclei remained intact, as well as the ventral nuclei; on the right these were all destroyed. Thus, at this level most of the thalamus was obliterated by the section.

Sections passing through the hypothalamus just caudal to the chiasm showed the whole dorsal portion of this region destroyed in the midline and the presence of only a small portion of tissue above the third ventricle. Laterally, the section differed on the two sides; on the right the entire pulvinar was destroyed and with it the nucleus ventralis and the dorsal lateral geniculate body; the temporal lobe and the nucleus amygdalae remained intact on this side; on the left there was almost complete destruction of the pulvinar, with softening in the nucleus ventralis *a*, with a small hemorrhage in the nucleus ventralis *b* and with destruction of the lateral geniculate body and of the temporal lobe. Thus the hypothalamus and the nuclei in and around the third ventricle, including the nucleus filiformis, and the nuclei hypothalamici anterioris, medialis and lateralis, ventromedialis, dorsomedialis, ventrolateralis and periventricularis, were all intact.

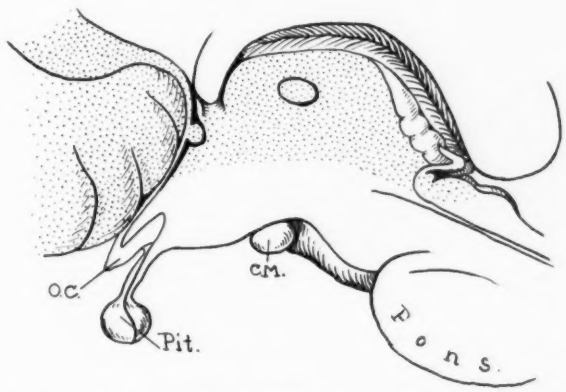

Fig. 2 (cat 1).—Sagittal diagram representing the position of the lesion; the stippled area represents tissue destroyed or removed. The entire hypothalamus is intact from the chiasm to the mamillary bodies. In this and succeeding figures, *O.C.* indicates the optic chiasm; *Pit.*, the pituitary; *C.M.*, the corpora mamillaria; *O.T.*, the optic tract; *Inf.*, the infundibulum; *Thal.*, the thalamus; *III*, the third ventricle; *Temp.*, the temporal lobe; *Int. cap.*, the internal capsule; *Put.*, the putamen; *Pall.*, the pallium; *Hem.*, hemorrhage, and *Nec.*, necrotic tissue.

In sections passing through the corpora mamillaria there was little evidence of destruction, except in the most dorsal portion of the brain stem. The pulvinar was destroyed in its outer portions, but was otherwise intact except for the ganglion habenulae which had been cut away on both sides. The corpora mamillaria, nuclei hypothalamici, corpus subthalamicum and nucleus periventricularis were all intact. The hypothalamus at this level was therefore intact, and only a small portion of thalamus had been removed.

Below the level of the corpora mamillaria the brain stem was intact except for a small area of hemorrhage in the superior colliculi.

The general level of the section is indicated diagrammatically in figure 1, and is demonstrated in more detail in figures 2 and 3.

This cat was regarded on both physiologic and histologic grounds as the one with the most anterior section of the series. Though it lived only a short while and was consequently not given any detailed examination, it apparently recovered temperature control as soon as the effects of the anesthetic wore off (within twelve hours of the operation), and a slight hyperthermia developed, which may have been a febrile reaction to the operation. At 9 a. m. on the following morning it was fed and cleaned, all heat was turned off, and the room was aired and cooled, yet the rectal temperature was well maintained, in strong contrast with other animals without temperature control in the room at the same time, which all showed a fall in rectal temperature of from 1 to 1.5 C. This morning routine accompanied the morning feeding almost invariably and

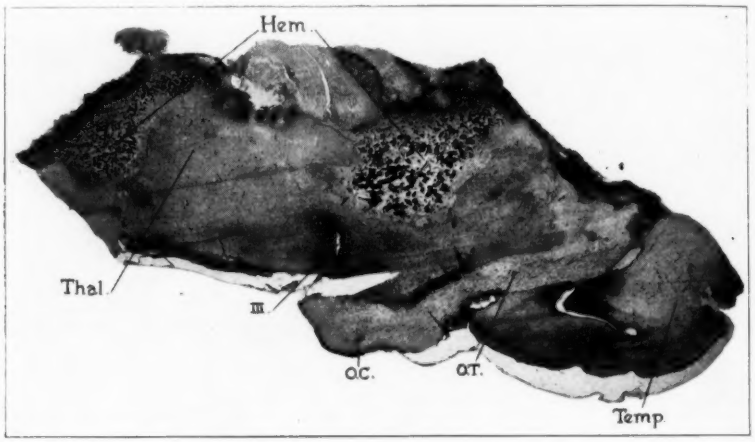

Fig. 3 (cat 1).—Photomicrograph of a section through the optic chiasm with the hypothalamus intact.

afforded an excellent test of the ability of the animal to maintain its temperature; the rapid fall commonly seen in the absence of control is well illustrated in figure 1 in cat 4 at the times of its first two morning feedings. In less than twenty-four hours cat 1 was therefore able to prevent this fall of temperature, though it did so perhaps a little more effectively the following morning. Presumably it also had some capacity to regulate against hyperthermia, since the rectal temperature after the first day fluctuated over a range of only 1 C. in spite of violent bursts of extreme muscular activity in a warm and very humid atmosphere. The respirations were fast but very irregular, and seemed to be mainly determined by the extreme condition of apparent excitement. An adequate temperature control must have been present and was able to function immediately after operation. Histologically, the corpora mamillaria, hypothalamus and a small portion of the thalamus were intact;

there had been entire destruction of the base of the brain cephalic to the optic chiasm, and of many of the dorsal structures. Presumably the thermal centers were situated within the intact area.

CAT 2.—Operation was performed on the morning of March 31, 1932. Brisk reflexes were observed on the following morning, with running movements and righting reflexes. On the morning of the fifth day, the cat was removed from the warm room and was kept in an ordinary metal bath tub in a room at about 25 C. (dry bulb) but of low humidity. During the next two days it showed great activity, walked in a drunken manner and made springing, climbing and ill coordinated running movements, with intervals of rest. In spite of consequent considerable variations in metabolism, it maintained its temperature between 39 and 40.5 C. during these two days. The wound was split open as the result of the violent hitting of the head against obstacles, and became infected; the animal died of meningitis on the seventh day. Death was preceded by a fall of rectal temperature on the last day of life to 31 C. There was no vocalization except during the last few hours, when a mewing cry was occasionally made. The conditions within the warm room used for the first four days were the same as for cat 1. The rectal temperatures recorded for the first four days are shown in figure 1.

Histologic study of the brain stem was conducted as in cat 1. The most anterior sections passed through the optic tracts just posterior to the chiasm; the dorsal part of the brain stem was completely destroyed. The hypothalamus on the left was almost completely destroyed by softening and inflammation, and on the right it was badly disintegrated as the result of inflammatory foci around the vessels; on this side the nerve cells showed marked degenerative changes. Posterior to this the hypothalamus was a little better preserved on both sides. The nucleus filiformis was destroyed on the left side and much damaged on the other; the more lateral parts of the hypothalamus were destroyed on both sides, but the tissue surrounding the third ventricle in the posterior part of the hypothalamus, including the nuclei periventricularis, was on the whole in good condition. Parts of the nuclei hypothalamici (anterioris and lateralis) were destroyed.

More posteriorly a section passing through the optic tract on the left showed destruction by hemorrhage of the dorsal parts both of the nucleus lateralis thalami and of the pulvinar, of the ventral part of the nucleus posterioris thalami and at this level of the whole of the nucleus ventralis, the ganglion habenulae and the nucleus para-ependymalis. On the right the same area was involved, but destruction was less complete, as it was due to softening rather than to hemorrhage. The hypothalamic region was intact on both sides, except that there was a perivascular infiltration along the walls of the third ventricle, which, however, was not associated with much destruction of tissue.

Sections passing through the corpora mamillaria on the left showed destruction of the pulvinar, nuclei posterioris and ventralis thalami, medial geniculate body and habenular and para-ependymal ganglia; on the right the destruction involved only the nucleus posterior and pulvinar, but spread over into the medial geniculate body. Around the third ventricle the gray matter was intact as far laterally as the nucleus limitans. The corpora mamillaria were intact. The hypothalamic region was diffusely spattered with inflammation, particularly perivascular, from the basal meningitis. The inflammation was found along the walls of the third ventricle and in the supramamillary groups of nuclei.

More posterior sections passed through the posterior commissure. There was destruction of the commissure. On the left the destruction had involved the entire

lateral geniculate body and extended medially to the area just adjacent to the nucleus of the posterior commissure; on the right the destruction involved part of the lateral geniculate body but did not extend as far mesially as on the other side. There were areas of inflammation around the iter and through the gray matter ventral to it, but the degree of destruction was not great. Both medial geniculate bodies were intact. On the left the most anterior part of the nucleus ruber was destroyed; on the other side it was intact. Below this level there was no destruction. The general level of the section is indicated diagrammatically in figure 1, and is shown in more detail in figures 4 to 7.

Temperature control was more definitely established in this animal, though it may not have been regained quite so rapidly as in cat 1. Probably some temperature control was present after twenty hours, since on the first morning during cleaning and feeding there was little fall of rectal temperature; other animals without temperature control

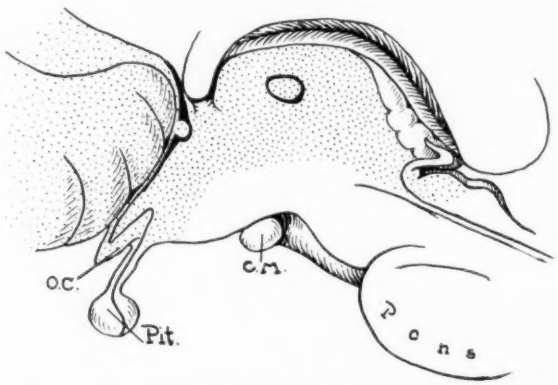

Fig. 4 (cat 2).—Diagrammatic representation of the lesion. The anterior part of the hypothalamus is destroyed; the posterior part is intact.

showed falls of temperature on this day of 1.5 C. However, if control was present at this time, it was not associated with fever, and the level of spontaneous control was not above that of the mechanical system. On the following morning, near the end of the second twenty-four hour period, there was no fall of temperature during cleaning (the other animals showed falls of from 0.5 to 1 C.), and temperature control was assuredly established, though neither fever nor complete independence of artificial heat was shown till early in the third day. (The high fever at about midnight on the third day was unusual. It could be interpreted either as an excessive febrile reaction or as a hyperthermia due to inadequate temperature control; more probably it had a simpler explanation in the thermal conditions of the room; for it may be noted that there was a general tendency in these animals to show maximal temperatures about midnight. After the evening feeding the room usually remained closed, and probably attained a much greater humidity than in

the day period, and the higher effective temperature was probably contemporaneous with the specific dynamic effect on metabolism of the evening feeding. If excessively violent movements happened to be made at this time and to add their effect to these other factors, it is likely that the cooling power of the room might be inadequate. Room tempera-

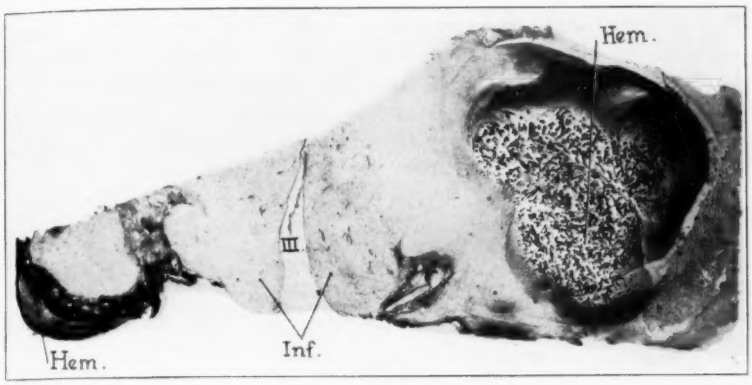

Fig. 5 (cat 2).—Section just caudal to the optic chiasm, showing the hypothalamic area preserved. Everything cephalic to this has been destroyed.

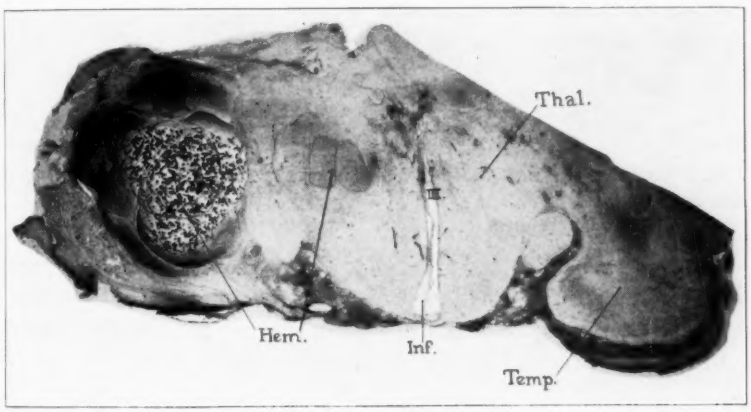

Fig. 6 (cat 2).—Section through the infundibular region. The hypothalamus is intact; the rest has been quite effectively destroyed.

tures were recorded with a maximum and minimum thermometer, and there was no evidence that on this occasion the room conditions differed much from their normal value. The whole phenomenon appeared at midnight on Saturday, with no data available except those of the graphic record, and consequently no deductions can be drawn as to whether the animal's thermal control was, or was not, normal at this time.) From

the beginning of the fifth day to the commencement of the seventh day, thermal control was at any rate adequate to maintain a normal temperature level (with moderate fever) under ordinary room conditions and with widely varying degrees of muscular activity. For the last twelve hours temperature control was again certainly lost, and presumably, therefore, temperature control was subserved by centers involved in the later inflammatory changes, but spared by the initial section.

In this cat, therefore, there was partial destruction of the anterior part of the hypothalamus bilaterally, and unilaterally less anteriorly; in the most posterior portions the hypothalamus was intact, especially around the walls of the third ventricle. The corpora mamillaria were

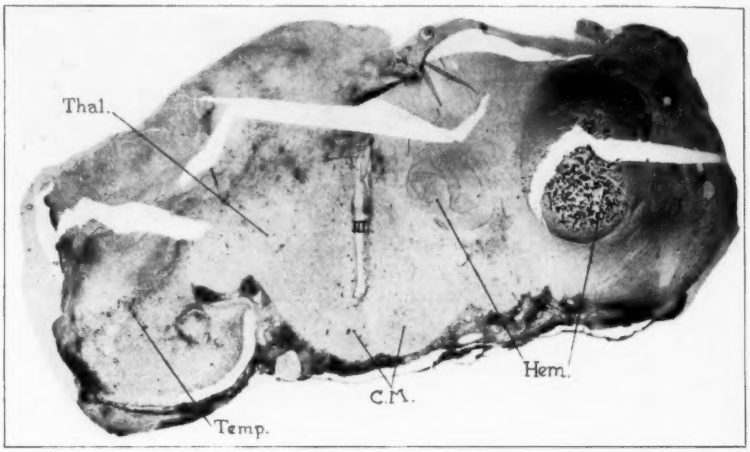

Fig. 7 (cat 2).—Section through the corpora mamillaria. The brain stem is in this area intact.

intact, but the thalamus and geniculate bodies were destroyed. It would appear, therefore, that temperature control was effected by nuclei in the most posterior part of the hypothalamus, and probably by one of the nuclei later involved in the inflammatory changes.

Cat 3.—Operation was performed on the morning of April 27, 1932. During the first twenty hours the cat was kept on a warm table in an ordinary room, and was placed on artificial control only at this time. At the end of the third day it was removed from the warm room (for cleaning purposes) and was kept for one hour without heat in an ordinary room. On return to its stall it was found to have maintained its temperature, and no artificial heat was used from this time till the time of the animal's death in the afternoon of the fourth day. The cat made moderately violent running movements and tried to right itself. All of these movements were incoordinate. It tended to turn to the left, and its efforts at righting usually resulted in its rolling over and ending on its back with the feet in the air. The conditions in the warm room were the same as for cat 1.

Death occurred from a hematopericardium as the result of an unsuccessful attempt at puncture of the heart. The rectal temperatures recorded are shown in figure 1.

Study of serial sections of the brain stem was conducted as for cat 1. In the more anterior sections, which passed through the optic chiasm, the entire brain stem, including the hypothalamus, was destroyed by hemorrhage on one side, and was almost completely destroyed on the other, but the nuclei para-ependymalis remained intact. Just posterior to this level the hypothalamus was almost completely destroyed on the right, except for a small portion along the walls of the third ventricle corresponding to the area of the nucleus hypothalamici and ventromedialis; on the left the whole hypothalamus was intact. In more posterior sections the destruction observed was similar until the region of the corpora mamillaria was reached, where the whole brain stem became intact except for a small area of destruction in the pulvinar of either side. Below this area there was no destruction. The level of section is shown diagrammatically in figure 1, and in more detail in figure 8.

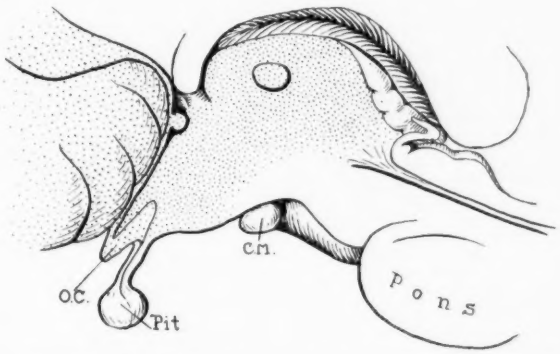

Fig. 8 (cat 3).—Diagrammatic representation of the lesion; the tissue cephalic to the corpora mamillaria is destroyed.

The evidence for temperature control in this animal at the end of the third day is similar to that for the other animals; though less complete, it is probably valid. It is equally certain that temperature control did not return for the first forty-eight hours. (The pronounced fall of temperature during cleaning near the end of the second day was similar in magnitude to those of other animals with lower sections and no temperature control. To prove the absence of temperature control more definitely, the heating lamps were disconnected at 9:15 a. m. near the end of the second twenty-four hour period both beneath this animal and beneath another control animal with a second lower transection and with no evidence of temperature control at any time; the fall of temperature in cat 3 is shown in figure 1, and almost exactly paralleled that of the control animal. The contrast seen twenty-four hours later when even removal to an ordinary room produced no fall of temperature is marked.)

In this cat the first really intact part of the brain stem was found at the level of the corpora mamillaria. Anterior to the corpora mamillaria there existed the nucleus hypothalamicus ventromedialis on the right and on the other side the whole of the hypothalamic nuclei.

It would seem logical to assume that the slow recovery of temperature control in this animal depended on an initial section which passed extremely close to the essential centers, and that they were temporarily incapacitated by the aseptic reactionary changes to the lesion.

CAT 4 (pregnant and nearly at term).—Operation was performed on the afternoon of March 14, 1932. On the following morning the animal showed only slight reflexes. By the beginning of third day reflexes were brisk; moderately active running movements were made, and righting reflexes were present. At the end of the fourth day (in the early morning), parturition had commenced and two live kittens were born. The animal mewed during efforts at parturition.

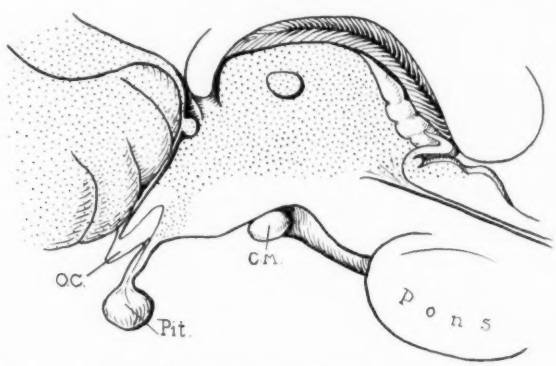

Fig. 9 (cat 4).—Diagrammatic representation of the lesion; the infundibular area is damaged, but the rest of the hypothalamus is intact.

Artificial heat was discontinued, and the thermometer was removed, as it was difficult to retain it in place. The rectal temperature was maintained between 40.5 and 41 C. Parturition continued very sluggishly, and the following morning not all the kittens had been born; consequently extract of the posterior lobe of the pitutitary gland (0.25 cc., intramuscularly) and later pitocin (0.5 cc., intraperitoneally) were given, and the last two kittens were born, one during the day and one during the following night; one placenta was retained. During this day (the sixth day), the rectal temperature (within the warm room but without other heat) was 36 C. in the morning, 36.5 C. in the afternoon and 35 C. in the evening (when the animal was wet with amniotic fluid). On the following morning (the end of the sixth day), reflexes and movements were still active, but the rectal temperature was only 33 C. The cat was warmed artificially, struggled considerably, vomited after feeding and died, apparently from asphyxia. Room conditions were the same as for cat 1. Autopsy showed the presence of the retained placenta and pus in the uterine horns. There was no other evidence of infection. The temperatures recorded are shown in figure 1.

Histologic study of the most anterior sections, which passed through the infundibulum and optic tract, showed everything dorsal to the third ventricle

destroyed on both sides. On one side of the third ventricle there was a small area still intact, including lateral and medial hypothalamic nuclei, as well as the nucleus periventricularis. On the other side the pulvinar and posterior nucleus of the thalamus were destroyed, but everything ventral to this was intact. More posteriorly the whole of the hypothalamus was intact to the level of the infundibulum, where there was quite marked destruction of the hypothalamic region involving the nuclei hypothalamici dorsomedialis and ventromedialis, and the nucleus periventricularis hypothalamicus ventralis; here the walls of the third ventricle were destroyed by hemorrhage, except for portions in the infundibular area. More posteriorly the brain stem was intact. The level of the section is shown diagrammatically in figure 1, and in more detail in figures 9 to 11.

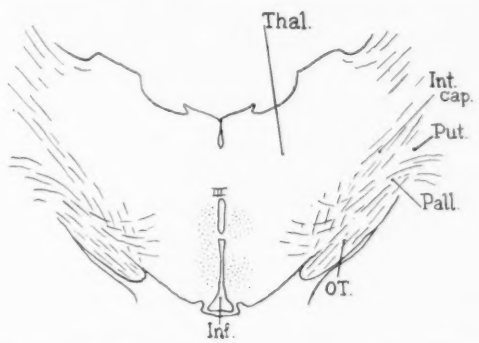

Fig. 10 (cat 4).—Diagrammatic representation of the infundibular area destroyed by hemorrhage, as seen in transverse section.

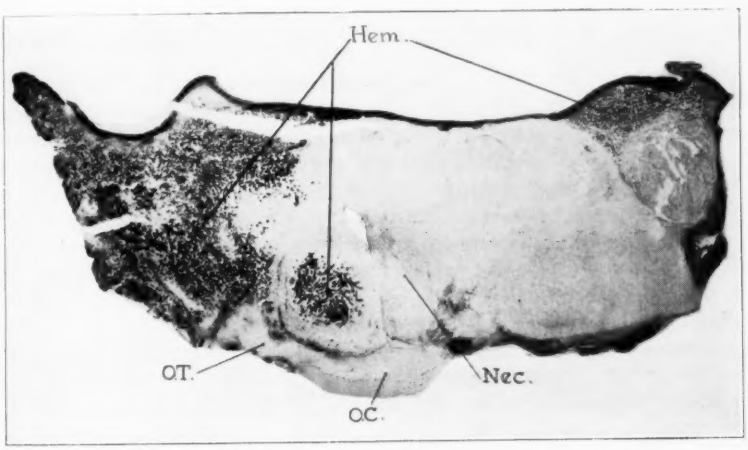

Fig. 11 (cat 4).—Photomicrograph showing a section through the optic chiasm with destruction of the hypothalamic area by hemorrhage and softening.

This animal resembled cat 3, in that temperature control was not regained during the first two days. (The fall of temperature during the morning feeding and cleaning was marked, and at the beginning of the

third twenty-four hour period the heating lamp was temporarily disconnected; the profound and rapid fall of rectal temperature even in the warm room is demonstrated in figure 1.) However, by the end of the third day pyrexia was developing, and the animal maintained a temperature not far from normal until the sixth day. At the beginning of this day its temperature control appeared somewhat inadequate, and at the end quite ineffective. Probably the data are to be interpreted as spontaneous control developing late, and perhaps never complete; possibly during the efforts of parturition some additional damage of the brain stem was induced by hemorrhage, which might account for the later failure in temperature control in the absence of meningeal infection.

The data on these four animals may be criticized in that no exact study was made of the mechanisms involved in temperature control; it was however, observed that these very excitable preparations appeared to survive better the less they were exposed to stimulation, and it was for this reason that more detailed study was not made. Consequently another preparation (cat 5), resembling in its main features cats 1 and 2, was used to test the responses of such animals to extremes of heat and cold. The brief protocol which follows demonstrates that such preparations can show the responses to cold that may be observed in the normal cat and that they can control their temperature, but that the reaction to heat (in this animal at least) was definitely subnormal.

Cat 5.—Operation was performed on the morning of Jan. 4, 1933. Within about twelve hours, temperature control appeared to be regained, and after twenty-four hours mechanical heating and control were discontinued. In the warm room, rectal temperature was maintained spontaneously between 38.7 and 39.5 C. Active running movements were made; fairly symmetrical righting reflexes were present, and the animal could walk in a clumsy manner. After forty-eight hours, the cat was cooled violently by wetting its fur and moving it to a stone floor in a room at 15 C. The rectal temperature fell from 38.8 to 37.2 C. in fifteen minutes, in spite of considerable activity (walking), when marked generalized shivering developed which prevented the temperature falling more than 0.2 C. in the next eight minutes. On return to the warm moist room at 25.5 C., the shivering continued and raised the rectal temperature rapidly at a rate of about 3 C. per hour. As soon as this temperature reached 38.7 C., the shivering became slight and the rectal temperature showed only a very slight tendency to rise; two hours after cessation of the violent cooling, rectal temperature reached 38.9 C. and was maintained constant without shivering. The room temperature was then gradually raised to 31 C. and the table on which the animal was placed was also heated; the rectal temperature rose in a hundred minutes to 41.7 C., when the heat was discontinued. There was no sweating on the pads of the feet; the respiration remained of normal depth, and the respiratory rate rose only to 80 (a normal cat after twenty minutes in the same room with no extra heat showed a rise of rectal temperature to 40 C., associated with a respiratory rate of 150 and marked sweating on the pads of the feet). The extra heat was then discontinued and the temperature of the room was allowed to fall to 26 C. The rectal temperature fell

in fifty-five minutes to 39.2 C., when it was maintained constant. The animal died on the seventh day, and during the last day had lost its capacity to maintain a normal temperature.

Histologic examination showed essentially the same picture as in cat 1. The thalamus was destroyed and the hypothalamus was almost intact, especially in its median portions. There was some destruction of the more lateral portions anteriorly; in the region of the mamillary bodies the entire tissue was intact. The infundibular region was practically intact and completely so in its median portion.

The fact that this animal lost its temperature control after some days in the absence of any demonstrable inflammatory reaction makes the cause of any such late loss of control uncertain, and unfortunately somewhat complicates the picture. Active animals of this type do not appear to thrive on the diet of simple milk employed.

Many control animals with lower sections have been frequently tested for ability to control their own temperatures or to make reactions of the normal type to changes in temperature, but no evidence of temperature control has been observed, except that a considerable increase in the rate of respiration accompanied a raised body temperature, though this rate fell far short of a true polypnea caused by heat. In this such observations agree with earlier observations by Bazett and Penfield [11] and by Sherrington.[12] Consequently details of a single control animal only will be given.

Cat 6.—Operation was performed on the morning of Jan. 14, 1932. Transection was performed through a level approximately the same as that of cat 1, followed by a second transection from between the colliculi to the anterior end of the pons. Good decerebrate rigidity was developed by the following day and was maintained throughout the period of survival. Occasionally, slight running movements were made. On January 29, artificial heat was turned off and the rectal temperature rapidly fell to 36.5 C., when the artificial heat was renewed. There was no sign of shivering or of any other response to the cooling. On February 1, when lying on its left side a tremor at the ankle joint of the right forelimb was noticed; this resembled a shiver, except that it accompanied flexion of this joint and immediately disappeared when the joint was passively extended, and appeared again as the joint became gradually flexed by the weight of the limb. When the animal was turned to lie on its other flank, the tremor disappeared. The tremor was observed when the rectal temperature was 38.6 C. and continued while artificial heat was used to raise the rectal temperature to 39.2 C. On the following day the cat was taken to an ordinary room and put on a cold metal table. This raised the respiratory rate from its normal value of about 25 to one of 36 per minute, and the rectal temperature fell from 38.7 to 37 C. without any sign of shivering or any tremor of the forelimb. Warming on a hot table till the rectal temperature reached 38.2 C. gave a respiratory rate of 27. Cooling by wetting with water at 11.5 C. dropped the rectal temperature from 38 to 30 C. in about forty-five minutes without any sign of shivering, but there was a greater tendency to assume flexed positions and to make slow movements. As the rectal temperature fell below 30 C. these movements became athetoid or choreiform and were incoordinated. During the brisk cooling the respiratory rate rose to 48.

Macroscopic examination demonstrated the presence of an anterior section similar to that of cat 1, and a second posterior section through the inferior colliculi to the anterior border of the pons which appeared to be complete.

A single instance may be quoted to show that these posterior sections, like the more anterior, develop no true polypnea caused by heat. A cat was observed three days after a complete section at the collicular level when suffering from an accidental hyperthermia induced by the extrusion of the thermometer in defecation. The rectal temperature was 43.2 C., and the respiratory rate was 96; the respirations were deep and not of the shallow type of true polypnea. Observations of a similar character have been made on other animals.

Finally a brief description must be given of a single animal (cat 7) in which a double transection of the type used for cat 6 was attempted, but in which the second section was incomplete. When the lower section has been slightly incomplete there has usually been evidence of righting reflexes but no evidence of temperature control, but this cat was exceptional in presenting a typical picture of maintained decerebrate rigidity without righting reflexes, but with some capacity for temperature control.

Cat 7.—Operation was performed on the afternoon of Oct. 11, 1932, with a double transection. On the following morning the cat showed good decerebrate rigidity with no movements or righting reflexes, and remained in this condition until it died. It was kept on artificial temperature control for the first two days, though pyrexia developed and it maintained its temperature above that of the control system and so received little or no artificial heat after the first twelve hours. In the morning at the end of the second twenty-four hour period, artificial heat was discontinued, and the rectal temperature fell somewhat but not below 36.7 C. At the beginning of the fourth day, it was moved to an ordinary room for one or two hours, and its rectal temperature fell to 34.5 C.; on return to the warm moist room (which in this case was at 27 C., dry bulb), it maintained this temperature without further heating, but showed no rise above it. Artificial heat and control were therefore renewed for half a day. On the beginning of the fifth day, it maintained a temperature of 36.7 C. without artificial heat. It was then cooled within the warm room by wetting the fur, particularly that of the limbs with cold water. The rectal temperature fell to 36.3 C. and shivering became visible, though it was not widespread but limited to a few muscles of one shoulder and one hindlimb. After one hour the rectal temperature had fallen to 34.8 C., mild shivering continued, and occasional spasmodic movements involving all four limbs were made. Artificial heat was renewed, and following this the spasmodic movements ceased before any appreciable rise of rectal temperature had occurred. The animal was not tested for reaction to excessive heat, as it died at the end of the fifth day from an unknown cause. Autopsy showed slight meningitis, but this was probably insufficient to account for death. The temperatures recorded during the first one and one-half days are shown in figure 1.

Histologic examination showed a lower transection from the inferior colliculi to just in front of the pons, which separated the hypothalamus from the lower part of the brain stem except for a small strand of fibers in the right lateral

column; this strand had, however, a cross-sectional area of only a few square millimeters. The corpora mamillaria were destroyed; above this the infundibular area was fairly well preserved on both sides, except for a small area of necrosis on the left side which involved the nucleus hypothalamicus ventromedialis and part of the periventricular gray matter. The more anterior part of the hypothalamus was destroyed on both sides, but slightly caudal to the chiasm there was on the left side a small intact area which included the nucleus hypothalamicus posterior, nucleus ovoideus and periventricular gray matter.

COMMENT

Cats 1, 2 and 5 appear to have had the capacity to control their own temperature at a normal level, and were probably able to develop a febrile response to injury or infection. The examination of cat 5 suggests that such cats were able to react to exposure to cold as efficiently as a normal cat, but that their reactions to excessive heat were subnormal and incomplete. The tendency of all the cats to show a rise in rectal temperature when the room became slightly more humid also suggests that the response to heat was subnormal in all of them. These three cats stand out in striking contrast with control animals with a lower transection in their response to cold, but in response to excessive heat there is no evidence that the normal mechanisms were adequately utilized, nor that they were more effective than in the control animals. In both types the respiration was increased moderately and when the excessive heat was discontinued the rectal temperature fell; this fall of rectal temperature was, however, arrested only at the normal temperature level in the animals with an anterior section. Centers capable of maintaining a normal temperature were also probably present in cats 3 and 4, but, in view of the slow recovery of heat control in these animals, the lesions were probably very close to the centers; in cat 4 they were probably partly damaged, for full control seemed never to be regained.

No assumption can be made on the basis of these animals that any nucleus is unessential for this degree of control unless it was absent on both sides, since it has been abundantly demonstrated that a single center may exert bilateral effects; thus hemidecerebration at the collicular level does not interfere with bilateral sweating (Bazett and Penfield [11]), unilateral stimulation of the hypothalamus produces bilateral sweating (Hasama [1]), and unilateral lesions of the corpora mamillaria produce no functional disability of the sympathetic system on either side (Beattie, Brow and Long [16]).

In cats 1 and 5 the hypothalamus was intact, but the tissue anterior and dorsal to the third ventricle was destroyed. In cat 2 the anterior portion of the hypothalamus was destroyed, but the posterior portion, especially that in the region of the third ventricle, was intact. In cat

3 the anterior part of the hypothalamus was also destroyed, but in addition the hypothalamic area cephalic to the corpora mamillaria was damaged, particularly on one side. Cat 4 was peculiar in that both the anterior and the posterior parts of the hypothalamus were intact, but there was considerable damage to the infundibular area. The transection level in control animals with no indication of temperature control was through the inferior colliculi and red nucleus.

It can therefore be definitely stated that the portions of the brain lying dorsal or cephalic to the third ventricle, including the thalamus, corpus striatum and geniculate bodies, are unessential for temperature control of this order. The anterior part of the hypothalamus seems unessential, for it was absent in cat 3; the posterior part of the hypothalamus was somewhat damaged in cat 2, yet control seems to have been rapidly regained and to have been well maintained until the onset of the terminal infection. The infundibular area appears to be particularly important, for in cat 4 temperature control was only very slowly regained, and even then appeared incomplete, although both the anterior and the posterior areas of the hypothalamus were relatively intact. The capacity of controlling temperature was thus associated in these animals with greater or lesser preservation of the tissue surrounding the third ventricle, the infundibular nuclei, the corpora mamillaria and the tissue between the corpora mamilaria and infundibulum; the center or centers appear to have a relatively mesial position in this area. The late inflammatory changes from infection in cat 2 help rather than hinder the substantiation of this hypothesis, since these areas were particularly involved in these changes, which destroyed thermal control.

Cat 7 is anomalous, though not inconsistent with the hypothesis that the infundibular nuclei may be essential, provided that connecting tracts can pass in the extreme edge of the lateral column. It is hoped that evidence of the course of the tracts may be obtained later, and in view of present ignorance of such tracts and the possibility of assumption of some reactions by lower centers, this animal has been only briefly described and no deductions, positive or negative, are drawn from it.

The evidence for the position of the thermal centers in the cat is therefore in good agreement with much of the recent literature already quoted, and also with the long series of experiments by Rogers,[21] who found temperature centers in birds to be in the thalamic area. The subject is somewhat complicated by the evidence advanced by Jelsma [22] that the center for antagonizing cold is in the medulla, by that of Hasamà [23] that centers concerned with sweating also exist in the medulla

21. Rogers, F. T.: Am. J. Physiol. **45**:553, 1918; **86**:639, 1928.
22. Jelsma, F.: Am. J. Physiol. **93**:661, 1930.
23. Hasama, B.: Arch. f. exper. Path. u. Pharmakol. **153**:257, 1930.

and by that of Keller and Hare [2] that though heat control may be lost in a cat following removal of the hypothalamus and no shivering may be observed in animals with a section at the collicular level, yet a capacity to shiver and to prevent a fall of temperature on exposure to cold is preserved in animals with division of the brain stem at a lower level in the medulla. Dworkin,[24] using acute preparations in rabbits, found shivering on exposure to cold with transverse sections almost as low as the calamus scriptorius; he did not observe absence of shivering with sections at the collicular level, but the functional level of his sections need not have been identical with the macroscopic lesion.

There appears good evidence that shivering may occur in medullary animals, at any rate when a profound fall of rectal temperature is induced, but under most circumstances (with the exception of Keller and Hare's experiments) the reactions appear to be those of subsidiary centers which are incapable of maintaining the body temperature at its normal level. These subsidiary centers seem frequently to be involved in hyperthermic responses to injuries of the brain, for such responses have been noted in animals with low sections by Keller and Hare. In the experiments here reported, definite instances of such hyperthermias have been very rare, and have been associated with subtentorial hemorrhage (e. g., in one animal a rectal temperature of 40.9 C., rising to 42 C., was observed immediately after operation; the rise of temperature was associated with violent shivering; death followed, and autopsy showed considerable subtentorial hemorrhage with a large hemorrhagic area in the pons and medulla). The data here advanced in favor of hypothalamic centers for temperature control should not therefore be taken as implying the absence of subsidiary centers in the medulla. On the other hand, evidence in acute preparations cannot always be accepted as conclusive, as stimulatory effects of the lesion can at times prove confusing, and Keller [25] is of the opinion that such effects cannot be definitely excluded even in semiacute preparations.

Lastly, attention may be drawn to the somewhat surprising association of only slightly asymmetrical bilateral righting reflexes in cat 2 in spite of partial damage to one red nucleus, and of completely incoordinated very asymmetrical righting reflexes in cat 3 without damage to the red nuclei. Other animals have given evidence that righting reflexes are not simply dependent on the red nuclei (compare Ingram and Ranson [26]).

CONCLUSIONS

The brain stems of cats with anterior decerebrations have been studied histologically. The animals had the capacity of reacting to cold

24. Dworkin, S.: Am. J. Physiol. **93**:227, 1930.

25. Keller: Am. J. M. Sc. **185**:746, 1933.

26. Ingram, W. R., and Ranson, S. W.: Am. J. Physiol. **102**:466, 1932.

and of regulating their own body temperature at a normal level (and probably of developing fever) in the absence of the corpus striatum and thalamus, which were not therefore essential. The presence or absence of temperature control appeared to be associated with the preservation of the hypothalamus just cephalic to the corpora mamillaria; the area included the nuclei surrounding the walls of the third ventricle and the infundibular nuclei. Such animals did not, however, show a normal hyperpnea when exposed to excessive heat.

CEREBRAL LOCALIZATION IN CEREBRO-VASCULAR DISEASE

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NEW YORK

The conception of cerebral localization has been evolved from many methods of investigation, such as the myelogenetic (Flechsig), embryologic, physiologic (Hitzig, Fritsch, Ferrier), pathologico-anatomic (Türck), clinicopathologic and histologic methods (Brodman, Campbell, Vogt and von Economo). Undoubtedly each method has certain shortcomings peculiar to itself, but when all the facts are gathered from these various forms of investigation a structure is built which cannot be shaken.

Ours is essentially a clinicopathologic method, limited to cerebral lesions due to vascular insults. We are fully aware that our method of approach may deservedly meet with many criticisms. Strict schematization and attempts at simplification of the anatomic basis of cerebral function are out of accord with present-day conceptions of neurophysiology. Nor have we dismissed lightly the obstacles in the way of clinicopathologic correlation in vascular disease. Just as studies of localization in cases of cerebral neoplasm are hazardous because of the inability to differentiate distance effects from those due to destruction of tissue at the immediate site of the growth, or as studies along lines of comparative anatomy and physiology may be misleading because the analogous structure in lower forms may have a different function, so localization in vascular disease presents its own problems. Cerebral arteriosclerosis is a generalized process; the common occurrence of multiple lesions often makes correlation of structural and functional disturbances impossible. Again, if the patient with a cerebral vascular insult dies within a short time after the ictus, the effects of diaschisis may have persisted and the patient may have presented a symptomatology out of all proportion to the lesion in the brain. Or, if the

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patient dies a long time after the initial ictus, the possibility of additional vascular compromises coming on gradually and imperceptibly must be borne in mind. Still another point to be remembered is that not every lesion found at autopsy necessarily has given rise to symptoms and signs. Not rarely one sees gross atrophy of cerebral tissue with very few disturbances of cerebral functioning manifested during life. Finally, there is the consideration stressed particularly by adherents of the psychologic school that similarly situated lesions may give rise to dissimilar disturbances of function. In the individual case it may well be impossible to eliminate these confusing factors. The study of a large series, however, allows for selection and control, and consequently for greater reliability.

It is well known that certain vessels supply certain areas of the cortex. It is also well established that certain areas of the cortex are endowed with special functions. It was Shellshear [1] who first attempted to associate vascular supply with definite areas of the cortex and with their particular functions. Foix [2] and his pupils went a step further and tried to establish definite neural syndromes on the basis of thrombosis of the main cerebral arteries or of their branches. Although we are able to confirm the findings of the French school to the effect that there is a definite relationship between vascular supply and certain functions, mediated by the parts of the brain supplied by these vessels, we shall not adhere too strictly to these interpretations. Among the factors which make for variability in this relationship are: (1) anomalies of the cerebral vessels, (2) the richness of anastomosis of the cerebral vessels at the base and in the cortex, (3) dominance of one part of the brain over another, or of one entire hemisphere over the other and compensation by new assumption of function, and (4) variability in the extent of the area irrigated by a certain vessel. All of these factors must be taken into consideration. When this is done we shall not be hesitant to state that certain areas of the brain have certain specific functions, and at the same time we shall not be baffled when we discover that lesions similarly situated result in somewhat dissimilar syndromes.

METHOD OF PROCEDURE

The material was selected from about two hundred cases of cerebral vascular disease in which the brain was available for study. Not all could be used for several reasons: 1. Cases which clinically did not lend themselves to careful

1. Shellshear, J. C.: The Basal Arteries of the Forebrain and Their Functional Significance, J. Anat. **55**:35, 1920.

2. Foix, C., and Hillemand, P.: Les syndromes de l'artère cérébrale antérieure, Encéphale **20**:209, 1925. Foix, C., and Masson: Le syndrome de l'artère cérébrale postérieure, Presse méd. **31**:361 (April 21) 1923. Foix, C., and Levy, M.: Les ramollissements sylviens, Rev. neurol. **2**:1, 1927.

*rovascular Disease**

	Insula		Sensory							Auditory and Olfactory						
	IA	IP	CP	PS	PI	PB	PR	GSM	ANG	PT	T_1	T_2	T_3	U	HI	FUS
AL ARTERY OR ITS BRANCHES																
	....	.....	L W part +	L W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
	....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
L ARTERY AND ITS BRANCHES																
IDDLE CEREBRAL ARTERY																
	R &W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	.....	.....	.....
	R &W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	R G&W part +	R G&W part +	R G&W part +	R G&W +	R G&W +	R G&W part +	.....	.....	.....
4.	R &W +	R G&W +	R G&W +	R G&W +	R G&W +	R W part +	R W part +	R G&W part +	R G&W part +	R W part +	R W part +	.....	.....	.....	.....	.....
5.	R &W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	R G&W +	R G&W +	.....	R G&W +	.....	.....	.....	.....	.....
6.	R &W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	.....	.....	.....	.....	.....
7.	L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....
8.	L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L W part +	.....	.....	.....	.....
9.	L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....
10.	L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	L G&W +	L G&W part +	.....	.....	.....	.....
11.	St L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....
12.	. L &W +	L G&W +	L G&W +	L G&W part +	L W part +	L W part +	.....	.....	.....	L G&W +	L G&W +	.....	.....	.....	.....	.....
	L &W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W part +	L G&W +	.....	.....	.....	.....	.....

	Psychic	Aphasia: Sensory	Aphasia: Motor	Pyramidal Tract	Sphincteric	Sensory Disturbances: Pain, Temperature, Touch, Vibration, Stereognosis	Sensory Disturbances: Visual	Cortical Discharges	Vessels Involved	Frontal: F_1	F_2	F_3	F_1O	F_2O	F_3O	F_3 pt	Motor: CA	Motor: PA	Operculu: OpR	Op
									I. Occlusion of the Anterior Cer											
1.	Sluggish mentality	—	—	R upper L lower	—	Impairment of position sense bilaterally; astereognosis on the right	—	—	R and L anterior cerebral; medial frontal branches	R&L G&W + part	R&L G&W + part	.....	.....	.....	.....	.....	R G&W part + L W part	R G&W part + L W part	.....	.....
2.	Poor memory; emotional	—	—	L complete	+	Vague sensory disturbances	—	—	R anterior cerebral; inferior, ascending frontal and precentral branches of middle cerebral	R G&W +	R G&W + part	R G&W part	R G&W +	R G&W + part	R G&W + part	R G&W + part	R G&W + part	R G&W + part	.....	.....
									II. Occlusion of the Middle Cere											
									1. complete occlusion of thi											
1.	Memory defects; mental deterioration; personality changes	—	—	L complete	—	All modalities affected, L	Suggestive homonymous hemianopia, L	.....	R middle cerebral, complete	.....	R W part +	R G&W +	.....	.....	.....	.....	R G&W +	.....	R G&W +	R G&W +
2.	Memory defects; mental deterioration; disoriented	—	—	L complete	+	Hemianesthesia, L	Unreliable	.....	R middle cerebral, complete	.....	.....	R G&W part +	.....	.....	R G&W part +	R G&W part +	R G&W part +	R G&W part +	R G&W +	R G&W +
3.	Memory defects; emotional instability	—	—	L complete	+	All modalities affected, L	Unreliable	Generalized convulsions	R middle cerebral, complete	.....	R W part +	R G&W +	.....	.....	.....	.....	R G&W +	R W slight +	R G&W +	R G&W +
4.	.....	—	—	L complete	—	All modalities affected, L	Unreliable	Convulsions at onset	R middle cerebral, complete	.....	.....	R G&W +	.....	.....	.....	.....	R G&W +	.....	R G&W +	R G&W +
5.	Mental deterioration	—	—	L complete	+	All modalities affected, L	Unreliable	.....	R middle cerebral, complete	.....	.....	R G&W part +	.....	.....	R G&W +	R G&W +	R G&W +	R W slight +	R G&W +	R G&W +
6.	.....	+ cleared up	+	R complete	—	All modalities affected, R	L primary optic atrophy with central scotoma	Convulsions 2 years after insult	L middle cerebral, complete	.....	L G&W part +	L G&W part +	.....	.....	.....	.....	L G&W part +	L W part +	L G&W +	L G&W +
7.	Mental deterioration; confusion	+	+	R complete	—	Hypalgesia, R	Homonymous	.....	L middle cerebral, complete	.....	L W part +	L G&W +	.....	.....	.....	.....	L G&W +	L W part +	L G&W +	L G&W +
8.	.....	+	+	R complete	+	Hypalgesia, R	Homonymous hemianopia, R	.....	L middle cerebral, complete	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
9.	.....	+	+	R complete	—	All modalities affected, R	Suggestive homonymous hemianopia on right; bilateral choked disks	.....	L middle cerebral, complete	.....	L G&W part +	L G&W +	.....	.....	.....	.....	L G&W +	L W slight +	L G&W +	L G&W +
10.	.....	—	+	R complete	—	Unreliable	Unreliable	.....	L middle cerebral, complete	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
11.	Stuporous	—	+	R complete	Vesical +	Unreliable	Unreliable	.....	L middle cerebral, complete	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L W +
12.	.....	+	+	R complete	+	Unreliable	.....	.....	L middle cerebral, complete	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	L W slight +	L G&W +	L G&W +
13.	Mental deterioration	+	+	R complete	—	Unreliable	Homonymous hemianopia, L	Convulsions 4 days before death	L middle cerebral, complete; R posterior cerebral, incomplete	.....	.....	L G&W + R W part	.....	.....	.....	.....	L G&W + R W part	L W part +	L G&W +	L G&W +
14.	Emotional instability	+	+	R complete	Vesical +	Unreliable	Unreliable	.....	L middle cerebral and L posterior cerebral, complete	.....	.....	L G&W +	.....	.....	L G&W +	L G&W +	L G&W +	L W slight +	L G&W +	L G&W +
									2. INCOMPLETE OCCLUSION OF THE											
15.	Emotional instability	—	—	L complete	—	All modalities affected, L	Suggestive homonymous hemianopia, L	.....	R middle cerebral and anterior cerebral, incomplete	R W +	R W +	R G&W +	R W part +	R W +	.....	.....	R G&W +	R G&W +	R G&W +	R G&W +
16.	.....	—	—	L complete	—	Hypesthesia; hypalgesia; hyperpathia, L	.....	.....	R middle cerebral, incomplete	.....	.....	R G&W +	.....	.....	.....	.....	R G&W +	.....	R G&W +	R G&W +
17.	.....	—	—	L complete	+	All modalities affected, L	.....	.....	R middle cerebral, incomplete	.....	.....	.....	.....	.....	.....	.....	R G&W part +	.....	R G&W part +	R G&W part +
18.	.....	—	—	L complete	—	Unreliable	.....	.....	R middle cerebral, incomplete	.....	.....	R W part +	.....	.....	.....	.....	R G&W +	.....	R G&W +	R G&W +
19.	.....	—	+	R complete	—	Unreliable	Homonymous hemianopia, R	.....	L middle cerebral, incomplete	.....	.....	L W +	.....	.....	.....	.....	L G&W +	.....	L W +	L W +
20.	.....	—	+	R complete	—	.....	.....	.....	L middle cerebral, incomplete	.....	L W +	L W +	.....	.....	.....	.....	L W +	.....	L G&W +	L G&W +
21.	.....	+	+	R complete	—	All modalities affected, R	.....	.....	L middle cerebral, incomplete	.....	.....	L W part +	.....	.....	.....	.....	L W part +	.....	L G&W +	L G&W +
22.	.....	—	Part +	R complete	—	.....	.....	.....	L middle cerebral, incomplete	.....	L W +	L G&W +	.....	.....	L G&W +	.....	L G&W +	.....	L G&W +	L G&W +
23.	.....	—	+	R complete	—	All modalities affected, R	.....	.....	L middle cerebral, incomplete	.....	L W +	L G&W +	.....	.....	.....	.....	L G&W part +	.....	L W +	L W +
24.	.....	—	+	R complete	—	All modalities affected, R	.....	Convulsions over a period of 10 years	L middle cerebral, incomplete	.....	.....	L W part +	.....	.....	.....	.....	L G&W +	.....	L W +	L W +
25.	.....	—	+	R complete	+	.....	.....	.....	L middle cerebral, incomplete	.....	.....	L W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
26.	.....	+	+	R complete	—	Unreliable	.....	.....	L middle cerebral, incomplete	.....	.....	L W part +	.....	.....	.....	.....	L G&W part +	.....	L G&W part +	L G&W part +
27.	Emotional instability	+	+	R complete	—	Unreliable	Unreliable	.....	L middle cerebral, incomplete	.....	L G&W +	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
28.	.....	+	+	R complete	+	All modalities affected, R	Homonymous hemianopia, R	.....	L middle cerebral, incomplete	.....	L W +	L G&W part +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
29.	Mental deterioration	—	—	Bilateral	+	Unreliable	Unreliable	.....	Bilateral, middle and anterior cerebral, incomplete	R&L W +	R&L W +	R&L W +	.....	.....	R&L W +	R&L W +	R&L W +	.....	.....	.....
									3. OCCLUSION OF THE CORTICAL BRANCHES OF											
30.	Mental deterioration; disorientation; confusion	+	—	.....	—	.....	.....	.....	L anterotemporal and L lenticulo-optic and striate	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
31.	Mental deterioration	—	—	L incomplete	—	.....	.....	.....	R branch of ascending precentral artery	.....	.....	R G&W +	.....	.....	.....	.....	R G&W +	.....	.....	.....
									4. OCCLUSION OF THE DEEP BRANCHES											
32.	.....	—	—	L complete	—	.....	.....	.....	R lenticulostriate	.....	R W +	R W +	.....	.....	.....	.....	.....	.....	R W +	R W +
33.	.....	—	—	L complete	—	All modalities affected, L	.....	.....	R lenticulostriate	.....	.....	R W +	.....	.....	.....	.....	R W +	.....	.....	.....
34.	.....	—	Transient +	R complete	—	.....	.....	.....	L lenticulostriate	.....	.....	.....	.....	.....	.....	.....	L W part +	.....	L W part +	L W part +
35.	.....	—	Transient +	R complete	—	....	Suggestive homonymous hemianopia, R	.....	L lenticulostriate and L posterior cerebral, incomplete	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
36.	.....	—	Transient +	R incomplete	—	Hypesthesia, R	.....	.....	L lenticulostriate branch to insula	.....	.....	.....	.....	.....	.....	.....	L W +	.....	.....	.....
25.	.....	—	+	R complete	+	.....	.....	.....	L middle cerebral, incomplete	.....	.....	L W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
26.	.....	+	+	R complete	—	Unreliable	.....	.....	L middle cerebral, incomplete	.....	.....	L W part +	.....	.....	.....	.....	L G&W part +	.....	L G&W part +	L G&W part +
27.	Emotional instability	+	+	R complete	—	Unreliable	Unreliable	.....	L middle cerebral, incomplete	.....	L G&W +	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
28.	.....	+	+	R complete	+	All modalities affected, R	Homonymous hemianopia, R	.....	L middle cerebral, incomplete	.....	L W +	L G&W part +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
29.	Mental deterioration	—	—	Bilateral	+	Unreliable	Unreliable	.....	Bilateral, middle and anterior cerebral, incomplete	R&L W +	R&L W +	R&L W +	.....	.....	R&L W +	R&L W +	R&L W +	.....	.....	.....
									3. OCCLUSION OF THE CORTICAL BRANCHES OF											
30.	Mental deterioration; disorientation; confusion	+	—	.....	—	.....	.....	.....	L anterotemporal and L lenticulo-optic and striate	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
31.	Mental deterioration	—	—	L incomplete	—	.....	.....	.....	R branch of ascending precentral artery	.....	.....	R G&W +	.....	.....	.....	.....	R G&W +	.....	.....	.....
									4. OCCLUSION OF THE DEEP BRANCHES											
32.	.....	—	—	L complete	—	.....	.....	.....	R lenticulostriate	.....	R W +	R W +	.....	.....	.....	.....	.....	.....	R W +	R W +
33.	.....	—	—	L complete	—	All modalities affected, L	.....	.....	R lenticulostriate	.....	.....	R W +	.....	.....	.....	.....	R W +	.....	.....	.....
34.	.....	—	Transient +	R complete	—	.....	.....	.....	L lenticulostriate	.....	.....	.....	.....	.....	.....	.....	L W part +	.....	L W part +	L W part +
35.	.....	—	Transient +	R complete	—	....	Suggestive homonymous hemianopia, R	.....	L lenticulostriate and L posterior cerebral, incomplete	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
36.	.....	—	Transient +	R incomplete	—	Hypesthesia, R	.....	.....	L lenticulostriate branch to insula	.....	.....	.....	.....	.....	.....	.....	L W +	.....	.....	.....
37.	.....	+	+	R complete	Rectal +	All modalities affected, R	.....	.....	L lenticulostriate and optic	.....	.....	.....	.....	.....	.....	.....	.....	.....	L W slight +	.....
38.	Emotional instability	—	Transient +	R complete	—	Hypesthesia; hypalgesia, R	.....	.....	L lenticulostriate	.....	.....	.....	.....	.....	.....	.....	L W part +	.....	.....	.....
39.	.....	+	+	R complete	+	Hypesthesia; hypalgesia, R	.....	.....	L lenticulostriate and optic	.....	.....	.....	.....	.....	.....	.....	L W +	.....	.....	.....
40.	.....	+	+	R complete	+	All modalities affected, R	Homonymous hemianopia, R	.....	L lenticulooptic	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
41.	.....	—	Transient +	R complete	—	.....	.....	.....	L lenticulostriate	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
42.	.....	—	Transient +	R complete	—	.....	.....	.....	L lenticulostriate	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
									III. Occlusion of the Posterior Cere											
1.	Mental deterioration; paranoid ideas	—	—	.....	—	.....	R upper temporal and L upper nasal quadrantic defects; bilateral central scotoma	.....	L calcarine branch of posterior cerebral and L precentral and postcentral branches of the middle cerebral	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
2.	.....	—	—	.....	—	Dysesthesia, R	L homonymous incomplete quadrantic hemianopia	.....	R calcarine and cuneus branch of posterior cerebral and L postcentral branches of the middle cerebral	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
3.	Mental deterioration	+	+	L complete	—	.....	Cortical blindness; bilateral	.....	Both posterior cerebral and L middle cerebral incomplete	.....	.....	L G&W +	.....	.....	.....	.....	L G&W +	.....	L G&W +	L G&W +
4.	.....	—	—	.....	—	.....	Sudden blindness of right eye; perceived only light	.....	R posterior cerebral	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....

* Abbreviations same as those in figures 2 to 17. Part = partly.

erculum	Insula		Sensory							Auditory and Olfactory							Visual						Corpus Callosum	Internal Capsule	Remarks
OpP	IA	IP	CP	PS	PI	PB	PR	GSM	ANG	PT	T_1	T_2	T_3	U	HI	FUS	L	CU	O_1	O_2	O_3	E			
CEREBRAL ARTERY OR ITS BRANCHES																									
.....	.....	.....	L W part +	L W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	
.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Anterior partly +	
CEREBRAL ARTERY AND ITS BRANCHES																									
THE MIDDLE CEREBRAL ARTERY																									
R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	R genu partly +	R +	T3 involved owing to an anomaly of the middle cerebral artery or involvement of small branch of posterior cerebral artery
R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	R G&W part +	R G&W part +	R G&W part +	R G&W +	R G&W +	R G&W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	R genu partly +	R +	T3 involved as in case 2
R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R W part +	R W part +	R G&W part +	R G&W part +	R W part +	R W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	R genu partly +	R +	
R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W part +	R G&W +	R G&W +	.....	R G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	R +	
R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	R G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	R genu slightly +	R +	
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu slightly +	L +	
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu slightly +	L +	
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu slightly +	L +	
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu slightly +	L +	
L W +	L G&W +	L G&W +	L G&W +	L G&W part +	L W part +	L W part +	.....	.....	.....	L G&W +	L G&W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu slightly +	L +	
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L G&W +	L G&W +	L G&W +	L G&W +	L G&W part +	L W part +	L W part +	L W part +	L W part +	L W part +	.....	L G&W part +	.....	.....	.....	.....	.....	.....	R W part +	R G&W part +	R G&W part +	R G&W part +	R G&W part +	L and R genu and splenium partly +	L +	Involvement of left middle cerebral artery and branch of right posterior cerebral artery
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L genu and splenium +	L +	No evidence clinically of involvement of posterior cerebral artery; patient uncooperative
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L G&W +	L G&W +	L G&W +	L G&W +	L G&W part +	L W part +	L W part +	L W part +	L W part +	L W part +	.....	L G&W part +	.....	.....	.....	.....	.....	.....	R W part +	R G&W part +	R G&W part +	R G&W part +	R G&W part +	L and R genu and splenium partly +	L +	Involvement of left middle cerebral artery and branch of right posterior cerebral artery
L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L G&W +	L genu and splenium +	L +	No evidence clinically of involvement of posterior cerebral artery; patient uncooperative
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R G&W +	R G&W +	R G&W +	R G&W part +	R W part +	R W part +	R W part +	.....	.....	R W part +	.....	R W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	R genu partly +	R partly +	
L W +	L W +	.....	L G&W part +	L G&W part +	L G&W part +	.....	.....	L W +	L W +	.....	L W +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L partly +	Left optic radiation involved
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L G&W +	L G&W +	L G&W +	L W part +	L W part +	.....	.....	.....	.....	.....	.....	L W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L partly +	
L G&W +	L G&W +	L G&W +	L W +	L W +	.....	.....	.....	.....	.....	.....	L W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	L genu and splenium partly +	L partly +	
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L G&W +	L G&W +	L G&W +	L G&W +	.....	.....	.....	.....	.....	.....	.....	L G&W part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Left optic radiation involved; G&W of right F3 and F4 also involved
.....	R&L W +	R&L W +	R&L W part +	R&L W part +	R&L W +	.....	.....	R&L part +	R&L part +	.....	R&L part +	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	R&L +	Forced grasping present; aphasia absent in spite of extensive lesion
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L G&W +	L G&W +	L G&W +	L G&W part +	L G&W +	L G&W part +	.....	.....	L G&W part +	L G&W part +	L G&W part +	R&L G&W part +	R&L G&W part +	R G&W part +	R G&W part +	R G&W part +	R G&W part +	R&L G&W +	R&L G&W +	R&L G&W +	R&L G&W +	R&L G&W +	R&L G&W +	Splenium +	.....	
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study—whether because of intellectual deterioration or for some other cause—were eliminated. 2. Cases of multiple lesions were discarded. Only brains were used in which there were not more than one or two clinical vascular insults. 3. We were concerned only with lesions of the cortex and its projection system. The diencephalic and mesencephalic structures were omitted from consideration. As a result of these limitations, forty-eight brains out of about two hundred remained for study.

As it was difficult to determine grossly the exact extent of cortical destruction, complete horizontal or coronal sections of most of the brains were stained with the myelin sheath and cresyl violet methods. We were thus enabled to observe areas of destruction in the gray and white matter when it was impossible to do so in the gross specimen.

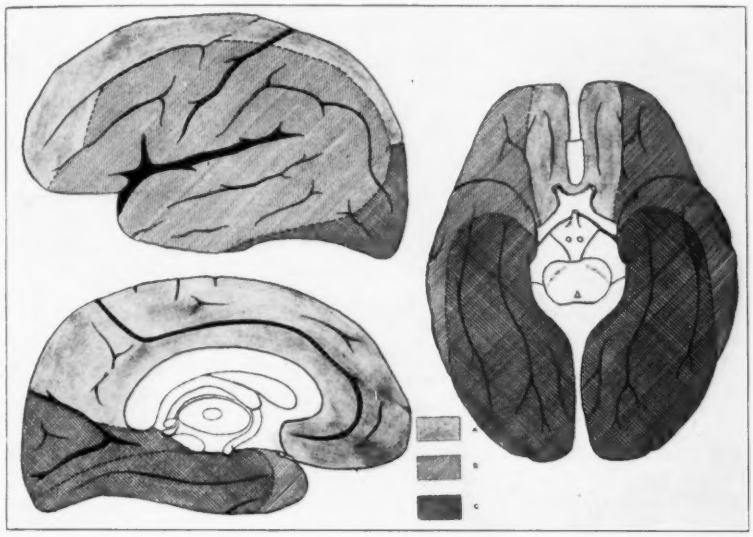

Fig. 1.—Areas of the cerebral hemispheres supplied by the three main vessels: *A*, area supplied by the anterior cerebral artery; *B*, area supplied by the middle cerebral artery; *C*, area supplied by the posterior cerebral artery.

The cases were classified in three main groups according to the three vessels supplying the cerebral hemispheres. A table and clinicopathologic correlations in each group are given to point out the significance of the vascular topography and the corresponding function of the cyto-architectural areas supplied by these vessels.

ANTERIOR CEREBRAL ARTERY

It is not necessary to review in detail the distribution of the anterior cerebral artery. Reference to figures 1 *A*, 2 and 15 will make clear the area of the brain supplied by this vessel.

CASE 1.—*Partial occlusion of both anterior cerebral arteries; sluggish mentality; crossed hemiplegia; sensory disturbances in both lower extremities, and astereognosis in the right upper extremity.*

History.—F. C., a man, aged 58, who entered the Montefiore Hospital on Oct. 10, 1931, had noticed, one year before, that his left foot turned inward when he walked. In August, 1931, there developed heaviness of the left foot as he attempted to lift it from the ground, in addition to slight weakness of both right limbs.

Neurologic Examination.—There were sluggish mentality, paresis of the right upper and left lower extremities and positive Rossolimo and Mendel-Bechterew signs in the left foot. The abdominal and cremasteric reflexes were absent. There was impairment in position sense in the right and left lower extremities, with astereognosis in the right upper limb.

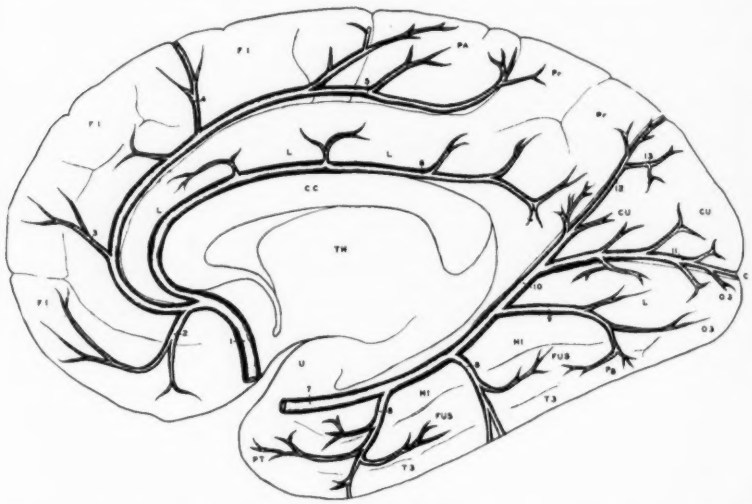

Fig. 2.—Cortical areas supplied by the anterior and posterior cerebral arteries and their branches (mesial view): *1*, anterior cerebral; *2*, internal orbital; *3*, anterior medial frontal; *4*, intermediate frontal; *5*, posterior medial frontal; *6*, corpus callosal; *7*, posterior cerebral; *8*, anterior temporal branch of the posterior cerebral; *9*, posterior temporal branch of posterior cerebral; *10*, occipitoparietal branch of the posterior cerebral; *11*, calcarine branch of the posterior cerebral; *12*, parieto-occipital branch of the posterior cerebral; *13*, cuneus, branch of the posterior cerebral. In this and the accompanying illustrations and table abbreviations are: F_1, first frontal convolution; F_2, second frontal convolution; F_3, third frontal convolution; F_1O, first orbital convolution; F_2O, second orbital convolution; F_3O, third orbital convolution; $F_3pt.$, triangular part of the third frontal convolution; *CA*, precentral convolution; *PA*, paracentral lobule; *OpR*, rolandic operculum; *OpP*, parietal operculum; *IA*, anterior insula; *IP*, posterior insula; *CP*, postcentral convolution; *PS*, superior parietal convolution; *PI*, inferior parietal convolution; *PB*, basal part of the parietal convolution; *Pr*, precuneus; *GSM*, supramarginal gyrus; *ANG*, angular gyrus; *PT*, parietotemporal convolution; T_1, first temporal convolution; T_2, second temporal convolution; T_3, third temporal convolution; *U*, uncus; *HI*, hippocampus; *FUS*, fusiform gyrus; *L*, lingual gyrus; *CU*, cuneus; O_1, first occipital convolution; O_2, second occipital convolution; O_3, third occipital convolution; *E*, Ecker's gyrus or gyrus descendens Ecker; *G*, gray matter; *W*, white matter; *Cf*, calcarine fissure; *CC*, corpus callosum; *TH*, thalamus.

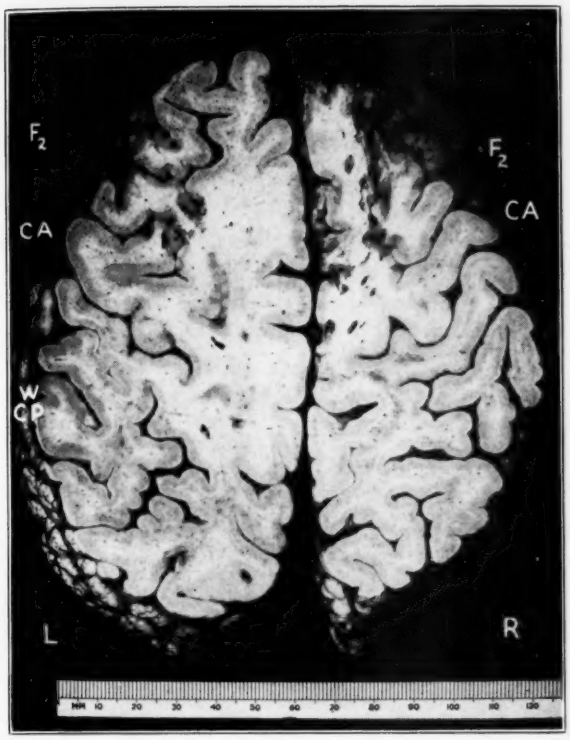

Fig. 3.—Horizontal section of the brain showing destruction of the right and left first and second frontal convolutions and the right paracentral area and slight involvement of the white matter of the left precentral and postcentral convolutions. The main lesion was due to partial occlusion of both anterior cerebral arteries.

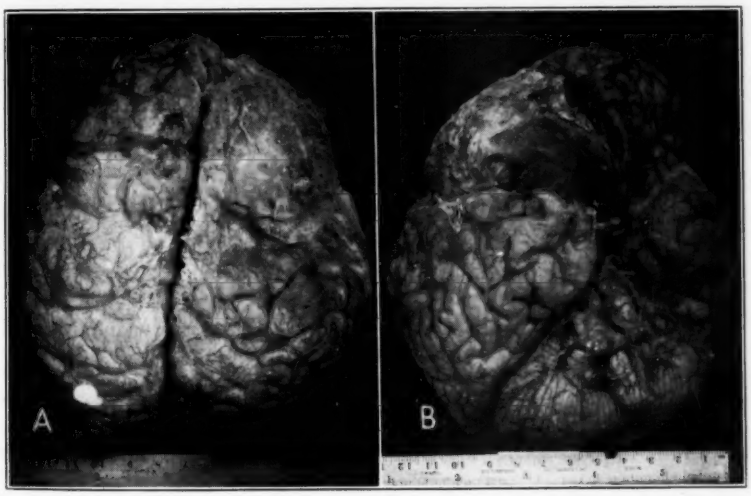

Fig. 4.—*A*, superior view showing softening of the right frontal and precentral convolutions; *B*, posterior view showing softening of the orbital convolutions.

Autopsy.—There was partial occlusion of both anterior cerebral arteries, the medial frontal branches being involved, predominantly on the left side. Part of the gray and white matter of the right first and second frontal convolutions and of the paracentral lobules was destroyed; on the left, there was less extensive involvement of the gray and white matter of the first and second frontal convolutions, with slight involvement of the white matter of the precentral and postcentral and superior parietal convolutions (fig. 3).

CASE 2.—*Occlusion of the right anterior cerebral artery; memory defects; emotional instability; paralysis of the left side of the body, and vague sensory disturbances in the left lower extremity.*

History.—L. E., a man, aged 63, was admitted to the Montefiore Hospital on April 19, 1923, with the history that in December, 1922, a left hemiplegia and incontinence had developed.

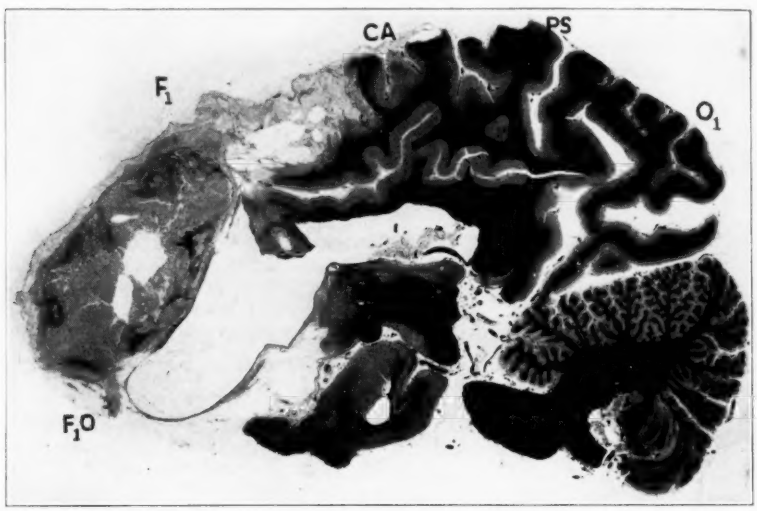

Fig. 5.—Sagittal view showing destruction of the first frontal, orbital, part of the precentral convolution and the anterior two thirds of the corpus callosum, with occlusion of the right anterior cerebral artery. Myelin sheath stain (Weil modification).

Neurologic Examination.—The patient was emotionally unstable, with a poor memory for recent and remote events. There was complete spastic paralysis of the left side of the body, with pyramidal tract signs on the left. There were some vague sensory disturbances in the left lower extremity. No apraxia was noticed. The patient died on March 14, 1925.

Autopsy.—The right frontal convolutions were destroyed as far as the precentral and sylvian fissures (fig. 4 *A* and *B*). Part of the softening was encapsulated by the pia-arachnoid (fig. 5). The brain was cut sagittally. All of the right frontal convolutions were involved as well as the right paracentral lobule, part of the right precentral convolution and the anterior two thirds of the corpus callosum. The second and third frontal convolutions were not so markedly involved as the first. The caudate nucleus was also partly destroyed.

Comment.—In case 1 the essential findings were sluggish mentality, crossed hemiplegia, disturbance of position sense in both lower extremities and astereognosis in the right upper limb. Clinically, as a result of the crossed hemiplegia, it was thought that the lesion was in the region of the pyramidal decussation. Pathologically, there was involvement of the right and left first and second frontal convolutions, as well as of part of the right precentral and paracentral convolutions which supply the leg area and part of the white fibers of the left precentral convolution which supply the arm area. The white fibers of the left postcentral and superior parietal convolutions were also involved partly; this, together with the implication of the paracentral lobule, accounted for the sensory disturbances. As is well established, the upper surface of the precentral, the whole of the paracentral and the first frontal and part of the second frontal convolutions are supplied by the medial frontal arteries (fig. 2), branches of the anterior cerebral artery.

The patient in case 2 presented emotional lability, memory defects, complete left hemiplegia, sphincteric disorders and vague sensory disturbances of the left lower limb. The convolutions implicated were the frontal, the paracentral lobule and part of the precentral convolution. The first frontal, the upper surface of the precentral convolution, all of the paracentral lobule and the anterior two thirds of the corpus callosum are supplied by the anterior cerebral artery (figs. 2 and 15). All the other frontal and precentral convolutions are supplied by the inferior and ascending frontal and the ascending precentral arteries, branches of the middle cerebral artery (fig. 6). The latter branches evidently were also slightly compromised by the arteriosclerotic process.

The complete paralysis of the left side of the body in case 2 was due to involvement of the entire precentral convolution, the paracentral lobule and the anterior two thirds of the corpus callosum.

As will be seen in the table, the internal capsule in these two cases was spared.

Of the cases of involvement of the middle cerebral artery, one also showed partial involvement of the right anterior cerebral artery, and another, involvement of both anterior cerebral arteries (table). The symptomatology of the lesion of the anterior cerebral artery in these two cases (15 and 29) was completely masked by the massive destruction caused by occlusion of the middle cerebral artery. For this reason these cases are considered under the latter group.

Closure of one anterior cerebral artery before its junction via the anterior communicating artery with the one on the opposite side would not always cause any significant symptoms or signs, for the opposite anterior cerebral artery, if not diseased, would adequately supply the opposite part of the hemisphere. Even a closure distal to the junction

with the anterior communicating artery might not cause marked symptoms for, as has been well established by Pfeifer [3] and Cobb,[4] the cerebral arteries and their terminal branches are not end-arteries as was formerly held by Cohnheim, Duret and others. Anastomosis takes place both in the gray and in the white matter. The anastomosis afforded by the middle cerebral artery may at times be sufficient to prevent serious damage to the area supplied by the anterior cerebral vessels. The only difficulty arising in this connection is that in cerebral arteriosclerosis most of the cerebral vessels, especially the middle cerebral artery and its branches, show changes in their walls which cause some interference with the circulation.

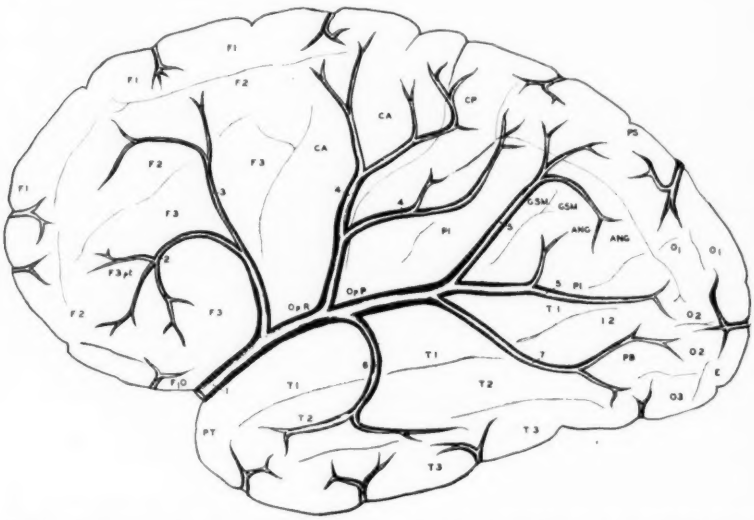

Fig. 6.—Lateral view showing the cortical areas supplied by the middle cerebral artery and its branches: *1*, middle cerebral; *2*, inferior frontal; *3*, ascending frontal; *4*, ascending precentral and postcentral; *5*, posterior parietal; *6*, anterior temporal; *7*, posterior temporal.

To establish a syndrome of the anterior cerebral artery is difficult. Generally, a complete occlusion of this vessel is associated with slight mental disturbances, a crural monoplegia, some sensory disturbances in the lower extremity (as a result of destruction of the paracentral lobule) and apraxia.

Destruction of the anterior portion of the corpus callosum induces an ideomotor apraxia on the left side of the body, provided the motor

3. Pfeifer, R. A.: Die Angioarchitektonik der Grosshirnrinde, Berlin, Julius Springer, 1928.

4. Cobb, S.: The Cerebral Circulation: XIII. The Question of "End-Arteries of the Brain and the Mechanism of Infarction, Arch. Neurol. & Psychiat. **25**:273 (Feb.) 1931.

power is intact. This is produced by interruption of the commissural fibers between the two frontal lobes. Neither of the patients in cases 1 and 2 showed any apraxia. In case 1 it was not expected in view of the absence of involvement of the corpus callosum. Apraxia in case 2 could not be detected because the left side of the body was paralyzed and, as is well established, this can be observed only when there is no paralysis of the limb. Aphasia, generally temporary, if encountered in anterior cerebral lesions, is due to edema or pressure. Psychomotor defects, such as forced grasping and groping observed in some cases by Critchley [5] and others, were not observed in our cases.

It is worth noting that closure of the anterior cerebral artery is rare.

MIDDLE CEREBRAL ARTERY

Occlusion of the middle cerebral artery is far more common. This artery, or its branches, is most frequently involved in cerebral vascular insults. (For the distribution and the supply of this artery the reader is referred to figures 1 *B*, 6 and 15.)

For the purpose of establishing definite syndromes resulting from closure of the middle cerebral artery or its branches it was found convenient to divide the material into: (1) cases of complete occlusion of the middle cerebral artery, (2) cases of incomplete occlusion of the main vessel, (3) cases of occlusion of some of the cortical branches of the middle cerebral artery and (4) cases of occlusion of the deep or profound branches of the middle cerebral artery (table).

COMPLETE OCCLUSION OF THE MIDDLE CEREBRAL ARTERY

Of fourteen cases with complete thrombosis of the middle cerebral artery, the right middle cerebral artery was involved in five. Clinically, the neurologic signs and symptoms in these cases consisted essentially of mental symptoms, complete left-sided paralysis, sensory disturbances, with all modalities affected, and left homonymous hemianopia. The left middle cerebral artery was involved in nine cases. The neurologic signs and symptoms in these cases were analogous to those in thrombosis of the right middle cerebral artery with, in addition, sensory and motor aphasia. In two cases (10 and 11) only motor aphasia was present. Convulsions occurred in four cases (3, 4, 6 and 13). In one case (9) there was bilateral choking of the optic disks, which made the diagnosis of cerebrovascular insult doubtful. In some of these cases the mental obfuscation was such as to render impossible a fine determination of sensation and visual fields.

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5. Critchley, MacDonald: The Anterior Cerebral Artery and Its Syndromes, Brain **53**:120, 1930.

In complete closure of the middle cerebral artery the following convolutions were affected: second and third frontal, precentral, opercular (rolandi and parietalis), anterior and posterior insular, postcentral, superior parietal, inferior parietal, parietotemporal, supramarginal, angular and first and second temporal convolutions and the internal capsule. As stated, structures belonging to the diencephalic region will not be considered. In a number of cases a few fibers of the genu of the corpus callosum were also involved. Nine cases (2, 3, 5, 6, 7, 9, 12, 13 and 14) disclosed slight destruction of the white matter of the paracentral lobule; in one case (2) the gray matter of this convolution was also slightly involved. In two cases (1 and 2) the third temporal convolution was also involved owing, possibly, to anomalies of the middle cerebral artery.

As demonstrated by other observers, the middle cerebral artery does not always have the same distribution and the same anastomoses, thus accounting for the minor variations in the clinical and anatomic findings. Two cases (10 and 11) did not present destruction of the second temporal convolution. This may have been due either to anomaly of the middle cerebral artery or to adequate collateral blood supply by the anastomotic branches of the posterior cerebral arteries. These two cases, in contrast to the others, presented only motor aphasia. At the time of the insults these patients might have had a sensory aphasia, which later cleared up. In complete closure of the left middle cerebral artery the aphasia persisted until the end, except in the two cases in which the sensory aphasia apparently disappeared. The convolutions that are usually considered to cause motor and sensory aphasia, i. e., the foot of the third frontal, the insular and the first temporal, were involved in all eight cases.

Convulsions occurred in four cases. In all of these the motor area was involved, and the convulsions were probably due to "irritation" in this region. The homonymous hemianopia in our cases was due to destruction of the optic radiations as they pass through the parietotemporal region. Auditory disturbances as a result of lesions of the temporal lobe were not found in our cases. This is most likely due to the bilateral cortical representation of the auditory pathways.

One case (13) also disclosed incomplete implication of the right posterior cerebral artery, and another (case 14) showed complete occlusion of the left posterior cerebral artery. In the former case there was left homonymous hemianopia; in the latter the visual disturbances were masked by the massiveness of the middle cerebral lesion and by lack of cooperation on the part of the patient.

As clinicopathologic illustrations we shall describe three cases of involvement of the right middle cerebral artery and of the left middle cerebral artery with aphasia and convulsions.

CASE 3.—*Thrombosis of the right middle cerebral artery; mental changes; left hemiplegia; left sensory disturbances, and left homonymous hemianopia.*

History.—C. A., a man, aged 65, was admitted to the Montefiore Hospital with a history of hypertension for several years. A complete left-sided paralysis appeared in February, 1931.

Neurologic Examination.—There were changes in personality, memory defects and deterioration. There was complete left flaccid hemiplegia, with all pyramidal tract signs, impairment of all modalities of sensation on the left and left homonymous hemianopia.

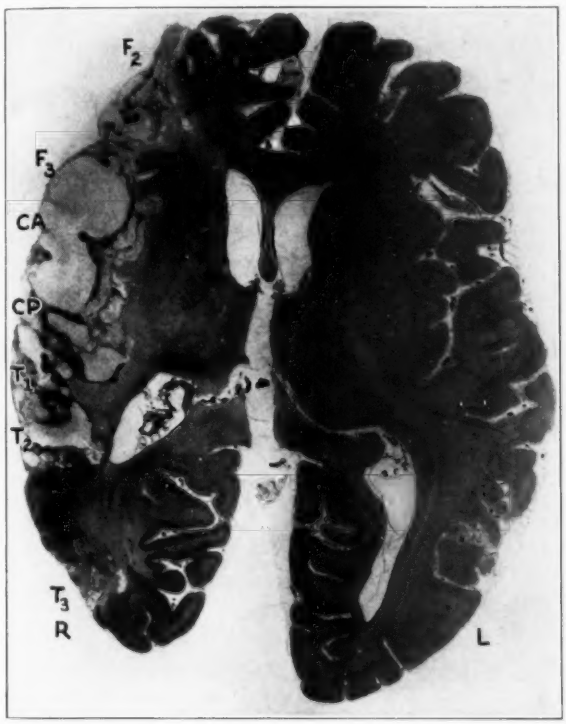

Fig. 7.—Horizontal section showing involvement of the second and third frontal, precentral, postcentral, insular and first, second and third temporal convolutions, with complete occlusion of the right middle cerebral artery.

Autopsy.—There was complete closure of the right middle cerebral artery, with softening of the following convolutions: part of the second frontal, all of the third frontal, precentral, opercular, insular, postcentral, superior parietal, inferior parietal, precuneus, supramarginal, angular, first and second temporal and part of the third temporal (fig. 7). The right internal capsule and part of the fibers of the genu of the corpus callosum were also involved.

Comment.—This case illustrates the typical syndrome of complete left hemiplegia, with sensory disturbances, homonymous hemianopia and mental changes. The unusual feature was the partial involvement

of the third temporal convolution. Anomalies of the middle cerebral artery are frequently encountered, and its posterior temporal branch may also supply the third temporal convolution. The possibility of the closure of a small branch of the posterior cerebral, supplying the third temporal convolution, also exists.

CASE 4.—*Occlusion of the left middle cerebral artery; mental changes; right hemiplegia; right sensory disturbances; questionable right homonymous hemianopia, and sensory and motor aphasia.*

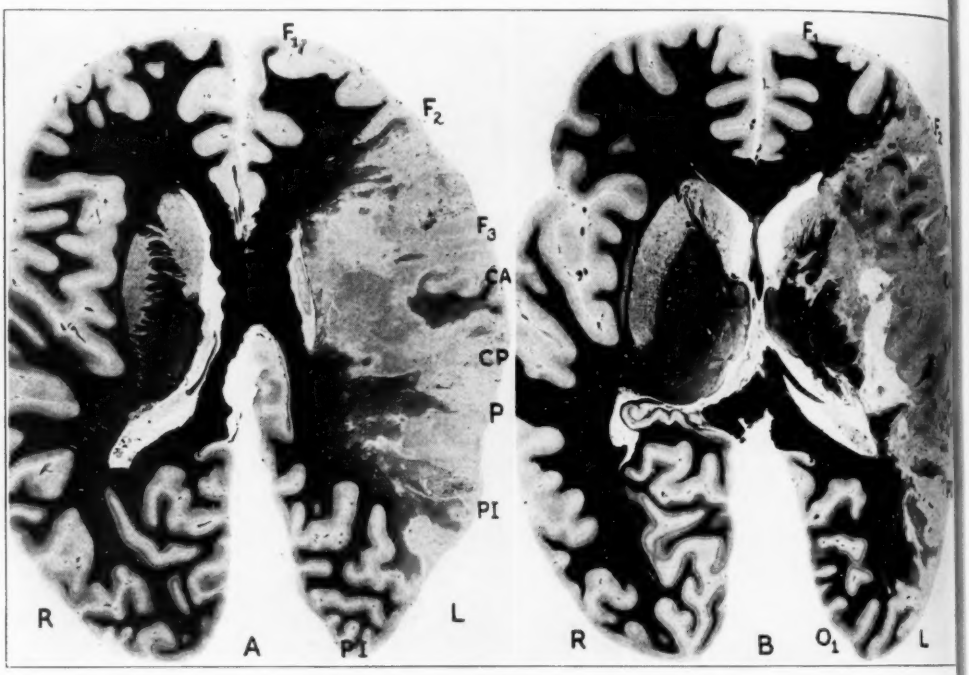

Fig. 8.—*A*, horizontal section of the brain through the middle of the neostriatum showing destruction of the second and third frontal, precentral, postcentral, parietal and inferior parietal convolutions as well as the opercular and insular convolutions. Notice the destruction of the neostriatum and internal capsule. Myelin sheath stain (Weil modification). *B*, section through the thalamic nuclei showing destruction of the same convolutions as in *A* as well as the optic radiations, with complete occlusion of the left middle cerebral artery.

History.—W. A., a man, aged 55, who was admitted to the Montefiore Hospital on Feb. 6, 1930, in August, 1929, had had several attacks of unconsciousness, and in October, 1929, paralysis of the right side of the body developed with loss of speech.

Neurologic Examination.—There were signs of mental deterioration which could not, however, be determined accurately on account of the aphasia. There was a complete right-sided paralysis with pyramidal tract signs, impairment of

all modalities of sensation on the right, a suspicion of right homonymous hemianopia, a motor and sensory aphasia and marked bilateral choking of the disks, with hemorrhages and thrombosis of the retinal vessels.

Autopsy.—There was occlusion of the left middle cerebral artery, with softening of the following convolutions: part of the second frontal and a few fibers of the paracentral lobule, all of the third frontal, precentral, opercular, insular, postcentral, superior parietal, inferior parietal, precuneus, supramarginal, angular, first temporal and second temporal convolutions. The internal capsule and a few fibers of the genu of the corpus callosum were also involved (figs. 8 *A* and *B*).

Comment.—Of interest in this case is the involvement of the left hemisphere, with complete sensory and motor aphasia. As the foot of the third convolution and the insular and temporoparietal convolutions were involved, it is difficult to establish the exact localization of each component of the aphasia. Clinically, owing to the presence of choked disks, the possibility of cerebral neoplasm was considered. On account of the aphasia and mental disturbances the suspected right homonymous hemianopia could not be charted accurately.

CASE 5.—*Occlusion of the left middle cerebral artery; right hemiplegia; right sensory disturbances; transient sensory aphasia; complete motor aphasia, and convulsions.*

History.—L. M., a man, aged 46, who was admitted to the Montefiore Hospital on March 18, 1930, in December, 1928, had suffered sudden paralysis of the right side of the body, with sensory and motor aphasia. Later, the sensory aphasia cleared up. In January, 1931, he had clonic convulsions which persisted until death.

Neurologic Examination.—There were complete right-sided paralysis with corresponding pyramidal tract signs, impairment of all sensory modalities on the right, motor aphasia, and primary optic atrophy on the left with a central scotoma. The presence of hemianopia could not be determined. The patient could not speak, read or write, but he understood what was said to him.

Autopsy.—The left middle cerebral artery was thrombosed, and the following convolutions were softened: part of the second and third frontal, precentral and paracentral (slight) and all of the opercular, insular, postcentral, superior and inferior parietal, precuneus, supramarginal, angular and first temporal convolutions (fig. 9). The internal capsule and a few fibers of the genu of the corpus callosum were involved.

Comment.—This case differed little from case 4, except for the improvement in the sensory aphasia and the presence of convulsions. As already pointed out, several patients with insults to the middle cerebral artery had convulsions due to irritative processes. We were unable to explain the primary atrophy of the left optic nerve; the central retinal artery was not obtained at autposy. Pathologically, the same convolutions were involved as in the previous case. The partial involvement of the second frontal convolutions was possibly due to the

adequate blood supply from the anastomotic branches of the anterior cerebral artery.

In summarizing we may state that, clinically, complete occlusion of the middle cerebral artery is characterized by: mental symptoms, complete hemiplegia, complete hemisensory disturbances, hemianopia and—if the left hemisphere is involved—sensory and motor aphasia. Patho-

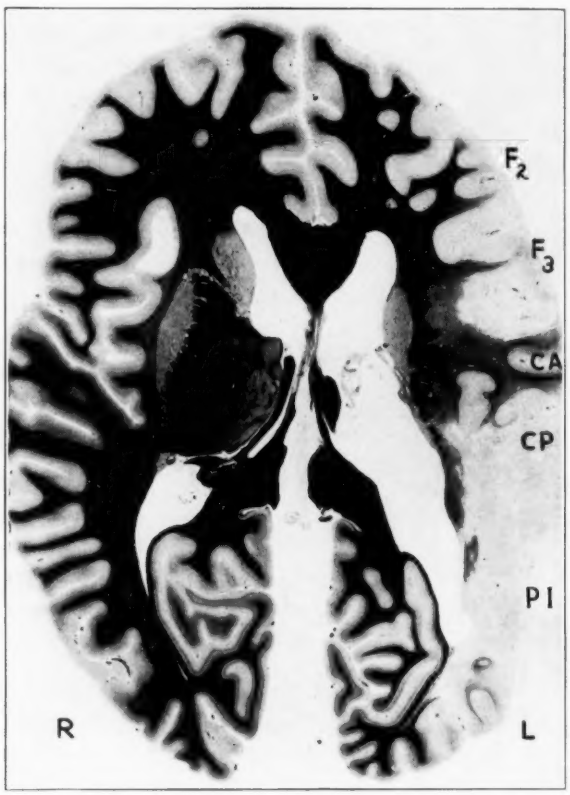

Fig. 9.—Horizontal section showing involvement of the second and third frontal, precentral, postcentral and inferior parietal convolutions. Other convolutions involved cannot be visualized in this section. This case was one of occlusion of the left middle cerebral artery with convulsions. Myelin sheath stain (Weil modification).

logically, the convolutions involved are: second and third frontal, precentral, paracentral (white matter slight), postcentral, opercular, insular, superior parietal, inferior parietal, supramarginal, angular and first and second temporal convolutions. Occasionally some of the fibers of the genu of the corpus callosum may be involved. When the first frontal and third temporal convolutions are involved there may be an anomaly

of the middle cerebral artery. If the white and gray matter of the second and third frontal convolutions are slightly involved, this may be accounted for by the adequate anastomosis from the branches of the anterior cerebral artery. The slight destruction of the white fibers of the paracentral lobule in nine of fourteen cases (table) would be in favor of partial supply of this convolution by the middle cerebral artery.

INCOMPLETE OCCLUSION OF THE MIDDLE CEREBRAL ARTERY

In this group were included cases that showed essentially involvement of only part of the convolutions supplied by the middle cerebral artery. There was not the massive softening seen in the previous fourteen cases. The essential lesion was that of extensive involvement of the superficial cortical branches or of incomplete closure of the middle cerebral artery.

Fifteen cases were included in this group. The right middle cerebral artery was implicated in four cases; the left in eleven cases. The neurologic symptoms and signs did not differ much from those in the preceding group. In cases of insult of the left middle cerebral artery complete aphasia was found in only four cases, motor aphasia in ten cases. Most likely these ten cases had shown a transient sensory aphasia at the onset, which had disappeared. Two cases (19 and 28) presented right homonymous hemianopia due to involvement of the temporal lobe and optic radiations. Convulsions were found in only one case (24) and probably were due to cortical irritation.

The convolutions involved in this group were the third frontal, precentral, opercular, insular, postcentral and first temporal convolutions. In a number of the cases the third frontal and first temporal convolutions were involved only partly. In some the second frontal and second temporal convolutions were also partly implicated. In eight cases a few fibers of the genu of the corpus callosum were also involved. The internal capsule was spared in three cases (15, 19 and 28). In two cases (20 and 24) the white matter of the convolutions was essentially involved; there was little involvement of the gray matter.

In one case (15), in addition to occlusion of the right middle cerebral artery, there was also partial thrombosis of the right anterior cerebral artery. Another case (29) disclosed bilateral closure of the superficial branches of both middle cerebral arteries and of part of the anterior cerebral artery. This is the only case that showed abnormal psychomotor activity in the form of forced grasping. Of interest is the absence of aphasia in spite of the bilaterality of the lesion. Another case was that of a left-handed person who had aphasia with involvement of the left middle cerebral artery. Most likely the left-handedness had been acquired late in life.

The following case is illustrative of the group:

CASE 6.—*Incomplete occlusion of the left middle cerebral artery; right hemiplegia; impaired sensation on the right; right homonymous hemianopia, and motor aphasia.*

History.—K. M., a woman, aged 55, was admitted to the Montefiore Hospital with a history that one year before sudden paralysis of the right side of the body had developed with loss of speech.

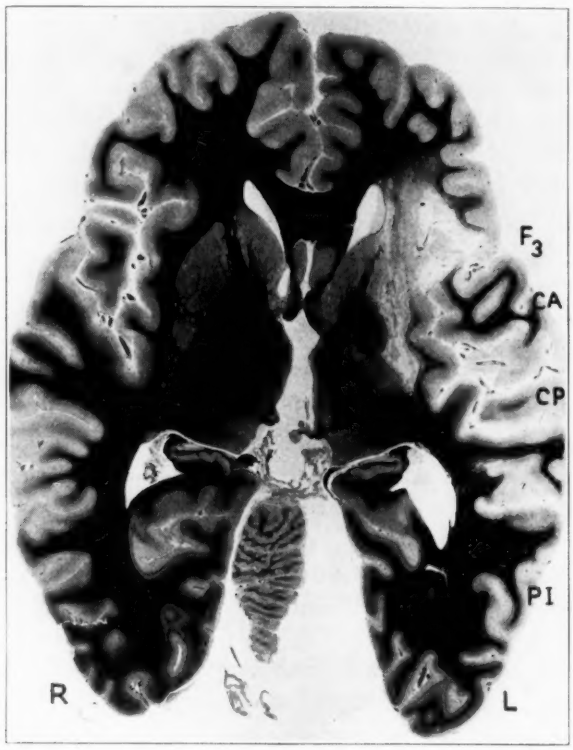

Fig. 10.—Horizontal section. Notice the involvement essentially of the white matter of the convolutions instead of the gray. The gray matter of the third frontal and parietal convolutions is involved but not extensively. There is incomplete occlusion of the left middle cerebral artery. Myelin sheath stain (Weil modification).

Neurologic Examination.—There were right-sided paralysis with pyramidal tract signs, impaired sensation on the right, motor aphasia and homonymous hemianopia. There were no mental symptoms.

Autopsy.—There was partial occlusion of the left middle cerebral artery with involvement of the white matter of the third frontal convolution, gray and white matter of the precentral convolution, white matter of the opercular and anterior insular convolutions, part of the gray and white matter of the postcentral, superior

parietal and inferior parietal, and white matter of the supramarginal, angular and first temporal convolutions (fig. 10). There was also partial involvement of the internal capsule.

Comment.—The neurologic signs and symptoms in this case differed little from those in complete closure of the middle cerebral artery, except that the sensory aphasia disappeared. Pathologically, however, there was not the extensive lesion seen in complete occlusion of the middle cerebral artery. Although almost the same convolutions were involved, the gray matter was less affected than the white.

We may summarize by stating that the clinical features of the cases in this group were essentially the same as in the first, except that the aphasia was not complete, but partook more of the expressive form. Pathologically, there was not the extensive involvement of the convolutions in the previous group. As will be seen in the table and figure 10, the white matter of the convolution was more involved than the gray.

CORTICAL BRANCHES OF THE MIDDLE CEREBRAL ARTERY

In this group were included cases of involvement of some of the smaller cortical branches of the middle cerebral artery. Implication of a single cortical branch is rare. It is more frequently associated with partial closure of other vessels. The following case is illustrative of the group.

CASE 7.—*Occlusion of the left anterior temporal branch and partial occlusion of the left lenticulostriate artery; mental deterioration; complete paralysis of the right side of the body, and sensory aphasia.*

History.—E. G., a woman, aged 68, was admitted to the Montefiore Hospital on May 23, 1930, with a history of four attacks of right-sided paralysis in the preceding ten years. The last attack occurred three weeks before admission to the hospital.

Neurologic Examination.—There were marked mental deterioration, memory defects, disorientation, emotional instability and loss of insight. There was right hemiplegia with pyramidal tract signs and sensory aphasia.

Autopsy.—There was partial closure of the left anterior temporal branch and of the left lenticulostriate and lenticulo-optic arteries. The main area of softening was in the region of the gray and white matter of the first and second left temporal convolutions (fig. 11). There was also independent partial destruction of the pulvinar and lenticular nucleus.

Comment.—The association of such marked mental symptoms with closure of only the temporal branch and lenticulostriate artery is striking. The other cerebral vessels showed atherosclerotic changes without complete closure. Undoubtedly the generally diseased cerebral vessels caused the mental symptoms. Of interest in this case was the sensory aphasia, due presumably to the involvement of the first temporal convolution.

In the second case of this group only the right ascending precentral branch was involved. The convolutions affected were the third frontal and precentral (fig. 12). The capsule was spared. The only neurologic sign was paresis of the left extremities, which was most marked in the upper limb. It will readily be appreciated that the syndrome in this group may be very variable, depending on the cortical branches involved.

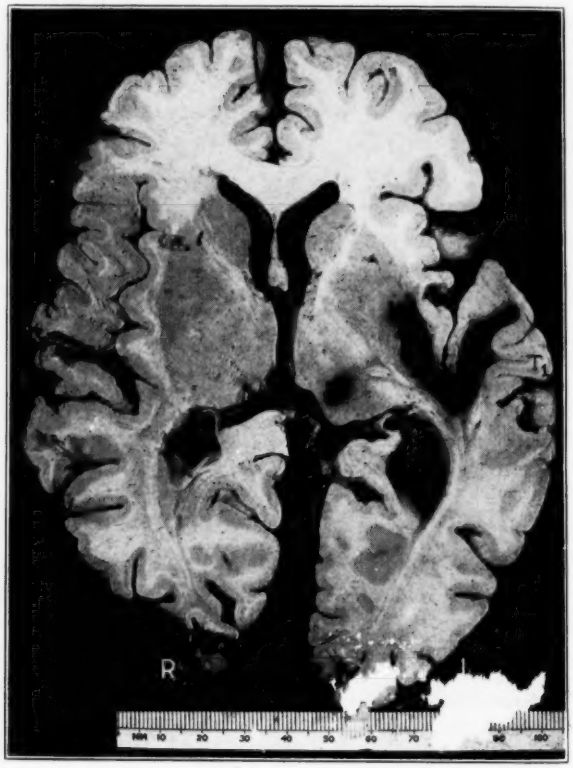

Fig. 11.—Horizontal section showing destruction of the first temporal convolution. Notice the softening in the left pulvinar and lenticular nuclei. There is occlusion of the left anterior temporal and lenticulostriate arteries, branches of the middle cerebral arteries.

DEEP BRANCHES OF THE MIDDLE CEREBRAL ARTERY

Eleven cases were included in this group. The main vessel involved was the lenticulostriate artery, the right in two cases and the left in nine cases. These cases were included in the series, despite preoccupation with cortical and subcortical pathologic changes, for two reasons: (1) because in most cases the white matter of some of the cortical convolutions was involved, and (2) because of the frequent occurrence of aphasia.

The neurologic signs and symptoms in the cases of this division showed many similarities to those observed in cases of incomplete occlusion of the middle cerebral artery. Of interest was the complete motor and sensory aphasia in three cases and the transient motor aphasia in the other six cases. The essential lesion was in the internal capsule. In some the white matter of the precentral, insular and postcentral convolutions was involved. In five cases the white matter of the first

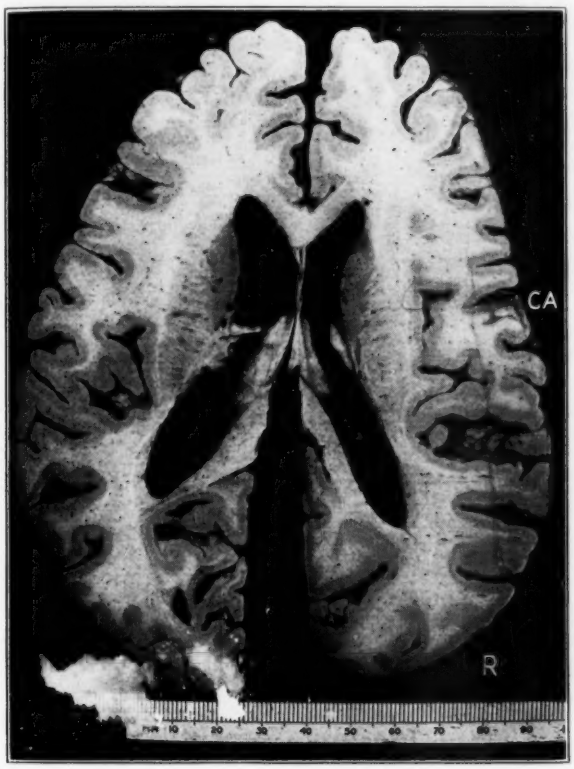

Fig. 12.—Horizontal section showing destruction of the precentral convolution only as a result of partial occlusion of the right ascending precentral artery, a branch of the middle cerebral artery.

temporal convolution was also involved. The sensory and motor aphasia in three cases and the transient motor aphasia in six were undoubtedly due to edema and pressure on the convolutions (foot of the third frontal and parietotemporal) subserving this function. That edema and consequent pressure were responsible for the aphasia appears probable in view of the fact that in six cases the motor aphasia was transient. The aphasia in the other three patients might have disappeared had they lived longer.

One case showed, in addition to occlusion of the left lenticulostriate artery, involvement of the left posterior cerebral artery (fig. 13). Accurate visual fields in this case were not obtained. Homonymous hemianopia was present in another case (40, table). The thalamic nuclei in this case were implicated.

CASE 8.—*Closure of the left lenticulostriate artery; paralysis of the right side of the body; right hypesthesia and hypalgesia, and transient motor aphasia.*

History.—G. B., a man, aged 74, was admitted to the Montefiore Hospital on Oct. 6, 1921, with the history that he had suddenly lost consciousness and that

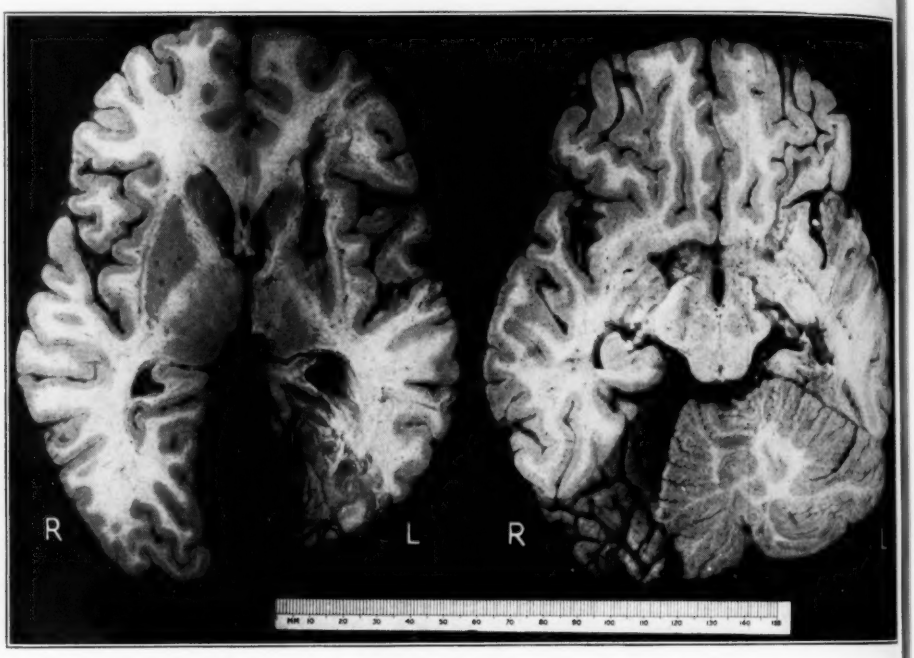

Fig. 13.—Thrombosis of the lenticulostriate and posterior cerebral arteries. Notice the convolutions involved, especially the white matter.

right-sided paralysis had developed with pyramidal tract signs, hypalgesia and hypesthesia on the right and motor aphasia. This patient formerly spoke Russian, Yiddish, French, German, Spanish, Italian and English fluently. A transient motor aphasia developed in which, interestingly enough, the first languages to return were Russian and Yiddish, which were the first that he had acquired.

Autopsy.—This revealed closure of the left lenticulostriate artery (fig. 14) with destruction of the internal capsule and part of the white fibers of the precentral, postcentral and superior parietal convolutions. The gray and white matter of the insular convolutions was also destroyed. Part of the striatum generally implicated in complete closure of the lenticulostriate artery was destroyed.

Comment.—This case emphasized that the distribution of the lenticulostriate artery is not strictly limited to the lenticular nuclei and internal capsule, but runs also to the insula, and occasionally to the white matter of the precentral and postcentral convolutions.

Study of this group of cases brought out the fact that the lenticulostriate artery sends branches not only to the structures which give it its name, but also to the white matter of the precentral and postcentral convolutions and the white and gray matter of the insular convolutions.

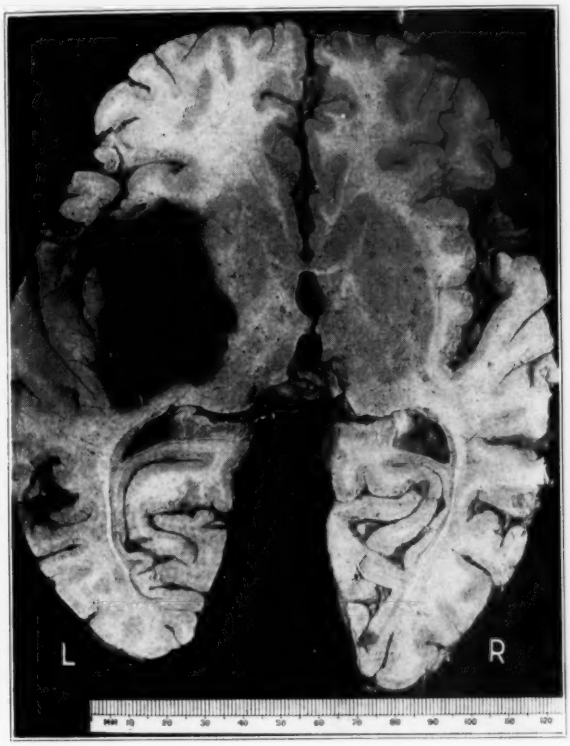

Fig. 14.—Hemorrhage due to closure of the lenticulostriate artery. Notice the destruction of the insular convolution in addition to the usual lesion seen in thrombosis of the lenticulostriate artery.

Of importance, furthermore, is the occurrence of transient motor aphasia encountered in this group as a result of edema and pressure on the convolutions or transcortical pathways mediating this function.

POSTERIOR CEREBRAL ARTERY

The posterior cerebral artery is less commonly involved in vascular disease of the brain than the middle cerebral artery and more frequently than the anterior cerebral artery.

As is well known, the posterior cerebral artery, in addition to supplying the territory of the third temporal, fusiform, uncinate, hippocampal, lingual, cuneate and all occipital convolutions, also supplies part of the optic thalamus and the subthalamic region (figs. 1 *C*, 2 and 15). In lesions of this vessel there is seldom an isolated involvement of the visual zone without associated foci in the thalamic and subthalamic regions. Our experience would tend to show that it is very unusual for

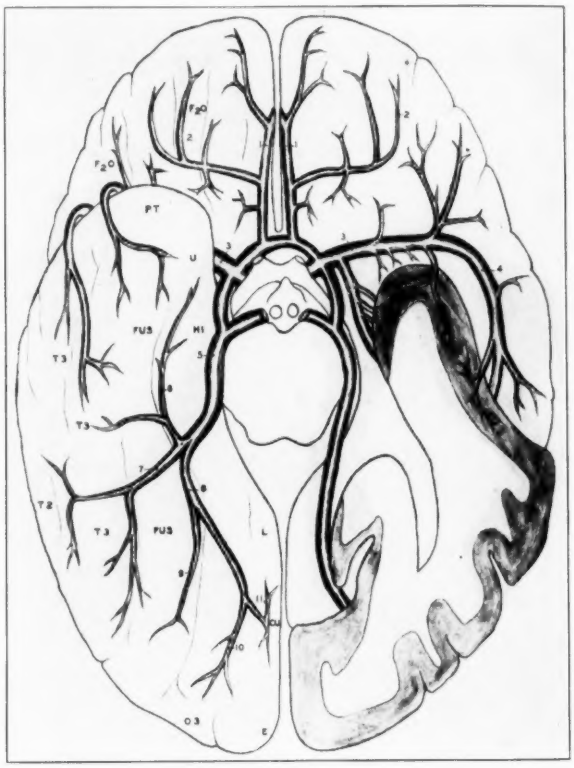

Fig. 15.—Inferior view showing the cortical areas supplied by the posterior and anterior cerebral arteries and their branches: *1*, anterior cerebral; *2*, internal orbital, branch of the anterior cerebral; *3*, middle cerebral; *4*, parietotemporal, branch of the middle cerebral; *5*, posterior cerebral; *6*, anterior temporal, branch of the posterior cerebral; *7*, posterior temporal, branch of the posterior cerebral; *8*, occipitoparietal, branch of the posterior cerebral; *9*, calcarine, branch of the posterior cerebral; *10*, parieto-occipital, branch of the posterior cerebral; *11*, cuneus, branch of the posterior cerebral.

the posterior cerebral artery to be the only vessel involved. There is frequently an associated occlusion of the middle cerebral artery or its branches. From this it can readily be seen how difficult it is to establish a syndrome of the posterior cerebral artery or one of its branches.

unless it is a fairly selective lesion. The syndrome, however, depends on which branches of the posterior cerebral artery are occluded. In this presentation we are concerned only with the branches that supply the cortical areas, especially the calcarine area.

The posterior cerebral artery is rarely obliterated at its origin. It has an anastomosis with the other cerebral vessels through the circle of Willis and also an anastomosis at the periphery with the terminal branches of the anterior and middle cerebral arteries (figs. 2 and 15). For this reason a syndrome of complete obstruction of the posterior cerebral vessel is rarely observed. Four cases occurred in this group. The clinical picture in two of the cases was somewhat obscured by concomitant lesions of the middle cerebral artery. All four cases, however, were characterized by some visual disturbances.

CASE 9.—*Occlusion of the left calcarine artery; right upper temporal and left upper nasal quadrant defect, and bilateral central scotoma.*

History.—S. B., a man, aged 66, was admitted to the Montefiore Hospital on Jan. 24, 1931, with a somewhat scanty history. He became depressed and irritable in January, 1930; later, he had right frontal headaches. Shortly before his admission to the Neurological Institute in July, 1930, his physician suspected hemianopia.

Neurologic Examination.—The pupils were irregular and not responsive to light, directly or consensually, but they responded promptly to convergence and in accommodation. There was impairment in visual acuity (right, 3/200; left, 20/200). The retinal vessels were sclerosed. There was a right upper temporal and a left upper nasal quadrant defect, with bilateral central scotoma. The patient repeatedly complained of dimness of vision. A careful neurologic study could not be made because of the severe mental deterioration. The patient died of bronchopneumonia on May 9, 1931.

Autopsy.—There was partial occlusion of the left middle cerebral and of the left calcarine artery, a branch of the posterior cerebral artery. The greatest obstruction was found in the calcarine branch. The convolutions essentially involved as a result of the middle cerebral closure were: left third frontal, precentral, opercular, insular and postcentral, and the white matter of the first and second temporal. The convolutions involved as a result of closure of the branch of the posterior cerebral artery were: white matter of the third temporal, gray and white matter of the fusiform, lingual and second and third occipital convolutions; the cuneus was not involved (fig. 16). The splenium of the corpus callosum was partly involved.

Comment.—The destruction of the fusiform and lingual lobules was undoubtedly responsible for the quadrantanopic defects. Of great interest is the bilateral central scotoma—on the basis of a lesion of a single hemisphere—especially since lesions in the visual area most frequently spare the macular representation. This raises the question of the dominance of one hemisphere in macular vision.

CASE 10.—*Partial occlusion of the right calcarine and cuneus arteries; left homonymous, incomplete quadrant defect.*

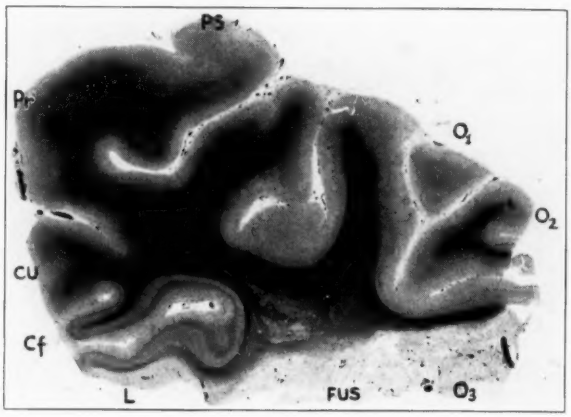

Fig. 16.—Coronal section through the calcarine area showing destruction of the lingual, fusiform and third occipital gyri as a result of a partial closure of the calcarine artery.

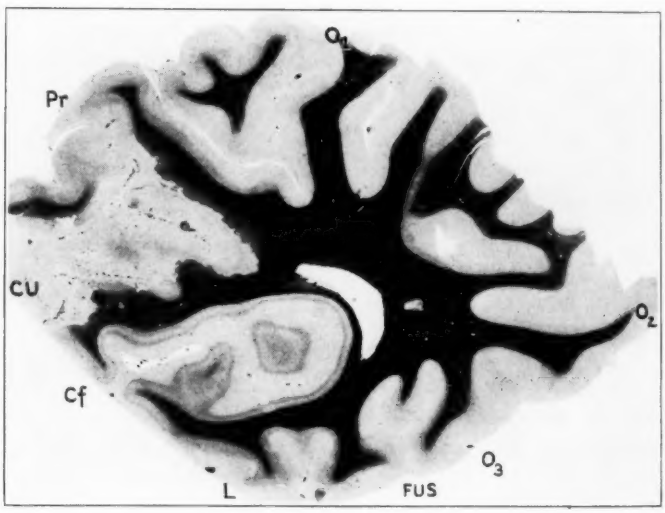

Fig. 17.—Coronal section showing destruction of the cuneus as a result of partial closure of the calcarine and cuneus, branches of the posterior cerebral artery.

History.—C. F., a man, aged 51, was admitted to the Montefiore Hospital on Dec. 8, 1928, complaining of dizziness, periodic attacks of spasmodic movements of the eyes to the right and numbness of the right side of the body. In October, 1928, the patient had attacks of dimness of vision followed by deviation of the eyes to the right and accompanied by a feeling of numbness over the entire right half of the body. A marked increase in blood pressure was observed during the attack, a rise of from 40 to 50 points in systolic pressure.

Neurologic Examination.—The fundi showed fulness of the veins and a tendency toward arterial spasm. During the spasmodic attack, which lasted from thirty to sixty seconds, the pupils were dilated and fixed, the patient could not see objects at his left and immediately following the attack complained of dysesthesia, i. e., a "pins and needles sensation," over the right side of the body. Vision in the right eye was 20/65, and in the left, 20/100. The fields showed contraction for blue, red and green, with an incomplete left homonymous quadrantic defect below, with normal blind spots. The patient died after a brief attack of unconsciousness.

Autopsy.—There was partial occlusion of the left postcentral artery, a branch of the middle cerebral artery, destroying part of the postcentral convolution. There was also partial closure of the right calcarine and cuneus branches of the posterior cerebral artery, destroying the cuneus (fig. 17).

Comment.—The lesion of the left ascending postcentral artery accounted for the dysesthesia following the oculogyric spasm.

The third case showed bilateral cortical blindness due to involvement of both posterior cerebral arteries. There were also aphasia and complete right hemiplegia, with mental deterioration due to involvement of the left middle cerebral artery.

In the fourth case there developed sudden blindness of the right eye except for perception of light. The patient cooperated poorly and could not be studied carefully. There was complete occlusion of the right posterior cerebral artery with destruction of the right third temporal, uncinate, hippocampal, fusiform, lingual, cuneate, first, second and third occipital and Ecker convolutions. The splenium corporis callosi in all, except case 10, was involved.

In two cases (13 and 35) in the group of insults to the middle cerebral artery there was also involvement of the posterior cerebral artery, but owing to involvement of the other vessels the symptoms and signs of a posterior cerebral lesion were completely masked.

These cases bring out the difficulty in establishing a definite syndrome for lesions of the posterior cerebral artery. As has been pointed out, the difficulty is due to the multiplicity of lesions. Foix and his pupils attempted to establish a syndrome of the posterior cerebral artery, and found that complete closure of the left posterior cerebral artery causes: (1) hemianopia, (2) pure alexia, or sensory aphasia with predominance of alexia, and (3) sensory and motor disturbances owing to involvement of the thalamus and pes pedunculi. In partial closure of the posterior branches without involvement of the thalamus, the syndrome consists of: (1) alexia, (2) hemianopia and (3) psychic blindness.

In involvement of the calcarine artery there is partial hemianopia. Our first two cases illustrate this well. If the lesion is above the calcarine fissure there is an inferior quadrantanopia; if it is below the fissure there is a superior quadrantanopia. These types of visual defect were best observed in injuries of the occipital lobe in the war. For alexia to develop, the lesion must include not only the visual cortex but also the lingual gyrus. Marie was of the opinion that there must be simultaneous involvement of the optic radiation and of the inferior longitudinal fasciculus. In our cases we did not succeed in demonstrating alexia, disturbances in visual orientation or hallucinations.

Scanty and inadequate as our material is, we have brought out one definite point of localization in the occipital lobe, i. e., visual disturbances in the nature of quadrantanopic defects associated with a lesion of one lip of the calcarine fissure.

CONCLUSIONS

This paper is limited to a simple exposition of disturbances of function in cases of cerebral vascular disease and alterations in the brain in these cases, with a view to establish a parallelism in the findings. We have not discussed the various doctrines regarding localization of function in the brain, nor weighed the validity of the beliefs of strict localizationists (Broca, Wernicke and Wilson) as against those, who, though accepting the presence of specific functional areas established by neurophysiology and other methods, argue for a more diffuse representation for cerebral functions (H. Jackson, von Monakow, K. Goldstein, S. Freud and H. Head). The objective anatomic approach, even at this late date and after the accumulation of so many observations, is still a necessary method of procedure. That two such authorities as Henschen and Niessl von Mayendorf, after studying about twelve hundred cases of motor aphasia, clinically and pathologically, concluded by localizing the function in two totally different regions is ample evidence of the truth of this statement. Anatomy must still provide the moorings for soaring psychologic speculations. On the other hand, the organicist must not remain unmindful of the dictum of Hughlings Jackson, who insisted that because a lesion in a certain area creates disturbances of a certain function it does not follow that the function is localized in that area.

As was stated at the outset, cerebral localization on the basis of vascular supply, though difficult and necessitating caution in interpretation, can still be definitely established. We were able, on the basis of a study of forty-eight cases, to demonstrate definite syndromes accompanying occlusion of the anterior and middle cerebral arteries or their branches; in cases of partial occlusion of the posterior cerebral artery the resultant quadrantic visual field defect was pointed out.

CEREBRAL CIRCULATION

XXIII. INDUCED VARIATIONS IN VOLUME FLOW THROUGH THE BRAIN PERFUSED AT CONSTANT PRESSURE

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During the last four years there has appeared from this laboratory a series of studies on cerebral circulation.[1] Many of these studies have been made by means of a cranial window which enables the investigator to make direct observations on the caliber of the pial arteries and veins and on the stream of blood flowing through them. Consistent results have been obtained in studying the effect on the pial arteries of sympathetic and vagus stimulation, hypertonic solutions, carbon dioxide and oxygen, histamine, acetylcholine, amyl nitrite and caffeine. These observations have been limited to measurements of the diameter of the pial vessels, and deductions have been drawn from these observations as to the flow of blood through the pial arteries. The experiments presented here deal with an attempt at measuring directly the minute volume cerebral flow of blood by a perfusion method in cats and monkeys during various experimental conditions. The effects of stimulating the cervical sympathetic, the vagus and the femoral nerves and the effects of epinephrine, caffeine, histamine and pitressin on the minute volume flow perfused through the carotid at a definite and constant pressure have been investigated.

Perfusion methods have been used by many investigators in studying the behavior of cerebral blood vessels. Wiggers[2] found evidence of

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1. For a review of this work see Cobb, S.: Am. J. M. Sc. **158**:528, 1929. Further studies in this series pertinent to this paper are: Wolff, H. G.: Cerebral Circulation: XIa. The Action of Acetylcholine, Arch. Neurol. & Psychiat. **22**: 686 (Oct.) 1929. Wolff, H. G., and Lennox, W. G.: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, ibid. **23**:1097 (June) 1930.

2. Wiggers, C. J.: Am. J. Physiol. **20**:206, 1907-1908; **21**:454, 1908

vasoconstriction on stimulating the sympathetic fibers along the carotid artery at the base of the brain. Ferrier and Brodie [3] and Wiggers [4] found that epinephrine causes a cerebral vasoconstriction. Dixon and Halliburton [5] found a slight dilation resulting from the use of epinephrine. Gruber and Roberts [6] found evidence of dilation of the cerebral vessels by acid and constriction by alkali. They believed that the inconstant results obtained by various investigators using epinephrine were due to the fact that the p_H of the epinephrine solution had not been carefully controlled. These investigators found that a strong solution of epinephrine with a p_H equal to that of normal blood caused a vasocon-

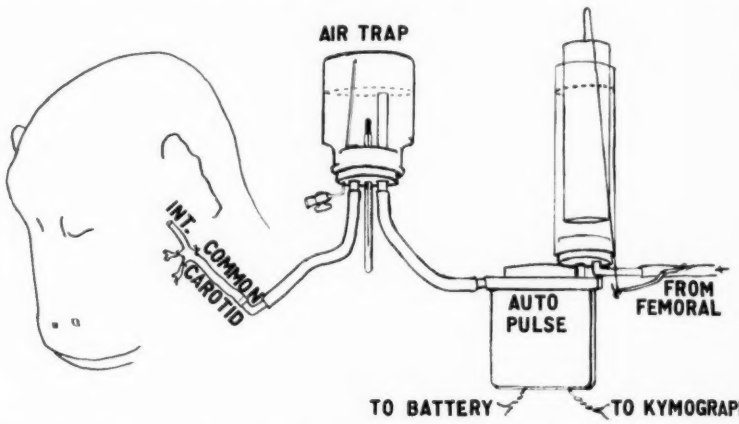

Fig. 1.—Sketch of the apparatus used for perfusion of heparinized blood into one internal carotid artery at a constant pressure.

striction in perfused brains. More recently, Schmidt [7] has studied the cerebral blood flow in dogs and cats during barbital and ethyl carbamate (urethane) anesthesia and following decerebration by the ligature method. In his experiments he measured cerebral arterial inflow through the central stump of the "subclavian arteries, all the branches of which had been tied except the vertebrals" by means of a Venturi meter and also by perfusing these arteries by the Richards-Drinker perfusion pump. He also made measurements of the venous return through the innominate veins. His results will be discussed.

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3. Ferrier and Brodie, quoted by Brodie, T. G., and Dixon, W. E.: J. Physiol. **30**:476, 1904.

4. Wiggers, C. J.: Am. J. Physiol. **14**:452, 1905.

5. Dixon, W. E., and Halliburton, W. D.: Quart. J. Exper. Physiol. **3**:315, 1910.

6. Gruber, C. M., and Roberts, S. J.: J. Pharmacol. & Exper. Therap. **27**: 335, 1926.

7. Schmidt, C. F.: Am. J. Physiol. **84**:202, 1928.

TECHNIC

In these experiments the technic used is that described elsewhere.[8] Essentially the experiments consisted in pumping heparinized blood at a constant pressure through the peripheral end of the common carotid artery in cats during amytal anesthesia, and in cats and monkeys during ether-morphine anesthesia (fig. 1). The source of the blood was the femoral artery or the central end of the carotid. Measurements of the number of pump strokes, the carotid or pump pressure and the systemic blood pressure from a femoral artery were recorded on a kymograph. In some cases the cerebrospinal fluid pressure was recorded. During various experimental procedures both the left and right cervical sympathetics and vagi in the neck were stimulated. Drugs were added to the perfusion fluid before it entered the carotid cannulas. In all the experiments the vertebral arteries were dissected and tied off close to the thorax, one carotid was connected with the perfusion apparatus, and the other carotid was clamped off. Three types of experiments are reported.

EXPERIMENTS

I. *Monkeys.*—In a series of rhesus monkeys, during ether-morphine anesthesia, the common carotid artery was dissected in the neck as far as the point at which it gave rise to the external carotid, internal carotid and maxillary arteries. The external carotid and the maxillary arteries were tied off, and the perfused blood was pumped into one internal carotid. Previous injections in a group of monkeys had shown that there were no important anastomoses between the internal carotid and the arteries of the facial muscles, tongue and neck. Both vertebral arteries were tied off before they entered the vertebral canals. The other carotid was clamped off high up in the neck, great care being exercised to clamp the internal and external carotid and facial arteries independently. Heparinized blood entered the perfusion pump at the animal's own blood pressure (recorded) from the femoral arteries or from the central stump of the carotid artery. The pressure at which the blood was pumped into the internal carotid was measured and kept constant. In most cases this perfusion pressure was a little higher than the animal's systemic pressure. This enabled us to feel that the error due to blood coming in through the anterior spinal artery could not be great. After the experiment, an injection mass of india ink and hot gelatin was pumped into the internal carotid artery in order to see if the brain and meninges alone had been perfused. In most cases dissection showed that very little of the injection mass reached any arteries except those of the meninges and the brain. The results of this series of experiments we consider the most accurate and important.

II. *Cats: Combined Technic.*—In this series of experiments cats were used, and the same experimental conditions were attempted as recorded in the experiments on monkeys. However, dissection showed that in cats the internal carotid artery is very small, and most of the blood entering the cat's brain flowed through the maxillary artery and the continuation of the external carotid. It was impossible to avoid perfusing the facial muscles, tongue, neck and cranium of the cat. In this series the perfusion technic was combined with the cranial window technic. This enabled us to record both the volume of blood perfused into the carotid artery at a constant pressure and the diameter of the pial artery. These experiments made it possible to correlate the results of perfusion of the common carotid and the actual observed behavior of the pial artery.

8. Putnam, T. J.: An Easily Assembled, Self-Recording Perfusion Apparatus, J. Lab. & Clin. Med., to be published.

III. *Cats: Simple Perfusion.*—In this series one common carotid artery was perfused with heparinized blood at a constant pressure. Both vertebral arteries were clamped before they entered the vertebral canal, and the other common carotid was clamped. In this series the whole head was perfused. These experiments add merely supplementary data.

SOURCES OF ERROR

1. We were unable to tie off the anterior spinal artery and its branches. In order to minimize this error we kept the perfusion pressure at a higher level than the systemic blood pressure which supplied the anterior spinal artery.

2. During the process of connecting the inflow tube from the perfusion pump to the carotid cannula there was always the danger that air emboli might enter the carotid cannula. In order to avoid this it was our procedure to remove the carotid clamp from the perfused artery and allow blood to run back through the cannula into the rubber tube to be sure that the air had escaped from the tube before the perfusion pump was started. In most cases we succeeded in eliminating the air from the tubes before the experiment was started. However, air bubbles were seen at times in the pial arteries during the combined experiments. Hence this possible source of error is included.

3. Often on stimulation of the sympathetic and vagus the cannula and inflow tube were accidentally displaced. This resulted in changes which were artefacts. If the difference in number of clicks between the periods before and after stimulation was greater than the change during stimulation, we considered these cases as ones in which the error was greater than the change. The experiments during which this happened are listed as "error greater than change."

STIMULATION OF THE CERVICAL SYMPATHETIC

I. *Monkeys.*—In these experiments six monkeys were used. The monkeys were given ether anesthesia until the experimental apparatus was in order and until the operative procedure had been completed. One milligram of heparin per kilogram of body weight was given intravenously. In all cases the procedure was to dissect the vertebral arteries on both sides and to clamp them before they entered the vertebral canal. The left carotid was then dissected in the neck and the external carotid and the maxillary arteries were tied off. The left common artery was cut and tied, and the central end was connected to the inflow tube of the perfusion pump by means of a metal cannula fastened to a rubber tube. Another metal cannula was tied into the peripheral end of the carotid and connected to the outflow tube of the pump beyond the air chamber (fig. 1). During this procedure the animal's head was supplied by the right carotid artery at the animal's own blood pressure. Ether was removed and the animal was given subcutaneously 3 mg. of morphine sulphate per kilogram of weight. The inflow tube of the pump was opened, and heparinized blood was pumped through the air trap. The carotid clamp was removed, and heparinized blood was perfused into the internal carotid artery at a pressure of about 120 mm. of mercury, care being taken to avoid the introduction of air emboli. When the perfusion system was working, the right carotid was clamped off, care being exercised to clamp the external carotid, the internal carotid and the maxillary arteries. This made it impossible for blood to enter the brain except through the pump and the anterior spinal arteries. The pump pressure was a little higher than that of the systemic pressure so that the amount of blood entering the brain through the anterior spinal arteries was at a minimum. Kymograph records were made of the number

of pump strokes in time and the system blood pressure. Records were kept of the carotid pressure and of the temperature of the blood just before it entered the carotid. In most cases the animals were breathing spontaneously, but in three cases artificial respiration was used during part of the experiment. At the end of the experiment the volume of the pump stroke was carefully calibrated and the actual blood volume per minute calculated. We were not so much interested in the absolute volume as in the percentage change in volume per minute, resulting from the experimental procedures.

After the apparatus was in order and blood was pumped into the carotid at a constant pressure for a preliminary period of from two to five minutes, the right sympathetic was stimulated by means of a bipolar electrode in secondary circuit attached to a Harvard inductorium supplied by one dry cell battery for periods varying from thirty seconds to two minutes. The coil distance was varied from 8 to 12 cm. Then the stimulating electrode was removed, and records were taken until the minute volume flow had attained its preliminary level. This was the general procedure in all of these experiments.

Calculation.—At the end of an experiment the perfusion apparatus was calibrated, and in one experiment it was found that at the perfusion pressure of 128 mm. of mercury each stroke of the pump delivered 1 cc. of blood. During

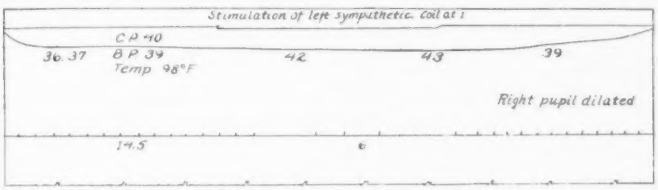

Fig. 2.—The effect of stimulating the left cervical sympathetic on the volume of heparinized blood perfused through the right internal carotid artery at a constant perfusion pressure of 80 mm. of mercury. In this and the following illustrations the second line from the bottom records the individual strokes of the perfusion pump. Every pump stroke in this chart on calibration represented 1 cc. of heparinized blood. Stimulating the sympathetic caused a decrease in the minute volume from 14.3 to 6 cc. There was a slight rise in the systemic blood pressure (third line from bottom) from 72 to 86 mm. of mercury. *C. P.* indicates cerebrospinal fluid pressure; *B. P.*, blood pressure.

the preliminary period the number of strokes during one minute was 14.5, and hence the volume of blood perfused into the internal carotid artery during this period was 14.5 cc. per minute. The right cervical sympathetic was stimulated for one minute with the secondary coil at 9. During this minute the volume of blood pumped into the left internal carotid artery at the same pressure was 6 cc. per minute. This decrease was due to an increase in the peripheral resistance of the arteries and arterioles of the brain. This increase in resistance could be caused only by a decrease in the size of the vascular bed, a vasoconstriction. Stimulation of the sympathetic was accompanied by a rise in systemic blood pressure and dilation of the right pupil.

After the stimulus was removed, the volume inflow increased to 17 cc. The actual decrease in volume flow during the period of stimulation was 62 per cent. In some cases in these experiments the change between the initial and final base line

periods was greater than the change during stimulation. We have classified these experiments under the group "error greater than change."

Data.—In six monkeys the right and left sympathetics were each stimulated thirteen times. Among these twenty-six stimulations, there was a decrease in minute volume in thirteen trials. In six trials the error was greater than the change, in six trials there was no change and in one instance there was an increase in minute volume. The decrease in volume flow per minute ranged from 2 to 62 per cent, with an average of 15.04 per cent.

In these cases the decrease of blood volume per minute was due to the increase in peripheral resistance, which in turn implied a decrease of the arterial bed in a vasoconstriction. If we eliminate the instances in which the error was greater than the change, our data indicate that in thirteen of twenty-six trials stimulation of the cervical sympathetics resulted in a decrease of blood volume per minute due to a vasoconstriction.

II. *Cats: Combined Technic.*—The procedure used in these experiments has been described. By using the perfusion apparatus in combination with a cranial window we were able to measure simultaneous changes in the volume flow per minute of the perfusion blood and at the same time the diameter of the pial artery. The combined experiments were carried out in eight cats during ether-morphine anesthesia. The animals were given ether until the operative and experimental procedures were completed. The animals were then given from one-fourth to one-half grain (16.2 to 32.4 mg.) of morphine sulphate subcutaneously, and the ether was removed. When the superficial reflexes had returned, the experimental changes were produced.

Eight experiments were carried out on as many cats. In five experiments a decrease in flow resulted, ranging from 11 to 25 per cent. In each instance there was a decrease in arterial diameter varying from 4.4 to 11 per cent, the degree of constriction corresponding in general to the change in minute volume. In three instances there was no change in either.

III. *Cats: Simple Perfusion.*—The procedure followed in these experiments has been described. In twelve animals, during amytal and ether-morphine anesthesia, the right sympathetic was stimulated twenty-one times; the left, fourteen times. In thirty of these trials, there was a decrease ranging from 4 to 70 per cent, with an average of 23.9 per cent.

Comment.—In our first series of experiments it was found that in thirteen of twenty trials there was a decrease in blood volume per minute. The range of this decrease was from 2 to 62 per cent, with

an average of 15.04 per cent. In the combined experiments on cats, five of eight showed a decrease in blood flow per minute with a simultaneous decrease in the diameter of the pial artery. In simple carotid perfusion a decrease in blood flow per minute was found in thirty of thirty-five experiments during amytal and ether-morphine anesthesia. These experiments show that in most cases stimulation of the cervical sympathetic resulted in a decrease in blood perfused per minute at a constant pressure, and offer evidence that the vasoconstrictor fibers have a direct action on the blood vessels of the pia and parenchyma of the brain. On sympathetic stimulation the blood vessels constricted in most cases even when the entire cerebral circulation was divorced from the general systemic circulation. We believe that these experiments afford additional evidence to prove: (*a*) the existence of vasoconstrictor fibers to the pia and parenchyma, and (*b*) their ability to act when the blood supply to the brain is independent of the animal's systemic aortic blood pressure.

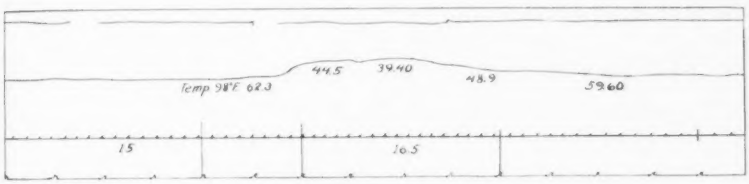

Fig. 3.—The effect of stimulating the central end of the left vagus at a constant perfusion pressure of 66 mm. of mercury. An increase in minute volume perfused and a drop in systemic blood pressure are recorded.

STIMULATION OF THE VAGUS

I. *Monkeys.*—These experiments were carried out precisely like those already described. The vagus in the neck was tied, cut and then stimulated for varying periods of time, from thirty seconds to two minutes. The stimulus was the secondary coil of a Harvard inductorium connected to a dry cell battery. In eight monkeys the right vagus was stimulated ten times and the left vagus ten times. Among these twenty stimulations, in eight instances the error was greater than the change recorded. In seven cases there was an increase in blood flow per minute ranging from 5 to 11 per cent, with an average of 7.5 per cent. In four cases there was no change, and in one instance there was a decrease in blood flow per minute. An increase in blood flow with a constant pressure head implies dilation of the vascular bed and of the arteries. In most of these experiments there were respiratory changes and a drop in blood pressure concomitant with stimulation of the vagus.

II. *Cats: Combined Technic.*—Seven experiments attempted on six cats were not very successful. In six of the seven the error was greater

than the change. In one experiment there was an increase of blood flow of 7 per cent, accompanied by a dilation of the pial artery of 5 per cent.

III. *Cats: Simple Perfusion.*—In thirteen animals the right vagus was stimulated eighteen times and the left sixteen times. There was an increased flow in twenty-eight trials, with a range of from 5 to 48 per cent and an average of 18.7 per cent. In five instances there was a decrease.

EPINEPHRINE

The effect of epinephrine on the blood vessels of the brain has been of great interest to students of vascular physiology. Using both direct and indirect methods, most investigators found that epinephrine caused vasoconstriction of the arteries.[9] A few, however, reported dilation[10] or dilation followed by constriction.[11] In our experiments we were able to introduce solutions of epinephrine of various strengths into the blood perfusate just as it entered the carotid artery (fig. 1). The effect which these solutions of epinephrine had on the minute blood flow are recorded later.

I. *Monkeys.*—In six monkeys, during ether-morphine anesthesia, epinephrine was introduced fifteen times. After every introduction there was a decrease in the number of pump strokes per minute and, as a rule, a rise in systemic blood pressure. In these experiments we felt confident that the blood was perfused through the internal carotid, which on injections of gelatin after the experiments showed no anastomoses with the vessels of the face, neck or tongue. Doses were used varying from 0.75 cc. of a 1:100,000 solution to 1 cc. of a 1:10,000 solution. In all cases there was a definite and significant decrease in blood volume per minute. The carotid and pump pressure was always constant; hence the change in peripheral resistance could have been due only to the decrease in the vascular bed or vasoconstriction. The range of

9. von Cyon, E.: Arch. f. d. ges. Physiol. **74**:97, 1899. Cushing, H.: Am. J. M. Sc. **124**:376, 1902. Hirschfelder, A. D.: J. Pharmacol. & Exper. Therap. **6**:597, 1915. Jacobi, W., and Magnus, G.: Arch. f. Psychiat. **74**:126, 1923. Sander, G.: Arch. f. d. ges. Physiol. **213**:492, 1926. Kahn, R. H.: Centralbl. f. Physiol. **18**:153, 1904. Pick, F.: Arch. f. exper. Path. u. Pharmakol. **42**:399, 1899. Neujean, V.: Arch. internat. de pharmacodyn. et de thérap. **13**:45, 1904. Berezin, I.: Russk. Vrach, 1916, no. 22, p. 513; abstr., J. A. M. A. **67**:844 (Sept. 9) 1916. Miwa, M.; Ozaki, M., and Shuoshita, R.: Arch. f. exper. Path. u. Pharmakol. **123**:331, 1927. Biedl, H., and Reiner, M.: Arch. f. d. ges. Physiol. **79**:158, 1900. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928. Wiggers.[2] Ferrier and Brodie.[3] Gruber and Roberts.[6]

10. Gerhardt, D.: Arch. f. exper. Path. u. Pharmakol. **44**:161, 1900. Dixon and Halliburton.[5]

11. Yamakita, M.: Tohoku J. Exper. Med. **3**:506, 1902.

change in blood volume per minute was from 12.5 to 64 per cent. The average was 30.9 per cent. In no case was anything but a decrease in minute volume recorded.

II. *Cats: Combined Technic.*—In this series of experiments seven cats were used during ether-morphine anesthesia. Records were taken of the blood volume per minute introduced into one carotid artery at a constant pressure, and at the same time observations were made on the diameter of the pial artery. Thirteen injections of epinephrine were made in seven cats. The doses ranged from 5 cc. of a 1 : 100,000 solution to 1 cc. of a 1 : 10,000 solution. In twelve of these trials there was a decrease in minute volume concomitant with a decrease in the diameter

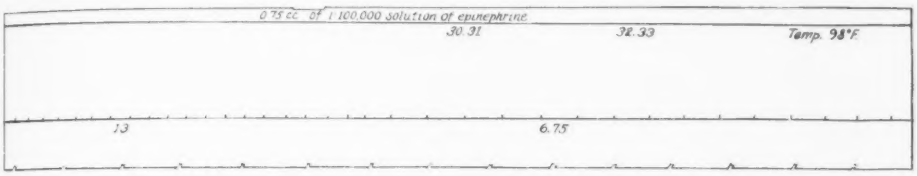

Fig. 4.—Effect of epinephrine. A decrease of blood volume at a constant perfusion pressure following the intracarotid injection of 0.75 cc. of a 1 : 100,000 solution of epinephrine (0.20 cc. per kilogram) during ether-morphine anesthesia. There was a slight rise in systemic blood pressure.

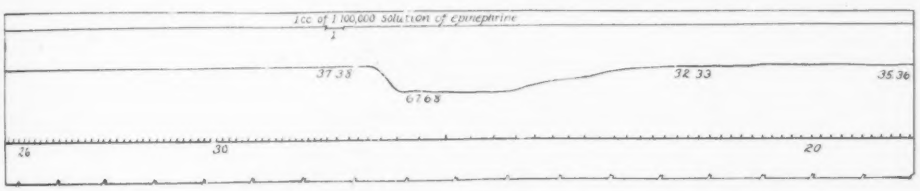

Fig. 5.—Effect of epinephrine. A decrease of blood volume at a constant perfusion pressure following the intracarotid injection of 1 cc. of 1 : 100,000 solution of epinephrine (0.33 cc. per kilogram) during ether-morphine anesthesia. There was a marked rise in systemic blood pressure.

of the pial artery. In one instance there was a decrease in minute volume without a corresponding change in arterial diameter. The range in volume decrease was from 28 to 70 per cent, the average for all trials being 43.6 per cent. The range of constriction of the pial artery was from 5 to 21 per cent, with an average of 9.6 per cent.

III. *Cats: Simple Perfusion.*—Five animals were used, two during amytal anesthesia and three during ether-morphine anesthesia. Fourteen injections were made with doses of epinephrine ranging from 1 cc. of a 1 : 500,000 solution to 1 cc. of a 1 : 10,000 solution. The result in thirteen cases was a decrease in blood volume. In only one instance was there

no change. The range of decrease varied from 10 to 60 per cent, and the average decrease was 41.8 per cent.

Comment.—The first series of experiments shows a consistent and significant decrease in the minute volume of blood perfused into the internal carotid artery. In most cases there was a rise in systemic blood pressure due to the epinephrine. In the second series of experiments there was a good correlation between a decrease in the minute blood volume and the observed constriction of the pial artery. The third group of experiments shows a significant decrease in blood volume flow after epinephrine. These results point definitely to the fact that in these experiments epinephrine caused a decrease in blood volume flow, owing to a decrease in the vascular bed in the vessels of the pia and parenchyma of the brain.

CAFFEINE

We also performed a series of experiments testing the effect of caffeine on the blood volume perfused into the carotid at a constant

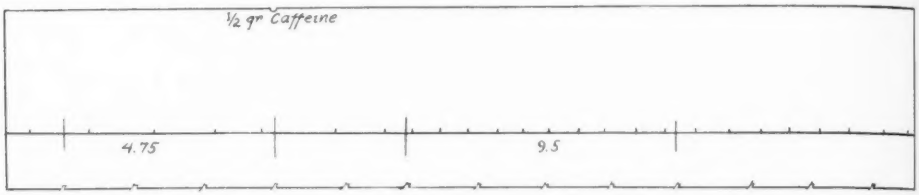

Fig. 6.—Effect of caffeine sodiobenzoate. An increase of blood volume at constant perfusion pressure following the intracarotid injection of one-half grain of caffeine sodiobenzoate (12 mg. of caffeine per kilogram) during ether-morphine anesthesia.

pressure. The literature on the effect of caffeine on the blood vessels of the brain has been summarized elsewhere.[12] It was found that during amytal anesthesia caffeine caused a marked dilation in the pial artery, a transient drop in blood pressure and an increase in cerebrospinal fluid pressure. After ether anesthesia, caffeine caused a slight preliminary transient constriction followed by a marked dilation of the pial artery. In these experiments we tested the effect of caffeine, as caffeine sodiobenzoate, on the volume of blood pumped into the carotid artery.

I. *Monkeys.*—Four monkeys, under morphine anesthesia, were used in these experiments. Caffeine sodiobenzoate was injected eight times in doses varying from 3 to 10 mg. of caffeine per kilogram of body weight. In all eight cases there was a marked increase in minute volume flow, ranging from 31 to 320 per cent, the average being an increase

12. Finesinger, J. E.: Cerebral Circulation: XVIII. Effect of Caffeine on Cerebral Vessels, Arch. Neurol. & Psychiat. **28**:1290 (Dec.) 1932.

of 116 per cent. In some cases there was a transient drop in systemic blood pressure, and in all cases characteristic respiratory changes occurred.

II. *Cats: Combined Technic.*—In this series, six cats were used, and caffeine sodiobenzoate was introduced in ten instances. In all cases there was an increase in blood volume concomitant with a dilation in the diameter of the pial artery. The range of percentage increase in volume was from 37 to 150, the average being 97. The range in percentage dilation of the pial artery was from 7 to 36, the average being 18. No definite correlation could be made out between the dose given, the change in volume flow and the arterial change.

III. *Cats: Simple Perfusion.*—Nine animals were used, two during amytal anesthesia and seven during ether-morphine anesthesia. In thirteen trials with doses ranging from 4 to 32 mg. per kilogram, an increase in blood volume was found in all cases. The range of percentage increase was from 5 to 268, the average being 81.

Convulsions.—It has been shown [13] that large doses of caffeine during ether-morphine anesthesia cause an acute constriction of the pial artery, followed by a convulsion with subsequent dilation of the artery. Large doses of caffeine were given to six cats. In all cases there was a marked slowing down in blood volume, in some an absolute shut-down for as long as from twenty to twenty-five seconds, followed by a typical caffeine convulsion. In one animal there was a series of convulsions, each one preceded by a period during which the volume had been considerably reduced. These findings are consistent with the direct observations on the diameter of the pial artery during experimental caffeine convulsions.

Comment.—Our experiments all consistently point to the fact that, during ether-morphine anesthesia and during amytal anesthesia, small and moderate doses of caffeine sodiobenzoate cause an increase in blood volume perfused per minute through the carotid artery at a constant pressure head. In the experiments on monkeys in which the internal carotid alone was perfused, the percentage of change is not as great as in the simple perfusion experiments on cats, in which we were recording the changes in the brain, face, tongue and neck. That these changes in volume per minute could be passive changes secondary to changes in systemic pressure is out of the question, because the carotid pressure level was always constant throughout an experiment. These changes in blood flow were due to an increase in the vascular bed in the pia and parenchyma—a vasodilation. In a previous study caffeine was found not only to dilate the pial vessels but also to cause an increase in blood velocity in the arterioles entering the parenchyma and in the venules

13. Finesinger, J. E.: Unpublished data.

coming out of the parenchyma. This led to the inference that the deep vessels in the parenchyma dilated as well. Our perfusion and combined experiments indicate that this is true, that the vessels throughout the whole pia and parenchyma react in the same general direction. Accompanying the results of the experiments on monkeys and the combined experiments on cats with the simple perfusion experiments on cats, it is obvious that there is an increase in blood volume when the brain alone is perfused as well as when the entire head is perfused. These varied types of experiments would lead us to believe that caffeine causes the same type of vascular reaction in the vessels of the pia and parenchyma and the head end of the animal. The direction of the change demonstrated by these experiments is in keeping with the results of most investigators studying vascular response to caffeine elsewhere in the body.

HISTAMINE

The importance of histamine has been recognized by physiologists as well as clinicians. In cats, Forbes, Wolff and Cobb[14] showed that, during amytal anesthesia, histamine brought about a marked dilation of the pial arteries. During ether anesthesia, when the pial vessels were initially dilated by the anesthesia, histamine caused little if any dilation and often an actual constriction. In man the intravenous injection of histamine causes flushing of the face, headache, throbbing,[15] a rise in cerebrospinal fluid pressure[16] and an increase in the volume of the brain.

We have performed experiments testing the effect of histamine on the perfused minute volume. In two monkeys, during morphine anesthesia, a 0.5 cc. of a 1 : 100,000 solution and 1 cc. of a 1 : 40,000 solution of histamine caused an increase in minute volume of 13 and 170 per cent. There was a marked drop of systemic blood pressure in each case. Three combined experiments in cats during ether-morphine anesthesia, using 1 cc. of a 1 : 100,000 solution showed a small increase in blood volume per minute, averaging 5 per cent, and a concomitant dilation of the pial artery in two instances, averaging 9 per cent. The changes were not great, but they were definite and in the same general direction. Simple perfusion of the head was done in five animals, using histamine ten times in doses ranging from 1 cc. of a 1 : 100,000 solution to 1 cc. of a 1 : 10,000 solution. In seven cases there was an increase in blood flow, ranging from 7 to 109 per cent. The average increase was 47 per cent. In one case there was a decrease in minute blood volume of 14 per cent, and in two

14. Forbes, H. S.; Wolff, H. G., and Cobb, S.: Am. J. Physiol. **89**:266, 1929.
15. Harmer, I. M., and Harris, K. E.: Heart **13**:281, 1926.
16. Weiss, S., and Lennox, W. G., quoted by Forbes, Wolff and Cobb.[14]

cases there was no change. In most of the cases there was a transient drop in systemic blood pressure, and the carotid pressure was maintained at a constant level.

Most of these experiments show that the introduction of histamine in varying doses brought about an increase in minute blood volume. The change in the two experiments on monkeys, which we consider most accurate, is definite. The percentage of change in the combined experiments is not great. In the combined experiments considerably more ether had to be administered because two experimental procedures had to be undertaken. It may be that in these animals the ether effect had not worn off completely, and the vessels were still dilated from the ether. Forbes, Wolff and Cobb [14] showed that during ether anesthesia histamine caused little if any dilation. The slight changes recorded might be due to the fact that in the combined experiments the animals were still under light ether anesthesia. The simple perfusion experiments in general support the view that histamine causes an increase in minute blood volume. The results of these experiments are in keeping with the results of other investigators.

PITRESSIN

We performed one experiment on monkeys using pitressin, the vasopressor component of pituitary. In this experiment, 0.5 cc. of pitressin gave a decrease in minute volume of 40 per cent. In a combined experiment, injection of 0.5 cc. of pitressin resulted in a decrease in minute volume of 19 per cent and a constriction of the pial artery of 8 per cent. In five simple perfusion experiments on five cats, during ether-morphine anesthesia, doses of from 0.25 cc. to 0.5 cc. of pitressin gave a decrease in minute volume in four cases. The range was from 6 to 26 per cent, the average being 18 per cent. In one case there was no change.

ADDITIONAL SIMPLE PERFUSION EXPERIMENTS

In addition to the experiments presented, many simple perfusion experiments were done under various conditions during amytal and ether-morphine anesthesia. In these cases, as already described, perfusion of the cat's own blood was done through one common carotid after both vertebrals and the other common carotid had been tied and the carotid pressure was higher than the animal's systemic pressure. Obviously this is a perfusion of the head end of the animal and not of the pia or parenchyma alone. These results are interesting to us only so far as they allow comparisons to be made with other studies when direct observations were made on the diameter of the pial artery. The results are presented in the accompanying table.

EFFECT OF CHANGES IN CAROTID PRESSURE

According to the observations of Schmidt,[7] variations in carotid blood pressure are of great importance in determining the rate of flow through the cerebral vascular bed. We also found that there were wide variations in flow as a result of changes of pressure. Specific observations were made in four monkeys, and it will be seen from figure 7 that variations of pressure within physiologic limits (between 80 and 220 mm. of mercury) caused changes in flow several hundred per cent greater than the changes produced by any of the other procedures employed.

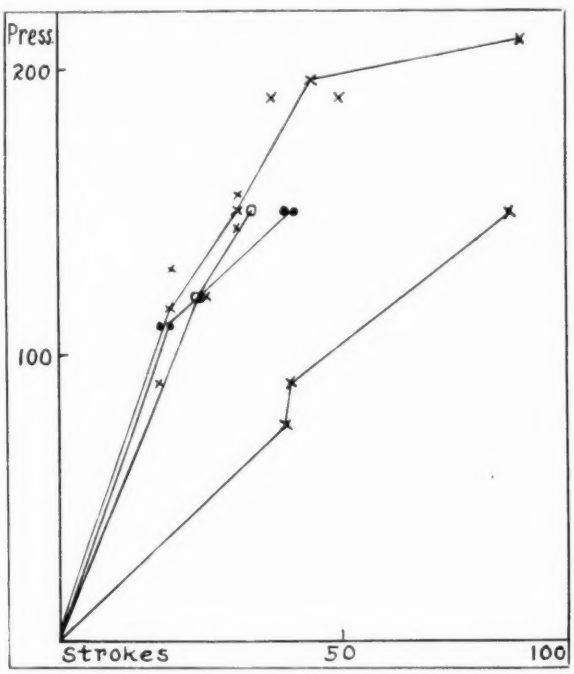

Fig. 7.—Effect of variations in carotid blood pressure on the rate of flow (in strokes per minute) in four experiments on monkeys.

Effect of Various Agents on Minute Volume Flow in Simple Perfusion Experiments in Cats During Amytal and Ether-Morphine Anesthesia

Procedure	Number of Animals	Number of Trials	Result	Average Change, per Cent
Ammonium sulphate	1	3	Increase	+ 8
Ephedrine hydrochloride	2	2	Decrease	—19
Ergotamine	1	2	Increase	+40
Stimulation of femoral nerve	1	4	Increase	+16
Glyceryl trinitrate	1	2	Increase	+70
Pilocarpine	2	3	Increase	+ 9
Solution of pituitary	2	2	Decrease	—29
Increase in carbon dioxide	1	1	Increase	+70
Decrease in carbon dioxide	1	1	Decrease	—30
Increase in oxygen	1	1	Increase	+ 7
Decrease in oxygen	1	1	Decrease	—10
Barium chloride crystals (sympathetic)	1	1	Decrease	—25
Barium chloride crystals (vagus)	1	1	Increase	+ 9

GENERAL COMMENT

Since the work of Bayliss and Hill, many investigators have stressed the idea that changes in the caliber of cerebral vessels are determined by changes in the aortic pressure. It has been assumed that the vasomotor nerves either were not present or were ineffectual in acting as an independent regulating mechanism. Schmidt [7] stated that in ordinary laboratory animals he has been able to show that changes in blood volume, as reflected by measured changes in venous return, are dependent on the systemic blood pressure level. Forbes and Wolff demonstrated significant changes in the diameter of pial arteries which seemed independent of the systemic blood pressure. They observed dilation of the pial artery on stimulating the vagus even when the systemic arterial pressure fell slightly. Cobb and Finesinger [17] showed that dilation of the pial artery occurred when the peripheral end of the seventh nerve, cut close to the medulla, was stimulated. This occurred often without a change in systemic arterial pressure. The recent anatomic work of Penfield demonstrated the presence of vascular nerves, and the physiologic studies already mentioned seem to indicate that there are significant changes in the pial vessels independent of blood pressure and respiratory changes.

We attempted to rule out the possibility of these so-called passive changes by interrupting the circulation between the brain and the rest of the animal. By our technic we were able to substitute the constant blood perfusion pressure for the normal aortic arterial pressure. In other words, during these experiments blood was pumped into the carotids at a constant pressure when the arterial supply, excepting that of the anterior spinal artery, had been tied off. No systemic change in aortic blood pressure due to vagus or sympathetic stimulation could in any way affect the pressure at which perfusion blood was pumped into the animal's head. In many preliminary experiments varied carotid perfusion pressures were tried. Of course, the minute volume increased as the perfusion pressure was elevated. During the actual experimentation the carotid perfusion pressure was kept constant, and in most cases was a little higher than the systemic aortic pressure of the animal to minimize the amount of blood which could enter through the anterior spinal arteries.

Hence we believe that in our experiments on monkeys the results of sympathetic and vagus stimulations are significant. These recorded changes in minute blood volume cannot be explained on the basis of

17. Cobb, S., and Finesinger, J. E.: Cerebral Circulation: XIX. The Vagal Pathway of the Vasodilator Impulses, Arch. Neurol. & Psychiat. **28**:1244 (Dec.) 1932.

their being passive to changes in systemic arterial pressure because in all cases the carotid perfusion pressure was absolutely and constantly controlled. We believe that the experiments on sympathetic and vagus stimulation in monkeys illustrate the independence of the vasomotor mechanisms from the systemic aortic pressure. These results also enable us to speak in terms of blood volume per minute resulting from sympathetic and vagus stimulation, whereas the previous work in this laboratory was reported in terms of changes in pial vessel diameter. Whereas the work of Forbes and Wolff was open to the criticism that some of the changes in the vessels might be due to changes in the animal's aortic pressure, these experiments are free from that particular criticism.

In all of the work done with the Forbes window, observations were made on the diameter of the pial arteries and pial veins and the rate of flow of blood within the arteries, arterioles, venules and veins. It was impossible to make any direct observations on the blood vessels of the parenchyma of the brain. In these experiments data are presented in regard to the minute blood flow throughout the whole brain. Gelatin-india ink mixtures perfused through the internal carotid in monkeys after the experiments had been completed showed definitely that all the blood vessels—those in the pia as well as those in the parenchyma—had been reached. As a result of this we believe that we were measuring changes in the vascular bed both of the pia and of the parenchyma. This fact brings added significance to our results.

In these experiments we were measuring changes in blood volume perfused per minute into one internal carotid in monkeys and into one carotid in cats at a constant pressure. In the case of cervical sympathetic stimulation the blood volume per minute decreased. During vagus stimulation the blood volume per minute increased. These changes were due to changes in peripheral resistance encountered by the perfused blood. In some experiments the cerebrospinal fluid pressures were read, and their variations were those described previously in the studies on pial diameter. As a rule, the spinal fluid pressure rose when the flow increased and fell when the flow decreased, which was parallel to the finding in the window experiments, that as a rule the cerebrospinal fluid pressure rose when the pial artery dilated and fell when the pial artery was constricted. The magnitude of these variations in the cerebrospinal fluid pressure could have influenced the peripheral resistance very little.[18] We took no measurements of intracranial venous pressure in these expeiments. Forbes and Wolff [19] measured the venous

18. Wolff, H. G., and Forbes, H.: Cerebral Circulation: V. Observations of the Pial Circulation During Changes in Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1035 (Nov.) 1928.

19. Forbes, H. S., and Wolff, H.: Cerebral Circulation: III. Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

pressure in the sagittal sinus on stimulating the sympathetic and vagus. They found a slight increase of pressure amounting to 4 mm. of water when the pial artery was dilated. Spontaneous changes of the same magnitude were recorded without any change in the pial artery. More recently, Forbes [20] reported no change in the diameter of the pial artery on marked changes in the systemic venous pressure. Loman and Myerson [21] reported an increase in venous pressure in the internal jugular vein in man on the intravenous administration of epinephrine. They believed that this increase was due to an abrupt rise in blood pressure following the administration of epinephrine. The intracranial changes in venous pressure during these experimental procedures have not been thoroughly investigated. The experimental data at hand indicate that changes in intracranial venous pressure could not have been responsible for the changes recorded in our experiments. The temperature of the blood was constant during each experiment. We had no occasion to believe that there were sudden viscosity or chemical changes in the perfused blood owing to mechanical artefacts or to respiratory changes during the process of an experiment. Hence, we were forced to the conclusion that the changes in peripheral resistance were due to changes in size of the vascular bed and changes in the size of the arteries, arterioles and capillaries and most likely of the veins and venules. Whenever the minute volume decreased there must have been a constriction in the size of the perfused arterial vessels in the pia and parenchyma, and whenever there was an increase in blood volume there was an increase in size or dilation of the perfused blood vessels. This was found to be true in the series of combined experiments on cats in most of which we observed that the blood volume increased concomitantly with a dilation of the pial artery and decreased concomitantly with a constriction of the pial artery. The same relationship between changes in minute volume and arterial size must have been true for the vessels of the parenchyma.

We were interested in comparing our results with those in the window experiments. On stimulation of the cervical sympathetic, Forbes and Wolff reported arterial constriction, while stimulation of the vagus caused dilation of the pial arteries. Our experiments on monkeys showed a decrease in minute blood volume on stimulation of the cervical sympathetic and an increase in blood volume per minute on stimulation of the vagus. In the window experiments, epinephrine locally caused constriction of arteries but not of capillaries; when injected into the left carotid, it usually caused a dilation, and dilation was usually found to

20. Forbes, H. S.: Personal communication to the authors.

21. Loman, J., and Myerson, A.: The Action of Certain Drugs on the Cerebrospinal Fluid and on the Internal Jugular Venous and Systemic Arterial Pressures of Man, Arch. Neurol. & Psychiat. **27**:1216 (May) 1932.

occur when epinephrine was injected intravenously, probably as a result of a rise of blood pressure. Caffeine, in small and moderate doses, and histamine caused dilation of the pial artery. In our experiments, epinephrine in all cases caused a decrease in minute volume, and caffeine and histamine caused an increase in minute volume flow. In our combined experiments an increase in minute volume was associated with dilation of the pial artery, and a decrease in minute volume was associated with a constriction of the pial artery.

It is also of interest to compare the quantitative change resulting from the various procedures. In our experiments on monkeys, when one internal carotid artery was perfused the average decrease in minute volume due to sympathetic stimulation was 15 per cent, while the average increase due to vagus stimulation was 7.5 per cent. In summarizing the effect of sympathetic and vagus stimulation on the pial artery, Cobb and Finesinger [17] mentioned that the average sympathetic decrease was 8.03 per cent and the average vagus dilation 15 per cent. According to Poiseuille's law, we should expect a much greater increase in per cent of minute volume flow than our results indicate. It is highly possible that our results offer evidence to support the idea that vessels down deep in the parenchyma do not react as actively as do the vessels in the pia. In other words, changes independent of the systemic arterial pressure take place in the size of the vessels in the parenchyma of the brain, but these changes are not as great in magnitude as the changes observed in the vessels of the pia. In this respect our results agree with those of Bayliss and Hill so far as their magnitude is concerned.

It has been our experience that the chemical mechanisms controlling cerebral blood flow are more powerful in causing changes than the vasomotor mechanisms. In our experiments on monkeys, epinephrine caused an average decrease of 31 per cent, caffeine an average increase of 116 per cent and histamine an average increase of 47 per cent. These changes are much greater than those resulting from stimulating the nerve-controlled mechanisms. The largest percentage changes resulted from alterations in blood pressure. A comparison of the results of our experiments on monkeys when the internal carotid was perfused with the results of the experiments on cats when the common carotid was perfused shows that vagus and sympathetic stimulation, epinephrine and histamine gave a much greater change in the experiments on the cats. The percentage change in minute volume flow was greater when all the vessels of the head and of the animal were perfused than when the internal carotid alone was used. This would indicate to us that the vessels supplying the facial muscles, skin, tongue and neck reacted more effectively than did the vessels of the pia and parenchyma. The combination of these results suggest that there may be a differential reactivity of these various blood vessels, those of the face, neck, tongue and muscles

reacting more actively than those of the pia, which in turn react more effectively than those supplying the parenchyma of the brain. This seems true in the experiments with sympathetic and vagus stimulation and with epinephrine and histamine. Caffeine seems to be exceptional in this respect.

SUMMARY

1. Experiments are described recording changes in minute volume of blood perfused through the internal carotid artery in monkeys.

2. Stimulation of the cervical sympathetic caused a decrease in minute volume flow of blood perfused through the internal carotid artery in monkeys during ether-morphine anesthesia. The perfusion method combined with the cranial window technic in cats showed that a decrease in minute volume flow was associated with a constriction of the pial artery.

3. Stimulation of the central and of the vagus caused an increase in the minute volume flow of heparinized blood perfused through the internal carotid artery in monkeys during morphine anesthesia.

4. Intracarotid injection of epinephrine resulted in a decrease in minute volume cerebral flow in monkeys. In combined experiments on cats this decrease in minute volume flow was associated with a decrease in the diameter of the pial artery.

5. Intracarotid injection of caffeine sodiobenzoate resulted in an increase in minute volume cerebral flow in monkeys. In combined experiments on cats this increase in minute volume was associated with an increase in the diameter of the pial artery.

6. Intracarotid injection of histamine resulted in an increase in the minute volume cerebral flow in monkeys. In experiments on cats this increase in minute volume was associated with an increase in the diameter of the pial artery.

7. Pitressin caused a decrease in the minute volume cerebral flow in a monkey.

8. Data are presented which indicate that the vessels of the parenchyma as well as those of the pia are subject to vasomotor and chemical control, irrespective of the systemic blood pressure.

9. Data are presented which suggest that in monkeys the blood vessels of the face, neck and tongue react more effectively to nerve stimuli and to drugs than do the vessels of the pia, which in turn react more effectively than do the vessels supplying the parenchyma of the brain, but all qualitatively in the same direction.

10. Variations in carotid pressure within physiologic limits were more effective in altering the rate of flow than any of the neural or chemical stimuli employed in this investigation.

DISCUSSION

Dr. W. Penfield, Montreal, Canada: This is an important contribution in that it shows that the dilatations and constrictions of the pial vessels, which have previously been proved by microscopic inspection after direct stimulation, really indicate a decrease in the blood flow through the brain, a conclusion not completely justified by the previous work.

Dr. Finesinger speaks of the fact that epinephrine, pituitary and ephedrine produce a decreased flow through the brain which is isolated in this particular experiment, but those drugs can act only in the intact organism, when they act on the rest of the body as well as on the brain. The nerves may act separately on the brain, but the drugs cannot. Is the same true with an intact animal? Does epinephrine then cause a decrease in flow through the brain?

Dr. Jacob Finesinger, Boston: It does not necessarily follow; it may well be that epinephrine in acting on the blood pressure, for example, may cause one effect to take place through the brain. On the other hand, epinephrine acting on the vessels of the brain may be the cause of another effect. In the intact animal, these results do not necessarily hold true. Forbes has recently shown that epinephrine causes a dilation in the pial vessels; he thinks that this is secondary to changes in the blood pressure.

MEGALENCEPHALY WITH DIFFUSE GLIOBLASTOMATOSIS OF THE BRAIN STEM AND THE CEREBELLUM

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"Megalencephaly is the enlargement of the brain without changes in its outer configuration and with a proportional increase of all its diameters" (Fletscher, von Hansemann). This condition may represent a true hypertrophy, an increase in the size of all the different neurons and neuroglial elements, or it may be a hyperplasia, an increase in the number of neurons and neuroglia. The latter condition, since Virchow, has been subdivided into true hyperplasia—an increase of neurons and neuroglia—and interstitial hyperplasia—an increase of neuroglia alone. If the hyperplasia of glial elements exceeds the normal bounds and spreads diffusely throughout the brain tissues, the interstitial hyperplasia becomes a diffuse glioblastomatosis (pseudohypertrophy, diffuse gliosis). French authors refer to Calmeil's division, "hypertrophies cérébrales simples par hypernutrition" and "processus hypertrophiques pathologiques."

If one reviews the literature on this subject,[1] one finds that most of the cases of megalencephaly that have been reported belong to the group of the interstitial hyperplasias. In no case has true hyperplasia with an increase in the number of neurons and glia cells been proved by exact measuring and counting of the different nerve elements in a well defined region and by comparing them with modern standards of cyto-architecture.

Only a few cases are recognized as instances of genuine hypertrophy, e. g., by Marburg,[2] the cases reported by Brouardel (brain of Tur-

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From the Institute of Neurology, Northwestern University Medical School.
Read before the Chicago Neurological Society, Nov. 17, 1932.

1. An index of literature may be found in the following more recent publications: Peter, K., and Schlueter, K.: Ueber Megalencephalie als Grundlage der Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:21, 1927; Schob, F.: Pathologische Anatomie der Idiotie, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11, pt. 7.

2. Marburg, O.: Hypertrophie, Hyperplasie und Pseudohypertrophie des Gehirns, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **13**:288, 1906.

genjeff), Variot,[3] Tsiminakis[4] and Haberlin.[5] But on closer analysis of even these few cases one will find that in none of them has the question been definitively answered as to whether the hypertrophy was due to an increase in size of all the nerve elements, or whether only interstitial hypertrophy, hypertrophy of the neuroglia, was responsible for the increase in size of the total brain.

Variot described the brain of a child, aged 16 months, which weighed 1,630 Gm. The outer appearance of the cerebral convolutions was somewhat irregular, especially in the central region. The occipitoparietal region seemed to be more enlarged than the frontal region. No histologic report was given. Tsiminakis reported the case of a child who had been born with a large head that gradually increased in size. The child developed normally up to the age of 3 years. Then periods of severe headache began, lasting until death, which followed scarlatina at the age of 8. The weight of the brain was 1,920 Gm. Tsiminakis reported that "the cyto-architecture of the cortex seems not to have suffered. The cells are of normal appearance. A marked increase or diminution cannot be demonstrated. Measurements of the pyramidal cells showed that their size had increased proportionally to the increase in the size of the brain." No detailed figures are published. Haberlin described the brain of a child, aged 2 years, who since the age of 3 months had shown a "disproportionate increase in the size of the head." The weight of the brain was 1,712 Gm., but no histologic examination was reported.

Marburg himself reported the case of a woman, aged 39, who had developed normally but who suffered from left hemiplegia five months before death. Bulbar symptoms, which appeared gradually, were added finally to the clinical picture. The weight of the brain is not given. The brain stem was enlarged in toto, with a more marked increase of the left side. The increase in size was due mainly to a proliferation of interstitial glia nuclei, which in places presented glioblastoma-like pictures. In addition, there seemed to be true hypertrophy of myelin sheaths and ganglion cells. "In the pyramidal tracts there were found, besides normal fibers, others which have a very thick myelin sheath. One also is able to demonstrate, by micrometric measurements of the cells of the hypoglossus nucleus, that their size in the average is one-third larger than normal. . . . In the cerebral cortex the myelinated fibers are prominent so much that one might speak here, too, of hypertrophy."

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3. Variot, G.: Hypertrophie simple du cerveau simulant l'hydrocéphalie chez un enfant de seize mois, Bull. et mém. Soc. méd. d. hôp. de Paris **19**:20, 1902.

4. Tsiminakis, K.: Zur Kenntnis der reinen Hypertrophie des Gehirns, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **9**:169, 1902.

5. Haberlin, J. H.: A Case of Hypertrophy of the Brain, J. A. M. A. **46**: 1988 (June 30) 1906.

The following case is reported because it presents, like Marburg's case, a combination of interstitial hyperplasia with diffuse glioblastomatosis and interstitial hypertrophy, demonstrating the intimate relationship between these different processes.

REPORT OF CASE

History (Dr. C. A. Aldrich).—The patient, a boy, seemed to be normal at birth and weighed 3,700 Gm. He grew up to be an intelligent child and showed no signs of an organic nervous defect. It was noticed, however, that his head was larger than that of other boys of his age (at death the parietal diameter was 15 cm. and the occipitofrontal diameter was 19 cm.). An elder brother has a head the size of which, according to the statement of his physician, is "at the upper limits of normal." The latter is now well developed at the age of 12.

The patient was first seen by the physician at the age of 6 years and 4 months (in October, 1931). His height was then 124 cm. (49 inches), and his weight was 25 Kg. (55 pounds), figures which are somewhat higher than those for the average boy of that age. The parents said that he had been less active recently, did not like to play, drooled, and slurred his words. Four weeks later the patient had several attacks of early morning vomiting, his gait became staggering, his speech became more slurred, and mentally he appeared somewhat apathetic. On examination, bilateral strabismus and bilateral nystagmus were found. The tongue deviated to the left. The tendon reflexes were exaggerated, and there was a bilateral Babinski sign, with ankle clonus. Both upper and lower extremities were ataxic; the Romberg sign was positive. Examination of the spinal fluid gave negative results; the blood leukocytes numbered 10,000. At this time a tentative neurologic diagnosis of chronic encephalitis was made. Two weeks later there was a slight improvement in the use of the arms but not in the use of the legs.

The condition remained unchanged for about three months, with remissions and exacerbations of the spasticity of both legs. In January, 1932, an ophthalmologist reported partial paralysis of both external recti. At this time the patient was unable to stand alone, but his mental attitude was described as much brighter. In February severe attacks of vomiting recurred, with difficulty in breathing; speech had become indistinct, and he could hardly talk. Paresis of the left side of the face developed later in the month.

By March the patient was almost inarticulate; the legs continued to show spasticity and were markedly contracted. There was difficulty in swallowing, and feeding by tube was instituted. The left arm had become completely paralyzed. On March 18 a sudden attack with coma was reported, accompanied by irregularity in breathing, violent clonus of the left arm and leg and contraction of the muscles of the left side of the face. Two days later the clonus and the attack of Cheyne-Stokes' respiration had disappeared, and the patient's condition seemed to improve. Two weeks after the first attack, however, a similar attack occurred, which was followed after another week by a third, from which the patient did not recover.

Report of Autopsy (Dr. F. D. Gunn).—There was atrophy of the skeletal muscles, especially of those of the hands; the thenar and hypothenar eminences were practically absent. The chamber of the left ventricle of the heart was somewhat dilated, and a very slight nodular thickening of the free margin of the mitral valve was noted. Microscopically, the fibers of the myocardium were pale and swollen, and the cross-striation was scarcely visible. Many of the nuclei were hypertrophic and hyperchromatic. The pineal gland was normal. In the hypoph-

ysis there was a mild proliferation of chromophobe cells. The medulla of the suprarenal glands was practically devoid of chromaffin tissue. The cortical cells were pale, swollen and finely granular. The right testis was undescended. The pathologic diagnosis was early bronchopneumonia and acute parenchymatous degeneration of the liver and kidneys.

Examination of the Nervous System.—The weight of the brain was 1,856 Gm. (2,010 Gm. after eight days of fixation in solution of formaldehyde). The diameters of the formaldehyde-fixed brain were as follows: diameter from tip of frontal pole to tip of occipital pole, left, 18 cm., right, 18.5 cm.; largest vertical diameter, both right and left, 11.5 cm.; circumference of the brain at the level of the tip

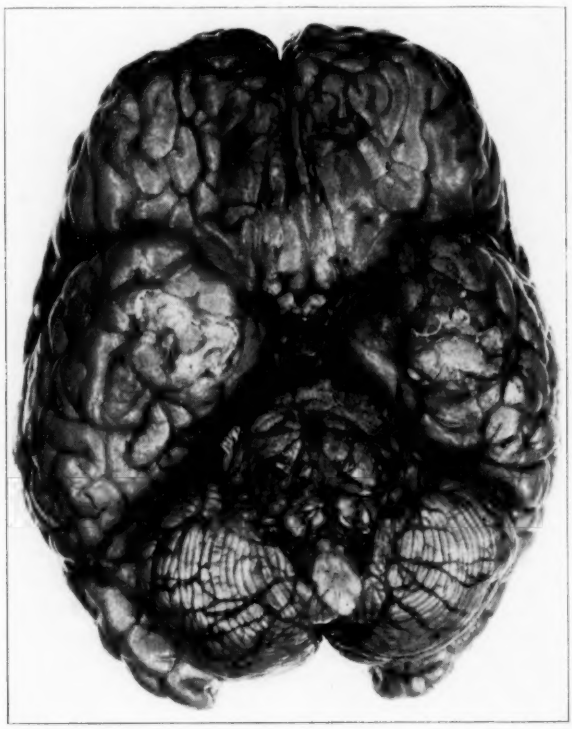

Fig. 1.—Photograph of brain showing the normal configuration of the cerebral cortex and the enlargement of the pons and medulla oblongata.

of the lateral ventricles, 34.5 cm., and at the level of the section through the anterior corpora quadrigemina, 43 cm. (fig. 1).

The pia-arachnoid covering the convexities of the hemispheres was mildly milky in color. The gyri appeared flattened but of normal configuration. There was an irregular bulging of the enlarged pons, with pontile vessels cutting deep fissures into it. The left part of the medulla oblongata seemed to be somewhat enlarged as compared with the right part. When the brain was cut vertically no gross abnormalities were found; the design of the cortical gray matter was normal throughout; that of the thalamus and of the nuclei of the midbrain, however, was indeterminate. After cutting the pons and medulla, with considerable resistance

to the cutting knife, one was impressed by the loss of structural design. In sections the tissue appeared rather homogeneous, without differentiation between gray and white matter. In the right cerebellar hemisphere, replacing the dentate nucleus, was a small, soft area, measuring approximately 1 cm. in diameter.

Microscopic Study.—In sections through the frontal, central, occipital and temporal cortex and the cornu ammonis the cyto-architecture appeared normal in its general outlines, but there seemed to be a uniform reduction in the number of ganglion cells within the microscopic field in comparison with normal slides. There was no increase in the glia nuclei, no marked disease of the ganglion cells, no marked pathologic changes of the myelin sheaths and axis cylinders. In the white matter there was a mild perivascular infiltration by lymphocytes, and in the pia-arachnoid mild edema was found, with some infiltration by smaller and larger round cells and an increase in collagenic fibers of connective tissue in isolated areas.

The corpora striata (the neostriatum as well as the paleostriatum) appeared normal, and the internal capsules were well developed. In sections stained with cresyl violet the different types of ganglion cells were well developed and no increase in glia nuclei was noticed. In various regions of the diencephalon and

Fig. 2.—Section through the medulla oblongata with the brachium pontis and both eighth nerves, showing the extent of demyelinization and destruction of the right brachium pontis by tumor. Weil stain.

the midbrain the outlines of the different nuclei in sections treated with a stain for myelin sheaths could be well recognized, although the peduncles stained somewhat lighter than normal.

In sections through the diencephalon and midbrain stained with cresyl violet, however, one was impressed by the tremendous increase in cellular elements. The whole microscopic field seemed to be densely packed with nuclei, which formed clusters around blood vessels and ganglion cells. The latter were fairly well preserved throughout the thalamic nuclei, in which the increase in cellular elements was less pronounced than in the densely infiltrated nuclei rubres and the substantia nigra. The ganglion cells of the two latter nuclei were somewhat shrunken and had darkly staining, clogged Nissl bodies and a prominent nucleus containing a deeply staining nucleolus.

The number of newly formed cellular elements gradually increased in the more caudal sections and diminished in the frontal sections. A vertical section of the brain just behind the optic chiasm indicated approximately the anterior limit of the glioblastomatosis. In sections through the pons and medulla oblongata stained for myelin sheaths the design of the different tracts had disappeared; both pyramidal tracts were stained the same uniform brown as the rest of the section

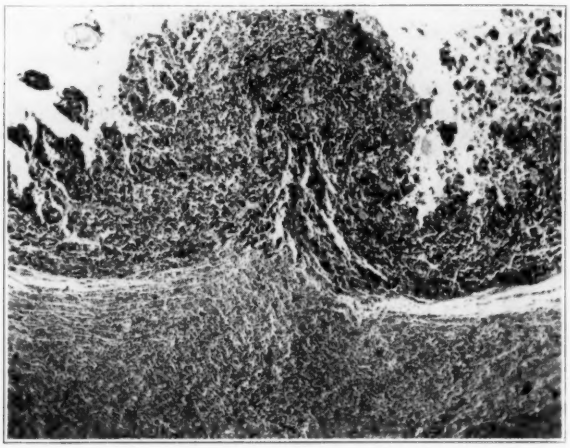

Fig. 3.—Section through the right brachium pontis. Hematoxylin and eosin stain; Leitz obj., 3 ×; ocul., 6 ×.

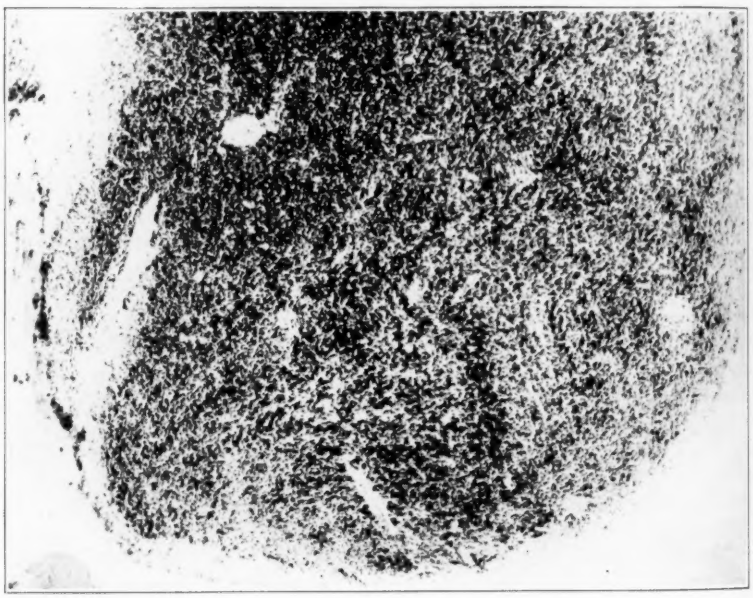

Fig. 4.—Section through the pyramid of the medulla oblongata showing transformation into neoplastic tissue. Cresyl violet stain; Leitz obj., 3 ×; ocul., 6 ×.

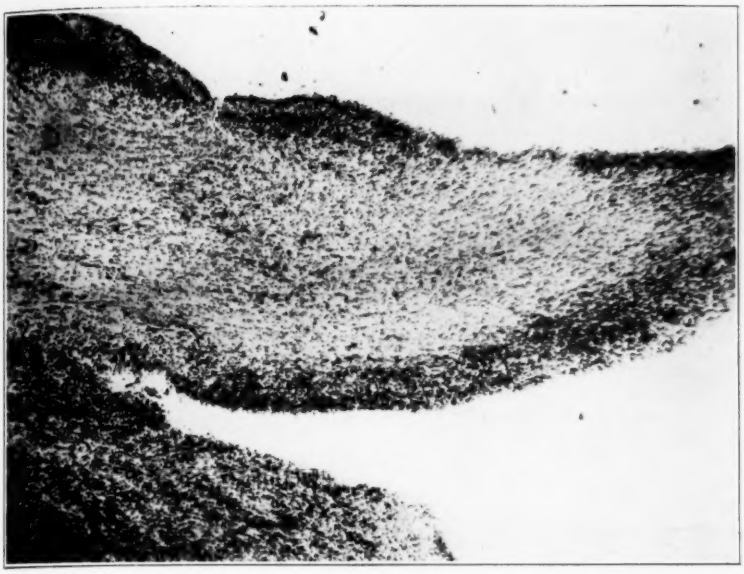

Fig. 5.—Longitudinal section through the root of the eighth nerve showing glioblastomatosis in the periphery of the nerve and in the adjacent medulla oblongata. Cresyl violet stain; Leitz obj., 10 ×; ocul., 10 ×.

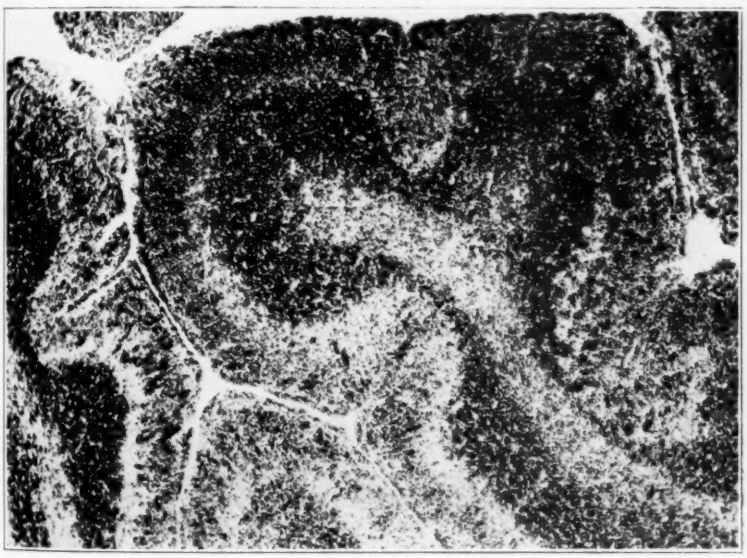

Fig. 6.—Dense infiltration of the outer molecular layer of the cerebellum by neoplastic cells. Cresyl violet stain; Leitz obj., 3 ×; ocul., 6 ×.

(fig. 2). In sections stained with cresyl violet both the pons and the medulla oblongata were densely infiltrated with cellular masses, which had transformed the right brachium pontis into a loose tumor, infiltrating the covering pia-arachnoid (figs. 3 and 4). The roots of the cranial nerves at this level were also involved in the neoplastic process, especially in their outer zones, which were densely infiltrated with newly formed cells (fig. 5).

In the cerebellum the outer molecular zones were mostly involved. In some places the histologic picture resembled that of the cerebellar cortex of a new-born child, with an outer embryonic marginal layer of cells. In other places the whole molecular layer was densely infiltrated with newly formed cells, which formed clusters around Purkinje cells (fig. 6). The white matter of the cerebellum was less involved in the neoplastic process, although it was not spared. The softened focus already described was a tumor-like accumulation of newly formed cells. In

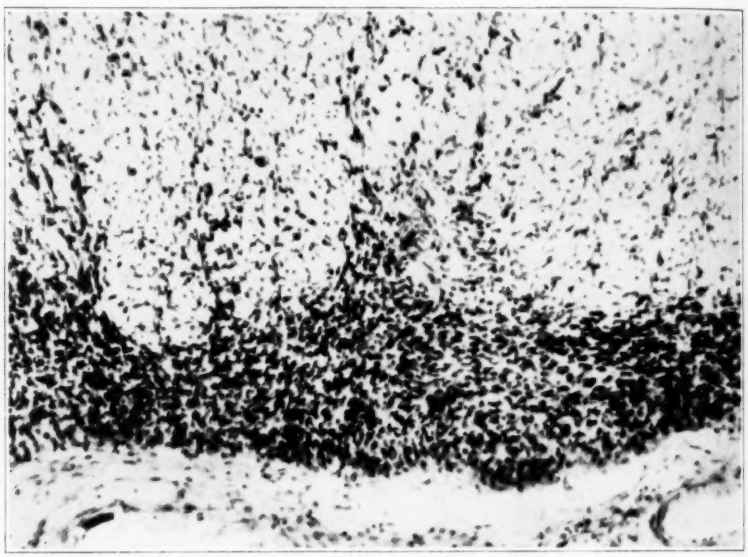

Fig. 7.—Transverse section through the first cervical segment of the spinal cord showing the dense infiltration of the outer zone by neoplastic cells. Cresyl violet stain; Leitz obj., 10 ×; ocul., 10 ×.

the pons isolated foci of intense perivascular infiltration by small round cells were seen. The basilar artery showed marked intimal proliferation, in contrast to the other cerebral arteries.

In sections through the lower end of the medulla oblongata and the upper part of the cervical spinal cord the infiltration by neoplastic cells subsided gradually and was confined to the posterior gray matter and the outer marginal zone, involving the proximal parts of the roots of the spinal nerves (fig. 7).

Throughout the area infiltrated by neoplastic cells the ganglion cells had been well preserved. In areas in which the myelin sheaths had preserved their staining qualities they appeared to be pushed aside by the proliferated interfascicular glia, showing swelling and fragmentation. The axis cylinders in sections stained by the Bielschowsky method seemed somewhat better preserved.

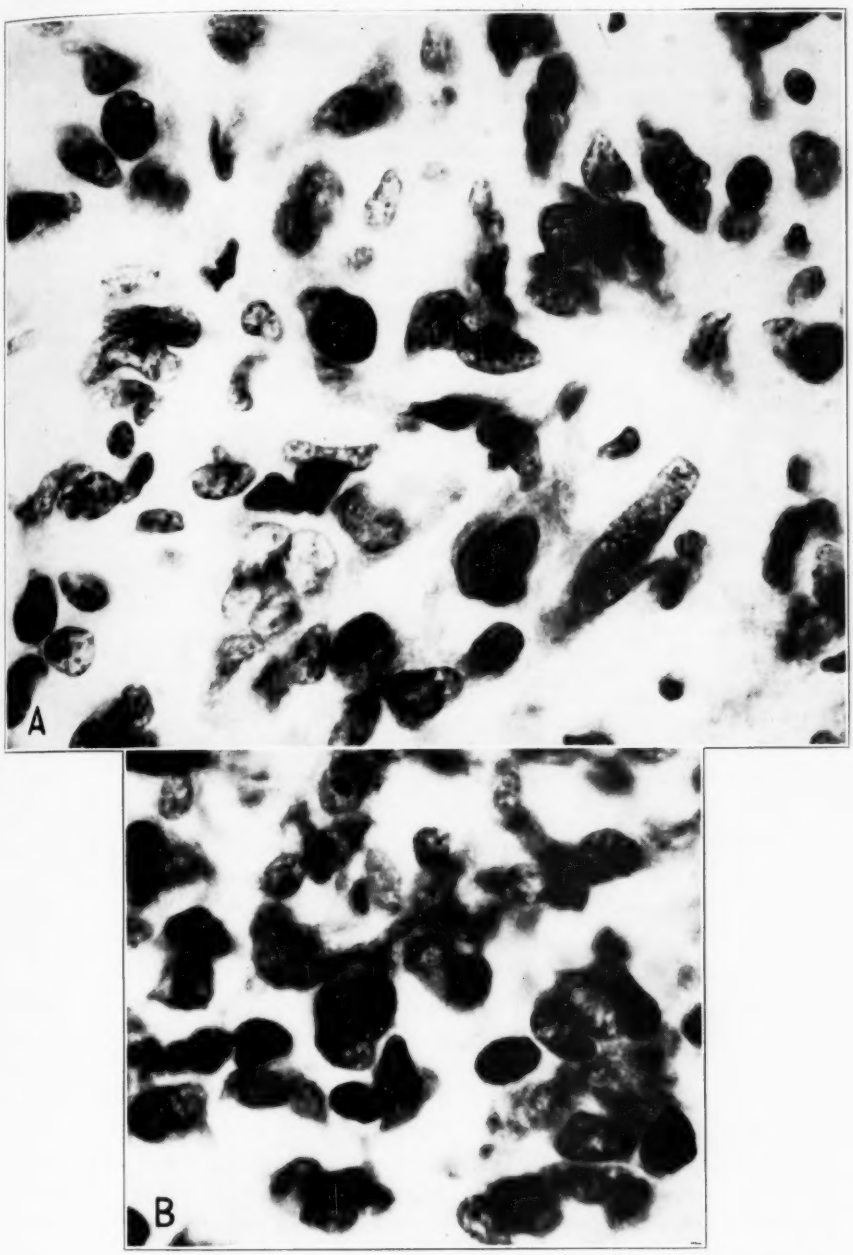

Fig. 8.—Polymorphous appearance of the neoplastic nuclei of the medulla oblongata. Zeiss obj., 3 mm. ap.; ocul., 10 × comp. *A*, cresyl violet stain; *B*, Davenport stain.

Detailed study of the neoplastic cells under higher magnification was made in sections stained by various methods. In preparations stained with cresyl violet the nuclei appeared either round or slightly oval and measured from 6 to 9 microns, or they were arranged as long, oval or spindle-shaped forms in long, streaming chains and measured from 10 to 15 microns in length and from 2.5 to 3 microns in transverse diameter. Frequently four or more nuclei were seen clustered together and surrounded by a common cytoplasm. The nuclei contained coarse granules of chromatin. The cytoplasm did not stain well with cresyl violet, but when stained with eosin, orange G or trinitrophenol it was well defined, surrounding the nucleus in a small zone and assuming round and oval forms. With different methods of silver impregnation (Cajal's gold sublimate method, the pyridine-silver method, Kanzler's modification of the del Rio Hortega method and the Stern and Bielschowsky methods) no cellular processes could be demonstrated. Only occasionally a neoplastic cell was seen with a short, tail-like broad extension of the cytoplasm (fig. 8).

COMMENT

The increase in the size of the pons, the medulla oblongata, the midbrain and the thalamus can be well explained by the diffuse glio-

TABLE 1.—*Comparison of Cortical Measurements Made on Sections of the Brain in Present Case with Those Given as Standard for Corresponding Sections of the Brains of Adults by Other Investigators*

		Cortical Thickness of the Crowns of the Gyri in Mm.					
	Area	Frontal			Temporal		Occipital
	Investigator	A	B	D	A	B	A
1	von Economo and Koskinas	4.5-3.5	4.0-3.2	3.0-2.4	3.0-2.8	3.0-2.9	2.6-2.3
2	Elliot Smith	4.0	3.0	2.5	3.0	3.0	—
3	Weil	4.2	4.3	3.7	4.1	3.6	3.8
	Difference between 2 and 3	+5%	+43%	+48%	+37%	+20%	—

blastomatosis, but the enlargement of the cerebral hemispheres and the corpora striata cannot be explained by such a neoplastic process.

Measurements of the cortical gray matter proved that it was definitively enlarged. The measurements given in table 1 were made from sections of the brain after fixation in formaldehyde. They were compared with the corresponding figures given by von Economo and Koskinas [6] for paraffin sections and by Elliot Smith [7] for formaldehyde-fixed sections from adult brains.

These figures indicate an increase in thickness of the frontal cortex of about 45 per cent, and of the temporal cortex of about 30 per cent. There was, however, no increase in glia nuclei as compared with sections from normal human brains, and the number of ganglion cells seemed to be less in a given microscopic field. In order to obtain

6. von Economo, C. F., and Koskinas, G. N.: Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen, Berlin, Julius Springer, 1925.

7. Smith, G. Elliot: A New Topographical Survey of the Human Cerebral Cortex, J. Anat. & Physiol. **41**:237, 1906.

figures for comparison in paraffin sections stained with cresyl violet, the number of ganglion cells of the different laminae was counted with the help of a squared ocular micrometer, and the average of twenty different squares in each lamina was calculated. Tables 2 and 3 give a comparison of the standards of von Economo and Koskinas

TABLE 2.—*Comparison of Numbers of Ganglion Cells in Present Case with Standards Recorded by von Economo and Koskinas*

		Number of Ganglion Cells per 0.1 Sq. Mm. of Lamina				
Case	Area	III (II)	III a	III c	V	VI a
von Economo and Koskinas	Frontal B	65	30	25	25	24
Weil	Frontal B	35	19	18	21	17
Difference		—46%	—37%	—28%	—16%	—20%
		III a	III b	V		VI
von Economo and Koskinas	Frontal A	30	29	16		25
Weil	Frontal A	11	12	11		10
Difference		—63%	—59%	—31%		—20%

TABLE 3.—*Comparison of Width of Laminae in Present Case with Standards Recorded by von Economo and Koskinas*

		Width of Lamina in Percentage of Total Cortex			
Case	Area	I	III	V	VI
von Economo and Koskinas	Frontal B	7	33	25	35
Weil	Frontal B	12	31	26	31
von Economo and Koskinas	Frontal A	5	40	22	33
Weil	Frontal A	8	45	15	32

TABLE 4.—*Comparison of Size of Ganglion Cells in Present Case with Standards Recorded by von Economo and Koskinas*

		Size of Cells in Lamina in Microns					
Case	Area	III (II)	III a	III b	III c	V	VI a
von Economo and Koskinas	Frontal B	7/8	17/12	30/15	35-65 20-30	30-40 20-25	30/15
Weil	Frontal B	15/8	22/12	36/17	42/26	34/25	30/27

with the figures in my case, together with the width of the different laminae.

Finally, the size of fifty ganglion cells in each lamina of the frontal B area was measured with the help of the ocular micrometer, and the average for one cell was calculated (table 4).

From the tables it may be concluded that, despite an increase of from 20 to 50 per cent in the width of the gray matter, the total

number of ganglion cells was not increased, because the density per unit was approximately from 15 to 50 per cent less than in the normal control. The increase in size of the outer layer, especially of the first layer, was somewhat more marked than that of the deeper layers, but in general the relationship between the width of the different laminae was the same as in the adult brain. The frontal area seemed to be more enlarged than the precentral or the temporal areas. The precentral area was very poorly developed. The number of ganglion cells per

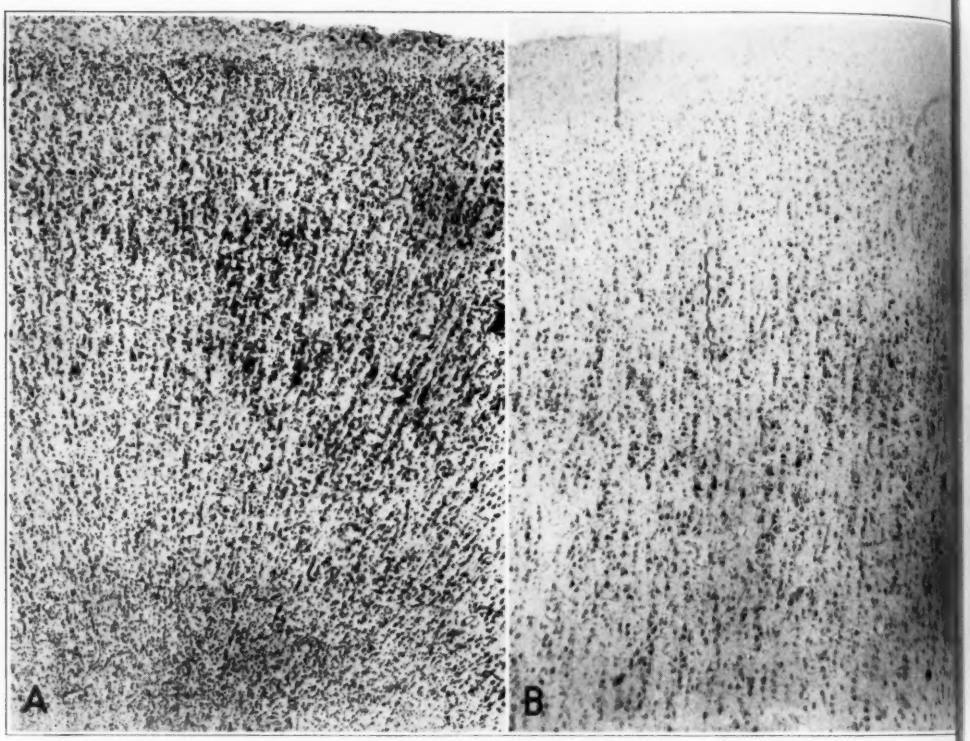

Fig. 9.—Cyto-architecture of frontal area, showing the reduction in the number of ganglion cells in comparison with the normal control. *A* is a copy from von Economo (Zellaufbau der Grosshirnrinde des Menschen, Berlin, Julius Springer, 1927); *B* is a section through the same area in the case reported in this article. Cresyl violet stain; Leitz obj., 3 ×; ocul., 10 ×.

one-tenth square millimeter was less than one half of that for the control. In the fifth lamina isolated Betz cells only could be found, and in the deeper layers ganglion cells which were arranged with their long axes perpendicular to the normal radiation were frequently seen. The coincidence of this underdevelopment of the motor area with the poorly developed skeletal muscular system as described by the general pathologist is interesting (fig. 9).

The size of the single ganglion cells seemed to be somewhat enlarged or at least at the upper limit of normal variations.

An increase in the number of neuroglia cells and fibers could not be demonstrated with any of the present methods of staining. The subjective impression was, however, that the protoplasmic astrocytes in the gray matter were larger than in normal controls. In the white matter of the cortex, a counting of glia nuclei in preparations stained with creysl violet did not show any difference in number in comparison with normal preparations from adult brains. Approximately forty nuclei per one-tenth square millimeter in a pyroxylin (celloidin) section 15 microns thick were counted as an average. In Cajal's gold sublimate preparations, however, one was impressed by the large astrocytes with abundant cytoplasm and thick, tortuous processes, which stood out in contrast to the more slender fibrous astrocytes of the controls. Oligodendroglia and microglia, in sections stained by Kanzler's method or by the modified Stern method, did not present any marked deviation from control preparations.

In order to explain the cortical hypertrophy one must assume, therefore, that it was due mainly to an isolated hypertrophy of the neuroglia, if one does not want to take refuge again in the assumption of an increase of the hypothetical Nissl gray. The megalencephaly of the cortex was an interstitial hypertrophy but not an interstitial hyperplasia. It was combined with congenital maldevelopment of certain areas.

The most interesting feature of the case is the fact that the interstitial hypertrophy was confined to the cerebral cortex and the corpora striata, while the glioblastomatosis was limited to the brain stem, cerebellum and upper part of the cervical spinal cord. If one wants to explain both processes on a common basis without being satisfied with the assumption of a mere coincidence, one might assume that there existed an inherent tendency for glial hypertrophy, which produced the megalencephaly (the size of the head of the elder, still living brother is at the upper limits of normal). In this case the hypertrophic glia first became hyperplastic, as is indicated by an increase of interfascicular glia and the new formation of the outer marginal embryonic layer of the cerebellum. Finally, the hyperplastic glia broke out of the normal boundaries designed for the adult cells, first in the hindbrain and gradually in the midbrain and thalamus.

This case, then, is another support of Marburg's idea that interstitial hyperplasia and primary diffuse gliosis are essentially similar processes. In each case one is dealing not with a tumor, a glioblastoma, which takes its origin from a given center, but with a diffuse process which begins simultaneously in different regions of the central nervous system. These characteristics seemed to justify the term "glioblastomatosis,"

which has been used in this paper in order to differentiate the process from diffuse gliosis; the term "diffuse gliosis" in most publications is used synonymously with "astrogliosis" referring to hyperplasia of adult, normal glia cells. A discussion of the clinical and anatomic differential diagnosis of the circumscript glioblastoma and the diffuse glioblastomatosis is given in Marburg's [2] paper.

The normally developed mental capacities of the patient and the absence of neurologic symptoms up to the age of 6 years, furthermore, justify the classification of this case as an interstitial hypertrophy, which, during the last six months of life, was converted into a hyperplastic, diffuse glioblastomatosis. That this condition was combined with maldevelopment of other systems is indicated by the underdeveloped precentral area, by the maldevelopment of the skeletal musculature and by the absence of chromaffin tissue in the medulla of the suprarenal glands.

A chronic infection was added to the pathologic picture, as is indicated by the endocarditis, with degeneration of the heart muscle and intimal proliferation of the basilar artery, and by the mild meningoencephalitis. Early bronchopneumonia and acute parenchymatous degeneration of the liver and kidney seemingly were the final and fatal events.

SUMMARY AND CONCLUSIONS

A case of megalencephaly in which the brain weighed 1,856 Gm., is described in a boy, aged 7, whose mental development had been normal up to the sixth year.

Hypertrophy of the cerebral hemispheres is combined with diffuse glioblastomatosis of the brain stem and the cerebellum.

A congenital, familial maldevelopment is suggested by the megalencephaly of the still living brother and by the congenital underdevelopment of the precentral area, the skeletal musculature and the chromaffin tissue of the medulla of the suprarenal glands.

ABSTRACT OF DISCUSSION

DR. PAUL C. BUCY: Why did Dr. Weil refer to the condition in the pons as glioblastomatosis? The condition is identical grossly with what was called by older pathologists hypertrophy of the pons and with what present day pathologists call glioma of the pons. As Dr. Weil pointed out, the growth is of the type which European observers call neurinoma centrale, and which in this country is called spongioblastoma unipolare. Certainly the case bears out this diagnosis. This type of involvement of the pons is not rare. At the Billings Hospital there have been four cases in the past year, which makes me doubt that the hypertrophy of the pons and the megalencephaly are anything but a coincidence. I think that in this case there are two conditions: one, a glioma of the pons and the other, an abnormal hypertrophy of the brain.

Did Dr. Weil examine the spinal cord, and if so, did it present the same hypertrophy as that seen in the brain?

Dr. G. B. Hassin: This is a remarkable case, and I wonder whether there was a normal area in the brain or spinal cord. It seems to me that the central nervous system presented conditions similar to those in Schilder's disease, multiple sclerosis and tuberous sclerosis, and that it also showed features of some glial tumors, such as glioblastoma and medulloblastoma, with a massive destruction of the brain tissues. The case presents a mixture of pathologic states that have been described under various names and that are present here in an accentuated form. I know of no other case like it recorded in the literature. It is not possible to explain the histologic changes on the basis of a tumor alone, as the extent of the lesion was too vast, the pons, cerebellum and upper spinal cord having been invaded. Probably it is a malformation, but that a malformation should show clinical symptoms and signs six years after birth is hard to understand. Has any one else seen a case like this reported in the literature?

Dr. A. B. Yudelson: Was there anything in the clinical history to indicate that there had been a febrile condition, trauma or other injury that might have caused the pathologic process? The wide dissemination and the character of the pathologic changes indicate an acute onset. Round cell infiltration about the blood vessels is shown in two of the slides.

Dr. Arthur Weil: I cannot agree with Dr. Bucy that we should call this neoplastic process a spongioblastoma, for spongioblastoma is a well defined tumor with characteristics different from this diffuse process. I tried to demonstrate with different silver stains the processes of neoplastic cells and forms resembling spongioblasts. Most of them were undifferentiated cells, which did not form any processes that could be stained by these methods. One cannot call this histologic process a spongioblastoma multiforme or a spongioblastoma unipolare. Cellular arrangements of the type of the central neurinoma could be demonstrated only in isolated areas.

Therefore I adopted Marburg's idea of the primary diffuse gliosis and called the process diffuse glioblastomatosis, indicating that one is dealing with a neoplastic process which did not arise in a given center, but which arose simultaneously in different parts of the brain. The neoplastic process gradually diminished in intensity in the more frontal sections, and the borderline was approximately a section through the optic chiasm.

Answering Dr. Yudelson, it may be added that the pathologist reported a chronic endocarditis, and there was marked proliferation of the intima of the basilar artery, resembling the arteriosclerosis of old age.

Replying to Dr. Hassin, Marburg reported a somewhat similar case under the title "Hypertrophie, Hyperplasie und Pseudohypertrophie des Gehirns," in 1906. The hypertrophy of the cortex, the maldevelopment of different areas and this diffuse glioblastomatosis, as well as the fact that the still living brother has an unusually large head, suggest a hereditary tendency toward hypertrophy of the brain, which at a certain period of life suddenly developed into hyperplasia and into a neoplastic process.

MYOTONIA ATROPHICA WITH CATARACT

REPORT OF THREE CASES

LEO L. MAYER, M.D.
AND
JOSEPH A. LUHAN, M.D.
CHICAGO

In 1876, Thomsen [1] wrote his famous dissertation on congenital myotonia, tracing the condition throughout three generations of his own family. He gave credit for the original description of this malady to Bell.[2] In 1886, Erb [3] elaborated the concept of myotonia.

Following the issuance of Erb's monograph there appeared reports of conditions that were considered at first to be atypical myotonia congenita. The earliest of these reports was that of Délèage,[4] in 1890. Good descriptions of such cases were given by Pelizaeus,[5] in 1897, and by Hoffmann,[6] in 1900. Rossolimo,[7] in 1902, gave the new clinical syndrome the name of *myotonie atrophique* (myotonia atrophica), although he considered the atrophy to have complicated a preexisting myotonia congenita. In 1909 the subject was clarified, and the clinical entity of myotonia atrophica emerged through the independent and almost simultaneous publications of Batten and Gibb [8] and Steinert.[9]

From the Departments of Ophthalmology and Nervous and Mental Diseases, Northwestern University Medical School.

A portion of the Scientific Exhibit of the American Medical Association, New Orleans, June, 1932.

1. Thomsen, J.: Tonische Krämpfe in wilkürlich beweglichen Muskeln in Folge von ererbter psychischer Disposition, Arch. f. Psychiat. **6**:702, 1876.

2. Bell, Charles: The Nervous System of the Human Body, ed. 3, London, H. Renshaw, 1844, p. 436.

3. Erb: Die Thomsen'sche Krankheit (Myotonia congenita), Leipzig, F. C. W. Vogel, 1886.

4. Délèage: Etude clinique sur la maladie de Thomsen, Thèse de Paris, Paris, Gaston Doin, 1890.

5. Pelizaeus: Ein Fall von Thomsen'scher Krankheit, Berl. klin. Wchnschr. **34**:609, 1897.

6. Hoffmann, J.: Zur Lehre von der Thomsen'schen Krankheit mit besonderer Berücksichtigung des dabei vorkommenden Muskelschwundes, Deutsche Ztschr. f. Nervenh. **18**:198, 1900.

7. Rossolimo, G.: De la myotonie atrophique, Nouv. iconog. de la Salpêtrière **15**:63, 1902; Neurol. Centralbl. **21**:135, 1902.

8. Batten, Fred E., and Gibb, H. P.: Myotonia atrophica, Brain **32**:187, 1909.

9. Steinert, Hans: Myopathologische Beiträge: I. Ueber das klinische und anatomische Bild des Muskelschwunds der Myotoniker, Deutsche Ztschr. f. Nervenh. **37**:58, 1909.

Greenfield [10] first emphasized the occurrence of cataract in myotonia atrophica. In 1911, he described a family of thirteen siblings of whom five suffered from myotonia atrophica (two with and three without cataract) and two from cataract alone. Similar reports by other writers soon followed, for example, Hoffmann's [11] report of four cases in 1912. In 1914, Curschmann [12] stressed the importance of cataract and other extramuscular symptoms in myotonia atrophica and suggested the name "dystrophia myotonica" for this disease. Hence Adie and Greenfield [13] in their excellent review suggested that the syndrome be called "dystrophia myotonica, type Batten-Steinert-Curschmann."

Fleischer,[14] in 1918, reexamined nearly all of the patients with presenile cataract who had been seen in the Tübingen clinic for several years previously. His exhaustive studies in tracing the family histories of thirty-eight patients with myotonia atrophica indicate that the disease is heredofamilial; therefore (as Adie and Greenfield pointed out), when the family history cannot be adequately traced (even back to the great-great-great-grandfather), even though the condition appears to be nonfamilial, it is much more likely that the investigations are incomplete rather than that the condition is nonfamilial. The disease may be transmitted latently through as many as six generations. The fully developed disease is usually confined to persons in one generation having the same relationship to a common ancestor. Not uncommonly, in the first generation cataract appears at an advanced age; in the second, it takes the form of a precocious cataract, and in the third, in which the disease attains full development, muscular troubles and presenile cataract occur, either in association or separately.

In spite of the fact that Fleischer did not use a slit lamp in his examinations, he was able to describe the typical cataract found in myotonia atrophica and to differentiate it from that found in tetany. With

10. Greenfield, J. G.: Notes on a Family of "Myotonia Atrophica" and Early Cataract, with a Report of an Additional Case of "Myotonia Atrophica," Rev. Neurol. & Psychiat. **9**:169, 1911.

11. Hoffmann, J.: Katarakt bei und neben "atrophischer Myotonie," Arch. f. Ophth. **81**:512, 1912.

12. Curschmann, Hans: Ueber familiäre atrophische Myotonie, Deutsche Ztschr. f. Nervenh. **45**:161, 1912; Beobachtungen und Untersuchungen bei atrophischer Myotonie, ibid. **53**:114, 1914.

13. Adie, W. J., and Greenfield, J. G.: Dystrophia Myotonica (Myotonia Atrophica), Brain **46**:73, 1923.

14. Fleischer, Bruno: Ueber myotonische Dystrophie mit Katarakt: Eine hereditäre, familiäre Degeneration, Arch. f. Ophth. **96**:91, 1918.

Hauptmann [15] and Naegeli,[16] he believed the disturbance to be of an internal secretory nature. After the advent of the slit lamp, cataracts of all types were more minutely studied. Vogt [17] gave a detailed description of the cataract in myotonia atrophica. In his atlas [18] are typical pictures of the condition, as observed in three cases. Early, the appearance of mixtures of shiny flakes, white dots and fine, dustlike opacities just under the anterior and posterior capsules is absolutely characteristic. Later starlike formations are noted. That the green and blue play of colors is caused probably by tiny cholesterol crystals was shown by chemical examination of an extracted lens. Vogt,[19] in 1922, after having seen five families with cataracts in myotonia atrophica, expressed the opinion that mild cases may easily pass unrecognized.

Weill and Nordmann [20] described a type of change in the lens with dots and precipitates through the cortex seen in mongolian idiots. This condition was also described by van der Scheer,[21] who was able to differentiate the cataract from that of myotonia.

Kennedy [22] pointed out that the appearance of patients with myotonia atrophica was strikingly similar, as if they all belonged to the same family. Other clinical studies and reports of cases of this disease include those of Hunt,[23] Bullowa,[24] Fearnsides,[25] Rohrer [26] (an excellent

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15. Hauptmann, Alfred: Die atrophische Myotonie, Deutsche Ztschr. f. Nervenh. **55**:53, 1916; Grundlagen, Stellung und Symptomatologie der "Myotonen Dystrophie" (früher "atrophischen Myotonie"), ibid. **63**:206, 1919.

16. Naegeli: Ueber Myotonia atrophica, speziell über die Symptome und die Pathogenese der Krankheit nach 22 eigenen Fällen, München. med. Wchnschr. **64**: 1631, 1917.

17. Vogt, Alfred: Neue Schweizer Stammbäume von myotonischer Dystrophie (atrophischer Myotonie) aus dem Aargau, St. Gallerland und aus dem Kanton Schaffhausen, Klin. Monatsbl. f. Augenh. **72**:421, 1924.

18. Vogt, Alfred: Atlas of the Slitlamp-Microscopy of the Living Eye, authorized translation by Robert Von der Heydt, Berlin, Julius Springer, 1921.

19. Vogt, Alfred: Weitere Ergebnisse der Spaltlampenmikroskopie des vorderen Bulbusabschnittes: IV. Präsenile und senile Linsentrübungen: 13. Die Katarakt bei myotonischer Dystrophie, Arch. f. Ophth. **108**:212, 1922.

20. Weill, G., and Nordmann, J.: La cataracte et ses rapports avec la pathologie générale, Ann. d'ocul. **163**:401, 1926.

21. van der Scheer, W. M.: Cataracta lentes bei mongoloider Idiotie, Klin. Monatsbl. f. Augenh. **62**:155, 1919.

22. Kennedy, Foster: A Case of Myotonia Atrophica, J. Nerv. & Ment. Dis. **40**:597, 1913; Myotonia atrophica, J. A. M. A. **61**:1959 (Nov. 29) 1913.

23. Hunt, D. J. Ramsay: Myotonia Atrophica, J. Nerv. & Ment. Dis. **35**:269, 1908.

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25. Fearnsides, E. G.: A Case of Myotonia Atrophica with a Family History of Cataracts, But No History of Familial Myopathy, and No Myotonic Manifestations, Rev. Neurol. & Psychiat. **13**:311, 1916.

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analysis and review of the literature up to 1916), Schmidt,[27] Hamill,[28] Broadwin,[29] Lüssi,[30] Abe,[31] Martin,[32] Heine,[33] Keschner and Finesilver,[34] Goulden,[35] Berg,[36] Steenaerts,[37] Breidenbach,[38] Pjatnizkij,[39] Duncan[40] and Kalinowsky.[41]

Reports of autopsy have been given for only nine cases, the last being one in the monographic thesis of Roques.[42] Reports were made by Hitzenberger,[43] Bramwell,[44] and Weil and Keschner.[45] The histologic picture of the muscular changes was best described by Heidenhain,[46]

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27. Schmidt, W. A.: Kasuistischer Beitrag zur "myotonischen Dystrophie" mit Katarakt, Ztschr. f. Augenh. **41**:199, 1919.

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35. Goulden, Charles: Some Unusual Forms of Acquired Cataract, Tr. Ophth. Soc. U. Kingdom **48**:97, 1928.

36. Berg, Wilhelm: Zur Kenntnis der myotonische Dystrophie, Deutsche Ztschr. f. Nervenh. **98**:29, 1927.

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42. Roques: La myotonie atrophique (maladie de Steinert), Thèse de Paris, Paris, Amédée Legrand, 1931.

43. Hitzenberger, K.: Ueber myotonische Dystrophie, Monatschr. f. Psychiat. u. Neurol. **47**:249, 1920.

44. Bramwell, Edwin: Observations on Myopathy, Proc. Roy. Soc. Med. (Sect. Neurol.) **16**:1, 1922.

45. Weil, Arthur, and Keschner, Moses: Dystrophia Myotonica, Tr. Am. Neurol. A., 1926, p. 473; Ein Beitrag zur Klinik und Pathologie der Dystrophia myotonica, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:687, 1927.

46. Heidenhain, Martin: Ueber progressive Veränderungen der Muskulatur bei Myotonia atrophica, Beitr. z. path. Anat. u. z. allg. Path. **64**:198, 1918.

in 1918, Slauck,[47] in 1923, and Adie and Greenfield,[13] in 1923. The pathologic physiology of myotonia was studied by Erb,[3] Kramer and Selling,[48] Adie and Greenfield,[13] Nylin[49] and others.

In 1929, Gifford, Bennett and Fairchild[50] reviewed the literature on myotonia atrophica and reported four cases. These showed the characteristic change in the lens and typical histologic appearances in the muscles on which biopsy was performed. Since then, most of the literature[51] has been by French authors, with etiologic theories and methods of treatment much in evidence. The general opinion of these writers is that the disease may be a form of parathyroid insufficiency. Thus, Faure-Beaulieu[51d] advanced as evidence in favor of this new theory: (1) the development of cataract, (2) the coexistence of signs of latent tetany and (3) biochemical changes (diminution of blood calcium and phosphorus, and deviation of the p_H toward alkalinity, with augmentation of the alkali reserve).

On the other hand, in 1931, Roquès,[42] who reviewed the literature thoroughly, opposed the view that the cause of the disease may be parathyroid deficiency. He pointed out that the cataracts of tetany and myotonia atrophica are not the same. In five cases, four of myotonia atrophica and one of Thomsen's disease, he found a normal calcium content of the blood. Treatment with parathyroid extract-Collip had no effect on the myotonia, even directly following the injection. However, he found that pulmonary hyperventilation induced augmentation of the myotonia in one patient without causing, at the same time, genuine tetanic spasms.

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47. Slauck, Arthur: Untersuchungen auf dem Gebiete der Myopathie und Myasthenie, Ztschr. f. d. ges. Neurol. u. Psychiat. **80**:363, 1923.

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49. Nylin, Gustav: Two Cases of Dystrophia Myotonica, "Batten-Steinert-Curschmann" Type, with a Graphic Investigation of Their States of Contraction and the Influence of Temperature Thereon, Upsala läkaref. förh. **31**:329, 1926.

50. Gifford, S. R.; Bennett, A. E., and Fairchild, Nora M.: Cataract in Myotonic Dystrophy, Arch. Ophth. **1**:335 (March) 1929.

51. (*a*) Paunesco, C.: Contribution à l'étude de la myotonie atrophique, Rev. neurol. **1**:789, 1928. (*b*) Faure-Beaulieu, Marcel, and Desbuquois, Georges: Dystrophie myotonique. Etude biochimique du syndrome endocrinien, ibid. **1**:713, 1928. (*c*) Rathery, F.; Mollaret, P., and Waitz, R.: Myopathie myotonique avec signe de Chvostek. Etude humorale. Rôle de l'insuffisance parathyroïdienne, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:395, 1930. (*d*) Faure-Beaulieu, Marcel: Dystrophie myotonique et insuffisance parathyroïdienne, ibid. **46**:534, 1930. (*e*) Rivoire, R.: Cataracte et métabolisme du calcium, Presse méd. **38**:723, 1930. (*f*) Achard, C.; Bariéty, M., and Desbuquois, G.: Sur un noveau cas de dystrophie myotonique, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1355, 1930. (*g*) Jung, Adolphe: L'hypocalcémie dans la dystrophie myotonique avec cataracte, Presse méd. **38**:1125, 1930.

Bencini [52] described the alterations of the lens in myotonic dystrophy. Terrien, Sainton and Veil [53] reported the characteristic pictures of changes in the lens and commented on the case of d'Antona,[54] in which a small sella turcica was found. They mentioned the theories of Foix and Nicolesco,[55a] who expressed the belief that pontobulbar lesions exist, and referred also to the theory of Nicolesco and Nicolesco [55b] that atypical senescence occurs in the axis-cylinders of the extrapyramidal and the vegetative nervous systems. However, the pathologic studies of these authors [55] were concerned with Thomsen's disease and with dystrophies other than myotonia atrophica.

Kuré and Okinaka [56] recently summed up the literature and observations concerning the treatment of muscular dystrophies with injections of epinephrine and pilocarpine combined. They stated that small doses given daily or every other day for a course of fifty injections stop further progress of the atrophy without causing untoward general effects. Monrad-Krohn [57] recently published a report of a case in which the intravenous administration of pilocarpine produced a diminution in the myotonia.

REPORT OF CASES

CASE 1.—*Myotonia of the fist-closing muscles of eleven years' duration; myopathic facies; difficulties in speech and swallowing; atrophy of the sternocleidomastoid muscles, muscles of the forearm and of the dorsiflexors of the feet; mechanical myotonia of the deltoid muscles; loss of tendon reflexes; abnormal electrical reactions; acrocyanosis; typical cataract on slit-lamp examination of the lens; normal blood calcium and phosphorus values.*

History.—Clyde W., an unmarried man, aged 32, was admitted to the Northwestern University Medical School Dispensary on April 4, 1930, complaining of stiffness in the ring and little fingers of each hand, weakness of the hands and legs and difficulty in speech. The mother was living and well at the age of 61. The father died of pneumonia at 51. There were two sisters; one was living and well,

52. Bencini, Alberto: Contributo allo studio delle alterazioni del cristallino nella distrofia miotonica, Boll. d'ocul. **8**:575, 1929.

53. Terrien, F.; Sainton, P., and Veil, P.: Cataracte héréditaire familiale et myopathie, Arch. d'opht. **46**:193, 1929.

54. d'Antona, S.: Sulla distrofia miotonica, Policlinico (sez. med.) **33**:389, 1926.

55. (*a*) Foix, C., and Nicolesco, I.: Note sur les altérations du système nerveux dans un cas de maladie de Thomsen, Compt. rend. Soc. de biol. **89**:1095, 1923. (*b*) Nicolesco, I., and Nicolesco, M.: A propos des données histologiques récentes concernant la maladie de Parkinson, la maladie de Thomsen, les myopathies, et la démence précoce, Rev. stiint. med., 1926, p. 353; abstr., Rev. neurol. **2**:499, 1926.

56. Kuré, Ken, and Okinaka, Shigeo: Behandlung der Dystrophia musculorum progressiva durch kombinierte Injektionen von Adrenalin und Pilocarpin, Klin. Wchnschr. **9**:1168, 1930.

57. Monrad-Krohn, G. H.: A Case of Myotonia with a Striking Reaction to Pilocarpine, Acta psychiat. et neurol. **5**:241, 1930.

and the other died at the age of 38 of "inflammatory rheumatism." The patient had fifteen cousins, all on the mother's side except one. They ranged in age from 10 to 40. So far as the patient knew, there was no one in his family who suffered from muscular weakness, difficulty in relaxing the hand grasp or cataract.

The past history was without significance except that nine years previously the right eye had been injured by a steel splinter. He had always been in good health prior to the present illness and had been athletically inclined, having been a member of track, basketball and football teams of the high school.

The present illness began eleven years before the patient's admission to the dispensary as a slowly developing stiffness in the ring and little fingers of each hand. This symptom was usually worse during cold weather. Next, weakness of the hands developed insidiously. The patient was forced to give up work as a machinist four years before admission because of weakness of the hands. The face began to show wasting seven years before admission, and two years later difficulty in speech developed. Enunciation became indistinct. At about this time the patient noticed trouble in swallowing; solid food would tend to "stick on its way down," and a hurried attempt to swallow liquids might be accompanied by regurgitation through the nose. During the four years prior to admission, there had been no aggravation and perhaps a slight recession of the difficulties in speech and swallowing. The eyes watered freely. Increased secretion of saliva and sputum was complained of. The patient had lost 30 pounds (13.6 Kg.) since the onset of the illness. He complained that his hands and feet were always cold. About a year before admission, when his attention was called to this by a physician, he first became aware of weakness of the feet. He noticed that the feet slapped down as he walked, and that the movements of lifting the toes and feet were very weak. He had impaired vision in the right eye, which dated from the injury to that eye; he did not think that this had progressed. Sexual desire and potency were not diminished.

Examination.—Only the positive findings, or those of special significance, will be recorded. The patient was intelligent and cooperative. His speech was indistinct, monotonous and somewhat nasal. [illegible]ght was 5 feet and 8 inches (172.7 cm.); the weight, 126 pounds (57.2 Kg.). The hair was sparse only at the vertex. The face revealed marked hollows in the temporal regions, sunken cheeks, a hatchet-shaped profile and absence of expression. The eyes were watery. Visual acuity was: right eye, 20/100; left eye, 20/60. With the slit lamp a characteristic picture (fig. 1) was demonstrable in the lens. There was a small, somewhat triangular opacity, which seemed to be in the posterior lamellae of the lens and was not sufficiently dense to interfere with ophthalmoscopy through the undilated pupils. This condition was bilateral, but was more marked on the right. The refracting media in the right eye were otherwise clear.

The temporal muscles were completely wasted; the masseters were normal. The facial muscles were atrophied, with facies myopathica of the Landouzy-Dejerine type and marked weakness of the frontalis muscle, the orbicularis muscles of the eyes and mouth and the buccinator muscles. A definite Chvostek's sign was elicited bilaterally. The soft palate moved well. No pharyngeal reflex was elicited. The vocal cords were not examined. The neck presented striking atrophy of both sternocleidomastoids, which were reduced to ribbon-like proportions. As a consequence, the patient was unable to lift his head from the table when he lay supine; when he raised the trunk to the sitting posture the head fell backward. The muscles of the upper parts of the arms appeared normal. The forearms showed definite atrophy, which was more marked on the extensor than on the flexor

surfaces, and more marked distally than proximally. The thenar and hypothenar eminences were well preserved. Flexion of the fingers was too weak to register on the dynamometer; however, it was stronger than extension. Pronation was fairly strong; supination was weaker and was done mainly with the biceps muscles. Movements of the fingers other than flexion and extension were only moderately weak. The thumb could be opposed to all of the fingers; Froment's thumb sign was not elicited. Abduction and adduction of the fingers were done with a fair

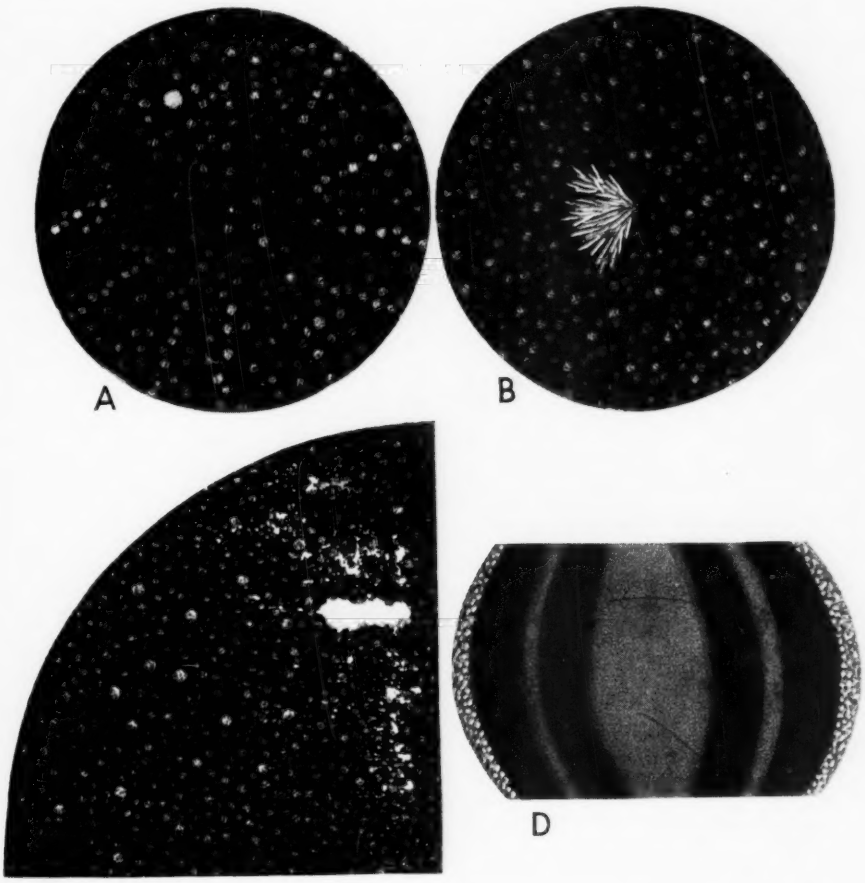

Fig. 1 (case 1).—*A*, anterior cortex of the lens seen with the slit lamp; *B*, posterior cortex of the lens; *C*, middle section of the cortex of the lens; *D*, optical section of the lens seen with the small bundle of the slit lamp.

degree of strength. No weakness of the truncal musculature could be demonstrated. All movements of the thigh and at the knee were strong. There was an atrophy of the anterolateral muscles of the legs, with marked weakness of dorsiflexion of the foot and toes and a steppage gait.

Active myotonia was shown only in the hand grasp, particularly in the ring and little fingers. Difficulty in relaxation decreased with repetition of the movement.

The accompanying ergographic record (fig. 2) shows plainly the *Nachdauer* (after-contractions) in the initial contractions. Mechanical myotonia was demonstrable in the deltoid muscle by the occurrence of a furrow at the site of impact, which persisted for about one second after the muscle was struck with a percussion hammer. Myotonia was less marked in the thenar and hypothenar muscles; none was found in the tongue.

The hands were moist with perspiration and cold to the touch. The penis was of good size and the testes were normal.

The tendon reflexes of the upper and lower extremities were absent; the superficial reflexes were normal. Coordination was normal. There were no tremors or loss of position, vibration, joint, stereognostic, touch or pain sense.

The temporal muscles were electrically inexcitable. The flexor carpi radialis muscle showed moderately diminished excitability both to faradism and to galvanism; there were no polar changes. With a current of the minimal strength necessary to elicit contraction the twitches were normally brisk and without a myotonic reaction; but with strong currents a definite after-contraction (*Nachdauer*) appeared. The tibialis anterior muscle showed the reaction of degeneration.

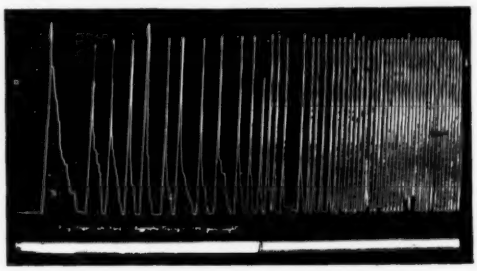

Fig. 2 (case 1).—Ergographic tracing of the left ring finger lifting a 100 Gm. weight.

Laboratory Findings: The blood was normal as to hemoglobin content, cell content and morphology. The blood calcium was 10.75 mg. and the inorganic phosphorus 3.5 mg. per hundred cubic centimeters. The urine was normal; the Wassermann reaction of the blood and of the spinal fluid was negative. The basal metabolic rate was —14 per cent. Roentgenograms of the skull revealed a normal appearing sella turcica.

CASE 2.—*A sister had well developed presenile cataracts; another sister showed early changes in the lens on slit-lamp examination. The patient had active myotonia in the hands after closing them, myopathic facies, monotonous speech, atrophy of the sternocleidomastoids and the muscles of the forearm, mechanical myotonia in the small muscles of the hands, testicular atrophy, some premature baldness, acrocyanosis, diminished deep reflexes, a low basal metabolic rate, a normal blood calcium and phosphorus content, and typical cataracts discovered on slit-lamp examination.*

History.—William A., an unmarried white man, aged 33, was admitted to the Michael Reese Hospital on Feb. 3, 1930. His complaints were numerous, foremost among them being pain in the left side of the abdomen, progressive generalized weakness and loss of weight and appetite. The patient was American born, of Russian-Jewish and Polish-Jewish extraction. His paternal great-grandfather

lived to be almost 100 years old, and his paternal grandfather died at 80. The maternal grandfather died in early adulthood of pneumonia; the maternal grandmother lived to be 86. The father was living and well at 61. The mother died of Bright's disease at 51. None of these antecedents presented any muscular wasting, difficulty in relaxing the hand grasps or cataract, so far as the patient was aware. A sister died of cerebral embolism following appendectomy, and a brother died of heart disease. A sister, aged 38, with three normal children, suffered from bilateral cataracts; her vision began to be impaired about a year before the patient entered the hospital. Another sister, Charlotte A., aged 27, had had an intra-abdominal cystic (ovarian?) tumor removed recently. Although she had no complaints referable to the eyes or to the neuromuscular system, the eyes showed incipient cataracts on slit-lamp examination.

The patient's birth and early development were normal. He had influenza in 1919 and pneumonia in 1924. He did not indulge in alcohol, but prior to his illness had smoked cigarets immoderately. He was apparently well until sometime in November, 1928, when he sustained a sacro-iliac strain while lifting a heavy object. After this he was no longer able to work as a shipping clerk. In January, 1930, he began to be troubled by a cramplike pain in the left side of the abdomen, coming on usually two hours after eating. Shortly thereafter he began to feel weak. He had lost 10 pounds (4.5 Kg.) within the three months preceding admission.

Examination.—During the patient's stay in the hospital, physical and roentgen examination and laboratory tests indicated that he ws suffering from a pathologic condition of the gallbladder and appendix, together with a spastic colon. The basal metabolic rate was —25 per cent; the gastric contents on two occasions showed achlorhydria, and the cerebrospinal fluid was normal with respect to cell count, globulin content and Wassermann and Lange reactions.

The neurologic consultant (Dr. L. J. Pollock) noted essentially the following: There was atrophy of the temporal muscles and, to a less extent, of other facial muscles. The sternocleidomastoid muscles were markedly atrophied, and the patient was unable to lift his head from the pillow. A myotonic reaction was present in the hand grasps. The deep reflexes of the upper extremities and also the knee jerks were diminished. The right ankle jerk was absent; the left, decreased. The fundi were normal, and no cataract was found on ophthalmoscopic examination. There was premature partial baldness. A diagnosis of myotonia atrophica was made on the basis of these neurologic findings. Electrical examination revealed a definite myotonic reaction in the muscles of the forearms. An examination of the blood made after the diagnosis was suggested revealed a calcium content of 12.7 mg. and a phosphorus content of 3.2 mg. per hundred cubic centimeters.

Course.—The patient was observed from time to time in the outpatient department of the Michael Reese Hospital. On Dec. 5, 1930, one of us found, with the aid of a slit lamp, the typical incipient cataract of myotonic dystrophy. In both eyes, under the anterior and posterior capsules of the lens, were tiny white dots and fine, dustlike particles, some of which reflected the light markedly; small stars made up of conglomerate flakes and particles were also noted. Gradually this condition progressed, with an increase in size and visibility of the various factors.

The patient was reexamined on June 11, 1932, at the Northwestern University Medical School. The following findings were noted: height, 5 feet and 7 inches (170.2 cm.); weight, 130 pounds (59 Kg.); frontal and vertical baldness;

myopathic facies, with marked weakness of the orbiculares oculi and wasting of the temporales and of the nasal and buccal mucles. The pupils reacted somewhat sluggishly and with small amplitude to light, and with small excursion in accommodation. The masseters were well preserved. The palate rose very slowly when the patient said "Ah!" Speech was monotonous and muffled. A slight degree of mechanical myotonia was elicited in the tongue. The sternocleidomastoid muscles were atrophied to ribbon-like proportions and were correspondingly weak. The platysma myoides muscles stood out in prominent relief. The strength of the deltoid, biceps, triceps, pectoral, latissimus dorsi and serratus anterior muscles was bilaterally adequate. The muscles of the forearms were markedly atrophic, considerably more so than when the patient was first seen about two years before. There was striking myotonia in the hand grasp, roughly proportionate to the degree of effort put into the act. When the patient clenched his fist strongly, it took about ten seconds for the contraction to relax so that the fist could be opened again. Repetition of the act led to more facile movement, so that finally less than a second was required for the firm closure of the fist and a similar time for its opening. Mechanical myotonia (a persistent furrow at the site of impact on percussion) was demonstrable in the thenar and hypothenar eminences, and to a less extent in the deltoid muscles. The hand grips were weak; dynamometer readings were: 35 for the right hand, and 37 for the left (normally about from 70 to 100). The hands were markedly cyanotic and cold to the touch. Although no atrophy or myotonia was unequivocally revealed in the lower extremities, there was slight weakness of dorsiflexion of the feet as compared with plantar flexion. (The patient stated that he did not walk as fast as he used to, and his sister said that at times he scraped his feet in walking.) No distinct abnormality in gait was detected at this examination. The ankle jerks were absent, the knee jerks diminished and equal, the biceps and triceps jerks present and the wrist jerks absent. The abdominal reflexes were brisk, the cremasteric reflexes diminished and the plantar reflexes absent. Touch, pain, vibration and joint sensibility was everywhere normal. The extremities showed no ataxia. The testes were soft and very small (about 2.5 by 1 by 1 cm. and 3.5 by 1.5 by 1.5 cm.), although the penis was of good size. The heart was not enlarged and revealed neither murmurs nor arrhythmia. The blood pressure was 104 systolic and 70 diastolic with the patient seated. The lungs were normal to percussion and auscultation. Tenderness to palpation was elicited in the left upper abdominal quadrant. The transverse colon was palpable. Slit-lamp examination showed the features previously noted.

Examination of Sister.—The patient's sister, Charlotte A., was examined at this time. She showed no evidence of either muscular atrophy or myotonia. However, a slit-lamp examination of the lens made by Dr. Sanford R. Gifford revealed several minute punctate opacities beneath the anterior, and to a greater extent beneath the posterior, capsule of the lens, with occasional particles showing a greenish iridescence. These findings were considered to be indicative of a very early cataract peculiar to myotonic dystrophy.

CASE 3.—*Myotonia of the hands and tongue for twelve or fifteen years; a family history of nervous disorders, two cousins presenting a condition similar to that of the patient and a third showing myotonia of the muscles of the thighs; advanced presenile cataracts; myopathic facies; atrophy of the sternocleidomastoid muscles; slight atrophy of the forearms; active myotonia of the muscles of mastication and less active myotonia of the muscles of the thighs; diminished tendon reflexes in the upper extremities; acrocyanosis, and possibly testicular atrophy; normal blood calcium and lowered inorganic phosphorus values.*

History.—W. H., a white man, aged 41, married, a farmer, was admitted to the Diagnostic Center of the Michael Reese Hospital on Nov. 27, 1931, complaining of failing vision, stiffness and weakness of the hands, a peculiar stiffness of the tongue and "sinusitis." The family history, obtained from the patient, revealed that the father died of "heart trouble" and that the mother was living at the age of 88. No history of cataract or muscular symptoms in the parents was elicited. A sister died of meningitis following mastoiditis. Three brothers and one sister were living and well. The patient stated that a cousin (on his mother's side) suffered from weakness of the hands. (Later investigation showed that this person was suffering from arthritis deformans.) Another cousin, on the mother's side, was said to have a similar condition ("eye trouble, stiffness of the hands, thin fingers like those of a girl of 11, and clumsiness in walking"). This cousin could not be examined, but other members of the family stated that she was feeble-minded. Another cousin (on the mother's side), a woman, aged 63, had suffered for fifteen years from weakness of the legs (foot drop) and marked weakness in lifting the head from the pillow when she lay supine. In a letter responding to our inquiries, she did not complain of myotonia or of ocular disturbance.

The patient's illness began with an insidiously developing stiffness in the hands and tongue which he said began "a long time ago," perhaps from twelve to fifteen years before we saw him. He noticed that if he grasped something tightly with his hands he had difficulty in releasing his grip. This became progressively worse; at the time of admission to the hospital it required a few minutes for his hands to "limber up" before he could do much work with them. During the past five years a slowly increasing weakness of the hands had been present. He had much difficulty in milking cows. He had not noticed that the difficulty in relaxing the hand grasps was any more marked in cold weather. The stiffness of the tongue also had been present for a long time. When the patient began to speak the tongue was thick and heavy, interfering with speech; but as he continued to talk it gradually "loosened up," so that finally it became free and mobile again and speech was unimpeded. This lingual difficulty was definitely worse in cold weather. At times, when he began to chew food vigorously the jaws would momentarily lock, slowly relaxing and becoming less stiff with continuation of masticatory movements.

Questioning revealed that the patient experienced a similar form of stiffness in the thighs, which was present when he stood up from a sitting posture and began to walk. He had to "walk off" this stiffness gradually. People had told the patient within the past few years that his face was becoming thinner. The visual difficulty dated back at least five years, and had progressed slowly from its inception. Three years before we saw him the patient consulted a physician for this trouble and was told that he had cataracts. Two years before he became unable to read with the left eye. At the time of admission to the hospital the sight of the right eye was also impaired; when he read with this eye an image like that of a bird followed the line of print.

The patient had had nasopharyngeal trouble for years. He had had severe frontal headaches which he ascribed to sinusitis. The hands and feet were always cold. There was no history of increased secretion of tears. However, the patient noticed that the face tended to sweat excessively during the eating of the noon meal. There was no history of any difficulty in swallowing. Neither weakness of the feet nor difficulty in walking was noted. He said that there was no diminution of potency or libido.

Examination.—The patient was adequately nourished. There was a good growth of hair on the head. There was a myopathic facies with hollowing out of the temporal fossae and a hatched-shaped profile. The sternocleidomastoid muscles were considerably atrophied and very weak, in contrast to the normal musculature in the remainder of the neck. The forearms were slightly atrophied, in contrast to the excellent muscular development of the upper part of the arms. The hand grasps were relatively weak and showed myotonia. No atrophy or weakness was found in the lower extremities, where the muscular development was excellent.

A marked myotonia, somewhat proportional to the amount of effort put into the movement, was demonstrable in the hand grasp. After forcible closure of the fist, relaxation required several seconds; it became progressively more facile with repetition of the movement until alternate opening and closing of the fists proceeded with normal ease and rapidity. A slight degree of mechanical myotonia (*Dellenbildung*) was elicited in the tongue and in the deltoid muscles.

The pupils were 3 mm. in diameter and regular in outline; they responded normally to light and in accommodation. The anterior cortex of the lens in each eye contained numerous fine, highly refractile points. The nucleus of the lens appeared clear. A stellate opacity was seen in the posterior cortical layers of each lens. The cataract was more marked in the left eye. The fundus of the right eye was normal.

The achilles and knee jerks were present and of about normal intensity, although they were slightly greater on the left side. The abdominal reflexes were active, slightly more so on the right. The triceps jerks were diminished, the biceps jerks were markedly diminished, and the wrist and ulnar jerks were absent.

All forms of sensation were intact.

The external genitalia were normal, although the testes were soft and somewhat small. The thyroid gland appeared normal.

Physical and neurologic examination otherwise revealed nothing of significance, except for mild chronic nasopharyngitis and laryngitis.

The significant laboratory findings were: The urine was normal chemically and miscroscopically. The blood was normal morphologically. The Wassermann and Kahn tests of the blood were negative. The blood chemistry revealed, per hundred cubic centimeters of blood: nonprotein nitrogen, 29 mg; sugar, 81 mg.; calcium, 10.7 mg., and phosphorus, 2.7 mg. The basal metabolic rate was +9 per cent. Roentgenograms of the nasal accessory sinuses revealed slight clouding of both frontal sinuses.

SUMMARY

Myotonia atrophica (myotonic dystrophy) is a distinct nosologic entity characterized by: (1) myotonia, in the active form usually limited to the hand grasps; (2) muscular atrophy of a selective distribution, and (3) dystrophic extramuscular phenomena, chief among which is a distinctive form of presenile cataract. The disease is probably heredofamilial, as the careful studies of Fleischer indicate. It usually begins between the ages of 18 and 35 and predominantly affects males.

Active myotonia is ordinarily limited to the fist-closing muscles, but sometimes involves the tongue and other groups of muscles. Mechanical myotonia, shown by a persistent dimple or furrow at the point of impact

when a muscle is percussed, is most commonly found in the thenar and hypothenar muscles and in the deltoids. The myotonic electrical reactions are often influenced by the presence of atrophy in the muscles examined. All three forms of myotonia are not usually found in the same muscle. Myotonia tends to appear early, before the development of atrophy, and may disappear with the advance of the atrophy.

The muscular atrophy is selective, involving the facial muscles, the sternocleidomastoids, the muscles of the forearms, the vasti of the thighs and the dorsiflexors of the feet. The hatchet-like physiognomy, combined with ribbon-like sternocleidomastoids and wasting of the muscles of the forearms, gives rise to a strikingly characteristic picture.

The extramuscular symptoms include cataract—essentially a presenile cataract—revealed on gross examination in about one half of the published cases. However, cataract will probably be found to be one of the most nearly constant findings in this condition if the lenses are examined by means of a slit lamp. Early, the appearance of fine, dust-like opacities under the anterior and posterior capsules is characteristic of this form of cataract; later, starlike formations may be found. Cataract is of great significance in the hereditary transmission of the disease, since members of affected families may present cataract alone (without muscular symptoms).

Testicular atrophy, monotonous, nasal speech, acrocyanosis, premature baldness, increased secretion of tears and loss of tendon reflexes even in healthy appearing muscles are dystrophic phenomena that are encountered with varying frequency in myotonia atrophica.

The pathologic basis for the atrophy appears to have been found within the muscles themselves (rather than in their related motor cells within the spinal cord). There is some histologic evidence to suggest that the vegetative nervous system within the central neuraxis may be pathologically implicated as the cause of the myotonia. The occurrence of cataract and of tetanic muscular phenomena in states of parathyroid deficiency has led investigators to search for evidences of parathyroid insufficiency in myotonia atrophica. In this regard, certain recent observers have stressed a diminished calcium content of the blood, signs of latent tetany and the cataract itself as indicating that parathyroid insufficiency is involved in the pathogenesis of myotonia atrophica.

VERIFIED TUMOR OF THE TEMPORAL LOBE

A CRITICAL REVIEW OF FIFTY-TWO CASES

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The temporal lobes of the brain have long been regarded as silent areas. Writing on the "Localization of Intracranial Tumors" in 1896, Bramwell stated: ". . . , and last of all, the most difficult to diagnose and locate, tumors of the temporosphenoidal lobe and especially, of course, tumors of the right temporosphenoidal lobe." Again, Oppenheim in 1899 remarked: "Wir haben niemals das Recht die Lokaldiagnose Tumor des rechten Schläfenlappens zu stellen." (We never have a right to make a local diagnosis of tumor of the right temporal lobe.) Even today, in spite of much progress, the frequency with which a mass lesion in one or the other temporal lobe may reach a considerable size while producing few symptoms is only too well known to the neurologist and neurosurgeon. Accordingly, a review and analysis of a fairly large group of cases of verified tumor of the temporal lobe in an effort to add to knowledge of the symptom complex which they present seem worth while.

Before presenting the clinical aspects of the subject, however, the physiology and anatomy of the temporal lobes may be briefly reviewed. Lying in the middle cranial fossa on either side of the cerebrum posterior to and below the sylvian fissures, these lobes present three surfaces. The superior aspect, immediately below the sylvian fissure and covered over by the frontal lobe, is traversed by two or three gyri running obliquely forward and outward in the horizontal plane. These, the transverse gyri of Heschl, undoubtedly comprise the auditory cortex, or auditosensory area, for the direct reception of auditory stimuli. The lateral surface of each temporal lobe comprises three gyri running anteroposteriorly, the superior, middle and inferior temporal convolutions, separated by sulci of the same names. On the inferomesial aspect of the lobe the long fusiform gyrus may be seen just mesial to the inferior temporal sulcus, and running roughly parallel with these structures is the hippocampal lobe, which terminates anteriorly in a small rounded gyrus, the uncus. The temporal convolutions and the fusiform gyrus are devoted, as far as their function is known, to the association and correlation of auditory stimuli and may be called the audito-

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psychic area. Further subdivision of the auditory cortex is still somewhat controversial (Börnstein [1]), but recent work suggests that a vestibular center does exist in the temporal cortex (Meyers [2]). The hippocampal gyrus and uncus are portions of the archipallium and represent the cerebral centers of taste and smell. These, then, are the cortical areas of the temporal lobes and, in a general way, their functions. The subcortical anatomy is of clinical importance chiefly through the presence of three structures: (1) the inferior horn of the lateral ventricle (sometimes known as the temporal horn); (2) the optic radiations which traverse the lobe from posterior to anterior and bend around the ventricle in a narrow band, and (3) the auditory radiations, running laterally from the internal capsule and lying in the upper portion of the lobe close beneath the auditory cortex.

The history of the attack on the problems of diagnosis of lesions of the temporal lobe is interesting. The first step was the discovery, in the last century, by Wernicke, Marie, Dejerine and others that damage to certain portions of the left temporal lobe in right-handed persons produced aphasia. This fact has continued to be a most important localizing weapon ever since. The remaining part of the left and all of the right temporal lobe were still regarded as uncharted seas, and it was at this point that Oppenheim made the statement quoted, in spite of the fact that it was vaguely known that disturbances of taste, smell and hearing did sometimes occur in diseases of the temporal lobes.

In 1905, Knapp [3] made another highly important contribution. He reasoned that, even though the temporal lobes, particularly the right, were relatively silent areas, the diagnosis of a tumor of the temporal lobe could be made by the grouping of the neighborhood symptoms which it produced. With this in mind, he studied a series of ten cases of his own and reviewed all those reported up to 1905. He concluded that in cases which did not show aphasia three groups of symptoms were of great significance: (1) transient paresis of the oculomotor nerve of the same side, (2) hemiparesis of the opposite side and (3) pseudocerebellar ataxia and disturbances of equilibrium. Furthermore, he was able in one case to diagnose a tumor of the right temporal lobe, which was subsequently found and removed at operation.

Kennedy,[4] studying nine cases in London, in 1911, shifted the emphasis again from general and neighborhood symptoms to localizing

1. Börnstein, W.: Ueber die funktionelle Gliederung der Hörrinde, Nervenarzt **2**:223 (April) 1929.

2. Meyers, I. L.: Cerebellar Phenomena in Lesions of the Temporal Lobe, Arch. Neurol. & Psychiat. **19**:1014 (June) 1928.

3. Knapp, A.: Die Geschwülste des rechten und linken Schläfenlappens, Wiesbaden, J. F. Bergmann, 1905.

4. Kennedy, F.: Symptomatology of Temporosphenoidal Tumors, Arch. Int. Med. **8**:317 (Sept.) 1911.

clinical manifestations. His cases were noteworthy for the frequency with which they displayed some form or other of epilepsy—most often peculiar alterations of consciousness usually associated with gustatory or olfactory hallucinations, which Hughlings Jackson named "dreamy states." These transient psychic variations or petit mal attacks were first described by Jackson,[5] but Kennedy reemphasized their important relationship to the temporal lobes.

In 1918, Knapp[6] reviewed the work in Germany since the appearance of his first paper, but though he now added to his symptom complex symptoms which were "characteristic but not particularly frequent" (hallucinations of taste and smell) and symptoms of "limited importance and significance" (neuritic disturbances from continued pull on the posterior roots, psychic abnormalities, epileptiform seizures, hemianopia and similar symptoms), he maintained in general his original conception of the basis for diagnosis of tumors of the temporal lobe—aphasia, oculomotor changes, hemiparesis and pseudocerebellar signs.

A fourth substantial advance came with the recognition of the frequency and importance of defects in the visual field in tumors of the temporal lobe. Cushing,[7] in 1921, reported that thirty-three of fifty-nine cases showed definite alterations of the visual field, and that these constituted the one most constant clinical finding in his series. Subsequently, many authors, notably Lillie,[8] have confirmed this work.

There have been a number of studies of series of tumors of the temporal lobe in more recent years, largely confirming the worth of the symptoms and signs emphasized by earlier writers, but also tending more and more to verify the opinion expressed by Kolodny[9] in 1929 that: "The temporosphenoidal lobe is too large an area of brain for it to be possible for lesions in it, variable in type and extent, to produce any one definite train of symptoms and signs."

The present study is based on the records of fifty-two patients with verified tumors of the temporal lobe in the neurosurgical service of the University Hospital. The ages ranged from 10 to 66 years, the majority being young adults. In thirty patients the tumor was right-sided and in twenty-two left-sided. Other than to note that in this

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5. Jackson, H.: On a Particular Variety of Epilepsy, Brain **2**:179, 1888-1889.

6. Knapp, A.: Die Tumoren des Schläfenlappens, Ztschr. f. d. ges. Neurol. u. Psychiat. **42**:226 (April) 1918.

7. Cushing, H.: The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341, 1921.

8. Lillie, W. K.: Ocular Phenomena Produced by Temporal Lobe Tumors, J. A. M. A. **85**:1465 (Nov. 7) 1925.

9. Kolodny, A.: The Symptomatology of Tumors of the Temporal Lobe, Brain **51**:385 (Oct.) 1928.

series most pathologic types of tumors were included, the pathology of the neoplasms will not be discussed in this paper. The material to be presented may be conveniently considered in five divisions: (1) the onset and duration of illness, (2) the symptoms of increased intracranial pressure, including a discussion of mental symptoms and epileptic seizures, (3) localizing symptoms, (4) neighborhood symptoms and (5) the roentgenologic findings (table).

Comparative Frequency of Eleven Symptoms Occurring in Five Series of Cases of Tumors of the Temporal Lobe

	Kennedy	Kolodny	Gibbs	Schlesinger	Rowe
Date	1911	1928	1932	1933	1933
Number of cases	9	38	197	11*	52
Symptoms due to increased intracranial pressure	Per Cent	Per Cent	Per Cent†	Per Cent	Per Cent
1. Epilepsy	77	50	31	90.0	36
Generalized	77	10	24	54.0	25
Focal	0	40	7	36.0	11
2. Mental symptoms	..	50	..	100.0	50
Focal symptoms of damage to the temporal lobe					
3. Aphasia:					
Per cent left-sided tumors	100	57	48	85.0	31
Per cent right-sided tumors	0	0	7	0.0	3
4. Uncinate attacks	77	17	15	36.0	11
5. Dreamy states	77	18	..	0.0	6
6. Auditory changes:					
Tinnitus	22	0	..	0.9	27
Hallucinations	0	2	..	0.0	2
Deafness	22	8	7	0.9	17
7. Visual field defects:					
Per cent of total cases	0	18	..	63.0	57
Per cent of tested cases	0	25	..	87.0	88
Neighborhood symptoms					
8. Hemiparesis	22	84	..	100.0	50
9. Third nerve	0	55	..	63.0	23
10. Fifth nerve	0	21	..	0.0	23
11. Cerebellar signs	44	18	13	36.0	53

* This series was confined to patients with fibrillary astrocytomas of the temporal lobe.
† These percentages were obtained by study of the tables presented in Gibbs' paper and may vary slightly from his actual statistics.

ONSET AND DURATION

The initial symptoms varied widely. When the cases are divided into three groups, it is seen that increased intracranial pressure caused the first symptom of the majority of patients (71 per cent). The gradual development of headache, dizziness, blurred vision or nervousness found in most instances was occasionally varied by cases of explosive onset, such as a sudden attack of unconsciousness or epilepsy. In a second but smaller group (9 per cent), damage to neighboring areas caused the first symptom—hemiparesis, jacksonian attacks or neuralgic pains over the forehead suggestive of irritation of the fifth nerve, for example. In the third group of patients (4 per cent), the initial symptom was of value in localizing the lesion to the temporal lobe, consisting of a brief attack of aphasia in one instance and in another of dreamy

states. The remaining patients of the series showed several early symptoms of varying causes and could not be classified in these rough groupings.

A comparison of the early symptoms with the chief complaint at the time of admission reveals that the damage done by increased pressure to the vision was the most common factor bringing the patient to the neurosurgeon. The intervals between the onset and the admission to the hospital varied from one month to fifteen years, and averaged twenty-nine months; but if six exceptional cases are excluded, the average duration of symptoms is reduced to twelve and a half months. In two of the cases the tumor was of a slow-growing type (osteoma in one and chondroma in the other), and in the remainder the actual relationship of the long-standing symptoms—mental disturbances, headaches and similar symptoms—to the lesion was not certain.

PRESSURE SYMPTOMS

Of the signs and symptoms due to increased intracranial pressure, headache was the most common, being absent in only three cases. Forty-two patients showed some degree of papilledema, and diminution of vision was found in twenty-one of the forty-six patients tested. Weakness of one or the other abducens nerve was present either objectively or subjectively in almost half of the cases (48 per cent). The clinical picture of intracranial hypertension has been too frequently described to justify any detailed discussion here, but two facts appear worthy of emphasis. First, there was no patient who did not show at least one or more symptoms of increased intracranial pressure, and more than 80 per cent presented definite abnormalities of the optic disks at the time of admission to the hospital. Secondly, in thirty-six patients no symptoms were noted until those of increased pressure appeared. It has been suggested by Kolodny [9] that the stages in the development of a tumor of the brain are: (1) no symptoms, (2) focal symptoms and (3) symptoms of general pressure. In neoplasms of the temporal lobe, to judge from this series, apparently the sequence is more apt to be: (1) no symptoms, (2) symptoms of increased pressure and (3) focal symptoms.

The difficulties in evaluating and classifying mental abnormalities in cases of tumor of the brain are well known. Resulting in part from the damage to the local tissue and in part from the effects of increased intracranial pressure, their localizing value, except in early cases, is not great. Nevertheless, it is of some value to consider the various mental changes observed in twenty-six (50 per cent) of this series of patients. The largest portion of this group showed principally disturbances of consciousness, described variously as drowsiness, stupor, mental dulness and impaired consciousness, and occurring, as might be expected, when

considerable degrees of choked disk were present. It is possible also that the proximity of the third ventricle and its possible neighboring sleep centers may be in part responsible for the high incidence of this picture in patients with tumors of the temporal lobe. Impairment of memory was noted in six cases; four patients were confused or "delirious"; two were restless or irritable, and one was jocose at intervals and lethargic at other times. In general, then, no characteristic mental picture of tumors of the temporal lobe can be described, and in most cases pressure seems to play an important rôle. The extensive German investigations have resulted in the description of almost every type of psychotic symptom-complex as the result of a tumor of the temporal lobe. Korsakoff's syndrome has been emphasized by Knapp and others, although in Marburg's [10] experience this has been rare.

The relatively high frequency of epilepsy in cases of tumor of the temporal lobe has been emphasized by many writers. including principally Kennedy,[4] Knapp,[3] Kolodny [9] and Gibbs.[11] In the present series "fits" were found nineteen times (36 per cent). They include generalized and focal convulsions and dreamy states. The latter will be considered later. The grand mal type of attacks occurred in ten patients, varying from a single convulsion with unconsciousness to one extreme instance in which the seizures had been present for thirteen years. Usually no localizing features existed, but in three cases postconvulsive paresthesias in one arm, mild residual and transient hemiparesis and occasional dreamy states, respectively, gave some indication as to the side or lobe involved.

Jacksonian convulsions or twitching were noted in six patients. In two these were associated at times with loss of consciousness.

The explanation of the frequency of convulsive seizures in cases of tumor of the temporal lobe must be largely theoretical in the present state of knowledge. It is possible that the mere contiguity of the lesion to the motor cortex is an important factor. Or the situation of the expanding lesion against the unyielding base of the skull may result in pressure of the cortex against the vault, with consequent damage or irritation of the prerolandic area. MacRobert and Feinier [12] have suggested that the proximity of the sylvian artery to this area is important, and that the continued upward pressure of a neoplasm against this rather thin-walled artery may result in a moderate ischemia of a large area on the lateral surface of the cerebral hemisphere with a consequent marked increase in cortical irritability.

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10. Marburg, O.: Die Tumoren der Schläfenlappen, in Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1929, vol. 11, p. 2.

11. Gibbs, F. A.: Frequency with Which Tumors in Various Parts of the Brain Produce Certain Symptoms, Arch. Neurol. & Psychiat. **28**:969 (Nov.) 1932.

12. MacRobert, R. G., and Feinier, R.: The Cause of Epileptic Seizures in Tumors of the Temporal Lobe, J. A. M. A. **76**:500 (Feb. 10) 1921.

LOCALIZING SYMPTOMS

Of the localizing symptoms of lesions of the temporal lobe, aphasia is the best known and most reliable. Fortunately for the patient, but unfortunately from the standpoint of diagnosis, it has become apparent in recent years that the early belief that aphasia was a constant accompaniment of tumor of the temporal lobe is incorrect. In this study aphasia was found in only slightly less than one third (31 per cent) of the patients with left-sided tumors. Furthermore, the early impression that a pure sensory aphasia results from a lesion in this area is not borne out by this group. Twice the motor aspect of the speech difficulty seemed predominant, the patients using words incorrectly. In two further cases inability to carry on conversation as well as failure to name objects correctly or carry out commands was present. In the remaining four cases the sensory difficulties were prominent, difficulties in understanding commands, failure of word memory, word deafness and word blindness being outstanding features. One patient with a right-sided tumor had suffered from aphasia. He was in stupor on admission so that no tests could be made, but a reliable history of inability to recognize familiar objects and periods of jargon speech was obtained. Unfortunately, the patient's handedness was not noted. In only one instance was the patient under observation soon after the onset of aphasia. Here, however, the early defects described as "paraphasia" by Knapp [3] and as elliptic or figurative speech by Kennedy [4] were evident. The patient's speech was often normal with the exception of the occasional substitution of a word or phrase which was obviously similar to, but not exactly synonymous with, the word or description which she intended to use. She recognized these errors promptly, and if the right expression was used by the examiner would reply, "That's what I wanted to say."

When these results are compared with those obtained from the study of other series of cases, it is noticed that the frequency of aphasia is somewhat lower than that usually reported. Kolodny,[9] for example, found aphasia in approximately half of his cases of left-sided tumors. Kennedy [4] noted it in five of nine cases, and Gibbs' [11] statistics showed again that almost 50 per cent of the persons with tumors of the left temporal lobe display aphasia.

Abnormalities of the auditory system were present in a rather high percentage of the cases in this series. While some patients presented obvious causes for this (previous scarlet fever, disease of the middle ear and other conditions), in a considerable number no etiologic factor was evident in the past history, and the symptoms seemed definitely related to the present illness. It was therefore considered justifiable to consider the abnormalities in this group as part of the symptom complex of tumor of the temporal lobe, in spite of the fact that the majority of the patients were not examined by an otolaryngologic consultant or by

the use of the audiometer. However, since the results of more gross tests (watch, whisper, and other voice tests) have been used, it is likely that too few rather than too many hearing defects have been found. Moreover, in comparing these tests and the audiometer readings in recent cases, there have been no instances in which deafness reported after routine examination was not substantiated by the more exact studies.

Auditory disturbances may be conveniently divided into two groups, subjective and objective. Of the subjective changes tinnitus was the most frequent, occurring in fourteen cases, or 27 per cent. Only one of these patients also complained of hearing voices at times, a somewhat lower percentage than that reported by Courville,[12a] who found auditory hallucinations in four of ninety-nine patients. It seems probable that these symtoms are the result of irritation rather than destruction of the auditory cortex, although the possibility of an effect produced by increased intracranial pressure must be considered. In most cases the tinnitus was not localized as to side; three times it occurred contralaterally and once ipsilaterally. Three patients complained of partial deafness, while no impairment could be determined by examination. It is possible that in these cases hearing of simple stimuli (watch) was normal, but that damage to the auditopsychic area led to impaired understanding of more complex auditory patterns, which was interpreted by the patient as deafness.

Nine patients showed objective partial deafness, in five the defect being almost entirely contralateral, in three bilateral and in one ipsilateral.

In considering the propriety of classifying partial deafness as a symptom of damage to the temporal cortex, two questions may be raised: (1) Does the symptom occur as the result of damage to the eighth nerve? (2) May it be due to increased intracranial pressure? Cases such as those of Wernicke and Friedländer,[13] Misch [14] and Mills [15] have shown beyond doubt that bilateral destruction of the transverse gyri of Heschl produces complete deafness, but the effect of a unilateral expanding lesion of the temporal lobe is less definite.

Knapp [3] placed little emphasis on auditory changes. In his second paper he did point out that occasionally auditory hallucinations may

12a. Courville, C. R.: Auditory Hallucinations, J. Nerv. & Ment. Dis. **67:** 265 (March) 1928.

13. Wernicke, C., and Friedländer, C.: Ein Fall von Taubheit in Folge von doppelseitiger Läsion des Schläfenlappens, Fortschr. d. Med. **1:**177, 1883.

14. Misch, W.: Ueber corticale Taubheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **115:**567 (July) 1928.

15. Mills, C. K.: Lesions of the Superior Temporal Convolutions Accurately Locating the Auditory Centre, Univ. Pennsylvania Med. Mag., November, 1891, p. 1.

occur. Spiller,[16] in 1908, reported a case in which bilateral diminution of hearing occurred. Kennedy [4] noted contralateral impairment in two of his nine cases, neither with any evidence of peripheral auditory disease, but concluded that in most cases of gradual destruction of one temporal lobe auditory compensation by the opposite center occurs. In Kolodny's [9] thirty-eight cases progressive deafness occurred three times, once as the initial symptom. In two patients the defect was ipsilateral. A fourth patient, whose epileptic attacks were preceded by auditory aura, showed no objective changes. Marburg [10] has rather thoroughly reviewed this subject. He concluded that there are no characteristic disturbances of hearing in tumors of the temporal lobe, that bilateral lesions lead to complete deafness and unilateral tumors result in chiefly contralateral impairment of hearing, but that in cases of homolateral diminution the possibilities of increased intracranial pressure or damage to the medulla or eighth nerve as etiologic factors must be carefully considered.

In one of Dandy's cases in which hemispherectomy was done, studied by Bunch,[17] hearing was apparently cared for by the opposite cortex, being found normal four months after operation. Unfortunately, no tests could be made within the first month after operation. Ruttin,[18] on the other hand, has suggested two characteristics of central deafness: (1) moderate bilateral diminution of hearing and (2) disproportion between the distance over which voice sounds and spoken words can be recognized. As it is generally accepted that most of the auditory fibers pass from the ear to the opposite cerebral cortex (though some are connected with the ipsilateral cortex center), one might expect, as occurred in Lawson's [19] patient, that central deafness would be largely contralateral, whereas changes due to a lesion damaging the eighth nerve would be ipsilateral.

Among the cases of this series with auditory symptoms, five were found in which the tumor did not appear to involve the auditory cortex directly. In all of these the lesion was below the lobe, but in only one instance could it conceivably have extended sufficiently far caudally to impinge on the acoustic nerve. There was no constant relation between the location of the tumor and the laterality of the hearing loss.

The effects of increased pressure are difficult to evaluate. In the majority of this group there was evidence of choked disk. On the other

16. Spiller, W. G.: Tumor of the Gasserian Ganglion: A Report of Two Cases with Necropsy, Am. J. M. Sc. **2**:712, 1908.

17. Bunch, C. C.: Auditory Acuity After Removal of Entire Right Cerebral Hemisphere, J. A. M. A. **90**:2102 (June 30) 1928.

18. Ruttin, E.: Ohrbefunde bei Tumoren der mittleren Schlädelgrube, Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres **27**:461, 1929.

19. Lawson, L. J.: Apparent Effects of Cerebral Tumors on Auditory Acuity: Report of a Case, Arch. Otolaryng. **15**:583 (April) 1932.

hand, the average incidence of impairment of hearing in lesions not affecting the auditory mechanism directly in Gibbs'[11] series was only approximately 9 per cent as compared with 17 per cent in this group.

Greene,[20] studying the ability of patients with tumors of the brain to localize sound, was unable to rule out the effects of intracranial hypertention and consequently could not come to any definite conclusions.

In general, then, one may conclude that partial deafness, occasionally more marked on the contralateral side, does occur from damage to the auditory cortex in tumors of the temporal lobe, rarely from damage to the nerve and possibly occasionally from increased intracranial pressure.

Disturbances of taste and smell were not prominent in this series. Hallucinations of taste or smell, i. e., uncinate attacks, which are the most valuable symptoms of this type from a diagnostic standpoint, were found in only six patients, or 11 per cent. These were usually of a disagreeable nature—gases, food burning and "a bad taste."

Attacks of a petit mal variety, apparently examples of Jackson's[5] "dreamy states," were found only three times. These peculiar transient psychic variations may possibly occur more frequently than is noted, but since their recognition depends to a large extent on the intelligence and alertness of the patient, it would not be surprising if they were occasionally overlooked. In only one case was the symptom prominent. This woman, aged 21, had suffered from "blank spells" almost daily for two and a half years. They came on as one of the earliest symptoms at a time when she was working in an electric power house, and she noticed that the sound of the dynamos assumed an intensely oppressive sound and that "everything else seemed to stop" for from a few seconds to fifteen minutes. There never was an unconsciousness, though for a moment or two she was not aware of external stimuli. She had also noted the sense of reminiscence, the feeling of having been caught in exactly the same situation before, that Jackson described.

The final definitely localizing sign of a lesion of the temporal lobe is of great importance. In thirty-two cases changes in the visual field were found—nineteen showing homonymous hemianopia, six homonymous cuts and five homonymous quadrantanopia (four in the upper quadrants). Two patients had peculiar restrictions of the visual fields of doubtful diagnostic value. It is to be noted that in eighteen cases no fields were charted, in several because the patient was seen some years before their importance was recognized, but in a considerable number because the patient's condition prevented his cooperation (stupor, psychotic upsets and similar conditions). The value and methods of

20. Greene, T. C.: Ability to Localize Sounds: Study of Binaural Hearing in Patients with Tumor, Arch. Surg. **18**:1825 (April) 1929.

perimetry in the diagnosis of tumors of the brain have been so frequently presented in the past (Cushing, Lillie,[8] Cave [21] and others) that further discussion is not necessary.

NEIGHBORHOOD SYMPTOMS

A tumor of the brain causing symptoms referable to a single lobe is a rarity indeed. Unfortunately, the almost invariable presence of symptoms due to pressure on contiguous structures is as frequently a hindrance as it is a help. Nevertheless, as Knapp [3] has emphasized, it is frequently possible to diagnose a tumor of the temporal lobe solely through the symptoms due to the damage of neighboring structures. In the present series no case failed to display these symptoms, and in approximately half of them the localization depended in a large measure on such findings. The chief effects of this injury to surrounding areas may be grouped under (1) frontal lobe, (2) parietal lobe, (3) cerebellum and (4) cranial nerves.

The principal manifestations of damage to the frontal lobe were jacksonian attacks and hemiparesis or hemiplegia. The former have already been discussed. Some evidence of motor involvement was noted in half the cases, 50 per cent. In five of these a unilateral exaggeration of tendon reflexes was the only finding, but in the remaining patients a definite spastic weakness was detected. Two cases were of especial interest in that they presented a homolateral hemiparesis.

Symptoms of involvement of the parietal lobe are at best not striking and did not appear frequently in this group. Six patients had astereognosis, and an additional seven had experienced subjective and in two cases objective sensory disturbances on the side opposite the tumor.

Symptoms of cerebellar involvement, on the other hand, were frequently and confusingly present. Of the forty-four patients tested for cerebellar signs, twenty-three (53 per cent) showed some variations from the normal. In general, these were less definite and appeared later in the history of the patient than in cerebellar lesions, but in some instances the similarity of the picture to that of a tumor of the posterior fossa was marked. Unsteadiness of gait, a positive Romberg reaction, dysmetria, nystagmoid movements of the eye, and even what was thought to be true nystagmus were found.

The explanation presented for this group of symptoms and signs includes: (1) the effects of pressure (Grant,[22] Alexander [23]), (2)

21. Cave, H. A.: Temporal Lobe Lesions: Disturbances of the Visual Pathways, California & West. Med. **36**:13 (Jan.) 1932.

22. Grant, F. C.: Cerebellar Symptoms Produced by Supratentorial Tumors, Arch. Neurol. & Psychiat. **20**:292 (Aug.) 1928.

23. Alexander, G.: Choked Labyrinth, Surg., Gynec. & Obst. **46**:361 (March) 1928.

damage to a vestibular center in the temporal lobe (Meyers [2]) and (3) interference with temporopontocerebellar tracts. It is probable that all of these mechanisms play a rôle, but that the last is the most important.

Damage to the cranial nerves by tumors of the temporal lobe was limited chiefly to the third, fifth and sixth nerves. The latter lesion is too frequently the result of increased intracranial pressure to have localizing value. Oculomotor changes, however, consisting most frequently of a mild ptosis of the eyelid or a dilated ipsilateral pupil, appeared twelve times (23 per cent) and formed an important diagnostic aid. Impaired pupillary reactions and slight weakness of the extra-ocular motions were observed in three additional cases on the contralateral side. Schlesinger [24] has also noticed this and suggested that damage to the optic tracts may be an underlying mechanism. The proximity of the gasserian ganglion to the temporal lobe is to be remembered in examining patients suffering with neuralgic pains in the face. Spiller,[16] in 1908, reported two cases in which pain of this origin was a predominant symptom. In the present series suggestive symptoms were found twelve times. Five patients showed homolateral and seven contralateral sensory or motor disturbances of fifth nerve type, consisting most frequently of paresthesias in the first or second divison. Again the contralateral findings are difficult of explanation. In the present series symptoms suggestive of injury to the fifth nerve were found twelve times. Miscellaneous neighborhood symptoms occurred in a few additional cases, but were of such variability and rarity as to be of little significance.

ROENTGENOLOGIC FINDINGS

While the lay idea that tumors of the brain are always disclosed by the x-rays is still far from correct, it is true that this diagnostic method is continually assuming a larger part in their localization. Including eleven cases in which ventriculography was used, twenty tumors in this series were definitely localized through roentgen studies. In an additional six instances the changes in the sella turcica were indicative of a cerebral lesion. Eleven cases could not be examined roentgenologically for one reason or another, and thirteen showed normal films.

SUMMARY

It is difficult, if not impossible, to formulate a definite symptom complex for tumors of the temporal lobe. With the infinite variations which occur, one can describe only an average picture and point out some of the more frequent departures from this which have occurred

24. Schlesinger, B.: Syndrome of the Fibrillary Astrocytomas of the Temporal Lobe, Arch. Neurol. & Psychiat. **29**:843 (April) 1933.

in the cases studied. A brief review of the material presented in this paper with this purpose in mind may serve to emphasize several important features of the symptomatology of tumors of the temporal lobe.

Even with the accumulation of facts by many observers of an ever-increasing number of cases, the temporal lobes seem destined to remain more or less silent areas. The early symptoms are as a rule not sufficiently severe or clearcut to bring the patient to the hospital, and it is only with the advent of increased intracranial pressure that he becomes aware of his disease. As a result, the picture is confused by the presence of intracranial hypertension and the localization rendered more difficult. On the other hand, the surgeon, while hampered by the presence of the increased pressure to some extent, is greatly aided in his effort to give the patient permanent relief by the fact that he is working in a silent area and may remove relatively large portions of the temporal lobe without causing serious postoperative disabilities.

Prominent in the symptomatology of these cases were mental abnormalities. Apparently in a large measure due to the presence of increased intracranial pressure, they showed no characteristic form, varying from changes of consciousness to mild alterations in personality.

Epilepsy was an important feature of the picture in nineteen patients (36 per cent). The fact that of these ten suffered from generalized convulsions and one had endured them for thirteen years serves to emphasize the need of careful study of epileptic patients to avoid overlooking a tumor as an etiologic factor.

Three of the recognized symptoms of damage to the cortex of the temporal lobe—aphasia, uncinate attacks and dreamy states—did not occur in a high percentage of the cases in this series. Aphasia was found in approximately one third of the patients with tumors on the left side and in one patient with a lesion on the right. Hallucinations of taste or smell were noted in six patients. These findings are in general keeping with those reported by others, though the frequency of aphasia has been found to be greater by some. Auditory abnormalities, on the other hand, were somewhat more frequent in this group than in those previously reported. While the possibilities of the effects of increased intracranial pressure or of coincidental peripheral changes must be kept in mind, it seems that tinnitus, auditory hallucinations and impairment of hearing, particularly for spoken words, occur rather frequently in patients with tumors of the temporal lobe.

Visual fields, though not always obtainable, were of great diagnostic importance in 57 per cent of the cases.

An evaluation of the oldest method of diagnosis of tumors of the brain, namely, through their damage to the surrounding structures by pressure, shows that in the main the signs and symptoms of injury to the motor system are still highly important in the localization of tumors

of the temporal lobe. Furthermore, in cases in which the lesion is situated at the base of the lobe, pressure on the fifth or the third nerve occurs relatively frequently. Finally, one finds that the information derived from the x-ray, particularly through ventriculography, is becoming more and more helpful.

REPORT OF ILLUSTRATIVE CASES

CASE 1.—*Headaches and vomiting of one year's duration; bilateral tinnitus, attacks of blindness, and several brief periods of unconsciousness within a few months of admission. Tubular vision in the left eye; nasal hemianopia in the right visual field, bilateral choked disks; anosmia on the right. Right temporal glioma removed in two stages with much improvement. One generalized convulsion, with several series of roentgen treatments. No signs of recurrence of the tumor after eight years.*

History.—Mrs. T. P., a white woman, aged 30, entered the neurosurgical service in October, 1923, complaining chiefly of headaches and sore eyes. Headaches over the vertex sometimes associated with attacks of vomiting had troubled the patient for one year. One month after the onset she noticed that things "seemed to go around" at times, and that occasionally her "sight would leave her" for five or ten minutes. Later she had bilateral tinnitus and sudden brief attacks of unconsciousness. The remainder of the history was without significance.

Examination.—Physical examination gave essentially negative results.

Neurologic examination showed marked contraction of the left visual field, with a nasal hemianopia in the right visual field; loss of sense of smell on the right; no other abnormalities of the cranial nerves, reflexes, motor or sensory systems. The eyegrounds showed bilateral choked disks of 3 diopters.

The roentgenogram was negative for any evidence of tumor.

Lumbar puncture showed a pressure of 28 mm. of mercury; there were 4 cells; there were no changes in the blood.

Operation.—First Stage (October 19): The right temporal lobe was exposed through an osteoplastic flap, and a tumor was seen presenting on the surface and involving the dura.

Second Stage (November 9): A tumor, fairly well encapsulated with the exception of one surface, was completely removed from the temporal lobe. The section was made quite wide of the tumor, apparently in normal tissue, in the region where no line of demarcation could be detected.

The pathologic diagnosis was astrocytoma.

Postoperative Course.—The patient had one generalized convulsion almost two years after the operation and was consequently readmitted for study. Neurologic examination gave negative results. Vision was nearly normal, and there had been some widening of the fields. No choking of the disks could be detected. She was given two courses of roentgen treatments. The last letter from her physician (1931) stated that aside from occasional headaches and a sensation of dizziness at times she showed no subjective or objective evidence of an intracranial pathologic process.

Comment.—This case is of considerable interest for two reasons: First, the symptomatology was sufficiently characteristic to localize the

lesion clearly. Second, the end-result shows that wide excision of even an infiltrative tumor of the temporal lobe can result in a complete cure.

CASE 2.—*Sharp paroxysmal pain in the right side of the forehead for eleven months; headaches and loss of vision; objective impairment of the function of the right fifth and right eighth nerves; bilateral choked disks of 6 diopters; slight increase in the left tendon reflexes; thickened bone in the right middle fossa. Removal of a fibroblastoma from beneath the right temporal lobe in two stages. Marked improvement. General condition good after seven years.*

History.—Mrs. M. A., a Mexican woman, aged 40, who was admitted to the neurosurgical service on Oct. 16, 1925, eleven months before had felt a sharp pain in the right temple, as though a nail were being driven into it. This lasted only a few minutes but recurred occasionally within the next six months. Subsequently she noticed numbness and crawling sensations over the right side of the face, in the tongue and in the right upper extremity. About eight or ten months before, she had a feeling of cold and a little later a ringing in the right ear. Generalized headaches and a gradual progressive impairment of vision were present for four months prior to admission. The past history revealed no pertinent findings, and the family history was essentially without significance.

Examination.—Physical examination showed a well developed and well nourished woman. There were small umbilical hernia and moderate deafness on the right.

Neurologic examination revealed nystagmus on left lateral deviation of the eyes; deviation of the jaw to the right on opening; hypalgesia in the first and second divisions of the right fifth nerve, with diminution of the corneal reflex; questionable weakness of the right eighth nerve of the peripheral type. The visual fields were not obtained owing to lack of cooperation and language difficulties. The eyegrounds showed 6 diopters of choking in each eye.

A roentgenogram revealed a marked thickening of bone in the region of the right middle fossa, particularly below and behind the lesser wing of the sphenoid.

Lumbar puncture revealed a pressure of 30 mm. of mercury, 3 cells and no changes in the blood.

Operation.—First Stage (November 2): Right temporofrontal craniotomy was performed by Dr. Frazier, and the thickened bone was exposed. For fear of penetrating the tumor, the right ventricle was not tapped, and in the presence of such high intracranial pressure it was not thought wise to try forcibly to lift the temporal lobe to obtain better exposure.

Second Stage (November 18): With the patient in a sitting posture, the flap was reopened; when the dura was opened a red granular-appearing tumor adherent to the dura was exposed beneath the temporal lobe. This was removed without difficulty, together with the dura of the middle fossa.

The pathologic diagnosis was meningioma.

Postoperative Course.—For a time following the operation the patient had mild mental change—acted somewhat childishly—but this gradually improved. A slight complete hemiparesis (face, arm and leg) also developed. This was not sufficiently marked to prevent the patient from walking well. Hearing was normal, and the subjective and objective evidences of involvement of the fifth nerve completely disappeared.

A letter (from Yucatan, Mexico) in November, 1932, stated, "Although her general conditions are good, she still complains of her left hand and foot . . .

remarking that the left foot suffers certain contractions that make difficult her normal walking . . ." and added that the patient also complains of neuralgic pains in the head and neck on the right.

Comment.—In this case the roentgen evidence was of great importance in determining the site of the tumor, but the damage to the adjacent cranial nerve was also valuable in the localization. Interestingly enough, only one of the signs (nystagmus) described by Elsberg [25] as characteristic of fibroblastoma beneath the temporal lobe was present in this case.

CASE 3.—*Six months before admission, dazed by a blow over the right eye; subsequently, headache, one attack of unconsciousness and loss of vision; uncertain, variable slight palsies of the cranial nerves. A cyst in the right temporal lobe drained on three occasions. Wall of cyst removed three months later. Marked improvement for approximately one and one-half years. Death two years after last operation.*

History.—J. H., a boy, aged 12, entered the neurologic service on June 10, 1927, complaining chiefly of right temporal headache. In December, 1926, he was struck over the right eye by a basketball. He became very dizzy and was dazed for a moment, but did not lose consciousness. Two weeks later he had severe right temporal headaches and vomited several times suddenly without warning. Subsequently the headaches had become more severe, and on June 3, 1927, he stiffened out and was unconscious for twenty hours. For the last six months before admission he had slight impairment of vision. The family and past history was irrelevant.

Examination.—Physical examination showed that the boy was normal physically.

Two examiners differed considerably in their findings on neurologic examination. The first thought that the only positive neurologic signs were hypesthesia and hypalgesia of the left side of the face. The second reported impairment of sensation and the corneal reflex on the left side of the face, weakness of the motor function of the right fifth nerve, and slight weakness (of the peripheral type) of the left side of the face, with moderate impairment of hearing on the left. The abdominal reflexes were absent on the left. The eyegrounds showed choked disks of 4 diopters on both sides.

Lumbar puncture revealed a pressure of 26 mm. of mercury. There were no changes in the blood.

Operation.—1. There was a considerable divergence of opinion as to the diagnosis, but as the location of the trauma and the patient's headache coincided over the right temporal region, it was decided to do a right subtemporal decompression and if nothing was found to tap the right ventricle to relieve the pressure. This was done, and when a cannula was introduced 40 cc. of yellow fluid, which did not coagulate, flowed out.

2. Nine days later, evidence of pressure recurred, and the cyst was tapped again.

3. Following this, the visual fields showed a left homonymous hemianopia, which did not disappear after a third emptying of the cyst.

25. Elsberg, C. A.: The Meningeal Fibroblastomas on the Under Side of the Temporal Lobe and Their Treatment, Bull. Neurol. Inst. **2**:95 (March) 1932.

4. A transcortical incision was made, the cyst was opened, and though no nubbin of tumor could be seen, a considerable portion of the wall of the cyst was removed after fixation with Zenker's solution.

The pathologic diagnosis was fibrillary astrocytoma.

Postoperative Course.—Immediately following the operation, a slight facial weakness appeared, but this disappeared before discharge. The patient returned to his home in Oklahoma greatly improved, a letter one year later stating that "he could ride his bicycle and his eyesight improved so that he could read well, and he finished the 8th grade with better grades than his brother," but in 1929 a left hemiparesis appeared and the patient died in September, 1930.

Comment.—In this case the localization was very obscure and the right temporal lobe was suspected chiefly because this was the site of the patient's headache. The fact that a cyst containing 40 cc. of fluid could produce so few and uncertain neurologic findings is characteristic evidence of the relative "silence" of lesions in that area.

DISCUSSION

DR. WILLIAM G. SPILLER: Dr. Rowe called attention to the well known fact that tumors of the temporal lobe, especially of the right lobe, are considered difficult to diagnose, and that this lobe is often regarded as silent. Experimental work has revealed some interesting findings. Spiegel demonstrated in dogs and cats that the application of strychnine to the arcuate gyrus behind the sylvian fissure, corresponding to parts of the temporal lobe in man near the occipital and parietal lobes, establishes a vestibular center. Rotation of animals so treated produced labyrinthine reflexes and convulsions. Barre, Vincent and Helle report a case of tumor of the temporal lobe which induces them to place the vestibular center in man in the middle portion of the first and second temporal convolutions.

Equally interesting are the statements that Silbermann and Tamari experimented on five persons with trephining defects over the third temporal gyrus, and three of these were over the right lobe. The brain at this part, which corresponded to the projection of Heschl's convolution, was frozen for three minutes with ethyl chloride, and audiometer tests were made before and after the freezing. A decided alteration in the perception of tones was produced. This seems to explain the fact that persons with lesions of the basal portion of the temporal lobe frequently complain of disturbing noises which interfere with their hearing. These authors conclude that the normal apparatus of the outer surface of the third temporal convolution has the function of a damper and regulator of the heard tones of human speech.

Similar results were obtained by Hoff and Silbermann in fracture with removal of bone over the right second temporal convolution. In another similar case epileptic attacks occurred with an aura of an unpleasant noise.

In another case a defect of bone over the right first temporal convolution existed. Freezing of this area with ethyl chloride caused the patient's speech to sound strange to her and as though a strange person in the room were speaking the patient's thoughts.

The projection field of the acoustic tract is only in the Heschl convolution, but almost the entire temporal lobe forms an important apparatus necessary for normal hearing, which on the left side is combined with the speech mechanism.

Chronic epidemic encephalitis often involves the periventricular gray matter of the interbrain. Hallucinations of sound, which begin about 10:30 p. m. and last

until 4 or 5 a. m., developed during the past month in a patient whom I saw recently in the care of Dr. Ornsteen. He hears footsteps on the floor above or below him, and has heard an automobile stop at his door and some one try the lock. He has never heard voices. He is convinced he hears burglars and awakens his mother and sister, who hear nothing. It is to be noted that he hears sounds and not voices, which would seem to imply that these hallucinations are less associated with the left first temporal convolution.

Cerebellar symptoms have been reported in tumors of the temporal lobe, and it has been demonstrated by Dejerine that the temporopontocerebellar tract, known as the fasciculus of Türck, has its origin in the posterior part of the second and third temporal convolutions. Some investigators believe that it arises partly in the occipital lobe. It degenerates toward the cerebellum in lesions of the convolutions mentioned. I have had the opportunity to observe this in sections in Dejerine's collection. Tracts in the central nervous system degenerate in the direction in which they transmit impulses. The cerebello-rubro-thalamo-cortical system must also be considered in this connection. It is striking that Kalodny in a study of cases of tumors of the temporal lobe at the National Hospital found no support for regarding the temporal lobe as an organ of balance, and stated that pseudocerebellar signs are rarely seen in tumors of the temporal lobe.

The typical thalamic syndrome of Dejerine and Roussy, consisting of hemianesthesia, involving deep sensibility more than superficial sensibility, with persistent, paroxysmal, spontaneous pains on the affected side, little or no hemiplegia, hemiataxia and frequently irregular involuntary movements of the athetoid or choreic type in the affected limbs, is not common in tumors of the temporal lobe, nor are the typical dystonias with athetoid or choreiform movements of striate disease.

Stephan Weisz, quoting Stertz, gives as symptoms of tumor of the interbrain: hypersomnia, disturbance of the pupils, vegetative vasomotor disturbances, polyuria, pollakiuria, increase of temperature, sudden death and psychic manifestations. He reports six cases in which symptoms of this character occurred with tumors of different types in the interbrain, which he studied in serial sections by the method of Nissl. He was not able to draw conclusions of localizing value from this study, and he attributed much importance to the brain swelling with tumors. Pette recently also emphasized this as a cause of diencephalic symptoms in tumors of the temporal lobe and spoke of it as Reichardt's *Hirnschwellung*. In a paper read by me before a joint meeting of the New York Neurological Society and the Section of Neurology and Psychiatry of the Academy of Medicine, Nov. 11, 1913, and published in the *American Journal of Medical Sciences* (**147**:28 [Jan.] 1914), I showed that the enlargement of the brain as described by me, even from small tumors, was a persistent condition, probably of glia overgrowth, and caused persistent symptoms. This was very different from Reichardt's *Hirnschwellung*, as described by him in 1911, which he stated may develop rapidly and disappear equally rapidly, and cannot be explained by hypertrophy, hyperplasia or histologic changes. He thought that it might be caused from an intimate combination of fluid with the brain substance, and yet the brain might not appear moist.

While clinical cases occur in which diencephalohypophyseal symptoms are prominent, and especially the hypersomnia, as in a recent case of mine in which this symptom was of such striking value as to assist in the proper localization of a tumor in the region of the periventricular gray matter of the third ventricle, other cases occur in which lesions of this region seem to be silent. This peculiarity has been well emphasized by Cushing in his monograph entitled, "Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System."

This is seen in hydrocephalus implicating the third ventricle or in large tumors filling the third ventricle without the slightest indication of the symptoms to be expected from the known function of this area; even after the removal of such a tumor, symptoms such as personality changes, polyuria, adiposity, somnolence, hyperthermia or vasomotor changes may be wanting. The absence of such symptoms does not vitiate positive findings obtained in other cases.

The conditions mentioned by Cushing are slow development and an adaptability of the brain tissues to slowly developing pressure.

Psychic symptoms are mentioned by many writers on tumors of the temporal lobe. Rowe found them in 50 per cent of his cases. Pette describes them. There may be merely a loss of mental energy, or hallucinations of sight, taste or smell, apathy, disorientation, mental depression, or euphoria and maniacal periods, or hallucinations of hearing of tones or words. Karl John made a critical review of this subject, but when such symptoms occur with abscess of the temporal lobe, as in a case reported by John, it is difficult to exclude toxic conditions. Horrax, in 1923, reported visual hallucinations in seventeen of seventy-two cases of tumor of the temporal lobe, and in twelve of these definite hallucinations of figures occurred, and in thirteen of the seventeen cases the hallucinations were associated with uncinate attacks. Psychic symptoms of diencephalic origin may be mistaken for symptoms of tumor of the frontal lobe.

Time does not permit a discussion of the importance of aphasia in tumors of the temporal lobe. I may mention that often an early indication of word deafness is the use by the patient of a wrong word to express his meaning, and the untrained examiner may consider the condition to be motor aphasia. The study of the representation of music in the brain still affords a large field for investigation. One of the most recent studies is by Somogyi. It may be assumed that the sensory musical center lies in the middle third of the left first temporal convolution, but the right hemisphere cannot be excluded.

Occasionally tumors of the temporal lobe may produce symptoms of paralysis of the cranial nerve by distant pressure. The most remarkable manifestation of this fact was observed by me in a case in the service of Frazier. A large occipitotemporal tumor caused successive paralysis of the abducens nerve and successive paralysis of peripheral type of the facial nerves. There were no signs of involvement of the pyramidal or sensory tracts. Dr. Alpers and I determined that the tumor did not invade the pons. I, as well as others, have seen paralysis of the abducens nerve from pressure by a tumor of the temporal lobe, but paralysis of each facial nerve from distant pressure is much more uncommon.

AKINESIA ALGERA

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Akinesia algera was described and named by Möbius in 1891.[1] He spoke of it as the loss of voluntary motion because of pain produced by motion, and considered that it lacks an organic basis. It occurs in patients of a neurotic type, the *déséquilibrés* or the mentally maladjusted. At first only the more intense movements produce pain leading to paralysis, but later all or almost all movements cause pain. The pain may occur simultaneously with or after the movements, and may occur not only in parts of the body which have been moved but may extend to other parts which have not been moved. Finally, almost complete immobility may result, simulating general paralysis. Signs of a psychoneurosis may be found, namely, hypochondriasis, hysteria, neurasthenia, etc. Möbius described two cases. He expressed the strongest conviction that he was dealing with a functional disturbance only, and spoke of hallucinations of pain. He acknowledged that the syndrome described by Neftel in 1883 [2] as atremia was very similar to the disorder that he described, but Neftel considered that the atremia in his patients was a hypochondriac psychosis, stating that the patients were affected only when walking, standing or sitting, and that they did not show the disturbance when in bed.

Oppenheim, in his "*Lehrbuch,*" gave an excellent and concise description of akinesia algera. He considered the pains as psychalgias and stated that they may increase the rapidity of the breathing and of the pulse. In dysopsia algera the pains from ocular movements or fixation of gaze may be severe. This was well illustrated in my patient. Intent listening and the taking of food may cause pain, and if the patient eats little, he may become emaciated. This condition is called aphagia algera.

The prognosis is grave. Oppenheim obtained recovery in a few cases by long continued psychoneurotic treatment, in one case after a half year; in another case, a severe one, he obtained incomplete recovery after several years.

In a case reported by Erb,[3] the patient, a man, aged 47, was a member of a highly neuropathic family and had severely taxed his

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1. Möbius: Deutsche Ztschr. f. Nervenh. **1**:121, 1891.
2. Neftel: Virchows Arch. f. path. Anat. **91**:464, 1883.
3. Erb: Deutsche Ztschr. f. Nervenh. **3**:236, 1892; **5**:424, 1894; **8**:345, 1896.

endurance by excessive intellectual work. Rapid heart beats occurred on every physical exertion; he became unable to stand or sit, and pains like electric shocks in the shoulders and thighs occurred after motion. After two weeks in bed he was able to stand for twenty minutes at a time and to recline in a chair for a little over three hours; more than this caused pains throughout the body. He became unable to read or write, because of the pains these acts produced. He was unable to listen to reading and was obliged to keep the horizontal position always; he avoided every possible voluntary movement because of fear of pain in all his limbs. If he moved a limb occasionally, it appeared for some time afterward as though paralyzed. He asserted that movement of any muscle produced pain in the corresponding muscle of the other side of the body. He remained in a horizontal position for ten years, day and night. He slept little. Then pain developed deep in the ears and he was unable to listen to more than two or three spoken words, although he could talk without discomfort. At the time of the report he had been complaining for twenty-two years, and because of pain had remained in the horizontal position for fourteen years with only the head movable. When friends visited him he did all the talking; they were permitted to speak only one or two words. His mind was clear. All treatment until the time of this report had failed. Erb regarded the condition of this patient as typical of akinesia algera and was doubtful of recovery.

A year later, Erb received an unexpected and favorable report from the patient. Erb had ordered certain medicines, with strict attention to details, largely for psychic effect, and the patient had followed the directions carefully. He could listen to reading aloud, but not to conversation. He had a relapse, but later was convinced that some of the pain was caused by his mental attitude; he began to fight against the pains.

In 1896, two years after his second report, Erb reported further improvement which amounted almost to complete recovery and which had been obtained by psychotherapy, especially in the form of suggestion.

Von Bechterew,[4] in his paper published in 1894, as a result of his findings in a patient with akinesia algera under hypnosis, concluded that the painful sensibility of the muscular and osseous systems was not imaginary. This view was disputed by Oppenheim.

Moyer,[5] reported a case which he said closely resembled, in some respects, the cases reported by Möbius and Erb. A man, aged 45, with a neurotic ancestry, five years before he came under Moyer's observation had pains in the upper and lower limbs that came on some hours

4. von Bechterew: Deutsche Ztschr. f. Nervenh. **5**:430, 1894.
5. Moyer: Med. Standard **13**:10, 1893.

after rising in the morning. The pains became worse during the day. He descended the stairway of his house on one occasion and had to crawl back on hands and knees. Thereafter he confined himself to one floor. He was able to move from one room to another, but only slowly and with care. The use of the lower limbs produced more pain than that of the upper limbs. The head was freely movable. Repeated examinations failed to show any objective condition accountable for the pains.

Ingelrans,[6] writing in 1905, said that the number of case reports of akinesia algera did not exceed forty; this included brief reports; no cases had been reported in France. He wrote a review of the subject and gave brief abstracts from some of the published reports. He did not consider the disorder distinct from other neuroses and questioned the propriety of the inclusion of some of the reported cases.

Dejerine, in the second edition of his "Sémiologie des affections du système nerveux," which appeared in 1914, described the symptoms of the disorder and referred to some of the early cases, but he mentioned no case of his own. He considered the condition as belonging to the central algias, and spoke of it as of rare occurrence.

"The General Index of Subjects of the Journal of Nervous and Mental Disease" from volumes 1 to 50, covering the period from 1874 to 1919, contains only two references to akinesia algera. One is to an abstract of the report of a case by J. J. Putnam at a meeting of the American Neurological Association in June, 1892; the other is to the papers by Erb and von Bechterew, of which I have made mention.

For many years akinesia algera has been almost ignored in medical literature. Most textbooks on neurology do not describe it or even refer to it, and I have frequently been informed by capable neurologists that they have never heard of it. It may not be amiss therefore to describe a case, especially as the case is unusual in that the pseudoparalysis from motion of the body was confined to the head and neck.

Miss A. B., aged 25, who consulted me on May 19, 1933, had been well until five years previously, at which time "a heavy feeling" developed in her eyes and the lower part of her face when she attempted to use the eyes even for a few minutes. At the onset, this disturbance was mild and did not prevent her from performing household duties, but it gradually became worse, especially on the left side of the face, and eventually implicated the entire head and neck down to the upper portion of the trunk. In about two years she became practically an invalid. The only position in which she obtained any degree of comfort was sitting in a chair with the eyes directed forward and the lids partly closed. As I watched her in this position she reminded me of the statue by Saint-Gaudens in Rock Creek Cemetery in Washington, D. C. Her pose and features were similar. A cervical sympathectomy, possibly for supposed atypical neuralgia, had been performed with the result that the symptoms were made worse.

6. Ingelrans: Gaz. d. hôp. **78**:783, 1905.

Physical examination revealed no important findings. I could not obtain any history of previous nervous strain, nor could I obtain any information of psychoneurosis in her family. No signs of a previous attack of epidemic encephalitis were obtainable.

She appeared in sitting almost statuesque, because any exertion, any movement of the head or eyes caused pain, and she maintained the one position. The pain was not sharp; it was not like the pain of toothache; she described it as a burning or cold sensation, or one "like needles." It was a sensation of heaviness, or as though she had a tight veil drawn about her face; it caused great discomfort but did not cause agony, and was not of the character of tic douloureux; it was a form of paresthesia.

She did not change the expression of her countenance, because to do so would produce the sensory disturbances. The pain and other paresthesia never extended below the neck or into the upper limbs. A draft, as from a window, or a current of hot air, as from a radiator, would produce the sensory phenomena. Walking in the wind, lifting some heavy object with the upper limbs and general fatigue had the same effect. She had no photophobia. She did not think that she was affected by sunlight, but the symptoms were more pronounced when she was lying down, because, as she explained, she was lying on the back of her head.

The pupils were equal and responded well to direct and indirect light and in convergence, and convergence was good. It was difficult to examine the pupils, because the patient did not open her eyes widely and allowed the upper lids to droop, making it difficult to see the pupils well; if I attempted to raise the upper lid with my finger or asked her to do so she resisted because of the discomfort produced. It caused her great discomfort to put her head back; if she attempted this motion on request, she placed her hand to the back of her neck and complained because of an increase in the symptoms. She did not wrinkle her forehead and did not raise her eyes toward the ceiling when requested to do so, because of the discomfort produced. When she was asked to show her teeth she did not comply for the same reason, and the corners of the mouth were not drawn upward. The face was kept masklike. She protruded the tongue a little beyond the lower lip on request, but not to a normal extent. The face felt a little tense to gentle palpation, and slight pressure on the face caused discomfort. When asked to bite, the masseter and temporal muscles contracted equally on the two sides, but she employed little force, and yet she tried to accomplish what I requested. Tactile, pain and temperature sensations were normal in the face.

The grasp of the hands was equal, but not as strong as it should be. A dynamometer registered 45 in the right hand and 30 in the left hand. Examination of the lower portion of the body as regards reflexes and objective sensation of different types revealed no striking abnormal findings.

COMMENT

The case appeared to me to have no organic basis, but to belong to the group which Dejerine called "algies centrales ou psychiques." The patient was discouraged and depressed by her years of suffering. I began psychotherapy by suggestion, enforced by very weak electrical currents and gentle massage applied to the face under the direction of Dr. Nylin, in charge of the department of psychotherapy of the University Hospital, but I found within two or three days that no treat-

ment directed to the face would be successful. Recalling that the patient was convinced that the symptoms in her face could be produced through other parts of the body than the face, I began to treat her through these other parts, and had she been able to remain she might have been benefited, but she was not able to stay more than eight days. The success obtained by Erb in his case should always be a source of encouragement in treatment in such cases.

HUGHLINGS JACKSON'S VIEWS ON MENTATION

THEIR VALUE FOR THE PSYCHIATRIST

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Few physicians have analyzed the nature of mental processes as clearly as Hughlings Jackson. Modestly disclaiming any knowledge of psychiatry and lacking extensive clinical experience in mental disorders, Jackson inductively worked out certain general principles of mental functioning which are profoundly illuminating—principles, be it shamefully admitted, which the world of psychiatry has ignored and virtually forgotten. In the half century that has elapsed since his Croonian lectures, facts have accumulated which demonstrate the soundness of his inductions most brilliantly. My purpose in this and in succeeding papers is to present some of the more important of these facts and to show their significance in the light of Jackson's views.

Three doctrines of Hughlings Jackson will be particularly considered. (These doctrines did not originate with Jackson, but it was he who most effectively demonstrated their medical importance.)

First Doctrine.—The nervous system is, in essence, a series of sensorimotor reflex arcs, superimposed one on the other. This system of arcs is built up in accordance with an evolutionary scheme whereby the lowest arcs are the most organized, the least complex and the most automatic; the highest arcs are the least organized, the most complex and the least automatic.

Jackson spoke more specifically of lowest motor centers (the anterior spinal horns and the nuclei of the motor cranial nerves), middle motor centers (precentral gyrus) and highest motor centers (frontal lobes). These centers, with their corresponding sensory centers, constitute the lowest, middle and highest levels of the nervous system (II, 399).[1]

In diseases of the nervous system there is a "taking to pieces," or dissolution, of this system of arcs. In cases in which the dissolution is "uniform" rather than "local," the highest arcs are most affected, the lowest arcs least. Jackson cited the following illustration: "An injurious agency, such as alcohol, taken into the system, flows to all parts of it; but the highest centres, being more organised, 'give out' first and most; the middle centres, being more organised, resist longer;

1. Bracketed figures refer to the volume and page of the "Selected Writings of John Hughlings Jackson" (London, Hodder & Stoughton, Ltd., 1931-1932).

and the lowest centres, being most organised, resist longest. Did not the lowest centres for respiration and circulation resist much more than the highest do, death by alcohol would be a very common thing" (II, 47).

Second Doctrine.—Each arc (save the lowest), in addition to performing its own specific function, in a measure inhibits the activity of the arcs below it. Consequently, an interruption of any but the lowest arc manifests itself both in negative symptoms (the loss of the specific function of the diseased arc) and in positive symptoms (the uninhibited activity of intact lower arcs). This is the doctrine of "duplex symptomatology."

Third Doctrine.—Mental phenomena occur *during* the activity of certain nervous arcs. Mental phenomena can neither cause, nor be caused by, physical phenomena. Physical phenomena can cause only other physical phenomena. Therefore, the activity of certain nervous arcs does not cause consciousness, but is accompanied by consciousness. It follows from this doctrine of "concomitance" that in trying to understand the nature of mental phenomena one must not ignore the activity of the underlying physical substrate.

THE PHYSICAL SUBSTRATE OF MENTATION

It is fair to assume that the highest motor and sensory centers constitute the "organ of mind;" in other words, mental phenomena occur during activity of these centers. Stressing the assumption that the highest level of the nervous system possesses, like the lower levels, a sensorimotor organization, Jackson affirmed that the organ of mind is a mechanism for the coordination of impressions and movements. This view I shall now examine in detail.

One may begin by considering what transpires when one sees an object. Many physicians would say that seeing an object represents a "purely sensory" act. Jackson emphasized that it really represents a sensorimotor act. To quote from his third Croonian lecture (II, 69):

> I suppose that I am seeing a brick. . . . What first happens is that there is a peripheral impression (upon the retina), impulses then pass through the lowest, through the middle, and up to the highest sensory centres. . . . So far we have only stated one half of the reflex action, have only reached the physical condition in the highest sensory centres correlative with the colour of the brick. It and all other objects have shape, and this as much requires to be accounted for as the colour. The shape of an object is the relation of its several positions one to another; our knowledge of this relation is by movements, in this case ocular movements. . . . By currents passing from the highest sensory centres, so to speak, "across" to the highest motor centres, and from these downward, through middle and lowest motor centres to muscular periphery, there is development of movements of the eyeballs. . . . Here we have . . . reflex action.

Confining himself to reflex actions in which the highest centers are engaged, Jackson spoke of two varieties (II, 69): "(1) complete and strong, those in which the highest centres are strongly engaged along with all lower centres; (2) incomplete and weak, those in which the highest centres are alone engaged, and are in but slight activity."

In connection with the example of the brick, Jackson expounded the difference between complete and incomplete reflexes in a passage of great importance (II, 70):

> The vivid image, the mental state we have [when we see a brick], arises during (not from) the physical condition in the two divisions of the highest centres, and is strongly and definitely "projected," because the lower centres are engaged; it *seems* part of the outer world. Next day, we can think of the brick in its absence, have "an idea of it," or, as I prefer to say, have a faint image, where, yesterday, we had a vivid image. In this case the reflex action is incomplete and weak; the lowest and the middle sensory centres and the middle and the lowest motor are not engaged. The highest sensory and motor centres are alone engaged; there is still reflex action, but only the central links of the great sensori-motor chain are engaged; the central part only of the whole process which occurred in perception is done over again, and, the excitations being slight, the image arising is faint, and, the lower centres not being engaged, it is feebly and indefinitely projected, *seems* more part of ourselves. [On the other hand, when we actually see the brick] we have complete and strong reflex action, complete because all orders of centres, sensory and motor, are engaged; and strong, because the highest centres are in great activity, consequent on the multiplication of energy-liberations upwards.

This doctrine of "incomplete and weak" reflex action is for the psychiatrist, as I shall presently try to show, one of Jackson's most important teachings.

The argument so far has applied only to the act of seeing an object. It may with equal propriety be applied to all other commonly termed "sensory acts." There may be taken as instances the acts of hearing a sound, smelling and tasting a substance, and touching an object. Ordinarily, when a person hears a sound he reflexly makes some movement enabling him better to comprehend its origin; generally he turns his head in the direction of the sound. This is "complete and strong" reflex action. Later he "thinks of" the sound, or, in Jackson's terms, has a "faint" image in place of the "vivid" image,[2] and now there is no visible movement. In this instance there is "incomplete and weak" reflex action, only the highest sensory and motor centers being engaged. Sometimes a sound is heard but no visible movement is made; here there is an intermediate type of reflex action, the lowest, middle and highest sensory centers being engaged, but only the highest motor. The sensorimotor nature of the act of smelling is most obvious, as

2. I follow Jackson (II, 165, footnote) in speaking not only of visual but also of auditory and other sensory images.

one cannot smell without inhaling (a movement). When one smells a flower, there is a vivid image; when later one thinks of it, there is a faint image. Tasting and touching are generally accompanied by appropriate movements. In such instances there is activity of all orders of sensory and motor centers. In instances of tasting or touching unaccompanied by movement, one again deals with that intermediate type of reflex action in which all orders of sensory centers are engaged, but only the highest motor. When one thinks of an object once tasted or touched, one has faint images, concomitant with activity of highest centers only. (Jackson discussed faint tactual images in detail [II, 403]).

Moreover the argument applies to complex as well as to relatively simple images. Just as one can "think of" a brick in its absence, so one can think of a football game, a concert or a lecture which on a previous occasion one has attended. In these instances, as in the instance of the brick, one deals with "incomplete and weak" reflex action.

Turning now for a moment to movements and quoting Jackson (II, 95, footnote):

> When I actually move my arm . . . there is a process from highest motor centres, through lower centres, then by nerves to some muscles, which are discharged in a particular way. This is a purely physical process. . . . When we think of the movement, or remember it (popularly "have an idea of it"), the physical process is limited to the highest centres; *the very same* nervous arrangements of the centres are engaged, but they are slightly engaged, and the physical state concomitant with the slighter process is faint.[3]

To Jackson, then, thinking of a movement is comparable to thinking of an object; in either case neural activity is "incomplete" (i. e., limited to the highest centers) and "faint."

Bearing in mind the generalization that all popularly styled sensory acts are really sensorimotor acts, one may go one step further by extending this generalization to popularly styled motor acts (with one exception to be noted presently). When one scratches one's nose or shifts the position of one's legs, the motor act is obviously but part of a sensorimotor act. Similarly, when, thinking of a letter in one's pocket needing to be mailed, one walks toward a mail-box, the motor act is the sequel to a sensory process concomitant with a "faint image" (the image of the unseen letter). Indeed, every "voluntary" motor act and nearly every "involuntary" motor act arises in response to a sensory process concomitant with a vivid or faint image. I say "nearly" every involuntary motor act, because it seems to me that there is one exception: in epileptic attacks which *begin* in some motor center one deals with a "purely motor" act.

3. Italics in original.

I conclude, then, that there is no "purely sensory" act and, with one exception, no "purely motor" act. For practical purposes all acts are reflex acts. Some acts involve the highest centers only slightly, if at all, as when one automatically brushes a fly off the face while deeply absorbed in reading a book. Those reflex acts that strongly involve the highest centers fall into four groups: 1. Those in which both the lowest sensory and the lowest motor centers are also engaged (Jackson's "complete and strong" reflex actions). An example is the act of seeing an object. 2. Those in which the lowest sensory centers are engaged but not the lowest motor, as when one hears a sound but refrains from turning the head or making any other movement. 3. Those in which the lowest motor centers are engaged but not the lowest sensory, as when one walks toward a mail-box in response to having thought of a letter lying in one's pocket. 4. Those in which neither the lowest motor nor the lowest sensory centers are engaged, the reflex action being confined to the highest motor and sensory centers (Jackson's "incomplete and weak" reflex actions). An example is the act of "thinking of" an unseen object.

Consideration must now be given more closely to the nature of the act of "thinking." I have already considered that kind of thinking implied in the expression "I am thinking of" an object or a movement. I shall now be concerned with certain other components of mentation: "knowing," "remembering" and "reasoning."

It may be taken for granted that knowing and remembering the state of the environment are acts comparable with that of thinking of an object. Seeing a book on the table, I automatically "know" it is there. (More accurately, I know that if I look at the top of the table, I shall have a visual image corresponding to book; if I place my hand on a certain part of the table, I shall have a tactual image corresponding to book.) A large part of what one knows is bound up with perceptions (things one has read and seen, things one has been told, etc.). Clearly, knowing what is going on in the environment is correlative with being conscious of images. Likewise, "remembering" means once more "thinking of" objects formerly perceptible. Knowing and remembering, then, are concomitant with the same nervous process which occurs when one thinks of an object, i. e., an "incomplete and weak" reflex process, in which only the highest sensory and motor centers are engaged.

In the last paragraph attention was confined to knowing and remembering as they pertain to objects in the environment. These acts may now be considered as they pertain to movements. Two elements enter into knowing what movement one is making: (1) a vivid kinesthetic image and (2) an "idea of the movement." Obviously, then,

remembering a movement already performed involves (1) a faint kinesthetic image and (2) an "idea of the movement."

Jackson cited (II, 140, first footnote) the following statement of Herbert Spencer:

> To remember the colour red is to have, in a weak degree, the physical state which the presentation of the colour red produces. To remember a motion just made with the arm is to have a feeble repetition of those internal states which accompanied the motion—is to have an incipient excitement of those nerves which were strongly excited during the motion.

In this statement one must construe "those internal states which accompanied the motion" to include both faint kinesthetic images and "ideas of movements."

"Knowing" and "remembering" are closely similar; "reasoning" is different from either of these. Knowing and remembering are acts involving the consciousness of images; reasoning involves, one might say, the "manipulation" of images. A primitive and therefore instructive example of reasoning is found in one of Koehler's chimpanzees. This animal knew how, with the aid of a bamboo stick, to reach for a banana lying outside its cage. When the banana lay just beyond the reach of the stick, the animal was helpless, until one day it fitted one stick into another, making a stick long enough to reach the fruit. This act of reasoning is, in essence, a motor act, involving in part the physical manipulation of objects. One can only infer what "went through the chimpanzee's mind" just before it performed this manipulation, but one knows definitely what would go through a human being's mind in the same situation. Just before the intentional performance of a movement there is an "idea of the movement." One comprehends the situation which confronts him, and ponders how he can reach the banana. Specifically, there is a train of "ideas of movements," which are discarded one after the other. Presently there occurs an idea of the correct movement, which is then executed. The idea of the movement occurs during activity of the highest motor centers; the execution of the movement occurs during activity of highest, middle and lowest motor centers and the muscles.

Suppose now one wishes merely to solve the banana problem as an intellectual pastime, without wishing to gain actual possession of the fruit. In this case the efforts culminate in "saying to onself:" "I can reach the banana if I fit one bamboo stick into the other." In this instance of unexecuted movement the highest motor centers are engaged but not the lowest.

Suppose one is watching a chess player, *A*, pondering his next move while his opponent, *B*, is at the moment out of the room. If *A* is so constituted that he "thinks out loud," one may hear him say,

"If I move my bishop here, *B* will interpose his knight; I shall then move my queen *there*." One not only hears him speak, but very likely sees him execute fragments of arm movements appropriate to the projected moves. One sees here that reasoning is associated with movements of articulatory and other muscles. Suppose, now, that *B* had been in the room throughout the period of *A's* meditation. *A's* reasoning would have been the same, but one would have heard and seen nothing to reveal his strategy. Instead of spoken words there would have been unspoken words. To state the matter differently, instead of articulatory movements there would have been only ideas of articulatory movements. Similarly, instead of arm movements there would have been only ideas of arm movements. *These ideas of articulatory and of arm movements would have constituted his reasoning.*

Jackson (II, 209) expressed himself on the nature of reasoning as follows:

> When I arrange books on a table there are visual and tactual images, and there are actions.[4] Physically there are imprints on the retinae and on finger-tips and there are movements of the arm . . . Now suppose I think of arranging the books. I have faint visual and tactual ideas, and there are faint actions, and physically there are slight central, cerebral discharges, the peripheral parts not being engaged. . . . It sounds grotesque to say that manipulating and certain other gross operations, or rather the correlative actions, are reasoning, but I think there is reasoning in its lower form—or that there is at least that out of which what is called reasoning has been gradually evolved. To return to the former illustration. The action during actually arranging books is reasoning in its lowest form; the action when thinking of arranging them is a next higher grade; a purely symbolic arrangement of them in thought, by actions concomitant with activity of new nervous arrangements representing modified parts of the operations, is a sort of reasoning. Certainly when words come to be symbols of the actions (symbols of symbols) in the case supposed there is what is commonly called reasoning.

Jackson, I believe, was unnecessarily cautious when in the last citation he added the clauses "there is at least that out of which what is called reasoning has been gradually evolved." His immediately preceding statement, "there is reasoning in its lower form," seems free from overstatement. Indeed, it might even be said to contain a

4. The reader is reminded that Jackson used the word action to denote an "idea of a movement" (II, 208, line 8). He occasionally used the phrase "idea of a movement," but usually in quotation marks. He evidently considered the term "action" superior. Jackson, a great master of clear statement, laid himself, in this instance, open to misunderstanding. Readers may confuse his term "action" with "act" or "movement," which would be fatally misleading, since "movement" involves highest and lowest motor centers while "action" involves only the highest. For this reason, throughout this paper I employ the cumbersome phrase "idea of a movement." An "idea of a movement" is to that movement what a "faint image" is to the corresponding "vivid image."

bit of understatement. I would not assent to the statement, "The action during actually arranging books is reasoning in its lowest form; the action when thinking of arranging them is a . . . higher grade." The "action" when actually arranging books is *not on a lower but on the same* evolutionary level as the "action" when thinking of arranging them. In the former instance there is "action" (Jackson's sense of the term) plus movement; in the latter, "action" without movement. Expressed in other terms, when actually arranging books one reasons no less than when thinking of arranging them.

A further remark on the rôle of words in reasoning. One commonly says that he "thinks in words." But, as Jackson has emphasized, words are the psychic correlates of certain (articulatory) movements. Reasoning, then, comprises ideas of movements in a twofold manner: (1) ideas of manipulative movements (e. g., the arm movements of the chess player); (2) ideas of articulatory movements correlative with words symbolic of these manipulative movements. Many instances of reasoning involve ideas of both manipulative and articulatory movements, as when one ponders how to repair a piece of machinery. Other instances of reasoning involve ideas of articulatory movements only, e. g., the "abstract" reasoning of the philosopher. (It may be said that the philosopher writes down the "words in which he thinks." Writing movements, however, are, for the present purpose, to be regarded as equivalent to articulatory, rather than manipulative, movements.)

Valuable confirmatory evidence of the existence of motor discharges during reasoning may be found in those movements and postures which characteristically accompany acts of "mental concentration." A glance at the forehead would enable one instantly to distinguish the photograph of a man listening to music from that of the same man doing difficult mental arithmetic. In recent years it has been found that laryngeal movements of small amplitude occur during mental arithmetic. This fact was not known in Jackson's time, as is seen from his statement (II, 131): "The same nervous processes are concerned in internal as in external speech. The difference is that the excitation of these nervous processes in speaking to one's self is so slight that the nerve currents developed do not spread to the articulatory and vocal muscles . . . ." It is known today that when people "think to themselves" the laryngeal muscles do contract, even if rudimentarily. I allude, for example, to the observation of Golla,[5] who graphically recorded the movement of his larynx and found that when he merely *thought* of the successive notes of an octave he obtained a curve identical, save for a difference in amplitude, with that obtained when he sang the octave audibly.

5. Golla, F.: The Objective Study of Neurosis, Lancet **2**:115 (July 16) 1921.

Thinking, then, is a composite function occurring during activity of the highest sensorimotor arcs, this activity being generally combined with that of lower arcs as well. When one "thinks of" something—whether it is an object once seen or a movement once performed—there is activity of both highest sensory and highest motor centers. The last statement applies also to "knowing" and "remembering," whether these pertain to the state of the environment or to one's own movements. "Reasoning" occurs during activity of motor centers, there being activity always of the highest centers and often (if not always) of the lowest. In actual practice one never reasons without reasoning about something, that something usually being a set of objects. "Thinking of" these objects occurs during activity of sensory and motor centers. Therefore, in actual practice an act of reasoning is concomitant with activity of sensory as well as motor centers.

The Localization of Mentation.—If any apology were needed for devoting so much space to Jackson's views on mentation, I should point to certain prevalent misconceptions on the localization of mentation. According to common belief, mental symptoms constitute evidence of a disturbance in the frontal lobes. Thus, in a recent comprehensive article on a certain nervous disorder, the author, a deservedly esteemed neurologist, described the respective symptoms arising from involvement of the different parts of the brain. Under the heading "Frontal Lobe Symptoms," he wrote: "Psychic activity is diminished, thought is retarded, and memory is impaired. . . . Ideas become incoherent and confused and there are subjective feelings of confusion, anxiety and unrest." One may assume that the anterior part of the brain is chiefly motor and the posterior part chiefly sensory—an assumption that few will dispute. Any one who accepts Jackson's views will reject the assumption that thinking occurs during activity of only the anterior part of the brain. The unnamed author whom I have cited listed impairment of memory as a frontal lobe symptom. It must be clear that remembering necessitates activity of sensory as well as motor centers. If I remember that I met my friend John Doe on the steps of the public library on a very hot day in 1932, that we had a steak dinner and then attended an outdoor concert, surely certain sensory processes concomitant with visual, auditory, gustatory and other images help to form the groundwork for this act of memory. Nearly fifty years ago, Jackson said (II, 54): "The highest (chiefly) sensory centres—parts behind Ferrier's sensory region—and also the highest (chiefly) motor centers—parts in front of the so-called motor region—make up the physical basis of consciousness." I see no reason today to dispute this statement. The reader must not suppose that Jackson intended this statement to apply to consciousness and not to mentation; to Jackson the two were synonymous (II, 424).

Allusion has already been made to the evidence suggesting that reasoning occurs during activity of motor centers. This, however, does not entitle one to assume that impairment of reasoning necessarily points to involvement of the frontal lobes. As has already been indicated, one cannot reason without at the same time having images—a function concomitant with sensory as well as motor activity. (This was recognized by the makers of our language. One way of praising a person's intelligence is to say that he is "sensible" or has "good sense.") Therefore, when a patient reasons poorly, one cannot easily say whether the disturbance is in the sphere of reasoning proper (motor) or in that of imagining (sensory and motor). Conceivably a patient with an intact anterior brain may reason poorly because of a disturbance in the posterior brain hampering those processes concomitant with "faint images."

One must conclude that thinking disorders are by no means pathognomonic of a disturbance in the frontal lobes. I am aware of statements that mental symptoms occur with relative frequency in cases of tumor of the frontal lobe. However, they *do* occur also in cases of tumor elsewhere in the brain. Moreover, statements of the relative infrequency of thinking disorders in cases of tumor of the posterior part of the brain must be taken with a grain of salt, owing to the carelessness with which most patients are psychiatrically studied. Methods of studying mental functions are at best exceedingly crude. When, in addition, these methods are carelessly and hastily employed, patients are inaccurately put down as mentally normal in spite of having fine disturbances of thinking. I once attended a clinical lecture at which a good neurosurgeon presented a patient in whom because of a tumor he had removed the entire right frontal lobe, with the statement that the extirpation had caused no impairment of mentality. I question whether painstaking investigation of this patient's thinking processes would not have revealed fine abnormalities. There is great need for research in which neurologists, neurosurgeons and psychiatrists will collaborate in the detailed and thoroughgoing study of the thinking processes of patients with discrete lesions of the brain. Such research will place on a more satisfactory basis than at present the question of the localization of mentation.

CLINICAL APPLICATION

In the remainder of this paper I shall present clinical facts understandable in the light of Jackson's views on the nature of the physical processes concomitant with mentation. First I shall consider a few comparatively simple facts that require no discussion of the evolution and dissolution of the nervous system. Later I shall consider certain

more complex mental phenomena that are understandable only in the light of Jackson's views on dissolution.

1. *"Tonic Innervation" Accompanied by Perseveration.*—In case 3 of Wilson and Walshe,[6] the patient, when asked to write her name, wrote (with her right hand) "Fanny Fanny" instead of "Fanny Flynn." This little fragment of an observation becomes impressive when one remembers that the patient had "tonic innervation," i. e., inability to relax her (left) hand when anything was in its grasp. As the patient persevered in the comparatively simple grasping movement, so also did she persevere in the more complex movement of writing "Fanny." This is in accord with the obvious fact that writing a word is a movement, much more complex but essentially of a piece with simpler movements. There is, then, a parallel between the central processes correlative with the complex movement, writing, and those correlative with the simpler movement, grasping.

The fact that the writing was with the right hand and the tonic innervation in the left does not weaken the force of the illustration.

2. *Association of Tic and Forced Thinking.*—Some cases show the association of tic and forced thinking or forced utterance. I cite the case of a girl at the Harrisburg State Hospital, who at the age of 9 began to have a compulsion to utter certain words; at 10 she began to have tics of certain parts of the face. Here one sees once more a parallel between a complex movement (uttering a word) and a simple (facial) movement.

3. *Association of Oculogyric Crises and Forced Thinking.*—In reading Jelliffe's[7] digest of the literature on oculogyric crises in encephalitis one is struck by the frequency with which forced thinking occurs *during* these crises. If oculogyric crises are due to the excitation of agonists rather than the inhibition of antagonists, there is here a remarkable instance of the parallelism of the processes concomitant with thought and movement: These patients, while having a discharge of the centers for the upward movement of the eyeballs, have at the same time a discharge of the nervous arrangements concomitant with certain words or groups of words.

In some of these cases the patient is compelled to *think* of certain words, in others to *utter* them. Physiologically, the difference is that

6. Wilson, S. A. K., and Walshe, F. M. R.: The Phenomenon of "Tonic Innervation" and Its Relation to Motor Apraxia, Brain **37**:199 (Oct.) 1914.

7. Jelliffe, S. E.: Oculogyric Crises as Compulsion Phenomena in Post-encephalitis: Their Occurrence, Phenomenology and Meaning, J. Nerv. & Ment. Dis. **69**:59 (Jan.); 165 (Feb.); 278 (March); 415 (April); 531 (May); 666 (June) 1929.

in the first group the highest centers, exclusively or chiefly, are engaged; in the second group the lowest centers also are engaged.

4. *"Recurring Ideas" After Cerebral Trauma.*—Jackson called attention to "recurring utterances" in aphasia (II, 172). When the recurring utterance had "propositional value," Jackson found that in a number of cases it was the utterance that the patient was about to make at the moment when he was taken ill (II, 188). Thus, a man whose left cerebral hemisphere was injured in a brawl thereafter had the recurring utterance "I want protection." In one of his most penetrating expositions Jackson used this fact in constructing a hypothesis to account for these utterances. He suggested that the nervous arrangements for the words last spoken, or about to be spoken, at the moment of the injury remain excessively "dischargeable" or "excitable" (II, 192). (Through repetition these arrangements become more and more "organized" and "automatic"—a fact with which I am not concerned here.) Significantly, a *movement* occurring at the moment of the injury may recur, exactly like a recurring utterance. Jackson cited the following instance (II, 202, footnote): "A woman . . . who fractured her skull by a fall when laying down the oilcloth on a staircase, kept, during partial unconsciousness a few hours before death, manipulating the counterpane of her bed. We supposed this to be a continuance of the action of laying the oilcloth."

I now come to the reason for mentioning this topic. There are some cases in which the *idea* that was "in the patient's mind" at the moment of injury continues to manifest itself after he has recovered consciousness. Jackson cited two cases of this sort: Abercrombie's case (II, 202) and Conolly's case (II, 204). I shall cite two cases in which I questioned the patient carefully. An intelligent young woman was driving an automobile to New York; the car skidded on the wet road, turning completely around, and the woman was thrown out. She "came to" a moment later on the roadside. Subsequently there was complete amnesia for the passage from the car to the ground. "On coming to," she said later, "I couldn't get the conviction out of my mind, 'I'm in the car on my way to New York.'" This "recurring idea" lasted a fraction of a minute. The other case is that of a farmer who, while riding a mule, was struck by a truck. He was thrown into the air and fell on his head on the concrete highway. Whether he was for a short time unconscious I do not know. If he was, he "came to" while still lying on the highway. For several hours thereafter he was "bewildered, like in a dream." During the early part of this period of bewilderment, he said, "I *knew* the mule was killed—they (friends) told me that—but I *couldn't get it into my head* that the mule *was* dead."

Both in "recurring utterances" and in "recurring ideas" certain nervous arrangements remain, for a variable length of time after the injury, highly "dischargeable." In the former instance the arrangements are those correlative with certain (articulatory) movements, and include lowest as well as highest centers; in the latter instance the arrangements are those correlative with an idea, and therefore include only (or chiefly) the highest centers.

The cases cited in the four numbered paragraphs are understandable only if one adopts Jackson's view that the physical processes concomitant with thinking obey the same laws as those concomitant with having impressions and making movements.

THE EVOLUTION OF MENTATION

During the course of a person's growth his nervous system evolves from a state of least to a state of greatest complexity. It follows, from the doctrine of concomitance, that this evolution is accompanied by a corresponding evolution of mental functions. As the nervous system evolves, its parts become more organized, more automatic and less voluntary. Correspondingly, the mental functions occurring during the activity of these parts likewise become, in a sense, more organized, more automatic and less voluntary.

Saying that a part of the nervous system becomes more organized is another way of saying that it becomes more independent. In considering the nature of this independence, I shall begin with an illustration from the sphere of motor activity.

The younger the infant, the more it moves large parts, rather than small parts, of its body. A very young infant rarely moves an arm without at the same time moving the other arm. In the course of time it "learns" to move one arm independently. Its early efforts in this direction are accompanied by movements of facial and other muscles. (Note, for example, the strong facial contractions indicative of "mental concentration" in a child just learning to use a crayon.) As the person reaches a higher level of evolution he becomes able to perform the finest manipulations, involving the smallest parts of the hand, while the rest of the body is still. People differ according to the extent of motor independence achieved. Thus (1) there are some children who cannot write without making "mirror-image" movements of the opposite hand; (2) people differ in their ability to close one eye without the other.

An instructive piece of research was made by Becher,[8] who found that "a large percentage of children, when told to open the mouth

8. Becher, H.: Fingerspreizphänomen im Kindesalter, hervorgerufen durch weites Mundöffnen, Wien. klin. Wchschr. **45**:1155 (Sept. 23) 1932; abstr., J. A. M. A. **99**:1897 (Nov. 26) 1932.

wide and put out the tongue, spread the fingers." The older the group of children investigated, the less frequently does this "co-movement" occur.

Movements in the course of time become independent not only of each other but also of the activity of the highest centers; i. e., the nervous parts engaged during movement become more and more "automatic." To take a concrete instance: A person just learning to drive an automobile is unable to attend to other matters while driving. He must "put his mind on" his stream of visual and auditory images and on the movements of his limbs. In the course of time the parts of the brain engaged during driving become more automatic. The driver is now able to make the correct movements while talking or listening to a companion or while thinking of matters unrelated to driving.

Any one who watches children eat will observe now and then that a child stops eating and remains apparently wrapped in deep thought until reminded to finish his meal. In some cases this tendency is so marked that parents complain of it. In my view of this problem, the lowest centers in the brain of a young child have not yet sufficiently achieved their independence of the highest centers. As a consequence, should some thought closely engage the child's attention, the lowest centers suspend activity and eating movements stop. On the other hand, a healthy adult continues to perform "automatically" the movements of eating even while engaged in deep mental concentration.

One may observe two stages antecedent to the complete independence of the lowest centers. In the first and earliest stage, the lowest centers are so slightly independent that they function only when the child puts his attention directly on the movement to be performed. In a later stage, the lowest centers have become partially independent to the extent that the child no longer must attend closely to the movement in question yet must refrain from attending too closely to matters unrelated to the movement. This is the stage of the child who ceases to eat the moment he becomes wrapped in thought.

Not only do the lowest centers in the course of time become independent of the highest, but—and this is of the greatest importance here—the highest also become independent of the lowest. Jackson has stated this as follows (I, 375):

> As evolution progresses the highest centres not only gradually develop (become increasingly complex, etc.), but also become more and more detached from, and more independent of, the lower centres out of which they have been evolved. . . . There are degrees of detachment and of independence . . . [When independence has been attained] our highest sensory and highest motor centres (together the "organ of mind") can energise, to a large degree, independently

of the lower centres out of which they have been evolved, and by aid of which they have been developed; consequently they can act independently of the environment.

Certain concrete data are strikingly in accord with this view. I shall consider these data under two headings.

Association of Activity of Highest Centers with Activity of Lowest Sensory Centers.—The phenomenon known as eidetic imagery is of great importance. The reader will find in Wertham's article[9] a convenient summary of the work of the Jaensch school. Eidetic images are differentiated from ordinary after-images and from representation or memory images. The after-image is seen only immediately after the object has been gazed on. The eidetic image may be seen long after the object has been gazed on, and is capable of being "produced voluntarily and by thought associations." There are also certain other differences between eidetic images and after-images.[10] The memory image is, so to speak, imagined but not actually seen. Eidetic phenomena occur in connection not only with vision but also with the other special senses. From the point of view of this discussion, the significant thing is the demonstration that most normal children are capable of eidetic imagery, losing this power as they become adults. Wertham cited E. R. Jaensch's theory that in childhood "there is an undifferentiated stage in which representation and perception are practically unified to become two different phenomena only in later life." This may be restated as follows. In earliest life the highest sensory centers are relatively dependent on the lowest sensory centers, acting in unison with them. Activation of the highest sensory centers "from within" (i. e., when not caused by an external object) is apt to be accompanied by activation of the lowest sensory centers (a "spreading" of innervation similar to that described by Becher). As evolution proceeds, the highest centers become more and more able to act independently of the lowest centers. Prior to this stage of independence, when the child "thinks of" an image he is apt actually to *have* the image. It is difficult or impossible for him to "imagine" an object without activation of the corresponding lowest sensory centers, the result being that he "sees" an absent object with relative ease, but "imagines" it with difficulty. In Jaensch's terms he has eidetic images more easily than memory images; in Jackson's terms he has vivid images more easily than faint images. (I am, of course, not saying that vivid image and eidetic image are synonymous terms.) After the stage of independence has been reached, the highest sensory centers are able to act alone.

9. Wertham, F.: Progress in Psychiatry: V. Eidetic Phenomena and Psychopathology, Arch. Neurol. & Psychiat. **24**:809 (Oct.) 1930.

10. Wertham,[9] p. 811.

The child—now no longer a child—has become capable of imagination in the true sense of the term.

The notion that imagination is an adult, rather than an infantile, trait conflicts with the popular belief that children have a "rich imagination." This belief is erroneous. It springs from the fact that children like to play, and during their play attribute animate characteristics to inanimate objects and human characteristics to subhuman creatures, thus "pretending" to converse with a doll. This, strictly speaking, is not imagination. Imagination refers to the ability to have faint images in the absence of vivid images—the ability to "think of" objects in the absence of the corresponding perceptions. The child who pretends that the doll is a playmate has a low, not a high, level of imagination; a high level of imagination is seen in the child who pretends the presence of a playmate *in the absence of a doll or other concrete equivalent*. For further illustration I may consider two instances of a high level of imagination. The average woman cannot imagine how she will look in a given hat, but must put it on and study herself in the mirror. On the other hand, a competent milliner has a better imagination, and does not need to *see* her customer wearing the hat. A composer of music can imagine how a composition will sound without hearing it; Beethoven wrote great compositions while stone-deaf. It is said that the deaf Beethoven was to be pitied. Without denying this, I suggest that the grounds for pity are not as compelling as some might think. Beethoven was able to imagine the "Ninth Symphony" infinitely more keenly than the average man who hears it through good ears.

A fact which has not been accorded the attention it deserves is the habit of young children of requesting that a story be read to them over and over again. Some adults mistakenly assume that the child asks for the repetition of the story because he has no clear recollection of it. The truth is quite to the contrary. The child usually remembers every word of the story, and if the reader should omit only one word the child will not infrequently correct him. Why, then, does the child ask for so many repetitions of a story that he already knows word for word? I suggest that the answer lies in the fact that in very young children representation and perception have not yet been differentiated. The child likes the story, and wants to enjoy over and over again the pleasure of thinking it through as a fantasy. An adult, in whom imagination has become independent of the lower function perception, would, in a similar situation, be able to "think of" the events of the story without external aid. The young child, on the other hand, must *hear* the story in order to be able to think it.

Daily language shows how mentation has evolved from perception. A person will say, "*Something tells me* I won't enjoy the play this

evening," instead of "I *think*." Expressions pointing to a visual root are frequent. People say, "It seems to me" instead of "I am of the opinion that." When one comprehends an explanation presented, he says, "I see." One "sees through" a person's trickery. In the olfactory sphere, when a situation arouses suspicion one "smells a rat." In the gustatory sphere, when one regards something as improper, it is "in bad taste." One speaks of "bitter care" and, on the other hand, of a "sweet melody." Examples are found even in the sphere of cutaneous and muscle senses. An ironic tongue is a "sharp" tongue. One speaks of "hard necessity." The colloquial expression for a life of ease is "a soft life."

Association of Activity of Highest Centers with Activity of Lowest Motor Centers.—Young children talk "to themselves" in such a way as to make it plausible to conclude that their usual way of thinking is to think "out loud." Sometimes one overhears both sides of a conversation between a child and an imaginary playmate. As the child grows older he becomes more and more able to think without speaking. Complete independence, however, is never achieved. In the first place, as has already been stated, laryngeal movements of small amplitude occur during silent thought. In the second place, certain forms of mentation are aided by speech. Thus, when travelers inquire the direction and are told "three blocks down and turn right," they usually repeat the instructions out loud. This is done perhaps partly for the purpose of checking up. I believe that a more potent reason is that one remembers a group of words better when one has spoken them. The activation of the nervous arrangements engaged when one utters a certain phrase renders them that much more "organized."

The behavior of the average person when doing mental arithmetic illustrates the association of activity of the highest centers with activity of both lowest sensory and lowest motor centers. One can more easily add 27 and 19 when one "writes" them with the fingers on the table or, better, on the thigh. During this "writing," lowest motor and lowest sensory (kinesthetic) centers are engaged. When one does the "writing" on a part of the body, there is also engagement of the lowest centers of cutaneous sense.

I conclude, then, that as evolution proceeds, the parts of the nervous system tend to become independent in a twofold way: 1. At least in the motor apparatus, parts become independent of other parts belonging on the same level, permitting the isolated movement of a smaller and smaller segment of the body. I may call this "horizontal independence." 2. Parts become independent of both higher and lower parts ("vertical independence"). When a person learns to drive an automobile "automatically," there is "independence of lowest centers." To the extent

that a person acquires the ability to think in the absence of activation of the lowest centers, there is "independence of highest centers."

Evolution manifests itself also by an increase in the complexity of imagery and of reasoning. In the present article I shall not concern myself with this manifestation.

MENTAL SYMPTOMS AS EVIDENCE OF DISSOLUTION

Mental symptoms may be studied from many angles, but they can be understood only as evidences of dissolution of the nervous system. Negative symptoms must be carefully distinguished from positive symptoms. Thus, destruction of the highest centers manifests itself in: (1) reduction of the ability to think complexly—a negative symptom; (2) unchecked activity of intact lower centers, e. g., in the form of overactivity and violence—a positive symptom.

Dissolution implies the "reversal of evolution." "The statement, 'to undergo dissolution' is rigidly the equivalent of the statement, 'to be reduced to a lower level of evolution' " (II, 46). In the remainder of this paper I shall try to show how this statement applies to certain concrete symptoms. I shall confine attention to symptoms interpretable as evidences of loss of "vertical independence." From the foregoing discussion it is evident that one must consider loss of "independence of lowest centers" and loss of "independence of highest centers."

Loss of "Independence of Lowest Centers."—Patients sometimes complain that they can no longer perform certain movements automatically—a fact that is not sufficiently well known, perhaps because the patient must be very intelligent and comparatively intact in order to notice and report it. As an instance I cite the case of an intelligent schizophrenic patient which I reported as case 1 in a recent paper.[11] This patient, a cutter in a dress factory, complained that as his illness progressed he lost the ability to perform automatically certain movements incident to his trade. He referred particularly to the handling of cloth and pattern. Formerly he was able to make the required movements automatically, whereas "now I have to stop and *think what I am doing.* I can't get my mind working the way it should." [12]

The incomparable observer Pavlov, during his advancing years, made a noteworthy observation in himself. He said: [13]

> It is a common occurrence that, being predominantly preoccupied with some one activity, we can simultaneously perform some other activity which has long been

11. Levin, M.: The Basic Symptoms of Schizophrenia, Am. J. Psychiat. **11**:215 (Sept.) 1931.

12. Levin,[11] p. 231.

13. Pavlov, I. P.: Conditioned Reflexes, translated by G. V. Anrep, London, Oxford University Press, 1927, p. 406.

practised; i. e., those parts of the cortex involved in this older response, although in a state of partial inhibition through negative induction, still continue to function in a normal manner. That this interpretation is somewhere near the mark I become more and more convinced, through observing the diminution in the reactivity of my own brain through my advancing age (my diminished memory of recent events). Moreover, with time I progressively lose the faculty, when busy with one activity, of performing correctly another also.

In both of these instances there is some degree of loss of independence of the lowest centers, which therefore function poorly unaided and must have, so to speak, the support of the highest centers. Expressed in psychologic terms, the lowest centers, in order to function, require to an unusual extent the "attention" of the subject.

Jackson often spoke of "reduction to a more automatic condition" (for example, II, 51). Some readers may wonder whether there is a contradiction between such cases of reduction and the two instances of loss of automatic function just cited. There is no such contradiction. In cases showing "reduction to a more automatic condition," the centers that have become automatic are intact; they function more freely because of impairment of higher regulative centers; the analogy is with the increase of the knee jerk in hemiplegia. By contrast, in such cases as that of my schizophrenic patient who complained of inability to perform certain movements with their former automaticity, the centers that have become automatic *are no longer intact;* there is impairment either of the centers or of their horizontal connections; the analogy is with the loss of the knee jerk in tabes.

Loss of Independence of Highest Centers.—This may manifest itself in two ways, according to whether the activity of the highest centers is accompanied by an abnormal degree of activity of the lowest motor or of the lowest sensory centers.

(*a*) Cases in Which Activity of the Highest Centers Is Accompanied by an Abnormal Degree of Activity of the Lowest *Motor* Centers: The increased tendency of patients with disease of the highest centers to "think out loud" is well known to every physician. I cite two specific instances of unusual interest.

A woman, aged 37, was admitted to the Harrisburg State Hospital in a catatonic stupor. Six weeks after admission she emerged from the stupor and became for a time very nearly normal mentally. A former high school teacher, she gave, during this period of relative normality, an intelligent retrospective account. The four days that followed her emergence from the stupor she designated as "horrible." During these four days she worried over every trifling wrong of her life. She was overtalkative. "I had no speech control. It seemed as if I couldn't *think* things, but could only *say* them. *There was a great fear in my mind that I would never again be able to think without speaking,* and I thought how horrible it would be to have to go through life that way."

Lindemann [14] described the effect of amytal on six normal subjects. Under the influence of the drug the following subjective statements were made: "It's funny I am just telling you things which I wasn't going to tell you. . . . No matter what comes to my mind it wants to be expressed too. . . . I feel like saying all sorts of things. The words kind of just come out of my mouth. . . . The words just go rambling on my tongue."

In these instances, through dissolution the highest centers have lost their independence of the lowest motor centers, with the result that thinking silently has become difficult or impossible.

(*b*) Cases in Which Activity of the Highest Centers Is Accompanied by an Abnormal Degree of Activity of Lowest *Sensory* Centers. Hallucinations: I shall not be concerned here with "elementary" hallucinations, such as flashes of light and ringing in the ears, which may, perhaps, occur in consequence of an irritation in the sense organs or in the lowest nervous pathways. I shall concern myself only with more complex hallucinations, in which the patient hears words or sees objects. It is clear that such hallucinations must be understood in terms of the physiology of the *highest* centers; they occur *when the highest centers have lost their independence of the lowest sensory centers.* In the healthy adult the highest centers have achieved the power of acting more or less independently; he is therefore able to think without at the same time having vivid images. So long as the highest centers have not yet achieved this independence, or if having achieved it they have lost it, their activation is accompanied by activation of the lowest centers; in other words, thinking is in such cases accompanied by vivid images "projected into the outer world."

Simplest to understand are the hallucinations in which the patient hears words or sees images corresponding to his thoughts of the moment. German writers term these respective phenomena *"Gedankenlautwerden"* and *"Gedankensichtbarwerden."* Bleuler [15] gave instances of *Gedankenlautwerden.* Krisch [16] gave instances of *Gedankensichtbarwerden.* His first patient noticed that his answers to the examiner's questions "were written letter for letter by an invisible hand before his spiritual eye in indistinct script." I have observed an intelligent schizophrenic patient, in his twenties, who ruminated about masturbation.

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14. Lindemann, E.: Psychological Changes in Normal and Abnormal Individuals under the Influence of Sodium Amytal, Am. J. Psychiat. **11**:1083 (May) 1932.

15. Bleuler, E.: Dementia praecox der Gruppe der Schizophrenien, Leipzig, Franz Deuticke, 1911, p. 81.

16. Krisch, H.: Die Interpretation schizophrener Symptome als Funktionsabbau, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:109, 1931.

He believed that some day he would be brought to trial because of it, and would be prosecuted by a certain famous criminal lawyer. In fantasy he dwelt on the details of this trial. He plainly heard the lawyer's speech of denunciation. When during such fantasies he passed a news-stand, he saw headlines in the newspapers: "Declared Immoral"; "Youth's Silence Causes Much Disturbance in Court Room." The patient had excellent insight and knew that the voices and the headlines were "imaginary." He said, "They are *a reflection of my thoughts.*"

In addition to the foregoing type of hallucination, there are the commoner instances in which the content of the hallucination bears no immediately apparent relation to the thoughts of the moment. In such instances there are two possibilities: 1. The content of the hallucination may consist of a "translation" of the thoughts of the moment into pictorial terms. I shall illustrate with a dream-hallucination from my own experience.

I had examined a criminal and was contemplating the contents of the report that I would present to the court. I continued my contemplation into the evening, and while gradually falling asleep I pondered the question of determinism and free will. Becoming more and more sleepy, I reflected that this question is, at least for the present, insoluble. I then had an image of a wooden chest; the chest was closed, and I "knew" that it was locked and that the key was nowhere to be found. At that moment I awoke and realized that for a few moments I had been asleep. My accidental awakening so early was fortunate in that it allowed me to see the relation of hallucinatory images to thoughts belonging on a higher plane of mentation. While awake one thinks in terms of an insoluble metaphysical problem; these terms, on a more primitive level of thought, are translated into a locked wooden chest to which no one has the key.

2. The content of the hallucination may bear a relation to the "unconscious" thoughts of the moment. Opponents of Freud have derided his view that one is not aware of all that is going on "in one's mind." I am sure that Jackson would not side with these opponents. It seems plausible that, besides the activity of the nervous arrangements concomitant with the thought of the moment, there is activity of many other nervous arrangements. One is conscious of only the thoughts concomitant with those arrangements *that for the moment are in the most intense activity.* To say that there is no activity of the highest centers save that which is concomitant with the thought of the moment is almost as absurd as to say that there is no diffusion of gases through cerebral capillaries because one is not aware of it.

Neurophysiology teaches that there are two possible states of a nerve cell: The cell is either able or else (temporarily or permanently) unable to be irritated. Likewise, a nerve fiber is either able or unable to convey impulses. I believe that the facts already given warrant the assumption (so far as the highest centers are concerned) of an intermediate state—that in which the center is still capable of being activated but "requires assistance" from lower centers. I offer a crude

analogy. A child learning to walk first walks on all fours. Later the two legs (and their corresponding nerve centers) become strong enough to transport the rest of the body unaided. Disease of the walking apparatus may occur in two forms: (1) The legs may be completely paralyzed, in which case the patient cannot walk at all; (2) they may be paralyzed incompletely, to an extent that the patient is able to get about on all fours or with the aid of a crutch; i. e., he returns to a previous stage in which the use of the upper limbs was necessary in locomotion.

Too little is known about the highest centers to permit one to say with certainty that this is a satisfactory analogy, but from the data now available it seems probable that the analogy roughly holds. I allude to the evidence that the highest centers early in life act in unison with the lowest centers; that in the course of growth they become more and more independent of them, and that in some cases of mental disorder (where one may safely postulate disease of the highest centers) they again become dependent on the lowest centers, acting in unison with them. In these cases the highest centers are not completely paralyzed, for one would then expect to find coma or profound dementia; they are, I suggest, incompletely paralyzed, in such a way that they can still act, but with "greater need of support" from lower centers. Expressed in psychologic terms, the patient is still able to think, but this thinking is more apt to occur in association with movements and perceptions.

"Projection."—The term projection has been used in two senses, one more literal and the other more figurative: 1. Accepting Kant's idea that one may testify not to the existence of matter but only to one's perception of it, one may say that one's images are projected into one's surroundings so as to give the impression that "matter is there." This more literal use of the term is the one to be found in Jackson's writings (e. g., II, 70). 2. In recent years the term projection has been applied, metaphorically, to one of the "mental mechanisms." For instance, a patient hears imaginary voices denouncing him; in this way certain difficulties within himself are said to be projected outward. This metaphorical use of the term seems permissible so long as one means only that processes within the patient give him the impression of processes without. Many present-day physicians, however, go beyond this by including in the concept of projection a causative psychologic motive. Thus they assert that a forbidden wish is "disowned by the ego," as a result of which it becomes "necessary that the wish should appear to come from the outside; it is accordingly projected." (The quotation is from a recent formulation of the theory of hallucinations.) Against such a formulation an emphatic protest must be rendered, on

the ground that it rests on a spurious anthropomorphic conception of the physiology of the brain. Lest the reader think it paradoxical to protest against the anthropomorphizing of the human brain, I point out that "brain" and "human being" are obviously not synonymous. One may properly ascribe human qualities only to human beings and not to their component organs. A human being obeys the law of human motivation; the brain obeys only the laws of physiology. To try to explain on the basis of human motives the brain processes concomitant with hallucinations is as unsatisfactory as to say that when a man is confronted by a tiger his heart beats fast "because" he is afraid. He is, to be sure, afraid, but this does not explain the tachycardia. The tachycardia must be explained in terms of nervous processes concomitant with images, efferent nervous impulses, liberation of chemical agents acting on cardio-accelerator centers, etc., i. e., in physical and physiologic, and not in psychologic, terms. Similarly, though people wish to disown certain obnoxious thoughts, this human trait does not cause hallucinations. Hallucinations represent thoughts expressed in perceptual form. One may say that in hallucination there is fusion of mentation and perception. To understand the cause of hallucinations, therefore, one is required to think, not in psychologic terms, but in terms of the physical processes concomitant with mentation and perception. Psychologic data do not help one to understand the mechanism of hallucination; they help only so far as to indicate that certain thoughts, more easily than others, gain expression in hallucinatory form.

The error of ascribing hallucinations to the human desire to disown one's faults is facilitated by the apparent obviousness with which the patient "blames the environment." Thus a schizophrenic woman angrily denounces those imaginary beings who taunt her with the remark "You are (or She is) a prostitute." I shall try to show that this seeming tendency to "project" the blame on others is in reality determined by physiologic laws. To do this, I shall show that a hallucination connected with the idea "I am a prostitute" could not readily be couched in the first person singular, but only in the second or third person. Nervous arrangements concomitant with particular images and words are not originally inherent in the brain, but are established through use. For example, a person who has never seen the Mona Lisa, or a copy or photograph thereof, has no image of a particular person when he hears or sees the words "Mona Lisa." A person who knows English has a particular image when he hears or sees the word "cloud;" a person who knows no English will have no such image. Now, barring two exceptions to be noted later, no person has heard the word "I" *designating himself* issuing from lips other than his own; pronouns

designating the subject and issuing from other lips are invariably "you" or "he." Accordingly, in the subject's brain there are nervous arrangements concomitant with the auditory images "you" and "he" (designating the subject) capable of being energized when the speech apparatus is inactive; also, there are arrangements concomitant with the auditory image "I" that are energized *only in conjunction with* the arrangements for *saying* "I;" but there are no arrangements concomitant with the auditory image "I" capable of being energized when the subject is not speaking. Therefore, when the idea "I am a prostitute" gains expression in hallucinatory form, the energizing of the arrangements concomitant with the words "I am a prostitute" is a physiologic impossibility; the patient has no nervous mechanism enabling her to hear the word "I," designating herself, when she is not the speaker—exactly as I, in my ignorance of Sanskrit, have no mechanism enabling me to have an image "cloud" when I hear the corresponding Sanskrit word. Thus one sees that physiologic laws make it inevitable that the patient's thoughts, when woven into auditory images, will be expressed in terms of the second or third person.

I now state the first exception noted in the last paragraph. Suppose John says to Henry: "Last week you said, 'I should like you to lend me this book as soon as you have read it.' Well, I've finished it. Here it is." In the inner quotation Henry, though not speaking, hears the word "I" designating himself. I do not believe this exception constitutes a serious objection to the hypothesis set forth in the last paragraph. It is an exception fictitious rather than real; one may be certain that in real life John would say, "Last week you said you would like me to lend you this book . . ." The second exception noted in the last paragraph consists of a case of *Gedankenlautwerden* reported by Jankowska.[17] The patient, during an alcoholic delirium, "heard on the left side word for word his own thoughts, expressed in the first person ('I lose my job.' 'What is happening to my son?') as an echo of his internal speech, without objective or subjective signs of movement or sensation in the articulatory muscles." This case is in sharp conflict with the hypothesis set forth in the last paragraph. Whether it invalidates the hypothesis or is merely an unimportant exception to the rule, I am now unable to say.

"Soundless Auditory Hallucinations."—In describing their auditory hallucinations, patients sometimes specify that the voices do not have the sound of real voices but are more like thoughts within themselves. Thus, Bleuler,[18] said:

17. Jankowska, H.: Ein Fall von Gedankenecho oder Gedankenlautwerden, Rocznik psychjat., 1928, p. 44; abstr., Nervenarzt **2**:118 (Feb.) 1929.

18. Bleuler,[15] p. 90.

There are all gradations from normal representations *(Vorstellungen)* to hallucinations with perfect sensory distinctness. . . . Even intelligent patients often do not know whether to say they hear voices or must only *think* them; there are "such vivid thoughts," which however even by the patients themselves are designated as voices; then also there are "loud thoughts," "soundless voices," two expressions which designate perhaps the same thing, or at any rate very nearly the same thing. . . . Sometimes it seems to the patients "as though they heard."

Some physicians might be inclined to think that these soundless hallucinations are not really hallucinations at all, but represent merely a normal manifestation of thought. This interpretation is not permissible in cases in which the thoughts are couched in the second or third person. After emerging from a catatonic stupor, an intelligent schizophrenic patient gave a retrospective account in which she related how she had heard voices seemingly emanating from "that power that seemed to control me." Thus, "it said to me, 'You'll never see your family again.'" The "voice" was absolutely silent. "It was more like my own thoughts." I submit that one cannot regard this as normal thought. Normal thought would express itself in the first person: "*I'll* never see my family again." "*You'll* never, etc.," is a hallucination, its soundlessness notwithstanding. The difference between such a soundless hallucination and an ordinary audible hallucination is on the order of that between a faint and a vivid image.

A case bearing decisively on this point is that of a woman, aged 52, who reported that ever since she joined the church, at the age of 15, she had been hearing the voices of God and the devil. (Is it as loud as an ordinary speaking voice?) "No—it's a quiet voice; nobody can hear it but me." (If I were right next to you, would I be able to hear it? "No. It's not intended for you to hear—it's the voice of conscience." (Does it come from the outside?) "No, it's a voice in my own head." (Why do you call it a voice?) "I can *hear* it." The voices speak *to* her in the second person and *about* her in the third person. Examples of the second person: God's voice says, "Love me and despise the devil." The devil's voice says, "Worship me instead of the Lord." Examples of the third person: God's voice says, "Margaret (patient) is a good person." The devil's voice says, "I'm going to try to win her from God." *The patient carefully distinguishes her "own thoughts" from those of God and the devil.* Though the voices of God and the devil are soundless, she describes her own thoughts as being even "quieter." Moreover, *her own thoughts are couched in the first person;* e. g., the thought of needing a handkerchief occurs in the form "I need a handkerchief."

This case shows conclusively that soundless voices bearing messages in the second or third person are really hallucinations, and are to be differentiated from normal thoughts, in which the subject is designated by the first personal pronoun.

Delusions.—The criterion of a delusion is not its falsity but the insufficiency of its supporting data. Ordinarily one does not know or believe a given fact unless one "has reason" to do so, i. e., unless

one has heard or seen or otherwise perceived the fact in question, or else inferred it from other facts coming within the grasp of the senses. To know or believe something when the evidence does not warrant such belief is to have a delusion. At once one sees a parallel between delusion and hallucination: in hallucination one, e. g., *sees* something "for which there is no adequate external basis;" in delusion one *knows* something "for which there is no adequate external basis." Moreover, this parallel is not without meaning if one bears in mind that (as I tried earlier to show) cognition and perception are related in the closest way. If I see a book on the table, I have a vivid image, concomitant with activity of lowest and highest centers; if I later think of the book, or if I reflect that I know it is lying on the table, I have (in either case) a faint image, concomitant with activity of the highest centers. I therefore submit that delusion is but a special instance of hallucination; in hallucination there is a *vivid* image, in delusion a particular kind of *faint* image, "without adequate external basis." When a patient believes that men are outside waiting to hang him, he has a faint image; when he *hears* them, he has a vivid image.

This view is in accord with a fact that has attracted little, if any, attention: I refer to the frequency of delusions in dreams. Every one realizes that one hallucinates while dreaming but I do not know of any one who has called attention to the fact that one also has delusions, i. e., one knows things for which one has no evidence. Thus a woman has a dream in which she enters her house, whereon (while still dreaming) she suddenly becomes aware that her mother has died, *although she sees or hears nothing to indicate it.* This is an exact duplicate of what in waking life would be called a delusion. I refer again to my own dream, in which, seeing a wooden chest, I "knew" that the key thereto was nowhere to be found, though I saw and heard nothing on which to base this belief. I believe that there is profound significance in this occurrence of delusions in the hallucinatory state that accompanies sleep.

The need of uniform terminology would warrant one in speaking of delusions as "cognitive hallucinations." Thus a patient with "cognitive hallucinations" has certain faint images "without adequate external basis," while a patient with visual hallucinations has certain vivid images. Cognitive hallucinations are of the same order as "memory hallucinations," of which Bleuler has already written.[19]

Though delusion and hallucination are essentially of a piece, there is a certain difference. Confining attention to the sensory centers, one may say that during perception there is engagement of lowest and highest

19. Bleuler,[15] p. 317.

centers; during cognition the highest only are engaged. In hallucination, therefore, the highest ("thinking") centers "lean for support" on a very low level of the nervous system; in delusion they lean on a very high level. Delusions indicate a relatively shallow dissolution, hallucinations a deep dissolution. Returning to a previous analogy, a deluded patient who does not hallucinate is like a man who needs a cane; a hallucinating patient is like a man who needs a crutch. This is in keeping with the well known fact that patients who hallucinate are generally more deeply disintegrated than those who have delusions without hallucinations.

These views on the nature of delusion will find disfavor with those who look on cognition, perception, memory, etc., as separate faculties that do not touch each other. Nevertheless, I believe that if one accepts Jackson's ideas about the sensorimotor constitution of the "organ of mind," there is no inherent absurdity in the view that delusion and hallucination are but different degrees of the same thing, however far apart they may seem to those who fail to view mental phenomena from the standpoint of their evolution.

Clinical Notes

A CASE OF INTRAPONTILE GLIOMA

Differentiation of Syndromes Referable to Progressive Involvement of the Pontile, Mesencephalic and Bulbar Regions

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In the diagnosis of lesions at the base of the brain, the history of the development of the malady, with particular reference to the chronologic sequence of the symptoms, may be of the utmost importance. The so-called brain stem includes the medulla oblongata, the pons and the midbrain—structures in which the third to the twelfth pairs of cerebral nerves have their nuclei of origin and of termination. A thorough knowledge of the anatomy (gross and microscopic) and the physiology (human and experimental) of these areas, as well as of the architecture and functions of their component mechanisms, is essential for finding the way to diagnostic conclusions that make any attempt at precision with regard either to the localization of the organic lesions or to the nature of the malady on which these lesions depend. There are now known a whole series of bulbar syndromes, pontile syndromes, peduncular syndromes and quadrigeminal syndromes; in each group one has gradually become acquainted with markedly different complexes of symptoms, the total constitution of each being dependent on the exact site of the lesions that underlie it, and the chronologic sequence of the symptoms often being determined by the nature of the disease.

A patient now under observation in the Johns Hopkins Hospital will serve well in illustration of the difficulties of diagnosis of disturbances in the region of the brain stem and of the kind of investigation that is of help in their solution.

REPORT OF CASE

History.—Richard C., aged 21, single, a glazier, was admitted to the Neurosurgical Department (service of Dr. Dandy) on Feb. 18, 1933, complaining of weakness of the left side of the body, headache and vomiting. The family history contributed nothing of importance. The patient had always been healthy, except for measles and tonsillitis in early childhood and appendectomy one year before admission. He had been in two automobile accidents—in December, 1931, when he suffered a bruise of the right leg, and again in October, 1932, when he hit his forehead against the windshield frame (without loss of consciousness or evidence of bruise), after which he had mild headaches and occasional vomiting. Despite these symptoms he continued at work until the latter part of December.

On Dec. 28, 1932 (about seven weeks before admission), on awakening in the morning, he noticed that his left arm and leg were weak; though he could walk with difficulty, he dragged his left foot. A day or two later he began to have

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A clinical demonstration to the Clinic for Senior Students of the Johns Hopkins Medical School, March 2, 1933.

headaches on the right side; they increased in severity and became generalized over the head. He complained also of a "dead" feeling in the lower half of the right side of the face. He entered a hospital in Washington, D. C., for observation, and while there he noticed that his eyesight became dim and that he saw double, symptoms that have persisted since. One week before admission to the Johns Hopkins Hospital, the weakness of the left arm and leg and of the trunk became more marked, so that he said that he was unable to sit up in bed. The headaches became more severe and he had vomiting spells (apparently of the projectile type) every afternoon or evening. At this time, too, he first noticed ringing in both ears and numbness of the left half of the body and of the right side of the face. There was some involuntary jerking of the left arm and leg, but there were no general convulsive seizures or loss of consciousness. The headaches recently had apparently been excruciating, and the vomiting had persisted. There had been no incontinence of urine or feces, dysarthria or dysphagia. Aside from a tendency to drowsiness, there had been no disturbances of consciousness and he had remained mentally clear.

Examination.—Physical examination showed variability of the pulse rate with a tendency to tachycardia; slight fever; a respiratory rate of 20; a blood pressure of 110 systolic and 70 diastolic; slight ptosis in the right eye; active and equal pupils; paralysis of the right lateral rectus muscle, with constant diplopia; poor visual acuity; slight papilledema in the left eye; weakness of the muscles of the jaw, of the sternocleidomastoid muscle and of the muscles of the left side of the tongue; hemiplegia on the left side, with loss of the left abdominal reflex, but patellar and ankle clonus and a positive Babinski sign on the left side; hemihypesthesia on the left side and hypesthesia of the right side of the face; a normal sense of smell and taste; normal hearing; active responses to caloric stimuli in Bárány tests.

Examination of the blood showed no anemia; white cells, 8,200; Wassermann test, negative. The urine had a specific gravity of from 1.022 to 1.024; there was no polyuria and no albumin, sugar or casts. The cerebrospinal fluid was clear; there were 4 cells per cubic millimeter, and the Queckenstedt test was negative. Roentgen examination revealed that the sella turcica was normal; the ventriculograms taken after an injection of air were normal; the paranasal sinuses were normal.

Ophthalmologic examination (Dr. F. B. Walsh, February 19) showed slight papilledema in the left eye; complete paralysis of the right abducens nerve, partial paralysis of the right trochlear nerve and a suspicion of weakness of the left levator palpebrarum; anesthesia of the right cornea. Visual acuity was greatly reduced in both eyes at the time of examination, though two days later vision was approximately normal, with practically normal fields.

Course.—Vision has varied greatly from day to day. On February 20, numbness appeared in the left side of the face, and there was corneal anesthesia on the left side. The patient continued to be rather drowsy and vomited frequently. There was no rigidity of the neck. Slight pyrexia was present. After an injection of air on February 21, the temperature rose to 101.2 F., the pulse rate to 120 and the respiratory rate to 36. On February 22, the temperature was lower, and the patient took more fluid; the severe headache and vomiting continued. On February 23, the temperature became normal, the headache was less severe and there was less vomiting. The patient continued to complain of blurred vision and of seeing double constantly. Nystagmus appeared, with the rapid component

to the left. The corneal reflexes returned, though the right was still rather sluggish. Slight anesthesia of the left side of the face was still present, and there was a slowed response to sensory stimuli over the whole left side of the body, though the nature of all stimuli could be recognized and there was no astereognosis.

Conjugate movement of both eyes above the horizontal level was normal, but conjugate movement of the eyes horizontally to the right was lost. On February 28, there were temporary dilatation and fixation of the left pupil. On conjugate deviation of the eyes to the left definite nystagmus appeared, with the rapid component to the left.

COMMENTS

This man, aged 21, except for headaches and occasional vomiting after a motor accident four months before admission to the Johns Hopkins Hospital, had been healthy until about two months before admission, when he suddenly noticed weakness and rigidity of the left arm and leg which made walking difficult. Right-sided headaches soon followed, along with dimness of vision and diplopia due to paralysis of the right abducens nerve. Later, severe attacks of vomiting set in, and at about the same time, bilateral tinnitus, hypesthesia of the left arm and leg, hypesthesia of the right side of the face and involuntary jerkings of the muscles of the extremities on the left.

On examination, in addition to spastic hemiplegia on the left side, the hypesthesias mentioned, paralysis of the lateral rectus muscle of the right eye, loss of horizontal associated movements of the eyes to the right, nystagmus on looking to the left, weakness of the muscles of the jaw and of the sternocleidomastoid and the muscles of the left side of the tongue, there was evidence of slight ptosis in the right eye, of beginning papilledema in the left eye and of corneal anesthesia on the right side. Later there was marked oscillation of the visual acuity, and slight numbness of the left side of the face with anesthesia of the left cornea developed. Temporary dilatation and fixation of the left pupil were noted, but these signs disappeared. On March 1, the patient was more drowsy and apathetic, and there was slight dysarthria as well as some hiccup.

Localization of the Focal Lesions.—The hemiplegia on the left side must be due to a lesion of the pyramidal tract somewhere above the lower part of the pons, and since it is accompanied by paralysis of the right abducens nerve, it is evidently one of the forms of hemiplegia alternans that point to a lesion of the right side of the upper part of the pons. The hemihypesthesia cruciata also points to a lesion of the right side of the pons, involving slightly the lemniscus and the nucleus (or the root fibers) of the right trigeminus nerve. The vomiting and headaches may be of pontile origin also rather than the effect of increased intracranial pressure, since ventriculograms show no evidence of blocking of the aqueduct and there is no bilateral choked disk (merely beginning papilledema on the left). That the nuclei of the cerebral nerves on both sides (or the roots of the nerves) have been injured is obvious from the symptoms referable to the second, third (left), fourth (right), fifth (both sides), sixth (right) and eighth nerves (tinnitus without deafness). The nystagmus with the rapid component to the left that recently appeared is probably due to a partial involvement of the fasciculus longitudinalis medialis.

Judging from the chronology of the appearance of the symptoms, the injury to the right side of the pons occurred first and was followed by injury either to multiple nerve roots or to their nuclei in the pons and the midbrain; these

later injuries were not confined to the right side but irregularly involved the left also. One must therefore assume a preponderant injury to the right half of the pons, with irregular bilateral asymmetrical injuries of structures above and below it.

Nature of the Lesions.—The mode of onset of the symptoms and the history of the development of the syndrome strongly favor the view that the process is *intrapontile* rather than extrapontile. Its rapid progress suggests either a neoplasm or an inflammatory process (tuberculoma or encephalitis). I believe that a gliomatous tumor (a glioblastoma multiforme or possibly an astrocytoma or a unipolar spongioblastoma) is most probable. Intrapontile tumor is unique as a type of tumor in the posterior fossa of the skull that need not give rise to marked increase of intracranial pressure or to changes in the ventriculograms; severe pain and vomiting suggestive of increased intracranial pressure may be due to local pontile lesions.

Pontile lesions due to compression from above by a pineal or other neoplasm seem to me to be improbable since in compression from such tumors the initial symptoms are most often those due to increased intracranial pressure because of early blocking of the aqueduct, symptoms of involvement of the midbrain (early pupillary changes with loss of associated movement of the eyeballs upward) are more pronounced than pontile symptoms, and peripheral involvement of the fifth, sixth, seventh and lower cerebral nerves (so often found in pontile tumors) is relatively infrequent.

The so-called tumors of the median line—one group of tumors of the fourth ventricle—yield evidences of marked increase of intracranial tension early, with severe headaches and vomiting and, usually, rapidly developing choked disk; with many of them there are symptoms referable to involvement of the vermis of the cerebellum; with some, there are symptoms due to nuclear lesions in the floor of the fourth ventricle, especially lesions of the nuclei of the fifth and sixth nerves. But in the case reported here, the involvement of the pyramidal tracts, the absence of cerebellar symptoms and the late appearance of only slight papilledema of a single optic disk favor a diagnosis of intrapontile tumor and seem to rule out a tumor of the median line.

An ordinary tumor of the cerebellopontile angle (or acoustic neurinoma) seems to me to be ruled out, first, because there has been no deafness in either ear, despite some tinnitus, and the Bárány tests have been negative, and second, because in acoustic tumors the chronologic sequence of symptoms is characteristic, i. e.: (1) cochlear and vestibular manifestations, (2) occipitofrontal pain with suboccipital discomfort, (3) ataxia of cerebellar type, (4) signs of injury to other cerebral nerves of the same region, (5) development of increased intracranial pressure with choked disk and (6) disturbances of speech, swallowing and respiration. Tumors originating within the pons do not exhibit any similar set order of sequence of the symptoms; nor are the general symptoms of increased intracranial pressure likely to be prominent early, choked disk appearing late, if at all. Hemiplegia alternans and hemihypesthesia cruciata do not belong to the picture of an acoustic tumor, though they are often early signs of an intrapontile growth. Finally, the slow development of the syndrome due to acoustic neurinoma is in marked contrast with the "galloping" development of the syndrome due to intrapontile tumor.

Aside from tumors of the pons, inflammatory lesions due to abscess of the brain, to syphilis, to tuberculosis, to epidemic encephalitis, to acute multiple sclerosis or to Schilder's disease (encephalitis periaxialis diffusa) must be briefly

discussed since any one of these conditions may give rise to a syndrome that simulates in greater or less degree that of intrapontile neoplasm.

Abscess of the brain seems improbable, for there has been no evidence of a primary infection elsewhere and no leukocytosis.

Syphilis is ruled out by the negative Wassermann reaction of the blood and of the cerebrospinal fluid.

A tuberculoma of the pons cannot be so easily dismissed, since it may be unilateral, may involve the nucleus of the sixth nerve, causing paralysis of the medial rectus muscle of the eye, may injure the pyramidal tract and give rise to contralateral hemiplegia or hemiplegia alternans, and may not cause any great increase in intracranial pressure. As a rule, however, when there is a tuberculoma of the pons, signs of tuberculosis elsewhere in the body are evident, and one expects also a family history of tuberculosis. Thus far, nothing suggestive of tuberculous infection has been discovered in the patient or in any member of his family.

The fact that the patient has had some fever and has been somewhat drowsy might make one think of epidemic encephalitis of bizarre localization. But with such extensive involvement of the brain stem as is evident in this case it would seem surprising not to find signs of involvement of other parts of the central nervous system if the condition were epidemic encephalitis; moreover, the cerebrospinal fluid showed nothing suggestive of that infection. The recent increase of drowsiness and the appearance of hiccup make one cautious, however, in denying the possibility of epidemic encephalitis. Unfortunately, the sugar content of the cerebrospinal fluid was not determined.

Acute multiple sclerosis might conceivably be localized predominantly in the pons, but such a localization must be of extreme rarity and, besides, would scarcely be compatible with the mode of development of the syndrome presented in this case.

One or two members of the staff have suggested the possibility of Schilder's disease, but in the diffuse periaxial encephalitis to which that name has been given the lesions are more widespread in the brain and tend to be bilaterally more or less symmetrical, involving the cerebral hemispheres, especially the parietal and occipital lobes, as well as the brain stem.

I come to the conclusion, therefore, that the weight of evidence is strongly in favor of the diagnosis of an intrapontile glioma, though the bare possibility that the condition may be a tuberculoma or epidemic encephalitis will be kept in mind.

Therapy.—From the standpoint of treatment, a correct diagnosis is of the utmost importance, for if this patient has an extrapontile tumor surgical intervention may be of promise, whereas if, as seems most probable, he has an intrapontile glioma, surgical treatment is definitely contraindicated.

High voltage roentgenotherapy or radiotherapy might be tried, but these forms of treatment have been unavailing in similar cases. It seems all too probable that the malady presented by this patient is not amenable to any form of therapy and that death may be expected, perhaps in the course of a few weeks or months.

NOTE.—Dr. Woodhall of Dr. Dandy's staff reported that the patient died on March 6 (four days after the report was made at the clinic). There were no further manifestations except progressive paralysis of the respiratory tract. At autopsy there was a large pontile glioma occupying the entire half of the right side of the pons and probably infiltrating toward the left side. There was also congenital absence of the left occipital sinus.

IMPACTION OF A NEUROEPITHELIAL CYST IN THE THIRD VENTRICLE OF THE BRAIN

CARL O. RINDER, M.D., AND PAUL R. CANNON, M.D., CHICAGO

Cystic tumors occurring in the third ventricle of the brain, associated with the choroid plexus, are uncommon, and the literature contains but few references to them. Fulton and Bailey,[1] in reviewing the subject in 1929, found less than twenty instances. From the clinical point of view, antemortem diagnosis is extremely difficult, and the process may be suspected only from certain peculiarities of symptoms, such as hypersomnia, visual disturbances accompanied by choking of the optic disks, a tendency to intermittency of attacks, and severe headaches, often associated with nausea and vomiting, from which the patient obtains sudden relief by a change in posture. Some of these symptoms, however, have been associated with tumors of the third ventricle, pineal body and posterior fossa. We wish to record a case of impaction of a cystic tumor in the third ventricle in which death occurred suddenly, owing to acute internal hydrocephalus.

REPORT OF CASE

History.—B. Y., a woman, a secretary, aged 47, was first seen by one of us (C. O. R.) in January, 1920. At that time she stated that in May, 1919, she had had attacks of severe headache, usually ushered in by pain over the bridge of the nose. The headaches would increase until nausea and vomiting occurred; often the vomiting would relieve the pain. The attacks were associated with vertigo and abnormal drowsiness and usually lasted for about twelve hours, although at times they persisted for from twenty-four to thirty-six hours. Relief from pain and vertigo was frequently obtained by reclining with the head thrown back. Following the relief from pain the desire to sleep was so pronounced that she frequently slept for about twelve hours, during which time she could be aroused, but she complained bitterly at any attempt to awaken her. She attributed her trouble to a visual defect, as her first attack followed a change in glasses. It is of significance, however, that previous to 1920, three oculists had observed no lesions of the optic nerve or of the retina, only a marked myopia. She believed, furthermore, that a saline purge would often stop an attack. There was an unusual feature of periodicity in that at one time she reported severe attacks recurring every Monday morning for seven weeks.

The previous history was not particularly significant. At the age of 18, during a severe illness accompanied by diarrhea, she was told that a hemorrhage had occurred in the right eyeball. She had malaria at 22 years of age, and was in a sanatorium for a "nervous breakdown" at the age of 26. Her sister stated that she was very emotional, and that she worried over trivial matters.

From 1920 she was practically free from symptoms for nine years. While on a vacation six months prior to death, she had an attack that resembled the former ones. An oculist told her that the optic nerve was involved, and that there was a narrowing of the field of vision. Her condition improved, and she did not consult a physician again.

From the Department of Pathology, the University of Chicago.

1. Fulton, J. F., and Bailey, Percival: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1, 1929.

The fatal ending began on the afternoon of Nov. 27, 1929. The patient stopped work because of a severe headache. At home she began to have attacks of vomiting which increased until they became projectile. There was excruciating pain over the right eye and in the temporal region, and she complained of dimness of vision. She refused to call a physician, as she believed that the attack would stop as had the previous ones. At about 3 a. m. on November 28, she was found lying on the floor in a coma; she was cyanotic and breathed with difficulty. Death ensued shortly thereafter.

Necropsy.—Necropsy was performed six hours after death and revealed the following: The dura mater was under increased tension and, when removed, showed that the leptomeningeal surfaces were dry, the convolutions flattened and

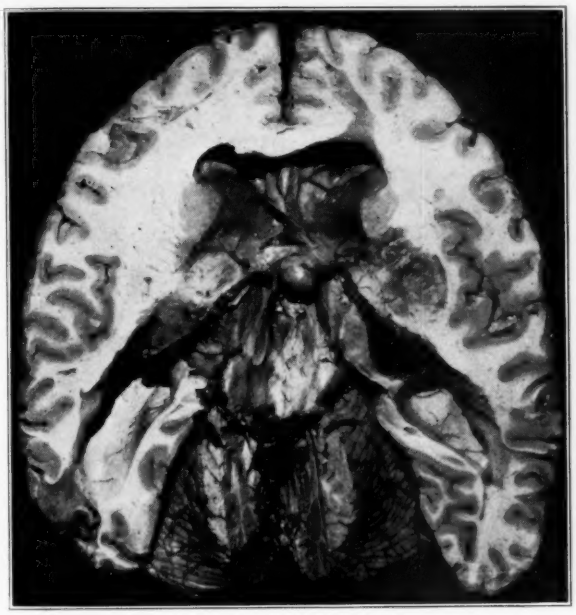

Fig. 1.—The spherical cyst is shown impacted in the foramen interventriculare.

the sulci compressed. There was an increased quantity of cerebrospinal fluid around the medulla and the pons. A horizontal incision through the brain showed both lateral ventricles moderately dilated by a clear fluid. A spherical cyst (fig. 1), 15 mm. in diameter, was impacted in the foramen interventriculare, completely occluding the third ventricle. The cyst was attached by a stalk to the anterior margin of the right choroid plexus and could be removed easily from its site of lodgment. The third and fourth ventricles were not significantly dilated. The brain, emptied of fluid, weighed 1,140 Gm.

The only other pertinent findings were acute distention of the right side of the heart and acute pulmonary edema.

The cyst had a smooth wall and contained a translucent, gelatinous, grayish-yellow material. Sections stained with hematoxylin and eosin (fig. 2) showed that the wall consisted of an outer fibrous coat and an inner layer of cuboidal

and columnar ciliated epithelial cells, some of which were swollen and contained coarse yellowish-brown granules. Others contained numerous small blue granules arranged in a row along the inner borders of the cells. The contents of the cyst were somewhat granular and stained bluish-pink with hematoxylin and eosin and red with scarlet red; they did not take the mucicarmine stain. Concentrated sulphuric acid caused the contents to become bluish, indicating a lipochrome substance.

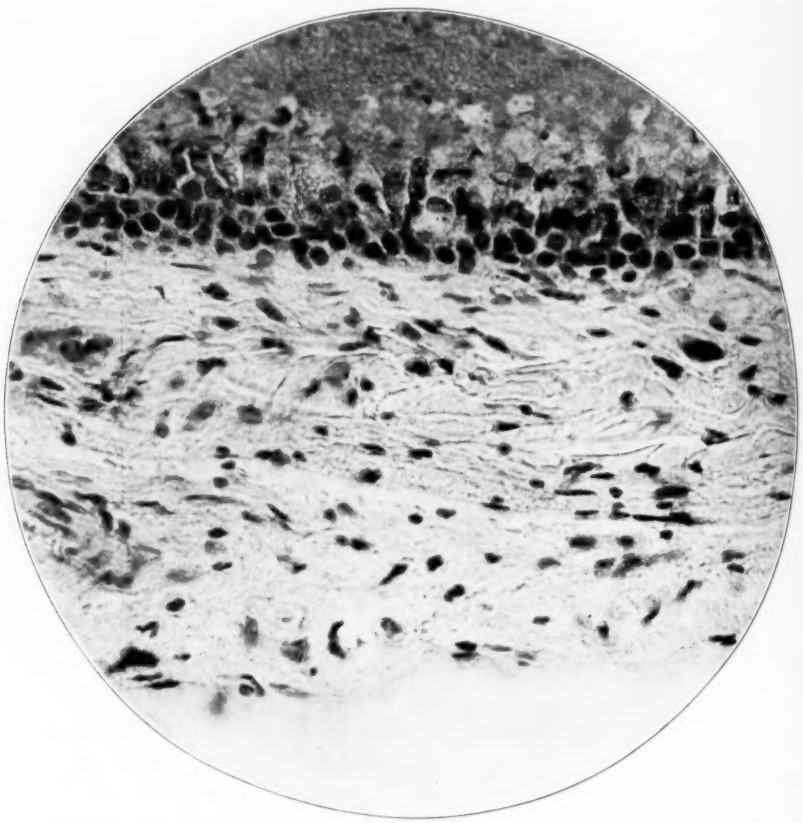

Fig. 2.—Section through the wall of the cyst stained with hematoxylin and eosin; × 400.

COMMENT

Tumors such as this have usually been described as "colloid cysts," but as their exact origin is still uncertain and the term "colloid" quite indefinite, we are, at the suggestion of Bailey, calling this one a neuro-epithelial cyst. According to Sjövall,[2] these tumors probably originate in the paraphysis, a structure which is

2. Sjövall, E.: Ueber eine Ependymcyste embryonalen Charakters (Paraphyse?) im dritten Hirnventrikel mit tödlichem Ausgang, Beitr. z. path. Anat. u. z. allg. Path. **47**:248, 1909-1910.

extremely rudimentary in man, but which in lower vertebrates arises from the extreme anterior end of the third ventricle (Bailey [3]).

Drennan [4] recently described two cases quite similar to that reported here. These were in patients under 26 years of age; in each instance death occurred rather suddenly under circumstances which led to a coroner's investigation. In one the patient had apparently been in good health, while in the other the patient had had severe headaches for two years. In both cases necropsy disclosed a smooth colloid cyst impacted in the third ventricle, with a resulting internal hydrocephalus affecting the lateral ventricles.

Kennedy [5] described what seems to be one of these cysts in a patient in whom operation effected a cure. He stated: " . . . on opening the dura over the affected brain area there was a tremendous extrusion of brain cortex, which suddenly burst, emitting a fountain of cerebrospinal fluid through the thinned out and ruptured ventricular wall. Sir Victor Horsley, who performed the operation, digitally explored the interior of the ventricle and removed a tumor the size and shape of a large pea, which had been attached to the choroid plexus, and apparently had blocked interventricular communication. This tumor was epithelial in structure and had two small cystic areas on its surface; it was benign and the patient entirely recovered." So far as we know this is the only instance of successful treatment in a condition of this sort.

Of significance in most of these cases is the intermittency of symptoms, perhaps explained by the ability of the cyst to act as a ball-valve in blocking the foramen of Monro. In several of the cases reported the symptoms were at times relieved by a change of posture or by movements of the head. In our case an interesting point is the apparent absence of symptoms for a period of nine years, followed by a sudden fatal attack. We suggest that during the earlier attacks the cyst may have been small enough to enter and leave the foramen interventriculare, but grew too large to enter readily; when impaction occurred after the long interval, the cyst, unable to dislodge itself, caused rapid death by acute internal hydrocephalus.

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3. Bailey, Percival: Morphology of the Roof-Plate of the Fore-Brain and the Lateral Chorioid Plexuses in the Human Embryo, J. Comp. Neurol. **26**:79, 1916.

4. Drennan, A. M.: Impacted Cyst in Third Ventricle of Brain: Report of Two Cases, Brit. M. J. **2**:47, 1929.

5. Kennedy, Foster, in Nelson Loose-Leaf Living Medicine, New York, T. Nelson & Sons, 1920, vol. 6, p. 122.

SPECIAL ARTICLE

"CORTICALIZATION" OF FUNCTION AND FUNCTIONAL LOCALIZATION IN THE CEREBRAL CORTEX

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The problems of "corticalization" of function and functional localization in the central cortex are intimately linked, but for purposes of exposition it is desirable to discuss them to some extent separately. Functional encephalization is the underlying principle of the progressive development of the central nervous system as observed in the animal scale. I shall not deal here with the problem of encephalization in general, which would mean a survey of the shift of functional dominance from the spinal cord up through all levels of the central nervous system. I shall confine myself to the problem of functional corticalization and give first of all the major physiologic evidence available at present for the shift of functional dominance toward this highest level as one ascends the animal scale.

CORTICALIZATION OF FUNCTION

The Motor Functions.—Fairly normal posture and progression are possible within a few hours after the total extirpation of the cortex in the cat. The decorticate dog can stand and walk within twenty-four hours. The decorticate monkey can sit upright to some extent, as demonstrated by the experiments of Karplus and Kreidl, but needs support for his upper extremities. Real progression has, so far as I know, not been recorded in such an animal, even in the monkey of Karplus and Kreidl which survived twenty-eight days after the extirpation of the second hemisphere.

There are a few human "experiments of nature" on record, comparable to some extent to the total extirpation of the cerebral hemispheres in animals. The best known examples of human beings without cortex are the children described by Edinger and Fischer, and

Read as part of a symposium on cortical localization at a meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 28, 1932.

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Gamper. Both children were incapable of assuming a sitting position, though the child described by Gamper showed some indication of this postural function when the legs were held down. In other respects posture and locomotion were impossible. Even with less extensive lesions, e. g., large porencephalic bilateral defects of the sensorimotor cortex, active standing and progression are impossible in man.

In the cat and the dog relatively little motor impairment is present after extirpation of the sensorimotor cortex of one hemisphere. Occasionally a little loss of muscle tone, as it reveals itself in resistance against passive movements, can be observed; but even this is not constant and disappears quickly. In these species a true motor paralysis or even paresis is not observed. The most prominent symptoms are the sensory ones, about which I shall speak later.

In the monkey (Macacus, green monkey) the picture after a circumscribed lesion of the so-called motor cortex is much more marked, though it is always astonishing to observe the rapid recovery from the initial severe symptoms. For two or three days there is a contralateral monoplegia, with marked diminution of muscle tone and depression of the tendon reflexes. Then (sometimes even earlier than the second day) motility reappears: Some coarse movements occur first in the proximal joints and then in the more distal joints of the limb. Within a week movements of the fingers may come back, but they are as yet clumsy and ataxic. For the finer movements, such as picking up food from the floor, the impaired limb is used much less extensively than the normal one, but during excitement, anger or fear or in fighting or climbing, in short, in the grosser movements, the affected limb is used much more and effectively. Fine movements in the distal joints of the affected extremity remain impaired for a long time, though here also recovery is obvious, so that finally it is often difficult to state which extremity was affected.

Interesting is the observation that if for some reason, such as intestinal trouble, the general condition of the animal becomes poor, even long after the operation, the symptoms of cortical deficit may reappear to a certain extent. This demonstrates the relative fragility of the functional recovery.

In the higher apes, the gibbon and the chimpanzee, the motor impairment after circumscribed lesions of the motor cortex is much more profound and long-lasting (Beevor and Horsley, Sherrington and co-workers). The recent work of Fulton and Keller on extirpation of the leg area in these primates has given further valuable information on this point, from which I take the following data: There is areflexia for from two to three days; return of "voluntary power"

occurs in the hip after from two to four days, in the knee after four days, in the ankle only after twenty-five days and in the toes after from forty to sixty days. Here again one sees a much more pronounced impairment in the musculature of the distal joints. The extensor muscles are more and longer affected than the flexor muscles of the leg. Of interest is the observation of these authors that after extirpation of the cortical leg area a positive Babinski sign appears permanently in the chimpanzee and temporarily in the gibbon. Some of the other signs of lesion of the pyramidal tract, however, persisted in the gibbon.

In the cat and the dog the extirpation of a whole hemisphere results in little more evidence of motor deficit than is present after a circumscribed lesion of the sensorimotor area. In the monkey the result is different; the symptoms of motor deficit are distinctly more pronounced and of longer duration after total ablation of one hemisphere than after extirpation of the electrically excitable portion of the cortex alone. This indicates that in these higher animals other parts of the hemisphere participate in the elaboration of motility.

In man the disturbances in motility caused by localized lesions of the precentral cortex have the same character as in the anthropoid apes, but are more profound and of longer duration; as in monkeys, however, recovery of function may be strikingly rapid and far-going.

The increase in the functional importance of the motor cortex in the higher animals expresses itself also in stimulation experiments.

The yield in motor responses from the cortex of cold-blooded animals is meager. The older observations are mostly not beyond the criticism that the effects obtained might be due to spread of current to subcortical mechanisms. More recent work, such as that of Richter on the alligator cortex, indicates that the cortex in cold-blooded animals is excitable.

In the lower mammals, including the cat and the dog, the movements elicitable from the cortex on electrical stimulation are rather coarse flexion and extension in the various joints of the limbs, with slight pronation and supination at the wrist and ankle and adduction and abduction of the shoulder and hip. These movements, together with some responses of the facial musculature and lateral and vertical deviations of the eyes from parts of the occipital cortex, are practically the only responses obtainable.

In the monkey many more finely graded responses can be obtained, predominantly in the distal parts of the limbs. Movements of each of the fingers and toes, especially of the thumb and index finger and of the hallus, are readily elicited. Movements of the eyes can be produced from a rather large frontal and occipital area. The representa-

tion of the facial musculature and that of the tongue and larynx are much more extensive. Not only is the excitable area relatively much larger in the monkey than in the lower mammals, but it is striking that it can readily be subdivided into at least three parts, which subserve the musculature of the leg, the arm and the face. Moreover, these subdivisions do not overlap much if strong stimuli and facilitation are avoided. In the chimpanzee and the gorilla the production of fine, highly coordinated movements is still more marked (Leyton and Sherrington, Fulton and Keller).

The cortex in gyrencephalic monkeys is characterized by the presence of a well marked central sulcus or rolandic fissure. Hitzig

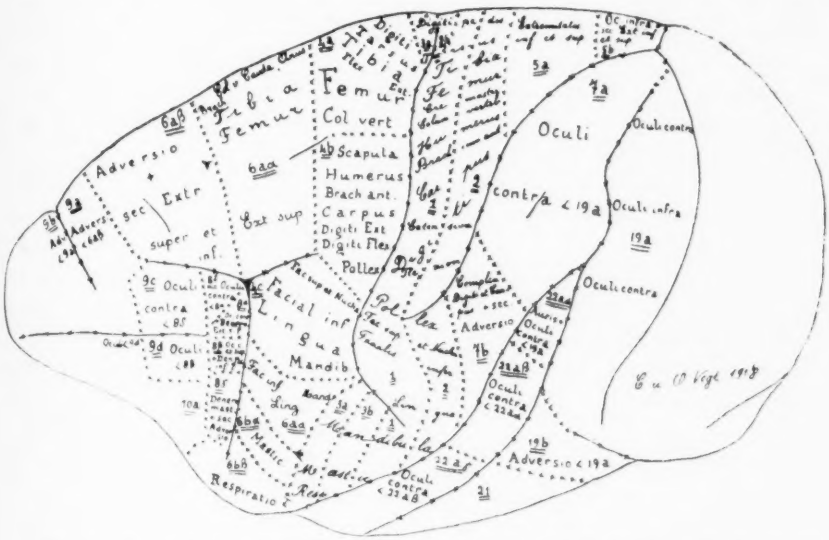

Fig. 1.—Synopsis of stimulation experiments of C. and O. Vogt on the brain of Cercopithecus (1918).

showed for the first time, in 1874, that in Macacus rhesus the excitable foci lie on the precentral cortex—a statement which was denied by almost all later investigators, until Grünbaum (Leyton) and Sherrington rediscovered this important fact and showed that it extended to the brain of the higher apes, the chimpanzee and the gorilla. At present this conception is almost universally accepted. It cannot be denied, however, that motor responses can be obtained, though less readily and with less differentiation, from the postcentral gyrus. Graham Brown furnished evidence that these postcentral responses cannot be explained on the basis of escape of current to the precentral cortex, but must be regarded as responses to efferent excitations arising in the postcentral

cortex. The tendency of recent stimulation experiments in monkeys (C. and O. Vogt) and in man (O. Foerster) is again to extend the electrically excitable cortex over the precentral and postcentral regions. The excitability of the motor cortex was found to be the same in the cat, the rhesus monkey and the chimpanzee (Sherrington).

In the lower mammals there are indications of a bilateral representation of motility. In the cat and the dog increase of the cortical stimulation often results in bilateral movements; under special conditions, such as isolation of a motor focus, bilateral movements may appear even with stimuli which normally give rise only to unilateral responses (Dusser de Barenne and Marshall). Even in the higher species motility seems to be represented bilaterally. Fulton and Keller gave special attention to this question. They found that in the higher monkeys, from the baboon upward, after the cortical foot area on one side has been removed, subsequent removal of the second foot area results in a distinct increase of motor impairment and a change in the Babinski response observed in the ipsilateral leg, i. e., the leg affected by the first lesion. Fulton and Dusser de Barenne found an analogous indication of bilateral representation of the motility of the tail in their experiments on monkeys with a prehensile tail.

Noteworthy here is the fact that the excitability of the motor cortex appears earlier after birth in the lower mammals than in the higher species. Recent experiments of Marinesco, Kreindler and Sager showed that in the guinea-pig the cortex reacts to galvanic stimuli on the fifth day after birth, whereas in the cat motor reactions can be obtained only after fourteen days, a statement in agreement with the early findings of Soltmann and others that in the dog the excitability for faradic stimuli appears from nine to eleven days after birth. Bechterew stated that it is possible to provoke epileptiform convulsions, apparently with strong faradic stimuli, in the new-born guinea-pig but not in the new-born puppy.

The Sensory Functions.—The cortex subserving the various qualities of cutaneous and so-called deep sensibility covers a large area in the higher animals.

In the lower mammals, as in the cat and the dog, this sensory area covers the precruciate and the postcruciate cortex, besides extending farther occipitally to the middle portion of the gyrus marginalis, reaching the border of the anterior ectosylvian fissure. In the cat and the dog the sensory cortical area to a great extent coincides with the electrically excitable region, thus indicating the existence in these species of a true sensorimotor area.

After experimental lesions in this sensorimotor field symptoms of deficit are readily observable in the initial stages: distinct impairment

of cutaneous sensitivity to touch, pain and thermal stimuli, and also of deep sensibility. The former group of symptoms rapidly diminish, so that in a few weeks or even less they may become undetectable by means of observation available in animal experimentation. An exception is the persistence of the loss of the "local sign," by which rather unfortunate denomination is designated the fact that apparently the animal is not able to locate the exact place of stimulation on the skin; this impairment is permanent. The symptoms of deficit in deep sensibility remain observable much longer and are to some extent permanent, so far as abnormal positions given to the distal parts of the limbs are permanently less promptly corrected than on the normal side. Munk's *Berührungsreflexe* are also permanently lost in the contralateral

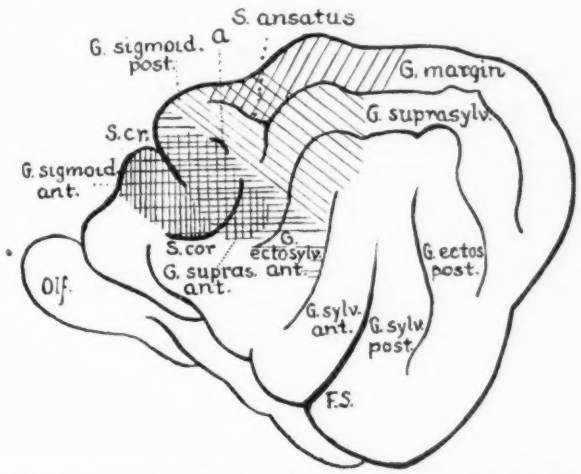

Fig. 2.—Sensory cortex on the convexity of the cat's brain, as determined by the method of local strychninization of the cortex (Dusser de Barenne, 1916). The vertical lines indicate the face area; the horizontal lines, the fore leg area; the diagonal lines (downward from right to left), the hind leg area; the diagonal lines (downward from left to right), an area of "crossed symptomatology."

extremities, which is probably also a symptom of impairment in deep sensibility, though this interpretation is still controversial. All these symptoms are more pronounced in the distal parts of the extremities than in the proximal parts.

In the monkeys from Cercopithecus upward, in which there is a well developed central sulcus, the sensory area, according to the results of extirpation experiments, lies exclusively in the postcentral gyrus and the adjacent parts of the parietal cortex. This would leave the central fissure as the boundary between a precentral motor and a postcentral sensory area. In man exactly the same observation is to be

made: Precentral lesions are not followed by apparent sensory defects, and postcentral lesions are not followed by definite motor impairment except for a certain amount of ataxia. This must be explained, however, not as a motor symptom, but as a sequence of disturbances in deep sensibility. The well known experiments of Cushing and of van Valkenburg, in which electrical stimulation of the postcentral gyrus in the conscious patient resulted in sensations localized in definite parts of the contralateral half of the body, add to this evidence, especially since Foerster stated that he never was able to elicit any sensation by stimulation of the precentral cortex.

The symptoms in the higher mammals after circumscribed lesions of the postcentral cortex are essentially the same as those described for the cat and the dog; they are, however, more intense and observable over a much longer period than in the lower animals. Still, recovery is often amazingly quick in "clean" postcentral lesions, especially in cases of clinical extirpation in which the excision does not penetrate too far into the white matter and thereby involve fiber tracts from other cortical regions. Permanent damage is done, just as in the lower animals, to the various qualities of spatial discrimination, so far as the cutaneous sensibility is concerned, and to deep sensibility. In most cases also a slight hypesthesia for touch, mild pain and thermal stimuli is permanent, whereas the initial impairment of perception for strong painful and excessive thermal stimuli subsides practically entirely. These disturbances are usually most marked in the distal parts of the limbs and around the mouth and nose.

This conception of a more or less strict separation of a precentral motor and a postcentral sensory cortex in the higher mammals has to be modified, since it has been found that the precentral cortex also, at least in the Macacus, is endowed with sensory functions. As this point will be discussed at some length in the section on functional localization, I shall confine myself here to the statement that the whole precentral cortex between the arcuate sulcus and the rolandic fissure in the Macacus has to do with sensory functions. This result was obtained in experiments with local strychninization of these parts of the cortex, in which distinct and typical symptoms of sensory excitation appeared on local application of a minimal quantity of strychnine to a definite region of the cortex, located posterior and anterior to the central sulcus. It is interesting to note here that these symptoms of sensory excitation were always present in the distal parts of the region of the body in which they could be established. About the explanations offered for the marked recovery from the severe initial symptoms I shall speak in the second part of the paper.

The Visual Functions.—In the visual function also functional corticalization is apparent.

A decorticate frog is hardly distinguishable from a normal one. It snaps at flies as readily and promptly and escapes from a vessel and avoids obstacles just as adroitly as a frog with an intact central nervous system (Schrader, 1887 and 1892). The pigeon is certainly not blind after total extirpation of the cortex. The most accurate data for this species are those given by Schrader (1888 and 1892). A decorticate pigeon can avoid obstacles and locate a small surface on which to land when thrown into the air. But distinct visual disturbances can be observed; the behavior of the bird is such that one is induced to assume that it does not recognize the objects depicted on its retina.

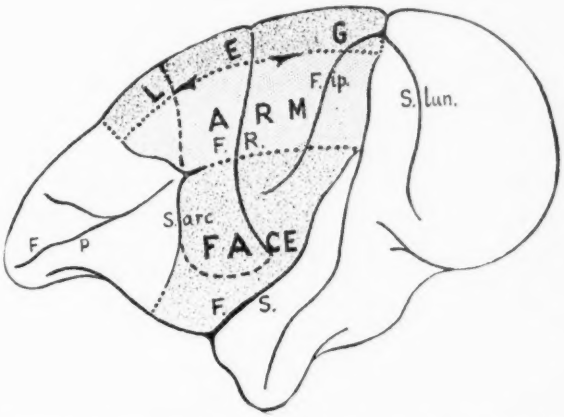

Fig. 3.—Sensory cortex on the convexity of the hemisphere in Macacus as revealed by the method of local strychninization of the cortex (Dusser de Barenne, 1924). The dotted lines indicate the boundaries between the three subdivisions of the sensory zone, and the broken line, the frontal boundary of the electrically excitable cortex. Between the leg and arm areas probably lies the trunk area. *F.R.* indicates fissura centralis; *F.S.*, fissura sylvii; *F.ip.*, fissura interparietalis; *S.lun.*, sulcus lunatus; *S.arc.*, sulcus arcuatus; *F.P.*, fissura principalis.

It manifests no fear under conditions in which the normal pigeon does. The conclusion is that, though important visual functions are subserved in this animal by subcortical centers, the cortex has obtained influence on the highest, most complicated activities, which govern through vision the relations of the animal with its surroundings. The same picture is found in other representatives of the avian class (Schrader).

In the cat and the dog, the animals most extensively and thoroughly investigated with regard to visual cortical localization, the disturbances after bilateral extirpation of the hemispheres or of the visual

cortex are much more profound. It is at present, I think, universally accepted that the primary visual cortex in mammals coincides with the area striata, as delimited by architectonic studies; the earlier statements about the localization of the visual cortex on the convexity of the occipital lobe are erroneous, owing to imperfect extirpations.

The higher mammal with total bilateral extirpation of the area striata acts as if blind. Visual stimuli no longer elicit any behavioristic reactions. Still there seems to be a residuum of visual activity, namely that of light discrimination in the rat (Lashley) and even in the dog (Marquis). How the monkey stands in this respect has not yet been investigated. In man bilateral destruction of the area striata results, so far as reliable evidence goes at present, in complete blindness.

The Auditory Functions.—Much less is known about the cortical representation of hearing, and the exact location and extent of the auditory cortex have not yet been delimited entirely satisfactorily. Grossly, it is known that in the cat and dog at least the anterior and posterior sylvian gyri are part of this region; perhaps the adjacent parts of the anterior and posterior ectosylvian gyri play a rôle in this respect. The difficulty in making an exact delimitation of this region lies in the fact that highly organized, complex auditory reflexes can still be observed in decorticate animals. Even the decerebrate cat exhibits some acoustic reflexes (Forbes and Sherrington). In a cat in which the whole neocortex had been extirpated, I observed during several weeks (beginning six or seven weeks after the total decortication) that the animal was able to localize sounds. She could be induced, especially when hungry, to walk and run promptly in the direction from which she was called.

Even the method of training and of conditioned reflexes has not as yet yielded unequivocal results with regard to the exact location of the auditory cortex in the higher mammals (Kalischer, Rothmann, Pavlov). Von Monakow was inclined to think that even in a human being with bilateral total destruction of the auditory cortex, taking as such the middle portion of the first temporal gyrus and Heschl's gyrus (cases of Mills and of Mott), there may still be retained some traces of audition.

The Olfactory and Gustatory Functions.—The cortical representation of the higher senses discussed so far lies in the neocortex, the latest acquisition, phylogenetically speaking. The lower senses, smell and taste, do not have their representation here, but in the phylogenetic old cortex, the allocortex or paleocortex. About the activities of this part of the cortex little is known as yet, either from the experimental or from the clinical point of view.

Smell reactions in a cat in which only the allocortex was retained and all neocortex was extirpated (Dusser de Barenne) were found practically normal. This animal was able to find its food and take it spontaneously. Apparently in the cat highly organized olfactory reflexes with prompt orientation in space can be evoked by olfactory stimuli in the absence of the whole neocortex. The question as to which parts of the cortex in man subserve these functions is one of the most obscure in neurology. So far as I know the literature on this problem I have the impression that the clinical observations do not allow any definite statement. The same is true with regard to the gustatory functions. Strong negativistic reactions toward unpleasant (bitter) food can be observed not only in the decorticate cat and dog, but also (and this is of greater significance) in anencephalic children. These general reactions, therefore, are largely subcortical, displayed by levels of the brain stem.

The Frontal Lobe.—The development of the cortex is characterized not only by the progressive evolution of the large projection areas of the neocortex but by the evolution of the regions surrounding or adjacent to these projection areas—the frontal and parietal lobes. The experimental and clinical literature on the activities of the frontal lobe is contradictory. This region has important connections with the motor cortex, the basal ganglia and the cerebellum. Through these connections it has influence, not directly, but indirectly, on motor activities of different functional dignity. Frontal lesions cause no actual defects in voluntary power; among the symptoms described as resulting from such lesions are defective coordinative adjustment in movements of the eyes and head, in the locomotion and in posture, abnormal tonus distribution, forced grasping, forced crying and catalepsy. The recent observations of Richter and Hines are of special interest: unilateral extirpation of the premotor region (area 6 of Brodmann) on the lateral and medial surface of the hemisphere in the monkey led to temporary forced grasping in the contralateral arm; bilateral destruction gave rise to bilateral and permanent forced grasping. "Psychic" disturbances have also been observed in lesions of the frontal lobe. Broadbent, in 1872, claimed that this part of the brain is the "psychic centre"; ever since those early days there has been argument on this problem. Loss or defects in apperception, memory and spatial orientation are among the most frequently reported symptoms.

The Parietal Lobe.—The anterior part of the parietal lobe has associations with sensation in man as in the monkey. In the posterior parts there is a specific human feature, the supramarginal and angular gyri, which subserve apparently activities of a more associative nature. Their destruction leads to agnosia, apraxia, acalculia and defects in

writing and reading. The interpretation of these symptoms and their relation to various parts of the cortex is still controversial. The left hemisphere in man has become especially dominant in this respect. So far as I know, no indication of such dominance of one hemisphere over the other is available in animal experimentation.

FUNCTIONAL LOCALIZATION

The classic localization theory with its assumption of a sharp, point-to-point, geometric projection of the body on the cortex, with its centers for separate psychic functions, must be changed. It was born prematurely. The workers in the years immediately following the discoveries of Hitzig and Fritsch were carried away by enthusiasm. I do not mean to belittle the work of these men; it is so easy for a generation living nearly sixty years later, and standing on their shoulders, to point out where and why they went wrong. This is the almost inevitable fate of all who share, with the privileges, the dangers of working in a period of great momentum; and as such one certainly can consider the years immediately after 1870 in the field of neurophysiology and neurology.

The classic localization theory must be changed. The great problem of today is: To what extent? Many neurologists agree that with regard to the higher psychic activities the classic conception is wrong. They can look no longer on the classic speech diagrams of Wernicke and Lichtheim and their numerous modifications as the true representation of the neurodynamic processes going on in the brain of man when he talks, understands speech, reads, writes and thinks. Though a certain focal concentration of activity may be present, in all probability the whole cortex participates in these processes. What one can and may localize in these functions is one of the most difficult and controversial problems of cortical activity.

But I do not want to dwell on this particular topic. I shall confine myself, as befits a neurophysiologist, to lower functional levels and discuss some points of the problem of localization with regard to somatic functions. Even here, notwithstanding the enormous scientific activity for more than sixty years, one finds a wide diversity of opinions, ranging from that of the modern advocates of the classic localization theory to views which are more or less a revival of Flourens' thesis of the uniformity of cortical activity.

Concerning the sensorimotor functions, one may take as a starting point a paper published in 1925 by Niessl von Mayendorf (a present-day protagonist of the classic theory) on the localization of cutaneous sensibility. He discussed the well known experiments reported by Cushing in 1909, and later confirmed by van Valkenburg and Foerster,

on electrical stimulation of the cortex of the postcentral gyrus in conscious patients. Such stimulation of limited postcentral foci gives rise to distinct elementary paresthetic disturbances; these sensations are localized by the patient in various parts of the skin according to the location of the electrical stimulation. These experimental facts, according to Niessl von Mayendorf, "prove undoubtedly that the touch perception of the skin occurs in very circumscribed cortical areas" ("Es ist damit zweifelsohne festgestellt, dass die Berührungsempfindung der Haut in ganz umschriebenen Rindenterritorien sich abspielt"). Furthermore, he concluded: "It is, therefore, admissible to draw the negative conclusion, that without the stimulated cortical area the skin regions concerned can no longer be perceived" ("Man hat daher auch ein Recht, den negativen Schluss zu ziehen, dass ohne die gereizte Rindenpartie die betreffenden Hautregionen nicht mehr empfunden werden können").

It is rather irrelevant, I think, whether, as van Valkenburg believes, the stimulation affects the endings of the sensory radiations "before any elaboration of the impulses carried by them" or whether one assumes with Niessl von Mayendorf that in these experiments not only fibers are stimulated, but also nerve cells. The latter is the more probable point of view, of course. The main question is whether one is allowed to conclude from the facts of these experiments of Cushing as Niessl von Mayendorf did. In my opinion, decidedly not.

One does not know whether the excitations set up by these stimulations remain restricted to the few square millimeters of cortex under the electrodes. This is highly improbable; I imagine that the neurodynamic processes evoked by such stimulations spread to other parts of the cortex, and probably to other levels, especially to the thalamus opticus. One does not know as yet anything about this spread, but only if it had been proved that such a spread did not exist would von Mayendorf's conclusion seem warranted. As regards his second conclusion, I think that experimental and clinical evidence disproves its correctness. After extirpation of only a few square millimeters of the cortex of the postcentral gyrus in, e. g., the arm region, sensibility is not abolished in circumscribed regions of the opposite arm; this exact experiment has not been made clinically, but one can be confident of its result, as even larger extirpations need not result in abolition of cutaneous sensation in circumscribed parts of the skin.

I shall discuss a few results of experiments with local strychninization of the sensory cortex which bear on this problem. These experiments showed that in the monkey not only is the postcentral cortex endowed with sensory functions, but also the percentral cortex, as far frontally as the arcuate sulcus, is associated with these functions

(fig. 3). This can be shown in the following manner: If one strychninizes a few square millimeters in the middle part of the precentral cortex, i. e., of the arm area, marked symptoms of sensory excitation (a strong hypersensitivity of the skin to various stimuli, tactile, painful and thermal) arise in both arms, especially in the distal parts of the extremities. Hypersensitivity of the deeper structures to pressure is present in most cases on the contralateral side only and in some bilaterally. It was shown that these symptoms still occur after extirpation of the whole postcentral and precentral sensory arm area of the contralateral hemisphere and of the homolateral postcentral arm region. This is even so when also the cortex of the homolateral precentral arm area is put out of function by local procaine hydrochloride anesthesia, with the exception of the small strychninized area. This result can be obtained irrespective of the location of the small strychninized area within the precentral sensory arm region (fig. 4). The inter-

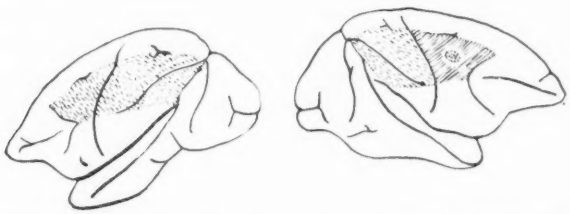

Fig. 4.—Extirpation of the whole sensory arm area of one hemisphere (the left in this figure). Extirpation of the postcentral and parietal sensory arm area of the other hemisphere; procainization of the precentral sensory arm area of this hemisphere, except for a small region which was strychninized locally in the usual manner. The diagonal lines indicate the procainized area; the broken lines, the extirpated area, and the dots the strychninized area.

pretation offered at the time (1924) was that, although the symptoms of sensory excitation were brought about by the strychninization of a few square millimeters of cortex, they were not due to the hyperactivity of only this small part of the cortex. It was assumed that probably this poisoning induced along corticothalamic neurons a hyperactivity of the corresponding thalamic nuclei and, in experiments with the other parts of the sensory cortex intact, of the other parts of the sensory arm region. The alternative conclusion from these experiments would be that in a cortical area of only a few square millimeters the sensitivity of the skin of both arms and of the deeper structures of either one or both arms is represented. This conclusion, in itself improbable, becomes almost impossible in my opinion when one takes into consideration that the other inevitable logical conclusion would be that in the whole sensory arm region, precentral and postcentral, of

one hemisphere there would be at least from a fifty to a hundredfold repetition of such a focal sensory representation. I cannot help thinking that this view is, as I stated, almost impossible. Ottfrid Foerster, in 1926, however, embraced this second alternative, apparently discarding my objections to it.

At present I am convinced even more than in 1923 that the conclusion then chosen is the correct one. Experiments on cats, done in 1929-1930 in collaboration with Dr. O. Sager of Bucharest, showed that exactly the same symptomatology is brought about by local strychninization of the optic thalamus. This was true in acute experiments even after extirpation of the cortex of both hemispheres. From this fact one cannot escape the conclusion that the functional level with regard to sensation reached in the thalamus is very high, almost of cortical dignity. This, I think, is another strong argument in favor of the conclusion that the sensory cortex functions in close mutual relation with the thalamus, a view which is supported by the abundance of corticothalamic connections.

Interesting with respect to the problem at hand is the fact that apparently definite functional boundaries exist between the various large subdivisions of the sensory cortex, the face, arm and leg areas. This conclusion presents itself if one considers the fact that the symptoms of excitation always remain confined to the arms if strychninization is kept within the boundaries of the arm region, no matter how close to the leg or the face area. As soon, however, as such a boundary is crossed, e. g., between the arm and the face region, sensory disturbances appear also in the face. This experimental fact shows that inside the large subdivisions of the sensory cortex no distinct functional barriers exist, at least to such an extent that they cannot be broken down by strychnine, whereas even this drug, though producing the maximum of sensory excitation, does not violate the subdivisional boundaries. What this actually means is still an open question.

The fact already mentioned that in one sensory cortex both sides of the body are represented, at least so far as cutaneous sensibility is concerned, may be looked on as one of the reasons why disturbances in cutaneous sensibility are apt to disappear rather quickly after unilateral cortical lesions in the sensory region. The much longer and partly permanent persistence of the disturbances in deep sensibility after such lesions finds a ready explanation in the fact that this sensibility is in the majority of the cases represented only in the contralateral cortex. In the experiments with strychnine the disturbances were most pronounced, and usually observed exclusively, in the distal parts of the limbs. This is in harmony with clinical observations in which irritative lesions of the postcentral cortex are accompanied sometimes

by paresthetic disturbances which nearly always are said to exist in the distal parts of the extremities.

In conclusion, the marked recovery from sensory disturbances after cortical lesions is, I think, readily accounted for by three facts brought out in these experiments: (1) that the sensory area is much larger than was known (fields 1, 2, 3, 5, 7, 4 and 6 of Brodmann), (2) that cutaneous sensibility of both sides of the body is represented in the sensory cortex of one hemisphere or, to put it in another way, that cutaneous sensibility of one half of the body is represented in the sensory cortex of the two hemispheres and (3) that the sensory cortex functions in close correlation with the optic thalamus.

The Motor Functions.—The electrically excitable cortex in the higher mammals (from Cercopithecus on) is confined almost entirely to the posterior part of the precentral cortex (Hitzig, 1874; Grünbaum [Leyton] and Sherrington). This area, however, is larger than the gigantopyramidal area (area 4 of Brodmann). The adherents of the theory of strict cortical localization look on this region as the cortical zone which subserves voluntary movements. Their opponents claim that this conclusion is unwarranted and that other cortical fields influence motor activity. As was mentioned, clinical and a few physiologic observations (C. and O. Vogt) point first of all toward the premotor cortex (area 6 of Brodmann) and then toward the postcentral gyrus. But even for the electrically excitable cortex itself there is evidence at present that the relations between the foci and the peripheral striped musculature are by no means as fixed and rigid as the classic localization theory asserts. These relations are on the contrary rather loose, being easily disturbed and broken down. The well known experiments of Graham Brown and Sherrington (1911) gave many examples of the instability of the responses elicitable on electrical stimulation of the motor cortex. The experiment of Lashley with four separate stimulations in the same monkey is also of interest here. If one keeps external and internal conditions of the cortex (temperature, moisture, degree of anesthesia, strength and time relations of the successive stimulations, etc.) as constant as possible, the motor responses from the various precentral foci are fairly constant. Slight deviations in the internal conditions, the external conditions being left constant, are apt to bring about a change in the responses. The functional "history" of a cortical point, immediately preceding the stimulation, is of great importance. My recent experiments with Dr. Clyde Marshall have given another striking example of this changeability of motor cortical responses. A functional blocking of the cortex by local procainization around a motor point, which primarily yields isolated flexion of a finger on liminal stimulation, may give rise after a latency of ten or

fifteen minutes not only to a marked increase of the initial response, but to a spread of response to other joints of the same limb and even to other limbs on both sides of the body. Sometimes an epileptiform after-discharge can be observed, although the stimulus is kept rigorously constant all through the experiment.

The fact that in these experiments after the procainization bilateral responses may appear on liminal unilateral stimulation points to bilateral functional relations of one motor cortex with both sides of the body musculature, which normally do not show up but come into being under special conditions. In what way these changes are effected is still unknown, but they are another instance to show that the functional relations between the motor cortex and the musculature are flexible instead of rigid, and adaptable to prevailing conditions and demands. This is also stressed by the well known fact that functional reparation is greatly enhanced if one compels the animal to use the impaired extremity. Wilhelm Trendelenburg, especially, has given impressive evidence of this fact in his experiments in which ablation of one cortical arm area in the monkey was combined with exarticulation in the shoulder of the homolateral arm.

The Visual Functions.—It is generally acknowledged nowadays that the visual radiations in the higher mammals (cat, dog, monkey and man) arise only in the external geniculate body and end entirely or at least almost exclusively in the area striata. The tendency of modern physiologic and clinical evidence points in the direction of a rather localized projection of the retina, via the external geniculate body, on the visual cortex; this, however, certainly is not a point-to-point, geometric projection as advocated by Munk. The most tenable view is, I think, that of Minkowski. In his excellent experiments in this field he showed that the excitations of a retinal element spread over a small, limited area of the visual cortex and that this area is larger for those retinal elements nearer the fovea; even the fovea is represented focally, but has the largest diffusion area. The conception of von Monakow of an extensive diffuse spread of visual impulses over the greater part of the occipital lobe and a diffuse representation of the macula is highly improbable. Recovery from visual disturbances after lesions of the area striata is observed only to a limited extent; quadrant hemianopia and total homonymous hemianopia are permanent symptoms even in the lower mammals. Goldstein and Gelb showed that the disappearance of such hemianopia is not a true, but only an apparent, disappearance; it is brought about by a largely subconscious, partly conscious, correction and readjustment of the position of the eyes, with formation of a pseudofovea. Under strict conditions, as in taking the visual fields, the hemianopia was found to be persistent. This is,

of course, quite another mechanism of functional recovery than the one I have discussed in the sensory field. It seems that the functional organization of visual activities is much more intimately linked with cortical levels than that of the other somatic functions; furthermore there is no physiologic evidence as yet available, so far as I know, of mutual relations of this function with its subcortical center. The existence of some corticogeniculate connections, however, has recently been demonstrated by Brouwer and Biemond, indicating the probability of such relations.

CONCLUSIONS

It seems to me that, with regard to the cortical representation of the somatic functions, there is not merely one type of functional localization in the cortex, but more; perhaps as many as there are senses. I have tried to point out briefly, for the two best known instances, some pertinent facts and considerations:

Vision is, I think, the function which in the higher mammals has become most corticalized. This is suggested by the following evidences: (1) distinct, rather sharply defined localization, with stable relations between the periphery and the cortex; (2) little or no evidence of functional correlation between the area striata and its subcortical center, the external geniculate body; (3) little reparation of disturbances after lesions of the area striata, at least permanence of quadrant and total homonymous hemianopia after extensive lesions of the area striata.

For the sensorimotor functions there is evidence suggestive of another type of cortical organization: (1) a more diffuse localization, at least within the large subdivisions of the sensory area; (2) within the motor sphere, distinct instability and changeability of functional relations between the cortex and the body musculature; (3) probably intimate functional correlation between this cortical region and its subcortical center, the optic thalamus; (4) marked reparation of functional disturbances.

Niessl von Mayendorf ended an interesting inaugural address in 1926 with the statement that "we possess at present a reliable knowledge of the location and extent of the central organs of our senses in the cerebral cortex; we know what they look like grossly and in detail and also—and I emphasize this in spite of all objections that have been expressed—what they mean physiologically and psychically." ("Wir besitzen nunmehr ein zuverlässiges Wissen von der Lage und dem Umfang der Zentralorgane unserer Sinne in der Hirnrinde; es ist uns bekannt, wie sie im groben und feinen aussehen und ich betone dies trotz aller geäusserter Bedenken, auch was sie in pysiologischer und psychischer Beziehung bedeuten.")

Although I cannot share in this optimistic attitude, there is no reason for pessimism. One need only be conscious of the immense complexity, anatomic and functional, of the cerebral cortex. Carefully planned experimentation and thorough observation with painstaking anatomic control and deliberate argumentation will undoubtedly advance the knowledge of the functions of this highest level of the nervous system.

Abstracts from Current Literature

THE CEREBELLUM. G. JELGERSMA, J. f. Psychol. u. Neurol. **44**:505, 1932.

This article is an extensive contribution of ninety-eight pages in which the author discusses: (1) the anatomy of the cerebellum, (2) secondary atrophy of the cerebellum following cerebral lesions, (3) the cerebellum as a sensory organ, (4) experimental extirpation of the cerebellum in animals and cerebellar atrophy, (5) higher coordination in man, (6) cerebellar atrophy in human pathology, (7) pathology of the coordination system (cerebellar symptoms in disease of the frontal and temporal lobes, Friedreich's disease, pseudoglossolabiolaryngeal paralysis, subcortical motor aphasia, chorea and paralysis agitans), (8) intercalations, (9) developmental defects in the cerebrocerebellar coordination system and (10) the theory of coordination.

According to Jelgersma, coordination in its broadest sense is a property of all organic processes; it is nothing more than an orderly cooperation serving a definite purpose in the existence of the organism. In the course of every volitional act the coordination of that act has been previously prepared, and its representation exists in the nervous system long before the coordination is manifested. If the execution of a certain coordinated movement is desired, the image of that particular movement must preexist in the psyche. In this sense every nerve process may be said to be coordinated. This applies to the simplest reflexes (Sherrington) as well as to the highest and most complex psychic processes. All kinds of possible transitions occur between the normal coordination of a simple reflex like that of winking and the bizarre pathologic intrapsychic incoordination in schizophrenia.

The principle of higher coordination is best illustrated by a purposeful movement which, to achieve the purpose for which it is designed, must be executed by the proper muscles alternatingly contracting and relaxing in proper succession at the right time and with the correct amount of power and speed. Highly coordinated movements are mediated through the cerebellum, the impulse for the movement being transmitted through the cerebrum. It is in the cerebrum that the composite images of movement of higher coordination are formed by central stimuli reaching it from the labyrinth and the muscles. These pictures of movement are composite processes of association which represent a reproduction of simple coordinations. They are the objective images of what are designated as images of movement. This composite complex leaves the cerebrum by two main pathways: The first is by way of the pyramidal system, at the origin of which, the anterior central convolution, the simplest images of movement are collected, whence they descend to the ganglion cells in the anterior horns of the spinal cord. At the same time the images of movement localized in the frontal and temporal lobes also leave the cerebrum by way of the pathways descending through the pes pedunculi; on reaching the various nuclei in the pons, they decussate in the raphe, descend by way of the pontile brachia along the granular cells and reach the Purkinje cells in the cerebellum. From there the processes pass by way of the axis cylinders to the central nuclei, the site of origin of the superior cerebellar peduncles. Collaterals from the peduncles extend to the cord and terminate, as do the pyramidal pathways, in the large motor cells of the anterior horns. Of these two important pathways, the pyramidal is the simpler. The second pathway, going through the pons, cerebellum and other bodies, is interrupted by various intercalations consisting of accumulations of ganglion cells, and reaches the anterior horn cells in a roundabout way. Through this pathway the stimulus reaches its destination in the anterior horn cells at a time when the stimulus that previously arrived by way of the pyramidal system has already begun to be elaborated. The various stimuli for movement conveyed by the second

pathway reach the ganglion cells engaged in the elaboration of the simple stimuli. After these simple stimuli have been converted into a complex form, they represent the image of a higher coordinated movement. This is discharged through the axis cylinders of the ganglion cells and reaches the muscles, which finally execute the purpose of the stimuli.

In this sense the Purkinje cells may be regarded as the central factor of higher coordination. The pathways coming from the spinal cord, which convey the stimuli from the periphery, terminate as arborizations in the protoplasmic prolongations of the Purkinje cells. Through the axis cylinders of these cells stimuli are conveyed to the ganglion cells of the central nuclei, whence they are further conveyed through the superior cerebellar peduncles. According to Ramón y Cajal, the cerebellofugal pathway has two components. One of these reaches the spinal cord in the form of collaterals. This component arises from the ganglion cells of the nucleus dentatus and from the Purkinje cells, in which, as has been pointed out, there is deposited the image of a higher coordinated movement derived from the cerebrum. When the defective image of movement reaches the Purkinje cells from the periphery, it meets the true image from the cerebrum, and a correction of the peripheral image results. The second component of the cerebellofugal pathway goes to the cerebrum. The Purkinje ganglion cell, therefore, occupies a unique position in the central nervous system. From the same cell there arises an axis cylinder which is divided in two parts, one of which extends to the periphery and the other to the cerebrum. A single ganglion cell is thus connected with the periphery as well as with the cerebrum. A second collateral connects this cell with the ganglion cells of the red nucleus, from which the periphery is again reached. The superior cerebellar peduncles are connected with the optic thalamus; in lower mammals, according to Cajal, this connection is slight and terminates farther up in the cerebrum. The composite images of movement which reach the Purkinje cells from the periphery produce an image of movement and do not reach the cerebrum until later. In the cerebrum these images are elaborated and descend again as composite images of movement from the frontal and parietal lobes through the cerebellum and the Purkinje cells to the periphery.

In the Purkinje cell, therefore, one finds two sets of images of movement, one from the periphery and the other from the cerebrum. When these are in harmony, there results at the periphery a properly executed higher coordinated movement; when, however, the two sets of images do not coincide harmoniously, the movement is defective, and a reflex correction occurs in the cerebellum. This correction assumes the character of a reflex because when the movement has already reached this stage there is no further necessity for it to reascend to the cerebrum. The advantage of such an arrangement is that the correction can occur with the rapidity of a reflex. When it is realized that the higher coordinated movements consist of innumerable simple movements which follow each other in quick succession, it is obvious that a very rapid correction which must be reflex is essential to an orderly execution of the desired movement.

This, briefly, is the basis of Jelgersma's theory of higher coordination. If it is true that higher coordination occurs in this manner, one may regard it as an automatic function of the cerebellum. It is not a pure reflex because it came into existence after the development of the cerebrum and cerebellum had already begun. It is an automatic function of the cerebellum that has the rapidity of a reflex.

According to Jelgersma, the nonexistence of a purely motor localization in the cerebellar cortex is due to the peculiar property of the Purkinje cell. There occurs in this cell an absolute union of sensory and motor impressions; this union is so close that one can hardly speak of motor processes and sensory processes. Nowhere else in the central nervous system, not even in the mechanism of the simplest reflex process, does such a close union exist. In the simplest reflex there are always two individual processes (motor and sensory); the sensory impression is received in one ganglion cell, and the result is conveyed to another ganglion cell, whence the reflex is conveyed to the muscles as a motor impulse. These two functions occur in the same Purkinje cell. According to the author, the purpose of such a union must be the necessity for an unusually rapid correction of the elements that

contribute to the formation of a composite movement. There passes through the Purkinje cell a crossed innervation impulse: An impulse from the periphery conveys a composite innervation to the cerebrum; another conveys a more complex innervation from the cerebrum to the periphery. These innervation impulses produce projections of images in the Purkinje cell; when these projections coincide, nothing further happens, but when they vary a correction occurs in the cell. It must be borne in mind, however, that in all probability other phenomena also occur in the Purkinje cells; the baskets which climb around these cells must be of further significance; perhaps they are associative, although they are strikingly few in number in the cerebellum.

The higher coordinating mechanism of the central nervous system shows still another peculiarity. Each of the paths of conduction to and from the cerebrum is interrupted in two places by ganglion cells—the cerebropetal pathway by the pontile ganglia and the nuclei of the cerebellar cortex, and the centrifugal pathway by the dentate nucleus and the optic thalamus. These ganglia are regarded by Jelgersma as intercalating mechanisms which enable an impulse coming to or going from the cerebrum to become connected with various nerve structures, so that every higher coordination may be learned during a person's lifetime. Every acquisition of a higher coordination is a vital process which demands function and practice on the part of the elements of the central nervous system. With sufficient practice and repetition, higher coordinated movements may be inculcated into the central nervous system. However, as the psychic component of higher coordination is continually being withdrawn during practice and repetition, the result is that the movement assumes in time an automatic character and becomes fixed. But when something additional is to be acquired in coordination the psychic factor reappears, and the previously described process is repeated. Every animal is capable of movements of higher coordination peculiar to that animal. The acquisition of such movements is always at the beginning a psychic process which disappears after the movement has been acquired. The only difference between higher coordinations in man and those in other animals is that in man the coordinations are much more complicated and more numerous and consequently many more must be acquired.

Every higher coordination presupposes a period of psychic practice, because it always represents a product of the psychic sphere, and only the anlage for the coordination is inherited. In this way the well formed and complete higher coordinations are indexes of the psychic development of the species; at the same time they demonstrate and explain the uniformity of this function and of the structural system subserving it in the particular species. The unusual development of this system in man, as well as his great capacity for psychic activity, is striking and bears witness to his superiority in this respect.

KESCHNER, New York.

DIFFERENTIAL DIAGNOSIS OF LESIONS OF THE ANGLE WITH ESPECIAL REFERENCE TO TUMORS. CARL F. LIST, Ztschr. f. d. ges. Neurol. u. Psychiat. **144**:54, 1933.

List stresses the fact that the type of tumor in the angle has significance for operability and for postoperative prognosis. He divides the angle into three portions and gives the symptom complex of each division: (1) the upper angle syndrome (Gradenigo) with involvement of the fifth and sixth cranial nerves; (2) the middle angle syndrome, with involvement of the seventh and eighth nerves; (3) the lower angle syndrome, with involvement of the ninth, tenth and eleventh (and sometimes the twelfth) nerves. For diagnosis the points to be stressed are: (1) careful history with chronological sequence; (2) objective neurologic findings; (3) careful otologic, cochlear and vestibular studies; (4) roentgen examination of the base of the skull with special reference to the petrous bone.

Cushing's material, consisting of one hundred and seventy-five cases of verified tumors in the angle, is carefully analyzed. The most common tumor is the neurinoma of the eighth nerve, usually manifesting itself between the ages of

25 and 60. There occurs, according to Cushing, a definite chronological sequence of symptoms: In three fourths of the cases, often years before the other symptoms manifest themselves, there occur auditory manifestations. True vertigo, facial spasm and hemiparesis are not common, even less frequent is a true trigeminal neuralgia. The disease does not begin with diplopia; the paresis of the muscles of the eye is usually transient and seldom severe. As later symptoms there occur hemiparesis and hemihypesthesias, epileptic attacks (also uncinate fits), homonomous and binasal hemianopia and polyuria. Bilateral and contralateral symptoms do not rule out acoustic neuromas. In more than half the cases there are roentgen evidences of changes in the petrosa and the internal auditory meatus.

Atypical cases can be divided into: (*a*) cases with headache, visual disturbances and eventually cerebellar manifestations, with late-appearing or complete absence of signs of the eighth nerve; (*b*) cases beginning with symptoms of the fifth, seventh, ninth and tenth nerves; (*c*) cases with psychotic symptoms predominating.

The clinical course of the meningioma is more rapid than that of the neurinoma. While the symptoms of the ear are usually the first manifestations of the disease, the other symptoms follow quickly. Dizziness, facial spasm, symptoms of the ocular muscles, unilateral symptoms and dysarthria are more marked and more frequent than in the neurinoma. On the contrary, the symptoms of the eighth nerve are less constant. The meningioma usually causes less marked roentgen changes, but a local hyperostosis is usually pathognomonic.

The cholesteatoma of the angle is an extremely slowly growing tumor, usually well spread out at the base, the characteristic onset and true trigeminal neuralgia sometimes being its only signs. There are also a relative frequency of facial spasm, epileptic attacks, marked hemiparesis, psychotic symptoms and a fairly low intracranial pressure.

Glioma of the pons occurs at all ages, especially in childhood. The course is usually much quicker than in other groups of tumors. There occur cases with protracted courses and marked signs of the eighth nerve. The diagnostic points are: severe subjective dizziness, mild headache and late signs of cerebral pressure. Facial spasms are more marked in this than in the other tumors. Disturbances of the ocular muscles occur frequently and early, with eventual disturbance of lateral associated movements and trigeminal symptoms, the motor division being especially marked. The symptoms of the ear are often bilateral, but partial. Marked dysarthria and hemiparesis occur as in other tumors. The roentgenogram shows no abnormalities.

Non-Neoplastic Diseases: 1. True cysts of the angle are uncommon. In most cases of "cysts" in the literature there were either pseudocysts in or around tumors, or frequently widened arachnoid spaces, i. e., arachnoiditis cystica adhesiva serofibrosa, or a so-called cystic and hyperplastic lateral recess of the fourth nerve. 2. Under the inflammatory diseases, arachnoiditis shows the following manifestations: occurrence after trauma or infection, remittent course, prevalence of pressure on the brain and cerebellar signs. 3. Multiple neuritis of the basal cranial nerves often begins suddenly, but can be remittent, with residual symptoms between the exacerbations. The symptoms are usually bilateral; pressure on the brain is absent, as are also cerebellar signs. 4. The first (pontile) manifestations of multiple sclerosis are often difficult to distinguish from a beginning tumor of the pons; the further course makes clear the diagnosis. 5. Syphilis in tumor of the angle must also be considered. In cases of severe intracranial pressure with positive findings in the blood and spinal fluid, one must be skeptical of the diagnosis of gumma, since actual tumors can give a positive reaction. 6. Tuberculoma of the angle usually presents cerebellar signs rather than manifestations in the cranial nerves. At times the roentgenogram shows characteristic calcification. 7. In older people there occur symptoms of the angle through arteriosclerotic changes of the posterior inferior cerebellar artery; they occur suddenly and later show improvement. 8. Aneurysm of the basilar or vertebral artery can simulate a tumor of the angle (cholesteatoma). 9. Ménière's disease may simulate a tumor of the angle.

WINKELMAN, Philadelphia.

CHANGES IN THE CENTRAL NERVOUS SYSTEM IN SCARLET FEVER AND IN DIPHTHERIA. A. JAKUBOWICZ, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **34**: 136, 1932.

Thirteen cases of scarlet fever, diphtheria, and scarlet fever complicated by diphtheria were studied. In all, as in the other acute infectious diseases, there was a general hyperemia of almost every organ as well as of the central nervous system. In the latter the hyperemia was more marked in the white substance, and in most cases it was most marked in the zone between the gray and the white matter. It is also noteworthy that the acute hyperemia was most extensive in the caudal portions of the central nervous system.

Every case disclosed evidences of vascular involvement, varying from swelling of the walls of the vessels to complete homogeneization of the media and the adventitia. Proliferation was also found in the intima, and in one case there was a moderate obliterating endarteritis. In many cases the arterioles were rigid, reminding one of atherosclerosis. The hemorrhages caused by diapedesis that were observed in the cortex are evidence of damage to the walls of the vessels, especially of those with flattened surfaces. The diseased condition of the arteries led in several cases to tissue necrosis in various parts of the brain and cord. Examination of substance taken from the vessels revealed no clue as to the nature of the infectious micro-organism. The anatomic changes in the vessels were identical, whether the disease was due to a virus, the diphtheria bacillus, a streptococcus or a pneumococcus. The more virulent the infectious agent, the more extensive were the lesions in the vessels and the parenchyma.

Associated with the vascular disease and hyperemia were edema and disintegration of the tissues in the nervous system. In many cases the edema was inflammatory; in others, it was due to passive congestion. The edema was followed in some cases by perivascular disintegration and in others by status lacunaris. The disintegration was most marked in the oral portions of the nervous system, although some was also observed in the caudal portions. It was most marked in the basal ganglia and the cortex, especially in the area of transition between the gray and the white matter.

It is noteworthy that almost all cases showed some meningeal reaction. The reaction was serous in some cases and serofibrous in others; in still others it was accompanied by a nonpurulent infiltrate. In most of the cases in which serous meningitis was present the inflammation was local rather than general. In one case the meningitis was serous over one frontal lobe and purulent over the remaining portions of the hemisphere, but the occipital lobe was free from meningeal involvement.

So far as the parenchyma of the nerves is concerned, the ganglion cells showed two types of alterations which ran parallel to each other—colliquation and coagulation. The degenerative processes in the cells seemed to have a predilection for certain structures. The sites of predilection were in most cases the inferior olive, the dentate nucleus, the substantia reticularis and the third cortical layer, especially in the frontal lobes, where the large pyramidal cells were particularly affected.

The ectodermal as well as the mesodermal reaction was minimal, in contrast to the other inflammatory processes in the central nervous system. It was more intense in the cases of diphtheria than in those of scarlet fever. In the cases of scarlet fever complicated by diphtheria the glial reaction was also more marked. In the cases of pure scarlet fever there was no glial response whatever. The mesodermal reaction was much more marked in the uncomplicated cases of scarlet fever than in the cases of pure diphtheria. The metabolic disturbances in the central nervous system were more marked in diphtheria than in scarlet fever; apparently there was no relation between their intensity and the duration of the disease. It is also of interest that of all the neural structures the pallidum and the pineal body showed the most extensive deposits of calcium or of pseudocalcium.

Bacteriologic examination of the nervous system disclosed three types of microorganisms: cocci, bacilli and peculiar structures resembling fungi. The cocci included streptococci and pneumococci that are probably identical with Friedländer's bacillus. Further differentiation of the bacilli could not be carried out. Of the cases of pure diphtheria, two showed cocci without rods, one, cocci with rods and one, peculiar fungus-like structures without bacteria. Cocci were found in one case of pure scarlet fever with rods and in one case without rods. In one case of scarlet fever complicated by diphtheria, cocci were found without rods, and in another case with rods. The peculiar fungus-like structures were found in scarlet fever without bacteria four times, and with bacteria twice. In five cases bacteriologic examination of the nervous system gave entirely negative results. In discussing the bacteriology in these cases Jakubowicz points out that although he does not know the origin of the fungus-like structures, their occurrence in so many cases, especially in those of scarlet fever, cannot be accidental. He believes that they may be related to the lymphocytes, but he does not understand their significance.

KESCHNER, New York.

POSSIBLE DETRIMENTAL EFFECTS OF EXPERIMENTAL HYPNOSIS. MILTON H. ERICKSON, J. Abnorm. & Social Psychol. **27**:321 (Oct.-Dec.) 1932.

Since the time of Mesmer there has been a general attitude of prejudice against and fear of hypnosis. This scientific antagonism is giving way before the realization that hypnosis is a normal psychologic phenomenon. It is chiefly valuable as a means of scientific experimentation. There is also a slow development of its use in the field of therapeutics. Instead of expecting magical results and discarding the procedure altogether if astounding results are not forthcoming, the procedure should be appreciated for its worth as one of the many approaches to the difficult problem of psychotherapy.

The author has reviewed the literature on the subject and finds there mostly the expression of personal opinions, often supported by hearsay. There is little evidence of scientific investigation properly controlled and impartially evaluated. Taking up, one by one, certain theoretical possibilities of harm that may result from evoking the phenomenon, the author attempts to give reasonable answers to these questions. The conclusions deduced are chiefly from his own experience with approximately three hundred subjects in whom he has induced several thousand trances.

The first of the theories of possible detrimental effects centers around the question of the development of hypersuggestibility. As an answer to this, the author notes that even after a subject's hypnotization as many as five hundred times over a period of years it was found that continuous care must be exerted lest the cooperation of the subject be lost or even a compensatory negativism be engendered. Even the most ideal subject of one hypnotist is practically as difficult a subject for a new operator to handle as if he had never before submitted to hypnotic suggestion. Relative to the question of the possibility of effecting alterations in personality, the author explains that in cases in which members of the family and personal friends, who could be observed over a long period, were hypnotized over a period of four years no alteration in any way attributable to hypnosis was observed. But an even more forceful answer may be derived from the experience of psychotherapeutists who have deliberately and carefully utilized the method to induce desired alterations in the personality of their patients, and have usually failed. It is possible that various dissociated personalities have been created by the overzealous investigations of the hypnotist, but personal experience suggests that this is improbable. On the question of the possibility of weakening the subject's perceptual powers relative to distinguishing reality from unreality, the author offers his opinion (based on his subjective feeling) that there is no permanent alteration in the subject's capacity to test reality. It is admitted that this is contradictory to the opinion (also arrived at by subjective impression) of an eminent practitioner in the field of behavior disorders who was working therapeutically with unstable personalities.

The last of the questions asked and answered by the author concerns the possibility of the subjects acquiring through the experience of hypnosis unhealthy escape mechanisms. This speculation arose from a scheme which one of the author's subjects evolved of employing the trick of crystal gazing (which he had learned) to find suitable material for drawing or theme-writing to be used in his university assignments. Could this trick be turned to evading the demands of reality through self-deception? In the author's experience there was noticed only a tendency to utilize the hypnotic experience for profit, a finding corroborated by the experience of other trained workers in the field of hypnosis.

The conclusion from the entire study is that marked changes in the subject's personality as the result of experimental hypnosis appear questionable.

WISE, Howard, R. I.

STUDY OF THE MACROGLIA OF THE CEREBRAL CORTEX OF THE NORMAL DOG WITH THE NEW LUGARO METHOD. P. E. MASPES, Riv. di pat. nerv. **40**:414 (Sept.-Oct.) 1932.

Maspes has used for this study a new method of silver impregnation of protoplasmic neuroglia, devised by A. Lugaro, and reports details of the cytologic structure of both the protoplasmic and the fibrous neuroglia. He discusses questions concerning the small astrocytes, satellites, the so-called bipolar cells, twin cells and mixed elements. Under mixed elements he includes elements that occupy an intermediate position between protoplasmic and fibrous neuroglia. He finds, in the first layer of the cortex, the so-called molecular layer in which the neuroglia occupies the most external stratum, that fusiform elements with a rod-like nucleus are frequent, whereas in the deeper strata of the same layer there are larger fibrous neuroglia similar to those in the white substance. The protoplasmic neuroglia is represented in this layer exclusively by mixed elements. A more distinct type of protoplasmic neuroglia exists at the boundary between the first and second layers of the cortex.

In the layer of small pyramidal cells, only two types of the protoplasmic neuroglia are present. Bipolar neuroglia exist almost exclusively in this layer. In the layer of middle and large pyramidal cells, a large amount of protoplasmic neuroglia is present, particularly the perineural satellites. No mixed cells occur. In the layers of granules, the glial elements are smaller and the perineural satellites are scarce. In the layer of large pyramidal cells, protoplasmic neuroglia is abundant, and the larger elements have rich and abundant processes. The perineural satellites are abundant and at times two or three surround a single nerve element. In the layer of polymorphic cells, protoplasmic neuroglia is more scarce; among them appear the first elements of fibrous neuroglia.

Lugaro's method for neuroglia was reported in the *Schweizer Archiv für Neurologie und Psychiatrie* (**29**:282, 1932). Blocks are fixed for from two to four days in an 18 per cent solution of formaldehyde and kept preferably in an icebox. The blocks are then transferred to silver solution prepared as follows: Three flasks are used, each containing 1,000 cc. of a 9 per cent solution of sodium hyposulphite. To each flask silver bromide and silver iodide are added—to the first, 1.3 Gm. of silver bromide and 0.7 Gm. of silver iodide are added; to the second, 1 Gm. of silver bromide and 1 Gm. of silver iodide; to the third, 0.7 Gm. of silver bromide and 1.3 Gm. of silver iodide. Altogether the amount of silver should not exceed 2 Gm. per thousand cubic centimeters. These are stock solutions. (The silver bromide and silver iodide should be dissolved separately in a concentrated solution of hyposulphite, each being afterward diluted to 500 cc.; the two solutions are then mixed together.) For use, a 9 per cent solution of sodium hyposulphite must be added in the following proportions—in one container, to 15 cc. of solution of silver, add 1 cc. of the hyposulphite solution; in another container, 2 cc. of hyposulphite is added to 14 cc.; in a third container, 3 cc. is added to 13 cc.; in a fourth container, 4 cc. is added to 12 cc., and in a fifth container, 16 cc. of silver solution without addition of hyposulphite. Small blocks of nerve

tissue are put in each of the containers and left for three hours at room temperature (from 16 to 20 C.). Three hours later, 10 cc. of a 25 per cent solution of formaldehyde is added to each container and the containers are placed in an oven at 37 C. for two days. Forty-eight hours later, the blocks are ready for frozen sections, which must be as thick as 50 or 60 microns; dehydrate and mount. Blocks of tissue may be kept in the previously mentioned formaldehyde-silver solution for months in an icebox.

FERRARO, New York.

SUBCORTICAL DEMENTIA. F. G. STOCKERT, Arch. f. Psychiat. **97**:77 (June) 1932.

The attempts of Berze to gain insight into the anatomic substratum of the schizophrenic process by histologic and psychiatric studies of postencephalitic psychoses have not proved successful because there does not seem to be any definite relationship between the psychologic pictures of these two mental disturbances. Nevertheless, the interesting fact that certain types of mental disturbances may follow encephalitic lesions with few or even no signs of organic involvement opens up the question of localization of these mental symptoms. Of special interest are cases in which "rigidity without hypertonia" occurs. Stockert discusses this form of disturbance and reports the case of a man, aged 45, who was referred to the clinic because acute confusional states with concomitant glycosuria but without acetone in the urine had developed. The attacks had been manifest for about eight months before admission. Between the attacks the patient showed loss of interest, irritability and disturbances in memory and speech, and for about six months he was unable to work. Two days before entrance to the clinic, while he was occupied with preparations for a festival in honor of the confirmation of his daughter, an attack developed.

When examined, he showed an apathetic and listless attitude. There were constant chewing and swallowing movements, and he seemed perplexed. The most important mental symptom was a disturbance of retention memory with Korsakoff-like confabulations. The patient believed that he was brought for the purpose of participating in the confirmation ceremony and was disoriented as to time and place. He had difficulty in naming objects, although he seemed to know the purpose of the objects and their uses. He had difficulty in reading and also in carrying out written commands. He could, however, carry out simple oral commands. There was a tendency to perseveration and imitation. Physical examination showed no positive pathologic findings, although all the movements were retarded and there was a certain amount of stiffness in the facial expression. Serologic tests were negative; the urine did not show any sugar. Throughout the patient's stay in the hospital there were a marked tendency to a steadily increasing somnolence and an increase in most of the symptoms. However, the symptoms came to a standstill shortly before discharge, following treatment with iodine preparations.

Stockert discusses the mental picture under the concept of dementia characteristic for this type of disease. He regards the stickiness of attention, with inability to turn to new situations and stimuli, as the central point. It is because of this stickiness that the retention memory is disturbed, for there is an inability to perceive new stimuli. With this there is also a disturbance in the appreciation of the symbolic significance of objects as well as of written characters, particularly numbers. The patient recognized them as figures and was able to differentiate one from another but could not grasp their significance as symbols expressing certain quantities. The inability to recognize the symbolic significance of contents was also carried into the field of events. Sensory impressions which should call forth certain associations in connection with the situations into which they fit were perceived but not in their proper relationships. All the symptoms are regarded by the author as indicative of deterioration, but one which is essentially different from that of schizophrenia. As to localization, he is not definite, but suggests that the pathologic chewing and swallowing, the rigidity and the slowness are dependent on a lesion in the substantia nigra and surrounding structures.

MALAMUD, Iowa City.

ARACHNOIDITIS FIBROSA SPINALIS SYPHILITICA PRESENTING THE CLINICAL PICTURE OF PSEUDOTUMOR. MARIANNE ÖSTERREICHER, Jahrb. f. Psychiat. u. Neurol. **49**:57, 1933.

A woman, aged 65, in 1923 had severe pains and weakness in both lower limbs. In 1924 the weakness ascended to the right upper extremity. She was admitted to a hospital where she received injections the nature of which is not stated. The weakness of the extremities persisted and gradually progressed, so that by 1929 she had become bedridden. At this time diplopia also developed. Examination in March, 1929, revealed normal pupils, nystagmus on looking to the extreme right and left and spastic paraparesis, with hyperreflexia, ankle clonus and a bilateral Babinski sign. There were no sphincteric disturbances. Several weeks later the pupils reacted sluggishly to light and in accommodation, the nystagmus had become more pronounced, the corneal reflex was absent on the right side and diminished on the left, and the upper and lower extremities showed more definite evidences of involvement of the pyramidal tracts, which was more marked on the right side. Bilateral hypalgesia had also appeared (the level was not stated). The Wassermann reaction was negative in the blood and positive in the spinal fluid, which contained large quantities of albumin and 17 cells per cubic millimeter. (No record was made of manometric studies of the spinal fluid.) Myelography with iodized sesame oil 40 per cent showed arrest of the latter between the fourth and fifth cervical vertebrae. Laminectomy revealed dense adhesions between the meninges and the spinal cord at the fourth cervical segment. A piece of tissue was removed for examination; the dura was sutured and the wound closed. Recovery from the laminectomy was uneventful. The patient was subjected to antisyphilitic treatment, but cystopyelitis soon developed, and she died from sepsis.

Necropsy revealed an extensive syphilitic process throughout the entire neuraxis, involving especially the cord in the region of the middle and lower cervical segments. The process was proliferative and degenerative; there were marked alterations in the walls of the meningeal and spinal blood vessels. Although the macroscopic appearance was that of hypertrophic cervical pachymeningitis, histologic examination showed that the dura was intact, while the arachnoid had undergone fibrous changes and was adherent to the dura and the pia. The plastic arachnoid disclosed marked changes in the vessels, many of which were thrombosed. Recent lesions in the form of lymphocytic infiltrations were also observed throughout, especially in the medulla oblongata. In the cord the pathologic process gave rise to severe marginal degeneration as well as to degeneration of the anterior and posterior horns and some pallor of the posterior columns. The anterior horns showed bilateral symmetrical involvement consisting of necrotic areas with replacement by glial tissue. Here and there the lateral columns also showed areas of degeneration.

Österreicher comments on the paucity of neurologic signs, especially the absence of amyotrophy, in the upper extremities in the presence of extensive lesions in the lower cervical region of the cord. She believes that this may have been due to the fact that the changes in this portion of the cord did not appear until after the performance of the laminectomy, although she admits that the arrest of iodized sesame oil 40 per cent prior to operation points to the existence of meningeal adhesions in this part even at that time.

KESCHNER, New York.

ACUTE GLOMERULAR NEPHRITIS IN CHILDREN: TREATMENT OF CEREBRAL MANIFESTATIONS. KENNETH D. BLACKFAN and CHARLES F. MCKHANN, J. A. M. A. **97**:1052 (Oct. 10) 1931.

Of the therapeutic agents that Blackfan and McKhann have employed in the treatment of patients exhibiting cereberal manifestations with acute glomerular nephritis, magnesium sulphate has proved to be of most value. Magnesium sulphate given by mouth and, if necessary, by rectum usually suffices to control and relieve the cerebral symptoms if the administration of the salt is begun with the appearance of an elevated blood pressure during the stage of headache and vomiting and

before the development of coma and convulsions. Very large doses of the drug are necessary. As much as from 1 to 2 ounces (from 30 to 60 cc.) of a 50 per cent solution by mouth or by rectum given every four hours is often required in order to secure the desired effect. As pointed out by Aldrich, magnesium sulphate in children with the hemorrhagic type of nephritis does not cause diarrhea even when massive doses are used. Rarely are there more than two or three stools daily until after the prophylactic result is obtained. The action appears to be one of general dehydration with resultant diminution of cerebral edema. Evidences of improvement are relief of cerebral symptoms and fall in blood pressure. The improvement is gradual and is seldom obtained without loss of body weight. The medication may be and should be continued until the blood pressure approaches a normal level. In comatose patients or in those with convulsive twitchings, the action of magnesium sulphate administered by mouth and by rectum is not sufficiently rapid to prevent a fatal outcome. In 1928, the observation was made that a 25 per cent solution of magnesium sulphate, when injected intramuscularly, had almost as prompt an effect in relieving cerebral symptoms and in reducing blood pressure as did the intravenous injection of a 1 per cent solution of the anhydrous salt. Since then, the authors have employed this intramuscular injection as the method of choice when the presenting symptoms became so severe as to indicate emergency treatment. By way of illustration, with the blood pressure continuing to rise and with the development of cerebral symptoms, despite large amounts of magnesium sulphate by mouth and by rectum, a 25 per cent solution of magnesium sulphate is given intramuscularly. The amount used is determined by the weight of the patient. It is seldom necessary to use more than 0.2 cc. per kilogram, although in exceptional instances 0.4 cc. per kilogram of body weight was used. The effect as measured by fall in blood pressure and diminution in cerebral symptoms is obtained usually in from fifteen to thirty minutes and is analogous in all respects to the results derived from the intravenous injection. If results do not follow the first intramuscular injection, a second can be made with relative safety after a period of two or three hours. In some cases repetition of the intramuscular injection may be required several times before the blood pressure remains low and the cerebral symptoms disappear. No difficulties have been encountered from the intramuscular injection of magnesium sulphate either as regards alarming toxic symptoms of the drug or as regards local irritation or sloughs. Since the introduction of this mode of administration of the drug, patients who develop cerebral symptoms have responded to the intramuscular injections in conjunction with the use of the salt by mouth and by rectum, and in no case has recourse to intravenous injection been necessary.

EDITOR'S ABSTRACT.

GRANULES, SPHERULES AND MULTIPLE SCLEROSIS. A. MORSELLI and A. GUARDINCERRI, Riv. di pat. nerv. **40**:335 (Sept.-Oct.) 1932.

Following a new report by Purves Stewart and Hocking concerning the existence of spherula insularis in the cerebrospinal fluid in multiple sclerosis, Morselli and Guardincerri have again undertaken investigations. They describe, in the cerebrospinal fluid in eleven cases of multiple sclerosis, granules and spherules which have not been found in control material (dementia paralytica, one case; transverse myelitis, two cases; pseudobulbar palsy, one case; hematomyelia, one case; dementia praecox, two cases). They speak of granules and spherules that are morphologically somewhat different. For their detection they use a cultural medium made from the muscular tissue of beef to which extract of pancreas is added in the proportion of 50 cc. to 2,500 cc. of aqueous solution of beef cardiac muscle. The medium must have a p_H of 7. Before the medium can be used it is necessary to add a small percentage of normal human serum filtered through a Berkefeld filter. In the tubes the amount of serum should be two portions to ten portions of the culture medium, in a test tube 4 cm. in diameter. Into this solution at 37 C., 10 cc. of the cerebrospinal fluid is allowed to drop directly from the puncture needle. The tubes are kept at 37 C. and not disturbed; after from forty-

eight to fifty-six hours, the fluid appears opalescent, and a thin reticulum is formed on the outer surface. In the reticulum with the ultramicroscope having a 2 mm. objective and a 17 mm. ocular, the spherules and granules may be studied. The spherules are rounded bodies 0.2 microns in diameter and highly refractile, with an irregular contour and a bright halo, almost a photosphere, which is more developed on one side. In the central part may be seen a ring of different refractility and with a central black dot. The granules are smaller and rounded, but with a slight caudal prolongation recalling a small drop of water in the process of falling. The granules are less refractile and have a more definite contour and a smaller photosphere. The internal portion of the granule has a uniform luminosity. The spherules and granules always appear together, but the granules are always more numerous than the spherules. Both granules and spherules have movement, which the authors have divided into: (*a*) massive movement, (*b*) brownian movement, (*c*) oscillating movement, (*d*) movement of laterality and (*e*) movement of progression. After the slide has been left under the microscope for a few hours, there is progressive diminution in the number of spherules and granules up to total disappearance.

Concerning the significance of the spherules, the authors are not sure if they are identical with those described by Chevassut. They think that, though they may be the same, they may also be new elements which have not as yet been considered by other authors. They believe that there is a certain relationship between the spherules and the granules, but are not in a position to establish exactly the nature of the relationship. They express, however, the possibility that the granule may be the primary and essential element, the spherule being a secondary element derived from the granules because of the pathologic condition of the fluid. Whether the granules may be directly related to the causal infection of multiple sclerosis and be considered as granular elements at the limit of visibility, in harmony with Nicolle and May's conception, is as yet problematic.

FERRARO, New York.

GLUCOSE INSULIN ADMINISTRATION IN PROLONGED NARCOSIS. J. H. QUASTEL and R. STROM-OLSEN, Lancet **2**:464 (March 4) 1933.

The development of narcotic treatment in certain types of mental disease has been greatly retarded by the knowledge that prolonged narcosis is often accompanied by severe toxic symptoms. These symptoms may necessitate abrupt cessation of the treatment before there is any chance of alleviation of the abnormal mental reaction. About fifty patients have been treated with a barbituric acid derivative during the past two years. The results have been extremely encouraging, except that toxic symptoms appeared in a large proportion of the cases. A frequent accompaniment has been the development of ketonuria, which becomes more marked as the narcosis proceeds. The degree of ketonuria varies from person to person; in some patients there is little or no ketonuria after seven days of narcosis under a barbituric acid derivative, whereas in others the ketonuria may become marked in forty-eight hours or less from the commencement of the treatment.

Previous investigations by the authors have shown that all narcotics have the property of inhibiting specifically, at low concentrations, the oxidation by the brain of substances important in the metabolism of carbohydrates, viz., dextrose, lactic acid and pyruvic acid; of narcotics belonging to the same chemical type, those with the greater narcotic activity have the greater inhibitive action on oxidations in the brain. There is a definite parallelism between the inhibitive power on oxidation of dextrose by the brain and the narcotic power of the drug. It was found by certain preliminary experiments that the simultaneous administration of dextrose and insulin to narcotized animals brought about a decrease in toxicity of the narcotic.

Twenty cases have been investigated. The usual procedure has been to administer 2 cc. of a barbituric acid derivative intramuscularly from two to four times in twenty-four hours, most patients receiving three doses a day. As soon as definite ketonuria appeared, the following modified procedure was adopted.

Simultaneously with the next intramuscular injection of a barbituric acid derivative, from 5 to 15 units of insulin were given hypodermically, the dose of insulin from then on being administered twice or thrice a day with each subsequent dose of the narcotic. With each injection of insulin the patient received 50 Gm. of dextrose in water or milk. The result of the modification of the narcotic treatment with insulin and dextrose was the entire disappearance of ketonuria within forty-eight hours. The patient, moreover, showed no ketonuria during the remainder of the course of the narcotic treatment, which lasted from fourteen to sixteen days. Of the twenty patients in the cases investigated, thirteen have had dextrose-insulin treatment, with the result that they have finished the course of narcotic treatment without development of ketosis or other serious complications.

While only few patients have been as yet subjected to the modified treatment, the results have been so satisfactory that the authors have considered it advisable to publish this preliminary note.

BECK, Buffalo.

NECROTIZING ARTERITIS AND SUBACUTE GLOMERULONEPHRITIS IN GONOCOCCIC ENDOCARDITIS. MILTON HELPERN and MAX TRUBEK, Arch. Path. **15**:35 (Jan.) 1933.

There is considerable difference of opinion concerning the origin of the necrotizing, nonsuppurative, inflammatory arterial lesions usually designated as periarteritis nodosa. Whether these lesions are a disease of the blood vessels, sui generis, caused by a specific bacterial agent or virus or whether they represent a specific vascular reaction to any of a great variety of toxic agents is as yet unsettled.

In a case of subacute glomerulonephritis of ten weeks' duration, death occurred from uremia with pericarditis. The onset of this illness occurred eight weeks after an attack of gonococcic urethritis complicated by gonococcic ophthalmia. At necropsy, right-sided subacute gonococcic endocarditis of the pulmonic valve and typical subacute glomerulonephritis were found. In addition, isolated necrotizing inflammatory lesions of the small arteries were found in two widely separated regions of the body, namely, the choroid coat of the eye and the testis. These vascular lesions exhibited many of the morphologic features described in periarteritis nodosa and were considered as belonging to that group. The larger arteries of the body were not involved, and the distribution of the lesions was not extensive enough to produce clinical manifestations. The renal lesion represented a severe reaction of a sensitive organ to the toxin produced by the gonococci growing on the pulmonic valve. The vascular lesions, which in this case were anatomically dissociated from the kidney, were also considered a specific reaction of sensitive vessels to this toxin.

The findings strengthen the conception that these vascular lesions and those of periarteritis nodosa do not represent a specific disease, but a specific reaction of the blood vessels to any of a whole group of variable toxins.

The histologic features of the vascular lesions in the choroid coat and the testis in the case described conform to many of those that are characteristic of periarteritis nodosa, so well enumerated by Wohlwill. Thus, medial fibrinoid necrosis, disintegration of elastica interna, subendothelial intimal proliferation resulting in fibroblastic obliteration and canalization of the lumen, vacuolation of the endothelial cells, eccentric involvement of the walls of vessels, absence of suppuration and the occasional periarteritic nodule were present. A few of the more frequent findings were absent: thromboses, true aneurysms of the walls of the vessels and an abundant cellular infiltration of the coats and periadventitial regions.

In the fully developed lesions of periarteritis nodosa medial necrosis is always present, transforming that layer into a homogeneous eosinophilic substance resembling fibrin in its staining characteristics. This medial reaction was the

most striking lesion in the vessels in the case described, and although periadventitial cellular infiltration was absent, there was abundant fibrinous exudate within and beyond the adventitial regions. WINKELMAN, Philadelphia.

DEPERSONALIZATION. E. STOERRING, Arch. f. Psychiat. **98**:462 (Jan.) 1933.

Krishaber was the first to describe the peculiar disturbance of personality that was subsequently named by Dugas depersonalization. Following the descriptions of these two men a number of theories as to the manner of the development and the etiologic factors of the process were advanced by Janet, Schilder and others. The author discusses these theories in relation to a number of cases of his own and those from the literature. The most significant features of the clinical picture consist in the development of a feeling of strangeness of reality in the person himself and outside objects. The person speaks of his experiences as occurring in a dreamlike state, of the loss of the sense of reality of contents both personal and external, of the loss of interest in these contents and sometimes of an actual change in the size and the shape of objects. In his summary Stoerring points out the following facts: 1. For an appreciation of this phenomenon it is important to work with cases that do not show the complicating features of hallucinations or delusions. 2. A fundamental feature in the analysis of this phenomenon is the concept, first pointed out by James, that human beings show a split in their ego, with the differentiation of an ego as an observing subject and as an observed object. The subject-ego may detach itself from the object-ego and observe it as something that exists outside of itself. 3. Most authors have searched for a single factor that will explain the occurrence of this phenomenon; some have regarded it as resulting from a disturbance of sensations, from emotions, from the feeling of activity, or from compulsive self-observation. The author, however, is of the opinion that depersonalization develops on the basis of a change in a number of these functions. 4. One of the most important of these is the compulsive tendency toward self-observation, and when this tendency is the predominant factor a special type of depersonalization develops. It usually follows the existence of a marked tension in the psychic experiences of the person; this leads to an abnormal diminution of the normal ego-consciousness which is replaced by a feeling of ego-strangeness. The loss of the sense of reality of outside objects should be regarded as secondary to the aforementioned occurrence and is due to an abnormally increased introspection and analysis of perceptions received. 5. Another factor of importance is the disturbance of the feeling of activity. In this disturbance the person feels that activities performed by him are not on the basis of a voluntary decision to act, but are in the nature of an automatic activity into which the person is forced by some drive from outside himself. It, too, is closely related to the increased tendency toward self-observation. 6. The theory that this phenomenon develops on the basis of actual changes in sensibility cannot be substantiated, because no actual sensory disturbances are found in cases of this type. 7. Stoerring believes that in the development of depersonalization one must recognize the definite etiologic significance of dream states which precede this phenomenon and are usually combined with anxiety. 8. A discussion is undertaken of psychotherapeutic methods of treatment for this phenomenon and of the fact that depersonalization may occur in different degrees of depth and intensity. MALAMUD, Iowa City.

LIPOIDGRANULOMATOSIS (TYPE, HAND-SCHÜLLER-CHRISTIAN): REPORT OF A CASE. WILLIAM CHESTER and V. H. KUGEL, Arch. Path. **14**:595 (Nov.) 1932.

Rowland, in 1928, collected twelve instances of a disease described under various titles in the literature and characterized by the symptom complex of defects in the membranous bones, exophthalmos and diabetes inspidus. He entitled the disease "Schüller-Christian's syndrome." To these cases from the literature he added two striking cases of his own, one of which was studied post mortem. Hand, in 1893, under the tile of "Polyuria and Tuberculosis," described this symptom complex in a boy, aged 3 years, who, in addition to exophthalmos and polyuria,

showed at necropsy yellow nodules in the defects of the internal and external tables of the skull, grayish nodules in an enlarged liver and enlargement of the spleen. Only the nodules in the liver were studied microscopically; they revealed chronic inflammatory granulation tissue. In the absence of significant criteria, the condition was named tuberculosis in the pathologic report, although syphilis was also considered. The author noted, however, that he believed the lesion was neither that of tuberculosis nor that of syphilis. Kay, in 1905, reported an instance of "acquired hydrocephalus with atrophic changes in the bones, exophthalmos and polyuria" in a boy of 7 years, which he ascribed to a tumor at the base of the brain. Schüller, in 1915, described two cases in an article entitled "A Peculiar Syndrome of Dyspituitarism." The first was that of a girl, aged 3, with the same symptom complex. Schüller thought that the condition was due to a disturbance of the pituitary gland. In the second instance, the patient suffered, in addition, from dystrophia adiposogenitalis. Schüller attributed the condition to a tumor at the base of the brain.

Christian, in 1919, under the title, "Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus: An Unusual Syndrome of Dyspituitarism," reported the case of a girl, aged 5. None of the cases except that of Hand came to autopsy. The other authors ascribed this unusual symptom complex to dyspituitarism or to a tumor at the base of the brain. In view of the apparent historical priority, it has been suggested that the symptom complex be designated as Hand's disease. Subsequently, instances of the disease were reported by numerous investigators.

A case of lipoidgranulomatosis (type, Hand-Schüller-Christian) in a man, aged 31, with diffuse skeletal involvement, diabetes insipidus, dyspituitarism and extensive changes in the central nervous system is described. Postmortem examination revealed: (*a*) lipoidgranulomatous lesions in the skull, femur, pituitary gland and lungs and (*b*) increased vascularity in the anterior lobe of the pituitary gland, marked diminution in the number of eosinophilic cells, adenomatous hyperplasia and hypertrophy of the basophilic cells, a predominance of altered chromophobe cells and an increase in the stroma. The posterior lobe showed an increase in the stroma, marked fibrosis and infiltration by round cells.

The atrophy of the testes, with its attendant clinical picture, was subsequent to a primary lesion of the pituitary gland.

WINKELMAN, Philadelphia.

SLEEP AND CEREBROSPINAL FLUID PRESSURE. VLADIMIR VUJIĆ, Jahrb. f. Psychiat. u. Neurol. **49**:113, 1933.

Vujić studied experimentally the effects of sleep on the spinal fluid pressure. His conclusions are as follows: 1. During spontaneous sleep there occurs a rise in the spinal fluid pressure. The only exceptions to this rule are in epilepsy and in conditions in which the initial pressure is abnormally low. 2. The rise in pressure persists to a greater or lesser degree during sleep. 3. As a general rule a drop in pressure almost to the level of the initial pressure occurs on awaking from a spontaneous and short sleep. This phase of the problem, however, needs further investigation. 4. Spontaneous heavy sleep and sleep induced by hypnotics are frequently accompanied by a rise in pressure. As a rule this rise is greater and more prolonged than that occurring during spontaneous light sleep. It is conceivable that in the latter case the pressure is lower because the sleep is not so deep and the patients awake more readily. 5. Occasionally hypnotics may produce a fall in pressure before sleep sets in, and, rarely, during actual sleep. The effect of hypnotics on the spinal fluid pressure is also manifested by the fact that certain characteristics of the pressure curve are more pronounced in some cases, while in others they are indefinite and are eventually lost. 6. During the process of falling asleep, as well as for some time during sleep, periodic variations in pressure occur, ranging from 1 to 9 cm.; the variations bear no relation to the pulse rate nor are they synchronous with the respirations; each variation may last from twenty to forty seconds. The variations are especially marked in dementia

paralytica and catatonia, but they may also occur in other diseases of the central nervous system. Marked variations may be regarded as objective evidence that the patient is asleep. 7. In a large number of patients with epilepsy the pressure curve is characteristically labile; this is due to the marked tendency to low spinal pressure in this condition. 8. In chronic encephalitis (the type is not stated) there is a characteristic deviation of pressure during sleep which is manifested by a marked tendency toward equalization of the pressure during sleep and that during the waking state. 9. In sleep induced by hypnosis the pressure rises, although the rise is not so high as that which occurs during spontaneous sleep or during sleep induced by hypnotic drugs. 10. Sleep has no effect on the spinal pressure in cases of subarachnoid block when lumbar puncture is performed below the block; this fact may be helpful in the determination of the presence of subarachnoid block. 11. As alterations in the cerebrospinal fluid pressure indicate changes in the innervation of the cerebral blood vessels, it may be concluded that circulatory changes in the brain in the form of hyperemia are not indispensable for sleep.

KESCHNER, New York.

PHEOCHROMOCYTOMA OF THE SUPRARENAL MEDULLA (PARAGANGLIOMA): A CLINICOPATHOLOGIC STUDY. A. A. EISENBERG and HARRY WALLERSTEIN, Arch. Path. **14**:818 (Dec.) 1932.

The purposes in this article are: to collect all the recorded cases of pheochromocytoma of the suprarenal gland; to present the salient clinical and pathologic features of all these cases, and to attempt to reduce them to a common denominator, i. e., to present their clinicopathologic cross-section, and to report the fifth case of malignant pheochromocytoma of the suprarenal gland, one that is associated with another primary malignant growth (of the thyroid gland) and an unusual blood picture. Fifty-three cases of pheochromocytoma of the medulla of the suprarenal gland collected from the literature are tabulated with their main clincial and pathologic features.

A new case of malignant pheochromocytoma of the medulla of the suprarenal gland is presented, with the following unusual features: (*a*) coexistence of another primary malignant neoplasm (of the thyroid gland), (*b*) widespread metastases from the pheochromocytoma, with none from the carcinoma of the thyroid gland, and (*c*) a very unusual blood picture. Only five of the fifty-three cases previously reported were malignant, but all of them showed widespread metastasis.

Association of benign pheochromocytoma with other tumors is not rare, several cases having been reported of its association with multiple neurofibromas, with adenomas (of the thyroid gland, liver and pancreas) and with hypernephromas. In only the one case was a malignant pheochromocytoma associated with another primary malignant tumor. All known cases of malignant suprarenal pheochromocytoma were bilateral. The incidence of the tumor is about even as to sex; it is greatest on the right side and in patients in the fifth decade of life. The most striking histologic features are: the greatest imaginable irregularity in the size and shape of the cells and of the nuclei, the reaction to the chromaffin and the rich vasculature.

The most interesting feature is the relation of these tumors to hypertension. About one half of all the patients showed hypertension, some with atherosclerosis and others without it. While in some cases of tumor of the suprarenal cortex hypertension was continuous, in a large majority of the cases of tumors of the suprarenal medulla in which it was present it was of paroxysmal type—but only in the cases in which the tumor was benign, as all patients with malignant medullary tumor showed either no hypertension at all or hypotension. The attempts to correlate hyperplasia of chromaffin tissue with hypertension are not successful because of the absence of proof that hypersuprarenalemia exists in such cases, and also because it is not at all established that hypersuprarenalemia is responsible for hypertension.

WINKELMAN, Philadelphia.

THE RÔLE PLAYED BY MASTURBATION IN THE CAUSATION OF MENTAL DISTURBANCES. W. MALAMUD and G. PALMER, J. Nerv. & Ment. Dis. **76**:220 (Sept.); 366 (Oct.) 1932.

For centuries the belief has existed that masturbation is one of the chief causes of mental and physical abnormalities. With the work of Kraepelin, Freud, Bleuler, Krafft-Ebing and Havelock Ellis the time-honored theory has had to be revised. Few studies on the subject have been scientifically controlled. Of 190 male college students averaging 25 years of age studied by Peck and Wells, only 7 per cent denied the habit. According to K. B. Davis, of 1,183 unmarried female college graduates, from 30 to 68 years of age, 64.8 per cent admitted the practice. The general concensus of students of this problem seems to be that the practice is an important factor in the development of mental disease by virtue of certain psychic attitudes adopted by the patient toward the possible sequelae of such a practice, and not because of the effects of the masturbation itself.

The authors reviewed 500 consecutive cases of patients admitted to the Iowa Psychopathic Hospital. In 10 per cent, masturbation was found to have played an important rôle. The degree of importance of the symptom can be represented in three groups of cases: (1) those in which masturbation was apparently the most important cause of the disturbance; (2) those in which masturbation was only one of several causative factors; (3) those in which masturbation was only a precipitating cause. Of the 50 patients, 35 were male and 15 female; 34 were unmarried, 15 married and 1 widowed. The period of maximum evidence in the male is between 16 and 20; in the female between 36 and 40. Seventy per cent of the cases showed the presence of mental deviation in the family history. Distribution according to diagnostic type was an follows: psychoneuroses, 12 cases; depression (reactive), 11 cases; paranoid state, 7 cases; schizophrenia, 7 cases; organic psychoses, 7. The signs of the disease seem to have no definite relationship to the duration of the practice. In some cases the mental disturbance began during the practice, and in others after it had closed. In all cases the disturbance seemed to be related to fear of consequences, feelings of guilt and inability to stop the habit. The authors conclude that the development of an abnormal mental state is not an invariable concomitant of masturbation; and in cases in which abnormal mental states existed there were constitutional peculiarities, poor heredity, abnormal personality traits, lack of proper sex education and frequently unsatisfactory general environmental situations. Psychotherapy was effective in the readjustment of the patients.

HART, Greenwich, Conn.

TWO CASES OF THALLIUM POISONING. PAUL CHALIONGUI, Lancet **2**:1433 (Dec. 31) 1932.

Thallium acetate has proved of value in the treatment for favus and ringworm. Chaliongui has had the opportunity to observe two cases of severe poisoning. Brief case histories follow.

About four hours after an accidental second dose of thallium acetate, a girl, aged 6, complained of pains in the calves and vomiting. The pains rapidly became excruciating, and on the following day she could neither walk nor stand; she swayed and fell at the slightest attempt. Vomiting became obstinate, so that she could take nothing by mouth. Drowsiness and, later, coma occurred. At first this state was interrupted by intervals of consciousness, but it soon became constant. The pains and vomiting diminished and ultimately disappeared as coma developed. On the tenth day after the onset of the illness, she was immobile; the limbs and body were flexed, and the head was retracted. At times she uttered a plaintive, monotonous cry. All the hair of the head had come out, except a few thin patches. The face was pale and pinched; the eyes were wide open and the eyeballs prominent. The pupils were dilated and immobile to light. There was much loss of weight. On the eleventh day, there were peculiar convulsive attacks, during which the child lay on her back with the upper limbs tonically contracted; they were flexed at the interphalangeal and extended at the meta-

carpophalangeal, wrist and elbow joints. This tonic stage was followed after a short interval by slow movements of pronation and supination in the extended forearms and arms, which lasted for a few minutes. Three such attacks were observed before death, which occurred on the thirteenth day.

Choreo-athetoid movements of the four limbs and face, with conjugate deviation of the eyes to the right on the day after treatment, developed in a boy. The pupils were widely dilated but active; reflexes were diminished. The eyegrounds appeared normal. There were bilateral pyramidal tract signs in the upper and lower limbs. Incontinence of urine and feces occurred. The spinal fluid was under slightly increased pressure, but otherwise was normal. Two hours later the patient was conscious but had amaurosis, left hemiplegia, with typical reflex changes, and conjugate deviation of the eyes to the right. The blindness disappeared in about an hour, while the other symptoms persisted for about three hours. The boy made an uneventful and complete recovery. BECK, Buffalo.

THE RELATIONSHIP BETWEEN STATUS LYMPHATICUS, THE THYMUS AND THE SUPRARENAL GLANDS. EDWARD H. CAMPBELL, Arch. Otolaryng. **15**:517 (April) 1932.

Status lymphaticus is defined as a constitutional defect dependent on an inadequacy of some function of the suprarenal glands, sex glands and autonomic nervous system, associated with lowered resistance to a great variety of agents. There is a tendency to leukocytosis, hypotension, a longer coagulation time, a lowered blood sugar and a lowered alkali reserve. Owing to the frequent sudden deaths during tonsillectomy, this matter has become of particular interest to laryngologists. It is probable that many people, especially infants and children, suffer in various degrees from this condition, which greatly impairs their ability to resist infection. Various authors are quoted who sustain this point of view in pneumonia, tetanus, cholecystitis and other diseases. Owing to the disagreement as to the exact method of examining and the importance of the interpretation of the findings, accurate statistics for the frequency of status lymphaticus are not available. Twenty-two per cent of patients at Bellevue Hospital who had attempted suicide or were drug addicts, degenerates or gunmen had some of the stigmas of status lymphaticus. It is frequently found in children and especially in children who have died suddenly. Death from status lymphaticus has been known to be precipitated by slight infections or intoxications, various emotions, psychic shock, electric shock, shock from hypodermics or vaccination, traumatism, coitus, anesthesia, flogging, cold water, burns, bathing, muscular exertion, hemorrhage and drugs. Some persons whose death has been due to status lymphaticus have had previous experiences that might have been expected to kill them.

Enlargement of the thymus does not always indicate status lymphaticus. Many healthy children show an enlarged thymus. The thymus changes during starvation, acute infection and intoxication and during many diseases. The various methods of taking roentgenograms and of using roentgenotherapy are discussed. The relationship between the thymus and the suprarenal glands is emphasized, and also an appreciation of the fact that a mild state of status lymphaticus may exist and may help to combat chronic and acute intoxications in those who seem to be constitutionally imperfect. Interesting problems for future investigations are outlined. HUNTER, Philadelphia.

PURIFICATION OF POLIOMYELITIC VIRUS. M. A. SCHAEFFER and W. B. BREBNER, Arch. Path. **15**:221 (Feb.) 1933.

The fact that experiments on viruses are generally carried out in the presence of proteins and other substances necessarily contained in emulsions of infected tissues may partially explain the variability of results. Because of the protective or inhibitive manifestations of these substances, it is desirable to remove them in order to arrive at truer conceptions of the behavior of viruses.

The phenomenon of absorption has long been employed as a practical means of selective separation and recovery of substances from heterogenous biologic mixtures. Andrejew showed that antibodies could be absorbed from serum on kaolin and kieselguhr. Lewis and Andervont reported that the viruses of vaccinia and fowlpox were adsorbed by powdered Berkefeld filters, kaolin and charcoal, and the virus of Rous' sarcoma on aluminum hydroxide. Since Willstätter and his school have developed methods for the purification of enzymes by adsorption and elution, many investigators have applied this technic to viruses and bacteriophage.

Rhoads used poliomyelitic virus adsorbed in alumina gel for immunization of monkeys. He observed that the virus was adsorbed and inactivated in an acid solution, but that when the "p_H" was raised to neutral or the basic side, the virus was actively present in the supernatant liquid. However, he did not apply these observations toward purposes of purification. In the summary the authors state that poliomyelitic virus can be adsorbed and "eluted" on aluminum hydroxide; it yields a potent solution of the virus which gives no reactions for protein unless the solution is concentrated, in which case the results of the tests are sometimes positive. The optimum "p_H" for adsorption is apparently between 5.8 and 6.4; for elution, between 8 and 9. Lipids can be extracted with ether from emulsions of the cord without injury to the virus. The extracted solutions can subsequently be effectively adsorbed and "eluted" on alumina gel. Purified preparations are probably unstable, but the period of inactivation has not yet been definitely limited.

Attempts to purify the virus of poliomyelitis by several other methods have been unsuccessful. The results obtained with safranin may nevertheless prove interesting, because the virus is definitely attenuated.

WINKELMAN, Philadelphia.

RAYNAUD'S DISEASE, WITH SPECIAL REFERENCE TO THE NATURE OF THE MALADY. THOMAS LEWIS, Brit. M. J. **2**:136 (July 23) 1932.

The two theories of the causation of Raynaud's disease are discussed. The author discounts the hypothesis that sympathetic nerve impulses due to the irritability of vasomotor centers cause this disturbance and brings forth the following evidence to prove that it is a local condition of the artery: A spontaneous attack may develop by simple exposure to a room temperature of 15 C. (59 F.). If the subject's body and hands are warm in a room at 22 C. and one hand is placed in water at 20 C., an attack will develop in this hand. If the subject is taken into a cold room at 15 C. and the right hand is placed in water at 30 C., an attack develops in the left hand only. If the subject is exposed in a cool room, the hands being kept at a temperature of about 25 C., an emotional disturbance or pain develops in the patient, there is a rise in vasomotor tone, and an attack supervenes. In this case the vessels are already abnormally narrowed, though not occluded, and an increase in vasomotor tone is sufficient to complete the closure. It is possible that a normal vasomotor impulse might close a digital vessel at a higher temperature, if that digital vessel has much intimal thickening. A patient has an attack in a cool room, and anesthetization of the ulnar nerve fails to abolish it. Thus removal of normal vasomotor tone is insufficient to release spasm in vessels that are closed owing to local abnormality. A patient who has lost the sympathetic nerve supply to one arm dips both hands in water at 20 C. while in a cool room. An attack develops in both hands, but it is more severe on the nonsympathectomized side. Finally, if the body of a patient on whom cervical sympathectomy had been done on one side long before is kept very warm while the two hands are cooled by immersion in cold water, the attack may be confined to the sympathectomized side. This apparent paradox is due to the fact that after sympathectomy full vasodilatation is not maintained; hence, when there is a conspicuous vasodilatation, as from heating the body, the vessels of the intact side become wider than those on the sympathectomized side. This leads, curiously, to an attack which is clearly the result of a local cause, being confined to the limb from which the sympathetic nerves have been removed.

FERGUSON, Niagara Falls, N. Y.

INFLUENCE OF VITAMIN B AND OF IODINE ON THE CALCIUM AND PHOSPHORUS METABOLISM OF RABBITS WITH HYPERPLASTIC THYROIDS. MARTA SANDBERT and OLIVE M. HOLLY, J. Biol. Chem. **99**:547, 1933.

Various authors have presented evidence that vitamin B is concerned with thyroid metabolism, as the requirement of this vitamin is greater when the caloric factor is increased, as in hyperthyroidism. In rabbits kept on a diet consisting principally of cabbage, simple goiter develops. Steaming of the cabbage, a process which destroys the heat-labile vitamin B, increases the goitrogenic activity. The authors found that either the adding of vitamin B to the diet or the giving of iodine increased the excretion of calcium and made a striking change in the ratio of calcium and phosphorus retention in rabbits in which thyroid hyperplasia had been produced by the feeding of cabbage. The experiments which they present in detail were made in order to determine whether iodine and vitamin B would act similarly on rabbits kept on a standard diet of alfalfa, hay and oats if the ratio of calcium to phosphorus in the food was kept the same as in the diet of steamed cabbage (i. e., 1 : 0.8). Throughout the experiments this ratio was kept constant. Five rabbits were kept for nine weeks on a vitamin B deficient diet. (Hyperplasia of the thyroid gland developed.) Two of the rabbits were then given potassium iodide and the retention of calcium and phosphorus changed so that the ratio of calcium to phosphorus shifted from 1 : 0.3 to 1 : 216. After this high point of excretion of calcium, the ratio of calcium retention to phosphorus retention and the excretion of calcium proceeded in wavelike cycles, increases being followed by decreases. Vitamin B was given to the three other rabbits, and the form of the curve of excretion was the same. After three weeks the calcium-phosphorus ratio had changed from 1 : 1 to 1 : 226, and from 1 : 0.3 to 1 : 177.

Autoclaved yeast and autoclaved vitavose showed no influence on the calcium and phosphorus metabolism, supporting the assumption that vitamin B is the active agent in yeast and vitavose which influences calcium and phosphorus metabolism of rabbits with hyperplastic thyroids.

DAILEY, Boston.

SUICIDE: POSSIBILITIES OF PREVENTION BY EARLY RECOGNITION OF SOME DANGER SIGNALS. R. E. FAIRBANK, J. A. M. A. **98**:1711 (May 14) 1932.

The author states that the only possible cure of suicide is prevention. She enumerates some of the guide-posts one can use in this connection thus: 1. Most suicides occur in patients who are depressed, but suicide is also relatively frequent in schizophrenic and paranoid patients, especially those whose conversation reveals depression. 2. Disappointment over some situation which seems unmodifiable to the rigid individual is perhaps the most common motive in suicide. A common feature in cases studied by the author is the talk of hopelessness, of wanting to die, of a fear of "going crazy"; such expressions as "a feeling of emptiness," of "guilt," or the special preoccupation with various delusions of persecution and with autistic fantasy. 3. The "rigid personality" is present in about one third of the cases and shows the need of careful watching. 4. A family history of suicide is apt to reduce the resistance. 5. Methods show the things from which patients need to be protected. In the hospital the impulsive plungers are especially difficult to take care of. On the outside, suicides from gas, gun-shot wounds and drowning are frequent. 6. Warnings are to be found in previous attempts and the frequent talk of suicide. Some patients, however, give no warning; others apparently try to protect themselves, while a third group conceals the means of suicide. 7. Special problems involve such questions as when to put a patient on suicidal observation and when to take him off, and how much risk to take in order to encourage an interest in occupation or to avoid unnecessary chafing against restrictions. The methods to be adopted must in the end rest with the personnel in charge, depending to a large extent on the rapport with the patient and the willingness of the family to share the responsibility which such a risk involves. 8. Finally, regarding prevention, the author suggests the restriction of the loose

handling of firearms, poisons and sedatives, if possible, and urges the cultivation of a sensitiveness to the aforementioned symptoms, warnings and mistakes. It is necessary to realize that a suicidal patient must never be left alone.

EDITOR'S ABSTRACT.

THE DEPRESSIVE PSYCHOSES DURING THE AGE OF REGRESSION. E. FÜNFGELD, J. f. Psychol. u. Neurol. **45**:1, 1933.

This contribution is based on anatomicoclinical investigations in twenty-three cases of depressive psychosis occurring during the age of regression. The clinical material is divided into three groups. The first group includes cases of the cycloid form. The patients in this group were subject to periodic attacks of the disease; some cases disclosed anatomic alterations in the brain after death, but these bore no relation to the psychosis. When such conditions run a malignant course or present clinically organic manifestations referable to the brain, necropsy always reveals pathologic cerebral changes. It is also emphasized that in cases of this type the clinical picture does not vary fundamentally, whether the process in the brain is arteriosclerotic, senile or involutional. The second group includes cases of depressive psychosis that bear no definite relation to the circular forms, the onset of which apparently depends on pathologically increasing phenomena of regression. The third group includes cases of genuine senile psychosis, with changes in the brain that appear early in the course of the disease and a peculiar accumulation of "Drusen."

The uncomplicated cases of circular insanity and those in which the disease runs a pernicious course occur during the natural years of regression and of the senium. The involutional psychoses appear strikingly between the ages of 53 and 63 years. It is noteworthy that in the twenty-three cases studied only two patients were men. However, it need not necessarily be assumed that the female sex has a greater tendency to involutional processes. The greater incidence in women is most likely due to the fact that this sex reacts to such processes with psychotic manifestations—a fact in full accord with general observations in regard to the occurrence of other endogenous psychoses.

Fünfgeld's material shows conclusively that there is apparently no justification on clinical or on anatomic grounds for including the involutional psychoses among the schizophrenias.

KESCHNER, New York.

TYPOLOGY IN THE LIGHT OF THE THEORY OF THE CONDITIONED REFLEX. J. S. ROSENTHAL, Character & Personality **1**:56 (Sept.) 1932.

Experiments on dogs and pigeons demonstrated that, with the removal of the cerebral cortex, the animal was unable to seek for food or for a mate, and unable to avoid danger. The result was that these decorticated animals speedily perished. This established the first requisite for conditioning a reflex: a cortex. There are several other requirements: The animal must be living as a unit, and not in the course of gestation; reflexes cannot be conditioned in utero. Other essentials are excitability, attention and reenforcement. As an instance of the latter, Rosenthal cites the case of conditioning a dog by operating a metronome during feeding, so that the tick of the clock alone will cause saliva and gastric juice to flow. If, however, this is attempted repeatedly without actually giving food to the animal, the metronome will in time lose its power as a stimulus to the salivary and gastric glands. The ticking must be reenforced.

Inhibitions as well as excitations can be conditioned. It is possible to accustom an animal to a stimulus which will actually check the secretion of a gland. These stimuli, and excitatory ones also, have a tendency to radiate, so that forces similar to the conditioned stimulus can often bring a response.

Human and animal types can readily be classified on the basis of their receptivity toward stimuli; five such groups are found: choleric, sanguine, central, phlegmatic and melancholic. In the first three classes, new stimuli are readily accepted and

soon can replace the old ones; in the latter classes, resistance toward conditioning is considerable. To an extent it is possible to change the temperament of a human being or animal through a process of education and reconditioning. Unfortunately, most of the alteration that occurs in nature is in the downward direction, that is, the enfeeblement of previously strong types as a result of adverse environment. In an intelligently controlled environment, however, there is no reason why reconditioning should not result in strengthening and improving the stock.

DAVIDSON, Newark, N. J.

THE CALCIUM AND PHOSPHORUS CONTENT OF THE BRAIN IN EXPERIMENTAL RICKETS AND TETANY. A. F. HESS, J. CROSS, M. WEINSTOCK and F. S. BERLINER, J. Biol. Chem. **98**:625 (Nov.) 1932.

During the course of a metabolism study of rickets, the authors found a marked decrease in the total calcium of the brain in rats. Their calcium values were determined by a modification of the Fiske and Logan method; the phosphorus values, by the method of Fiske and Subbarow. In twenty-seven normal rats the total calcium ranged from 100 to 260 mg. per hundred grams of dried weight, averaging 182 mg.; the total phosphorus, from 1,000 to 1,400 mg., averaging 1,278 mg. per hundred grams. In twenty rats in which rickets had been induced, the calcium values were definitely low, ranging from 37 to 76 mg. and averaging 59 mg. The total phosphorus was about the same as in the normal group.

The rickets-inducing diets were altered in an attempt to ascertain the factor leading to the withdrawal of calcium from the brain. Not only the usual rickets-inducing ration high in calcium and low in phosphorus, but one low in calcium and high in phosphorus caused a marked reduction of the calcium in the brain. The authors then attempted to bring the calcium in the brain back to normal level by antirachitic agents. No change either in phosphorus or in calcium resulted from ultraviolet irradiation or cod liver oil. Substitution of an adequate ration induced a slow return toward normal values.

Parathyroidectomy was carried out in another series of rats. Three days after operation, with a serum calcium below 7, but on normal diet, the calcium in the brain was normal. In rachitic rats on which parathyroidectomy was performed, the calcium in the brain was low. The authors conclude that there is no relationship between the calcium content of the brain and that of the serum. In rickets the total calcium is normal in the blood and diminished in the brain; in parathyroid tetany it is low in the blood and undiminished in the brain.

DAILEY, Boston.

TREATMENT OF OBSTINATE CHOREA WITH NIRVANOL. T. D. JONES and J. L. JACOBS, J. A. M. A. **99**:18 (July 2) 1932.

The histories of three obstinate cases of chorea, with emphasis on their response to nirvanol therapy, are reported. In each of the three cases, "nirvanol sickness" was produced. The dosage was halved after three days and discontinued on the first appearance of rash. A definite rash occurred in each case; on the sixth day in case 3, and on the eighth and ninth days respectively in cases 1 and 2. Case 1 at no time showed a temperature reaction, and in case 2 there was a single rise to 101 F. (rectal), sixteen hours prior to the appearance of the rash. Definite eosinophilia occurred in all cases, with an inversion of the neutrophilic and lymphocytic ratios. There was a definite increase in the total eosinophils. Case 3 failed to show the usual variation in neutrophilic and lymphocytic elements until quite late, probably because of the complication of hemorrhage. The most interesting phase of the report is concerned with the unusual reaction in case 3 to nirvanol therapy. A definite rash appeared on the sixth day, preceded by a rise in temperature to 102 F. (rectal). On the ninth day after therapy was begun, bleeding occurred, first from the gums, then into the skin and subcutaneously. Blood platelets disappeared from the smear. There was a conspicuous prolongation of bleeding time, with the coagulation time unchanged. A sudden pulmonary

episode occurred on the ninth day, possibly best explained as bleeding into the lung tissue. Each of two transfusions was followed by definite improvement. The blood picture resembled suppression of bone marrow as produced with nirvanol in studies of rabbits by Leichtentritt and Lengsfeld, and that seen in human beings, in benzene and arsphenamine poisoning. In addition, there was a secondary reaction, three weeks after therapy was begun, consisting in a rise in fever of two days' duration. The first reaction with its unusual pulmonary complication was nearly a fatal issue and shows clearly that the drug is one not to be used indiscriminately.

EDITOR'S ABSTRACT.

HYPERPARATHYROIDISM WITHOUT PARATHYROID TUMOR. LEWIS H. HITZROT and BERNARD I. COMROE, Arch. Int. Med. **50**:317 (Aug.) 1932.

A woman, aged 42, was admitted to the hospital complaining of weakness and aching in the bones. Her diet, consisting mainly of starch and vegetables, had always been deficient in calcium and in fat-soluble vitamins. She had grown shorter during the few years preceding her admission to the hospital. The symptoms began with dull, boring pain in the legs, which progressed and was accompanied by rapidly advancing weakness. Blood calcium was 13.2 mg. per hundred cubic centimeters (normal, 9 mg.). X-ray films revealed extreme rarefaction of almost all the bones, with flattening of the vertebrae. A diet high in calcium proved ineffective; three of the parathyroid glands were removed, part of the thyroid gland being excised during the operation. Tetany developed three days later, the calcium of the blood having fallen to 6.8 mg. This was controlled by the daily administration of 15 Gm. of calcium lactate, by the intravenous injection of 20 cc. of calcium gluconate and by 20 units of Collip's parathyroid extract given intramuscularly. A diet high in calcium and high in phosphorus, and containing viosterol, was administered. Within two months the symptoms had disappeared, and the x-ray pictures showed that there had been a marked increase in lime deposits. The blood calcium at the time of discharge was 9.8 mg. On a regimen of calcium salts by mouth the patient remained free from tetany. The authors speculate as to the possibility that parathyroid overactivity is required to make up the calcium needs of the body owing to the inadequacy of this salt in the diet. This case is an addition to the few that have been reported in the literature hitherto, in which hyperparathyroidism without tumor has been successfully treated by removal of the glands.

DAVIDSON, Newark, N. J.

COMPRESSION FRACTURE WITH COMMINUTION OF BODY OF THIRD LUMBAR VERTEBRA AND NEUTRAL ARCH OF FOURTH VERTEBRA WITH PARAPLEGIA. H. D. ISAACS, Brit. M. J. **1**:835 (May 7) 1932.

Crush fractures of the vertebral body are produced by a bending or hyperflexion of the spine, associated in some cases with compression in the long axis of the column. Falls on the back of the neck from a height or a heavy weight falling on the back while it is in a stooping position are examples of accidents causing this form of fracture. The reduction of such fractures depends on the integrity of the anterior common ligament. The process of hyperextension puts this ligament into tension, which, in its turn, presses the fragments into position and so molds the vertebrae back into form.

The case is reported of a man, aged 50, in whom roentgenograms showed a marked comminution of the body of the third lumbar vertebra, with a forward displacement of the greater part of the body into the abdominal cavity, and fracture of the spine and neural arch of the fourth lumbar vertebra. Examination of the lower limbs showed a complete flaccid paralysis, with the exception that there was ability to contract the left quadriceps extensor muscle. Reflexes and sensation were absent. The patient was unable to void urine or to evacuate the bowels.

Reduction of the fracture was accomplished by placing the patient face downward, resting on his elbows and thighs. The thighs were then lowered until the shoulders were about 2 feet higher than the knees. A plaster of paris cast was applied from the shoulders to the greater trochanter. A roentgenogram taken the next day showed complete reduction of the fracture. There was immediate improvement. In one month the patient was out of bed; two weeks later he was able to walk unaided, and at the end of six months he was completely well.

FERGUSON, Niagara Falls, N. Y.

CISTERN PUNCTURE: GENERAL REVIEW AND COMPARISON BETWEEN DIRECT AND INDIRECT METHODS. GIRSCH D. ASTRACHAN, Am. J. Syph. **16**:321 (July) 1932.

Because there is less pain, less chance of breaking the needle and less likelihood of bleeding, Astrachan prefers the direct or Ayer method of making cisternal punctures to the indirect or Eskuchen procedure. In the former method, the needle is inserted just above the spine of the axis and directed in line with the external auditory meatus and glabella. In this way the needle penetrates only soft tissue, and as no periosteum is irritated, pain does not result. In the Eskuchen procedure it is necessary for the operator to feel his way along the occiput toward the lower edge of the foramen magnum, thus scratching the sensitive periosteum. The anastomoses connecting the external and internal venous vertebral plexuses constitute a formidable hazard of bleeding during the practice of indirect puncture. Because of these unfavorable features, the author much prefers the Ayer approach. He recommends choosing the location for the puncture while the patient is in a standing position, because this posture offers clearer landmarks. During puncture the patient lies on his right side, with the head moderately flexed and held in place by an assistant or nurse. The most serious contraindications to cisternal puncture are tumor of the brain and injury of the skull, because of the danger that these conditions might displace vital structures toward the median line. The chief therapeutic advantages of the procedure are its availability in cases of spinal block and the strategic location of the cistern for the distribution of drugs and serums in both the spinal and the cerebral direction. Owing to the negative pressure, postpuncture headaches do not occur.

DAVIDSON, Newark, N. J.

PSYCHIATRIC ANNEXES OF PRISONS. H. CARRILHO, An. assist. a psicop., 1931, p. 21.

Carrilho recommends the creation of psychiatric annexes to prisons for the anthropologic study of delinquents, such as have been established in Belgium under the leadership of Dr. Vervaeck. Several countries have already followed Belgium's example: Germany, Austria, Italy, Portugal, Soviet Russia, Argentina and Cuba. The author gives a proposed draft of a law, consisting of three sections. Section 1 would provide that all penal institutions shall be equipped with a psychiatric annex that will pursue certain definite objectives. It will examine the interned inmates who, because of their peculiar criminal conduct or through indications noted by the Instituto de antropologia, are suspected of mental abnormalities. It will study, in the cases indicated, the probable abnormal mental condition of the inmates at the time of the crime, the circumstances of the crime and the revelations of the individual examination, in order that the courts of justice may be better informed concerning the cases that require a "therapeutic sentence" instead of a penal sentence properly so called. It will also define, for the purposes of social defense, the extent to which the interned prisoners may be dangerous in view of their anomalous mental condition. Section 2 would provide that the observation period to decide whether a subject should be retained permanently in the psychiatric section, transferred to the institution for the criminal insane or returned to the penitentiary proper could normally extend over three weeks,

but, in special cases, previously certified to the court having jurisdiction, it could be prolonged. Section 3 would provide that the management of the psychiatric section shall be entrusted to a professional psychiatrist.

EDITOR'S ABSTRACT.

PATIENT WHO CONSIDERS HIMSELF A HERMAPHRODITE. I. L. POLOZKER, J. Nerv. & Ment. Dis. **75**:1 (Jan.) 1932.

The case of a man, aged 42, calling himself by a variety of names, Emily W., Edmund P. and Emily P., was referred to the Psychopathic Clinic of the Recorder's Court at Detroit. He wore bobbed hair, a khaki shirt and knickers, women's tan shoes, women's fur trimmed blue coat, and carried a lady's pocketbook containing cosmetics. He claimed to have given birth to a male child and that his husband had died during the war.

The family history was obtained from several agencies as the patient's statements were unreliable. The paternal grandfather, the father and the sister of the patient exhibited psychopathic traits, with marked sex delinquency and promiscuity. The patient's personal history, which was actually verified, revealed that he had been married to Emily W., who bore him three sons. Between 1917 and 1926, he was involved in numerous charges: of threatening to cut off a woman's fingers, of stealing, absence from work, living with juvenile girl prostitutes, larceny of clothing, disorderly conduct, etc. He lived in a portable car with a child whom he neglected. A psychometric examination revealed much scattering, but indicated about an average level. He was irrelevant, incoherent and circumstantial in speech and produced some neologisms. He indirectly admitted homosexual experience. He derived much satisfaction from fantasy and romancing about having given birth to twelve children by different men, and he assumed an identity with his wife and also with his sister. The pleasure that he obtained from being dressed in women's clothing more than compensated for the ridicule to which he was subjected because of his singular appearance. The case was diagnosed as schizophrenia with constitutional homosexuality.

HART, Greenwich, Conn.

OLIGODENDROGLIA OF THE SENSORY GANGLIA. J. M. ORTIZ PICON, Rev. españ. de biol. **1**:19 (June) 1932.

The spinal ganglia of cats and rabbits were used in this study. They were stained with Rio-Hortega's silver carbonate method (for oligodendroglia). The endocapsular cells (satellite cells or amphicytes) are spindle-shaped elements or cells, with irregular contour and prolongations of unknown length and distribution. In a general way, it may be said that the endocapsular cells appear clearly separated from one another, except in an area which may correspond to the initial glomerulus of the ganglion cell; in this area they are crowded and may even give rise to a syncytium. The histochemical reactions of the endocapsular cells are identical with those of the oligodendrocytes of the central nervous system. In fact, these cells seem to be functionally homologous with the oligodendrocytes located in close proximity to the neurons of the nerve centers, although they probably represent a special type found only in the sensory ganglia. Free or scattered oligodendrocytes were also observed outside the capsules enclosing the ganglion cells; most of these oligodendrocytes appear in the vicinity of the nerve fibers within the ganglion, and their few prolongations are directed toward these fibers. Their histochemical reactions differ from those of the elements of connective tissue occurring among the neurons of the ganglion.

The observations reported favor the view advocated by Rio-Hortega, that the oligodendrocytes of the central nervous system are homologous with the cells of Schwann of the peripheral nerves and the subcapsular (satellite) cells of the ganglia.

NONIDEZ, New York.

PERICYTES OF THE CENTRAL NERVOUS SYSTEM. L. URTURBEY, Rev. españ. de biol. **1**:25 (June) 1932.

The microglia methods of Rio-Hortega and the methods of Golgi-Kopsch and Bielschowsky were used for staining. Intravenous injections of lithium carmine and carmine in physiologic solution of sodium chloride and subcutaneous and intraperitoneal injections of trypan blue and india ink were also employed. Intraspinal injections were made in some cases. Dogs, rats and rabbits were used. In the opinion of Urturbey, the pericytes wrapped around the capillaries of the nervous system seem to be nonmuscular cells of histiocytic nature. While it is true that in many blood vessels these cells may be transformed into typical fibrocells, this is interpreted as a normal process, since smooth muscle fibers may arise from histiocytes. The fact that in some cases the capillaries show constrictions at the level of the prolongations of these pericytes, wound around their wall, seems to indicate that the pericytes regulate in some way the circulation of the blood in the capillaries of the nerve centers. It is not possible to demonstrate the transformation of the pericytes into microglia cells. Since in the nerve centers neither the pericytes nor the endothelium takes up injected carmine, trypan blue or india ink, Urturbey thinks that the argument used by some investigators as to the ectodermic origin of the microglia, based on the fact that the latter does not ingest particles of these stains, has no value.

NONIDEZ, New York.

VENOUS ANGIOMA OF THE RETINA, OPTIC NERVE, CHIASM AND BRAIN. E. F. KRUG and BERNARD SAMUELS, Arch. Ophth. **8**:871 (Dec.) 1932.

The presence of a venous angioma of the retina, optic nerve, chiasm and brain was confirmed by autopsy following the suicide of the patient. The right eye, orbital contents and brain were removed. The angiomatous lesion extended from the right retina along the right optic nerve, chiasm and tract to the right of the midbrain and via the right superior cerebral peduncle to the right lobe of the cerebellum and the dentate nucleus. The microscopic observations explain well the interesting neurologic features which the patient presented. They have not been included in this abstract.

Venous angiomas are one of three classes of vascular malformations; the first is telangiectases, or capillary formations (cavernomas); the second, venous angiomas (entirely venous), and the third, arterial or arteriovenous angiomas. The second group, of which the case reported is one, may be subdivided into three groups: (1) simple varices; (2) serpentine varices (i. e., single, much enlarged vascular channels), which at times are associated with the varices belonging to the third group; (3) a small racemose variety, forming a mass of interwoven, at times pulsating, blood vessels.

SPAETH, Philadelphia.

EFFECT OF PITUITRIN IN MALIGNANT DISEASE. E. W. RICHES and M. KREMER, Brit. M. J. **1**:877 (May 14) 1932.

The authors review the work of Susman, published in October, 1931, on the effect of pituitary and ovarian extract, plus a low carbohydrate diet, in malignant conditions. Their results in similar cases do not confirm Susman's findings. Except in one case in which there was a local diminution in the edema of the tongue overlying a growth, there was no beneficial effect that could be attributed to the injections of solution of pituitary and theelin. In no case was life prolonged, nor was there regression of any growth. The physiologic effects of the prolonged administration of solution of pituitary were also investigated. In most cases the immediate effect was to lower the blood pressure, the systolic being lower than the diastolic. Electrocardiographic studies revealed little change. Pallor came on soon after the injections were given in all cases and lasted from twenty to thirty minutes. A flush sometimes followed the pallor. Urinary excretion was diminished, though not to the extent seen in normal subjects. In

two cases faint traces of sugar appeared at the start but disappeared later. The effect on the bowels was surprisingly slight. Constipation was the rule. Only two cases showed stimulation.

FERGUSON, Niagara Falls, N. Y.

NARCOLEPSY: RESULTS OF TREATMENT WITH EPHEDRINE SULPHATE. JOHN B. DOYLE and L. E. DANIELS, J. A. M. A. **98**:542 (Feb. 13) 1932.

A survey was made of information obtained concerning sixty-seven patients who were given a diagnosis of narcolepsy in the clinic and who had not been treated with ephedrine. The duration of the disorder ranged from one to forty years. No patient had recovered completely. Thirty patients wrote that they had improved. In fourteen instances, however, the improvement was very slight. Twenty-five patients reported that they were the same, and eight that they were worse. Four patients had died. Fifty patients were treated with ephedrine, including those treated by others as well as those treated by the authors. The treatment was a total failure in two instances. Two patients, who at first were improved, no longer appear to receive any effect from the drug. Eight patients have been moderately improved symptomatically. Seventeen patients have made marked symptomatic improvement, and twenty have been completely relieved symptomatically. In the two groups mentioned in the preceding sentence, symptomatic relief continues as follows: in four patients after nine months, in two after eight months, in two after five months, in three after four months, in six after three months and in four after two months.

EDITOR'S ABSTRACT.

BISMUTH ARSPHENAMINE SULPHONATE (BISMARSEN) IN THE TREATMENT OF TABES DORSALIS. SAMUEL HADDEN and GEORGE WILSON, Am. J. Syph. **15**:316 (July) 1931.

Over a period of eighteen months, Hadden and Wilson studied the effect of bismarsen on thirty-one tabetic patients. They used the drug synthesized by Raiziss, containing 12 per cent arsenic and 25 per cent bismuth. Butyn was included as a local anesthetic. Afraid of destroying the patient's protective mechanism by too intensive treatment, they gave these injections a week apart; forty treatments made up the average course. Among comparatively early cases, 57 per cent of the patients were rehabilitated sufficiently to return to work; 35 per cent were improved, and only 8 per cent were no better. In the older cases, 30 per cent of the patients were relieved, 40 per cent improved and 30 per cent unimproved or worse. In three patients a positive Wassermann reaction became negative following the injections. Hadden and Wilson conclude by recommending bismarsen because of its ease of administration and freedom from toxic effects, as well as for its favorable effect on gastric crises, bladder disorders and ataxia.

DAVIDSON, Newark, N. J.

RIGIDITY IN DEAFFERENTED LIMBS. S. W. RANSON, J. Comp. Neurol. **52**:341, (April) 1931.

For the experiment, seven cats were used in which three of the dorsal roots of the nerves entering into the formation of the brachial plexus were cut on one side—the fourth cervical to the second thoracic, inclusive—without the dura being cut. Similar operations from the fifth cervical to the second thoracic dorsal root, inclusive, were performed on four other cats. In none of the cats did overactivity of the extensor muscles characteristic of the completely deafferented hindleg develop. The forelimb on the operated side at first was atonic. Later, it could bear the weight of the body in standing and walking. In from one to five months, the cats were decerebrated by a transection through the thalamus. When these animals were supported on a hammock with four openings in it through which the legs hung pendent, some rigidity occurred in all four legs. When these animals were quiet the rigidity was less marked in the deafferented

legs than in the normal hindlegs. The observations were rendered difficult by the occurrence of running movements during which the deafferented forelimb was held in rigid extension.

ADDISON, Philadelphia.

GASTRO-INTESTINAL MOTOR FUNCTIONS IN MANIC-DEPRESSIVE PSYCHOSES: ROENTGENOLOGIC OBSERVATIONS. GEORGE W. HENRY, Am. J. Psychiat. **11:** 19 (July) 1931.

By means of the x-rays and the fluoroscope, Henry studied the gastro-intestinal functions in psychotic patients and found changes in position, tone and motility. Thus, the stomach in manic patients was found to be about 2 inches (5 cm.) above the normal position, while in depressed schizophrenic patients it was about 1 inch (2.5 cm.) above the normal. Sixty-four per cent of hypomanic patients had increased tone in the descending colon, while no depressed patient had hypertonicity of the colon. Henry considers first a physiologic explanation, presenting the hypothesis that these changes are indexes of the function of the vegetative nervous system in pleasant and painful emotional states. He also speculates as to the possibility of a psychoanalytic mechanism, suggesting that the retardation of visceral function might be a melancholic expression of narcissistic identification with the love object. He observes that whereas in hypomanic patients function is increased, in acute mania visceral function has already passed the limit of acceleration and begins to be retarded. Unless they were given laxatives, some of the depressed patients retained residues of food for more than two weeks.

DAVIDSON, Newark, N. J.

CHOICE OF NEUROSIS: MOLDING FACTORS OF NEUROTIC SYMPTOMS. A. KRONFELD, Arch. f. Psychiat. **93:**274, 1931.

This paper was presented at the International Congress for Individual Psychology, Berlin, Sept. 26 to 28, 1930. The author takes the stand that in the neurosis it is not only the flight into the disease process that can be understood psychologically, but also the choice of the particular type of neurosis. The whole problem is approached from the adlerian point of view. The neurotic reaction in general is considered as the expression of the concentration of efforts toward the gaining of a fictitious goal. Each one of the symptoms developed, however, must have a definite set of determinants in the structure of the patient's personality and its development.

Kronfeld presents a case in which there was, during the development and course of the neurosis, a shifting from one set of symptoms to another one. On the basis of the personality study of this particular patient and of material in his own experience, as well as in that of other workers in this field, he concludes that organ inferiorities are usually the deciding factor in the choice of a symptom.

MALAMUD, Iowa City.

FURTHER STUDY OF THE SYMPATHETIC INNERVATION TO SKELETAL MUSCLE: ANATOMICAL CONSIDERATIONS. SARAH S. TOWER, J. Comp. Neurol. **53:**177, (Aug.) 1931.

Using the muscles of the forelimbs of cats, dogs and goats, the author studied the innervation in normal material, in sympathetically denervated material and in material in which each of the three components of innervation had been isolated by degenerative section of the other two. In some animals the dorsal root ganglia were removed; in some the corresponding ventral roots were sectioned; in others the corresponding spinal nerves were cut distal to the dorsal root ganglia to eliminate both dorsal and ventral roots, and in others one or more sympathetic ganglia were extirpated. This material was studied after staining with methylthionine chloride, U. S. P. (methylene blue), and after the use of Bielschowsky and Ranvier's gold chloride technics. The nerve endings seen on the skeletal

muscle fibers were formed either by a myelinated nerve fiber or by a non-myelinated branch of such. The somatic origin of these fibers was demonstrated by degenerative section. The author concludes that the innervation of the intrinsic muscles of the forepaw of kittens 1 month old is not assisted by nerve fibers from the sympathetic ganglionic chain.

ADDISON, Philadelphia.

TUMOR OF THE RIGHT TEMPORAL LOBE. M. HARTMANN, Arch. f. Psychiat. **94**:847 (July) 1931.

Hartmann reports the case of a man, aged 40, who for two years had been having attacks, gradually increasing in frequency, during which he experienced overpowering olfactory hallucinations and marked dizziness. Prior to his coming to the hospital, the attacks occurred practically daily, and on one occasion an attack was accompanied by unconsciousness. At the same time he began to show signs of increased intracranial pressure, that is, headache and choking of the disks. Left facial weakness and ataxia of the left arm also developed. At the time of entrance, however, the attacks had ceased. The other symptoms persisted and were not relieved, even following a decompression operation. Four years after the first appearance of the symptoms, the patient died; autopsy showed a large tumor on the base of the right temporal lobe. The tumor had invaded the cortex toward the frontal lobe, but the olfactory nerve and the adjacent cortical structures were not involved. Histologically, the tumor was a glioma. A discussion of similar cases reported in the literature and their relationship to the development of olfactory hallucinations is included.

MALAMUD, Iowa City.

ABSENCE OF THE CERVICAL SPINE: KLIPPEL-FEIL SYNDROME. G. I. BAUMAN, J. A. M. A. **98**:129 (Jan. 9) 1932.

Six cases of the Klippel-Feil syndrome are reported in one man and five women. This condition consists in a numerical variation in the cervical vertebrae with more or less complete fusion into one mass. The deformity remains stationary and is not affected by any treatment. It is disguised with difficulty and unfortunately does not become much less conspicuous as the patient develops. The mirror movement, when present, does become less noticeable, but does not disappear. The deformity does not interfere with longevity. The classic symptoms, as given by Klippel and Feil, are: (1) absence or shortening of the neck, (2) lowering of the hair line on the back of the neck and (3) limitation of motion. Other symptoms occurring in a certain percentage of cases are: torticollis, mirror movement, facial asymmetry, dorsal scoliosis, other deformities, difficulty in breathing or swallowing and shortness of breath. No treatment is of any benefit. Operations, as for congenital torticollis, or active treatment, as for Pott's disease, should be avoided by making a correct diagnosis.

EDITOR'S ABSTRACT.

BACTERIAL PROTEIN FEVER IN THE TREATMENT OF SYPHILIS IN THE RABBIT. JOHN KOLMER, Arch. Dermat. & Syph. **24**:546 (Oct.) 1931.

Rabbits were given intratesticular injections of spirochetes, and then were subjected to bacterial protein fever by the intravenous introduction of typhoid-paratyphoid vaccine. A million organisms per kilogram were given on the first day; the dosage was increased until on the thirtieth day, a tenth injection was administered carrying 100,000,000 bacteria per kilogram. An increase in temperature of from 2 to 5 degrees Fahrenheit followed each injection and lasted for five hours. Following this treatment, the rabbits were examined, and chancres with actively motile spirochetes were found. The course was repeated with another set of infected animals, the administration of arsphenamine accompanying each inoculation with protein. On a third occasion, bismuth was used with the production of fever. Coley's fluid was similarly employed. In every case the testicular lesions were

reduced or disappeared entirely, but lymph glands remained infected and reproduced the disease when transplanted. From this, Kolmer concludes that bacterial protein fever has no curative value in the treatment of syphilis in the rabbit.

DAVIDSON, Newark, N. J.

MENTAL HYGIENE. JOSEF LUNDAHL, Acta psychiat. et neurol. (supp. 1), p. 1, 1932.

This article is a supplement to the *Acta psychiatrica et neurologica* and is a presentation in monograph form of the author's views on mental hygiene. In the first section he discusses the relationship between the individual and the environment, and the effect that particular environments have on particular individuals. This is a general introduction covering many of the concepts of modern social psychiatry. In section B he discusses the effect of the family and of the various types of family discords on the child, the influence of ordinal position in the family, and the way in which physical defects affect the psychic equilibrium. In the final section he discusses certain problems of social treatment, euthanasia and sterilization, the boarding out system for psychotic patients, the use of a vocational guardian and general child welfare activities. Many of the data he presents are well known to psychiatrists in this country, but certain of the chapters—that on the size of the family and on the boarding out system—are informative and well worth reading. The monograph is a detailed and thoughtful presentation of many of the well known concepts in social psychiatry. PEARSON, Philadelphia.

METABOLISM IN MYOTONIA ATROPHICA. SERGIUS MORGULIS and ALEXANDER YOUNG, Arch. Int. Med. **48**:569 (Oct.) 1931.

In common with other diseases of the muscles, such as pseudohypertrophic dystrophy, myositis fibrosa and amyotonia congenita, myotonia atrophica is accompanied by inability to fix creatine. Morgulis and Young report a case in which weakness and atrophy of the muscles of the limbs, face and neck and atrophy of the left testis developed in a man aged 28. There were: absent knee jerks, foot drop and opacities in the lens. The basal metabolic rate was persistently below normal, averaging —13. Creatine appeared in every specimen of urine. A diet low in nitrogen was administered, but the output of creatinine nitrogen was unchanged. From this, the authors postulate an inability to convert creatine into creatinine. Creatine administered orally was eliminated without retardation and without change through the urine. In healthy muscles a combination of phosphoric acid and creatine is formed, which is hydrolyzed and resynthesized during the course of muscle activity; the muscles in a patient with myotonia atrophica are unable to hydrolyze and reconstruct this compound.

DAVIDSON, Newark, N. J.

THE NEUROTIC CRIMINAL. PHILIP GETSON, J. Nerv. & Ment. Dis. **75**:498 (May) 1932.

The author describes the case of a man, aged 25, the oldest and much pampered son of poor Jewish parents, who possessed a quiet, retiring, masochistic make-up, with an unconscious incestuous attachment to the mother. After a period of irritability, loss of weight, insomnia and vomiting, he sought to punish his guilty ego by committing three burglaries in such a planless fashion as to indicate a desire for detection and punishment. When admitted to the Mount Sinai Hospital, he showed further masochistic and self-punishment tendencies by asking for needles and other means to discomfort, and welcomed his ultimate transference to jail after his family's funds had given out. The author wonders if centuries of such experiences as the Babylonian captivity, the Spanish inquisition and the Russian massacre may have caused the development of masochistic tendencies in a certain class of Jews, and hopes that the courts will ultimately discern the difference between the neurotic and the constitutional criminal. HART, Greenwich, Conn.

PROPHYLAXIS OF NEUROSYPHILIS. W. PIRES, An. assist. a psicop., 1931, p. 53.

Pires recalls that Kyrle, on examining systematically the cerebrospinal fluid in latent syphilis, ten years after the onset of the infection, found in a large number of cases humoral changes without any sign of a syphilitic lesion of the neuraxis. This fact shows the need for examination of the cerebrospinal fluid as the only means of securing a sure criterion for the prophylaxis of neurosyphilis. The author does not relegate to a secondary plane the clinical examination, which he regards as indispensable, but merely emphasizes the value of the biologic symptoms, which make it possible to catch the preclinical period when it is still possible to prevent the definitive invasion of the nervous system. Medicine has advanced much in recent years and is nearing the point where it can demolish the aphorism of Fournier, "Syphilis sleeps but never dies." Medicine is in possession at present of semiologic and therapeutic factors capable of giving to the syphilitic person a guaranty as to the future of the nervous system. Thus is realized the purpose of social medicine, which is to prevent diease.

EDITOR'S ABSTRACT.

PSYCHIATRIC REACTIONS FROM DYSINSULINISM IN A DIABETIC PATIENT. HERBERT J. CRONIN, J. Nerv. & Ment. Dis. **74**:478 (Oct.) 1931.

The case of a college girl, aged 21, with definite evidence of constitutional inferiority, feelings of inadequacy, inability to face reality, fears of the future and a desire to remain in a state of protection and support is described in detail. Prior to the discovery of glycosuria and high blood sugar, she had given a history of diplopia of two or three weeks' duration. After diabetic treatment with 15 units of insulin daily, diplopia recurred with mild confusional states. Analysis with the object of uncovering some hidden psychic material of traumatic character was given up as impossible. Subsequent attacks of diplopia were followed by a stuporous state in which silly, childish, assaultive activity, with delusions of poisoning and negativism suggesting an early schizophrenia, developed. The exact relationship of the mental phenomenon to the use of insulin is, however, not made clear.

HART, Greenwich, Conn.

TRACHEATION OF GRASSHOPPER NERVE GANGLIA. L. S. ROSS and R. R. TASSELL, J. Comp. Neurol. **52**: 347 (April) 1931.

Ganglia of grasshoppers were prepared by "Bensley A O B method" and cut at 4 microns in paraffin. The ganglia appeared richly provided with air tubes, varying in size from 1 or 2 microns to 20 or 25 microns in diameter. Trachea of from 10 to 20 microns are common at the boundary between the *Punktsubstanz* and mass of cytons. These send branches both to the *Punktsubstanz* and to the cell mass. Trachea and tracheoles are much more numerous in the *Punktsubstanz*, which the author suggests may mean that metabolism is more active in the *Punktsubstanz* than in the mass of cytons, where there is a small proportion of tracheoles. In a few instances tracheae were seen to have penetrated the cyton. The authors cite no references to the literature. They believe this to be the first record of the presence of air passages to have penetrated within a nerve cell.

ADDISON, Philadelphia.

OBSERVATIONS ON THE TREATMENT OF TRIGEMINAL NEURALGIA. WILFRED HARRIS, Brit. M. J. **2**:87 (July 16) 1932.

The author reviews twenty years of experience with injection of the gasserian ganglion since his first published paper on the subject. He concludes that when injections are made slowly and with care and patience, with light anesthesia produced by morphine-scopolamine or by procaine only, used locally, the results are most gratifying to both operator and patient, with no risk to life and at a minimum of expense and time. There can be no guarantee against eventual recurrence of neuralgia unless total and permanent anesthesia is produced. Many

patients may be free from pain for years following production of less than total anesthesia. Others may be permanently cured, but so long as there is some conduction of sensation, especially in the lower branches and even in the upper, recurrence must be considered. A second injection is as effective and is usually as easy to make as the first, if required. FERGUSON, Niagara Falls, N. Y.

THE TOPICAL DIAGNOSIS OF HEADACHE. EDGAR TRAUTMANN, Deutsche Ztschr. f. Nervenh. **110**:67 (Sept.) 1929.

The entire investigation of headache is founded on self-observation and exploration. One can differentiate primary localizations, irradiations and secondary localizations, for the specific etiology of which one is referred to the primary center. The establishment of primary centers is the first task to be undertaken. Delimitation of irradiation is accomplished by the exploration of zones of the slightest degree of painfulness. The pain center itself should be studied for character, degree and duration of the pain itself. The author analyzes the following five types of headaches: (1) migraine; (2) traumatic; (3) frontal lobe syndromes; (4) psychic; (5) headaches occurring in the vegetative neuroses. He regards headaches in which there is absence of cerebral symptoms as relatively harmless. In their presence, however, the importance depends on the localization and functional significance of the part of the brain affected. The establishment of a clinic for headaches is recommended for more accurate topical diagnosis.

HART, Greenwich, Conn.

BATH TREATMENT FOR DEAFNESS. JAMES ADAM, Brit. M. J. **1**:621 (April 11) 1931.

Six cases of chronic progressive deafness are reported, along with two cases of Ménière's disease. Treatment consists of hot baths containing a pound of commercial magnesium sulphate. One infers that the frequency of the baths is every other day the first week, once during the following week, then once every fortnight. Ten or fifteen minutes' duration is advised. Startling results are reported in some of the cases. One patient suffering from the Ménière complex was unimproved; the others showed pronounced improvement but only after the quantity of magnesium sulphate was doubled.

The author asserts that this treatment is as yet in the tentative stage, worthy of trial, but likely to succeed only in a minority of chronic cases. It fails when it fails to sweat the patient. It is not certain that magnesium sulphate is essential.

FERGUSON, Niagara Falls, N. Y.

ACID-BASE EQUILIBRIUM OF BLOOD IN PSYCHOTIC PATIENTS. K. E. APPEL, C. B. FARR and P. J. HODES, J. Nerv. & Ment. Dis. **75**:22 (Jan.) 1932.

The authors indicate that chemical measurements of the electrolytes and of the acid-base equilibrium in the blood serum by newly developed methods offer little that is enlightening in regard to 120 psychotic patients and 15 normal persons studied. The total base content of the blood plasma in manic-depressive psychoses and in other psychoses studied for comparison is normal. The blood chlorides in the same cases are also normal. There is an increased "acid residue" in the involutional depression of a degree, however, that is not markedly significant. The carbon dioxide content of the plasma, in the psychoses studied, lies within normal limits, except in cases complicated by "new admission" factors, toxic conditions, physical abnormalities and resistance to venipuncture. No relationship exists between habitual motor activity and the degree of acidosis in cases uncomplicated by resistance to venipunture or "new admission" factors.

HART, Greenwich, Conn.

THE SIGNIFICANCE OF CEREBROSPINAL FLUID SUGAR. ERNEST F. WAHL, Arch. Int. Med. **48**:446 (Sept.) 1931.

Although the normal cerebrospinal fluid sugar content is commonly reported as lying between 40 and 60 mg., Wahl found consistently higher values; his average is 89 mg. He also studied the ratio between spinal fluid sugar and blood sugar, emphasizing the importance of drawing the specimens simultaneously. This ratio is normally 76 per cent. In encephalitis he found a ratio of 77 per cent; in syphilis, 74; in meningitis, 34; in multiple sclerosis, 75; in posterolateral sclerosis, 72; in functional mental and nervous disorders, 79; in brain tumor, 76; in epilepsy, 79, and in diabetes mellitus, 75 per cent. In the latter disease the spinal fluid sugar was 170 mg. instead of the usual 89, but the glycemia was correspondingly high. Study of the spinal fluid sugar offers some diagnostic aid in differentiating meningitis from similar clinical pictures. A high reading for spinal fluid sugar is not in itself of any diagnostic value.

DAVIDSON, Newark, N. J.

REMARKS ON A CASE OF INTRACRANIAL TUMOUR. A. F. TREDGOLD and E. T. RUSTON, Brit. M. J. **2**:555 (Sept. 26) 1931.

The clinical symptoms and autopsy report are given in the case of a man who suffered from a tumor in the nasopharynx which presented some resemblances to a chordoma, though microscopic examination suggested more the probability of a malignant endothelioma arising from the basisphenoid bone. When first seen, the patient had a hard swelling in the nasopharynx which had been present for two years but which, up to that time, produced symptoms mostly referable to the nasopharynx. Three years later, it was apparent that the growth was causing much pressure on all the cranial nerves of one side, below and including the eighth, and that, though there was no actual involvement of the brain by tumor, the man presented marked and persistent dulling of perception, loss of memory and general intellectual deterioration.

FERGUSON, Niagara Falls, N. Y.

CONTACT INFECTION IN ACUTE POLIOMYELITIS. A. S. MACNALTY, Lancet **2**: 1186 (Nov. 28) 1931.

Two cases of acute poliomyelitis are described in which the infection appears to have been acquired through direct contact. The chief points of interest are: One patient contracted the disease in a hospital ward while undergoing treatment for a surgical condition, the probable source of infection being an undetected carrier, also an in-patient. The true nature of the illness was not recognized while the patient was in the hospital, which illustrates how liable the acute febrile stage of poliomyelitis is to escape detection. The second patient contracted the disease through kissing the first patient. The incubation period was two days, thus falling within the range of from two to ten days given by Wickman, Flexner and others. The resulting paralysis in both patients was of almost similar distribution, the condition affecting mainly the left shoulder girdle muscles.

BECK, Buffalo.

SEX-LINKED INHERITANCE IN MENTAL DEFICIENCY. AARON J. ROSANOFF, Am. J. Psychiat. **11**:289 (Sept.) 1931.

After analysis of data in ninety-five cases of mental deficiency in one or both members of pairs of twins, Rosanoff finds that sex is an etiologic factor in feeblemindedness. He postulates that the genes of intelligence may be carried not only in the autosome, but also in the x-chromosome. In thirty-three of his thirty-five pairs of monozygotic twins, both members were mentally deficient; in only thirty-two of the sixty pairs of dizygotic twins were both members of each pair feebleminded. Two thirds of the feebleminded patients in his series were males. Of twenty-seven pairs of twins of opposite sex, there were sixteen in which

only one member was deficient mentally; of these sixteen mentally deficient members, eleven were males. Rosanoff calls attention to the slight but consistent margin of superiority shown by girls over boys in scholastic records and intelligence tests.

DAVIDSON, Newark, N. J.

THE DIAGNOSIS OF DRUNKENNESS FROM THE EXCRETION OF ALCOHOL. SYDNEY SMITH and C. P. STEWART, Brit. M. J. **1**:87 (Jan. 16) 1932.

The authors report the results of their research on the excretion of alcohol in the breath and urine as a test for drunkenness. They found that the estimation of the amount of alcohol in the breath was valueless, except to prove that the individual had or had not been drinking recently. There was no constant relationship between the alcohol of the breath and that of the urine. It was found also that the differences in the alcohol concentration of the urine in different experiments with the same consumption of alcohol in similar circumstances cannot be correlated either with body weights or with the habits of the subjects in regard to the drinking of alcoholic liquors. Thus these findings would discount the value of tests for alcohol in urine and breath as criteria of drunkenness.

FERGUSON, Niagara, Falls, N. Y.

TUMORS OF MUSCLE TYPE: REPORT OF A GROUP OF CASES, WITH SPECIAL REFERENCE TO METASTASIS OF LEIOMYOSARCOMA TO THE BRAIN. J. STANLEY COHEN, Arch. Path. **13**:857 (June) 1932.

The incidence of muscle tumors varies with the type. Leiomyoma occurs frequently, especially in the uterus. Leiomyosarcoma is less frequent, according to the author's studies, than is generally claimed. What appears to be the first case of metastasis of leiomyosarcoma to the brain is described. Rhabdomyoma occurs rarely. Rhabdomyosarcoma is rare. The diagnosis of muscle tumors depends on close observation of the type of cell, i. e., the finding of spindle-shaped cells arranged in whorl formation or of cross-striations in large, irregular cells. Mallory's and van Gieson's differential stains are of diagnostic aid. The possible theoretical origins are enumerated.

WINKELMAN, Philadelphia.

THROMBO-ANGIITIS OBLITERANS (BUERGER): VI. CHEMISTRY OF THE BLOOD. MAE FRIEDLANDER and SAMUEL SILBERT, Arch. Int. Med. **48**:500 (Sept.) 1931.

In thrombo-angiitis obliterans there seems to be a tendency to concentration of the blood. This is evidenced by a comparison between the organic and the mineral matter content of the blood in Buerger's disease and in normal persons. Friedlander and Silbert report on the chemistry of the blood of forty persons with thrombo-angiitis obliterans, and contrast the results with those of the blood of a series of nonsmoking normal persons. The results were: ash content, 1.2 mg. (normal, 0.9); protein, 23 (normal, 17); calcium, 12 (normal, 10); phosphorus, 2 (normal, 2.2); chlorides, 55 (normal, 49), and cholesterol, 235 (normal, 165). No striking abnormalities were found in the amount of sugar.

DAVIDSON, Newark, N. J.

ACUTE DERMATITIS DUE TO OPIUM PREPARATIONS. N. B. HELLER, Arch. Dermat. & Syph. **24**:417 (Sept.) 1931.

Clinicians are warned to consider the possibility of opium causing an acute dermatitis in susceptible persons. Heller reports a case of generalized papulovesicular eruption following the external application of lead water and laudanum. A month later, the patient developed a similar rash after he had been given a proprietary cough medicine, presumably containing opium. Patch tests with a variety of drugs disclosed a marked reaction at the site of application of powdered

opium, and also at the area that had been treated with the proprietary drug. To round out his study, Heller then readministered the cough medicine internally, and this was promptly followed by the appearance of a rash.

DAVIDSON, Newark, N. J.

THE RELATION BETWEEN THE PITUITARY GLAND AND THE TUBER CINEREUM: IS THE PITUITARY GLAND INDISPENSABLE? L. N. KARLIK and I. A. ROBINSON, Arch. f. d. ges. Physiol. **227**:480, 1931.

Contrary to the opinion of Cushing and Biedl, the authors find that in dogs total extirpation of the pituitary gland is possible. The animals lived for from two months to three and one-half years after the operation, and showed the well known disturbances of growth, metabolism and development of the genitals. Efforts to extirpate the lobus bifurcatus necessarily result at the same time in injury of the infundibulum. Contrary to the opinion of Koster and Geesing, they found no hypertrophy of the lobus bifurcatus following extirpation of the other parts of the gland.

SPIEGEL, Philadelphia.

AN IMPROVED METHOD OF PROTEIN FEVER TREATMENT IN NEUROSYPHILIS. M. O. NELSON, Am. J. Syph. **15**:185 (April) 1931.

Because it is dangerous, often inaccessible and usually uncontrollable, malaria is not an ideal fever for therapeutic purposes. Ordinary foreign protein inoculation, on the other hand, does not produce a sufficiently high temperature to be of value. An effort to combine the efficiency of malaria with the safety and convenience of protein therapy is made by Nelson. He gives two intravenous injections of dead typhoid bacteria daily, the second being administered at the height of the fever produced by the first. The dosage is increased from about twenty-five to two hundred million organisms. In this way he produces fever, often as high as 107 F., by relatively small doses of vaccine.

DAVIDSON, Newark, N. J.

THE EXCITABILITY OF THE TONIC AND NONTONIC FIBERS OF A MUSCLE. WACHHOLDER and VON LEDEBUR, Arch. f. d. ges. Physiol. **228**:183, 1931.

The tonic fibers of the muscle, which react to acetylcholin with a contracture, form a separate bundle in some frogs' muscles (ileofibularis and gastrocnemius). It is therefore possible to compare their excitability with that of the nontonic fibers of the same muscle. If one stimulates the nerve, both parts of the muscle show the same excitability. If one stimulates the muscle fibers directly, one finds that only the tonic fibers have the same excitability as the corresponding nerves, whereas the nontonic fibers are less excitable (longer chronaxia). These results show that Lapicque's law of isochronism of nerve and muscle is not valid in all cases.

SPIEGEL, Philadelphia.

FORCED SPINAL DRAINAGE IN ITS RELATION TO INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. GEORGE M. RETAN, J. A. M. A. **99**:826 (Sept. 3) 1932.

Retan used forced spinal drainage in twenty-one cases of various infections of the central nervous system. In four autopsies in cases of septic meningitis no hydrosis of any organ was found. There was evidence of a washing of fluid through inflammatory areas. Products of inflammation were washed from the depths of affected areas. The field of greatest usefulness for forced spinal drainage was in diseases of the central nervous system characterized by perivascular round cell infiltrations. Forced spinal drainage was shown to be a safe procedure. Over two thousand hours of treatment have produced no alarming symptoms.

EDITOR'S ABSTRACT.

THE BLOOD GROUPING OF MONGOLIAN IMBECILES. L. A. PENCORE, Lancet **1**: 394 (Feb. 20) 1932.

A marked difference in the distribution of the four blood groups between Europeans and Mongols has been observed. In fact, the grouping seems to be characteristic for each race. It was thought, therefore, that this test could give data as to the correctness of Langdon Down's theory that Mongolian imbecility is due to an admixture of Mongolian blood among Europeans. The blood grouping in 158 definite Monoglian imbeciles of English extraction was studied. The results do not support the hypothesis, for the distribution of the four blood groups of English nonimbeciles closely resembles the groupings in the defectives.

BECK, Buffalo.

THE THERAPEUTIC PENITENTIARY. L. VERWAECK, Arch. de neurobiol. **11**:587, 1931.

In Belgium the penitentiary is being changed into a psychiatric hospital. In all cases a detailed study is made, and when indications are found psychiatric treatment is carried out in a special hospital penitentiary. Punishment has thus proved to be unnecessary.

CRANIOGRAPHY ENCEPHALOGRAPHY AND VENTRICULOGRAPHY. A. SUBIRANA, Arch. de neurobiol. **11**:616, 1931.

This is an excellent review of actual methods. The author presents numerous photographs of patients that show clearly the advantages and disadvantages of the two methods. A complete bibliographic list makes the review of great value for Spanish readers.

FUNICULAR MYELITIS OF LICHTHEIM IN PERNICIOUS ANEMIA: CURE WITH LIVER DIET. G. R. LAFORA and M. BUSTAMANTE, Arch. de neurobiol. **12**:23, 1932.

A new case of nervous complications in pernicious anemia is added to the list published by Woltmann (*Am. J. M. Sc.* **157**:400, 1919). The importance of early diagnosis and treatment with liver extract is stressed.

MUSICAL APTITUDE AND ACOUSTIC HALLUCINATIONS IN THE FAMILY OF A PATIENT WITH CATATONIC SCHIZOPHRENIA. J. M. SACRISTAN, Arch. de neurobiol. **12**:40, 1932.

In several members of the family of a patient musical aptitude appeared together with acoustic hallucinations and other psychopathic symptoms.

A CASE OF ENCEPHALOMYELITIS AFTER MEASLES. W. LÓPEZ ALBO, Arch. de neurobiol. **12**:50, 1932.

A new case is added to the lists of Foerd (*Bull. Johns Hopkins Hosp.* **43**:140, 1928) and Greenfield (*Brain* **52**:171, 1929).

LORENTE DE NÓ.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Feb. 14, 1933

BYRON STOOKEY, M.D., *Chairman*

EFFECTS OF LESIONS OF THE INFERIOR CEREBELLAR PEDUNCLE AT VARIOUS LEVELS IN MONKEYS. DR. ARMANDO FERRARO and DR. S. E. BARRERA (by invitation).

As the initial part of a general analytic study of the interrelations between the various cerebellar components and the vestibular apparatus, we present an experimental report on the effects of lesions of the dorsal spinocerebellar component of the inferior peduncle in monkeys (Macacus rhesus). The presentation emphasizes the importance of correlating behavior disturbances with careful anatomic control. In evaluating the symptomatology following lesions of the dorsal spinocerebellar tract (Flechsig) three typical levels may be considered and typical cases of monkeys, in the acute and chronic stages after operation, illustrated. The spinal level is a lesion of the dorsal spinocerebellar tract at about the third cervical segment. The next higher level is a lesion of the same tract in the area ovalis at a point near the middle region of the nuclei of Goll and Burdach. The third level is a lesion of the tract at the zone of entrance of the eighth nerve.

In the spinal cord with a unilateral lesion of the dorsal spinocerebellar tract in the acute phase, the monkey showed ipsilateral ataxia, dysmetria, diminution of the deep reflexes, hypotonia and loss of the placing and hopping reflexes, with, however, normal sensory functions and a well retained grip. With a bilateral lesion at the same level the same changes were present. The animals showed a rapid amelioration of the symptoms, with practically normal function at the end of from two to three weeks and practically no residual symptoms after three months. At this stage the animal showed only slight diminution of elasticity in the limbs on jumping. At the next higher level, in the acute phase, with both unilateral and bilateral lesions, the same changes, including weakness, ataxia, dysmetria, hypotonia, hyporeflexia and loss of the placing and hopping reflexes, were present. The degree of disability, however, seemed in some cases to be slightly greater than that at the lower levels, although essentially of the same type. This is explainable in the light of the involvement of some fibers originating from the nuclei of the posterior columns, the nucleus funiculi lateralis and possibly the inferior olives, which might partly enter the area ovalis, mixing with the fibers of the dorsal spinocerebellar tract. At the still higher level of entrance of the eighth nerve, the same findings were again obtained; here, likewise, the involvement was slightly more severe, and is explainable on a basis similar to that already mentioned. In both of the last two groups of animals the symptoms again disappeared rapidly, just like those caused by lesions in the levels of the spinal cord; the monkeys were likewise essentially normal in the chronic stage at two or three months.

We never found the rolling movements which have been described by the majority of the authors who previously experimented on the corpus restiforme. The absence of rolling movements was also true in the presence of lesions of the corpus restiforme involving the olivocerebellar fibers at high levels. The rolling movements described, among others, by Ferrier and Turner, and by Bechterew are the expression of a complication occurring in the vicinity immediately surrounding the corpus restiforme.

As an example of the tremendous increase in symptoms and the addition of new ones that follow involvement of the area adjacent to the vestibular nuclei, moving pictures of an animal were projected showing rolling movements in the acute stages and tremors of the head and limbs in the chronic stage. From a topographic standpoint we believe that the area of the inner portion of the cerebellar peduncle (Innere Abtheilung des Kleinhirnstiels), bundle of Monakow, should be considered entirely separate from the corpus restiforme; the symptoms following lesions of this area should not be confused with those that follow involvement of the various components of the corpus restiforme itself.

The nervous system of each of the animals operated on and studied physiologically was cut in serial sections and stained, according to the period of the investigation, by the Marchi, Weigert or Nissl stain. The extent of the surgical lesion was documented by a number of serial sections projected with lantern slides.

DISCUSSION

DR. RICHARD M. BRICKNER: The dorsal spinocerebellar tracts conduct impulses which should be identical with those traveling in the dorsal columns, because the dorsal spinocerebellar tracts arise from the cells of the column of Clarke, and these cells are innervated by collaterals from the dorsal columns. The technic of Ferraro and Barrera, now that it has been worked out, could be used to study the differences in result between section of the dorsal columns and section of the dorsal spinocerebellar tracts. It would be interesting to hear the results of any such experiment if it has been made.

DR. J. G. DUSSER DE BARENNE, New Haven, Conn.: These are actually among the first well made and controlled sections of the various cerebellar peduncles of which I know. I will ask only one of many questions. There can be no doubt that in the monkey shown there is some hypotonia after section of the inferior peduncle. Until now I have had no experience with total cerebellar extirpation in the monkey. Have you had experience with it? If so, did you also find indications of atonia or hypotonia? I cannot accept that phenomenon after total ablation of the cerebellum in the cat and dog.

DR. FRANK H. PIKE: I wish to add one confirmatory remark; in the cat, for instance, if there is a lesion of the vermis one notes movements of the head for a time. These movements may practically disappear, becoming apparent only when the cat is regarding something intently, when one sees a fine tremor. Ordinarily, both internal ears may be removed in the cat without giving rise to any permanent movements of the head. However, if the ears are taken out, a year after the cerebellar lesion, I have never seen recovery from the movements of the head which then appear. The two lesions together do a great deal more than one might expect as the sum of the two.

DR. LOUIS HAUSMAN: It is accepted that the dorsal spinocerebellar tract is more or less associated with Clarke's column and not particularly with the function of the hind limbs, which we attribute to the ventral spinocerebellar tract of Gowers. It seems to me that in this presentation the fact was stressed that the hind limbs were as much affected as the forelimbs. I wish to know if there is any particular explanation for that manifestation.

I wish also to emphasize that this presentation brings out once more the indefiniteness of the cerebellar functional mechanism. I mean this: I had the opportunity to work on the roof nuclei in cats several years ago, and to a great extent I observed the same defects noted after section of the restiform body. Yet the restiform body does not go to the roof nuclei, or, in fact, to any of the nuclei of the cerebellum. I mention this to stress that it is very difficult to come to any conclusions about the specific cerebellar mechanisms and their functions and the localization of these functions in the cerebellum.

DR. ARMANDO FERRARO: We thought that our experimental work on the effects of lesions of the cerebellar peduncle might have the double advantage of clarifying some anatomic questions and some of the clinical manifestations follow-

ing such a procedure. It would be premature now to compare the results of our physiologic experiments with the clinical symptoms in man. We expect to reach this point as an ultimate stage of our investigation.

From an anatomic standpoint we are also interested in several questions, one of which has been touched on by Dr. Hausman. We, as well as he, have been puzzled by the question of what the course of the two spinal cerebellar tracts really is. We think that because of the similarity in function there should be a closer anatomic relationship between the dorsal and ventral spinocerebellar tracts. Though we have not as yet examined the material showing the degeneration following section of the ventral spinocerebellar tract alone, we believe from the study of the course of the dorsal spinocerebellar tract and from the study of the course of other components of the corpus restiforme that we may eventually dissent from the majority of authors who make too sharp a differentiation between the course of the dorsal and ventral spinocerebellar tracts. As Bruce has established experimentally, we think that it is possible that fibers of the ventral spinocerebellar tract follow the same course as those of the dorsal tract. Unfortunately, Bruce did not follow the course of the tract high enough; we expect to fill this gap in his investigation.

With regard to Dr. Brickner's question, we are fortunately in a position to answer this because in our series of experiments we have included a certain number of cases in which experimental lesions of the nuclei of Goll and Burdach were made. In a few instances the nuclei of Goll and Burdach alone, and in some others the nuclei of Goll and Burdach plus one or both restiform bodies, have been damaged. The symptoms after lesions of the nuclei of Goll and Burdach differ essentially from those following lesions of the dorsal spinocerebellar tract. I shall not discuss the details of this, as the material will form the subject of a separate communication in which the symptoms following lesions of the nuclei of Goll and Burdach will be compared with those following lesions of the restiform body. I wish, however, to ask Dr. Barrera to answer the question of Dr. Dusser de Barenne concerning the tonus in acerebellar monkeys.

DR. S. E. BARRERA: We have serial sections of a completely acerebellar monkey. In this animal there was no evidence of hypotonia; in fact, the animal showed a general slight increase in tone. The same type of phenomenon occurs with lesions in some other regions, as, for example, in the unilateral motor area, when the tone may be diminished, while in bilateral lesions there may be an increase in tone. I do not think that we can reason accurately concerning abnormalities of tone from the conditions in partial lesions to those in total ablation.

With regard to Dr. Brickner's question, I may add that in some lesions of the partial type of the dorsal columns below the nuclei of Goll and Burdach, the symptoms may have some elements similar to those in bilateral dorsal spinocerebellar lesions in the monkey. When the lesion is at the level of the nuclei, however, or if it involves a considerable portion of the posterior column, an entirely different picture ensues, as Dr. Ferraro has stated. The picture in these lesions does not seem to show an appreciable degree of cerebellar symptoms.

In answer to Dr. Pike, it is of interest that associated symptomatology of the vestibular and cerebellar apparatus is apparently very important, as he has found. We note in the monkey certain twists of the head that do not follow cerebellar lesions alone or lesions of the eighth nerve alone, but occur with combined lesions of the two. Apparently simple vestibular lesions, particularly of the eighth nerve, are much more important in the cat than in the monkey, whereas in the monkey the predominant symptoms of vestibular type seem to be associated with central lesions of the vestibular apparatus, in contrast to the marked vestibular disability which results in the cat with a purely peripheral lesion. Regarding the tremor of the head and extremities, we have noticed the same type of tremor with isolated lesions of the central apparatus in monkeys, that is, in vestibular nuclear lesions.

THE HUMORAL TRANSMISSION OF CHORDA TYMPANI STIMULATION. DR. HAROLD G. WOLFF (by invitation).

Loewi (*Arch. f. d. ges. Physiol.* **189**:239, 1921) observed that stimulation of the vagus branches to the heart causes the fluid contained in the heart chamber to be so altered as to be capable (if removed during the period of stimulation) of reproducing the initial action of the vagus on the same or another heart when later introduced into its chambers. Loewi (*Arch. f. d. ges. Physiol.* **214**:678, 1926), his co-workers and others during the next few years defined the nature of this liberated material, called by Loewi "vagus stuff." This substance, as tested in the Straub preparation, slows the rate of the heart and decreases the height of its contractions. It causes a tested strip of intestine to shorten its initial length and to contract more frequently. It is destroyed by extracts made from heart muscle, liver and kidney and by blood. This takes place rapidly at 37 C. and at a p_H of from 6 to 7.5, and is delayed at 0 C., and p_H 4. The ability of the organ extract to break down "vagus stuff" is abolished if the extract has been heated to 56 C. or exposed to fluorescent or ultraviolet rays. The potency of a solution containing "vagus stuff" is not increased by acetylization. Its action is abolished by atropinizing the test objects mentioned and is prolonged or accentuated by previously physostigminizing the tissues.

With such a means of prolonging or exaggerating the effect of stimulating parasympathetic nerves, it became possible to test more readily for the existence of similar phenomena in mammals and thus lend support to the conception of humoral transmission of autonomic effects. For this purpose the chorda tympani nerve with its end-organ, the submaxillary gland, was selected for the following reasons: 1. Stimulation of the chorda tympani produces vasodilator effects; therefore it should be possible to demonstrate the liberation of a vasodilator substance through its action on other vascular beds. 2. The chorda tympani induces salivation; hence it should likewise be possible to demonstrate the liberation of a substance inducing salivation in the other, or nonstimulated gland. 3. It is technically simple to manipulate.

In the cat, Babkin, Gibbs and Wolff (*Arch. f. exper. Path. u. Pharmakol.* **168**:32, 1932) exposed the submaxillary gland with its chorda tympani and salivary duct, and insulated it from the rest of the animal. A cannula was placed in the salivary duct so that the saliva produced could be measured, and the veins were exposed so that venous outflow could be blocked by clamping when desired. A cannula was placed in the femoral artery and connected with a mercury manometer. Physostigmine in doses of 0.25 mg. was given one or more times.

It could be shown that following stimulation of the chorda tympani there was a fall in the systemic arterial pressure as measured in the femoral artery. Thus, apparently, a vasodilator substance produced in the submaxillary gland during stimulation of the chorda was carried into the systemic circulation and affected other vascular beds. This conception was supported by the observation that stimulation of the chorda after blocking venous outflow from the gland, by clamping the veins, was not followed by a fall in systemic arterial blood pressure.

To determine whether there was also liberated a substance capable of activating the salivary gland, Babkin, Alley and Stavraky (*Tr. Roy. Soc. Canada*, 1932, sect. V, p. 89) placed a cannula in the duct of the right submaxillary gland as before mentioned, but then, after physostigminizing the animal, stimulated the left chorda tympani. It was observed that stimulation of the chorda tympani on the left side increased the production of saliva on the right side, and also accelerated the blood flow in the right denervated submaxillary gland. In addition, it lowered the systemic blood pressure. Reflex influences, including an increased output of epinephrine and the effect of the lowering of the blood pressure, were excluded as causative of the phenomena. Atropine abolished it. Since the whole phenomenon was abolished or greatly diminished after clamping the vein of the submaxillary gland, since the latent period preceding the fall of the systemic blood pressure was much longer than in the case of stimulation of a depressor nerve, and since the acceleration of the secretion in the control gland was always delayed in compari-

son with that of the stimulated gland, it was postulated that a special chemical substance is formed in the submaxillary gland, is preserved from inactivation by physostigmine and is transferred in the blood stream, causing secretion and vasodilatation in the opposite gland and a fall in the systemic blood pressure.

There remained one further step to complete the evidence, namely, the isolation (in vitro) of the chemically active substance resulting from stimulation of the chorda tympani. In the original experiment, in a few instances, blood collected from the submaxillary gland during the period of stimulation of the chorda, when reinjected, caused a drop in systemic arterial pressure, an effect not produced by control samples of blood. This depressor effect, however, was inconstant and technically unsatisfactory.

However, Gibbs and Szelöczey (*Arch. f. exper. Path. u. Pharmakol.* **168**:64, 1932) utilized a perfusion pump, by means of which they were able to perfuse the submaxillary gland with physiologic solution of sodium chloride (Tyrode) both before and during the period of stimulation of the chorda. The perfusate collected during stimulation of the chorda contained a substance which has the following properties: It causes vasodilatation and increases salivary production; it has a negative inotropic action on the isolated heart; it decreases the initial length of the intestine and increases the rate of contraction; it breaks down in alkaline solution at temperatures of about 37 C., and is stable for days in the cold and in acid solution; it is destroyed by blood and by tissue extracts, unless the latter have been previously treated with physostigmine. These effects are increased by, but not due to, physostigmine, since the perfusate collected from nonphysostigminized animals has qualitatively similar, if quantitatively less, striking properties. Its action is abolished by atropine, for when tissues are atropinized the perfusate has no effect. However, the perfusate collected from an atropinized submaxillary gland during stimulation of the chorda is still effective, in the manner described on unatropinized tissue. In brief, "chorda stuff" is very similar to Loewi's "vagus stuff" and both simulate acetylcholine in their effects.

These experiments demonstrate that there is liberated by stimulation of the chorda tympani an intermediate substance soluble in body fluids. They further demonstrate in mammals the humoral transmission of the effects of autonomic nerve stimulation.

DISCUSSION

DR. MCKEEN CATTELL: Dr. Wolff has given a clearcut presentation of his experiments on the salivary gland, in which he has demonstrated a functional control by a humoral mechanism. The number of organs in the body in which such control has been shown to exist has increased in an interesting way during the last few years. As Dr. Wolff has mentioned, it was only twelve years since Loewi first demonstrated the existence of a humoral mechanism in nervous activity. This was a somewhat revolutionary doctrine to most physiologists and has been rather slowly accepted, especially in this country. It is only perhaps in the past few years that one can talk about this in physiologic circles with perfect freedom.

In connection with this work by Dr. Wolff, which is particularly interesting as the first demonstration, I believe, of the control of a gland by a humoral factor, I may mention the work of Dr. Cannon, who has shown that through the stimulation of the sympathetic various effects may be mediated. For example, if he stimulates the sympathetic fibers to the tail, producing pilomotor and vasoconstrictor responses, a substance is liberated which produces effects elsewhere in the body, resembling the effect produced by the injection of epinephrine. Among other experiments which might be mentioned are those of Bain with a perfusate obtained during stimulation of the vasomotor nerves to the tongue, which may produce effects elsewhere; also the experiments of Finkleman, who showed that the perfusate from a portion of the intestine contains a sympatheticomimetic substance when the sympathetic nerves going to it are stimulated. There are many other examples.

With this impressive demonstration I feel that one may have a certain assurance in guessing that the functions of the autonomic nervous system in general may

be mediated by such means, i. e., through a chemical substance which is liberated by nervous activity. After all, this is more satisfying than to regard it as a purely mechanical thing. It is difficult for me, at any rate, to understand how such effects as that of the vagus on the heart or the chorda tympani on the salivary gland can be mediated in a mechanical way. It is much easier to think of chemical stimulation for such effects.

I wish to ask Dr. Wolff two questions. Has he tried the effects of sympathetic stimulation of the salivary gland? Have his experiments thrown any light on the action of atropine under such conditions?

DR. J. G. DUSSER DE BARENNE: In the lantern slide in which Dr. Wolff showed the effects of stimulation of the left chorda tympani and investigated the influence of the perfusate on the other gland, he clamped the vein of the stimulated gland and found that the perfusate had no influence on the salivary secretion of the other gland. The second part of the record showed a marked influence on stimulation of secretion when the clamp was released. Is that a continuous record? I mean, was this procedure done only a few seconds later?

DR. H. G. WOLFF: There was no time relationship between the two records.

DR. J. G. DUSSER DE BARENNE: Then why has the release of the clamp as such no influence? Is it because the substance is destroyed too quickly or is it in too small a concentration?

DR. LOUIS HAUSMAN: When Dr. Wolff stimulated the fibers of the chorda tympani, was that nerve cut or were the central fibers intact?

DR. H. G. WOLFF: The central end of the nerve was cut. We were dealing with the peripheral apparatus at the time. No reflex activity was possible.

DR. LOUIS HAUSMAN: There was, therefore, no chance for reflex activity to be established through the central mechanism.

DR. H. G. WOLFF: In answer to Dr. Cattell's first question, unfortunately I have no data on the effects of stimulation of the sympathetic on the salivary gland.

In answer to the question concerning the action of atropine, it was possible through the use of the perfusion pump to atropinize the animal in such a way that stimulation of the chorda produced no salivation. Examination of the perfusate, however, demonstrated that it still had the properties that were found in the perfusate of the animal which had not received atropine. In other words, atropine does not paralyze the parasympathetic nerve endings. There was found in the perfusate a substance which was capable of simulating the effect of stimulation of the chorda tympani in a test animal, though not in the animal that had been atropinized. Thus, the effect of atropine seems to be to antagonize "parasympathetic stuff," in this instance, "chorda stuff."

In answer to Professor de Barenne, it might be said that the subsequent release of the clamp on the vein of the gland in no instance was followed by a drop in blood pressure or by an increase in salivation on the opposite side. Plattner was able to show that "vagus stuff" in contact with blood was usually destroyed in approximately twenty seconds. The concentration in the experiment was an amount equivalent to 0.05 gamma of acetylcholine. It is our opinion that the retention of the "chorda stuff" in the gland causes its destruction.

SOME EXPERIMENTS RELATING TO THE ORGANIZATION OF THE MECHANISM FOR RESPIRATION. DR. F. H. PIKE, Columbia University (by invitation).

The localization of the central mechanism for respiratory movements in the lower portion of the medulla oblongata was indicated by Lorry and definitely shown by Legallois. Flourens' announcement of the *noeud vital* came some years later. The fact that bilateral vagotomy produced severe respiratory disturbances was known considerably earlier. In conformity with the general point of view

with regard to the nervous system, the idea of a circumscribed "center" for respiration arose. In some way which has never been made quite clear, a "center" was supposed to preside over the entire execution of any motor response; but so long as there was only one center for any given activity, the difficulty did not become acute.

Marckwald's experiments on the effects of transection of the brain stem at the lower border of the midbrain combined with bilateral vagotomy introduced a certain element of perplexity into the situation. An animal will continue to breathe indefinitely after bilateral vagotomy so long as the midbrain is intact. Transection below the midbrain alone does not give rise to any severe respiratory disturbances. But after both of these procedures the respiratory rate falls very low—to 3 or 4 a minute—and the movements of the diaphragm are irregular and spasmodic, giving rise to the sobbing type of respiration. The assumption of accessory centers in the midbrain did not really clear up the perplexity.

While it has long been known that stimulation of the central end of an afferent nerve, e. g., sciatic or brachial, is generally followed by great acceleration of the respiratory rhythm, little consideration was given to the relation of the dorsal spinal roots to respiratory movements. Either clinical observation of respiratory movements in such conditions as advanced tabes dorsalis has been absent or the records have been so well buried that we have been unable to find them. One does find statements, however, that the quadratus lumborum muscle fails to act normally, so that in the descent of the diaphragm in tabes the ribs are pulled in at the lower border of the thorax, thus giving rise to the "girdle" effect. Experimental division of the dorsal roots of the thoracic portion of the spinal cord abolishes all movements of the ribs, so that the whole burden of the respiratory activity falls on the diaphragm. There is, however, no actual paralysis of the thoracic musculature, since costal movements are resumed following section of the phrenic nerves or after the stomach or abdominal cavity is filled so full of fluid that the diaphragm is no longer able to contract.

Respiratory movements have a rhythm and depth sufficient for the purposes of the animal when either bilateral vagotomy alone or division of the dorsal roots alone is done. But when both are done the movements become extremely slow—3 or 4 a minute—with the sobbing type of respiration. It is possible, therefore, to duplicate by section of peripheral nerves and nerve roots alone, without any actual invasion of the central nervous system, the results of combined bilateral vagotomy and transection below the midbrain. Nor does transection below the midbrain add anything to this picture.

The effect of anatomic division of all the thoracic and cervical dorsal roots without any actual injury within the central system is more severe than the effect of transection below the midbrain, since the latter does not so profoundly affect costal movements.

The inadequacy of the idea of a "center" is shown by lesions of the dorsal roots alone. For without afferent impulses the "center" is powerless to control the response of the effectors. It is believed that the afferent impulses from the thoracic and abdominal muscles do not reach the "center" in the medulla directly, but only indirectly by way of ascending paths to the midbrain and thence by descending paths to the medulla. The relation of afferent impulses over the vagi to the mechanism in the medulla seems more direct. The midbrain is not regarded in the light of an accessory center, since there is no evidence that any cells in it are more sensitive to carbon dioxide or hydrogen ion changes than any other cells. It is simply a region through which afferent impulses pass on their way from the costal musculature to the central mechanism in the medulla. The midbrain seems to have acquired its importance as a part of the respiratory mechanism in fish in connection with afferent impulses from the mandibular musculature over the mandibular division of the fifth cranial nerve. But the fifth nerve has lost its respiratory importance in mammals.

The central course of the afferent fibers of the phrenic nerves is not known. Frequently greater changes of respiratory rhythm follow section of the dorsal roots of the cervical nerves than section of the thoracic nerve. But the movements of the diaphragm are even and regular as long as the vagi remain intact.

DISCUSSION

DR. J. G. DUSSER DE BARENNE: I think that the facts which Dr. Pike has presented speak clearly for themselves. Will Dr. Pike state briefly what is his conception of the influence of the respiratory centers of the midbrain? Apparently there must be higher centers than the medullary respiratory center, which under special conditions, for instance, section of the vagi, give rise to the slowed respiration (4 per minute or even as low as 1 per minute) and the abnormal type of respiration with a very strong inspiratory gasping movement. From this old observation of Kronecker and Marckwalder, which has been confirmed everywhere when it has been investigated, I cannot think of any way other than that there are higher centers which are important, under certain conditions at least, for respiration. I have the impression that Dr. Pike is inclined, to some extent at least, to disregard these centers.

DR. F. H. PIKE: The number of different combinations that one may get from even such an apparently simple system as the respiratory system is rather bewildering. In regard to the specific question by Dr. Dusser de Barenne, it seems probable that the afferent impulses from the intercostal muscles go up through some pathway, which I do not at all know anatomically, to the midbrain. We are at a little disadvantage, anatomically, here because it is not really good form to eliminate the respiratory mechanism and keep the cat alive long enough for degeneration to occur. We must do the best we can without getting much degeneration. I think that this midbrain mechanism was probably established in fishes. I have not yet worked on this in Cyclostoma. It has been well worked out in fishes. There is a definite relationship between the mandibular muscles in the fish and the mandibular branch of the fifth nerve and the midbrain. The fifth and seventh are not important motor respiratory nerves in the mammal, but apparently this relationship of midbrain to respiratory mechanism, laid down in the fish, has persisted in the mammal.

I rather think that afferent impulses from the intercostal muscles go up to the midbrain first and then down to the bulbar mechanism. There are a number of experiments which I think show that. I do not know where the phrenic afferents end. I am inclined to think they are a little lower down. There is a closer connection between the vagi and the diaphragm than between the vagi and the control of the movements of the intercostal muscles. That seems to come out pretty clearly.

With regard to the afferent impulses from the intercostal muscles, I think that probably there are three points at which they work: (1) in the ventral gray of the spinal cord; (2) in the midbrain, where they come into connection with some central nucleus and find some pathway downward—what it is I do not know—and (3) the point at which these impulses coming downward from the midbrain are added to whatever is coming into the bulbar mechanism itself.

I have nothing to add except this, a remark of Hughlings Jackson about organization in general, that if all mechanisms were as highly organized as those for respiration, there would be little possibility of new attainments in the rest of the nervous system. We must look for different types of organization if it is admitted that man can learn things.

SOME OBSERVATIONS ON SPINAL ANIMALS (WITH DEMONSTRATION). DR. J. G. DUSSER DE BARENNE, New Haven, Conn. (by invitation).

In previous experiments, together with Dr. Y. D. Koskoff (*Am. J. Physiol.* **102**:75, 1932), the occurrence of a marked flexor rigidity of the hind legs was described, often associated with persistent priapism in the male cat on "secondary"

decapitation, i. e., when the animal was first decerebrated and subsequently decapitated. This syndrome appears only when the animal is put in the symmetrical prone position on the table. In the side or the supine position or when the animal is held in the air, this springlike flexor rigidity is not present in the hind legs. Subsequent experimentation showed that this syndrome is present, under the specified conditions, also in the "primary" low spinal preparation, in which the cord is transected at the level of the first lumbar segment. It could be proved that exteroceptive and proprioceptive impulses arising in the hind legs from the contact with the table are the adequate stimuli to produce this flexor rigidity. The latter group is especially important. The flexor rigidity shows constantly typical changes when the front part of the body is rotated. The flexor rigidity increases markedly in the "occiput legs," diminishing strongly in the "face leg." In a great number of cases, active extension of the face hind leg can be observed. These changes are looked on as due to afferent stimuli arising in the caudal vertebral column on rotation of the front part of the body, and if this interpretation is true, to be a new link, perhaps the most distal one, in the chain of Magnus-de Kleijn reflexes. Of course, these changes in flexor rigidity cannot be interpreted as due to tonic labyrinthine or neck reflexes, since they occur in the low spinal preparation. (See, however, the addendum at the end of the discussion, which proves that this interpretation was erroneous and must be replaced by the conception given there.)

DISCUSSION

DR. F. H. PIKE: Again I think that Dr. Dusser de Barenne's facts speak for themselves. Some years ago I became skeptical of this statement that everything of a reflex nature below the level of transection was abolished. One can show immediately after total elimination of the medulla that there is some tonic element of a reflex nature which goes through the spinal cord, affecting the skeletal muscles. For instance, the blood pressure of a spinal animal with the arteries to the head completely tied off will run to about 60 or 70 mm. of mercury. If one cuts all the dorsal roots of the spinal cord, the pressure falls to about 30 mm. There is a possibility that that may be vascular or that it may be maintained by the skeletal muscles, as von Länderer suggested. The separation is possible by means of curare, which throws out the skeletal muscles and leaves the vascular element intact. The blood pressure falls to about 30 or 33 mm. after an injection of curare. Therefore, I should say with von Länderer that there is some tonic element of a reflex nature in the skeletal muscles immediately after complete transection of the spinal cord. That being the case, I do not see why one does not get more reflexes in these animals than occur, provided the paths are what they are supposed to be. I have grown a little skeptical of that.

The change of position of the vertebral column, with its effect on the flexor mechanism, is of interest. I had never seen it before. There is no question that it is there. I think that the results speak for themselves.

DR. MCKEEN CATTELL: I wish to ask what the coordinating mechanism is by which this flexor reflex or flexor tonus is mediated when the animal's head is turned to one side or the other. What pathways are involved?

DR. HAROLD G. WOLFF: I observed that when you lifted the animal from the table the muscles became flaccid and the legs hung loosely. On turning the head and the body under these circumstances, can you get effects such as you observed when the hind parts of the animal were resting on the table?

DR. ISRAEL S. WECHSLER: I wish to ask three questions. I noticed that the leg of the animal on the chin or face side extended even though the tonus lessened. Now the leg extends on the chin side and flexes on the occiput side when eliciting the tonic reflexes of the neck, except that there is also increased tonus. The second question, then, is, How are these impulses mediated at all with complete section of the spinal cord, seeing that one cannot get tonic neck

reflexes in lesions below the upper cervical cord? Third, is this a question of torsion of the pelvis? Stenvers once described a reflex *du bassin*, and I wonder whether this is the same type of reflex.

DR. LOUIS HAUSMAN: Dr. Dusser de Barenne is such a great experimentalist that I hesitate to put a question, but in doing so I merely wish to clarify the problem in my own mind. I gather that in this animal the exteroceptive and proprioceptive impulses play an important part in maintaining the tonus of certain muscle groups. That seems to be apparent. When the animal was lifted, the flexor rigidity in the hind limbs was diminished. As soon as the animal was put on the table the flexor rigidity came into being. When Dr. Dusser de Barenne rotated the head of the animal, it was obvious that the flexor rigidity in the hind limb on the side of the occiput was increased. It occurred to me that there was this possibility: With the animal lying on the table with the head rotated in that manner, it was possible to transmit pressure to the opposite side; that is, rotation of the occiput to the left would produce greater pressure on the left hind limb than on the right hind limb. If that is so, one is really physiologically stimulating or augmenting the exteroceptive and proprioceptive impulses in that limb. That in itself should increase the flexor rigidity in that limb, and for obvious reasons one would expect the flexor rigidity in the opposite limb to diminish.

DR. DUSSER DE BARENNE: In reply to Dr. Cattell: I thought and still think, although the discussion by Dr. Hausman brought up a difficult point, that this change in flexor rigidity—the augmentation on one side and the diminution on the other—is brought about by the rotation and torsion in the caudal part of the vertebral column. Although it is rather difficult to put it to an experimental test, I think that the proprioceptors are involved there.

In reply to Dr. Wolff, although I looked for them, there were no changes in the tonus of the muscles of the two hind limbs when the front part of the body was rotated, that is, with torsion of the vertebral column, when the animal was held in the air.

In reply to Dr. Wechsler's question about tonic neck reflexes and tonic labyrinthine reflexes, these of course cannot play a rôle here. It must be a mechanism in the lower part of the body, caudal to the transection of the spinal cord, which gives rise to these changes. These changes in the flexor rigidity of course oppose the Magnus-de Kleijn reflexes. With regard to the influence on the extensors, they are exactly in the direction of and analogous to the reflexes of Magnus and de Kleijn. I think that we may look on all this as another link in that chain of reflexes which is active in the intact central nervous system, although with the intact spinal cord it is difficult to observe these changes with certainty. When the reflex is released and these mechanisms are brought about by transection of the cord, the tonic changes appear, and they are in the same line as the tonic neck and tonic labyrinthine reflexes. I do not know whether it is analogous to the reflex of the pelvis which Brouwer described.

In reply to Dr. Hausman, the difficulty is in differentiating between whether stronger pressure on the surface of the table might originate or give rise to stronger exteroceptive and proprioceptive impulses or whether the changes are due to the torsion of the vertebral column. It is difficult to evaluate this. I have tried to do so. When one lifts the animal from the table, all flexor rigidity disappears. Therefore, up to the present I actually do not see a way to differentiate between those two mechanisms, and certainly there is a great truth in the objection to the interpretation that the reflex is due to the torsion of the vertebral column alone. It might also be due to the stronger pressure on the table causing stronger exteroceptive and proprioceptive impulses.

ADDENDUM (Feb. 23, 1933, at the time of the correction of the notes): The point has been studied more closely since the discussion recorded. A way to differentiate between the two mechanisms has been found, and we are at present in the position to make a definite statement.

Section of the posterior roots of the twelfth and thirteenth thoracic and first, second and third lumbar nerves on both sides in the low spinal "primary" preparation (transection at the eleventh and twelfth thoracic level) leaves the changes in the flexor rigidity and the active extension in the "face" hind leg intact. Transection of all the posterior roots of one hind leg in a low spinal preparation (first lumbar level) abolishes the active extension in the "face" leg, present before the section. From the first set of observations it follows that abolition of sensory impulses from the caudal part of the vertebral column does not abolish the reflexes under observation in the hind legs. This, together with the result of the second set of observations, leads to the view that the changes in flexor rigidity and the active extension often seen in the "face" leg are *not* due to afferent impulses arising in the caudal vertebral column on rotation of the front part of the body, but to changes in afferent impulses by the rotation, arising in the hind legs themselves, the active extension of the "face" hind leg being another form of crossed extension reflex activity.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Secretary*

Four Hundred and Sixth Meeting, Feb. 16, 1933

E. S. ABBOT, M.D., *in the Chair*

A CASE OF PSYCHOSIS DUE TO LARGE DOSES OF ACETYLSALICYLIC ACID. DR. KARL M. BOWMAN.

Acetylsalicylic acid is commonly regarded as a drug of low toxicity; large doses are frequently given without untoward symptoms. For this reason, the report of a psychosis apparently precipitated by large doses of acetylsalicylic acid is of interest.

History.—The patient, a married woman, aged 44, was admitted to the Boston Psychopathic Hospital on Jan. 2, 1932, having been sent from a general hospital with the report that while under treatment for neuritis of the arms she began to have hallucinations, saw imaginary persons and became mildly agitated. The family history is unimportant. The patient was born in Boston on July 12, 1887. Little is known of her early life, but so far as could be learned, birth and early development were normal. She finished grammar school and was an average student. She then worked in a shoe factory until she married at 22 years of age. She did not use alcohol, tobacco or drugs. Her married life was uneventful. She never became pregnant, although contraceptives were not used; she was somewhat frigid. When she was 19, she was operated on because of an abdominal tumor and a gynecologic condition, the nature of which was not fully known. Since marriage, she has worked as a waitress two hours a day. Four years prior to admission she fell down-stairs. Following this she seemed somewhat depressed and did not eat or sleep well. However, after a year she seemed normal again. A year before admission she was operated on for exophthalmic goiter. Postoperative pneumonia developed, and she has been somewhat weak since. For four months before admission she complained of "neuritis" of the arms. In regard to personality, she was said to be sociable, cheerful and to have many friends. She was ambitious, energetic and a good housekeeper. She was not moody or given to fits of melancholy.

About a week before admission to the Boston Psychopathic Hospital she went to a general hospital complaining of neuritis. She was presumably in a normal mental condition at that time. When she was admitted to the general hospital the case was diagnosed as arthritis; she was given a routine treatment of acetyl-

salicylic acid in doses of 180 grains (11.6 Gm.) daily. This treatment was continued for five days. On the third day she began to show signs of a psychosis. On the fifth day she was transferred to the Boston Psychopathic Hospital.

Examination.—On admission she was quiet and cooperative. She thought that she was still in the general hospital; she said that some members of the Gustin gang were in the ward and were after her and that she was much frightened by them. She said also that the interns and nurses were having parties in the ward and were disturbing her. She believed that they were giving her poison. Apparently she had refused to submit to a certain medication; she had been fed by tube and had interpreted this as an attempt to poison her. She said that she had heard a friend talking in the next room, advising her husband to take her out of the hospital, but that later she had learned that this girl had not been there at all. She was correctly oriented as to time. She gave a fairly correct chronological account of her previous sickness and of her admission to the general hospital. She did the serial substraction of 7 from 100 in one minute and forty-five seconds, with three mistakes. She named the president, governor and mayor correctly, but named as the five largest cities New York, Boston, Massachusetts, Rhode Island and Connecticut. When it was pointed out that these were not all cities, she asked whether they were cities or states, started again, named New York, Boston and Washington and went no further. She had no insight into her condition.

Physical examination revealed a well developed, thin woman with arthritic changes in most joints and slight atrophy of the arms and legs. Neurologic examination gave essentially negative results. The heart was not enlarged, but there was a blowing systolic murmur at the apex. The blood pressure was 160 systolic and 100 diastolic. The hemoglobin content was 80 per cent by the Tallqvist scale; the white blood cell count was 10,100. The urine had a specific gravity of 1.022, was acid and contained no bile or sugar; a very slight trace of albumin was present; there were no casts or red blood cells, but there was an average of 5 or 6 white blood cells per high power field, with triple phosphate crystals. There were no signs of salicylic acid poisoning—no rash and no tinnitus. The temperature was normal throughout the patient's stay in the hospital.

Treatment and Course.—As the patient complained of pain and the relation of acetylsalicylic acid to the psychosis was not suspected, she was given acetylsalicylic acid, 10 grains (0.65 Gm.), and codeine, ½ grain (0.03 Gm.), once a day for two days, after which they were discontinued. Two days after the drugs were discontinued, the mental condition cleared completely. No further hallucinations appeared, and the abnormal ideas gradually faded. The patient had excellent insight into her condition and realized that her ideas were imaginary and were due to a psychosis. She was slightly confused as to the exact nature of the ideas and believed that she had been in a delirious state from which she had recovered without complete memory for everything that had happened.

Diagnosis.—It appears that in this case a toxic psychosis was precipitated by large doses of acetylsalicylic acid, namely, 180 grains a day for five days. The psychosis disappeared within forty-eight hours after the drug was discontinued.

It may be questioned what relation the arthritis had to the psychosis, and to what extent the condition was due to a particularly vulnerable personality. There seems to be little indication that the arthritis played any important rôle. It is probable that the patient had a special personality with, perhaps, some degree of idiosyncrasy for acetylsalicylic acid. Furthermore, there is a history of a somewhat atypical depression, of a year's duration, following a fall down-stairs, and also of an operation for exophthalmic goiter a year prior to the psychosis. These two facts suggest an unstable personality which was capable of being thrown out of normal equilibrium more easily than the average personality.

Subsequent Course.—The patient has apparently been making a successful adjustment during the year that she has been at home; there have been no acute psychotic episodes. She has gained 35 pounds (15.9 Kg.), and her general health

is much improved. She still uses small doses of acetylsalicylic acid for the arthritic pains and takes thyroid extract whenever her hands become blue and cold. She could not state the exact size or frequency of the doses of these two drugs. She has had occasional feelings of depression, but has been able to "walk them off." She has occasionally thought that people looked at her in a rather odd manner and knew that she had been at the Boston Psychopathic Hospital.

Although when she left the hospital she agreed that her ideas were not correct, she now maintains that the incidents which she imagined actually occurred; she is certain that she saw persons in the ward in the general hospital who were talking about her and trying to harm her. She has not elaborated these ideas to any extent and has not felt that any further attempts have been made to harm her in any fashion or that any organized group is "after her." Her recovery seems to be, therefore, essentially one without insight, and the patient apparently has such a degree of sensitivity in personality that she still has some ideas of reference.

DISCUSSION

DR. E. B. LANE: I never heard of a patient who took so much acetylsalicylic acid. I do not know of any other case of confusional psychosis resulting from this cause.

DR. TRACY J. PUTNAM: I wonder whether cases of this type are so uncommon. Dr. George Sears reported cases in which he gave acetylsalicylic acid until delirium occurred.

DR. ERIC ASK-UPMARK: In diabetic coma one can observe somewhat similar conditions. What did the studies of the blood chemistry show?

DR. KARL M. BOWMAN: The chemistry of the blood was not studied.

DR. W. BLOOMBERG: I saw this patient. From the clear history and especially from the rapid recovery, it would seem that there was a relationship between the drug and the psychosis. I saw another patient in whom 10 grains of acetylsalicylic acid taken for headache caused urticaria; he had a similar reaction to 1½ grains (0.09 Gm.) of phenobarbital. More acetylsalicylic acid was given to relieve pain until the patient discovered that a rash broke out.

DR. J. LOMAN: I saw a patient to whom 45 grains (2.9 Gm.) of acetylsalicylic acid and 15 grains (0.09 Gm.) of sodium bromide were given, the doses being reversed by mistake. Within one-half hour after the administration of the drugs the patient became actively psychotic, exhibiting great excitement and experiencing visual and auditory hallucinations. The acute psychosis disappeared within a few hours.

DR. E. S. ABBOT: I agree with Dr. Bowman that the condition was probably due to a combination of personal idiosyncrasy and acetylsalicylic acid.

INDUCED VARIATIONS IN VOLUME FLOW THROUGH THE BRAIN PERFUSED AT CONSTANT PRESSURE. DR. JACOB FINESINGER (by invitation) and DR. TRACY J. PUTNAM.

This article appears in full in this issue of the ARCHIVES, page 775.

DISCUSSION

DR. TRACY J. PUTNAM: I wish to give credit to Dr. Gibbs for pointing out that in the cat the facial artery is a more important channel of cerebral blood supply than the internal carotid artery, and that in this animal it is extremely difficult to separate the intracranial and extracranial circulation. I was impressed, on looking over the data when all were put together, to see to what extent they reconciled the two opposing schools of thought. Hill believed that the changes in the cerebral blood flow were purely passive. Forbes has shown that pial blood vessels have an active vasomotor supply. Our results lead to an intermediate point of view. Under most circumstances the passive changes outweigh the active

ones. Of course, it is possible that under pathologic conditions the reverse may be the case. We obtained a smaller proportion of positive results than Forbes. This is not difficult to understand, as the animals used by us were prepared by a lengthy operation and were seldom in as good condition as his.

DR. FRANZ FREMONT-SMITH: I agree with Dr. Putnam that the evidence from these experiments shows that the flow of blood through the brain is dependent chiefly on the blood pressure. In considering how applicable these data are to man, it must be remembered that these experiments were performed on animals under the influence of anesthesia. The vasomotor response of the unanesthetized human brain may be much more active, particularly near a pathologic process.

DR. H. C. SOLOMON: One is impressed by the fact that all these changes in the brain must have some effect on the function of that organ. It seems to me that it is an introduction to changes that are induced by emotional disturbances. One cannot say that acetylsalicylic acid causes trouble. One must think in terms of personality of the person. Certainly, disturbances in emotional states will cause reactions similar to those produced by caffein and other substances.

DR. F. GIBBS: I have been working on the same general problem with a slightly different technic. Everything that I have done so far has been in accord with the findings of Finesinger and Putnam. In my work with epinephrine I have found that the intravenous injection of the drug increases the cerebral blood flow. This would seem to be in conflict with part of the data presented tonight, but it is not necessarily so, for, as Finesinger and Putnam have pointed out, a marked increase in arterial pressure could force more blood through the cerebral vessels despite vasoconstriction.

DR. J. B. AYER: I wish to add my appreciation of the new experiments performed in Dr. Cobb's laboratory. The previous ones utilizing the window were convincing, but in these there seems to be even more conclusive evidence of variation in blood flow. Would it be possible to complete the experiment still more and perhaps tie off the middle meningeal artery and see whether the parenchyma alone responds as well as the parenchyma plus the pia? We are familiar with sudden blindness, temporary paralysis and aphasia of short duration. Can these be shown more conclusively to be due to decreased blood supply?

DR. TRACY J. PUTNAM: In reply to Dr. Ayer's questions: We have been able to follow microscopic changes in the living choroid and to compare them with those in the ventricle. I think that any experiments in perfusion would be very difficult, because almost all the deep vessels come in from the surface.

EXPERIMENTAL STUDY OF HEART RATE IN RELATION TO EMOTION. DR. JOHN C. WHITEHORN, DR. M. RALPH KAUFMAN and DR. JACKSON M. THOMAS.

A combination of recently developed apparatus, the Boas cardiotachometer and the Fleisch chronograph, makes it possible to record the time of each heart beat over long or short periods in a perspective which throws into graphic relief the almost ceaseless fluctuations in the heart rate. Under experimental conditions, approximating a natural social setting, important evidence has been obtained that emotional disturbances, even of the moderate degree common in every-day life, do effect the heart rate; some of this evidence has been presented.

From our experiments in word association it has also seemed probable that the frequent brief accelerations, which appear in many records, occur at moments of special emotional tension. In addition, under our experimental conditions, acute decelerations, which occur fairly commonly within the space of one heart beart, are also related to emotional situations. These decelerations are mediated through the vagus nerve. The quickness of acceleration in response to stimulus words points with some probability toward a parasympathetic release rather than a sympathetic excitation as a common mechanism for emotional acceleration.

The details of this new experimental set-up will be published in the near future.

DISCUSSION

DR. M. RALPH KAUFMAN: I wish particularly to call attention to one of our findings: the rather slow, steady heart rate in the agitated depression group. On the other hand, we obtained a heart rate of from 120 to 140 in several subjects with apparently deteriorated apathetic schizophrenia.

DR. JOHN C. WHITEHORN: We have reason to expect that some of the subjects will recover their normal state of mind; we can then compare the heart rates of these subjects with their own normal rates. The question of the qualities of emotion is one that has disturbed us slightly. We have not attempted seriously to follow Wundt's three-dimensional system of description. The attempt to correlate such descriptions with heart records is the kind of work in which none of us is interested, and we have neglected it, perhaps unduly, on that account. We have, in general, merely noted the occurrence of an emotional disturbance, describing it by whatever term of common speech seemed appropriate to the behavior.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 16, 1933

PERCIVAL BAILEY, M.D., *President, in the Chair*

VALUE OF ENCEPHALOGRAPHY IN DETERMINING CEREBRAL FUNCTION. DR. DOUGLAS N. BUCHANAN (by invitation).

There appears to be a fashion to regard encephalography in cases of congenital feeblemindedness and of idiocy as a procedure that has some virtue in itself and gives reliable information as to diagnosis and prognosis which is not obtainable by any other method. I present encephalograms in ten cases of idiocy uncomplicated by neurologic findings which could be definitely localized or lateralized in the nervous system. It is evident from these encephalograms that there is no correlation between the roentgenographic findings and the degree of mental defect, and it appears unjustifiable from a medical standpoint to subject patients to the discomfort and expense of such a procedure when no information is obtained which could not equally well be produced by clinical examination.

DISCUSSION

DR. PERCIVAL BAILEY: Several times we have had discussions about defective children in which it has been stated that we must always estimate the physiologic deficit; the only evidence I have ever seen was obtained from encephalograms. Such evidence is totally insufficient to permit conclusions concerning cerebral function.

MENINGIOMAS OF THE SPHENOIDAL RIDGE. DR. ARIST STENDER.

In two cases of meningioma of the sphenoidal ridge, the clinical, surgical and microscopic findings were strikingly similar. In both cases the tumors did not cause any subjective complaints of importance. In the histories there is an absence of the usual complaints associated with intracranial tumors. Both patients noticed swelling in the temporal region and unilateral exophthalmos, but paid little attention to it. In the second case the failure of vision was hardly noticed.

Several similar cases have been reported by Cushing (1922), Penfield (1923), Clovis Vincent (1923) and Hodges (1930). In the series of cases, including those collected from the literature, one of the most characteristic findings is the roentgen appearance. Regularly the sphenoid bone and especially the sphenoidal ridge and

wings are the sites of severe pathologic changes, namely, thickening and sclerosis of the bone. The changes may involve the posterior part of the orbit and eventually the lateral part of the orbital wall, sometimes including the superior orbital fissure and the optic foramen. The thickening and sclerosis may extend laterally into the temporal fossa and dorsally into the region of the clinoid.

It is noteworthy that the development of the clinical picture extends over several years or longer. As a rule there are no other neurologic symptoms or clear signs of increased intracranial pressure. Venous stasis or a beginning choked disk may be absent. These conditions were present only in Penfield's case. It is surprising that in none of the cases was there any damage to the optic nerve from pressure, as evidenced by optic atrophy or defects of the visual fields, despite the fact that in all cases the neoplasm had infiltrated the immediate vicinity of the optic nerve. This fact coincides with the observations of other authors.

Cushing has pointed out that the meningiomas at the base of the brain often do not produce signs of cerebral pressure. He observed two types of meningiomas in this region: the usual tumors of the spherical form with a small attachment to the dura which, depending on their size, usually produce clear phenomena of cerebral pressure; and a "tumors en plaque"—round, flat tumors with a broad attachment to the dura; the second type produces pressure phenomena only seldom. Cushing noted that it is these tumors that tend to infiltrate the bone, an observation made also by Elsberg, Penfield and Vincent. We confirm this fact on the basis of our cases. Some tumors of the sphenoidal ridge, especially of the spherical type, may be characterized by symptoms of pressure on the contiguous cerebral structures, particularly the temporal lobe.

DISCUSSION

DR. PETER BASSOE: In a recent article on exophthalmos in tumor of the brain, Elsberg made the statement that in no case did the cavernous sinus have anything to do with it. I wish to know whether there was any growth in the orbit in these cases, how the abducens nerve happened to be involved, and if so, whether it was by some kind of pressure at the superior orbital fissure.

DR. PERCIVAL BAILEY: I think that in the second case there was palsy of the abducens nerve before operation. In the other case reported, in which the tumor extended into the orbit, a tumor of considerable size had to be dissected out. It is probable that I should have disturbed the abducens nerve had it not already been involved by the tumor.

MENINGIOMA OF THE TUBERCULUM SELLAE WITH HYPEROSTOSIS. DR. F. E. KREDEL (by invitation).

The patient, a man, aged 42, had had gradual loss of vision in the left eye for fifteen years and in the right eye for four years with no other significant symptoms. On examination, the left eye was totally blind, while the right showed perception of light in the inferior nasal quadrant of the visual field. The basal metabolic rate was — 16 per cent. A roentgenogram revealed calcification above the anterior clinoids and thickening of the tuberculum sellae. Death occurred from hemorrhage during operation.

Necropsy revealed a large meningioma of a meningotheliomatous type. The tumor invaded the optic foramina and compressed the optic nerves more on the left. Microscopic section of the hyperostosis of the tuberculum revealed dense trabeculated bone containing masses of tumor cells in the cancellous spaces. New bone is laid down by osteoblasts and not by tumor cells directly. Hyperostosis is a rare concomitant of meningiomas of the tuberculum sellae.

DISCUSSION

DR. PERCIVAL BAILEY: When Dr. Penfield published his paper about meningiomas, he stated that these infiltrating tumors never occurred over the base, but always over the vertex. These cases show that his impression at that time was

erroneous and strengthen the belief that trauma is not related to such invasion of the bone. So far as I know, the structure of the meningioma has nothing to do with whether or not it invades the bone tissue, and just why some do while others do not remains to be determined.

CORTICAL PROJECTION OF THE RETINA IN MONKEY AND IN MAN. DR. STEPHEN POLJAK (by invitation).

My experiments concern the central portion of the visual pathway, from the lateral geniculate body to the striate area. The results obtained by means of the Marchi method have already been published. They showed that the visual radiation can be subdivided into three main portions: (1) the upper horizontal branch that terminates in the upper lip of the calcarine fissure and represents the upper homonymous quadrants of the retinas with the exclusion of the macula; (2) the lower horizontal branch terminating in the lower lip of the calcarine fissure and representing the lower homonymous quadrants of the retinas with the exclusion of the macula; (3) the perpendicular or the "axial" branch of the radiation that terminates in the posterior portion of the striate area around the occipital pole, which is placed between the aforementioned two "peripheral" branches, and conducts the macular impulses.

Experiments have been made with lesions in various parts of the striate area and of the visual radiation. To each lesion there corresponds a definite zone of degeneration in the lateral geniculate body (retrograde degeneration of cells). In such a way the gross quadrantic projection of the retina can be mapped out in the striate area.

In a special experiment, photomicrographs demonstrated a complete degeneration of the ipsilateral external geniculate body after unilateral and complete removal of the striate area. This proved that the hypothesis of a bilateral projection of each total macula had no anatomic basis. This is true also for the human macula.

Other experiments dealt with the problem of a detailed projection of the retina. For each minute segment of the lateral geniculate body there is a corresponding minute portion of the striate area. Hence the view of the so-called point-to-point projection of the retina is corroborated in an experimental way. In experiments with monkeys lesions were made in the macular cortex representing various figures; these gave zones of degeneration in the lateral geniculate body closely resembling in shape the figures of the lesions made. I conclude that it is probable that the figures of objects falling on the retina are transmitted without substantial alteration to the striate area of the cerebral cortex. (A brief account of these experiments will appear in the collective papers published by the Association for Research in Nervous and Mental Diseases, and a complete description will be given in the *Journal of Comparative Neurology* [**57**:541, 1933].)

DISCUSSION

DR. ERIC OLDBERG: In a recent review by Horrax and Putnam (*Brain* **55**:499, 1932) of about forty verified tumors of the occipital lobe, it was found that a large majority of the lesions spared the macula, in contradistinction to tumors of the temporal lobe. The authors considered that the clinical facts favored the theory that the macula is spared as long as a minimal number of visual fibers are still able to reach a partially intact occipital cortex, rather than that the macula is bilaterally represented in the occipital cortices.

DR. STEPHEN POLJAK: One has to consider that, but must remember that all fiber bundles of the visual radiation are close together at their origin; there is a chance that all fibers will be pressed by a tumor in the temporal lobe, whereas in the occipital lobe this might not occur. It is really an anatomic situation.

Book Reviews

Psychiatrie médico-légale. By Henri Claude. Price, 32 francs. Pp. 299. Paris: Gaston Doin & Cie, 1932.

This volume, based on Professor Claude's notes of lectures at the Faculté de Médecine, will have an appeal both to psychiatrists and to general practitioners of medicine. He stands on a sound foundation in asserting the social importance of the acts in certain psychopathic states and in stressing the socialized as opposed to the individualized therapy.

There are four parts to the volume: 1. The exercise of civil rights—appointments of guardians, opposition to and annulment of marriage, divorce and making of wills. In this part, great care is taken to protect the patient in the exercise of his legal rights. Mental disease in the partner is not a cause for divorce in France.

2. Penal responsibility. The Penal Code states that "there is neither a crime nor an offense if the person involved was in a state of dementia at the moment of the action, or if he has been subjected to a force which he could not resist." This at times has brought up some delicate legal points—a yes-no answer to the question of responsibility, or the establishment of "attenuated responsibility" through a certain constellation of events. Claude cautions against the latter practice, as it delegates by implication to the examining physician the fixing of the degree of punishment, provided the findings are accepted by the court. This he feels should be left strictly to the court. He warns against admission of children's evidence. The most interesting portion of this part is that which deals with the practical application of the law of June 30, 1838, concerning the methods of commitment of patients to mental hospitals. The "voluntary commitment" is made on application of a parent or friend, or of the patient himself, to the director of the hospital, accompanied by a medical report and identification of the patient. "Placement d'office," like our court commitment, is made on order of the prefect of police or of a department, and is resorted to when the patient is asocial or dangerous.

The medical certificate for voluntary commitment might well be copied for use in this country: "I certify that I have visited and examined ——— ———, and have found that he suffers from a mental trouble characterized by ——— etc.

"Therefore, I judge that, in the interest of the patient himself and to assure to him the care for the return of his health as well as the protection which cannot be given at his home, it is necessary that he be placed in a special establishment under the law of 1838 and should be kept there."

There is nothing about being *insane*, no reading of the certificate or order to the patient, or jury trial for insanity! Diagnosis is not entered on the certificate, and no mention is made of hereditary factors or of previous treatment, or of the difficulties the patient would likely meet in his environment because of his illness. This seems to be a telling, yet protective, sort of statement of the case.

The patient in the hospital retains all his civil rights, but an administrator is appointed to guard his interests. This administrative power ceases with the patient's release from the hospital. The patient under voluntary commitment may leave the hospital on demand of the person responsible for the commitment, unless the physician objects because of danger inherent in the release. The court may then change the voluntary commitment to "placement d'office," when release may be by medical certificate of health, by order of the prefect of police or of the department, or by the court.

The rest of this part deals with various types of psychopathy. France has the same need for special institutions for the constitutional psychopathic (asocial) person as America.

3 and 4. These parts are really a passing in review of mental reaction types with their special implications of a medicolegal nature with differential diagnostic

considerations. The "crime passionel" is of interest to American readers, with Levy-Valensi's differential diagnostic points between the character "passionel pur" and "delirant passionel." The author closes with a quotation from Rogues de Fursac: "Whenever the social defense cannot be assured by medical means, and indulgence risks the increase in the dangerousness of the subject, let the penal repression take full effect, even if the subject appears more or less mentally affected."

The book is clearly written and should be of considerable practical value to practitioners. It was especially surprising and gratifying to find that "voluntary commitment" can be made by friends of the patient with the greatest ease, in a perfectly orderly way and without embarassment of any sort. This, in a land where personal liberty has been a cornerstone of the social structure for a long while! How much more civilized than is the case in the United States, where "personal liberty" seems to mean something quite different. Those American opponents of commitment would doubtless be surprised to hear Claude assert that, on the whole, the patient gets the breaks against society in spite of the widespread belief to the contrary. One sees in this contrary belief the inherent struggle of the "I" against the "We"; and until this struggle is settled in a better manner, one cannot hope for a more rational rapprochement of mental medicine and the law.

Die Wissenschaft am Scheidewege von Leben und Geist. Festschrift Ludwig Klages zum 60. Geburtstag 10. Dezember 1932. Edited by Dr. Hans Prinzhorn. Price, 14 marks. Pp. 252. Leipzig: Johann Ambrosius Barth, 1932.

The title of this book ("Science on the Cross Road of Life and Mind"), in which thirty authors honor the German philosopher, Ludwig Klages, indicates the cause for Klages' far-reaching influence in the scientific and cultural world. His teaching asks for a biocentric instead of a logocentric orientation. Life is the important principle for the study of the personality and its cultural expressions.

Some of the psychiatric contributors based their studies on Klages' work. Pophal analyzes motility by distinguishing between the cause and meaning of movements, stressing the influence of strivings and counterstrivings and the differentiation between expressive and purposeful movements. Rothschild offers an attempt to utilize the distinction of sensation and vision in biologic problems. Haeberlin urges a psychotherapy which will do justice to the conflict of life and mind.

Prinzhorn stresses the importance of biologic security. To him psychopathies are disturbances of the relationship of the personality to the group. On this basis he also presents the performance of a leader as disturbing the integration of the group. Based on careful experimental work, Hansen was able to show that a nervous cardiac stimulation in the mother can affect the heart of the fetus. He therefore reopens the question of the psychic influence of the mother on the unborn child. Schroeder discusses the differentiation of feelings and mood. Kolle, in a study of various types of physicians, analyzes some of the personalities most frequently found among practitioners and specialists. Psychobiologic psychiatry and its approach to human personalities and problems are illustrated in a presentation of panic reaction by Diethelm.

The need for consideration of the total personality in tests is highly stressed by Stern in a discussion of expression and performance. Groos offers an analysis of time, and Uexkuell of space. The recent development and new orientation of German psychology are well demonstrated by Jaensch, who contrasts Fechner's psychophysics to biologic psychology, and substitutes for positivism and idealism the idealism of the near, real and living. A support for this attitude is Buytendijk's discussion of a vital guiding principle in animal movements, based on experiments with rats.

Klages' influence on the present-day literature is seen in Bode's discussion of the relationship of players and audience, Deubel's outline of the development of German tragedy and Cysarz' plea for esthetics on a vitalistic basis. This influence

is also seen in Fischer's consideration of the various stages of plastic art, in Schmitthenner's demand for a new architecture in the machine age and in Pinder's differentiation between naturally emerging and consciously formed styles in art. In the latter, man, and not the world and nature, is the central problem. Ackerknecht considers the cultivation of the instinctive urge to self-development, with relaxation in play instead of abreaction, the basis for a healthy education of the masses.

Curtius presents his latest study on phallus tombstones, Ninck an analysis of the Perseus myth. Their approach is based on physiognomy in its broadest sense, with willingness to see meaning and symbols instead of mere signs.

Kern clarifies Klages' relation to Goethe and the romantic schools, while Seillière does it more from the French romantic point of view, of which he considers the need for domination and a naturalistic mysticism characteristic. Thibon compares Thomas Aquinas and Klages. Seesemann's plea for the right of the individual and of individual peoples against universalism arises from such a philosophy. In some contrast stands Dessoir's personality analysis of Hegel.

A poetic tribute by Bernoulli closes this *Festschrift,* which gives an excellent view of Klages' cultural importance and shows how his various findings and theories have stimulated workers in the field of psychiatry and psychology.

Neurobiologie de l'hallucination. By Raoul Mourgue. With a Preface by Henri Bergson. Price, 91 francs. Pp. 416. Bruxelles: Maurice Lambertin, 1932.

The literature on hallucinations is enormous; surprisingly enough, it is almost entirely composed of papers dealing with isolated and specific issues. Large comprehensive monographs are rare, the only recent one being Mayer-Gross' chapter in Bumke's handbook. This is not the only reason, however, for the value of the present volume. Mourgue has written the best monograph on hallucinations that exists so far, and his book is an outstanding contribution to psychopathology.

Henri Bergson wrote a brief preface in which he recommends highly the biologic method of the author, who, in the words of Bergson, regards man "not only as a conscious being, but also as a living being."

An attempt to give a brief résumé of the author's facts and conclusions not only would do injustice to the book, but would be misleading. The author's point of view is synthetic, in the best meaning of this term, and he does not even attempt to arrive at any facile definitions of what hallucinations are or are not. This is a book that should be translated and made available in its entirety to English readers. It is distinguished by great erudition. The author seems to be at home equally in metaphysics and in all the allied branches of neuropsychiatry. The chief note struck is refutation of all "intellectualistic," "formalistic" and purely psychologic interpretations of hallucinations, and insistence on a biologic point of view.

This volume is recommended highly, not only to those interested in the problem of hallucinations but also to all who are interested in the development of a biologically oriented psychopathology.