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OCTOBER, 1932. NUMBER 4

Archives of Neurology and Psychiatry

VOLUME 28 NOVEMBER, 1932 NUMBER 5

FREQUENCY WITH WHICH TUMORS IN VARIOUS PARTS OF THE BRAIN PRODUCE CERTAIN SYMPTOMS

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PHILADELPHIA

This study was undertaken in the hope of obtaining additional evidence regarding cerebral localization of function and the mechanism by which certain symptoms are produced. The selection of intracranial neoplasm as the lesion to be studied is unorthodox. Vascular and traumatic lesions are usually chosen for this type of investigation. Vascular lesions are not, however, as strictly localized or as definitely localizable as is generally assumed. Traumatic injuries are rarely, if ever, tolerated in certain regions in which I am particularly interested. The method employed makes it possible to determine from a study of cases of tumor of the brain the intracranial area particularly concerned with the production of a given symptom.

PREVIOUS INVESTIGATIONS

It does not seem advisable at this time to attempt to review the formidable literature dealing with the symptomatology of tumors of the brain. A good bibliography of the old literature may be found in Oppenheim's [1] monograph. Cushing's [2] books and papers deal authoritatively with almost every phase of the subject. A recently published book by Sachs [3] gives numerous references to the modern literature.

In considering the effectiveness with which variously located tumors produce visual hallucinations, I am, for the most part, repeating the work

From the Department of Pathology, Johns Hopkins Medical School, the Departments of Neuropathology and Neurosurgery, Harvard Medical School, and the Johnson Foundation, University of Pennsylvania.

1. Oppenheim, H.: Die Geschwülste des Gehirns, ed. 2, Vienna, A. Hölder, 1902.

2. Cushing, H. W.: (*a*) The Pituitary Body and Its Disorders, Philadelphia, J. B. Lippincott Company, 1912; (*b*) Tumors of the Nervus Acusticus and the Syndrome of the Cerebellopontile Angle, Philadelphia, W. B. Saunders Company, 1917; (*c*) The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341, 1921; (*d*) Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C. Thomas, 1928; (*e*) Neurohypophyseal Mechanisms from a Clinical Standpoint, Lancet **2**:119 and 175, 1930.

3. Sachs, E.: Diagnosis and Treatment of Brain Tumors, St. Louis, C. V. Mosby Company, 1931.

of Horrax.[4] I have used many of the same cases on which his work was based. A study similar to mine on convulsions has been made by Parker.[5] His series, however, included only 313 cases. He did not consider focal and generalized convulsions separately. Martin[6] studied the incidence of choked disk in a series of 600 cases of intracranial tumor. An analysis of 100 unselected cases of tumor of the brain has been reported by Dowman and Smith.[7] Frazier and Gardner[8] analyzed 100 cases of supratentorial tumor.

The usual method of investigating the relation of symptom to position of the tumor is to select for study only patients with the lesion in a given area. Analysis of such a series yields information as to what symptoms are produced and the frequency with which they are produced by tumors in this area—information that is valuable for diagnosis but unsatisfactory for determining the function of the area considered. One may search the literature in vain for data on the frequency with which these symptoms are produced in tumors in other parts of the brain. Another somewhat less common method is to select for study cases that show a certain symptom or group of symptoms. Analysis of such a series yields information as to the frequency with which a given symptom is produced by variously located tumors—again, information that is extremely valuable for diagnosis. It is difficult, however, to draw conclusions regarding the function of various areas from such data, for tumors do not occur with equal frequency in all parts of the brain. It may well be that the greater incidence of tumors of the frontal lobe, for instance, in a series of cases of supratentorial tumors showing vomiting is not caused by a greater tendency for tumors in the frontal lobe to produce vomiting, but is simply the result of the greater frequency with which tumors occur in this area.

The fundamental question as to the relative effectiveness of variously located tumors in producing a given symptom can be answered only by analysis of a random series of sufficient size to contain a large number of cases of tumor located in each area considered, and of sufficient size to contain a large number of cases with each symptom considered.

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

5. Parker, H. L.: Epileptiform Convulsions: The Incidence of Attacks in Cases of Intracranial Tumor, Arch. Neurol. & Psychiat. **23**:1032 (May) 1930.

6. Martin, J. M.: Optic Neuritis in Intracranial Tumors, Lancet **2**:81, 1897.

7. Dowman, C. E., and Smith, W. A.: Intracranial Tumors: A Review of 100 Verified Cases, Arch. Neurol. & Psychiat. **20**:1312 (Dec.) 1928.

8. Frazier, C. H., and Gardner, W. J.: The Mechanism and Symptoms of Increased Intracranial Pressure Due to Encapsulated and Infiltrating Tumors of the Cerebral Hemisphere, in Intracranial Pressure, in Health and in Disease, Baltimore, Williams & Wilkins Company, 1929, p. 386.

MATERIAL

The data presented are obtained from an analysis of the records of 1,545 verified cases of tumor of the brain. Thirteen hundred and forty of these were obtained from Dr. Harvey Cushing's service at the Peter Bent Brigham Hospital. Among these there were 300 cases in which postmortem examinations were made. Two hundred and five cases with postmortem observations were obtained from the Johns Hopkins department of pathology. Only cases of primary intracranial neoplasm were included in the series. No case was included unless the position and extent of the tumor was determined at operation or at postmortem examination.

Reliance on operative notes for the accurate location of a tumor may seem unwarranted; some reassurance may be taken from the rarity of disagreement between operative notes and postmortem examination. The fact that more than two thirds of the cases included two histories of the present illness and two neurologic examinations increases the reliability of the clinical data. The lack of detailed study of postmortem material is regrettable, but since I have attempted

TABLE 1.—*Symptoms Studied and the Number of Cases with a Given Symptom*

Symptom	No. Cases	Symptom	No. Cases
1. Aphasia	205	15. Sexual hypoplasia	53
2. Focal convulsions	100	16. Acromegaly	40
3. General convulsions	141	17. Polydipsia	84
4. Tremor	42	18. Craving for sweets	38
5. Olfactory hallucinations	74	19. Rapid gain in weight	16
6. Gustatory hallucinations	32	20. Drowsiness	235
7. Visual hallucinations	51	21. Impairment of hearing	224
8. Irritability	27	22. Nystagmus	332
9. Jocularity	33	23. Positive Romberg sign	315
10. Difficulty in micturating	20	24. Choked disk of 4 diopters or above.	375
11. Urinary incontinence	164	25. Hemorrhage in nerve head or retina.	232
12. Projectile vomiting	162	26. Veins of eyelids dilated	95
13. Cessation of menses	113	27. Exophthalmos	145
14. Loss of sexual appetite	89		

to determine only in what gross area of the brain a tumor most effectively produces a given symptom, the relatively crude localization obtainable from the records alone was thought adequate. The assumption was made that the records were more often right than wrong, and that an analysis of 1,545 clinicopathologic records should yield significant data.

METHOD

The brain was divided into the following regions: frontal lobe, parietal lobe, temporal lobe, occipital lobe, hypophysis, suprahypophyseal region, caudate nucleus, lenticular nucleus, thalamus, pineal region, midbrain, pons, cerebellopontile angle, cerebellum and fourth ventricle. Lists were made of cases with tumor tissue in one of these areas. No attempt was made to describe a tumor as though it were confined to a single area. The left and right side were listed separately for the frontal, parietal, temporal and occipital lobes, for the caudate and lenticular nuclei, for the thalamus and for the cerebellopontile angle. The number of cases with tumor tissue in a given region is shown in table 2. A list was made of all cases showing a given symptom before operation. The symptoms considered are shown in table 1.

For greater accuracy the terms applied to certain of these symptoms are here defined: Under *aphasia* were included all cases with impairment of power of speech not resulting from impairment of the peripheral mechanism. Under *focal*

convulsions all cases were listed that showed a violent involuntary contraction or series of contractions of muscles on one side of the body. Under *general convulsions* were listed all cases that showed a violent involuntary contraction or series of contractions of muscles on both sides of the body, excepting cases in which the contraction took the form of opisthotonic rigidity. Under *tremor* were listed all cases showing a resting tremor of the arms or legs. Under *visual hallucinations* were included only cases with hallucinations of form; no cases were included in which the patient merely saw flashes of light or sparks. Under *irritability* were listed all cases in which ill humor seemed to be a symptom of the disease. Under *jocularity* were listed all cases in which euphoria or excessive good humor seemed to be a symptom of the disease.

The incidence of *loss of sexual appetite* was calculated for a series composed only of cases in which the patients were between 20 and 60 years of age. The incidence of *cessation of the menses* was calculated for a series composed only of cases in which the patients were between 15 and 45 years of age.

By comparing the lists of cases showing tumor tissue in a given area with the list of cases showing a given symptom it was possible to determine the frequency with which tumor tissue in a given area was associated with a given symptom. The percentage incidence of a symptom among cases with tumor tissue in a given region was considered an index of the power of tumor tissue in that area to produce the symptom in question. Curves were drawn showing the percentage incidence of each symptom for each area.

The application of a statistical method to such imponderables as jocularity may seem unwarranted, but imponderables of this kind are of interest and are continually dealt with in neurologic discussions. It was thought that figures relating to the occurrence of such symptoms might be welcome.

SOURCES OF ERROR

1. It is possible that certain mistakes in the records are consistently repeated.

2. It is possible that in many cases, especially in those of a tumor in the left hemisphere, certain symptoms escaped notice because the patient was markedly aphasic.

3. It is hazardous to group together tumors having widely different biologic characteristics and study them as though they were a single type of lesion. It is possible that the frequency with which certain symptoms are associated with tumors in a certain location is due, not to the position of the tumor, but to a biologic property of the type of tumor commonly found in that area, for example, to its rapid rate of growth.

4. The fact that tumors in a given area tend to affect different age groups (see chart 1) introduces a serious difficulty. It is possible that the frequency with which certain symptoms occur among cases of tumor in a given area is due, not primarily to the location of the tumor, but to the age of those commonly affected by a tumor in this region.

5. Though large, this series does not include a satisfactory number of cases of tumor in certain of the areas considered, or a satisfactory

number of cases with certain of the symptoms considered (tables 1 and 2). The figures regarding the incidence of these rare symptoms are not reliable, particularly as regards their incidence among tumors in areas in which tumors occur infrequently.

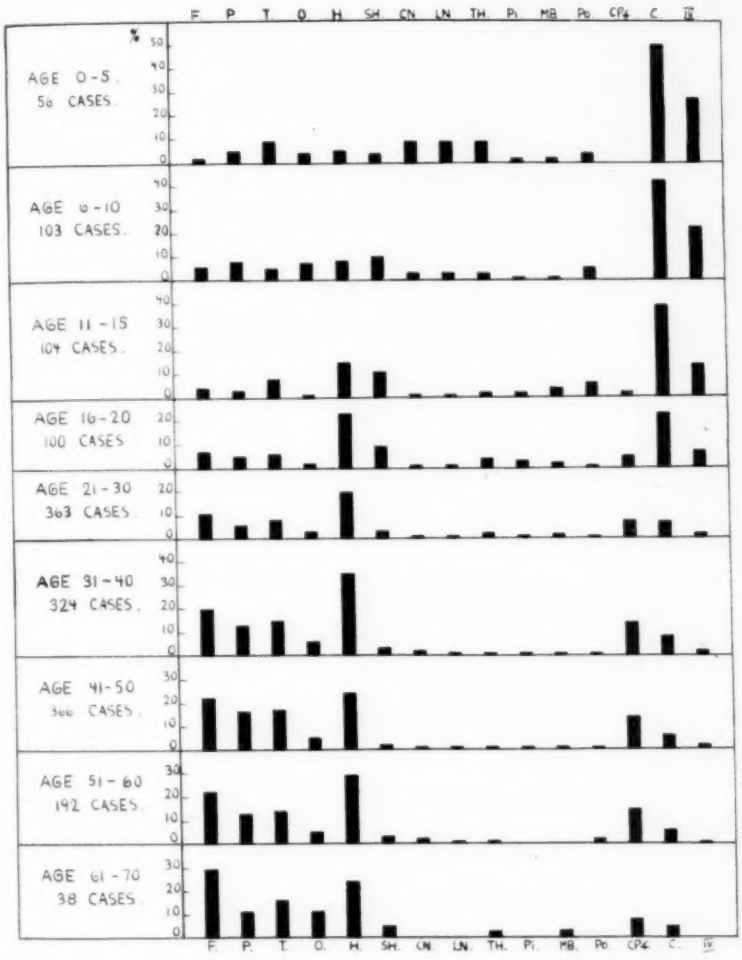

Fig. 1.—Percentage incidence of tumors in various locations in different age groups. F., frontal; P., parietal; T., temporal; O., occipital; H., hypophysis; SH., suprahypophyseal; CN., caudate nucleus; LN., lenticular nucleus; TH., thalamus; PI., pineal; MB., midbrain; PO., pons; CP., cerebellopontile angle; C., cerebellum; IV., fourth ventricle. The chart should be read in this manner: In the 0 to 5 year age group there were 56 cases; in 2 per cent of these the tumor involved the frontal lobe, in 5 per cent the parietal lobe and in 9 per cent the temporal lobe.

RESULTS

The results of this study cannot be stated more accurately than by curves showing the percentage incidence of a given symptom among cases with tumor tissue in a given region. These curves are shown in charts 2, 3, 4, 5 and 6.

The general level of the curve gives a rough indication of the commonness or rarity of a symptom; for more accurate information on this matter see table 1. The number of cases with tumor in a given area is shown in table 2. It will be seen that the series, though fairly large, is not large enough to afford a satisfactory number of cases with certain relatively rare symptoms, or a satisfactory number of cases with the tumor in certain areas in which tumors occur infrequently.

TABLE 2.—*Intracranial Regions Considered and the Number of Cases with Tumor Tissue in a Given Region*

	Left	Right	Left and Right	Total
Frontal	109	131	22	262
Parietal	71	88	9	168
Temporal	96	100	1	197
Occipital	46	25	4	75
Hypophysis	..	..	..	383
Suprahypophyseal	..	..	..	70
Caudate nucleus	11	10	3	24
Lenticular nucleus	11	11	2	24
Thalamus	11	14	4	29
Pineal	..	..	..	16
Midbrain	..	..	..	20
Pons	..	..	..	29
Cerebellopontile angle	85	83	1	169
Cerebellum	..	..	..	225
Fourth ventricle	..	..	..	85

Reference to the legend of charts 1 and 2 will show the meaning of the symbols. Here is an example of the way in which a curve should be read: The curve for the percentage incidence of aphasia shows a height of 21 above F., the abbreviation for frontal; this indicates that 21 per cent of all cases with tumor in either frontal lobe showed aphasia; the dot at 35 above F. indicates that 35 per cent of all cases with tumor in the left frontal lobe showed aphasia; the cross at 9 above F. indicates that 9 per cent of all cases with tumor in the right frontal lobe showed aphasia.

Summary of Results.—Curves showing the percentage incidence of certain symptoms among variously located tumors indicate: 1. Aphasia occurred most frequently among cases in which the tumor involved the left temporal lobe and somewhat less frequently among cases in which the tumor involved the frontal, parietal or occipital lobes.

2. Focal convulsions occurred most frequently among cases in which the tumor involved the parietal lobe and less frequently among cases in which the tumor involved the frontal lobe.

3. Generalized convulsions occurred most frequently among cases in which the tumor involved the left temporal lobe and somewhat less frequently among cases in which the tumor involved the frontal or occipital lobes or the suprahypophyseal or pineal regions.

4. Resting tremor of the arms or legs occurred most frequently among cases in which the tumor involved the left lenticular nucleus, less

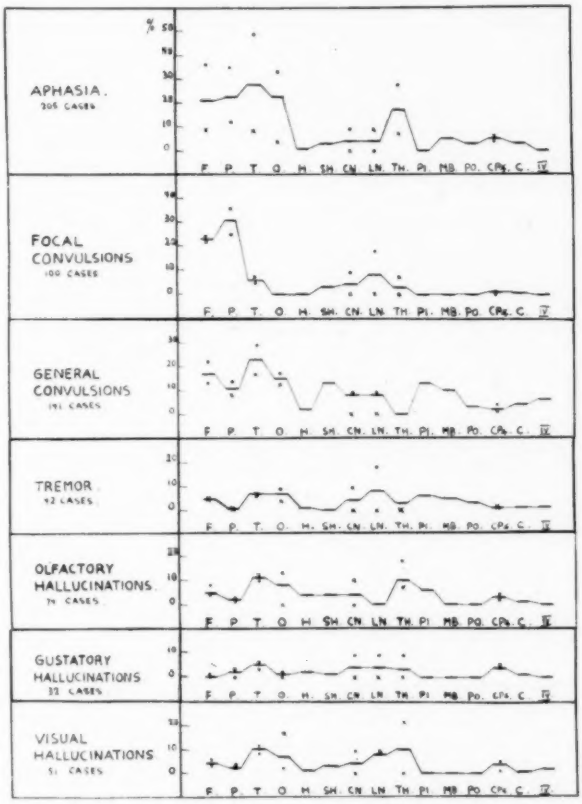

Fig. 2.—Percentage incidence of certain skeletal motor and sensory disturbances among cases with tumor tissue in a given region (e.g., 35 per cent of all cases of tumor of the parietal lobe showed focal convulsion). The dashes, joined together, indicate the percentage incidence among all cases with tumor tissue in a given region. The dots indicate the percentage incidence among cases with tumor tissue on the left side only. The crosses indicate the percentage incidence among cases with tumor tissue on the right side only.

frequently among cases in which the tumor involved the left caudate nucleus and still less frequently among cases in which the tumor involved the temporal or occipital lobes or the pineal region.

5. Olfactory hallucinations occurred most frequently among cases in which the tumor involved the left thalamus and somewhat less frequently among cases in which the tumor involved either temporal lobe or the left occipital lobe.

6. Gustatory hallucinations occurred most frequently among cases in which the tumor involved the left caudate or left lenticular nuclei or the left thalamus and somewhat less frequently among cases in which the tumor involved the temporal lobe or the cerebellopontile angle.

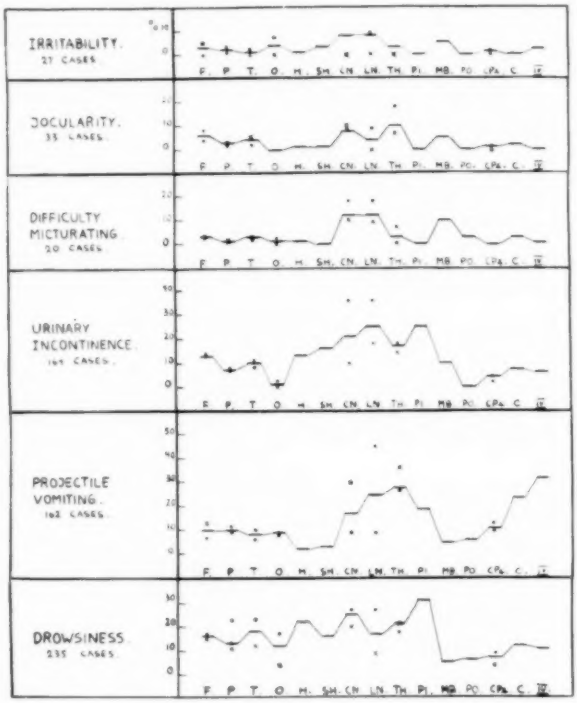

Fig. 3.—Percentage incidence of certain affective and visceral motor disturbances among cases with tumor tissue in a given region.

7. Visual hallucinations occurred most frequently among cases in which the tumor involved the right thalamus, somewhat less frequently among cases in which the tumor involved the right occipital lobe and more rarely still among cases in which the tumor involved the temporal lobe.

8. Irritability or ill humor occurred most frequently among cases in which the tumor involved both caudate or both lenticular nuclei.

9. Jocularity occurred most frequently among cases in which the tumor involved the left thalamus and slightly less frequently among cases in which the tumor involved the caudate nucleus.

10. Difficulty in micturating occurred most frequently among cases in which the tumor involved the caudate or lenticular nuclei or the midbrain.

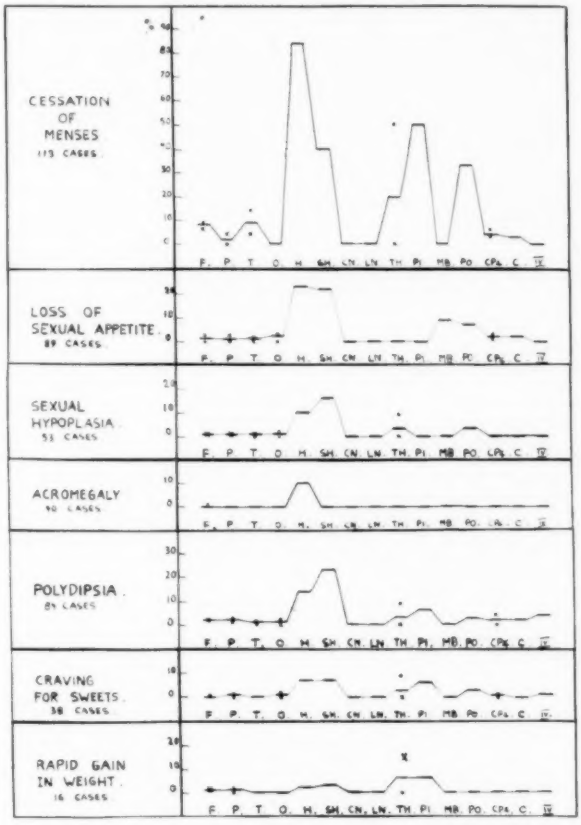

Fig. 4.—Percentage incidence of certain visceral and vegetative disturbances among cases with tumor tissue in a given region. It should be noted that the percentage incidence of cessation of the menses is calculated on the basis of a series composed of all cases in which the patient was a woman between 15 and 45 years of age. The percentage incidence of loss of sexual appetite is calculated on the basis of a series composed of all cases in which the patient was between 20 and 60 years of age.

11. Urinary incontinence occurred most frequently among cases in which the tumor involved the left caudate or left lenticular nucleus or the pineal region.

12. Projectile vomiting occurred most frequently among cases in which the tumor involved the right lenticular nucleus and less frequently among cases in which the tumor involved the thalamus or the fourth ventricle.

13. Drowsiness occurred most frequently among cases in which the tumor involved the pineal region and less frequently among cases in which the tumor involved the left caudate or the left lenticular nucleus.

14. Amenorrhea occurred most frequently among cases in which the tumor involved the hypophysis or the pineal region.

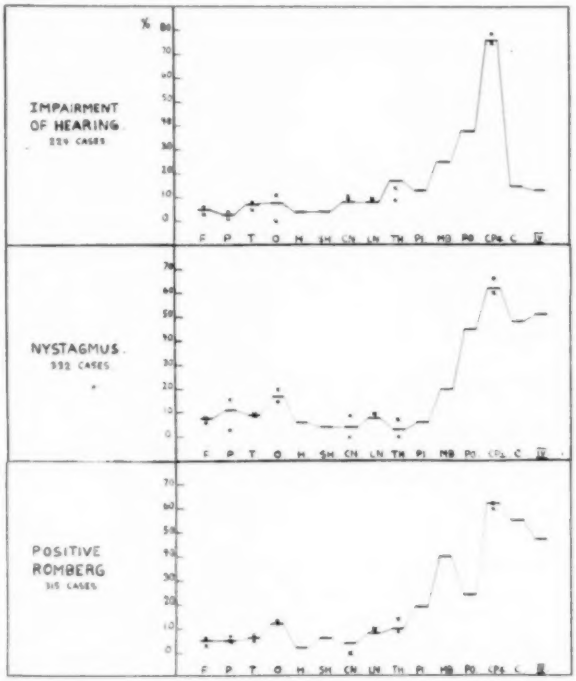

Fig. 5.—Percentage incidence of impairment of hearing, nystagmus, and positive Romberg sign among cases with tumor tissue in a given region.

15. Anaphrodisia occurred most frequently among cases in which the tumor involved the hypophysis or the pineal region.

16. Sexual hypoplasia occurred most frequently among cases in which the tumor involved the suprahypophyseal region and less frequently among cases in which the tumor involved the hypophysis.

17. Acromegaly occurred only among cases in which the tumor involved the hypophysis.

18. Polydipsia occurred most frequently among cases in which the tumor involved the suprahypophyseal region, somewhat less frequently among cases in which the tumor involved the hypophysis and still less frequently among cases in which the tumor involved the pineal region.

19. Craving for sweets occurred most frequently among cases in which the tumor involved the left thalamus, the pineal region, the hypophysis or the suprahypophyseal region.

20. Rapid gain in weight occurred most frequently among cases in which the tumor involved the right thalamus or the pineal region and less frequently among cases in which the tumor involved the suprahypophyseal region or the hypophysis.

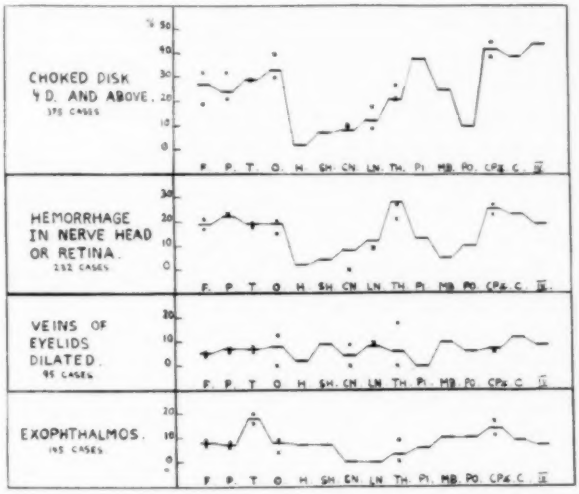

Fig. 6.—Percentage incidence of certain ocular signs among cases with tumor tissue in a given region.

21. Impairment of hearing occurred most frequently among cases in which the tumor involved the cerebellopontile angle. Among cases of supratentorial tumor; those in which the tumor involved both thalami showed the highest incidence of impairment of hearing.

22. Nystagmus occurred most frequently among cases in which the tumor involved the cerebellopontile angle.

23. A positive Romberg sign occurred most frequently among cases in which the tumor involved the cerebellopontile angle.

24. High grade choked disk occurred most frequently among cases in which the tumor involved the fourth ventricle or the cerebellopontile angle. Pineal tumors and cerebellar tumors were slightly less effective in producing this sign.

25. Hemorrhage in the optic nerve head or retina occurred most frequently among cases in which the tumor involved the thalamus, the cerebellopontile angle or the cerebellum.

26. Dilated veins of the eyelids were observed most frequently among cases in which the tumor involved the left thalamus, the left occipital lobe or the cerebellum.

27. Exophthalmos occurred most frequently among cases in which the tumor involved the temporal lobe or the cerebellopontile angle.

COMMENT

Aphasia.—Despite a lack of accord on many points, von Monakow,[9] Head,[10] Marie [11] and Goldstein [12] appear to agree that a cortical lesion bordering on the sylvian fissure, especially one in the temporal lobe, is more likely to produce aphasia than a similar lesion in another area. The lesions studied by these authors were chiefly vascular or traumatic. If what holds true for such lesions holds true also for tumors of the brain, one would expect to obtain a curve for percentage incidence of aphasia among variously located tumors much like that obtained here. The curve is in agreement with the generally accepted belief that lesions on the left are more effective in producing aphasia than lesions on the right.

Focal Convulsions.—It appears to be generally accepted that focal convulsions are usually the result of a lesion in the rolandic area.[13] The curve obtained for focal convulsions is in accord with such a belief. The higher incidence of focal convulsions among parietal tumors may indicate that a parietal lesion is more effective than a frontal one in producing a limited motor disturbance, whereas the curve for generalized convulsions seems to indicate that a frontal lesion is more effective than a parietal one in producing a diffuse motor disturbance.

General Convulsions.—The curve obtained for general convulsions indicates that tumors in very different areas are more or less equally effective in producing this symptom. The superior effectiveness of tumors in the temporal lobe is, however, definite; this calls to mind numerous instances in which lesions in the temporal lobe, more particularly in the cornu ammonis, have been reported in the brains of epileptic

9. von Monakow, C.: Die Lokalisation im Grosshirn und der Abbau der Funktion durch kortikale Herde, Wiesbaden, J. F. Bergmann, 1914.

10. Head, H.: Aphasia and Kindred Disorders of Speech, Brain **43**:87, 1920.

11. Marie, P., and Foix, C.: Les aphasies de guerre, Rev. neurol. **31**:53, 1917.

12. Goldstein, K.: Die Lokalisation in der Grosshirinde, in Bethe, A., et al.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10, p. 600.

13. Benisty, A.: Les lésions de la zone rolandique (zone motrice et zone sensitive) par blessures de guerre, Paris, Vigot Frères, 1918.

patients.[14] The cornu ammonis is believed to have a precarious blood supply;[15] it is possible that it is especially liable to injury by tumors. The frequency of general convulsions among tumors in the suprahypophyseal region is notable. Recent work[16] has indicated that lesions in certain ganglia in the floor of the third ventricle are found in association with epilepsy and that lesions in this region produce general convulsions in animals. The assumption does not appear altogether warranted that the convulsions produced by tumors in the pineal region and in the midbrain are secondary to internal hydrocephalus; tumors in the fourth ventricle are especially likely to cause hydrocephalus; it will be noted that these rarely produced general convulsions. General convulsions tend to be produced more readily by tumors on the left than on the right.

The greater effectiveness of tumors situated in areas containing few neurologic elements primarily concerned with skeletal movement suggests that general convulsions are most frequently produced by some mechanism other than direct injury to skeletal motor neurons. The nature of this mechanism is not apparent.

Attacks of opisthotonos were reported in 7 cases in which the tumor involved the cerebellum (3 per cent incidence), in 3 cases in which the tumor involved the fourth ventricle (4 per cent incidence) and in 1 case in which the tumor was situated in the cerebellopontile angle (1 per cent incidence).

Tremor.—Studies of cases of vascular and encephalitic lesions showing parkinsonian tremor[17] have indicated that this symptom is usually associated with a lesion in the lenticular nucleus. The curve obtained for the incidence of tremor among cases of variously located tumors shows the highest incidence of tremor among cases of tumor involving

14. Worcester, W. L.: Sclerosis of the Cornu Ammonis in Epilepsy, J. Nerv. & Ment. Dis. **24**:228, 1897. Steiner, P.: Epilepsie und Gliom, Arch. f. Psychiat. **46**:1091, 1909-1910. Wiglesworth, J., and Watson, G. A.: The Brain of a Macrocephalic Epileptic, Brain **36**:31, 1913. Bratz, E.: Das Ammonshorn bei epileptischen, paralytikern, senil-dementen und anderen Hirnkranken, Monatschr. f. Psychiat. u. Neurol. **46**:56, 1920. Koegerer, H.: Akute Ammonshornveränderungen nach terminalen epileptischen Anfällen, Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:211, 1923. Weimann, W.: Zur Frage der akuten Ammonshornveränderungen nach epileptischen Anfällen, ibid. **90**:83, 1924.

15. Spielmeyer, W.: Die Pathogenese der epileptischer Krampfanfällen: Histopathologischer Teil, Zentralbl. f. d. ges. Neurol. u. Psychiat. **44**:764 (Oct. 15) 1926.

16. Morgan, L. O.: The Nuclei of the Region of the Tuber Cinereum: Degenerative Changes in Cases of Epilepsy, with a Discussion of Their Significance, Arch. Neurol. & Psychiat. **24**:267 (Aug.) 1930.

17. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. f. Psychol. u. Neurol. **25**:633, 1920. Bielschowsky, M.: Weiter Bemerkungen zur normalen und pathologischen Histologie des striären Systems, ibid. **27**:233, 1922.

the lenticular nucleus. The general shape of the curve resembles that obtained for generalized convulsions except that the incidence of tremor among cases of suprahypophyseal tumor is low, whereas the incidence of generalized convulsions is high.

Olfactory Hallucinations.—The curve obtained for olfactory hallucinations is in accord with the belief that the uncinate region of the temporal lobe is concerned with smell.[18] The high incidence of olfactory hallucinations among cases of thalamic tumor suggests that a lesion in a lower center is more effective than a cortical lesion in producing this symptom.

Gustatory Hallucinations.—The location of the higher centers for taste is not known.[19] The curve obtained for gustatory hallucinations is in accord with the opinion that taste and smell are represented not by identical functional areas in the forebrain but by areas distinct from one another, though lying close together.

Visual Hallucinations.—Camus [20] believed that there is evidence that vascular and inflammatory lesions in any part of the visual pathway or in the occipital lobe may give rise to visual hallucinations of form. The curve obtained for the incidence of visual hallucination among variously located tumors indicates that a tumor in the temporal lobe or in the thalamus is more effective than one in any other area in producing visual hallucinations. If a tumor produces visual hallucinations by injuring neurologic structures concerned with vision lying in its immediate neighborhood, the curve obtained seems to imply that injury to the optic radiation or to the lateral geniculate body is more effective in producing this symptom than injury to the visual cortex.

Auditory Hallucinations.—Only 6 cases showed complex auditory hallucinations; in 4 the tumor was in the right frontal lobe, and in 2, in the left temporal lobe. Cases in which the patient reported hearing whistling and ringing noises were not included.

Irritability and Jocularity.—To the thalamus is generally ascribed responsibility for the development of emotional expressions.[21] It will be noted that the curve for jocularity is highest in the thalamus. The curve for irritability shows a peak in the caudate and lenticular nuclei. The more anterior situation of the areas in which tumors were most effective in producing irritability is in line with observations made on experimental animals. Fulton and Ingraham's cats with a lesion through

18. von Bechterew, W.: Ueber die Lokalisation der Geschmackszentren in der Gehirnrinde, Arch. f. Anat. u. Physiol., supp., 1900, p. 145.

19. von Bechterew (footnote 18). Henschen, S. E.: Ueber Geruchs- und Geschmackszentren, Monatschr. f. Psychiat. u. Neurol. **45**:121, 1919.

20. Camus, P.: Hallucinations visuelles et hemianopsie, Encéphale **6**:521, 1911.

21. Tilney, F., and Riley, H. A.: The Form and Function of the Central Nervous System, New York, Paul B. Hoeber, Inc., 1928.

the prechiasma region were extremely wild and irritable;[22] those of Beattie, Brow and Long,[23] with a lesion at the level of the mammillary bodies, were unusually docile.

Difficulty in Micturating and Incontinence of Urine.—Barrington[24] has shown that experimental lesions in a circumscribed region of the midbrain and anterior hindbrain produce abnormalities of micturition in cats. Lesions in the anterior end of the hindbrain result in incomplete emptying of the bladder. Lesions in the midbrain at the level of the anterior colliculus result in the animal micturating without first seeking a special place, without sniffing or in some other way evincing a desire to micturate. Karplus and Kreidl[25] reported contraction of the bladder on stimulation of the hypothalamus.

Neither difficulty in micturating nor urinary incontinence is perfectly analogous to the disturbances studied by Barrington. It is interesting to note, however, that the areas in which tumors most frequently produced these symptoms correspond in a general way to those regions which the work of Barrington and of Karplus and Kreidl tended to implicate in the control of micturition.

Projectile Vomiting.—The experimental work of Thumas[26] has localized a center for vomiting in the floor of the fourth ventricle. Opendowski[27] offered experimental evidence that there is a higher center for vomiting in the anterior inferior part of the junction of the caudate and lenticular nuclei. The curve obtained for the percentage incidence of projectile vomiting is in accord with the belief that there is a vomiting center in the floor of the fourth ventricle. It tends to corroborate Opendowski's localization of a higher center in the diencephalon.

Drowsiness.—Clinicopathologic studies of vascular and encephalitic lesions[28] and animal experiments have indicated that lesions in the walls

22. Fulton, J. F., and Ingraham, F. D.: Emotional Disturbances Following Experimental Lesions of the Base of the Brain (Pre-Chiasmal), J. Physiol. (Proc. Physiol. Soc.) **67**:xxvii, 1929.

23. Beattie, J.; Brow, G. R., and Long, C. N. H.: Physiological and Anatomical Evidence for the Existence of Nerve Tracts Connecting the Hypothalamus with Spinal Sympathetic Centers, Proc. Roy. Soc., London, s. B. **106**:253, 1930.

24. Barrington, F. J. F.: Central Control of Micturition, Quart. J. Exper. Physiol. **5**:81, 1925.

25. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: I. Zwischenhirnbases und Halssympathicus, Arch. f. d. ges. Physiol. **129**:138, 1909.

26. Thumas, L. J.: Ueber das Brechcentrum und ueber die Wirkung einiger pharmakologischer Mittel auf dasselbe, Virchows Arch. f. path. Anat. **123**:44, 1891.

27. Opendowski, T.: Ueber die nervösen Vorrichtungen des Magens, Zentralbl. f. Physiol. **3**:1, 1889.

28. Adler, E.: Zur Lokalisation des Schlafzentrums, Med. Klin. **20**:1321, 1924. Economo, C. V.: Die Encephalitis lethargica, J. f. Psychol. u. Neurol. **38**:253, 1917. Hirsch, E.: Zur Pathologie der Schlafzentren, Deutsche Ztschr. f. Nervenh. **102**:143, 1928.

of the third ventricle are especially likely to be associated with disturbances of sleep.[29] Hess [30] has shown that electrical stimulation of the periaqueductal and lenticular walls of the third ventricle produces sleep in cats. With his findings the curve obtained for drowsiness is in general accord.

Cessation of Menses.—Recent work by Hartman, Firor and Geiling [31] points to the primary importance of the anterior lobe of the hypophysis in maintaining the menstrual cycle. The present study indicates that amenorrhea is most readily produced by tumors of the hypophysis. Tumors in the pineal region, in the pons and in the thalamus are, however, relatively effective. In view of the low incidence of this symptom among tumors in the midbrain and fourth ventricle it would seem hazardous to assume that tumors in the pineal region, pons or thalamus produce amenorrhea indirectly by causing internal hydrocephalus.

Loss of Sexual Appetite.—Early experiments by Cushing on dogs [2a] showed that anaphrodisia frequently follows removal of the hypophysis. Camus and Roussy,[32] and Bailey and Bremer [33] have produced testicular atrophy with hypothalamic lesions that leave the hypophysis uninjured. The curve obtained for loss of sexual appetite tends to implicate the hypophysis and the suprahypophyseal region about equally.

In view of the low incidence of anaphrodisia among cases of tumor in the pineal region, cerebellopontile angle, cerebellum and fourth ventricle, it would seem hazardous to assume that midbrain and pontile tumors produced anaphrodisia indirectly by producing internal hydrocephalus.

Sexual Hypoplasia.—The finding of Camus and Roussy [32] and of Bailey and Bremer,[33] that testicular atrophy can be produced by a lesion of the hypothalamus which leaves the hypophysis uninjured, argues in favor of a neurologic basis for the sexual hypoplasia sometimes seen in cases of tumor of the brain.

The curve for sexual hypoplasia indicates a higher incidence of this symptom among tumors in the suprahypophyseal region than among those in the hypophysis. It may be that, in the production of this symptom, a possibly greater effectiveness of hypophyseal as compared with

29. Demole, V.: Pharmakologisch-anatomische Untersuchungen zum Problem des Schlafes, Arch. f. exper. Path. u. Pharmakol. **120**:229, 1927.

30. Hess, W. R.: Stammganglien-Reizversuch, Ber. ü. d. ges. Physiol. **42**:554, 1927.

31. Hartman, C. G.; Firor, W. M., and Geiling, E. M. K.: The Anterior Lobe and Menstruation, Am. J. Physiol. **95**:662 (Dec.) 1930.

32. Camus, J., and Roussy, G.: Experimental Researches on Pituitary Body, Endocrinology **4**:507, 1920.

33. Bailey, P., and Bremer, F.: Diabetes Insipidus and Genital Atrophy, Endocrinology **5**:761, 1921.

suprahypophyseal lesions is masked by the fact that the greater number of suprahypophyseal tumors occur in children (chart 1), whereas hypophyseal tumors are found most frequently in adults (chart 1), in whom it is necessary for retrogressive changes to occur before abnormalities of sex character become apparent.

Acromegaly.—The curve obtained for the percentage incidence of acromegaly indicates that it is produced exclusively by tumors of the hypophysis. This is in accord with the now generally accepted belief that acromegaly is a symptom complex resulting from an excess of secretion from the anterior lobe of the hypophysis.[34]

Polydipsia.—Camus and Roussy,[32] and Bailey and Bremer [33] have shown that polyuria and polydipsia can be produced in dogs with an intact hypophysis by a lesion in the infundibular region. Recent work by Richter [35] has shown that a persistent polydipsia can be produced in rats by a similar lesion. With these findings the curve obtained for polydipsia is in general accord. The curve suggests, however, that polydipsia may also be produced by a lesion in the pineal region.

Craving for Sweets.—It seems reasonable to suppose that craving for sweets is a symptom associated with disturbances of sugar metabolism. The work of Hiller and Tannenbaum [36] has cast doubt on the validity of most of the experimental work done on the localization of sugar centers. These authors offer evidence that injury to the dorsal nucleus of the vagus in the rabbit produces no greater rise of blood sugar than does injury to the cerebellum. Even before the publication of their work, Allers [37] believed that there was not satisfactory evidence in favor of a sugar center in the region of the fourth ventricle. He contended, however, that the tuber cinereum or some adjacent part of the hypothalamus is concerned with the regulation of sugar metabolism. The curve obtained for craving for sweets is in accord with Allers' theory. It shows that tumors in the hypophysis and suprahypophyseal region are especially effective in producing this symptom. The curve also shows a peak in the pineal region, as did the curves for polydipsia, cessation of the menses and a rapid gain in weight.

Rapid Gain in Weight.—According to Camus and Roussy [32] and Bailey and Bremer,[33] adiposity can be produced in dogs by lesions of the

34. Putnam, T. J.; Benedict, E. B., and Teel, H. M.: Studies in Acromegaly: Experimental Canine Acromegaly Produced by Injections of Anterior Lobe Pituitary Extract, Arch. Surg. **18**:1708 (April) 1929.

35. Richter, C.: Experimental Diabetes Insipidus, Brain **53**:76 (April) 1930.

36. Hiller, F., and Tannenbaum, A.: Nervous Regulation of Sugar Metabolism, Arch. Neurol. & Psychiat. **22**:901 (Nov.) 1929.

37. Allers, R.: Nervensystem und Stoffwechsel, Ztschr. f. d. ges. Neurol. u. Psychiat. **19**:209 and 321; 1920.

floor of the third ventricle. Recent work by P. E. Smith [38] on rats has corroborated this observation. The curve obtained for a rapid gain in weight shows a peak in the hypophyseal and suprahypophyseal region but a still higher peak in the thalamus and pineal region. It will be noted that this curve closely resembles that obtained for the craving for sweets.

Impairment of Hearing.—The relatively low incidence of impairment of hearing among supratentorial tumors is in accord with anatomic and physiologic evidence that the cortical areas concerned with hearing lie on both sides of the brain and that each side receives fibers from both ears.[39] It is believed that in order for a cortical lesion to produce gross impairment of hearing, it must involve the auditory cortex on both sides.

Nystagmus.—It is believed that central lesions producing nystagmus involve neurons forming part of the vestibular, cerebellar or oculomotor systems.[40] With such a belief the curve obtained for nystagmus is in general accord. The high incidence of nystagmus among cases of tumor of the cerebellopontile angle suggests that this symptom is most readily produced by a lesion of the vestibular pathways.

Positive Romberg Sign.—A positive Romberg sign is considered indicative of involvement of the afferent cerebellar pathways or of the vestibular apparatus.[41] The curve obtained here for a positive Romberg sign tends to corroborate such a theory.

Choked Disk: Four Diopters and Above.—It is generally believed that choked disk in tumor of the brain is a result of increased pressure of cerebrospinal fluid, the increased pressure being due to blocking of cerebrospinal fluid pathways and channels of venous drainage.[42] The curve obtained for high grade choked disk is in accord with this theory. It will be seen that regions near narrow parts of the cerebrospinal fluid pathway or near large venous channels are especially effective.

Hemorrhage in Nerve Head or Retina.—In tumor of the brain hemorrhage in the nerve head or retina is supposed to be an accompaniment of an especially high grade papilledema. That it is something more than this is indicated by the fact that the curves for high grade choked

38. Smith, P. E.: Hypophysectomies in Rats: Adiposity Produced by Purely Suprahypophyseal Lesions, Am. J. Anat. **45**:205, 1931.

39. Luciani, L., and Seppilli, G.: Die Funktion-Localization auf der Grosshirnrinde, Leipzig, Denike, 1886. Ferrier, D.: The Croonian Lectures on Cerebral Localization, London, Smith, Elder & Co., 1890.

40. Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System, Philadelphia, Lea & Febiger, 1919.

41. Fearing, F. W.: Experimental Study of Romberg Sign, J. Nerv. & Ment. Dis. **61**:449, 1925.

42. Paton, L., and Holmes, G.: The Pathology of Papilledema, Brain **33**:389, 1910-1911.

disk and for hemorrhage, though similar, are far from identical. In thrombosis of the central vein of the retina hemorrhage is marked, whereas edema is not. It might be argued, therefore, that the difference between the two curves is due to the greater importance of interference with venous drainage in hemorrhage in the retina. Differences between the two curves are not, however, readily explainable on this basis.

Dilated Veins of the Eyelids.—Dilated veins of the eyelids are supposed to be related to the utilization of the ophthalmic veins as emissaries following blockage of the normal channels of intracranial venous drainage. If this were the case, one might expect the curve for this symptom to resemble more closely that for high grade choked disk or hemorrhage in the nerve head.

Exophthalmos.—The peak of the curve for the incidence of exophthalmos in tumor of the temporal lobe must be due in part to the frequency with which endotheliomas in the middle fossa break through into the orbit, and also to the inclusion of a number of cases in which the tumor probably started in the orbit or in the gasserian ganglion. Unverricht [43] believed that exophthalmos in exophthalmic goiter is due to congestion and edema of the orbital tissue. He was unable to produce it in human beings by stimulation of the cervical sympathetic. It does not appear to be associated in this series, to any significant degree, with weakness of the third, fourth or sixth nerves. The incidence of exophthalmos in the whole series was 8 per cent. The incidence among patients with weakness of the oculomotor nerve was 11 per cent, among patients with weakness of the trochlear nerve 22 per cent and among patients with weakness of the abducens 7 per cent.

TABLE 3.—*Relationship Between the Side on Which the Tumor is Present and the Incidence of Certain Symptoms*

Symptoms Having a Higher Incidence Among Supratentorial Tumors on the Left	Symptoms Having a Higher Incidence Among Supratentorial Tumors on the Right
*Aphasia	*Visual hallucinations
*General convulsions	Projectile vomiting
Drowsiness	*Nystagmus
Impairment of hearing	*Choked disk of 4 diopters and above
*Exophthalmos	

* This symptom occurred more frequently among tumors of the cerebellopontile angle on the opposite side.

Relationship Between the Side on Which the Tumor is Present and the Frequency with Which Certain Symptoms Are Produced.—Table 3 gives a list of symptoms that appear to be produced more readily by

43. Unverricht: Experimentelle Untersuchungen ueber die Ursache des Exophthalmos, Klin. Wchnschr. **4**:878, 1925.

supratentorial tumors on one side than on the other. Whether this asymmetry is due to asymmetry of nerve tissue, blood vessels, bones or dural structures is difficult to determine. The well known tendency for aphasia to be produced more readily, in right-handed people, by tumors on the left is ascribed to the location of speech centers on the left and their absence on the right. It may be that the tendency for projectile vomiting to be produced more readily by tumors on the right is due to the presence of more nerve elements concerned with vomiting on the right side of the brain, as is suggested by the larger size of the right vagus nerve and the greater area of the stomach which it innervates.

The basic asymmetry of the venous drainage of the brain may be, in part, responsible for the greater ease with which certain symptoms are produced by tumors on a given side. The right lateral sinus is usually larger than the left and usually receives a larger branch from the superior sagittal sinus.[44] The left lateral sinus usually receives a larger branch from the straight sinus. Possibly there are other asymmetries of the cerebral vascular system. It seems reasonable to suppose that such asymmetries might result in a greater vulnerability of a given region on one side of the brain than on the other. It is interesting to note that of the nine symptoms listed in table 3, six were produced more readily by tumors of the cerebellopontile angle on the side opposite to that most effective for supratentorial tumors.

Internal Hydrocephalus.—Blockage of ventricular drainage with subsequent dilatation of the ventricles has been used as a *deus ex machina* to explain much that is puzzling about the symptomatology of tumors of the brain. The rarity of convulsions among cases of tumor in the fourth ventricle suggests that internal hydrocephalus is not an important factor in the production of convulsions. The dissimilarity of the subtentorial part of the curves for amenorrhea, anaphrodisia, sexual hypoplasia, polydipsia, craving for sweets and a rapid gain in weight does not suggest that these symptoms all are produced by a common mechanism, that is, by blockage of the ventricular system with subsequent compression of the floor of the third ventricle. The drowsiness that occurs so frequently in cases of pineal tumor can hardly be the result of internal hydrocephalus, for this symptom is rare among tumors of the midbrain and fourth ventricle.

Intracranial Pressure.—It is often said that drowsiness and hypersomnia are a usual accompaniment of a general rise in intracranial pressure. Projectile vomiting is likewise supposed to occur with a

44. Knott, J. F.: On the Cerebral Sinuses and Their Variations, J. Anat. **16**:27, 1882. Henrici and Kikuchi: Die Varietaeten der occipitalen Sinusverbindungen (Confluens sinuum) und ihre klinische Bedeutung, Ztschr. f. Ohrenh. **42**: 321, 1903.

generally raised intracranial pressure, as is also high grade choked disk. A glance at the curves for drowsiness, projectile vomiting and high grade choked disk makes it apparent that these three symptoms are not produced by an identical mechanism. High grade choked disk is the only one of the three that has a curve that could reasonably be accounted for on the assumption that this symptom is produced by a general increase in intracranial pressure. Choked disk, hemorrhage in the nerve head and dilated veins of the eyelids are, in fact, the only symptoms studied that have curves of incidence that suggest the possible etiologic importance of a general rise in intracranial pressure.

CONCLUSIONS

1. Generalized convulsions are not most readily produced by tumors that compress the motor cortex.

2. Visual hallucinations are not most readily produced by tumors that compress the occipital lobe.

3. The frequency with which tumors of the midbrain and the pineal region give symptoms usually associated with a lesion in the floor of the third ventricle is not satisfactorily explained by assuming that such tumors injure the floor of the third ventricle by producing an internal hydrocephalus.

4. Projectile vomiting is not a general pressure symptom.

5. Tumors that block the ventricular system are not markedly superior to all others in producing high grade choked disk.

7. Other symptoms besides aphasia are produced more readily, though to a less marked degree, by tumors on one side than on the other.

TUMORS OF THE THIRD VENTRICLE

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Tumors primarily located in the third ventricle are rather rarely encountered when one considers the relative frequency with which other portions of the brain are involved by neoplastic diseases. Weisenburg,[1] in 1910, found twenty-seven such cases in the literature, reporting at the same time three of his own. Since then many more cases of tumor of the third ventricle have been reported. Weisenburg grouped these tumors into three definite classes: those arising from the floor of the ventricle and producing no obstruction to the flow of cerebrospinal fluid; those obstructing the foramina of Monro, and capable of changing position by deviation of the head, and those extending into the aqueduct, affecting the surrounding structures by direct extension or by pressure alone.

It is the last type of tumor in which we are especially interested. That the diagnosis of a neoplasm in this region can be made if there is sufficient disturbance of the surrounding structures is obvious. However, tumors of the posterior part of the third ventricle often produce little if any clinical evidence of their existence in this particular location.

The following cases illustrate some of the difficulties that arise in the correct diagnosis of the position of this type of intracranial lesion. In only one case was a tumor of the third ventricle suspected from the clinical findings alone. In two others, death occurred before the patients could be properly studied. In a fourth, the frequent error of localizing the tumor in the cerebellum was made.

REPORT OF CASES

CASE 1.—N. A., a man, aged 23, was admitted to the University of Michigan Hospital in a semicomatose condition as presenting an emergency case. Three days previously, he had complained of severe headache. It became worse on the next day and was accompanied by nausea and attacks of projectile vomiting. On

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1. Weisenburg, T. H.: Third Ventricle Tumors, Brain **33**:236, 1910.

the day following, he became mentally confused and began to feel drowsy. When the latter symptom appeared he went to bed and summoned his family physician, who advised his removal to the hospital.

Although drowsy when he arrived, he responded correctly to questioning. The pupils were equal and regular and reacted to light and in accommodation. Except for a bilateral weakness of the sixth nerve, the extra-ocular movements were normal. The remaining cranial nerves were intact. There was no nystagmus or strabismus. The ocular fundi were somewhat hyperemic, but no actual choking was present. All tendon reflexes were equally active. There was bilateral ankle clonus but no patellar clonus. The plantar reflexes were normal. There was no atrophy, deformity, paralysis or muscle tremor, nor was there evidence of cerebellar disturbance. There were no sensory changes. The temperature and respirations were normal, and the pulse rate was 92 per minute.

Shortly after admission, the patient began to have generalized muscular twitchings, followed by severe convulsions. A few moments later, the pulse could not be obtained, and respirations ceased. Attempts to revive him were futile.

Postmortem examination showed marked internal hydrocephalus, produced by a spherical, thin-walled cyst blocking the posterior part of the third ventricle. The cyst measured 2 cm. in diameter and was suspended from the ventricular roof. Both the lateral and the third ventricle were tremendously dilated. The brain was edematous, but no evidence of degeneration was present.

Microscopic studies showed the tumor to be a cysticercus cyst, having the characteristic form of the parasite. Its origin was probably in the choroid plexus. There was no evidence of cysticercosis elsewhere in the body,

CASE 2.—D. U., a boy, aged 15, was admitted to the University Hospital in a comatose condition. While at school, six weeks previously, a playmate threw him to the ground. Shortly thereafter he began to have headaches, which progressed in severity until the onset of coma. He had seemed sleepy most of the time, often falling asleep while his parents were talking to him. Attacks of vomiting were frequent. Vision had failed since the onset of the symptoms, and he often saw double images. Two weeks prior to admission, the parents noticed that his eyes were crossed. Two days before coming to the hospital, he fell unconscious and remained so.

The boy was poorly nourished. The body was held somewhat rigidly, and he lay quietly except for purposeless movements of the left arm and leg. He neither responded to commands nor attempted to answer questions, although he seemed to recognize his parents. There were complete ptosis of the right eyelid and partial ptosis of the left. The diameter of the right pupil was about twice that of the left. Both pupils were irregular and did not react to light. There were spontaneous nystagmus and internal strabismus of the left eye. The right eye was definitely fixed. Ophthalmoscopic examination showed papilledema of 5 diopters bilaterally. The biceps and triceps reflexes were almost normal; the knee and achilles reflexes were equally diminished. The Babinski reflex was present bilaterally. There was no clonus. The abdominal and cremasteric reflexes were normal.

A lumbar puncture was done. The fluid was cloudy and under a marked increase of pressure. There were 230 cells per cubic millimeter, 80 per cent of which were polymorphonuclear neutrophils, the remainder being lymphocytes. No organisms were demonstrated, and cultures produced no growth. The globulin content was moderately increased; the Kahn test was negative, and the colloidal gold curve flat.

The patient's condition remained unchanged, and on the following morning a ventricular injection of air was done. The ventricular fluid was clear and colorless, containing only 3 lymphocytes per cubic millimeter, with no increase in solids. Ventriculograms showed internal hydrocephalus, with the right lateral ventricle displaced slightly laterally. The third ventricle was not visualized. The patient's condition became progressively worse, and he died shortly afterward.

At autopsy, a large, soft mass was found in the region of the pineal body, extending forward into the greatly dilated third ventricle. The tumor also extended laterally, involving the posterior and descending horns of the right lateral ventricle. The quadrigeminate bodies were destroyed by the growth. The peduncles, pons and cerebellum appeared normal.

Microscopic studies of the tumor showed a cellular type of glioma, with the cells packed more or less into bundles, characteristic of a spongioblastoma unipolare.

Case 3.—O. B., a boy, aged 11 years, was admitted to the University of Michigan Hospital with complaints of headache, projectile vomiting and increasing drowsiness. The onset of the symptoms was six weeks prior to admission. During this period, marked ataxia developed, the boy staggering considerably when attempting to walk. Progressive muscular weakness was also noticed. No mental symptoms had been apparent.

On examination, the patient seemed of normal intelligence and cooperated well. There was slight ptosis of the left eyelid. The pupils were equal and regular and reacted to light and in accommodation. The extra-ocular movements were normal, and there was no nystagmus. Ophthalmoscopic examination revealed a hemorrhagic neuroretinitis, with both optic disks swollen 1.5 diopters. There was no apparent weakness of the face or tongue. The tendon reflexes of the upper extremities were normal, as were also the abdominal and cremasteric reflexes. The right knee jerk was diminished, and the left absent. The achilles reflexes were absent. There was a Babinski response on the left. The extremities were definitely ataxic, but adiadokokinesis was absent. Roentgenograms of the skull showed marked increase in the digital markings.

Although a tumor of the cerebellum was suspected, ventriculographic studies were deemed advisable. These showed symmetrical dilatation of the lateral ventricles. The third ventricle was well outlined in the anteroposterior view. The lateral projections, however, were not distinct.

A suboccipital osteoplastic craniotomy was performed, but no evidence of tumor was encountered. The cerebellum was under terrific pressure. Brain plugs were taken, which failed to show a tumor. The condition of the patient became rapidly worse following operation, and he died within a few days.

Postmortem examination revealed symmetrical hemispheres with the convolutions markedly flattened. The lateral ventricles were equally dilated. In the posterior part of the third ventricle, apparently arising from its floor, was a soft, irregular tumor, measuring 3 by 4 cm. It extended backward, involving the aqueduct, and laterally, involving both optic thalami. The pineal body was flattened from the pressure of the tumor. The corpora quadrigemina were normal in appearance. The peduncles and cerebellum showed congestion and edema, while the pons and medulla appeared normal. On microscopic examination, the tumor proved to be an ependymoma.

Case 4.—F. H., a boy, aged 7 years, had had an injury to his head from a fall ten weeks before admission to the hospital. Since the accident, he complained of headaches, which had become progressively worse, and of blurring of vision,

He also had frequent attacks of nonprojectile vomiting. Two days before admission, he became drowsy, and at the time of entrance into the hospital was semicomatose.

He appeared emaciated, but showed no abnormalities of development. He would cry out at intervals, but could not be aroused. The left pupil was larger than the right; both reacted to light. Ophthalmoscopic examination showed edema of both disks, with a swelling of 1.5 diopters in each eye. There was no evidence of facial weakness. The neck was held rigidly. Brudzinski's and Kernig's tests were positive on both sides. The biceps and triceps jerks were normal, as were the abdominal reflexes. The knee and ankle jerks were equally active. The plantar reflexes were normal. It was not possible to test the cerebellar functions, but there was no history of ataxia.

Ventriculographic studies demonstrated symmetrically dilated lateral ventricles. The third ventricle was not visualized, although the lateral ventricles were filled rather completely with air. A diagnosis of tumor of the third ventricle was made.

The finding at operation of a large tumor, apparently arising from the right lateral wall of the third ventricle, confirmed the diagnosis. It filled the third ventricle, and only a portion could be excised. The patient's condition was poor following operation, and he died on the second postoperative day. At postmortem examination, the tumor was found to be extensive. It spread laterally to the right temporosphenoidal region and thence forward well into the right frontal lobe. Microscopic studies showed a vascular, but not very cellular, glioma, the architecture of which was characteristic of astrocytoma.

CASE 5.—F. G., a man, aged 29, gave a history of having had typhoid two years before admission, following which he was troubled with severe headaches. These were growing progressively worse, although they were relieved at times by large doses of acetylsalicylic acid. Three months before admission, he noticed that his vision was becoming impaired, and that objects appeared blurred when he tried to focus. He then began to have frequent attacks of projectile vomiting, which were usually preceded by nausea.

The patient was well nourished and of good development. He seemed normal mentally, answering all questions promptly and intelligently. The pupils were equal and regular and reacted to light and in accommodation. The extra-ocular movements were normal, and there was no nystagmus. Ophthalmoscopic examination showed papilledema of 3 diopters in the right eye and 2.5 in the left. The visual fields were contracted and rather bizarre. Two large scotomas were present near the central portion of the left field, and five smaller ones were scattered throughout the right field. There was no paralysis of the face, tongue or palate. The tendon reflexes of both the upper and the lower extremities were normal. The abdominal reflexes were active on both sides. No pathologic reflexes were present. There was slight dyssynergia on both sides, shown by the finger-to-nose test, but no evidence of dysmetria or adiadokokinesis.

Roentgenograms of the skull showed an increase in the digital markings and thinning of the posterior clinoids. When ventriculography was employed, the third ventricle was poorly outlined in the posterior portion (fig. 1).

At operation, a tumor about the size of a walnut was found in the posterior part of the third ventricle, obstructing the aqueduct. It was completely excised, but the patient did not withstand the operation. His temperature rose gradually following his return from the operating room, finally reaching 107 F., when death occurred. The tumor was characteristic of an ependymoma. Unfortunately, permission for postmortem examination was not obtained.

CASE 6.—F. K., a boy, aged 13, came to the hospital complaining of severe headaches and blurring of vision. These symptoms had appeared four weeks before admission and had become progressively worse. Two weeks later, the patient began to have projectile vomiting. Although the headaches were usually generalized, they were at times most prominent in the frontal region. He complained of no other symptoms.

On examination, the boy was alert mentally and well oriented and answered questions promptly. He was somewhat undersized, except for his head, which seemed relatively larger than normal. The pupils were large and equal, and reacted neither to light nor in accommodation. The extra-ocular movements were normal, and there was no nystagmus. Ophthalmoscopic examination revealed 2 diopters of choked disk with many small hemorrhages in the right eye, and 1.5

Fig. 1.—Ventriculogram from case 5 visualizing the posterior part of the third ventricle and showing the presence of a tumor.

diopters in the left. The visual fields were normal. There was no paralysis of the face or tongue. The tendon reflexes of the upper extremities were normal; of the lower, those on the right were more active than the left. The abdominal and cremasteric reflexes were normal. There were slight ataxia of the left hand and arm and suggestive adiadokokinesis.

Ventriculographic studies demonstrated the presence of a mass projecting into the posterior part of the third ventricle (figs. 2, 3 and 4).

At operation, the tumor was approached from the right occipitoparietal region, by splitting the posterior end of the corpus callosum. It apparently arose from the pineal body. The mass, measuring about 1.5 cm. in diameter, was completely excised. Its appearance was typical of a pinealoma.

The patient had a rather uneventful convalescence. He was, however, unable to rotate the eyeballs upward following the operation. Two and one-half years later,

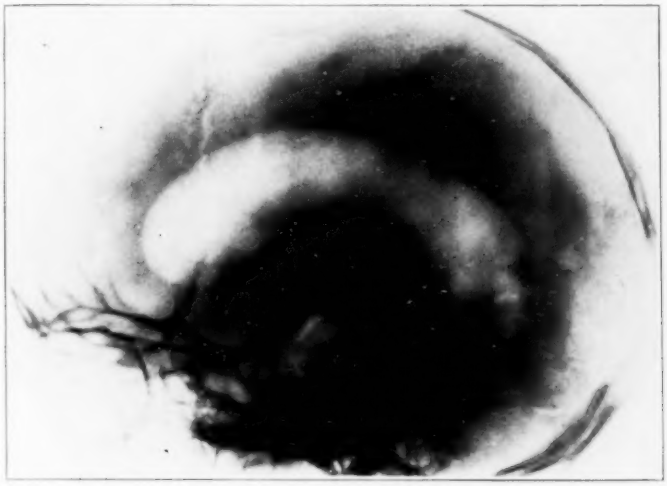

Fig. 2.—Ventriculogram from case 6 showing hydrocephalus. The outline of the third ventricle cannot be determined from this reproduction.

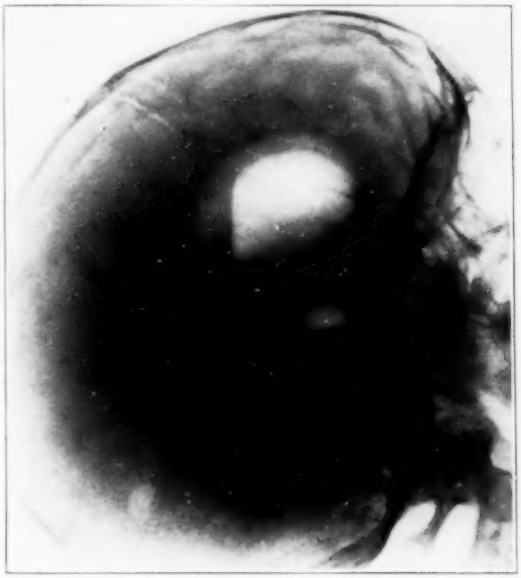

Fig. 3.—Ventriculogram from case 6 demonstrating visualization of the anterior portion of the third ventricle.

he seemed normal, except for a markedly leptosomatic appearance. He could rotate his eyes upward for a moment; they would then roll downward to the horizontal plane and diverge slightly. His mentality was not impaired.

Case 7.—E. W., a man, aged 19, entered the hospital complaining of double vision of two months' duration. Shortly after the onset of this symptom, he began to have occasional headaches and noticed a gradual loss in the acuity of hearing. Two weeks prior to admission, intermittent spells of drowsiness developed. Also associated were frequent attacks of projectile vomiting. All of these symptoms had been rapidly increasing in severity.

The patient was well developed and nourished. He appeared rather lethargic, but responded intelligently to questions. The pupils were equal and regular, and reacted to light and in accommodation. There were bilateral weakness of the

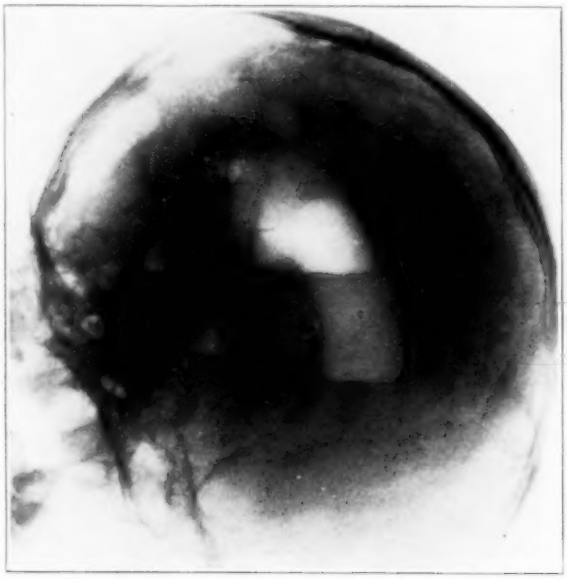

Fig. 4.—Ventriculogram from case 6 demonstrating the defect in the posterior part of the third ventricle, produced by a pinealoma.

external rectus muscles and nystagmus on lateral deviation of the eyeballs. When the patient attempted to fix his eyes on a close object, they would gradually rotate outward and downward, but there was no limitation of upward movement. Ophthalmoscopic examination revealed papilledema of 3 diopters bilaterally. The visual fields were normal. There was no evidence of facial or glossal weakness or of disturbance of sensation of the face. The biceps and triceps reflexes were equally diminished. The knee and ankle jerks were hyperactive, but equal. There was no patellar or ankle clonus, and the plantar reflexes were normal. There was some ataxia of the upper extremities, but no evidence of adiadokokinesis.

Ventriculographic studies showed well marked internal hydrocephalus and a large defect in the posterior part of the third ventricle, indicating the presence of a tumor (figs. 5 and 6) in that location.

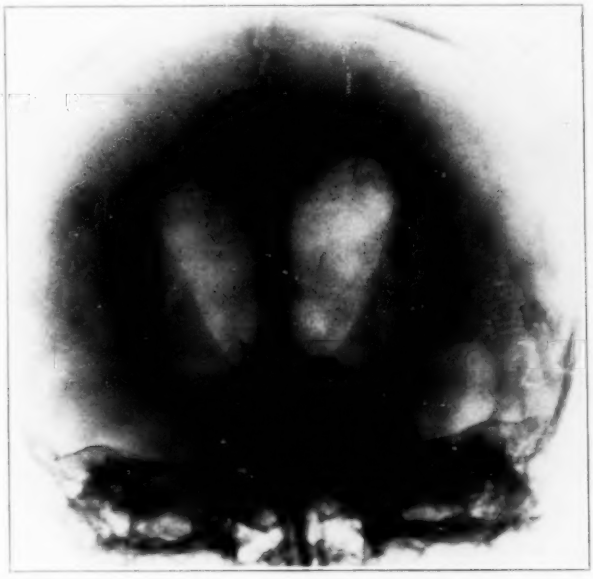

Fig. 5.—Ventriculogram from case 7 showing uniform dilatation of the lateral and third ventricles, the latter being well outlined although a tumor is present.

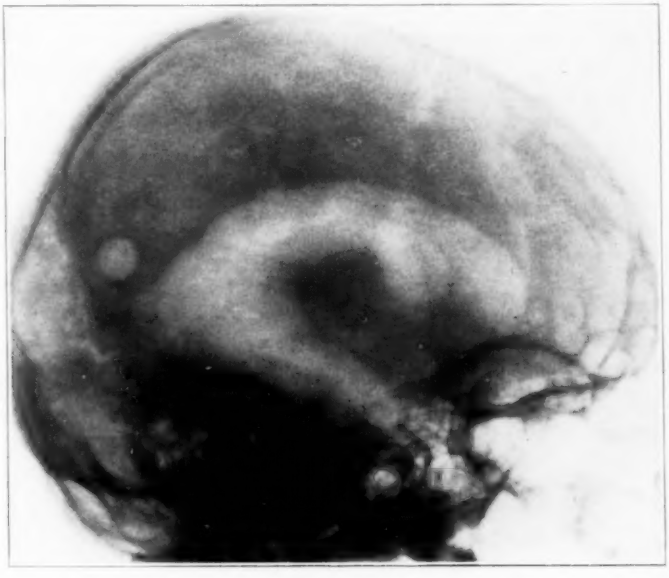

Fig. 6.—Ventriculogram from case 7 showing hydrocephalus. The outline of the third ventricle cannot be determined in this view.

At operation the lesion was approached through an occipitoparietal flap. A tumor about the size of a walnut was found in the region of the pineal body. It was completely removed, but following operation the patient remained in marked stupor for fourteen days. He then began gradually to improve, though he had a definite left hemiparesis. He was also unable to move the eyeballs upward, the same queer divergence still being present when he made the attempt. He became able to sit up, and the hemiparesis was improving slowly, when he suddenly began to fail. Death resulted about two and a half months after the operation.

Postmortem examination showed no evidence of tumor. The brain was extremely soft. The corpora quadrigemina were badly degenerated. Aside from the marked edema, no other lesion was noted. The tumor was a teratoma, chiefly adenocarcinomatous. Areas of squamous epithelium, possibly very young tooth germs, and primitive neuro-epithelium were present.

Case 8.—B. M., a woman, aged 44, gave a history of headaches and failing vision which had appeared about two months before she came to the hospital. Several weeks after the onset, a staggering gait developed. Two weeks later, she began to vomit profusely and complained of abdominal pain. A diagnosis of acute appendicitis was made, and the patient was subsequently operated on. Her condition was not improved, however, and although the vomiting subsided it did not cease. She then became exceedingly drowsy and failed to recognize those about her. At times she appeared much better, but she never attempted to talk and did not obey commands.

On examination, the patient seemed to understand what was being said to her but did not rely. She was incontinent of both urine and feces. The pupils were equal and regular, and reacted to light and in accommodation. There was bilateral weakness of the external rectus muscles. Convergence was normal. There was no nystagmus. The fundi were edematous, and 3 diopters of choking was measured in each eye. There was no weakness of the face or tongue. The biceps and triceps reflexes were normal. Hoffmann's thumb sign was suggestive on the left. The abdominal reflexes were absent. The patellar and achilles reflexes were slightly more active on the left than on the right. The Babinski test gave positive responses on the left. There was no ataxia.

Ventriculographic studies revealed symmetrically dilated lateral ventricles and an enlarged third ventricle with a tumor projecting forward from its posterior portion (figs. 7 and 8).

At operation, a tumor about the size of a marble was found. It completely obstructed the aqueduct of Sylvius. The tumor was entirely removed, but the patient did not withstand the operation.

Microscopic studies showed the tumor to be an ependymoma. At postmortem examination, aside from the large internal hydrocephalus, nothing of note was observed.

In addition to the cases presented, we were afforded the opportunity of observing the postmortem examination in a case of sudden death in a man, aged 26, who had been apparently perfectly well until the catastrophe. He had been active as a musician and was entirely asymptomatic. Yet at autopsy the brain showed a tremendous hydrocephalus due to obstruction of the aqueduct of Sylvius by a small, cherry-sized cysticercus cyst of the posterior part of the third ventricle, almost identical with that described in case 1.

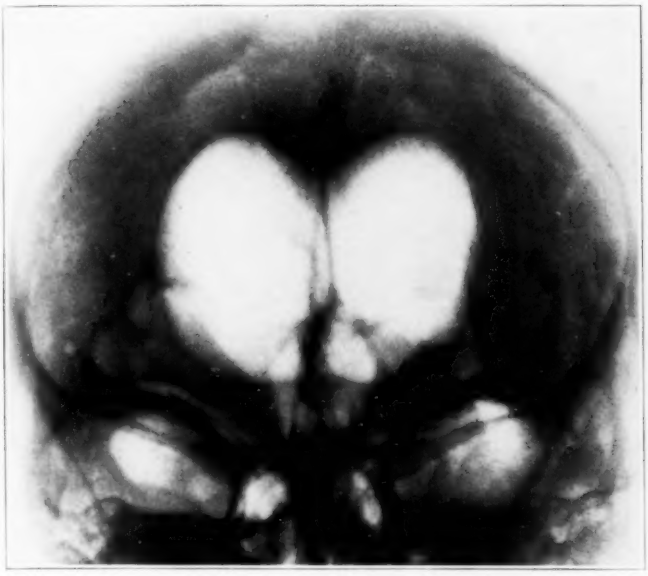

Fig. 7.—Ventriculogram from case 8 showing uniform dilatation of the lateral ventricles. The third ventricle is markedly dilated, and although the ventricle is well outlined a tumor is present.

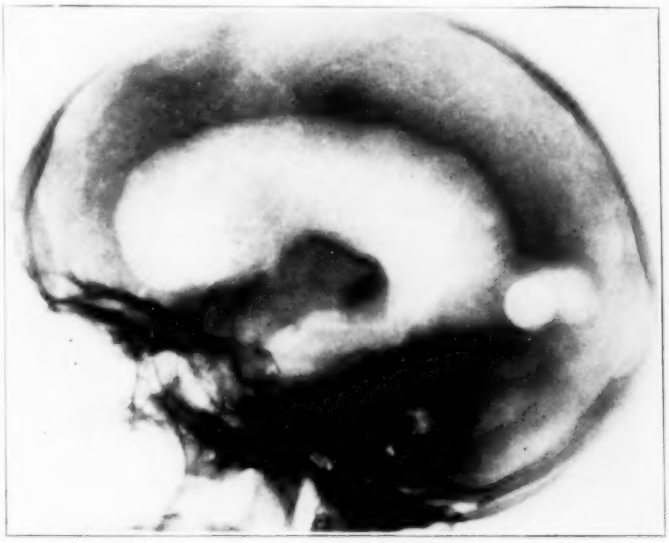

Fig. 8.—Ventriculogram from case 8 showing definite notching of the posterior part of the third ventricle by a tumor.

COMMENT

In this series there were three cases of ependymoma, one of astrocytoma, one of spongioblastoma unipolare, one of cysticercus and two of tumor of the pineal body. One of the last two growths was a pinealoma and the other a teratoma.

The types of tumors involving the third ventricle are the same as those arising from any other portion of the brain, except for the addition of neoplasms derived from the tissues of the hypophysis and epiphysis. Of tumors affecting the posterior part of this ventricle, those arising from the pineal body are the most common. Haldeman,[2] in 1927, collected from the literature reports of 113 cases of tumor of this structure, which included 22 cases of teratoma, 24 of sarcoma, 14 of cyst of the pineal body, 11 of unspecified glioma, 10 of pinealoma, 4 of hyperplasia of the pineal body, 4 of carcinoma, 4 of adenoma, 4 of psammoma and 18 of unclassified tumors. Cystic tumors[3] of the ventricle are frequently found, most of them arising in the choroid plexus, although cysts resulting from the remnants of Rathke's pouch in the anterior portion of the ventricle are much more common. Cholesteatomas[4] and parasitic cysts have also been found. Tuberculomas,[5] which are rapidly becoming less common as intracranial tumors, have been reported.

The symptoms and signs of tumor of the posterior part of the third ventricle depend entirely on two distinct features: (*a*) the production of generalized increased intracranial pressure by obstruction of the aqueduct of Sylvius and (*b*) the involvement of the structures adjacent to the ventricle either by direct extension of the neoplasm into these tissues or by pressure exerted on them by the tumor itself. Hence the

2. Haldeman, K. O.: Tumors of the Pineal Gland, Arch. Neurol. & Psychiat. **18**:724, 1927.

3. (*a*) Hassin, G. B., and Anderson, J. B.: Cystic Tumor of Third Ventricle, U. S. Vet. Bur. M. Bull. **6**:56 (Jan.) 1930. (*b*) MacPherson, D. J.: A Case Presenting an Epidermoid Papillary Cystoma Involving the Third Ventricle, Arch. Neurol. & Psychiat. **3**:395 (April) 1920. (*c*) Hall, A. J.: Two Cases of Colloid Tumor of the Third Ventricle Causing Death, Lancet **1**:89, 1913. (*d*) Drennan, A. M.: Impacted Cyst in the Third Ventricle, Brit. M. J. **2**:47 (July 13) 1929. (*e*) Guillain, G.; Bertrand, I., and Perisson: Étude anatomo-clinique d'une tumeur du IIIème ventricule, Rev. neurol. **41**:467, 1925. (*f*) Stedman, J.: Colloid Cyst, Presumably of the Choroid Plexus; Ventricular Dropsy, Boston M. & S. J. **109**: 135, 1883.

4. (*a*) Ford, F. R.: Cholesteatoma of the Third Ventricle with Bilateral Argyll Robertson Pupils, J. A. M. A. **82**:1046 (March 29) 1924. (*b*) Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.

5. Bristowe, J. S.: Clinical Remarks on Tumors Involving the Parts in the Neighborhood of the Third and Fourth Ventricle and the Aqueduct of Sylvius, Brain **6**:167, 1883.

syndrome produced by tumors of the third ventricle is not dependent on the filling or dilatation of the ventricle but on direct or indirect involvement of the surrounding brain.[6]

The symptoms that appear constantly but offer no aid in the localization of tumors of the third ventricle are those due to generalized increased intracranial pressure. This is the result, in almost every instance, of the tumor blocking the flow of the cerebrospinal fluid at either of the inlets to or at the outlet from the ventricle, producing an internal type of hydrocephalus. In Weisenburg's [1] series of cases, hydrocephalus was present in all but three, and he stated that it was also probably present in those, though not recorded. Each of our patients presented a well marked hydrocephalus from obstruction of the aqueduct. Severe headaches, drowsiness, progressive failure of vision and vomiting were the outstanding symptoms of pressure.

Various degrees of drowsiness were present in all but two of our cases. Although drowsiness, in itself, may be due entirely to increased intracranial pressure, it is nearly always a predominating feature of tumors of the third ventricle,[7] especially when there is involvement of the ventricular floor.[8] Two of our patients displayed definite hypersomnia. Disturbances in sleep are frequently found in tumors of this region and have often been interpreted as the result of epidemic encephalitis.[9] This symptom may be due to direct involvement of the basal ganglia, the midbrain about the aqueduct or the floor and sides of the ventricle, or merely to pressure of the dilated ventricle.[9b]

Progressive failure of vision was present in each of our cases. This was undoubtedly due to the high degree of choked disk,[2] as it has been demonstrated that localized destructive lesions of the midbrain are not accompanied by loss of sight.[10]

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6. (*a*) Fulton, J. F., and Bailey, P.: Tumors in Region of Third Ventricle; Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1 (Jan.), 143 (Feb.) and 261 (March) 1929. (*b*) Hogner, P.: Die klinische Erscheinungen bei Erkrankungen des III Gehirnventrikels und seiner Wandungen, Deutsche Ztschr. f. Nervenh. **97**:238 and 266, 1927.

7. (*a*) Hinds-Howell, C. M.: Tumors of the Pineal Body, Proc. Roy. Soc. Med. (Sect. Neurol.) **3**:65 (Feb.) 1910. (*b*) Mott, F. W., and Barratt, J. O. W.: Three Cases of Tumor of the Third Ventricle, Arch. Neurol., Path. Lab. London County Asyl. Claybury, London, 1900, p. 417.

8. Footnote 6. Stewart: Four Cases of Tumor in the Region of the Hypophysis Cerebri, Rev. Neurol. & Psychiat. **1**:239 (April) 1909.

9. (*a*) Bassoe, P.: A Case of Third Ventricle Tumor Mistaken for Lethargic Encephalitis, Arch. Neurol. & Psychiat. **4**:118, 1920. (*b*) Parker, H. L.: Tumors of the Brain Simulating Epidemic Encephalitis and Involving the Basal Ganglia, the Third Ventricle and the Fourth Ventricle; Report of Three Cases, J. Nerv. & Ment. Dis. **58**:1, 1923. (*c*) Guillain et al (footnote 3*c*).

10. Hoppe, H. H.: Tumor of the Corpora Quadrigemina, J. Nerv. & Ment. Dis. **39**:108, 1912.

Inequality of the pupils and disturbance of pupillary reaction were present in only three of the cases. The diagnostic value of this sign depends largely on the observer's interpretation of his findings, as the degree of optic atrophy present and not a lesion of the third nerve may well account for the loss of reaction. These pupillary disturbances are common, especially if the tumor invades the posterior wall of the ventricle. The Argyll Robertson [11] type of pupil has been described as due to such tumors, but the pupil in this instance may be contrasted with that seen in syphilitic lesions by its large and circular appearance.[4a]

We were able to have examinations of the visual fields made in only three of our cases, and in none of these were there any significant changes from the normal to aid in the diagnosis. If the tumor extends laterally for any distance, homonymous hemianopia may be expected by encroachment on the optic radiations as they approach the occipital lobe. This finding has been described by Shelden and Lillie [12] in a case of tumor of the third ventricle that produced no other localizing signs. It is unfortunate that in our second case, which showed this type of lesion, the field of vision could not be examined.

Of the extra-ocular palsies, those of importance that may be regarded as diagnostic in tumors of this region are conjugate paralyses of the eye movements. Paralysis of associated upward movement is perhaps the most significant of all neurologic signs of tumors of the posterior part of the third ventricle, particularly in those arising from the pineal body.[13] The paralyses undoubtedly result from the involvement of the midbrain in the region of the aqueduct of Sylvius, either by direct extension of the tumor into the brain or by pressure alone. Although impairment of conjugate movements of the eyes has long been attributed to lesions of the corpora quadrigemina,[14] it has been shown rather conclusively that destruction of these bodies alone will

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11. (*a*) Wilson, S. A. K., and Rudolf, G. de M.: Case of Mesencephalic Tumor with Double Argyll Robertson Pupil, J. Neurol. & Psychopath. **3**:140, 1922. (*b*) de Monchy, S. J. R.: Rhythmical Convergence Spasm of the Eyes in a Case of Tumor of the Pineal Gland, Brain **46**:179, 1923. (*c*) Glaser, M. A.: Tumors of the Pineal Gland, Corpora Quadrigemina and Third Ventricle, Brain **52**:226 (July) 1929. (*d*) Ford (footnote 4*a*).

12. Shelden, W. D., and Lillie, W. I.: Importance of Visual Fields as Aid in the Localization of Brain Tumors, J. A. M. A. **94**:677 (March 8) 1930.

13. (*a*) Duane, A.: The Extra-ocular Muscles, in Posey and Spiller: The Eye and the Nervous System, Philadelphia, J. B. Lippincott Company, 1906, chap. 5, p. 178. (*b*) Horrax, G., and Bailey, P.: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

14. Turner, W. A.: Localization of Intra-cranial Tumors, Brain **21**:341, 1892.

not produce this phenomenon.[15] Muskens[16] localized such a lesion ventral to the posterior longitudinal bundle near the raphe. It is surprising that upward paralysis of associated movement was not present in at least two of our cases, in which the lesion seemed to extend into this region, especially in case 7. This patient, however, was unable to maintain convergence for any length of time; his eyes rotated outward and downward, assuming a divergent strabismus when convergence was attempted. De Monchy[11b] described a case of rhythmic convergence spasm of the eyes in a boy, aged 14, suffering from a tumor of the pineal gland. In this instance there were both upward and downward paralysis also, associated with an Argyll Robertson type of pupil.

In only one of our cases was there impairment of hearing. There was no evidence of disease of the ears; yet both sides were equally affected, although not to a marked degree. This phenomenon has been described by Horrax[17] as occurring in four of eleven cases of tumor of the pineal gland. Lesions of the pons and tegmentum of the crura that involve the lemniscus more often produce deafness.[18] The symptom of deafness in our case was accompanied by tinnitus, which is not infrequently found in choking of the labyrinth from tumors producing increased intracranial pressure alone and not primarily affecting any of the pathways to the higher auditory centers.[19] The corpora quadrigemina were badly destroyed in this instance, but experiments have demonstrated that hearing and perception of tones were preserved following extirpation of these structures.[10]

Perhaps the most confusing symptom of all, not only in differentiation of tumors of the third ventricle from those of the cerebellum but in supratentorial and infratentorial lesions in general, is ataxia.[20] Definite ataxia was present in four of our cases, and a tumor of the cerebellum was thought to be present in three of these. In tumors of the pineal body it accompanies the other symptoms with marked regu-

15. (*a*) Spiller, W. G.: Importance in Clinical Diagnosis of Paralysis of Associated Movements of the Eyeballs, Especially in Upward and Downward Movement, J. Nerv. & Ment. Dis. **32**:417 and 497, 1905. (*b*) Hoppe (footnote 10).

16. Muskens, L. J. J.: The Central Connections of the Vestibular Nuclei with the Corpus Striatum, and Their Significance for Ocular Movements and for Locomotion, Brain **45**:454, 1922.

17. Horrax, G.: Differential Diagnosis of Tumors Primarily Pineal and Primarily Pontile, Arch. Neurol. & Psychiat. **17**:179 (Feb.) 1927.

18. Starr, M. Allen: Deafness Due to Lesions of the Brain, J. Nerv. & Ment. Dis. **37**:401 (July) 1910.

19. Alexander, G.: The Choked Labyrinth and Its Importance for Diagnosis and Indications in Brain Tumor, Surg., Gynec. & Obst. **46**:361 (March) 1928.

20. (*a*) Bailey, P.: Cerebellar Symptoms Produced by Suprasellar Tumors, Arch. Neurol. & Psychiat. **11**:137 (Jan.) 1924. (*b*) Bassoe, P.: Tumors of the Third and Fourth Ventricles, J. A. M. A. **67**:1423 (Nov. 11) 1916.

larity.[13b] As a rule, the nearer tumors of the third ventricle are to the midbrain the more likely is ataxia to be present, although it may be found in cases of hydrocephalus alone,[11a] with no involvement of the equilibratory tracts except indirectly by pressure. Pressure on the cerebellum by the dilated posterior horns of the lateral ventricles, however, may account for the symptom.[1] If the tumor extends caudad for any distance into the mesencephalon, the ataxia may be the result of destruction of, or pressure on, the red nuclei or the superior cerebellar peduncles.[1] The combination of ataxia with disturbances in movements of the eyeballs is often seen in tumors below the tentorium, but the chronological appearance of the symptoms may aid in the diagnosis; i. e., ocular symptoms first, followed by ataxia, indicate a tumor of the mesencephalon, while ataxia, followed by ocular symptoms, suggests a tumor of the rhombencephalon.[10]

Symptoms of involvement of the pyramidal and of the extrapyramidal tracts are not infrequently found. They were present in only four of our cases. In one, a tumor of the frontal lobe was suspected because of the lack of other localizing neurologic findings. Fulton and Bailey [6a] attributed these symptoms to pressure of the tumor on the lateral walls of the ventricle, or to involvement of the surrounding brain, affecting the internal capsule.

Hogner [6b] has stressed the frequency of disturbance of the vegetative nervous system in cases of tumor involving any portion of the third ventricle. This is evidenced by vasomotor symptoms, and by secretory and thermic disturbances. In case 5, severe hyperthermia occurred immediately after operation, the temperature reaching 107 F. when death occurred. In none of the other cases were any of the phenomena observed.

In only two of our cases did the tumor have its origin in the pineal body. Neither the pinealoma nor the teratoma presented the syndrome of "macrogenitosomia praecox," described by Pellizi and Frankl-Hochwart, and later stressed by Krabbe, de Monchy, Fulton, Bailey and Haldeman.[2] The case of pinealoma was in a boy who was considerably undersized and without abnormal sexual development. The patient with the teratoma was well past the age of puberty when the symptoms of tumor became apparent. Krabbe [21] concluded that pubertas praecox is found regularly with teratomas of the pineal body. This was first emphasized by Frankl-Hochwart [22] and later by Horrax and Bailey.[13b] In Haldeman's series there were sixteen cases of macrogenitosomia

21. Krabbe, K. H.: Pineal Gland; Supposed Significance in Sexual Development, Endocrinology **7**:379, 1923.

22. von Frankl-Hochwart, L.: Ueber Diagnose der Zirbeldrüsentumoren, Wien. med. Wchnschr. **9**:506 (Feb. 26) 1910; Ueber Diagnose der Zirbeldrüsentumoren, Deutsche Ztschr. f. Nervenh. **37**:455, 1909.

praecox, nine of which were in patients having a teratoma of the pineal body. The others included two cases of hyperplasia of the pineal gland, one each of adenoma, sarcoma, angiosarcoma, neuro-epithelioma and one of an unclassified tumor.[2] In de Monchy's series of thirteen cases, eight tumors were teratomas, three sarcomas, one an adenoma and one a glioma. In cases of teratoma in which macrogenitosomia praecox did not exist, all the patients were above the age of puberty.

That sudden death frequently occurs in cases of intraventricular tumors is a fact that has been emphasized by Hogner [6b] and others. Death may precede the development of symptoms that might lead one to suspect the presence of an intracranial lesion. It is of more than usual interest that in the two cases of our series terminating suddenly, in one of which the patient died before symptoms became apparent, solitary cysticercus cysts were the etiologic agents.

From the cases presented, it is seen how few localizing neurologic signs may be present to aid in accurate diagnosis of the position of the tumor, even though the severity of symptoms from obstruction of the ventricles or from generalized pressure by growth of the tumor may be extreme. Hogner [6b] stressed especially the lack of symptoms in tumors arising from the roof of the ventricle. If in all cases of tumor of the posterior portion of the third ventricle the structures of the midbrain were involved, diagnosis would be less difficult but the prognosis in general would be considerably worse than it already is. There is not a single diagnostic sign that may result from pressure alone. Not until the surrounding structures are involved by the growth of the tumor or by the resulting edema in the immediate vicinity do localizing signs become apparent. Often by the time these signs make their appearance the patient is in a practically hopeless condition. We may cite the case of a child, aged 4, who presented no symptoms other than those of increased intracranial pressure and ataxia. Ventriculograms were made which showed an obstruction in the region of the aqueduct of Sylvius. Death followed an exploratory operation on the cerebellum, and at autopsy a small but diffuse glioma was shown completely obliterating the entire lower two thirds of the aqueduct. We were at a loss to account for the lack of involvement of the cranial nerves.

It is in cases of tumor of the posterior part of the third ventricle that ventriculography displays one of its greatest values in the localization of intracranial lesions.[23] As hydrocephalus is such a prominent feature, considerable care is required in emptying the ventricles as thoroughly as possible and fractionally replacing the fluid with air. One naturally expects the lateral ventricles to be dilated (figs. 5 and 7),

23. Dandy, W.: Diagnosis, Localization and Removal of Tumors of the Third Ventricle, Bull. Johns Hopkins Hosp. **23**:188, 1922.

provided there is no obstruction in the region of the foramina of Monro. It is then essential that both the anterior and posterior parts of the third ventricle be visualized. This is the main point in the differentiation of a subtentorial lesion from one of the third ventricle. If, in the case of symmetrically dilated lateral ventricles, the third ventricle is well outlined, the lesion must of necessity lie posterior to the third ventricle. But if the posterior portion of the third ventricle is incompletely filled, the block in the ventricular system must be suspected in this region. Often a well defined notching may be demonstrated (fig. 8). In many cases it is extremely difficult to introduce sufficient air to be reasonably certain about the posterior part of the ventricle (figs. 2 and 6). Lateral exposures of the skull should then be taken with the body in a horizontal position and the face looking first upward and then downward (figs. 3, 4 and 1). These positions allow the air to gravitate to the anterior and posterior parts of the third ventricle, respectively, and these regions will be well outlined, even though the filling is inadequate to visualize these portions definitely in other views.

SUMMARY

1. Tumors arising in the posterior portion of the third ventricle are relatively infrequent. Eight cases are reported.

2. Hydrocephalus and increased intracranial pressure resulting from obstruction to the aqueduct of Sylvius are constant.

3. Lesions in this location usually produce no characteristic symptoms or localizing signs. The most commonly noted findings are papilledema, increased intracranial pressure, hypersomnia, disturbances of pupillary reaction, extra-ocular palsies, vegetative dyscrasias and precocious sexual development. Cerebellar symptoms are often confusing, and the lesion is erroneously ascribed to the hindbrain. Sudden death is frequent.

4. Paralysis of upward associated ocular movements and precocious sexual development in male children before the age of puberty are the most important clinical findings, in the absence of which the clinical diagnosis of pineal tumors is almost impossible.

5. Visualization of the lesion frequently by ventriculography makes this a most important diagnostic procedure.

DISORDERS OF OPTIC NYSTAGMUS DUE TO CEREBRAL TUMORS

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The possibility of exploiting optic nystagmus as an aid in cerebral localization depends on the fact that in certain cerebral lesions optic nystagmus may be present to one direction of movement of visual objects, but absent or defective in the other direction. This type of ocular behavior has been studied clinically by direct observation of the response of the eyes of a stationary subject to a moving visual field, such as a revolving drum or cylinder carrying alternate black and white stripes or a continuous series of figures or pictures. The test can be easily employed with practically all patients, providing they are sufficiently alert to direct their gaze to the drum. Optic nystagmus can be elicited with a low degree of visual acuity and even in the presence of a large central scotoma. Furthermore, hemianopic defects in the visual field, particularly those caused by infrageniculate lesions involving the optic tract, do not in themselves disturb optic nystagmus.

Fox and Holmes,[1] in their work, frequently noted responses of the eyes which they were unable to describe by unaided observation. They were compelled to limit their published results to those cases in which optic nystagmus was apparently normal to one direction of rotation of the field, and absent, or grossly disturbed to the other. Some form of graphic recording device is essential for the analytic and comparative study of the finer details of all types of eye movements. Various forms of apparatus for recording eye movements are now available to the student of optic nystagmus. Our nystagmograph employs the principle of photographing horizontal conjugate deviations of a closed eye. For a description of the technic, the reader is referred to the previous papers in this series.[2]

Read before the International Neurological Congress, Bern, Sept. 3, 1931.

1. Fox, J. C., and Holmes, G.: Brain **39**:333, 1926.

2. Dodge, R., and Fox, J. C., Jr.: Optic Nystagmus: I. Technical Introduction with Observations in a Case with Central Scotoma in the Right Eye and External Rectus Palsy in the Left Eye, Arch. Neurol. & Psychiat. **20**:812 (Oct.) 1928. Fox, J. C., Jr., and Dodge, R.: II. Variations in Nystagmographic Records of Eye Movements, ibid. **22**:55 (July) 1929. Dodge, R.; Travis, R. C., and Fox, J. C., Jr.: III. Characteristics of the Slow Phase, ibid. **24**:21 (July) 1930. Fox, J. C., Jr.; Couch, F. H., and Dodge, R.: IV. Physiologic Conditions, ibid. **26**:23 (July) 1931.

MATERIAL AND METHOD OF STUDY

This report concerns the detailed study of twelve cases with verified lesions variously situated in the cerebral hemisphere. Although a much larger clinical material has been made available during the course of our work, discussion is here limited to those cases in which the location was verified, either approximately at operation or precisely post mortem. All patients have been excluded in which the presence of a severe impairment of visual acuity, spontaneous nystagmus, weakness of any of the ocular muscles or heterophoria might interfere with the interpretation of the nystagmographic record. No case is included in which there was any uncertainty with respect to the alertness, intelligence and general capacity of the patient to cooperate at the time that the photographic record was obtained. In each instance, the photographic records appear to be satisfactory from the technical standpoint, and clearly show the character of the pursuit pattern to both directions of movement of the visual field.

The location of the lesions may be classified as follows: three parieto-occipital; one each of temporal, temporoparietal, parietal and frontoparietal; five frontal. Eleven of the twelve patients were operated on, in six cases more than once. The operative procedures were carried out by either Dr. S. C. Harvey or Dr. W. J. German. Despite the fact that the localization of a cerebral neoplasm can only be approximately verified at the operating table, it was believed that in this group of cases the estimation of the extent of the injury beneath the surface was fairly accurately estimated by incision, attempted extirpation and in two cases by frontal transection. The postmortem verification in two cases added little of value because of the elapse of time between the nystagmographic studies and the death of the patient.

As part of the complete neurologic examination, a thorough study of the visual and ocular functions was made in each patient. This examination included visual acuity, a Snellen chart at 20 feet and Jaeger type at 18 inches (45.7 cm.) being used; visual fields; ophthalmoscopic examination; conjugate eye movements on command, and pursuit of the moving finger. Visual attention was studied by the method of moving two objects (forefingers) simultaneously before the patient in extreme lateral fields at equal distance from the fixation point. In addition, frequent direct observations of the optic nystagmus were made in each case, both at the bedside and in the laboratory at the time of nystagmography. For this purpose a kymograph cylinder, 16 cm. in diameter, showing alternate vertical black and white stripes, 1 cm. in width, was slowly rotated at reading distance from the patients' eyes (45 cm.).

EXPERIMENTAL OBSERVATIONS

The cases are presented according to location of lesion rather than in sequence of observation:

PARIETO-OCCIPITAL LESIONS

CASE 5.—C. H., a man, aged 30, who was admitted to the hospital on Oct. 9, 1928, had originally been right-handed but, following an amputation in childhood, had learned to write with the left hand. Three months previously, he began to suffer with frontal headaches and attacks of weakness and vomiting, with transitory mental confusion and one spell of unconsciousness. Neurologic examination showed euphoria, impairment of the higher faculties, and difficulty in finding words, but no dyslexia. He could write well with the left hand. He had bilateral papilledema, right facial weakness, right hemiparesis and diminution of proprioceptive sensation in the right lower limb.

On October 18, in the performance of a ventriculogram, a needle was passed toward the left occipital horn, and at a depth of about 3 cm. there appeared 3 or 4 cc. of yellow fluid. A large parieto-occipital bone flap was then turned down on the left side. An incision was made in the ascending lip of the angular gyrus and carried down until it came in contact with gliomatous tissue 2 cm. beneath the cortex. Some of this was removed with the cautery and the growth followed back as far as the ventricle. Many small cysts were encountered; the glioma apparently spread out in all directions (fig. 1). Section revealed a blastocytoma.

On readmission to the hospital on Jan. 10, 1928, visual acuity was: right, 20/25; left, 20/20. There was a beginning right homonymous defect (fig. 1) and a disturbance of visual attention to the right. The eye movements on command were sluggish, more marked to the right than to the left, but there was no disturbance in pursuit. *Optic nystagmus* was vigorous for both directions of rotation of the drum.

Nystagmographic Records (fig. 1).—The pursuit pattern in both directions was normal in every respect.

The patient was again admitted in March, with almost complete motor aphasia and beginning secondary optic atrophy. On March 20, the bone flap was elevated; a considerable portion of the glioma was removed, and several cysts were also evacuated. Visual acuity was: right, 20/30; left, 20/20. The visual fields showed a generalized restriction with an hemianopic defect on the right (fig. 1). Command movements to the right were jerky, but to the left were normal. Pursuit of the moving finger appeared normal in both directions. *Optic nystagmus* was irregular in both directions, more so when objects were moving from the right to the left than from the left to right.

Nystagmographic Records (fig. 2).—The nystagmographic pattern was irregular for both directions of movement of the screen. However, in general, the response seemed to be more inadequate when the objects were moving from right to left, or toward the side of the lesion, especially at the higher speed.

CASE 4.—W. M., a man, aged 31, who was admitted to the hospital on Nov. 29, 1928, for seven years had suffered from dizzy spells, which were always preceded by a buzzing noise in the right ear. He had several attacks of unconsciousness. On regaining consciousness he was confused, disoriented and sometimes maniacal for a period of ten minutes. Severe pain in the right side of the head, blurring of vision and gradual change of personality developed. Neurologic examination revealed failure of attention, defect in memory, left facial weakness, clumsiness of

the left hand, left hemisensory disorder and astereognosis in the left hand. Visual acuity was: right, 20/40; left, 20/25. There were a left lower homonymous visual defect and complete visual inattention to the left (fig. 3). On command to look to the right, the eye movements were normal; on command to look to the left, the eyes moved in a succession of jerks.

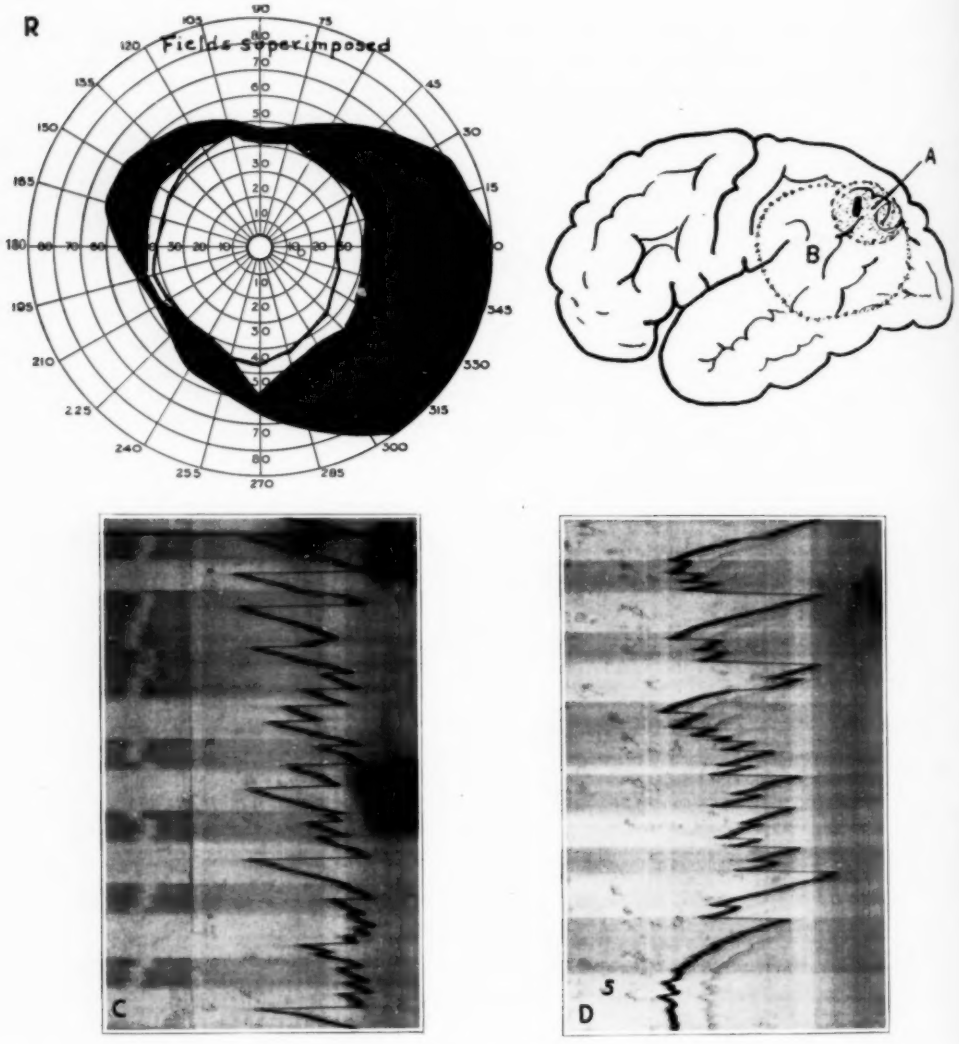


Fig. 1 (case 5).—Nystagmographic records made three months after the first operation. *A* indicates the extent of the lesion at the first operation and *B*, the extent at the second operation. In *C* and *D*, the ocular response is normal.

Optic nystagmus was normal with stripes moving from right to left. However, in the opposite direction, no definite nystagmus occurred.

A ventricular needle was passed into the right occipital lobe and a few cubic centimeters of yellow, gliomatous fluid obtained. In the region of the angular gyrus and posterior to it the overlying cortex was rather yellow in appearance.

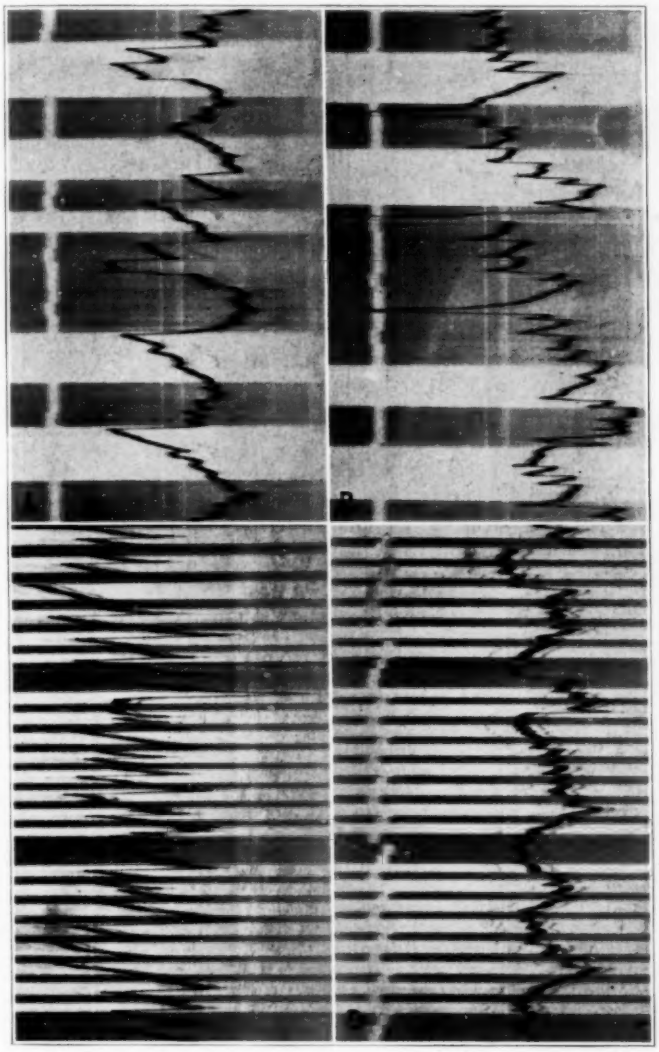
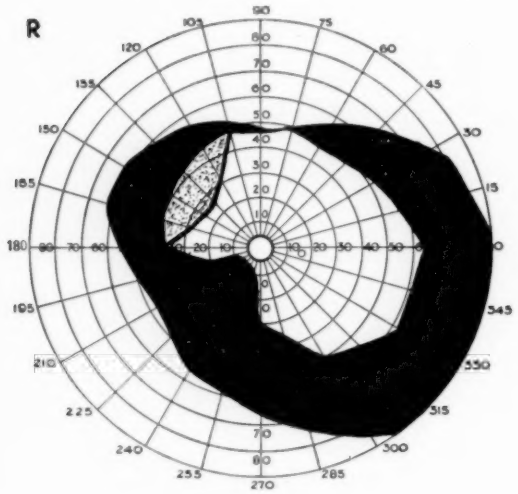
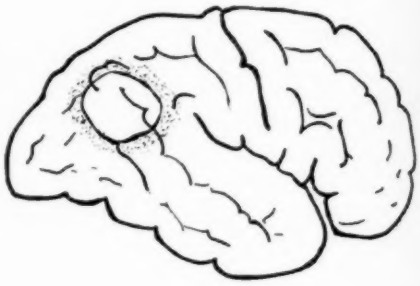


Fig. 2 (case 5).—Nystagmographic records made twenty-two and twenty-six days after the second operation (see fig. 1 *B*). In *A*, the ocular response is irregular; in *B*, defective; in *C*, normal, and in *D*, defective.

Incision with the electric cautery at once came down on cystic gliomatous tissue, which was found to be infiltrating in many directions. About 25 Gm. of tissue was removed. Section showed a spongioblastoma. On December 22, the visual

and ocular functions were identical with those described before operation. When the stripes moved from left to right, *optic nystagmus*, which before the operation had been absent, could now be elicited but was feeble and irregular.





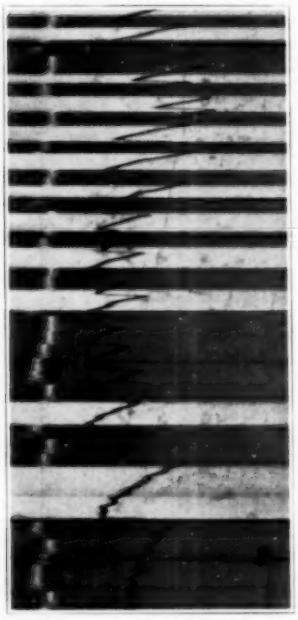


Fig. 3 (case 4).—Nystagmographic records made sixteen days after operation. In *A*, the ocular response is normal; in *B*, defective.

Nystagmographic Records (fig. 3).—When the objects were moving from right to left, the nystagmographic pattern was adequate. On the contrary, when the

bars were moving in a direction toward the side of the lesion, the pursuit pattern was inadequate, with shortening of both phases. Note the interruption of the first quick phase to the left by a succession of gropings. When the screen was rotating at a higher speed, there was at times a complete failure to pursue (not reproduced).

The patient was readmitted to the hospital on several occasions, until death took place on April 9, 1930, following an attempt to perform a more radical extirpation. During this entire period, whenever optic nystagmus was tested by means of the drum, the response was found to be either absent or markedly defective from left to right, but either normal or only slightly impaired from right to left. Postmortem examination of the brain revealed, in addition to the large cavity formed by the removal of the tumor mass at operation, an extensive infiltration of the posterior part of the right hemisphere. These findings indicating the wide extent of the tumor at death have no significant bearing on its localization at the time the nystagmograms were taken fifteen months previously.

CASE 1.—D. P., a woman, aged 29, right-handed, who was admitted to the hospital on June 6, 1927, had suffered for three months with headache, blurring of vision, dizziness and vomiting. Neurologic examination showed bilateral papilledema, slight left facial weakness, clumsiness of the left arm and dystereognosis in the left hand. Both blood and spinal fluid showed a positive Wassermann reaction.

On June 15, visual acuity was: right, 20/40; left, 20/30. A left homonymous hemianopia extended to within 10 degrees of the fixation point. The eye movements on command and in pursuit were normal in both directions except for a slight increase in positional nystagmus.

Nystagmographic Records.—When the screen was moving from right to left, the pursuit pattern was normal. On the other hand, when the screen was moving toward the side of the lesion, the pursuit movements were defective, as shown by a lag at onset and slow, inadequate pursuit. Also the quick phases were interrupted by periods of still fixations.

The patient failed to respond to antisyphilitic treatment, at first administered conservatively and subsequently more intensively, and died on Oct. 17, 1927. Postmortem examination revealed a large gumma in the right hemisphere, occupying chiefly the white matter, beginning in the centrum ovale, 5 cm. from the frontal pole, and extending to a point 2 cm. from the occipital pole, roughly ovoid in shape, and measuring 7 by 5 cm. beneath the fissure of Rolando. The optic radiation on the right was completely absent, and the internal capsule was invaded and destroyed from the genu caudally. Of course, the findings at postmorem examination do not give a true picture of the extent of the lesion at the time when the nystagmographic records were obtained four months previously. The sequence of symptoms indicated that the lesion had undoubtedly originated in the parieto-occipital region and had spread anteriorly.

Summary.—All three of the tumors situated in the posterior part of the hemisphere caused a disturbance of optic nystagmus when the visual objects were moving in a direction toward the side of the lesion. In one of these, case 5, when the lesion occupied the area marked *A*, the nystagmographic pattern was normal (fig. 1). On further extension and involvement of the region marked *B*, the ocular response became defective (fig. 2). The tumor in case 4 occupied a similar

location and disturbed optic nystagmus when the objects were moving toward the side of the lesion (fig. 3). The nystagmographic findings were similar in case 1.

TEMPORAL AND TEMPOROPARIETAL LESIONS

CASE 11.—D. S., a girl, aged 15, right-handed, who was admitted to the hospital on May 4, 1931, had a chronic discharge from the right ear after scarlet fever, ten years previously. Eight weeks before, pain developed over the right eye, with nausea and vomiting, and three weeks later impairment of vision. Neurologic examination showed bilateral papilledema and anosmia, but no localizing signs. Ventriculography on May 8 indicated a tumor in the posterior part of the right hemisphere. Exploration of the right temporoparietal region showed no evidence of tumor on the surface, but in the superior temporal region, just below the supramarginal gyrus, a resistant mass was encountered on tapping at a distance of 3 cm. below the cortex. The brain was incised at this point and a discrete tumor was encountered (fig. 4). The margins of the tumor were dissected free, and successive portions were scooped out. Section showed a meningioma. A complete removal will be attempted at a second stage.

On June 14, one month after operation, visual acuity was: right, 20/30; left, 20/100. A left homonymous hemianopia extended almost to the fixation point (fig. 4). The eye movements on command and in pursuit were defective in all directions. *Optic nystagmus* showed a very striking contrast. When the stripes were moving from the left to right, or toward the side of the lesion, there was no trace of nystagmus. However, in the opposite direction, there was a vigorous nystagmus.

Nystagmographic Records (fig. 4).—A similar phenomenon is demonstrated photographically. When the screen was moving from right to left, there was an adequate pursuit pattern. On the contrary, when objects were moving toward the side of the lesion, there was no trace of true pursuit. The entire ocular behavior consisted in periods of still fixation, interrupted by quick jerks in either direction.

CASE 7.—R. V., a girl, aged 17, right-handed, who was admitted to the hospital on Nov. 20, 1929, had a subacute discharge from the left ear for ten years with an acute exacerbation four days previously. Difficulty with speech developed, and she lapsed into unconsciousness. She was comatose, with a temperature of 101.6 F. and Cheyne-Stokes respirations. Bilateral papilledema and paralysis of the right side were present. The spinal fluid contained 454 white cells per cubic millimeter.

A ventricular needle was introduced for a distance of about 2 cm. into the left temporal lobe until pus was obtained. The needle was then removed and a small portion of the cortex transected at the needle hole and extending downward to the abscess cavity. A Penrose drain was inserted into the abscess cavity, and about 45 cc. of pus was removed with a sucker.

During the month following the operation the patient showed a steady, remarkable improvement. On December 17, visual acuity was: right, 20/25; left, 20/40. The visual fields were generally restricted to 30 degrees, with indentation of the upper right quadrants. Ocular movements were normal on command and in pursuit. Visual attention was normal. *Optic nystagmus* tired easily when stripes moved from right to left.

Nystagmographic Records.—The pursuit pattern showed many evidences of inadequacy for both directions of movement of the screen. However, the defects

were found to be more marked when the bars were moving from right to left. The quick phase also seemed to have a slower angle of velocity throughout the records. There were numerous periods of still fixation when the bars were moving in a direction toward the side of the lesion.

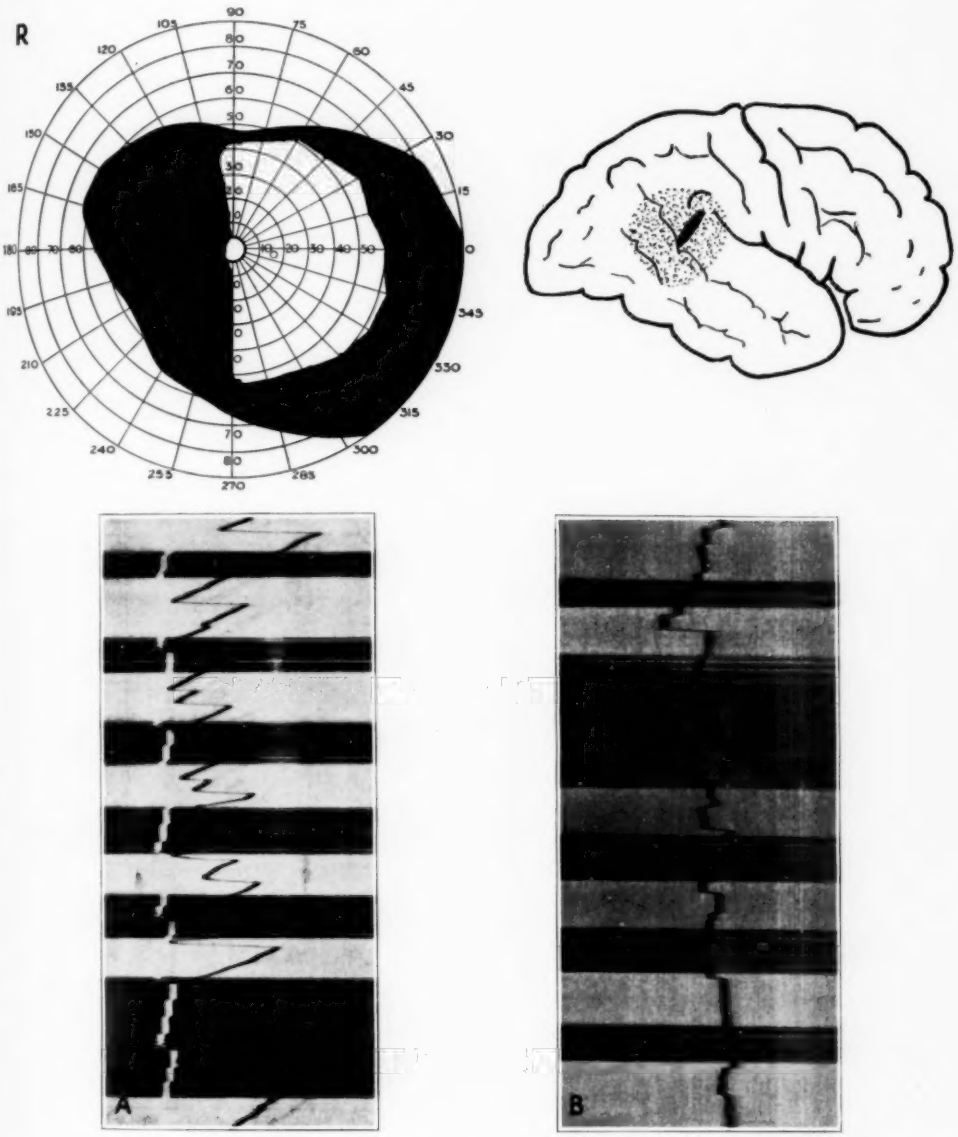


Fig. 4 (case 11).—Nystagmographic records made thirty-one days after operation. In *A*, the ocular response is normal; in *B*, absent.

Summary.—In case 11 (fig. 4), a tumor situated in the right temporoparietal region caused a complete absence of pursuit when the

objects were moving from left to right, or toward the side of the lesion. In case 7 an abscess in the left temporosphenoidal region disturbed optic nystagmus to both directions, but the pursuit pattern was more defective when the objects were moving toward the side of the lesion.

PARIETAL AND FRONTOPARIETAL LESIONS

Case 8.—B. D., a man, aged 29, right-handed, who was admitted to the hospital on Jan. 3, 1930, three years previously had sustained a fracture of the skull, with loss of consciousness. Three months later, he had a first convulsive seizure; these have recurred since with increasing frequency. Each attack began with a sensory aura in the left side of the face or arm, followed by twitching and then loss of consciousness. Neurologic examination gave negative results.

On January 9, a bone flap was turned down in the right parietal region. In the postcentral area, immediately adjacent to the fissure of Rolando, corresponding to the level of the arm and face, there was a cystlike structure which was evacuated on opening the dura. The cyst was filled with blood-tinged fluid, and the cortex about this area was markedly scarred for a distance of about 4 or 5 cm. The center of this scarred area was depressed below the level of the cortex for a distance of about 1 cm. Because of the proximity of the scar to the motor cortex it was deemed inadvisable to perform a cicatrixectomy.

On January 23, the visual and ocular functions were normal in every respect. *Optic nystagmus* was vigorous and equal in both directions.

Nystagmographic Records.—The pursuit pattern showed a number of irregularities, but no difference was noted between the two directions of movement of the visual field.

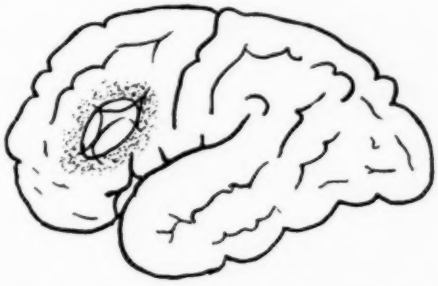
Case 3.—In W. O., a man, aged 27, right-handed, who was admitted to the hospital on April 2, 1928, right-sided jacksonian seizures developed at the age of 17. At first he retained consciousness throughout the attack, which started in the right foot and spread upward to involve the entire right side. In spite of a right hemiplegia, he had been able to work until recently. Speech was slow, with misplaced words and syllables. However, auditory and visual perception were normal. Attempted hand-writing and drawing with the nonparalyzed left hand showed a definite dysgraphia. There were blurring of both optic disks, right facial weakness, right spastic hemiparesis, diminution of proprioceptive sensation on the right and astereognosis and atopognosis in the right hand. Visual acuity was 20/25 in each eye. Visual and ocular functions were normal. *Optic nystagmus* was normal to both directions.

Nystagmographic Records.—The pursuit pattern was entirely adequate for both directions.

On April 23, a wide exploration of the left frontoparietal region revealed an enormously dilated patch of vessels, both arterial and venous, originating in the region of the sylvian fissure, and crossing upward over the brain. This massive telangiectasis of the meninges was thought to cover the brain from a point somewhat anterior to the precentral convolution as far backward as the supramarginal gyrus. In the center of this area the finger could be pushed down deeply into the varicosities.

Summary.—Neither of the lesions situated in the upper midportion of the hemisphere disturbed optic nystagmus. However, in both cases the pathologic process was confined chiefly to the surface of the brain.

In case 8, normal records were obtained following the evacuation of a cyst connected with a posttraumatic cicatrix situated in the lower postrolandic region. In case 3 a massive telangiectasis in the fronto-parietal region had no effect on the nystagmus.



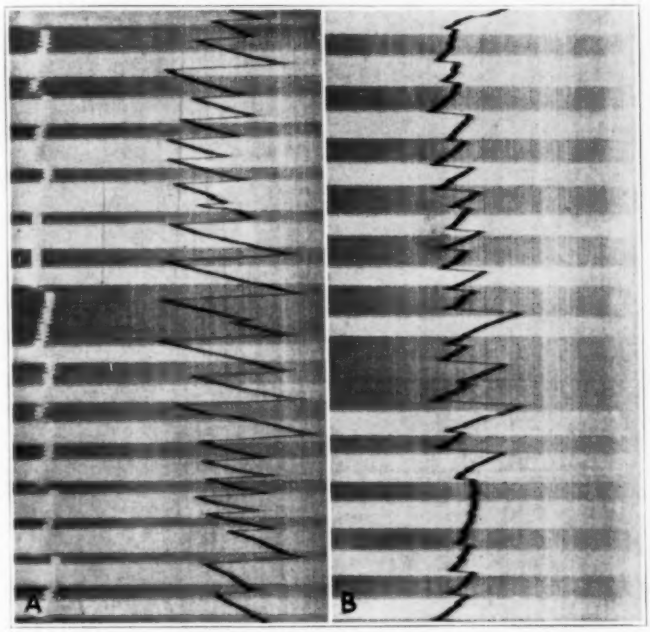


Fig. 5 (case 12).—Nystagmographic records made twelve days after operation. In *A*, the ocular response is normal; in *B*, defective.

FRONTAL LESIONS

CASE 12.—A. P., a man, aged 28, right-handed, who was admitted to the hospital on May 19, 1931, had sustained two head injuries in automobile accidents three years prior to admission. Two years before, he began to have spells of nausea and slight mental confusion. The first major epileptiform seizure occurred five months ago and since then they had recurred with increasing intensity and frequency. Neuro-

logic examination gave negative results except for left anosmia, blurring of the left optic disk and right facial weakness.

On June 1, a left frontoparietal exploration revealed, between the middle and inferior frontal convolutions, just anterior to the precentral gyrus, a gray tumor mass about 3 by 1.5 cm. in diameter (fig. 5). A needle inserted into the neoplasm disclosed an area of resistance extending downward to a depth of approximately 5 cm. Complete extirpation was carried out for a depth of 3 cm., and only a partial removal for a depth of 5 cm. in the process of scooping out until the ventricle was entered. In the opinion of the operator, the lower margin of the second frontal convolution was displaced upward by the tumor, which presented between this and the third frontal convolution. No cortical tissue at the surface was removed during the operation. Section showed a spongioblastoma multiforme.

On June 16 there was a slight residual right facial weakness and difficulty in writing. Visual acuity was 20/20 in each eye. Visual fields, visual attention and eye movements were normal. *Optic nystagmus* seemed to be normal.

Nystagmographic Records (fig. 5).—When the bars on the screen were moving from left to right, the pursuit pattern was unusually adequate. On the other hand, when the visual objects were moving in the opposite direction, from right to left, the pursuit pattern was grossly inadequate, with shortening of both phases and periods of still fixation.

Case 9.—M. H., a woman, aged 39, who was admitted to the hospital on April 2, 1930, was originally left-handed but had been taught to write with her right hand. Four months previously, she began to have headaches, vomiting, blurring of vision, diplopia, failure of memory and difficulty in speech and writing. Examination revealed a definite impairment of the higher faculties, disturbance of memory, dysphasia of the expressive type, dysgraphia, complete anosmia on the right and some impairment of smell on the left. A generalized asthenia, more marked on the left, was associated with left reflex pyramidal signs. The fundi showed primary optic atrophy on the right, papilledema on the left.

The patient was operated on in two stages on April 7 and 19. At the second stage a tumor was found occupying a large part of the right frontal lobe. Almost the entire frontal lobe was removed, the transection line running just anterior to the precentral gyrus, as shown in figure 6. A shelf of frontal lobe was allowed to remain over the floor of the anterior fossa, thereby preserving the anterior cerebral artery. The tissue removed weighed 49 Gm. and consisted of two structurally different types, meningioma and spongioblastoma multiforme.

On May 20, visual acuity was limited to light perception on the right, 20/25 on the left. The left visual field was restricted to 40 degrees. Visual attention and ocular movements were normal. *Optic nystagmus* was elicited in both directions. An irregularity was noted when the stripes moved from left to right, but the nature of this could not be determined by unaided observation.

Nystagmographic Records (fig. 6).—When the objects were moving from right to left, the pursuit pattern was almost normal. However, when the objects were moving from left to right, the pattern was defective both as regards amplitude and angular velocity of pursuit. Adequate pursuit did not appear until two seconds after the screen had started to move.

Case 10.—L. B., a man, aged 24, who was admitted to the hospital on May 11, 1931, was naturally left-handed but had been taught to use his right hand in early childhood. One year previously he had a series of generalized convulsions with a period of amnesia. Two months ago he began to have severe right frontal headaches. Vomiting, jerking of the upper part of the left limb, a tendency to profanity and undue irritability followed. Neurologic examination gave negative results

except for bilateral papilledema. Roentgen examination of the skull showed a localized area of bone absorption, suggesting a pressure atrophy of the right frontal bone just anterior to the coronal suture and above the plane of the supra-orbital plate.

On May 15, a right frontal exploration revealed in the region of the frontal pole, as shown in figure 7, a small discolored brownish area, palpation of which revealed increased resistance. It was decided to resect the major portion of the frontal lobe. The cortical vessels were clipped at a point 2 cm. anterior to the fis-

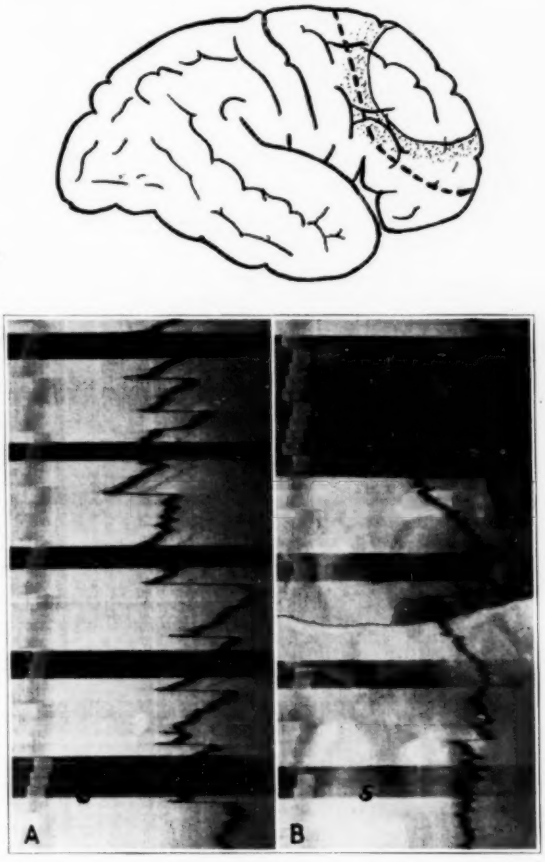
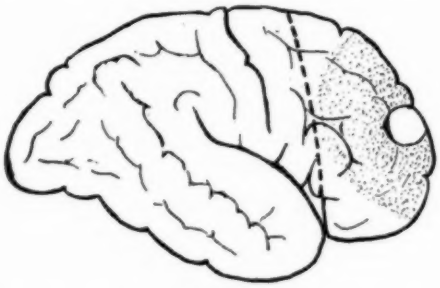


Fig. 6 (case 9).—Nystagmographic records made thirty-one days after operation. In *A*, the ocular response is normal; in *B*, defective.

sure of Rolando. The line of transection slanted somewhat obliquely forward at the inferior portion where it was noticed to run just anterior to the sphenoidal ridge. There was no evidence of tumor tissue in the cut surface or in the portion of the brain remaining. Section showed a spongioblastoma multiforme.

On June 8, visual acuity was 20/15 in each eye. The visual fields, visual attention and ocular movements in pursuit were normal. However, on command to look to the left, the eye movements were not as smooth as on command to look to the right. A vigorous *optic nystagmus* was obtained in both directions.

Nystagmographic Records (fig. 7).—The records showed a normal response for both directions of movement of the screen (even at higher speed than illustrated). There was no evidence of a defect of the quick fixation movement to the left. The pursuit pattern when the objects were moving from left to right, or toward the side of the lesion, was irregular, evidenced in some places in the records by brief periods of fixation at the beginning of pursuit. However, this cannot be classified



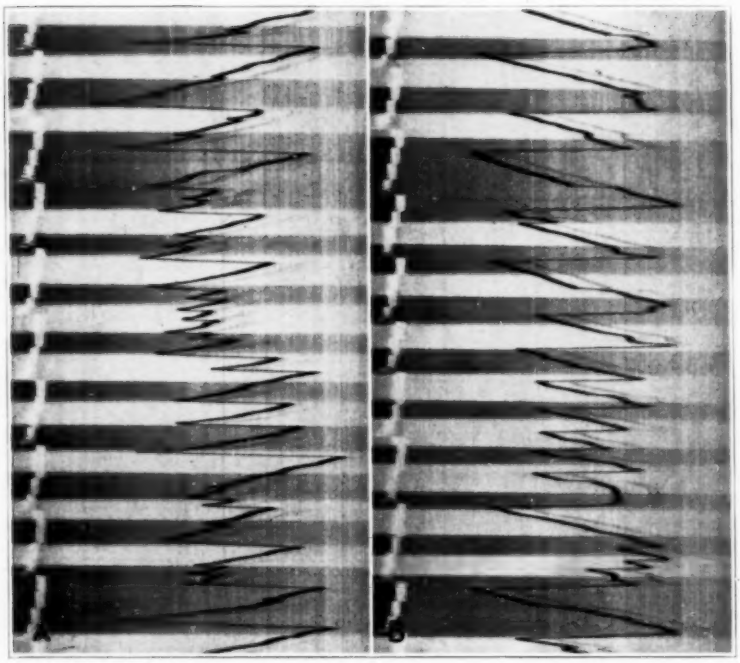


Fig. 7 (case 10).—Nystagmographic records made twenty-four days after transection. In *A*, the ocular response is normal; in *B*, irregular.

as a defective response in the pathologic sense, because such irregularties may occur in the records of normal subjects.

During the period of convalescence the patient was studied by Dr. Walter Miles. The patient's cooperation was found to be excellent in all the tests that were undertaken. He grasped the instructions readily and demonstrated good concentration in

carrying out the tasks asked of him. No evidence could be found of impairment of any of the higher intellectual faculties. His family and friends noticed no change in his personality. At times it was thought he might be a little euphoric; but in general his behavior was entirely normal. A study was made of the eye dominance. In ten tries he responded each time with the right eye. This was of some significance, because the photographic records were obtained from the seeing right eye with the recorder on the left eye. In every task examined in the laboratory, which called for spontaneous response, without the subject's knowing that handedness was being tested, he showed the left hand to be the natural one selected. However, in tests of rapid motion he did identically as well with the right hand as with the left. In dexterity of coordination with the two hands he was as accurate and somewhat more rapid with the left than with the right. In the use of pen or pencil he wrote with the right hand, and in feeding himself he also used the fork or spoon in the right hand. It must be assumed that the higher psychomotor centers are located in the left hemisphere in this patient, because of the absence of any disturbance following resection of the right frontal lobe. The patient was discharged on June 10 and has remained well since.

CASE 2.—A. M., a boy, aged 12, right-handed, who was admitted to the hospital on Dec. 30, 1927, was of normal birth and development, and had had generalized convulsive seizures since the age of 9, with a gradual change in personality. He has become irritable, subject to outbursts of temper and irresponsible in his behavior. With gradual deterioration he was obliged to give up school a year ago and recently has complained of headaches. Examination revealed an inability to call forth word memories and associations, dysgraphia, periods of hypomanic behavior with transitory mental confusion and irregular impairment of memory. The retinal veins were engorged. The right grip was weaker than the left. A roentgenogram of the skull showed an irregular, honey-combed area of calcium deposition in the left frontal lobe, extending 2 cm. on either side of the coronal suture. On January 5, visual acuity was: right, 20/30; left, 20/25. Visual fields, visual attention and eye movements on command and in pursuit were all normal. *Optic nystagmus* was vigorous in both directions.

Nystagmographic Records.—The records showed that the pursuit pattern was just as adequate when the objects were moving toward the side of the lesion as when they were moving from left to right.

On January 10, on exploring the posterior portion of the left frontal lobe, just in front of the rolandic fissure, at about the level of the arm and trunk areas, there was found a plexus of arterial and venous vessels of enormous size. These vessels plunged into the cortex, and on pressure one could express the blood so that there was a marked depression which would fill at once on release of the pressure. A needle, passed into the cortex, anterior to the mass of blood vessels, met resistance at a depth of about 1 cm., suggesting that the calcification seen on the x-ray plate was an old angioma deep in the frontal lobe.

CASE 6.—J. N., a man, aged 31, who was admitted to the hospital on Oct. 29, 1929, had complained of right frontal headache six weeks previously. Shortly afterward, vomiting, weakness in the left arm and leg and retardation of the mental processes developed. Neurologic examination showed mental clouding, apathy, bilateral anosmia, more marked on the right, bilateral papilledema, and left hemiparesis, including the face. Stereognosis was normal in the left hand. Ventriculography showed a multilocular cyst, well forward in the right frontal region.

On November 5, *optic nystagmus* seemed slightly more vigorous when the stripes were moving from right to left than in the opposite direction, or toward the side of the lesion. A right frontal exploration revealed a tumor mass presenting on the

surface. An incision was made through the cortex, somewhat below the tumor and well anterior to the precentral convolution. The tumor extended for a considerable distance inferiorly and medially, was well encapsulated, and appeared to permit complete removal. Section showed a metastatic adenocarcinoma.

On November 20, visual acuity was: right and left, 20/40 The visual fields were contracted to 50 degrees. Eye movements on command and in pursuit were normal. *Optic nystagmus* was vigorous and equal in both directions.

Nystagmographic Records.—The records showed an exceptionally adequate pursuit pattern in both directions with no evidence of a disorder of the quick phase to the left.

Summary.—In two of the five cases, optic nystagmus was disturbed when the visual objects were moving in a direction toward the side of the lesion. In case 12 (fig. 5), a glioma, which presented on the surface between the middle and inferior frontal convolutions and infiltrated deeply into the frontal lobe, had been partially extirpated. In case 9, the right frontal lobe had been transected anterior to the precentral gyrus along the broken line shown in figure 6. On the other hand, in case 10, in which the right frontal lobe had been transected at a level somewhat more posteriorly, as shown in figure 7, no significant alteration of the optic nystagmus could be observed. A massive hemangioma in case 2, and a metastatic lesion in case 6, also failed to disturb the ocular response, as revealed by nystagmography.

COMMENT

Cerebral Localization.—On account of their bearing on cerebral localization, the positive and negative groups of lesions have been projected on the lateral surface of a left cerebral hemisphere (fig. 8). One is immediately impressed with the fact that with one exception, case 5 (fig. 1 *A*), in all the cases in which optic nystagmus was unaffected the lesions were situated in the anterior part of the brain in the frontal or parietal regions. Also with a subsequent increase in the size of the lesion *A*, to that shown as *B* (fig. 1), the ocular response became defective.

On the other hand, with two exceptions, cases 9 and 12, all the lesions that disturbed optic nystagmus were located in the posterior part of the hemisphere in the temporal and parieto-occipital region behind the supramarginal gyrus. The intermediate region is not represented by positive cases.

The problem of neural integration of this interesting ocular phenomenon can best be discussed under three main headings: (1) the primary importance of the optomotor system or the corticofugal pathway of the optic radiation; (2) the secondary rôle played by the conjugate eye movement centers in the frontal lobe, and (3) the probable existence of a transcortical pathway connecting the occipital and frontal centers.

The Optomotor Pathway.—A patient with suprageniculate as well as infrageniculate hemianopia may develop a vigorous nystagmus, even when watching the visual objects emerging from the blind fields. The original contention of Bárány [3] that the failure of optic nystagmus was the direct result of a visual defect has been proved incorrect by numerous observations of Stenvers,[4] Ohm,[5] Cords,[6] Fox and Holmes,[1] and Nordman and Lieou.[7] While it is true that in many hemianopic patients optic nystagmus is absent or disturbed to the blind side, such as in cases 1 and 2, the defect in the ocular response must be due to

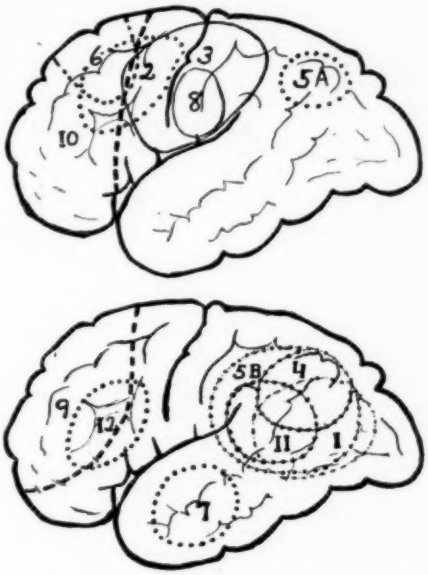


Fig. 8.—The upper drawing shows a projection on the lateral surface of a left hemisphere of lesions that did not disturb optic nystagmus. The lower drawing shows lesions that did disturb optic nystagmus.

some other cause than the hemianopia itself. This is substantiated by the fact that optic nystagmus is frequently disturbed by lesions in the temporoparieto-occipital region in which the contralateral visual fields are either normal or perhaps only slightly indented. Cases 4, 5 (fig. 2*B*) and 7 are examples of this. Comparison of the successive visual

3. Bárány, R.: Arch. f. Augenh. **89**:139, 1921.

4. Stenvers, H. W.: Schweiz. Arch. f. Neurol. u. Psychiat. **14**:279, 1925.

5. Ohm, Johannes: Zur Tätigkeit des Augenmuskelsenders, Bottrop (Westfalen) Selbsmverlag, 1928, vol. 1; 1929, vol. 2.

6. Cords, R.: Arch. f. Ophth. **117**:58, 1926. Cords, R., and Nolzen, L.: ibid. **120**:506, 1928. Cords, R.: ibid. **123**:173, 1929.

7. Nordman, J., and Lieou, Y. C.: Rev. d'oto-neuro-opht. **6**:81, 1928.

fields in case 5, which are superimposed in figure 1, is convincing proof that the disturbance of the optic nystagmus that developed with the spread of the lesion (*B*) was not due to a significant increase in the hemianopic disorder.

The admirable study of Cords [6] on the optomotor field and pathway, published in 1926, has served to clear up most of the confusion that had existed with respect to the influence of lesions of the optic radiation on optic nystagmus. He emphasized that the radiation of Gratiolet contained two main systems of fibers: (1) a corticopetal pathway or great sensory visual radiation—the external sagittal stratum of Sachs; (2) a corticofugal system or the optomotor pathway—the internal sagittal stratum of Sachs.

The cortical field for optically induced eye movements is thought by Cords to include the zone immediately surrounding the area striata, corresponding to field 18 of Brodmann. In this particular region of the brain arise the impulses that direct the searching movements, "Spähbewegungen." These impulses in turn are the direct result of visual impressions relayed from the neighboring calcarina and visual cortex of the opposite side through the corpus callosum.

The oculomotor system for directing the eye movements in response to moving visual stimuli is shown diagramatically in figure 9 (after Cords). The visual stimuli activate both halves of both retinae and pass along both optic nerves and tracts to the lateral geniculate bodies of both sides. The impulses then travel by the visual sensory pathways to the two calcarine areas. The optomotor fields are in turn activated from the calcarina of both sides. Here the optomotor pathway arises, travels along the radiation of Gratiolet, through the posterior limb of the internal capsule and the lateral part of the cerebral peduncle finally to reach the conjugate ocular deviation center in the pons, where the motor impulses are conveyed to the external rectus of one eye and internal rectus of the other.

Interruption of the visual sensory pathway at any point would not destroy optic nystagmus, because visual stimuli would be relayed to the optomotor field from the calcarina of the opposite side through the corpus callosum. On the other hand, interruption of the optomotor pathway at any point in its course would disturb the ocular adaptation to a certain direction of movement of the visual field. This defect of the ocular response has been found to take place uniformly when the visual objects are moving toward the side of the lesion.

The disturbances of optic nystagmus observed in lesions of the temporoparieto-occipital region such as cases 1, 4, 5 (*B*), 7 and 11 of this group, can be readily explained on this basis of involvement of the optomotor pathway. Of course, in all cases the neighboring visual sensory radiation was likewise injured to some extent, sufficient to

cause an hemianopia in cases 1 and 11. The normal nystagmographic pattern shown in figure 1 can be explained on the failure of the lesion to involve the optomotor pathway during the early stage of its growth, *A*, whereas with further infiltration, shown in *B*, the ocular response became defective.

Because of the proximity of the corticopetal and corticofugal fibers in the optic radiation, it is unusual to find a pure lesion of the optomotor pathway, at least in its proximal course. However, on restudy-

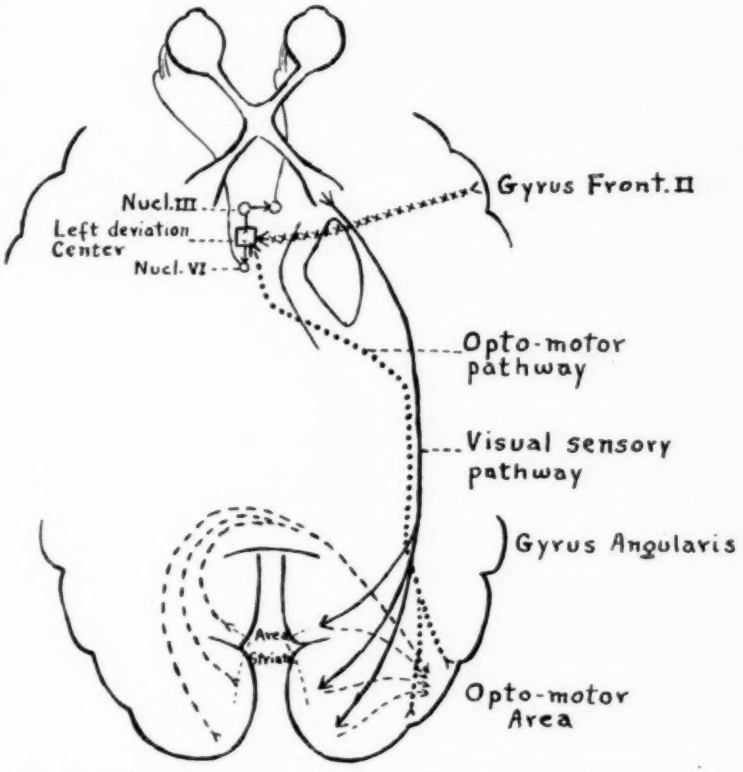


Fig. 9.—The centers and pathways in optic nystagmus (after Cords).

ing the verified cases reported by Fox and Holmes,[1] cases 6 and 7 seem to represent interruption of the optomotor pathway in its more distal course and for this reason are crucial cases. The visual fields in both instances were normal, but the quick phase of optic nystagmus was absent to the right. In case 6 (Fox and Holmes) an organized hemorrhage was found in the thalamus on the left side which destroyed the posterior limb of the internal capsule and part of the central white matter lateral to it. The external geniculate body escaped as well as the majority of the fibers of the optic radiation passing from it. In

case 7 (Fox and Holmes) a small localized glioma was found in the basal portion of the left temporal lobe, lateral to the posterior angle of the lenticular nucleus. It extended upward toward the optic radiations, the inferior fibers of which were probably involved as they turned around the horn of the ventricle.

The Frontal Eye Movement Center.—Electrical stimulation of the second frontal convolution, particularly in its inferior portion just anterior to the precentral gyrus, causes, in animals with binocular vision, lateral conjugate movements of the eyeballs toward the opposite side. An irritating lesion of this region in man may provoke clonic lateral conjugate movements of the eyes to the opposite side. A destructive lesion in this area may cause a transient inability to direct the gaze to the opposite side on command, or there may be difficulty in maintaining ocular deviation to the opposite side. The connection of the volitional eye movement center in the right frontal lobe with the left deviation center in the pons is shown in figure 9.

The rôle played by the frontal "Blickzentrum" in the reflex mechanism governing optic nystagmus has puzzled all investigators in this field. Lesions in the frontal lobe are notoriously inconsistent in their tendency to disturb optic nystagmus. This holds true not only for neoplasms but also for the vascular hemiplegias with aphasia. The presence of normal optic nystagmus in cases 2 and 6 and disturbance of the ocular response to one direction by a lesion similarly located (slightly inferior) in case 12 is difficult to explain. The pathologic process in case 2 had been of long duration and for this reason may have been less disturbing.

The results obtained on transection of the right frontal lobe just anterior to the precentral gyrus in cases 9 and 10 are also not in agreement. The ocular response is the better preserved in the case in which the resection was the more radical—case 10. The defective response in case 9 may have been caused by infiltration of the tumor beyond the boundaries of the resection, as indicated by the subsequent recurrence of the growth. The striking feature of these two cases is the lack of damage to the quick phase to the left in the nystagmographic pattern (fig. 7) in response to objects moving from left to right.

In only one instance has this author observed a complete loss of optic nystagmus caused by a frontal lobe lesion. In case 13 (Fox and Holmes) a previously normal optic nystagmus to the left disappeared following two deep operative incisions in the right frontal lobe—one in the anterior part of the third convolution, and a second in the posterior ends of the second and third gyri. Presumably the latter injured the center or, more likely, its connecting pathway just beneath. With respect to lesions of the frontal lobe, this definite statement can be made: Optic

nystagmus is frequently normal and is rarely abolished; when the ocular response is disturbed, it occurs with the visual objects moving toward the side of the lesion.

An Occipitofrontal Pathway.—In their earlier reports, Stenvers,[4] Cords[6] and Fox and Holmes,[1] contended that an occipitofrontal association system was necessary for the reflex mechanism underlying optic nystagmus. Theoretically, such a connecting transcortical pathway would correspond to the fasciculus longitudinalis inferior of Burdach. A detailed study of the literature on this subject convinced Cords that such a pathway does not exist, and he attempts to explain optic nystagmus without the aid of a connecting link between the occipital and frontal eye movement centers (fig. 9).

Optic nystagmus was undisturbed by either of the lesions situated in the upper midportion of the hemisphere—cases 3 and 8. However, in each instance the lesion did not penetrate sufficiently deep to have injured the white matter, and the negative evidence is therefore inconclusive. At this point reference must be made to two cases reported by Fox and Holmes.[1] In case 10, a deep operative incision was made into the lower end of the left postcentral convolution, cutting across the white matter of the inferior parietal lobule. Following the operation, optic nystagmus was absent when the visual objects were moving from right to left. Postmortem examination revealed that both the tumor and the incision had completely spared the optic radiations. Unfortunately, optic nystagmus had not been studied prior to operation, which deprives this experimental situation of some of its value. In case 8 (Fox and Holmes), a large tumor in the medial portion of the left hemisphere in the region of the central gyri, extending deeply into the white matter, abolished optic nystagmus to the one side. The tumor was well anterior to the optic radiations.

A disturbance of optic nystagmus has frequently been observed in association with astereognosis. Cords attributes this to a combined injury to the fibers of the sensory radiation and the optomotor pathway, as they run close together beneath the angular gyrus or in the internal capsule. However, consideration of all available data at the present time favors the existence of an occipitofrontal association system. Further study of the various problems of neural integration of the eye movements is obviously indicated. For this purpose a group of vascular, rather than neoplastic, lesions is preferable, in which actual degeneration of tracts can be determined post mortem.

Discussion in this paper has been confined to the effect of lesions situated in the cerebral hemispheres. Conjugate ocular movements occur not only in response to optic impulses to pursue a moving object, or to fix a new object of interest, but also as various reflex adjustments to changes in the position of the head and body, which depend

entirely on the activity of subcortical centers. In the final analysis, these factors, as well as those that require the intervention of the cortex of the forebrain, must be considered in a study of competition and rivalry for the final common ocular pathway.

SUMMARY

Some form of graphic recording device is essential for the analytic and comparative study of the finer details of all types of eye movements. Our "nystagmograph" employs the principle of photographing the horizontal deviations of the conjugately moving closed eye.

This report is based on the detailed study of twelve cases with verified lesions variously situated in the cerebral hemispheres. Satisfactory nystagmographic records were obtained from each patient, which clearly showed the character of the pursuit pattern for both directions of movement of the visual field.

A disturbance of optic nystagmus was demonstrated in seven of the twelve cases. Location of the lesion in the posterior part of the hemisphere, particularly in the region of the supramarginal or angular gyrus, or in the adjacent portions of the parietal, occipital or temporal lobes was certain to affect the optic nystagmus when the visual objects were moving in a direction toward the side of the lesion, although at an early stage one of the five patients had shown a normal response.

In two of the five cases in which the lesions were in the frontal lobe, optic nystagmus was also disturbed when the visual field was moving in a direction toward the side of the lesion. In one instance this observation was made following extirpation of the right frontal lobe just anterior to the precentral gyrus. On the other hand, the records of another patient showed a normal nystagmographic pattern, even after a somewhat more radical resection of the right frontal lobe.

Optic nystagmus was not affected by either of the two lesions situated in the upper midportion of the hemisphere, but in each instance the pathologic process was confined to the surface of the brain.

CONCLUSIONS

Disorders of optic nystagmus cannot be explained solely on the basis of imperfect recognition of visual objects emerging from the contralateral inattentive or blind fields. This is substantiated by the fact that the ocular response may be disturbed by lesions in the temporoparietooccipital region in which the contralateral visual fields are either normal or slightly indented and the visual attention unimpaired. Interruption of the corticofugal system or optomotor pathway—the internal sagittal stratum of Sachs—at any point in its course disturbs the ocular response to a certain direction of movement of the visual field, i. e., toward the side of the lesion. A defect in this corticofugal system is the primary

cause for a disturbance of optic nystagmus regardless of whether the neighboring corticopetal system or sensory visual radiation is also involved by the lesion.

The volitional eye movement centers in the frontal lobe obviously play a secondary rôle in the mechanism underlying optic nystagmus, as shown by the inconsistent and variable effects of frontal lesions. Whereas a definite answer cannot yet be given regarding the course of a transcortical association system, evidence at the present time favors the existence of such a connecting link between the occipital and frontal eye movement centers.

DESCRIPTION OF FIGURES 1 TO 7

The nystagmographic records were made by conjugate movements of a closed eye. They read from below upward. The actual direction of eye movement is reversed, i. e., movement of the line of regard to the subject's right appears as an excursion to the left. The speed of eye movement is shown by the obliquity of the excursions. Perfectly still fixation is shown by a vertical line (fig. 4). The greater speed of the rapid phase is shown by relatively finer record lines. Broad horizontal lines extending across the record occur at each 40 degrees of rotation of the screen. Each record represents a time interval of ten seconds.

Normal optic nystagmus to both directions is illustrated in figure 1. The nystagmographic pattern shows the pursuit of the fixed object by a slow phase, suddenly interrupted by the refixation of a new object of pursuit by a rapid phase. In the record on the reader's left the bars on the screen were moving from left to right. Consequently, the pursuit movement is directed to the right (to the left of record). Both movements are naturally reversed in direction in the record on the reader's right. The amplitude of the pursuit phases is consistently longer for the larger objects (bars) than for the intervening mesh. The pursuit phases may be broken by short fixation movements in either direction.

The left eye is recording while the right eye is seeing in all instances, except in the case of the two lower records in figure 2 and in figure 6. In each pair of records the one on the reader's left represents the ocular response when the objects are moving in a direction away from the side of the lesion. The disturbance in the nystagmographic pattern is, therefore, confined to or more marked in the record on the right of each pair. At the point marked *S* in some of the records the screen started to move following a preliminary period of still fixation.

The angular velocity of the moving visual field can be estimated by the width and frequency of the transverse bands. For example, in the upper pair of records in figure 2 the screen was rotating at an angular velocity of only 25 degrees per second, while in the lower pair the high speed of 110 degrees per second was maintained. The nystagmographic disturbances shown in the different records are described under the individual case reports.

CYTOGENESIS OF OLIGODENDROGLIA AND ASTROCYTES

O. W. JONES, Jr., M.D.
SAN FRANCISCO

Previous classifications dealing with the cytogenesis of neuroglia have formed a working basis for the study of the neoplasms of the glioma group. With the ever increasing interest in the field of neuropathology, largely owing to the advent of metallic staining methods, it will be necessary to modify these classifications from time to time in order to clarify the relationship between the embryonic and the pathologic cell types.

In the evolution of primitive spongioblasts to adult autonomous neuroglia can be distinguished cell types comparable to those constituting the various neoplasms arising from these cells.

A review of the literature on the phylogenetic development of neuroglia, in association with an ontogenetic study of their evolution in mammals, has suggested a possible simplification of the existing classifications.

The term neuroglia, as now used, applies first to the so-called classic neuroglia; this term includes the fibrous and protoplasmic astrocytes which differ only in the presence or absence of fibers in the cell cytoplasm. Normally, astrocytes in the gray matter of the brain and spinal cord are all protoplasmic, while in the white matter and subpial layer of the cerebrum they are fiber formers. All astrocytes show a definite vascular or pial connection by means of a sucker foot.

Second, the term applies to oligodendroglia, the interfascicular glia of the white matter and the satellite cells of the gray substance. It is most abundant in the white matter of the brain and spinal cord, appearing in rows of from four to eight cells, the structure of which closely resembles that of the astrocyte. Both have asteroid bodies, centrosomes and Golgi apparatus similar in appearance. The nuclei differ only in size, that of the oligodendroglia being smaller. The expansions of the oligodendroglia contain no fibers, nor are they connected to blood vessels or pia mater. The cell presents gliosomes similar in form, size and general distribution to those of the astrocytes.

From the Department of Neurosurgery, McGill University, Montreal, Canada.

Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 27, 1929.

HISTORY

The important technical investigations of Golgi,[1] in 1886, and of Weigert,[2] in 1895, led to the production of many methods of staining devised to demonstrate more clearly the interstitial element of the central nervous system. The application of these inadequate staining methods was responsible for the wide diversity of opinion regarding the origin and morphology of the cells forming this element. In 1913, Cajal's [3] gold chloride sublimate method provided a new and strikingly selective procedure for the staining of classic neuroglia. The results obtained by its application enabled him to separate these cells from the large group of small non-nerve cells which remained unstained by his new method. These he classified as the third element. It remained for del Rio Hortega,[4] in 1921, to demonstrate by his silver carbonate method that the third element of Cajal was made up of two groups of cells, oligodendroglia and microglia.

Although the older methods advanced our knowledge of the interstitial cells, it was only by the application of the more adequate metallic methods that the identification of the origin and morphology of these cells was made possible.

His,[5] in 1889 and 1901, pointed out that the medullary plate is made up of undifferentiated epithelial cells which give rise to the germinal cells, and differentiated epithelial cells or spongioblasts. In their development, the spongioblasts give rise to neuroglia, and the germinal cells by mitotic division produce neuroblasts which, emigrating from the epithelial layer, form nerve cells.

Schaper,[6] in 1897, concluded that in addition to the spongioblasts giving rise to neuroglia cells, the indifferent cells of spheroidal form arising from the germinal cells of His emigrate in great numbers from the epithelial layer, cross the nuclear zone and, arriving at the neuroblastic layer, again proliferate by mitosis, the daughter cells forming astrocytes or neurons. This conception was likewise held by Kölliker,

1. Golgi, C.: Sulla fine anatomia degli organi centrali del sistema nervoso, Milan, U. Hoepli, 1886; Opera omnia, Milan, U. Hoepli, 1903.

2. Weigert, C.: Beiträge zur Kenntnis der normalen menschlichen Neuroglia, Frankfurt, A. Weisbrod, 1895.

3. Ramón y Cajal, S.: Sobre un neuvo proceder de impregnación de la neuroglia y sus resultandos en los centros nerviosos del hombre y animales, Trab. d. lab. de invest. biol. Univ. de Madrid **11**:219, 1913.

4. del Rio Hortega, P.: Estudios sobre la neuroglia: La glia de ecasas radiciones (oligodendroglia), Bol. d. r. Soc. españ. de hist. nat., January, 1921.

5. His, W.: Die Neuroblasten und deren Entstehung im embryonalen Mark, Arch. f. Anat. u. Entwcklngsgesch., 1889, p. 249; Das Princip der organbildenden Keimbezirker und die verwandschaftender Gewebe, ibid., 1901, p. 307.

6. Schaper, A.: Die frühesten Differenzierungsvorgänge im Centralnervensystem, Arch. f. Entwcklngsmechn. **5**:81, 1897.

and von Lenhossék and His concurred. Bailey and Cushing [7] called this indifferent cell a medulloblast.

Von Lenhossék [8] in 1891, and Cajal,[9] in 1909, observed that the spongioblast early in embryonic life develops an external expansion which terminates at the external limiting membrane or pia mater, while at the opposite pole a short process is attached to the internal limiting membrane. This cell type was designated ependymal cell or spongioblast. It migrates outward, loses its ependymal attachment, forming what Cajal called a displaced epithelial cell and von Lenhossék termed an astroblast. It should be noted that the latter term as now used applies to a more adult type of cell. Its further evolution develops this cell into an adult astrocyte.

The researches of Held, Nausen, Muller, Retzius, Sala and others have led to a clearer understanding of the development of neuroglia.

Achucarro,[10] in 1915, demonstrated that the ontogenetic development of neuroglia is comparable to its phylogenetic development. De Castro,[11] in 1920, studied carefully the development of classic neuroglia in the olfactory lobes of man and animals. The origin of the neuroglia fibers has been studied for the most part by DaFano, Rubaschkin and Hortega. In 1921, Hortega [4] assumed an ectodermal origin for oligodendroglia, and in 1924 and 1928 Penfield [12] was able to demonstrate this conclusively in the spinal cords of young kittens.

MATERIAL AND METHODS

For this developmental study the brains of cat fetuses, measuring 7 cm. and 10 cm. in crown-rump length; kittens up to 1 month of age, and the brains of mice from 4 to 14 days of age were used. The staining methods employed were: Cajal's gold chloride sublimate, Hortega's silver carbonate, Gross-Bielschowsky's, Nissl's and Weigert-Pal's, with scharlach R as a counter-stain for fat.

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7. Bailey, P., and Cushing, H.: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of the Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

8. von Lenhossék, M.: Zur Kenntnis der Neuroglia des menschlichen Rückenmarkes, Verhandl. d. anat. Gesellsch. **6**:193, 1891.

9. Ramón y Cajal, S.: Histologie du système nerveux de l'homme et des vertébrés, Paris, A. Maloine, 1909.

10. Achucarro, N.: De l'évolution de la névroglie, et spécialement de ses relations avec l'appareil vasculaire, Trab. d. lab. de invest. biol. Univ. de Madrid **13**:169, 1915.

11. de Castro, F.: Estudios sobre la neuroglia de la corteza cerebral del hombre y de los animales, Trab. d. lab. de invest. biol. Univ. de Madrid **18**:1, 1920; Algunas observaciones sobre la histogenesis de la neuroglia en el bulbo olfativo, ibid. **18**:83, 1920.

12. Penfield, W.: Oligodendroglia and Its Relation to Classical Neuroglia, Brain **47**:430, 1924; in Cowdry, E. U.: Special Cytology, New York, Paul B. Hoeber, Inc., 1928, vol. 2, p. 1032.

CYTOGENESIS OF ASTROCYTES

The description of the evolution of the primitive spongioblast to the adult type of cell under consideration may be divided into two major parts: that of the supportive spongioblasts and that of the polar migratory spongioblasts.

Part I.—The type cell to be described is the supportive spongioblast or so-called ependymal epithelial cell.[13] In the 7 cm. and 10 cm. fetuses

Fig. 1.—Cat fetus. Section from the ependyma lining the third ventricle: *a* indicates supportive spongioblasts, cell bodies lying in the ependymal layer with long processes extending peripherally; *b*, dislocated epithelial cells; the peripheral attachments are not shown. Cajal's gold chloride sublimate method.

this is the predominating cell type. The cell body is located in the ependymal epithelium and is large and oval, and the nucleus, which is of the same shape, almost fills the cell body. A short process connects the cell with the internal limiting membrane. Extending peripherally

13. Ramón y Cajal, S.: Contribución al conocimiento de la neuroglia del cerebro humano, Trab. d. lab. de invest. biol. Univ. de Madrid **11**:255, 1913.

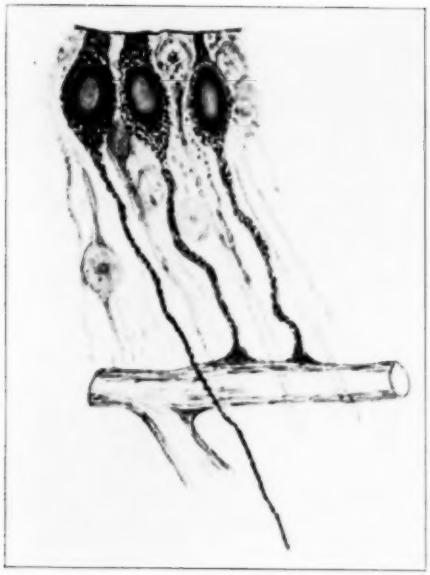

Fig. 2.—Mouse 9 days old. Section from the ependyma of the third ventricle. Supportive spongioblasts are seen, showing the vascular attachment.

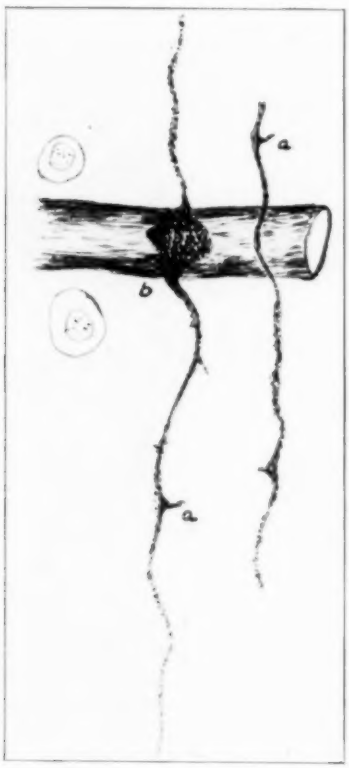

Fig. 3.—Cerebral white matter of a new-born kitten: *a* indicates collateral spines on the processes of the spongioblasts; *b*, broadening of a spongioblast process as it passes over a blood vessel forming a primitive foot plate.

from the cell body is a fine, irregular, tortuous process, which traverses the brain substance and ends on the external limiting membrane or a blood vessel in a foot plate (figs. 1 and 2). Along its course, in the new-born kitten, it presents many small collateral processes. The production of these is thought to be caused by a chemotactic influence of

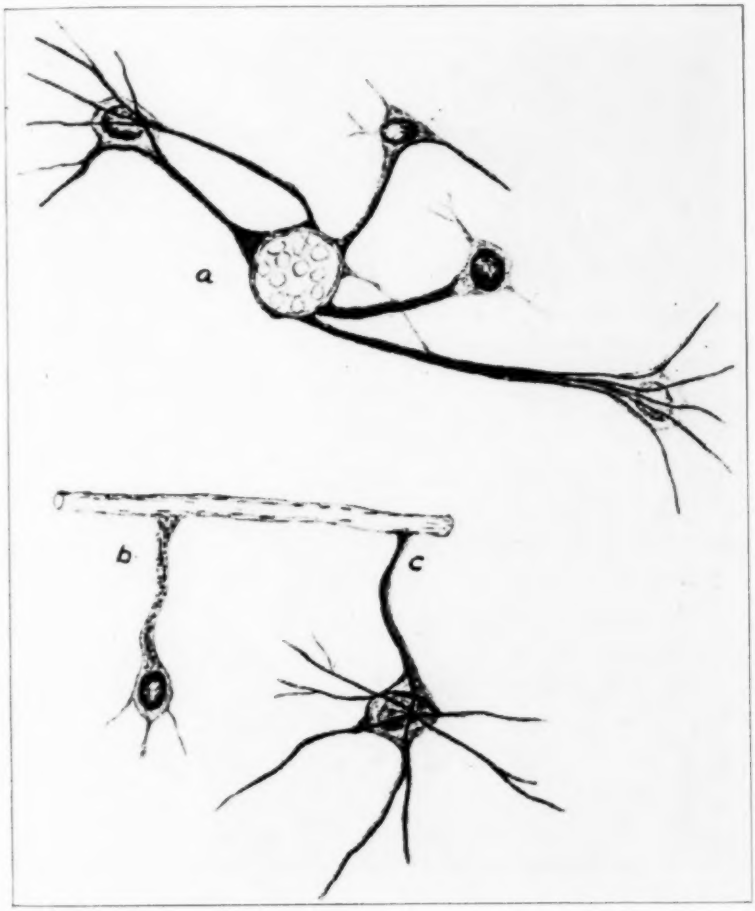

Fig. 4.—Cerebral white matter of a 1 month old cat: *a* indicates astroblasts attached to a blood vessel, showing various stages in the development of neuroglia fibers; *b*, an astroblast in which fiber differentiation has not yet appeared; *c*, an adult astrocyte. Cajal's gold chloride sublimate method.

the brain substance on the cytoplasm.[10] This phenomenon is best demonstrated in the brains of new-born kittens, but is found at earlier stages (fig. 3 *a*). The long processes at times broaden out as they pass over a blood vessel to the periphery, forming what appears to be a

vascular attachment. This formation has been described as a primitive foot plate and corresponds to a similar condition found in the forebrain of an adult frog (fig. 3 *b*).

At one stage in embryonic life the supportive spongioblast forms the only supporting element in the central nervous system. Achucarro has shown this cell to be the predominating supporting structure in adult

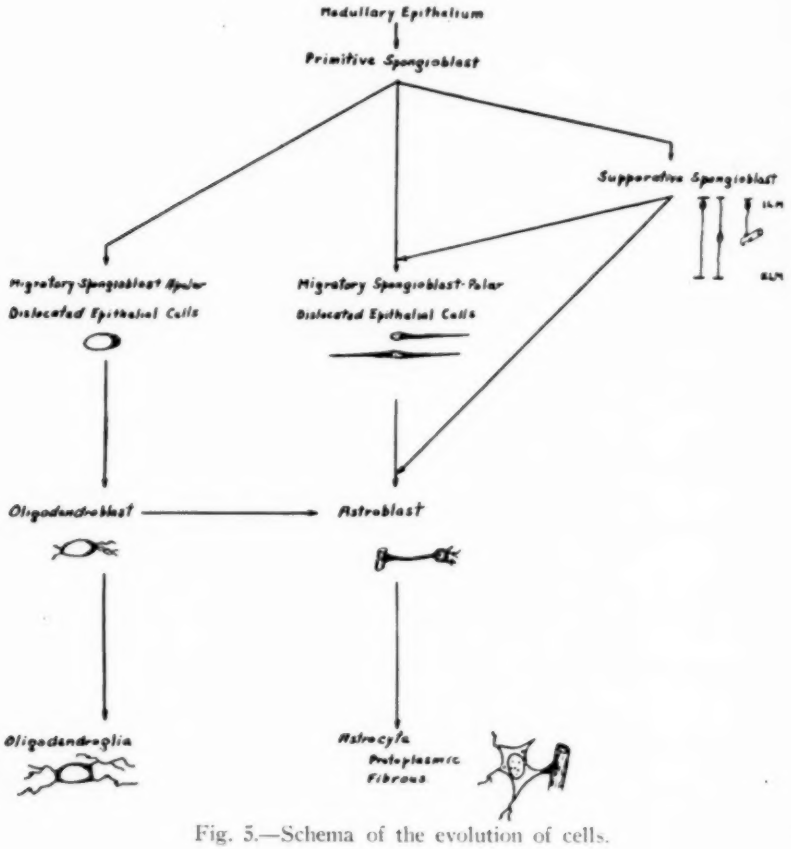

Fig. 5.—Schema of the evolution of cells.

teleost fish (Cyprinus), there being relatively few autonomous neuroglia cells in this species.

In mammals, as this cell develops, it migrates outward, losing its connection with the ependyma and forming a displaced epithelial cell.[9] Figure 1 *b* shows an early stage of a displaced epithelial cell; figure 4 shows the later stage of the same cell, now classified as an astroblast. The latter develops into an adult fibrous or protoplasmic astrocyte.

Numerous supportive spongioblasts migrate from the ependyma, retaining both a peripheral and an ependymal process. After migration,

many divide amitotically, forming an astroblast and a unipolar spongioblast, or two cells of the latter type, depending on the presence or absence of a vascular or pial attachment prior to cell division.

Part II.—The term migratory polar spongioblast (fig. 5) is applied to a type cell that arises from the ependyma and migrates out into the parenchyma free from vascular or pial attachments. A description of each type of migratory polar spongioblast follows.

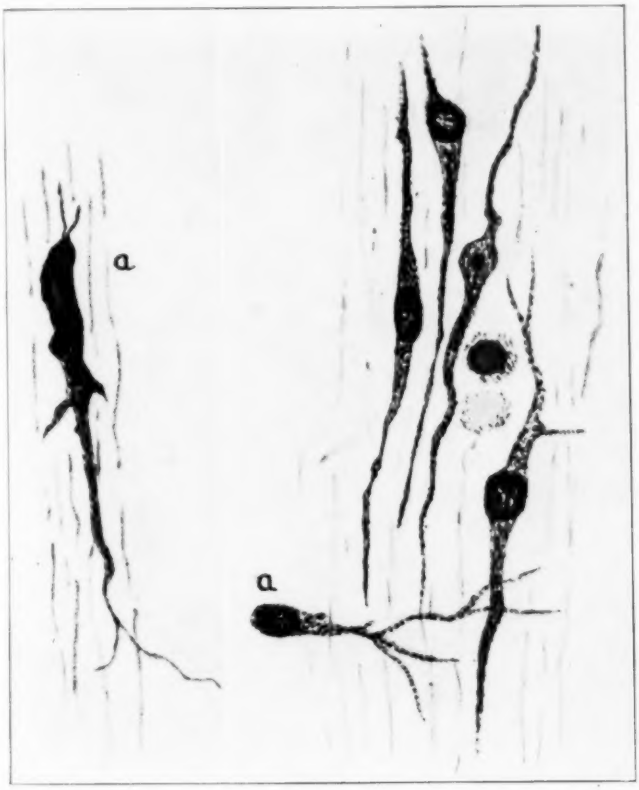

Fig. 6.—Cerebral white matter of a cat fetus: *a* indicates unipolar migratory spongioblasts. The remaining cells are bipolar migratory spongioblasts.

Unipolar Cell: The predominating type is the unipolar cell or unipolar migratory spongioblast. The cell body is round or irregularly oval, and the nucleus almost fills the cell, only a scant amount of cytoplasm surrounding it. The greatest amount of cytoplasm is in the form of a short tail, somewhat irregular in outline, directed, in most instances, peripherally, gradually tapering to a fine filament and at times showing minute terminal branching. Delicate collateral spines are present on the process, and the opposite pole of the cell may present one or two small

processes (fig. 6 *a*). Relatively few of these cells in the fetuses and new-born kittens show vascular attachments; the majority are free and migratory. In the 10 day old kitten, these cells have found vascular attachments and must therefore be considered to have reached the stage of astroblasts.

It is of interest to note that in the cerebellum of the adult Cyprinus, Achucarro [10] has described a migratory unipolar neuroglia cell similar to the type observed in the cat. The nucleus of this cell contains abun-

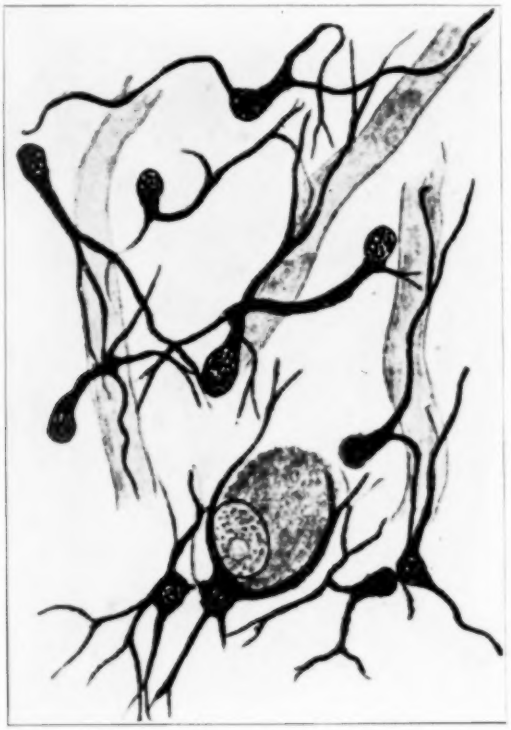

Fig. 7.—Autonomous neuroglia cells; valvula cerebelli (Cyprinus). (After Achucarro.)

dant chromatin, and the cytoplasm is eccentrically placed, in the form of a short process which divides terminally into two or three branches, which gradually taper off and are lost in the brain tissue. These cells are closely related to blood vessels and at times to nerve cells, have migrated from the ependyma, are primitive and polarized and remain free from attachments (fig. 7).

Bipolar Cell: A bipolar cell type similar to the unipolar migratory cell also can be distinguished. This cell type has been called a bipolar migratory spongioblast. One does not observe it leaving the ependyma

as such, but its bipolar form is first clearly defined in the subependymal layer. The majority of these cells, having lost their peripheral and ependymal attachments, undoubtedly correspond to the so-called displaced epithelial cells of Cajal. The nucleus is round or oval, almost completely filling the cell (fig. 6). The cytoplasm about the nucleus is scant and is seen in the form of short tails, somewhat irregular in outline, extending from either pole of the cell body. The lengths of the processes vary considerably, the peripheral being the longer. Short, fine, collateral spines arise from the polar processes. This cell migrates peripherally and develops a vascular attachment, forming an astroblast. As shown by Achucarro, both migratory bipolar and unipolar neuroglia cells are found in the vagus lobe of the adult Cyprinus. These cells are free from vascular or pial attachments (fig. 8).

Multipolar Migratory Spongioblast: Relatively few of these cells appear in the developing brain of the cat. The nuclei are round and

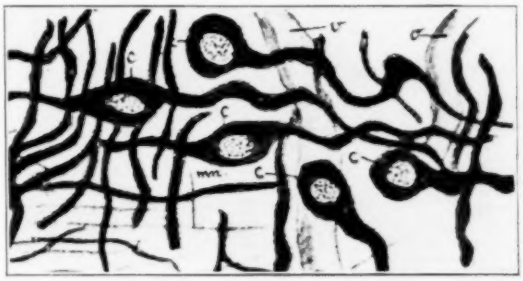

Fig. 8.—Monopolar and bipolar neuroglia cells in the vagus lobe of Cyprinus: *v* indicates a blood vessel; *c*, monopolar and bipolar neuroglia cells; *mm*, a nerve bundle. (After Achucarro.)

smaller than those of the cells just described. The cytoplasm is scant and is collected about the nucleus in the form of three or more short irregular processes. Amitotic division is observed infrequently. They migrate into the white and gray matter, establish a vascular attachment and develop into the small type of astrocyte.

Achucarro has described in the optic lobes of the lizard a similar cell. He said:

> The supporting element in this reptile is fundamentally ependymal. In the evolution of neuroglia we see here definite evidence of migration of epithelial cells. Everywhere in the cortex of the optic lobes the same small protoplasmic autonomous neuroglia cells are found which are similar to those described by Cajal in man and monkey. They present here however a greater simplicity. It is throughout the neighborhood of the ependyma that we find transitional forms distinct and undoubtedly immigrating. These cells detach themselves from the ependyma dividing in a perpendicular plane to the radial direction of the epithelial processes, progressing thus toward the surface (fig. 9).

CYTOGENESIS OF OLIGODENDROGLIA

Hortega,[4] in 1921, first successfully stained and observed the morphology of oligodendroglia. At this time he assumed an ectodermal origin for these cells.

Penfield,[14] in 1928, clearly demonstrated the ectodermal origin of oligodendroglia in the spinal cords of young kittens. He observed that

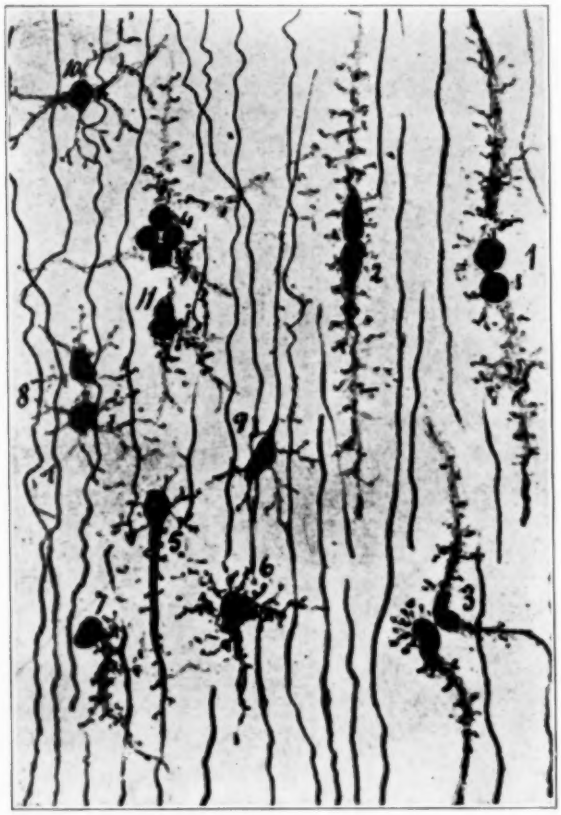

Fig. 9.—Optic lobe of a lizard; juxta-ependymal. Amitotic division of migratory polar spongioblasts is seen; the cells are emigrating toward the periphery. *1* and *2* show bipolar cells having a radial disposition; *3*, *8* and *11* show division of cells; *4* shows cell with four nuclei; *5*, *6* and *7* show polar spongioblasts; *9* and *10* are astrocytes. (After Achucarro.)

during the height of myelinization the white matter is densely packed with cells the nuclei of which are small and round, resembling those of the spongioblast, which leave the medullary epithelium during this period. The cytoplasm is scanty and collected at opposite poles of the

14. Penfield (footnote 12, second reference).

nucleus. These cells have no vascular attachments and multiply by direct division. Penfield named them migratory spongioblasts. From their cytoplasm short, fine, irregular, granular processes develop, forming oligodendroblasts.

My own observations on the cytogenesis of oligodendroglia in the cerebra of mammals show it to be comparable to that in the spinal cords of kittens.

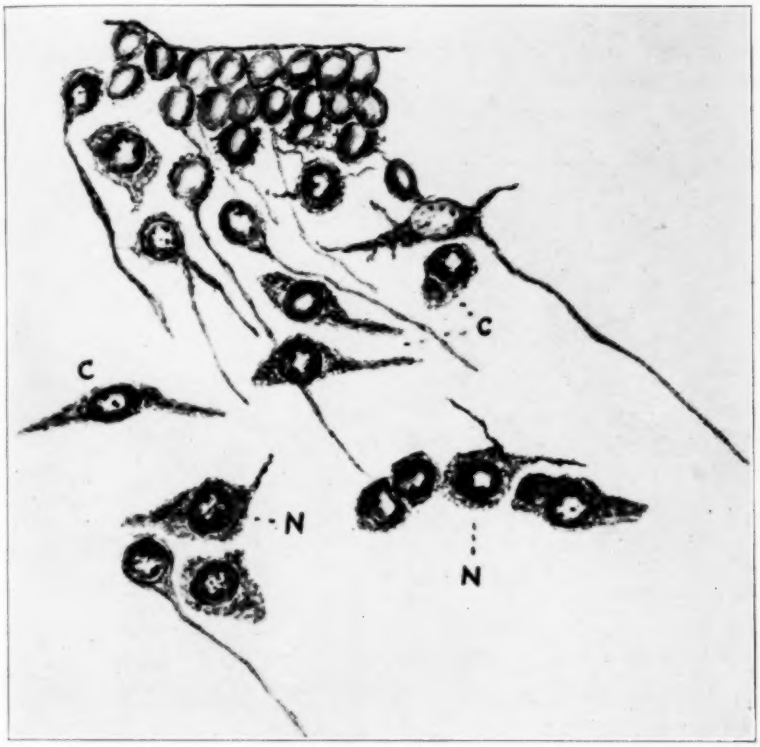

Fig. 10.—Ependyma, lateral ventricle, of a 14 day old mouse: *c* indicates apolar migratory spongioblasts; *n*, oligodendroblasts. Hortega's silver carbonate method.

Arising from the ependyma in the cerebra of young mice, during the height of myelinization, an apolar migratory spongioblast can be distinguished from the various cells. The nuclei are round or slightly oval, resembling those of the other spongioblasts arising from the ependyma at this time. The cytoplasm is abundant as compared with the amount present in the other spongioblasts, and it tends to collect at opposite ends of the nucleus. The cells are migrating away from the ependyma and are free from vascular attachments (fig. 10). They divide amitotically, and at times mitotic division was observed in what

appeared to be cells of this type. In the white matter they are closely packed together in rows of from four to six cells each.

During the period of migration, or when collected in rows, fine, short, granular processes develop from the cytoplasm (fig. 11). They then look like young oligodendroglia cells or, as called by Penfield, oligodendroblasts.

All stages of transition from the apolar migratory spongioblast to an adult oligodendroglia cell can be observed in the cerebrum of the mouse. Likewise, these cells may develop vascular attachments and, in so doing, form astrocytes. The latter cells form the intercalated astrocytes that appear in the rows of oligodendroglia. Similar transitions were observed by Penfield in the spinal cords of kittens.

Fig. 11.—Cerebral white matter of a 14 day old mouse: *c* indicates apolar migratory spongioblasts; *n*, oligodendroblasts, and *o*, an astrocyte.

In the cerebrum of the 4 day old mouse many mitotic figures are present in the ependymal layers and to a less degree in the white and gray matter. It is impossible to say, at this time, what cells are undergoing mitosis. The many mitotic figures scattered throughout the cerebrum lend further support to Schaper's idea that an indifferent cell exists which is capable of giving rise to either spongioblasts or neuroblasts. The form in which this cell leaves the ependyma is still unknown. Undoubtedly it is in the form of a migratory cell, but additional proof is needed to decide this point.

NEUROGLIA FIBERS

The investigations of Held, Rubaschkin, DaFano, Hortega and Cajal have shown that glia fibers differentiate late in the development of the

cell and appear in the granular cytoplasm. In the white matter of the spinal medulla of a 7 day old cat, Rubaschkin distinguished two types of cells: one, which stained only faintly, had a granular cytoplasm; the other possessed fibers. A short time after this period all the astrocytes in this area were of the fibrous type.

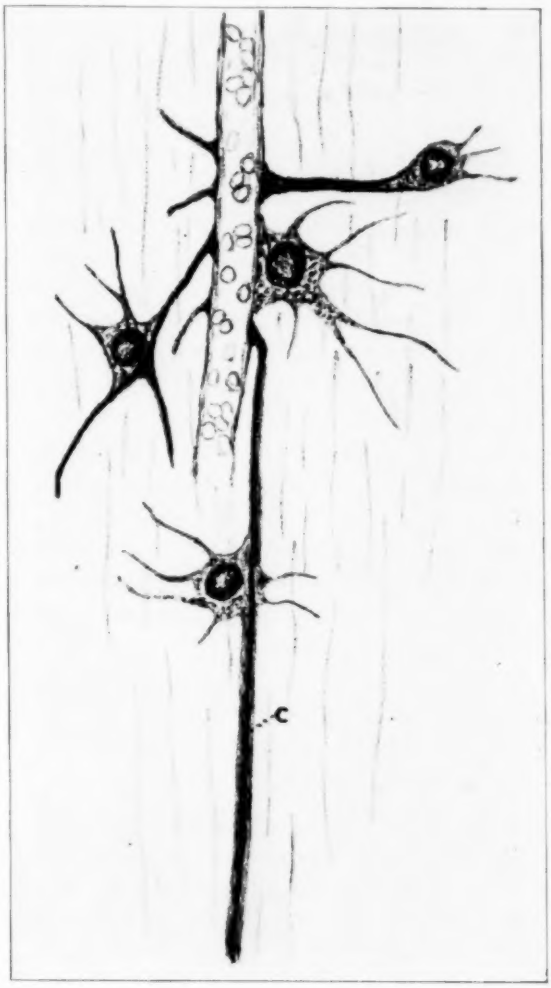

Fig. 12.—Cerebral white matter of a new-born kitten: *c* indicates an initial neuroglia fiber in the external radial process. Cajal's gold chloride sublimate method.

DaFano's investigations affirmed the previous observations. He observed that the glia fibers first appeared in the human embryo about the fourth month and that, in cat and chicken fetuses, they appeared just before birth. The fibers appear in one or more processes—usually

the external radial—and gradually invade the others. Cajal agreed with DaFano, but concluded that the fibers arise more frequently in the vascular process, from which they invade the other expansions.

The substance from which the fibers are formed has not been determined definitely.

Hortega stated that the glia fibers of Ranvier-Weigert arise by a progressive differentiation of the preexisting reticular protoplasm. Fieandt and Eisath concluded that the gliosomes are associated with fiber formation. Cajal did not agree with these authors. He believed that the gliosomes may play a secondary rôle in the formation of glia fibers, but not a primary one, and that the establishment of a vascular attachment plays a more important part.

In this study the development of glia fibers in astrocytes was observed in the white matter of young kittens. Glia fibers first appeared in the fetus of 10 cm. crown-rump length. They were fine in structure and were located close to the cell body in the external radial expansion, but they did not extend the entire length of the expansion. The majority of cells at this age were granular and without fibers. In the white matter at birth, almost all of the astrocytes contained fibers; a few remained granular. The fibers were found differentiating in the external radial process (fig. 12) or, more frequently, in the vascular process (fig. 4).

In the white matter of a 1 month old cat, all stages in the development of the fibers were observed. From their point of origin in the external radial process or vascular attachment they radiated toward the cell body, crossing it to invade the smaller processes (fig. 4). They were uniform in size and smooth in outline and had a granular structure. They differentiated in the granular cytoplasm of the cell.

PHAGOCYTIC ACTIVITY OF MICROGLIA

In the brains of kittens during the third week of life were found the original long processes of the supportive spongioblasts undergoing what appeared to be degeneration. It was during this period, rather than before or after, that the microglia cells, the phagocytes of the central nervous system, were engorged with fat. They were found in great numbers in the white matter of the cerebrum, in close relation to the degenerating processes, and appeared to be phagocytosing them. They were found collected about blood vessels into which they were discharging their contents. Microglia should not be confused with neuroglia. The former cells are of mesodermal origin while the latter are ectodermal.

SUMMARY

1. This study has shown oligodendroglia to be of ectodermal origin.

2. In the cerebra of mice, during the height of myelinization, apolar migratory spongioblasts are found quitting the ependyma in great numbers. During or after migration these cells develop processes forming oligodendroblasts. The latter develop into adult oligodendroglia cells.

3. The apolar migratory spongioblast described in this article is comparable to the migratory spongioblast described by Penfield [14] in the spinal cords of kittens.

4. The cytogenesis of oligodendroglia in the cerebrum is comparable to that in the spinal cord.

5. Astrocytes, fibrous and protoplasmic, are of ectodermal origin.

6. From the primitive spongioblast the adult astrocyte may develop in one of several ways: first, and most frequently, by passing through the stage of a supportive spongioblast; second, from the polar migratory spongioblast, and third, from the apolar migratory spongioblast. The intercalated astrocytes frequently develop from the latter cell type.

7. The ontogenetic development of neuroglia in general in the brains of cats and mice is comparable to its phylogenetic development.

8. Neuroglia fibers appear in the cat before birth. They differentiate in the cytoplasm of the cell, most frequently in the vascular process, from which they invade other expansions.

9. The various spongioblasts observed—supportive, migratory polar and apolar—permit a more thorough understanding of the various cell types occurring in the gliomas.

10. There is a marked similarity between the embryonic cell forms and those constituting the various tumors of the glioma group.

11. The degenerating spongioblastic processes are phagocytosed by the microglia cells.

EFFECTS OF NECROBIOTIC AGENTS ON THE WALLS OF CYSTS EXPERIMENTALLY PRODUCED IN THE BRAINS OF DOGS

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AND

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CLEVELAND

A variety of necrobiotic agents has been employed to supplement the surgical removal of malignant tumors. Of these, Zenker's fluid has been used in the operative field of tumors of the brain, especially gliomatous cysts, and Cushing[1] has recently emphasized its value, particularly for its hemostatic properties. In reviewing the literature, we have failed to find any experimental investigation of the relative merits of the various fixing agents used for this purpose. Zenker's fluid would seem particularly unsuited because of its slow penetration as compared to other commonly used fixatives.

This investigation was undertaken to test the necrobiotic and hemostatic properties of several of the more commonly used fixatives. For this purpose cysts were experimentally produced in the brains of dogs, and the various agents were tested on the lining of these cysts.

EXPERIMENTAL PRODUCTION OF CYSTS IN THE BRAINS OF DOGS

Technic.—Healthy, adult dogs were used. The skin of the scalp was shaved and prepared with alcohol and mercuric chloride. A lateral, frontal decompression was performed under interrupted ether anesthesia. A needle was inserted to a depth of about 6 mm. in the anterolateral frontal area, and 2 cc. of a sterilized paraffin-petrolatum mixture was injected slowly. This mixture was prepared of one part of paraffin and two parts of white petrolatum, and was warmed before injection.

Other methods of producing cysts, including the injection of liquid petrolatum and of gelatin and the embedding of glass beads, were unsatisfactory.

Histologic Methods.—Blocks for histologic study were fixed in a diluted solution of formaldehyde, U. S. P. (1:10), Zenker's fluid and formaldehyde bromide. Sections were stained by hematoxylin and eosin, Mallory's phosphotungstic acid-hematoxylin for neuroglia fibrils, Mallory's aniline blue for fibrous connective tissue and the Maresch modification of the Bielschowsky method for nerve fibers.

Reaction to the Injection Mass.—Seven Days After the Injection of the Paraffin-Petrolatum Mixture: Evacuation of the injection mass disclosed a smooth-

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From the Laboratory of Surgical Research and the Institute of Pathology of Western Reserve University School of Medicine.

1. Cushing, Harvey: Experiences with Cerebellar Astrocytomas: A Critical Review of Seventy-Six Cases, Surg., Gynec. & Obst. **52**:129, 1931.

lined, spherical cavity beneath the cortex. The lining membrane was pale, thin, friable and easily detached from an underlying layer of soft, pink granulation tissue. Microscopically, the lining membrane was composed of fibroblasts, which in places formed a compact lamella and in places were loosely organized. Beneath this membrane there was a broad zone of poorly organized granulation tissue, comprised almost entirely of fat-laden compound granule cells. Intermingled with them were a few endothelial cells, lymphocytes and polymorphonuclear leukocytes. These cells were supported on a delicate stroma of proliferating fibroblasts which contained newly formed blood vessels. There was no sharp line of demarcation between this zone and the adjacent substance of the brain, which was edematous, in places hemorrhagic, and which was the seat of granular and vesicular disintegration. The astrocytes appeared swollen, and the neurocytes were often degenerated, with karyorrhexis of the nuclei. There was no evidence of glial proliferation.

Fourteen Days After Injection: The lining of the cavity was smooth, and there was less edema in the adjacent substance of the brain. Microscopically, the fibrous lining membrane was thicker and the cells were more flattened and elongated. The inner portion of the membrane was dense as compared to the outer surface, which merged into the adjacent granulation tissue. The fibrous lining membrane was not of uniform thickness, being thickened at the site of the needle puncture wound, which was filled by a solid core of well vascularized fibrous connective tissue. Outside the membrane there was a zone of compound granule cells supported on a richly vascularized, fibroblastic stroma. This zone of granulation tissue contained fewer phagocytes and was more compactly organized than that around the seven day cyst. Masses of proliferating adventitial fibroblasts were frequently coalescent. The adjacent tissue of the brain showed less evidence of degenerative change and less edema. The junction of the intact substance of the brain and the granulation tissue was not sharp, and in places appeared frayed where neuroglial fibrils were prolonged into the granulation tissue. Astrocytes appeared swollen, but there was no gliosis.

On the deeper surface of the cyst there were several nodular outpouchings of the injection mass, several of which appeared to be isolated from the main mass. These had the appearance of simple defects in the tissue of the brain, and although the wall of some of them resembled that of the main cyst, others had no fibrous lining, no peripheral exudative zone and no apparent fixed tissue reaction in the substance of the brain other than a superficial condensation of neuroglial processes.

Twenty-Two Days After Injection: In addition to the main injection mass, there were several smaller masses of the paraffin-petrolatum mixture lateral to and beneath it. There was some flattening of the convolutions over the site of the cyst, but relatively little gross edema of the substance of the brain. The larger cyst had a smooth fibrous lining, which varied in thickness and compactness and was continuous with a vascularized core of fibrous connective tissue that followed the course of the needle puncture wound to the surface of the brain. The subcapsular zone of granulation tissue was similar to that seen in the fourteen day cyst, but with fewer phagocytic cells and more complete organization. The smaller, secondary locules varied as to the character of their lining, and in most instances were simple defects in the substance of the brain with or without a lining neuroglial feltwork.

Twenty-Eight and Thirty-Six Days After Injection: These two cysts were essentially similar on both gross and microscopic examination. The lining membrane was complete, tough and fibrous, and measured about 1 mm. in thick-

ness. In places the outer surface of the membrane was continuous with the adjacent tissue of the brain, and in other places the two were separated by small collections of compound granule cells. The deeper portions of the membrane, as well as the adjacent tissue of the brain, were richly vascularized, and occasional perivascular endothelial cells and lymphocytes were encountered. The subcapsular zone of granulation tissue had become organized as part of the fibrous capsule of the cyst. There was a superficial zone of gliosis in the brain, manifested by an interlacing feltwork of neuroglia fibrils.

Three Days After the Evacuation of the Contents of a Thirty-Day Old Cyst: Thirty days after injection, the head was opened through the old incision and the

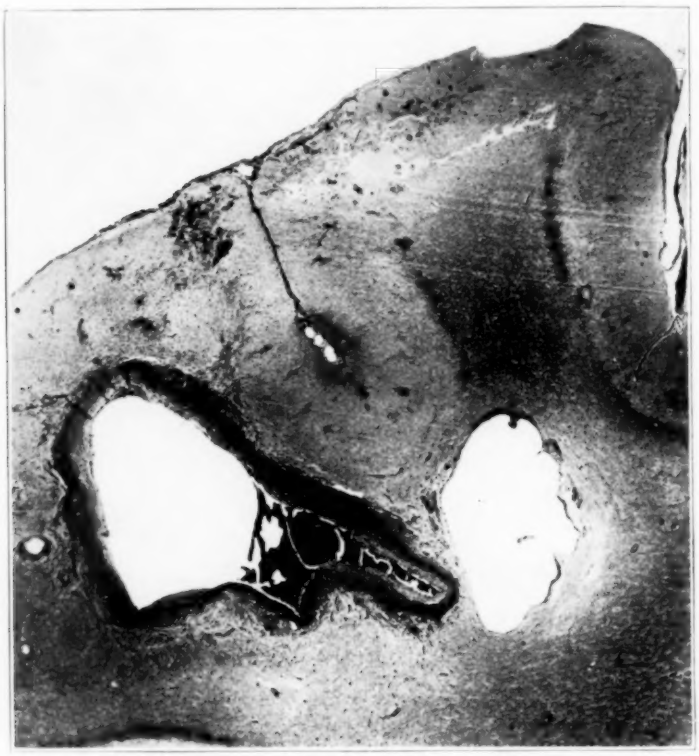

Fig. 1.—The brain three days after the removal of the paraffin-petrolatum injection mass from a thirty day old cyst. The smaller defect to the right in the substance of the brain represents an extruded mass of the injection mixture which was not removed at the second operation. Note the absence of a fixed tissue reaction around it in contrast to the thick fibrous wall of the primary cyst. Mallory's aniline blue stain: × 7.

dura divided. The injection mass was located by palpation and exposed by incision. Part of the paraffin-petrolatum mixture was removed with a small curet, and the rest washed out with warm saline solution. The wound was closed with silk, and the animal was killed after three days. The cyst was not collapsed and contained bloody fluid (fig. 1). There was some edema of the adjacent tissue of

the brain. Microscopically, the wall of the cyst resembled those previously described (twenty-eight and thirty-six days after injection). There were several small collections of extravasated erythrocytes in and around the fibrous capsule, and the adjacent tissue of the brain was hyperemic and edematous. Small collections of lymphocytes and endothelial cells were present beneath the fibrous capsule.

The sections disclosed a small accessory mass of paraffin-petrolatum mixture which had not been removed, and the tissue of the brain surrounding it showed relatively little change (fig. 1).

Thirty-Five Days After the Evacuation of the Contents of a One Hundred and Fourteen Day Cyst: One hundred and fourteen days after injection the paraffin-petrolatum mixture was evacuated in the manner described in the preceding experiment, and thirty-five days later the animal was killed. The diameter of the cyst was reduced to about 5 mm., and the capsule was thrown into folds, the crevices of which were filled by a loose pannus of fibroblasts to render the lining smooth. Within this newly formed connective tissue there were many pigment-containing phagocytes. The external surface of the capsule was approximated by the tissue of the brain, and at the junction there was a compact feltwork of neuroglial processes.

EFFECT OF NECROBIOTIC AGENTS ON THE TISSUE OF THE BRAIN

The fixatives to be tested were applied to the lining of experimentally produced cysts of about one month's duration. Animals to be used for the testing of fixatives were operated on again, and the injection mass was removed in the manner already described. After the cavity had been washed with saline solution and dried with cotton pledgets, the solution to be tested was introduced into the cyst with a pipet and agitated with a small curet throughout the period of application. At the end of the period of application, the solution was withdrawn and the cavity washed with saline solution and closed with silk.

TABLE 1.—*Results After the Application of 40 Per Cent Commercial Formaldehyde*

Age of Cyst	Application of Fixative	Survival After Treatment
35 days	1 minute	2 days
27 days	3 minutes	1 day (died)
27 days	5 minutes	1 day (died)
20 days	5 minutes	2 days

Forty Per Cent Commercial Formaldehyde.—Four cysts were treated with formaldehyde for from one to five minutes (table 1). Both on gross and on microscopic examination, the changes produced by formaldehyde were essentially similar in all four instances. An objective differentiation between the brains of animals that died and those that survived the experiment could not be made. The frontal lobe containing the cyst was edematous, and small hemorrhages were present in the brain for a considerable distance around the cyst. The cyst was collapsed. The fibrous lining, although intact, was elevated by hemorrhage and edema. The basophilic granular character of the

cytoplasm, with pyknosis of the nuclei, marked the extent of the necrosis of the lining, and only the inner portion of the fibrous capsule of the cyst was necrotic. A zone of intact and apparently unaltered fibrous connective tissue separated this necrotic superficial layer from the edematous tissue of the brain. In the adjacent tissue of the brain there were severe degenerative changes and focal hemorrhages. The blood vessels did not contain thrombi, and there were often perivascular collections of extravasated red blood cells, and exudation of endothelial cells and polymorphonuclear leukocytes (fig. 2). The

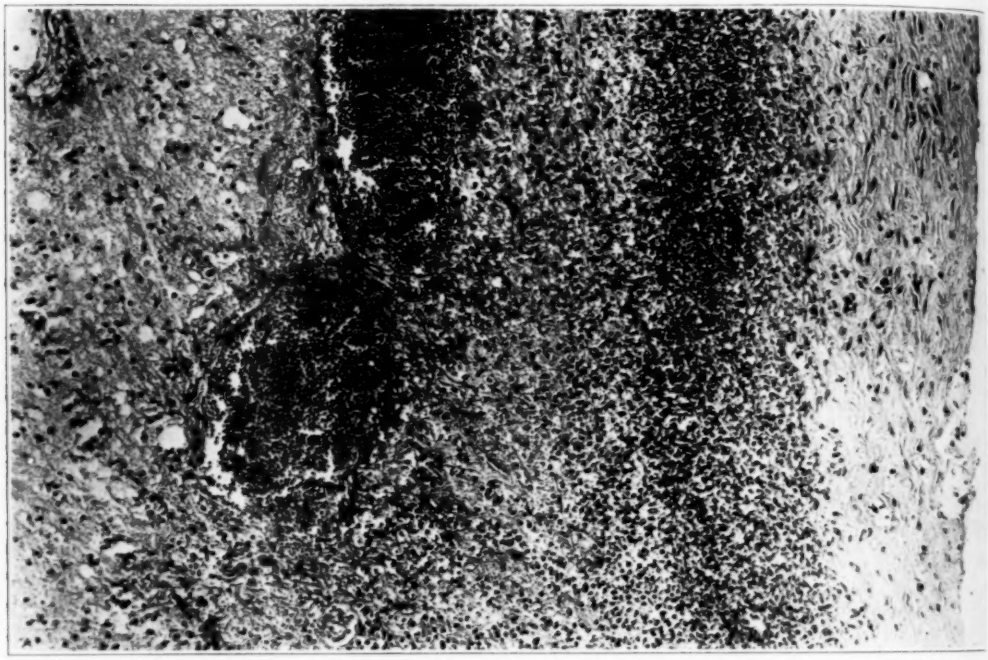

Fig. 2.—The wall of a twenty-seven day old cyst, one day after the application of 40 per cent formaldehyde for three minutes. There is necrosis of the fibrous wall, and also severe vascular damage with disruption of walls of the vessels. Note the wide, surrounding zone of acute hemorrhagic inflammation. Hematoxylin and eosin stain; × 120.

leukocytic infiltration extended for a considerable distance into the otherwise normal-appearing tissue of the brain.

Zenker's Fluid.[2]—Ten cysts were treated with Zenker's fluid for from one to five minutes (table 2). Immediately after the application

2. One part of glacial acetic acid was added to 20 parts of a solution consisting of 5 Gm. of mercuric chloride, 2.5 Gm. of potassium bichromate and 1 Gm. of sodium sulphate in 100 cc. of water.

of Zenker's fluid, the hemorrhagic oozing from the wall of the cyst incident to the removal of the mixture appeared to be lessened and the wall of the cyst was diffusely stained by the chromate. Four of the ten animals died with signs of severe cerebral disturbance within two days after the treatment, but no objective differentiation could be made between their brains and those from animals that were apparently in good health at the time they were killed. The four deaths were of animals that had been treated with Zenker's fluid for three minutes or more.

TABLE 2.—*Results After the Application of Zenker's Fluid*

Age of Cyst	Application of Fixative	Survival After Treatment
19 days	1 minute	5 days
23 days	1 minute	5 days
30 days	1 minute	4 days
31 days	1 minute	2 days
32 days	3 minutes	1 day (died)
37 days	3 minutes	2 days
28 days	5 minutes	3 days
27 days	5 minutes	2 days (died)
28 days	5 minutes	2 hours (died)
40 days	5 minutes	2 days (died)

TABLE 3.—*Results After the Application of Carnoy's Fluid*

Age of Cyst	Application of Fixative	Survival After Treatment
25 days	1 minute*	3 days
28 days	3 minutes*	3 days
26 days	5 minutes*	3 days
28 days	5 minutes*	3 days
25 days	1 minute†	36 days
30 days	1 minute†	7 days
28 days	3 minutes†	2 days
31 days	3 minutes†	1 day (died)
28 days	5 minutes†	2 days
28 days	5 minutes†	1 day (died)
51 days	5 minutes†	1 day (died)

* Absolute alcohol, 6 parts; chloroform, 3 parts; glacial acetic acid, 1 part.
† Carnoy's fluid, 9 parts; ferric chloride, 1 part.

Neither gross nor microscopic examination revealed any differences corresponding to the duration of application of the fixative or the length of survival after its use. Edema and hemorrhage into adjacent cerebral tissue were prominent and, in many cases, resulted in collapse of the cyst. The zone of hemorrhage and necrosis extended several millimeters into the substance of the brain, and the edema often involved the entire lobe of the brain. Microscopically, there was almost complete destruction of the fibrous capsule by liquefaction necrosis (fig. 3). The blood vessels beneath the capsule were dilated, did not contain thrombi and were often disrupted. There was considerable diffuse hemorrhage. Exudation was marked, included compound granule cells and was most severe in the cysts examined five days after the application of the fixative.

Carnoy's Fluid.—The linings of the cysts of the first four animals were treated with Carnoy's fluid and of the last seven animals with a mixture of ferric chloride and Carnoy's fluid. Carnoy's fluid was selected because of its known rapid fixing and penetrating properties, and ferric chloride was added to enhance the hemostatic properties of the solution and also because of its tanning effect on tissue (Sollmann[3]).

The application of Carnoy's fluid alone for periods of from one to five minutes resulted in blanching of the wall of the cyst and a diminution in the capillary oozing. After twenty-four hours, the wall of the

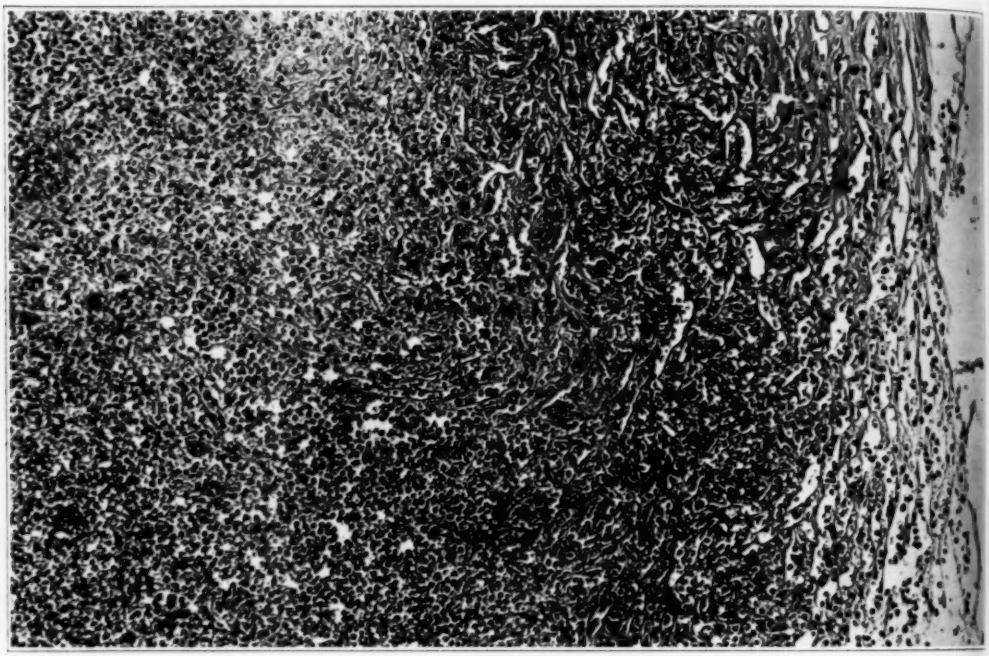

Fig. 3.—The wall of a thirty-seven day old cyst, two days after the application of Zenker's fluid for three minutes. There is an almost complete destruction of the wall of the cyst with acute hemorrhagic inflammation of the surrounding tissue of the brain. Hematoxylin and eosin stain; × 120.

cyst was firm, and no appreciable gross edema or hemorrhage was noted. Microscopically, the wall of the cyst was necrotic, but the necrotic tissue was compact and homogeneous in contrast to the liquefaction seen with Zenker's fluid. There was some perivascular hemorrhage, with sparse infiltration of compound granule cells, lymphocytes, endothelial cells and occasional polymorphonuclear leukocytes.

3. Sollmann, Torald: Manual of Pharmacology, ed. 3, Philadelphia, W. B. Saunders Company, 1926, p. 993.

Of the seven dogs treated with Carnoy's fluid to which ferric chloride had been added, three died within twenty-four hours. In none of these was there any considerable degree of hemorrhage or edema. The wall of the cyst had a tanned appearance and was tough, brown and thick. Hemostasis was secured with ease after removal of the injection mass. Microscopically, the tissue appeared similar to that seen after the application of Carnoy's fluid, except for the occlusion of blood vessels in the subcapsular tissue by hyaline thrombi and the presence of brown pigment granules. This pigment was both intra-

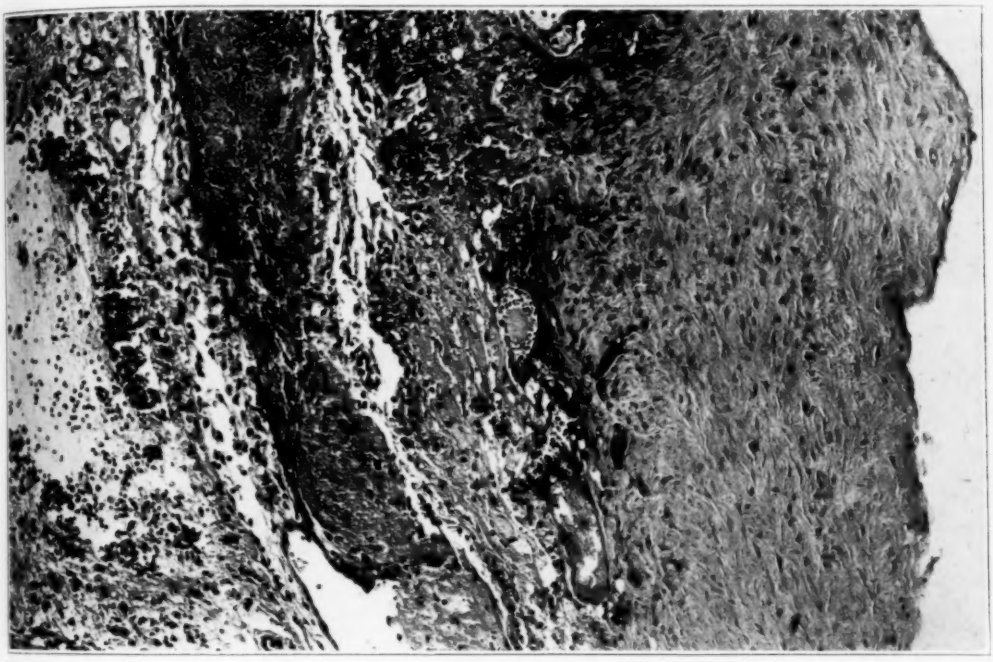

Fig. 4.—The wall of a twenty-eight day old cyst, two days after treatment with a 10 per cent ferric chloride solution in Carnoy's fluid for three minutes. The fibrous wall is necrotic despite the intact appearance of the nuclei. The subcapsular zone of tissue is the site of coagulation necrosis, and the blood vessels of the capsule and in the adjacent brain are occluded by hyaline thrombi. Hematoxylin and eosin stain; × 120.

cellular and extracellular. Phagocytic cells were seen in numbers that diminished with the time that had elapsed since treatment, but were in no instance so numerous as those seen with Zenker's fluid or formaldehyde fixation. Edema and hemorrhage in the surrounding tissue of the brain were not marked, nor was the extensive chemical encephalitis that was prominent following the use of some of the other fixatives (fig. 4).

Glacial Acetic Acid, Phenol and Trichloracetic Acid.—The walls of the cysts were treated with glacial acetic acid, phenol and trichloracetic acid, but these agents produced such severe inflammatory reactions following even short applications that they were rejected as being unsuitable for further study.

VARIATIONS IN MODES OF APPLICATION OF FIXATIVES

The different fixatives were also applied to the undisturbed pia and to freshly incised surfaces of brains. Neither method was found to be as satisfactory as the introduction of the necrobiotic agents into experimental cysts for comparative studies of tissue reaction.

COMMENT AND SUMMARY

Cysts were produced in the brains of dogs by the injection of a paraffin-petrolatum mixture. At the end of four weeks the injection mass could be removed, leaving a cavity lined by fibrous connective tissue which remained patent for at least thirty-five days. The fibrous wall of this cavity appeared to be derived in part from an extension of connective tissue along the needle puncture wound, and in part from the vascular adventitial connective tissue. In some instances the injection mass did not remain discrete, but small connected or isolated secondary cavities were found deeper in the substance of the brain. These did not characteristically acquire a fibrous capsule, nor was a glial proliferation of any consequence provoked (fig. 1). Such secondary cysts were examined from one to five weeks after injection, and around many there was no fibrosis, gliosis or phagocytic infiltration. The migration of phagocytes around the larger cysts was an indication of the degree of damage incident to the displacement of the substance of the brain by the injection mass. While this evidence of tissue damage was conspicuous around the large injection mass, it was inconspicuous or absent around the smaller injection masses. The fact that the large cysts acquired capsules of fibrous connective tissue, whereas there was little or no reaction around most of the smaller cysts, is in accord with the observation of Penfield and Buckley [4] that repair by fibrous granulation in the brain depends on the presence of injured tissue.

The genesis of the various types of phagocytic cells seen around the injection masses was not studied. Four morphologic types of wandering cells were identified as follows: compound granule cells, endothelial cells, lymphocytes and polymorphonuclear leukocytes. These

4. Penfield, W., and Buckley, R. C.: Punctures of the Brain: The Factors Concerned in Gliosis and in Cicatricial Contraction, Arch. Neurol. & Psychiat. **20**:1 (July) 1928.

cells diminished in number according to the time that had elapsed since the injection of the paraffin-petrolatum mixture. They were numerous around the primary injection mass and sparse or entirely absent from the tissue around the secondary masses. The first two types of cells were seen to persist the longest, and collected in the spaces of Virchow-Robin. Their subsequent fate was not learned.

Various necrobiotic agents, including 40 per cent formaldehyde, Zenker's fluid, Carnoy's fluid and a 10 per cent solution of ferric chloride in Carnoy's fluid, were applied to the lining of experimentally produced cysts. Of these, the solution of ferric chloride in Carnoy's fluid proved the most efficacious. The treated tissue was killed by coagulation for a depth of about 2 mm. following an application of the fixative for between two and three minutes. Blood vessels were the seat of thrombosis, and there was relatively little collateral inflammation or edema in the adjacent tissue of the brain. Other agents, including 40 per cent formaldehyde and Zenker's fluid, were as efficacious in producing necrosis, but were not desirable because of the severe collateral inflammation of the tissue of the brain.

NERVE DEGENERATION IN POLIOMYELITIS

V. CORRELATION OF FIBER CHANGES IN NERVES WITH CELLULAR CHANGES IN THE SPINAL CORD

W. P. COVELL, PH.D.
ST. LOUIS

The preceding papers of this series [1] dealt with a correlation between histologic evidence of degenerative changes in the roots and nerves supplying the affected extremities in experimental acute poliomyelitis and physiologic data concerning the concurrent dysfunction. The problem was undertaken with the view that the condition of the mensurable physiologic properties of the nerve fiber is the best index to the functional state of its cell of origin.

For the functional aspect of the study the cathode ray oscillograph was employed to record the physiologic properties of the nerves and roots in vitro. In addition galvanic stimulation was applied: (1) to the cord above the segments supplying the affected extremity, and (2) to the roots and nerves during the preparalytic stage and at intervals subsequent to the onset of paralysis. Standard neurohistologic procedures were also employed.

In order to interpret results, it was necessary to secure quantitative data concerning the physiologic properties of normal nerves of monkeys, not hitherto available. These data were presented in the second paper

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1. (*a*) Covell, W. P., and O'Leary, J. L.: Nerve Degeneration in Poliomyelitis: I. Vital Staining Methods with Neutral Red Applied to Nerve Degeneration, Arch. Neurol. & Psychiat. **27**:518 (March) 1932. (*b*) Bishop, G. H.; Heinbecker P., and O'Leary, J. L.: Nerve Degeneration in Poliomyelitis: II. A Histologic and Functional Analysis of Normal Somatic and Autonomic Nerves of the Monkey, ibid. **27**:1070 (May) 1932. (*c*) Heinbecker, P.; Bishop, G. H., and O'Leary, J. L.: Nerve Degeneration in Poliomyelitis: III. The Rate of Depression and Disappearance of the Components of the Conducted Action Potential in Severed Nerves; a Correlation with Histologic Evidence of Degeneration in the Several Groups of Fibers Essentially Responsible for the Various Components, ibid. **27**:1421 (June) 1932. (*d*) O'Leary, J. L.; Heinbecker, P., and Bishop, G. H.: Nerve Degeneration in Poliomyelitis: IV. Physiologic and Histologic Studies on the Roots and Nerves Supplying Paralyzed Extremities of Monkeys during Acute Poliomyelitis, ibid. **28**:272 (Aug.) 1932.

of the series.[1b] It was also necessary to know the rate of disappearance of the components of the conducted action potential in nerves severed from their cells of origin. For each of these components of potential, a histologically recognizable group of nerve fibers is essentially responsible, and it was therefore possible to correlate histologic with functional evidence concerning the rate of degeneration of the several fiber groups. The third paper of the series [1c] was concerned with this phase of the problem.

With these comparative data at hand, studies of the nerves and roots of affected extremities by the combined histologic and functional methods were conducted. The following results were obtained: Except for a period of increased irritability of root and nerve fibers during the preparalytic stage and first days of paralysis, the histologic and functional results secured indicated no difference between root and nerve degeneration occurring in poliomyelitis and in nerves severed from their cells of origin. This early irritability of nerves and roots supplying paralyzed extremities occurred in a sufficient number of cases to give the finding significance. Increased irritability was indicated by (1) lowered threshold, (2) a shorter refractory period and (3) an accelerated conduction rate. It was attributed to the effect of the virus on the cell. The functional loss, as revealed by oscillographic studies, indicated that the degeneration in roots and peripheral nerves of affected extremities rarely proceeded as rapidly as when nerves were severed from their cells of origin; indeed it was generally retarded, maximal loss sometimes not being apparent until from ten to fourteen days following the onset of paralysis. Different roots in the same animal were affected to varying degrees. By combined galvanic stimulation of cord, roots and nerves in vivo and oscillographic studies in vitro, it was shown that the site of first functional loss (coincident with the onset of paralysis) is in the anterior horn cell or at its synapse with the upper motor neuron. Dorsal roots, as compared with ventral roots, were only exceptionally found to be severely degenerated, but they may exhibit the primary stage of increased irritability equally with the ventral roots.

The purpose of this, the final paper of the series, is to attempt a correlation of these observations on nerve fibers with the injury to ventral horn cells caused by the virus. Much has already been written on the character of the changes in the cells, but they apparently have not been studied in the quantitative way that is necessary for this correlation. I wished particularly to ascertain: (1) the relative resistance of cells of different functional nature grouped in various cell columns in the cord; (2) the stage of the disease during which destruction of nerve cells is most marked, and (3) the part played by phagocytic cells in this destruction. In addition, newer qualitative methods

were applied in order to analyze further the character of the lesions. Chief among these was the intravital use of neutral red, which is selective for degenerating myelin [1a] as well as for certain granules and vacuoles within the nerve cells.

MATERIAL AND METHODS

The application of finer quantitative methods to the study of pathologic lesions is always a difficult matter because there are so many variables, of which individual differences in resistance are by far the most important and constitute the greatest obstacle. Fifteen of forty-eight monkeys given intracerebral injections of "mixed" virus of infantile paralysis secured from the Rockefeller Institute were selected for study because they reacted in the same way in that the period of incubation was of almost exactly the same length and the preparalytic symptoms were brief, intense and followed suddenly by paralysis of limb musculature, accompanied by marked prostration. The length of time during which the animals were paralyzed was not longer than forty-eight hours. They either were killed or succumbed to the disease at the end of this period, or prior to it. Autopsy was performed promptly in each instance.

Pieces from the following levels of the cord, 3 mm. thick, were fixed in Zenker's acetic or formaldehyde mixtures: cervical (4 to 6), thoracic region (7 to 9), and lumbar enlargements (3 to 5). Other parts of the central nervous system and of various organs were likewise preserved for subsequent study. Following the usual technical procedures, slides bearing 5 micron sections of the cord were colored in Giemsa's or Delafield's hematoxylin stain. Three slides, each carrying six serial sections, were prepared from each level, which means that attention was concentrated on relatively small areas. The conditions found in them, however, were of widespread occurrence.

The separation of cells into groups is usually made on rather an arbitrary basis. Definite information relating to the monkey is not available. The classification employed in this investigation is indicated diagrammatically in figure 1. Seven of the ten groups occur in the cervical level. On the lateral side of the ventral horn three groups of cells are recognizable, the ventrolateral, the intermediate dorsolateral and the dorsolateral. On the medial side there are two, the ventromesial and the dorsomesial. The central cell group lies between the medial and lateral cell columns. In the dorsal horn only the cervical and sacral nuclei of Stilling are considered. The thoracic level includes four groups: in the ventral horn, the dorsomesial, the ventromesial and the lateral splanchnic, and in the dorsal horn Clarke's column as represented by a definite cell group. In the lumbar region the groups are essentially the same as the cervical except for the addition of an extra group (the lateral basal) on the lateral side of the dorsal horn. As regards the functional significance of each group but little can be definitely said. Presumably the lateral groups of the ventral horns in the cervical and lumbar regions supply motor nerves to the musculature of the upper and lower extremities, respectively, and the medial groups the trunk musculature. The lateral splanchnic groups of the thoracic cord are visceral motor in function.

Before the extent of injury to these various cell groups could be estimated, it was necessary to reach an arbitrary decision regarding grades of injury. In the following account cells will be referred to as normal, partly destroyed and destroyed when certain criteria hold.

By normal cells are understood cells that showed no microscopically visible signs of having been injured by the virus. Obviously the possibility remains that they had nevertheless been injured in ways that at present are impossible to detect.

The partly destroyed cells were characterized by an irregular cell outline, chromatolysis, complete or incomplete, accompanied by some loss of ground substance, and a hyperchromatic, usually shrunken, nucleus with a distorted nuclear membrane. More detailed cytologic studies on this stage of cellular injury showed: (1) the shape of the mitochondria to be unaltered (Regaud's fixation, aniline acid fuchsin-methyl green staining); (2) the neurofibrillae to be normal or somewhat thickened, especially in the cell processes, with a tendency to fragmentation in the body of the cell (Ranson-Cajal silver pyridine preparations); (3) the Golgi apparatus to be apparently normal (Hirschler's osmic acid technic), and (4) intranuclear inclusions (Covell,[2] Hurst[3]) to be occasionally present.

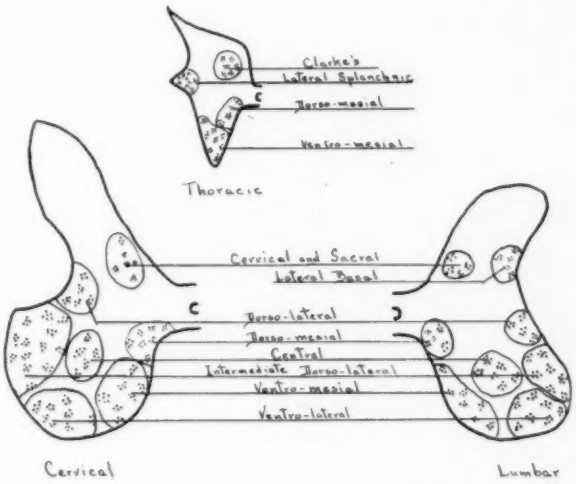

Fig. 1.—Diagram illustrating the approximate distribution of cell columns in the spinal cord of the monkey.

The more definitely injured cells were designated as destroyed because from all appearances there was no doubt that they were in process of complete removal. These cells really fell into two classes, as evidenced by the damage done by neuronophagia and the virus. Since these influences do not act equally, sometimes one being in the ascendancy and sometimes the other, considerable variability was encountered. Occasionally relatively normal cells were seen to be surrounded by neuronophages actively engaged in their destruction; the more common occurrence, however, was the invasion of the acidophilic staining masses of cytoplasm by phagocytic cells, or the persistence of clumps of phagocytes marking

2. Covell, W. P.: Nuclear Changes of Nerve Cells in Acute Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **27**:927, 1930.

3. Hurst, E. W.: The Occurrence of Intranuclear Inclusions in the Nerve Cells in Poliomyelitis, J. Path. & Bact. **34**:331, 1931.

the place in the group formerly occupied by cytoplasm. These neuronophages apparently attack cells in great numbers, regardless of the precise degree of degeneration that they exhibit. The converse type of reaction is characterized by profound injury in the almost complete absence of neuronophages. Such stages, according to Hurst,[4] illustrate a reaction to the more virulent strains of virus. The ground substance and chromidial substance of the cytoplasm are lacking, the staining reaction is modified, the cell outline is fairly regular and the nucleus may be clear and contain intranuclear inclusions. It is surprising to find that these cells, otherwise so drastically altered, have apparently unaltered mitochondria. The neurofibrillae, on the other hand, are usually noticeably fragmented and thickened; either the Golgi apparatus is not apparent or its remnants are in the form of short segments.

With this separation into three groups of cells on the basis of damage, no discrimination was attempted between those in the two halves of the cord, so that the final results were based on six separate counts, three on each side. The relative number of destroyed cells was estimated for each of the six observations and the weighted mean for all of the six counts obtained. The results are listed in the table.

RELATIVE NUMBERS OF CELLS DESTROYED IN COLUMNS OF THE SPINAL CORD

It has been pointed out in a qualitative way that the lateral columns of the ventral horns suffer most. In the cases under consideration, destruction was greatest in the intermediate dorsolateral group of the various levels. In the cervical enlargement for the fifteen monkeys it was 67.6 per cent, with a range of from 17.9 to 98.2 per cent. In the lumbar enlargement it was 71.3 per cent, with a range of from 47.3 to 93.6 per cent. The ventrolateral columns showed essentially the same degree of destruction without a significant variability in the two levels. In the cervical region it was 64.7 per cent, with a range of from 32.5 to 94.7 per cent. In the lumbar it was 67.5 per cent, with a range of from 41.6 to 92.3 per cent.

Although the relative numbers of destroyed cells in the ventromesial groups of the different levels were less than for the two lateral groups, they were approximately the same throughout the cord. In the cervical and thoracic cords the value was 52.2 per cent for the fifteen monkeys while that of the lumbar region was 47.5 per cent. It is also of some significance that the range for this column was greater than that for the corresponding columns on the lateral side of the ventral horn.

A comparison of the dorsolateral and dorsomesial groups in the different levels reveals a somewhat greater amount of destruction in the former group. In the cervical region the mean value for the number

4. Hurst, E. W.: The Histology of Experimental Poliomyelitis, J. Path. & Bact. **32**:457, 1929.

The Percentage of Totally Destroyed Nerve Cells in the Columns of the Ventral and Dorsal Horns Up to Forty-Eight Hours Following the Onset of Paralysis

Monkey	Ventrolateral		Intermediate Dorsolateral		Dorsolateral		Lateral	Ventromesial			Dorsomesial			Central		Cervical and Sacral		Lateral Basal,	Clarke's Column
	Cervical	Lumbar	Cervical	Lumbar	Cervical	Lumbar	Thoracic	Cervical	Thoracic	Lumbar	Cervical	Thoracic	Lumbar	Cervical	Lumbar	Cervical	Lumbar	Lumbar	Thoracic
3	35.5	41.6	50.1	47.3	12.6	15.1	30.4	21.2	33.4	22.1	16.7	37.4	5.8	12.5	14.3	0.0	2.0	11.8	9.1
9	47.4	63.0	87.8	64.6	62.9	48.8	81.8	38.9	36.4	34.3	22.2	25.0	17.4	11.8	9.3	0.0	0.0	0.0	0.0
16	77.8	62.1	86.3	62.5	33.3	55.1	45.4	80.9	72.7	70.9	50.0	40.8	47.2	63.2	63.2	29.2	57.1	39.6	23.5
31	39.1	76.5	17.9	75.6	0.0	31.4	8.3	49.7	75.0	43.3	40.0	30.8	43.9	12.2	30.5	0.0	0.0	46.7	50.0
33	87.2	76.8	93.6	80.8	51.5	38.6	26.4	66.7	40.0	51.1	28.4	0.0	7.5	76.2	61.1	29.4	6.3	9.4	26.3
38	32.5	73.6	57.3	93.6	27.6	31.6	23.5	19.8	63.7	22.8	0.0	15.4	19.1	35.5	53.2	0.0	5.6	2.3	35.3
40	63.8	62.2	57.7	69.6	42.3	75.0	30.1	20.6	22.5	34.6	17.4	10.6	24.9	55.3	66.7	0.0	5.4	0.0	8.7
44	67.5	64.8	45.3	53.6	17.2	29.7	15.2	62.5	68.8	58.4	32.3	41.2	39.5	29.7	35.0	27.8	26.5	37.1	11.1
46	85.4	80.6	98.2	70.1	57.6	23.1	27.8	52.2	58.3	65.9	28.2	27.3	15.9	44.1	26.1	10.5	4.4	13.0	42.8
47	87.5	92.3	46.2	79.0	23.1	88.9	34.5	84.6	54.5	85.3	17.6	33.3	86.8	64.7	76.1	37.4	53.7	73.3	43.7
61	63.1	79.6	77.8	75.7	53.4	34.9	11.9	57.5	50.2	47.6	57.1	50.0	68.6	73.6	57.4	32.2	23.1	40.4	29.6
63	80.0	48.5	70.3	66.7	61.5	2.2	0.0	91.4	66.7	39.0	65.9	40.0	29.8	72.5	15.4	13.0	23.9	0.0	36.4
76	94.7	68.4	90.9	84.2	68.4	61.3	0.0	61.9	55.6	38.9	45.5	0.0	50.0	76.5	18.8	35.7	0.0	21.1	62.5
175	52.6	57.7	58.3	67.7	42.5	35.3	19.6	35.6	37.5	33.3	5.6	0.0	0.0	27.8	48.8	0.0	8.3	11.8	41.2
187	56.5	65.0	76.0	78.9	26.7	58.2	0.0	40.0	48.2	64.7	17.6	15.8	35.7	45.5	58.8	45.8	30.0	27.8	23.1
Mean	64.7	67.5	67.6	71.3	38.1	41.3	23.6	52.2	52.2	47.5	29.6	24.5	32.8	46.7	42.3	17.4	16.4	22.3	29.6
Range	32.5	41.6	17.9	47.3	0.0	2.2	0.0	19.8	22.5	22.1	0.0	0.0	0.0	11.8	9.3	0.0	0.0	0.0	0.0
	to	to	to	to	to	to	to	to	to	to	to	to	to	to	to	to	to	to	to
	94.7	92.3	98.2	93.6	68.4	88.9	81.8	91.4	75.0	85.3	65.9	50.0	86.8	76.5	76.1	45.8	57.1	73.3	62.5

of cells destroyed was 38.1 per cent, while that of the lumbar region was 41.3 per cent. Contrasted with the averages for the dorsomesial groups, which were 29.6 per cent (cervical), 24.5 per cent (thoracic) and 32.8 per cent (lumbar), the damage to the former cell group was greater.

The central cell groups of the series represent in relative figures of destruction a transition point between the extent of damage to the lateral and medial parts of the ventral horn. The degree of damage in the cervical and lumbar regions for these monkeys was essentially the same. In the cervical level it was 46.7 per cent, and through the lumbar region, 42.3 per cent. In none of the monkeys was destruction entirely lacking, the range for the cervical level being from 11.8 to 76.5 per cent, while that for the lumbar was from 9.3 to 76.1 per cent.

Of considerable interest is the relatively mild destruction of the lateral splanchnic cell groups. This resembled the values found for the dorsal horn, the mean being 23.6 per cent, with a range of from 0 to 81.8 per cent.

One would expect the visceral motor group to be more affected than it is in a disease that involves so much of the somatic motor mechanism. Considering the degree of cell destruction in the dorsal horn it is noteworthy that in only one of the fifteen cases was Clarke's column free from injury to the cells. The mean value of the relative figures was 29.6 per cent, with a range of from 0 to 62.5 per cent. The lateral basal group was unaffected in three instances. The mean value of destruction was 22.3 per cent for the whole group of monkeys and the range from 0 to 73.3 per cent. The relative amount of damage in the cervical and sacral nuclei of Stilling was comparable to that of other dorsal horn cell groups.

Considering the degree of destruction for each animal in the three levels of the cord, it is noticed that in the case of the ventrolateral group, for instance, the lumbar and cervical regions showed essentially the same amount of destruction in about 50 per cent of the cases. Destruction in the cervical region in two instances exceeded that in the lumbar region by at least 15 per cent, while in five monkeys the lumbar region showed a greater amount of destruction. The degree of destruction was most consistent in the ventral horns from cell group to cell group in each case and least consistent in the dorsal horns.

STAGE OF THE DISEASE DURING WHICH INJURY IS MOST MARKED

For the purpose of examining more closely the rate of cell destruction in the spinal cord, the lateral groups of the ventral horns were selected for further study. This was done chiefly because of the susceptibility and lowered factor of variability in this group. The only

disadvantage in attempting this has been the inability to determine more precisely the relative numbers of cells affected by the disease yet capable of recovery. Perhaps the instances in which paralysis and symptoms of the disease have been less acute might be more profitably examined with this in view.

The program for classification of cells into groups was continued on the intermediate dorsolateral and ventrolateral columns of cells of the ventral horns from the cervical and lumbar levels of monkeys that were killed or succumbed to the disease at intervals ranging from the preparalytic to the postparalytic stages. The relative amount of damage in each case was ascertained by the method previously given. It was, however, necessary to determine the relative number of cells in the later stages of the disease that had completely disappeared and were no longer represented by focal accumulations of neuronophages. Glial proliferation replaced the appearance of the previous lesion. The average number of cells found in the sections at the various levels of the cord for the intermediate dorsolateral and ventrolateral columns was determined in twenty-nine monkeys with poliomyelitis, in which cell removal was not complete, and in eight normal monkeys. Tissues from three monkeys were studied for cell changes during the preparalytic stage, and from thirty-five monkeys for cell changes during the paralytic and postparalytic stages. In this instance also it was found necessary to consider only those monkeys which revealed essentially the same symptoms, degree of paralysis, etc., in order that the factor of individual variability might be limited and the results of greater significance. The latter group of thirty-five monkeys was chosen from a series of ninety-two monkeys. Of the thirty-five there were nine for the first twenty-four hours of paralysis, six for the interval from twenty-four to forty-eight hours, five from forty-eight to seventy-two hours, four from ninety-six to one hundred and twenty hours, and seven for varying periods of time ranging from five to thirty-three days.

The results obtained are illustrated graphically in the histogram shown in figure 2. During the first twenty-four hours following the onset of paralysis, 57.7 per cent of the cells in the ventrolateral and intermediate dorsolateral groups showed complete destruction and 24.7 per cent were partially destroyed, while 17.6 per cent revealed no changes. The group of cells destined for removal was increased to 75.6 per cent in the ensuing twenty-four hours while the number of discernibly altered nerve cells was diminished to 16.6 per cent in this interval, and likewise more of the previously unaltered ones had succumbed, so that only 7.8 per cent remained. From forty-eight to seventy-two hours revealed a further decrease in the latter groups, with only 1.9 per cent of the cells falling into the group of unaltered ones,

while 8.3 per cent remained partly destroyed cells, the remainder (89.8 per cent) being completely destroyed. The latter were at this time, as earlier, represented in part by an accumulation of neuronophages.

In from three to four days, 95.3 per cent of the cells were damaged and in part removed; 3.8 per cent showed mild changes; 0.9 per cent were normal. The values for from four to five days of paralysis were essentially the same: 97.7 per cent destroyed cells, 1.4 per cent partly destroyed and 0.9 per cent normal. Since the variability for individual animals following the fifth day of paralysis was found to be considerable, the results obtained in the seven monkeys used were grouped together.

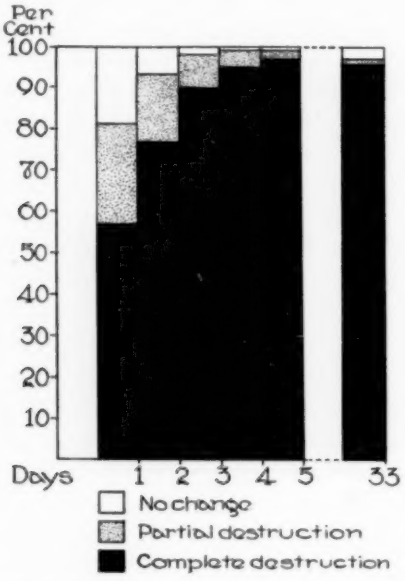

Fig. 2.—Histogram illustrating the relative numbers of destroyed, partly destroyed and normal cells in the ventrolateral and intermediate dorsolateral cell columns of the spinal cord.

Five of the seven monkeys survived from ten to thirty-three days after paralysis had commenced. It is possible that stages of recovery of certain cells are represented in this count since the remaining normal cells represented 3.3 per cent out of the total percentage, 95.6 per cent of the cells having been removed. The remaining 1.1 per cent still showed alteration.

PART PLAYED BY PHAGOCYTES IN CELL DESTRUCTION

There is much difference of opinion concerning the kinds of cells that participate in the process of neuronophagia. My observations are, however, in agreement with those of Hurst.[4] He found the number

of polymorphonuclear leukocytes to be conditioned by (1) the stage of the disease and (2) the virulence of the virus. After paralysis has persisted for some time (forty-eight hours) their number is decreased and other types of cells become more abundant. It is only in the most acute reactions that polymorphonuclear leukocytes are present in very large numbers. In order to clarify these qualitative statements, determinations of their existence in relative amounts were made. Sections of different levels of the cord from each monkey were colored with Giemsa's stain after the usual fixation in Zenker's fluid. The most striking thing about the occurrence of the leukocytes was the variation in their number in different parts of the cord. Quite regularly they were found to be more numerous in the lumbar region than at higher levels. In a few instances, however, examination of the cervical cord revealed large numbers of them. It is of interest, perhaps, to point out in this connection similar observations made by Warburg.[5] She also found that perivascular infiltration decreased progressively from the lumbar to the cervical and medullary levels.

In order to avoid confusion in actually counting the leukocytes, attention was concentrated on areas in which they were most abundant, so that maximum figures were obtained. Material from twenty-five monkeys representing the first forty-eight hours of paralysis was utilized. The total number of cells actively engaged in neuronophagia was counted by separating the polymorphonuclear leukocytes from other types of cells. In this way approximately 1,000 neuronophages were counted for each level before the relative numbers were determined. The results (fig. 3) were grouped according to the length of time, in twelve hour intervals, that the monkeys had been paralyzed. The first interval of twelve hours of paralysis is represented by results obtained from three monkeys; the second interval (twenty-four hours) by seven monkeys; the third (thirty-six hours) by four monkeys, and the fourth (forty-eight hours) by eleven monkeys.

At twelve hours of paralysis 63.6 per cent of the invading phagocytic cells were polymorphonuclear leukocytes, the remainder being represented by different types of cells. At twenty-four hours the values previously obtained were reversed so that 36.9 per cent were polymorphonuclear leukocytes while 63.1 per cent were other kinds of cells. At thirty-six hours there was a progressive decrease in the number of polymorphonuclears, there being 24.3 per cent against 75.7 per cent of other phagocytes. In forty-eight hours following paralysis the relative number of polymorphonuclear leukocytes was 17.1 per cent with 82.9 per

5. Warburg, B.: Experimental Poliomyelitis: Histology of the Persistent Lesions of the Central Nervous System, Arch. Neurol. & Psychiat. **25**:1191, (June) 1931.

cent of cells of other types. It is thus apparent, as illustrated in figure 3, that the rôle played by polymorphonuclear leukocytes is rapid and is terminated in from two to three days following paralysis. What the significance might be cannot at present be said. It seems highly probable that invading cells, different from the polymorphonuclear leukocytes, have something to do with their degeneration. The nuclei of the polymorphonuclear leukocytes become more compact, stain deeply and frequently fragment and dissolve. The cytoplasm of leukocytes is apparently more resistant to this undetermined lytic agent, because if the oxydase reaction is applied to material of later stages in which there is

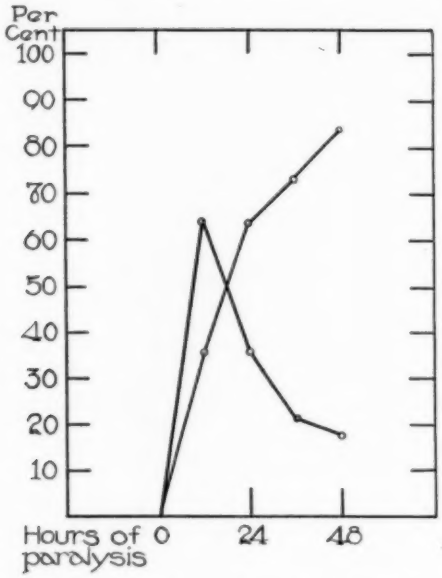

Fig. 3.—Relative numbers of polymorphonuclear leukocytes and other types of cells engaged in neuronophagia during the first forty-eight hours of paralysis. The curve that rises rapidly and then falls within the first twenty-four hours represents the polymorphonuclears. The other types of cells are represented by the curve that rises gradually to the forty-eight hour interval.

little evidence of polymorphonuclear leukocytes, numerous remnants of their protoplasm will still be seen to give this reaction.

LESIONS IN THE CENTRAL NERVOUS SYSTEM AND PERIPHERAL NERVOUS SYSTEM AS DEMONSTRATED BY NEUTRAL RED

It was during the study of the effects of staining with neutral red on the lesions in the central nervous system that its value as a stain of degenerating myelin in peripheral nerves came to light. This discovery has made possible determinations of the degree of change within the

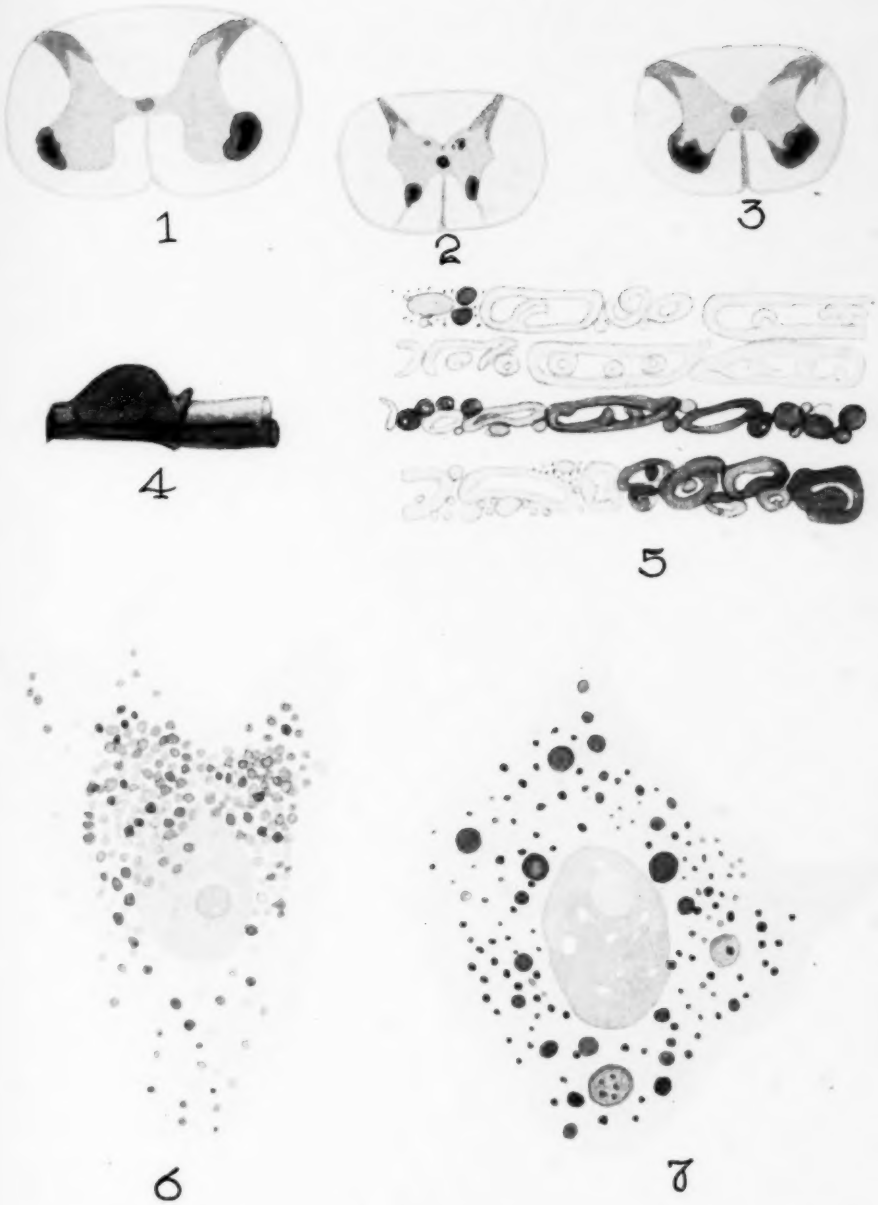

Fig. 4.—*1*, *2* and *3*, intravital staining, with neutral red, of the lesions in the spinal cord at various levels (fifth cervical, eighth thoracic and fourth lumbar) in a monkey after eight days of paralysis; × 5. *4*, neutral red staining of the fourth lumbar dorsal root ganglion and roots. The ganglion and ventral root are intensely stained; × 10. *5*, camera lucida drawing of the staining in the ventral root of *3*. Blocks of altered myelin stain deeply with the dye; × 550. *6*, camera lucida drawing of a large ventral horn cell from a monkey in the preparalytic stage, illustrating the location of neutral red stainable granules and vacuoles at one pole of the nucleus. This is in contrast to the normal cell, in which they are usually distributed evenly throughout the cytoplasm; × 1,000. *7*, camera lucida drawing of a large ventral horn cell from a monkey paralyzed for two days, showing the coalescence of neutral red stainable material, indicating a later type of change; × 1,000.

nervous system, since nerve cells and phagocytes contain neutral red stainable material, and the correlation of these with peripheral nerve alterations.

Nine monkeys in various stages of the disease and one normal monkey were given intravenous injections of the dye. One monkey was in the preparalytic stage, two had been paralyzed for from twenty-four to forty-eight hours and three had been in the paralytic stage for from three to four days, one for six days and two for eight and ten days. The femoral vein was exposed in each instance, and from 40 to 75 cc. of a 2 to 4 per cent solution of neutral red (Grübler) in physiologic solution of sodium chloride injected over a period of about one-half hour. After the desired staining had occurred, the animal was killed and the cord and brain were exposed. The dorsal root ganglia were intensely stained; likewise the gray matter of the cord. The white matter was distinctly pinkish, in contrast to the deeper red of the gray matter.

As illustrated in *1, 2* and *3* of figure 4, the region of the cord in which the lesion is found stains a deeper red than the less affected areas. Such a locus of deeper staining is seen to occupy most of the lateral parts of the ventral horns in the three levels shown. In figure 4, *1* represents the fifth cervical level, *2* the eighth thoracic, in which a smaller and deeper staining area in the region of Clarke's column was noted, and *3* the fourth lumbar. Microscopic examination shows that this degree of staining is not due entirely to the necrotic nerve cells ordinarily found in such areas, but also to the phagocytosed particles and vacuoles in the invading and infiltrating cells. The latter have not been figured because they do not differ in appearance from other phagocytic cells found elsewhere in the body. The numerous vacuoles of variable sizes, which are stained with neutral red, vary in their tinctorial properties. Gradations in color from yellow to red indicate that differences exist in the hydrogen ion concentration of different vacuoles in the same cell. It has been shown by Kubie [6] that vacuoles are present normally in the clasmatocytes distributed along the peripheral blood vessels in the central nervous system. Recent investigations on tissue cultures (Horning and Richardson [7]) apparently show that this formation of vacuoles is a phenomenon conditioned by changes in the hydrogen ion concentration.

The dorsal root ganglion and its attached roots of the fourth lumbar are illustrated in figure 4, *4*. The ganglion is colored intensely red,

6. Kubie, L. S.: A Study of the Perivascular Tissues of the Central Nervous System with Supravital Technique, J. Exper. Med. **46**:615, 1927.

7. Horning, E. S., and Richardson, K. C.: Cytological Studies on Cellular Degeneration of Differentiated and Undifferentiated Tissues in Vitro, Australian J. Exper. Biol. & M. Sc. **6**:229, 1929.

which is not due to the presence of many phagocytic cells, for comparatively few of these were found, but to the elective affinity for the neutral red of certain materials in the spinal ganglion cells. More stain seems to be taken up by these cells than by those of the gray matter of the cord. The ventral root is colored more intensely than the dorsal root—a difference probably caused by secondary degeneration in it, because in this case the monkey was allowed to live for eight days after the onset of paralysis. Figure 4, *5* illustrates the presence of a considerable amount of altered myelin taking the neutral red stain. The fragmentation and slipping of the myelin sheath and the staining of certain blocks of myelin are almost identical to those in preparations obtained by the much slower Marchi method. By contrast the dorsal root contained only a very few fibers which stained with neutral red. In another monkey, which was killed ten days after the onset of paralysis, the number of these degenerated fibers at this level in the dorsal root was increased, but no corresponding increase was detected in the ventral root. This was probably an individual difference in degree of response, and not simply the result of longer paralysis.

The nerve cell shown in figure 4, *6* illustrates the cellular change in a much earlier stage, being from the ventral horn of a monkey exhibiting pronounced preparalytic symptoms but no paralysis. In this case the coloration was secured by the intravenous injection of 50 cc. of a 4 per cent solution of neutral red over a period of twenty-five minutes, so that approximately the same degree of staining was obtained as for the other monkeys. It will be noticed that there is a distinct tendency for the neutral red stainable substance of the cytoplasm to collect about one pole of the nucleus. While this alteration is apparently slight, it is, nevertheless, of significance and rather striking in the number of cells that reveal it. In healthy monkeys used for control the same phenomenon was occasionally seen in a few isolated cells, but in the vast majority of the cells these granules and vacuoles were rather evenly distributed throughout the cytoplasm. It is evident, therefore, that the neutral red staining granules and vacuoles clump together in early injury to the nerve cells caused by the virus.

In the necrotic ventral horn cells of paralyzed monkeys, either the neutral red stainable material is absent, the whole cytoplasm being tinged a diffuse red color, or, occasionally, modifications in the cell similar to the one illustrated in figure 4, *7* are seen. It is obvious that the injury in this instance has been more severe, for the granules and vacuoles, which ordinarily take up the stain, are no longer fairly uniform in size, but appear to have coalesced. When the injury is further advanced to the stage of marked cell destruction by neuronophagia, it is usually impossible to observe any stained granules in the fragments of cytoplasm

that remain. The large collection of stained vacuoles in the phagocytes may be sufficient partly to obscure such vestiges. It is my contention that the neutral red staining material in the nerve cells is a more delicate indication of cell injury than the mitochondria, concerning the resistance of which information has been supplied by McCann.[8]

COMMENT

The foregoing results are in agreement with the indications of cellular injury and the evidence presented in the previous papers of this series relating to peripheral nerve alteration. A number of interesting correlations are thus made possible. These will be considered in the order of the progressive injury caused directly or indirectly by the virus.

Of primary interest is the stage of increased irritability of the peripheral nerves found during the late preparalytic stage and the first days of paralysis. That there are definite cellular alterations during this early period has been shown in a qualitative way by the unusual location of neutral red material in the cells, by the primary chromatolysis and by the beginning alteration in the neurofibrillae. It is unfortunate that these changes, while recognizable, are not sufficiently distinct to permit of quantitative treatment throughout the disease reaction. These early alterations speak for the direct action of the virus not only on the cell, but possibly also on the nerve fiber. This contention is supported by the fact that the fibers reveal increased irritability when removed from the body for study in vitro. Whether the first indications of the effects of virus activity are at the synapse, in the cell body or in peripheral nerves cannot be determined at present. With the sudden appearance of diversified lesions and the rapidly resulting consequences, a differentiation of this nature would be difficult to make even under the most favorable experimental conditions. The rapidity of the development of lesions in the next twenty-four hours is remarkable.

That the lesion becomes widespread during the first forty-eight hours of paralysis is evident from the study of the relative numbers of nerve cells injured in each column at the three levels of the cord examined. The more pronounced reaction of the cells of the lateral part of the ventral horn (ventrolateral and intermediate dorsolateral columns), especially at the lumbar level, explains the degree of degeneration of a secondary nature that is later so evident in the peripheral nerves to the limbs. This sudden destruction of the cell bodies with subsequent changes in peripheral nerves is comparable to that resulting from severing the nerves from their cells of origin. The chief functional difference is the usually longer time required for changes in the

8. McCann, G. F.: A Study of Mitochondria in Experimental Poliomyelitis, J. Exper. Med. **27**:31, 1918.

action potential to become apparent, for which the degree of cellular injury may be responsible. The proportion of visceral motor and sensory cells affected is less and corresponds to the number of degenerated fibers in the nerve trunks. The alterations in the nerve cells themselves are indeed sufficient to explain paralysis resulting at this stage of the disease in the limb musculature, but the possibility of changes in the motor end-plates must also be considered. The investigations of Kopits [9] are of interest in this connection.

The paralytic stage proper, in the series of thirty-five monkeys in which the ventrolateral and intermediate dorsolateral cells were estimated and the three types of injury determined, may be said to extend to the end of the fifth day following the onset of paralytic symptoms. Destruction is not actually at an end by this time, because one monkey that had survived an acute attack for thirty-three days revealed an occasional necrotic nerve cell still in process of removal. The experiments on the peripheral nerves, reported in other papers of this series, indicated that destruction was active from ten to fifteen days after paralysis. Recently Warburg [5] found evidence of degeneration of nerve cells in three levels of the cord in one monkey that lived for three hundred and nine days and commonly in the group of eight monkeys that survived from forty to seventy-two days. She was undoubtedly dealing with milder and more chronic phases of the disease than have been considered in this paper.

My co-workers and I have attributed the damaged nerve cells in the preparalytic and early paralytic stages to the action of the virus, but it is obvious that other factors may be operative, among which perivascular infiltration takes a prominent place. It occurs almost simultaneously with nerve cell destruction as well as with the penetration of phagocytes and the proliferation of cells within the cord. The extent of perivascular infiltration was, however, so variable in this series that one hesitates to assume a direct relation between it and cell destruction. Since the marked fluctuations in the number of polymorphonuclear leukocytes do not parallel changes in the rate of destruction of nerve cells, it is likely that this destruction is brought about by neuronophages as distinct from polymorphonuclears. The polymorphonuclear leukocytes are most numerous during the first hours of paralysis, reaching a maximum within twelve hours and becoming considerably fewer in number in forty-eight hours. It would appear that they are most active when for some reason the response of the neuronophages is delayed.

9. Kopits, I.: Beiträge zur Muskelpathologie: Histologische Befunde am Muskeln, Nerven und Blutgefässen in Spät und Endstadien peripher Lähmungen, mit besonderer Berücksichtigung der Poliomyelitis anterior acuta, Arch. f. orthop. u. Unfall-Chir. **27**:277, 1929.

Bearing in mind the experiments of Opie,[10] it is possible that the polymorphonuclears exercise a digestive action on injured nerve cells by the discharge of lytic ferments, in contrast to the phagocytic property of the neuronophages. Leukocytes have also been found to secrete substances capable of bringing about multiplication of cells in vitro (Carrel[11]). Thus they may influence the proliferation of microglia, which obviously plays an important rôle in the disease process.

SUMMARY

The relative numbers of cells destroyed in each column of the cord at three different levels during the first forty-eight hours of paralytic symptoms are greatest for the intermediate dorsolateral and ventrolateral groups. The ventromesial group is considerably injured, but to a lesser extent. The dorsal horn cell groups and the lateral splanchnic group contain about the same relative numbers of destroyed cells.

In a series of thirty-five monkeys more than half of the cells in the intermediate dorsolateral and ventrolateral groups were destroyed in the first twenty-four hours of paralysis and the number was gradually increased to more than 95 per cent by the fifth day. Nerve cell destruction continues during the later stages, but in this series it was not marked.

Early changes of the cell bodies in the preparalytic stage are recognizable by means of the characteristic change in the distribution of neutral red substance, which becomes clumped to one side of the nucleus. In later stages either this material is absent, the whole cell being diffusely stained, or it appears in the cytoplasm in the form of globules of variable size.

Polymorphonuclear leukocytes show considerable variation for the different levels, being found more often in the lumbar region. They are also variable in different monkeys showing similar severity of symptoms. In a selected group of monkeys they were found to be most numerous during the first twenty-four hours of paralysis and to be considerably less in relative numbers at forty-eight hours.

10. Opie, E. L.: The Enzymes in Phagocytic Cells of Inflammatory Exudates, J. Exper. Med. **8**:410, 1906.

11. Carrel, A.: Growth Promoting Function of Leucocytes, J. Exper. Med. **36**:385, 1922.

ENCEPHALITIS DISSEMINATA

A CLINICAL AND ANATOMIC REPORT OF A CASE WITH FEATURES AKIN TO MULTIPLE SCLEROSIS AND DIFFUSE SCLEROSIS

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AND
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Since the great epidemics of von Economo's disease of the preceding two decades, instances of sporadic, nonepidemic encephalitis, unassociated with any known virus or linked with one (vaccinia, variola, measles, etc.), are being reported from all quarters in steadily increasing numbers. The present report is made not only with the purpose of adding a new and somewhat unusual example, but also because the material affords data we consider pertinent to the old and currently active controversy respecting the nature and true nosological significance of multiple sclerosis, as well as to similar questions in the realm of the more recently elaborated disease concepts relating to the leukencephalitides of a diffuse kind (diffuse sclerosis, Schilder's disease, progressive subcortical encephalopathy, etc.).

REPORT OF A CASE

History.—Mr. Z., aged 23, a buyer for a tobacco company, entered the Presbyterian Hospital on June 10, 1929, with the history that on the evening of May 29 he had been lying down and on starting to get up fell. In a few moments he was able to get up and reach the couch, where he remained for about one hour, and was then able to walk to his bedroom, but noticed a weakness of the right arm and leg. On the next morning he was able to dress himself and be about the house, with the weakness continuing in the arm and leg. The feeling of weakness continued and was present at the time when he entered the hospital.

The family history was irrelevant in regard to nervous and mental disorders. The patient had had measles, chickenpox, whooping cough and mumps in childhood, frequent colds, not of sufficient importance to keep him in the house, and influenza in 1925, when he was in bed for a few days. He said that he had been slightly "under the weather" for two or three months preceding admission to the hospital. The gastro-intestinal tract was normal. There was a history of albuminuria five years previously. He said that he had not had venereal disease. The patient used tobacco and alcohol moderately.

Examination.—The patient was well nourished and did not seem acutely ill. The pupils were regular in outline and reacted to light and in accommodation;

From the Department of Neurology of Rush Medical College.
Read at a meeting of the Chicago Neurological Society, Dec. 17, 1931.

there was slight ptosis of the right lid; the eyegrounds were normal; all ocular movements were normal. There was slight paresis of the muscles supplied by the right seventh nerve, probably as part of the paresis of the right side. All other cranial nerves were normal. The right knee jerk was more lively than the left. Ankle clonus and positive Babinski, Gordon and Oppenheim signs were present on the right, and absent on the left side. The cremasteric and abdominal reflexes were present and normal. The reflexes of the upper extremities were normal. There was weakness of the muscles of the right arm and leg; the left limbs were apparently normal. No sensory disturbances were elicited. The teeth, from inspection, were in fair condition. The tonsils were injected, but not enlarged. There was no palpable adenopathy. The heart, lungs and abdomen were essentially normal.

Course.—The patient remained in the hospital for three days; he refused a lumbar puncture, and left the hospital with a diagnosis of right hemiparesis of undetermined origin. He was not seen again until the morning of March 29, 1930, when he reported that he had been feeling much better, and that the weakness of the right side had practically disappeared. No general examination was made at this time.

On April 30, 1930, he returned to the hospital complaining of a weakness of the left arm and leg, and inability to close the right eye. He stated that he had been in his usual health up to four days previously, when he awakened with a tired feeling; since then, he had gradually lost strength on the left side of the body.

Examination on Readmission.—Not much change was noted from the original examination except for the presence of weakness of the left arm and leg, with a positive Babinski sign and an increased ankle jerk. The positive Babinski sign that had been present on the right side at the first examination was now absent. A spinal puncture made on the day following readmission to the hospital, showed a cell count of 3, with the Kahn and Wassermann reactions negative. The gold chloride curve was essentially normal. A blood count showed: 5,090,000 red cells and 8,300 white cells. The blood pressure was 102 systolic and 62 diastolic. Urinalysis gave negative results. The temperature was normal, and remained so until about three days prior to death, when it gradually rose to 102.5 F.

Two weeks after the patient entered the hospital, examination showed a weakness of both sides of the body, with a bilaterally positive Babinski sign. The patient was lethargic and answered questions with difficulty. About two and one-half weeks after entering the hospital, difficulty in swallowing developed, and the patient became more lethargic. Respiration was irregular at times, and was stertorous. There was a gradual failure of respiration, and the patient died on May 26, twenty-six days after entering the hospital. A clinical diagnosis of encephalitis was made.

Autopsy.—This was done by Dr. C. W. Apfelbach on May 26, 1930, and was confined to an examination of the head. The pathologist's report showed: The bones of the skull were thick everywhere, the frontal bone averaging 1 cm. There was only fluid blood in the superior longitudinal sinus. The dura was tense and bulged more on the right side than on the left. The brain was swollen, particularly on the right side in the front half, where the convolutions were paler than those on the left, and also flatter and wider. The leptomeningeal veins on the right were less engorged than those on the left side. There was no noteworthy change in the large arteries at the base of the brain. In coronal sections of the brain there were light grayish-green, sharply circumscribed, soft regions in the white matter throughout the right cerebral hemisphere. These occupied from one third to two thirds of the white matter. They were irregular in shape, but the outlines were distinctly

convex or concave. There was no noteworthy change in the wall of the basilar artery. There was no change in the ear-drums. The large dural sinuses contained only fluid blood.

Bacteriology: In smears of the spinal fluid there were numerous leukocytes, but no organisms were found. On aerobic and anaerobic blood agar cultures and dextrose broth there was no growth.

Gross Appearances: After hardening in formaldehyde the brain weighed 1,450 Gm. Externally, there were no abnormalities except engorgement of the veins of the convexity and two small subpial hemorrhages, the largest 1 cm. in diameter. There was also some increase in the cloudiness of the leptomeninges along the veins. The normal configuration of the hemispheres and the brain stem was well maintained.

On all surfaces made by numerous frontal sections, from a level 3 cm. behind the tip of the frontal lobes anteriorly to one 3 cm. in front of the occipital poles poste-

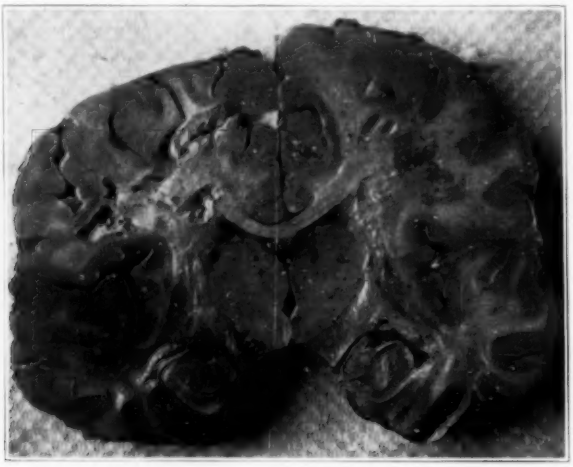

Fig. 1.—Frontal section, showing patches of softening.

riorly, there were marked changes. These consisted of extensive multiple areas of softening, lying wholly within the white matter of the hemispheres. They ranged from 2 mm. to 3 cm. in the greatest diameter, and were extremely irregular and diverse in shape, giving a maplike appearance to this part of the brain. The white matter in these regions of encephalomalacia was grayish yellow, soft and spongy; in places the regions were sunken as much as 1 mm. below the cut surfaces. They lay beneath the cortex, separated from it by zones of normal-appearing white matter. Much of the white matter in the vicinity of such regions was yellow, dull and soft to the touch (fig. 1).

While the lesions were found as far forward and backward as indicated, and were thus in the territories served by all three cerebral arteries, the following points in regard to distribution should be noted: They were more numerous and extensive in the right than in the left hemisphere; the greater number of them appeared in the centrum semiovale of the midportion of the hemispheres, and they tended to lie in the upper two thirds of the brain.

No other noteworthy changes were present, except an almost universal dilatation of the blood vessels, which was more marked in the white matter. Nowhere was

the cerebral cortex involved, nor was there any gross softening in the internal capsules, corpus callosum, basal ganglia or cerebellum. The ventricles were of normal size. There were no abnormalities of the large blood vessels of the base.

Microscopic Appearances: White matter of the cerebral hemispheres. Sections of the portions of the white matter of the cerebral hemispheres containing gross lesions, and of places near such regions, stained by the Pal-Weigert and Spielmeyer myelin sheath methods, presented innumerable patches of more or less complete demyelinization, patches that varied from 0.5 mm. to 3 cm. in diameter and were of the most diverse shapes. In regions that appeared to be normal on gross examination, many small, rounded, well delimited patches of partial demyelinization were

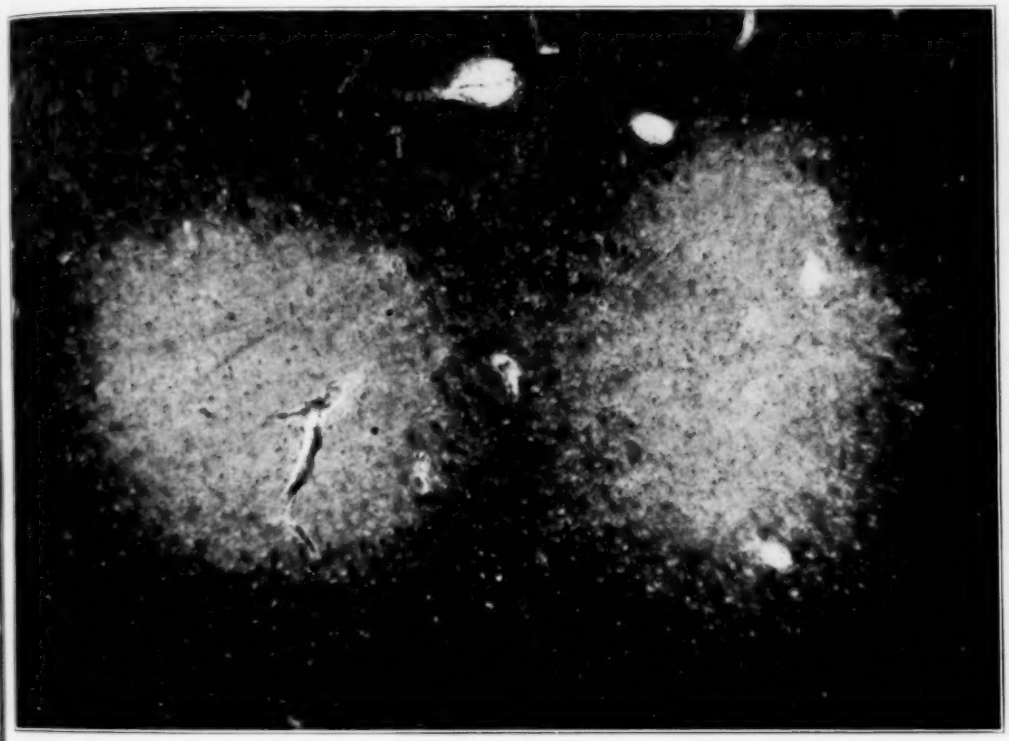

Fig. 2.—White matter from the right superior frontal convolution. Two islands of partial demyelinization are shown. Spielmeyer myelin sheath stain.

seen, through which some pale myelin fibers still passed. These had every appearance of small foci of multiple sclerosis (fig. 2). In sections that included regions of gross softening, such foci were seen to be completely devoid of myelinated fibers and were more or less filled with fat-granule cells, bearing granules stainable as myelin (fig. 3). These necrotic patches were sharply demarcated from the normal substance by a narrow zone of partial demyelinization of about the width of a high power field, in which were seen the usual twistings, swellings and fragmentations of retrogressive change in myelinated fibers. There was no relationship between the size of the lesion and the intensity of the damage to myelin. Figure 4 reproduces a small punctate region of complete degeneration, only 1 mm. in diameter.

While the changes in myelin were predominantly discrete and focal, this was not exclusively the case. Rather large areas were seen where the demyelinization was only slight, consisting simply of paleness in the fiber staining, fading off gradually from normal white matter. Such places were found particularly at the bases of the projections of the white matter into the convolutions. Conforming with the gross appearances of the cut surfaces of the brain, the myelin stains all revealed a striking tendency of the myelin damage to stop short of the cerebral cortex and to spare the subsulcine arcuate fibers. This is illustrated typically by figure 3, taken from a lesion which to the naked eye seemed to impinge on the cortical layer. However, such a distribution of myelin damage is not absolute. Places were found

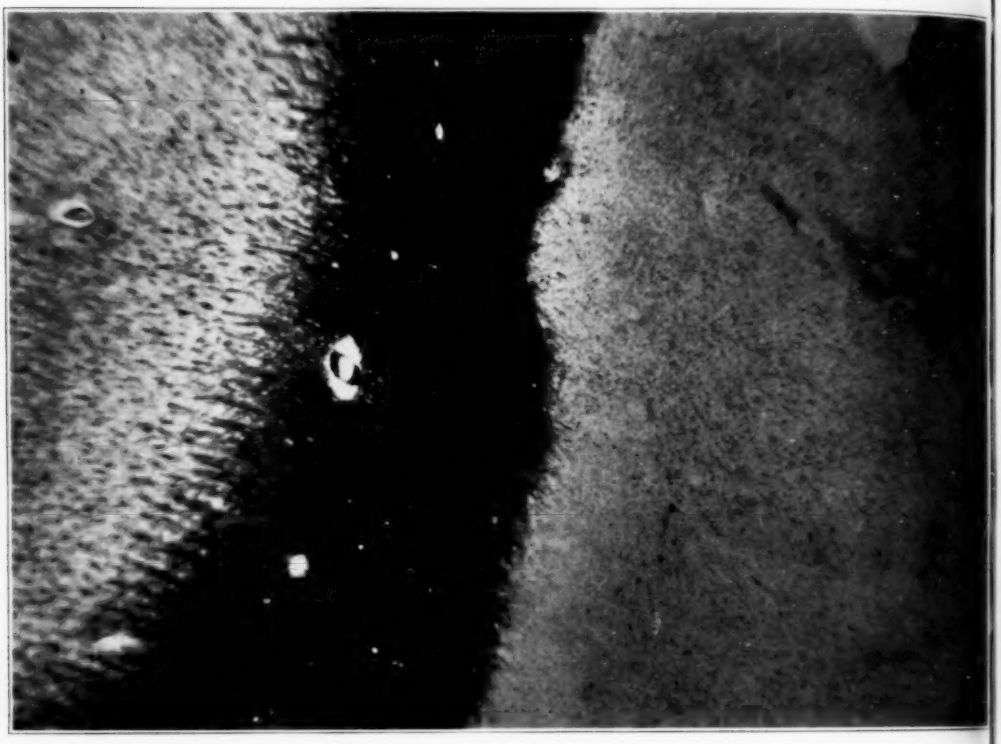

Fig. 3.—Cortex of the right postcentral convolution and the underlying white matter. The staining reveals a band of unaffected arcuate fibers between the lesion and the cortex. Pal-Weigert stain.

where the regions of demyelinization, both partial and complete, extended quite up to the junction of the white matter with the cortical gray, and in such places there was a distinct paucity of myelinated fibers in the deeper layers of the cortex.

Both Marchi and scharlach (Herxheimer) stains of the areas of softening revealed enormous amounts of lipoid degeneration products of myelin, some apparently free, but mostly collected within scavenger cells. In the central portions of these regions the fat-bearing cells were globoid and had the typical appearance of gitter cells, and, although very numerous, were dispersed in the field (fig. 5). At

the periphery of the lesion there was a bordering zone in which the phagocytic cells were packed closer together. Here the shape of the cells was more irregular; some of them appeared to possess short, blunt processes, so far as the contour could be made out from the fat content, and the included fat bodies were smaller and more uniform in caliber than in the cells of the central portion of the lesion. Moreover, in the portions of the white matter in which the changes were merely those of partial demyelinization without softening, there was a more or less rich sprinkling of black-stained bodies lying free along the longitudinal course of the fibers in the Marchi preparations. Corresponding pictures were not seen with scharlach. In all

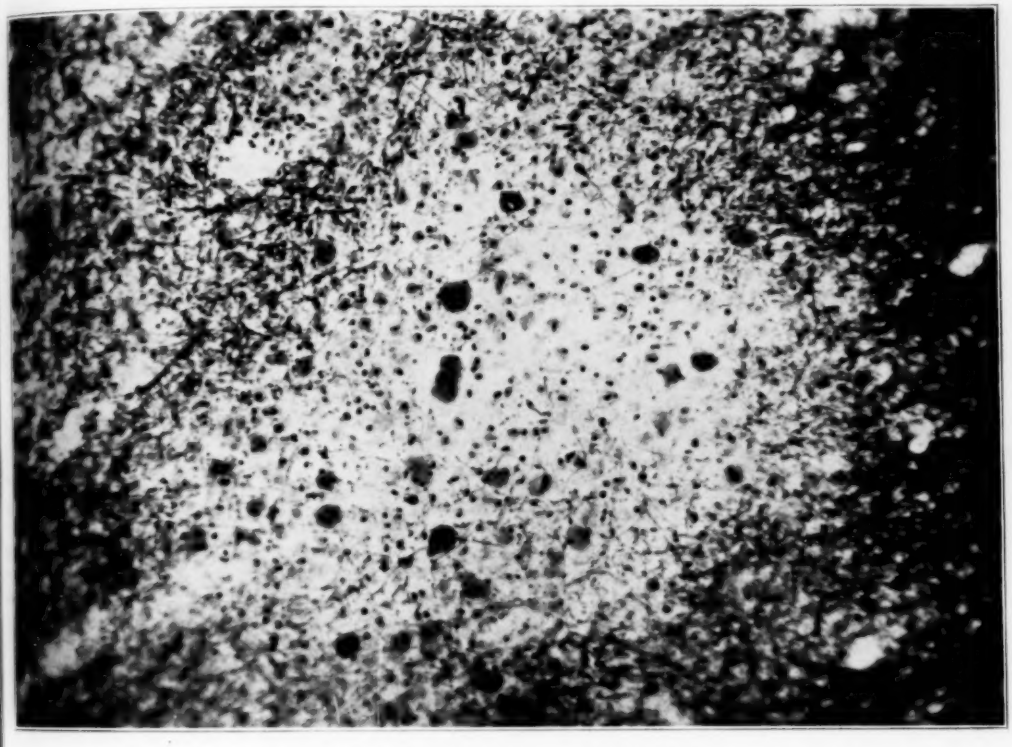

Fig. 4.—Section from the right superior frontal convolution with a minute area of complete softening, 1 mm. in diameter. Pal-Weigert stain.

parts of the involved white matter the perivascular spaces of the majority of the vessels were packed with fat-laden cells; few vessels were free from them.

Where the retrogressive changes in the white matter were confined simply to demyelinization, Bielschowsky preparations revealed, at most, only a somewhat fainter impregnation of the axis cylinders than in the normal portions (fig. 6). Where softening had occurred, the damage to axis cylinders was very great. At the edges of the necrotic areas they exhibited the usual pictures of advanced degeneration; some of them were extremely argentophile; some stained very faintly; they presented numerous localized swellings along their courses, and their edges were indistinct and uneven; many were contorted and some fragmented.

Such changes increased from the periphery to the center of the softened region. Centrally the axis cylinders were very sparse, and those present were thin, pale and badly broken up.

Impregnation with Cajal's gold sublimate and with silver diaminocarbonate revealed everywhere a progressive increase in the number of astrocytes as the border of an area of softening was approached, as well as an increase in the size of their cell bodies, so that they appeared from two to three times as large as the astrocytes in the normal white matter. The astrocytes bordering on and within the lesions possessed very large protoplasmic bodies, which were waxy and homogeneous. Their nuclei, relatively poor in chromatin, occupied an eccentric

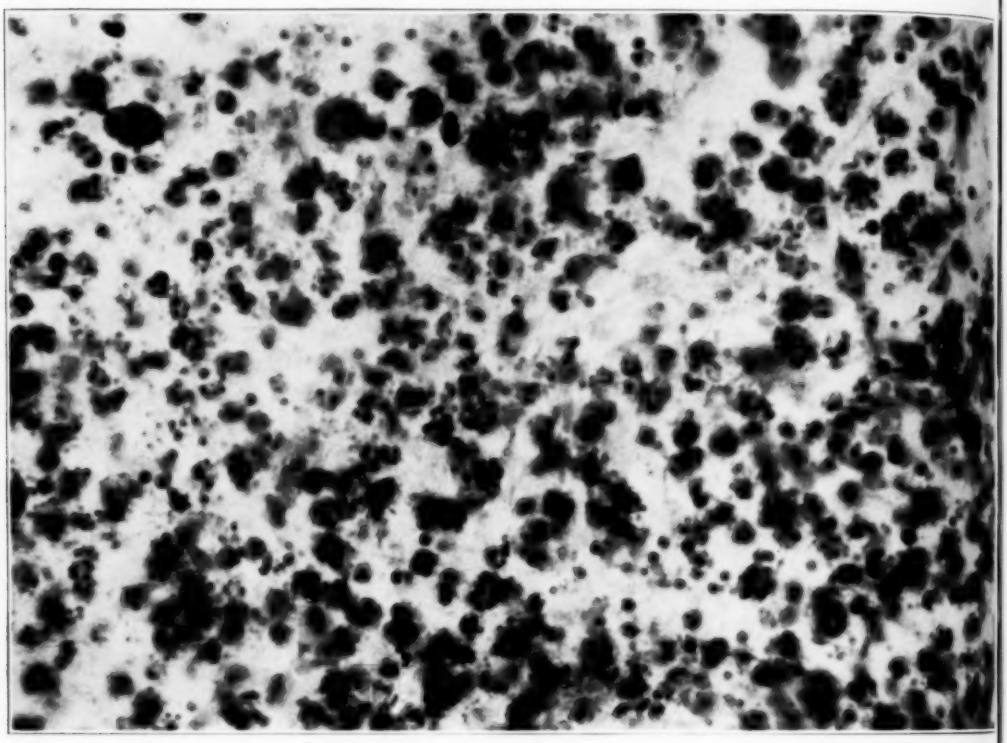

Fig. 5.—Fat-granule cells from a region of softening in the white matter of the right frontal lobe. Marchi stain.

position. A number of the cells possessed two nuclei, and most of them had numerous and sturdy processes. They all belonged to the class of gemästete glia (fig. 7). In Weigert preparations they were seen to be strongly fibroblastic.

Attempts to impregnate the microglia with silver did not yield satisfactory results on this material, but in all the silver methods, as well as in the preparations stained with hematoxylin and with aniline dyes, there was a distinct increase of microglia nuclei in the vicinity of the lesions and these nuclei corresponded in their essential features with those seen in most of the gitter cells, indicating a microglia origin for the latter. A few rod cells were seen toward the lesions, but the tendency toward the development of such forms was not striking.

In preparations stained for neuroglia fibers by the methods of Weigert, Holzer, Mallory and Benda and with Victoria blue, an energetic progressive fibroblastic activity of the glia was revealed in the vicinity of and within the foci of softening. In a rather narrow zonal region bordering the lesion, there was a marked increase of neuroglia fibrils toward the lesion, so that a dense feltwork of such fibers was produced. When the region of actual softening was reached, the arrangement of the fibers sharply took on a quite different appearance; they were more loosely

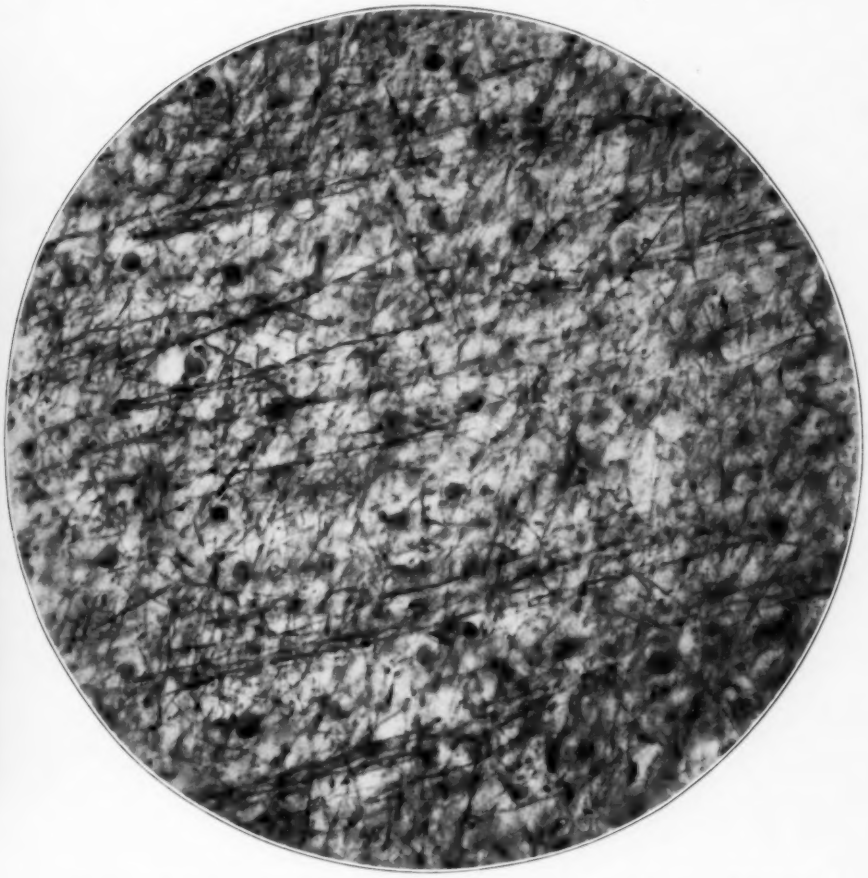

Fig. 6.—Intact axis cylinders in an area of demyelinization in the white matter of the right frontal lobe. Bielschowsky stain.

disposed and formed an areolar meshwork, the more so the further toward the center of the lesion one arrived. The fibers were derived from typical fiber-forming astrocytes, through which ran coarse, wirelike fibrils. But most of the fibers forming the fibrillary network were extremely fine-spun and delicate. Within their tangled meshes lay the fat-granule cells, as if caught in a spider's web (fig. 8).

About numerous blood vessels, in thionine and hematoxylin-eosin preparations, were perivascular infiltrations of varying grades of intensity, from a single layer of

cells up to four or five. The cells surrounded the entire vessel collar-wise, or occupied only a portion of the circumference of the perivascular space. The cells of this exudate consisted of lymphocytes, plasma cells and fat-granule cells in differing proportions. Veins and arteries alike were affected, the veins in a more striking manner. For the most part, the infiltrations observed the glial barrier and were confined to the perivascular spaces, although here and there a plasma cell was seen outside this boundary, but always very near an infiltrated vessel (fig. 9). Such infiltrations comprised the most important vascular alterations. Some of the arteries had thickened walls in the adventitial portion, but there was no endothelial

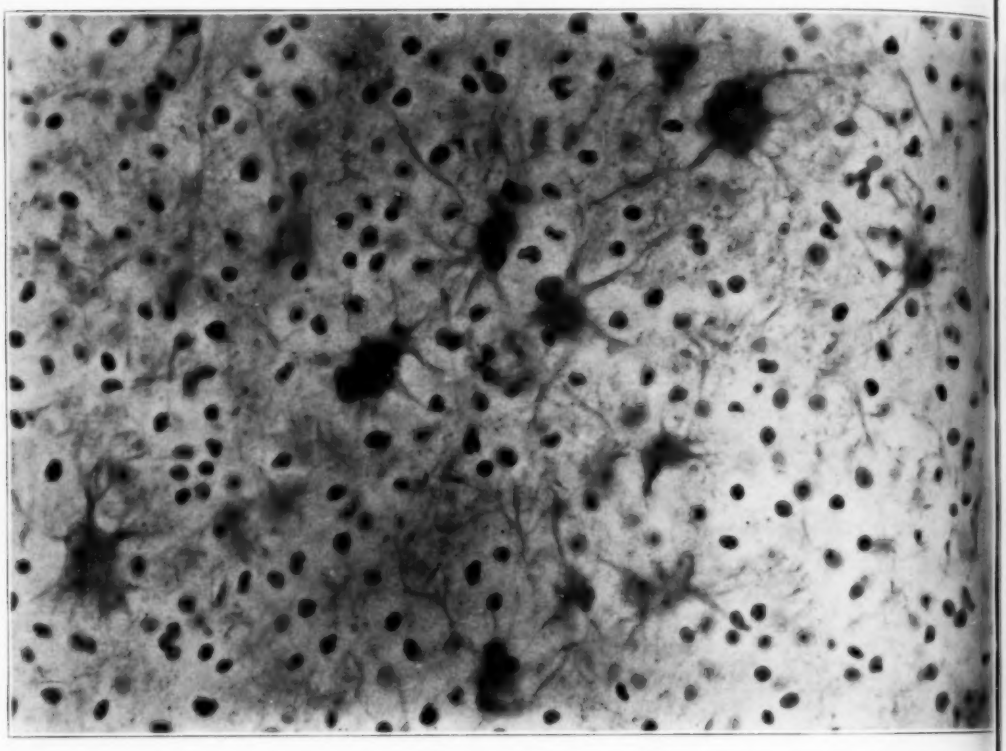

Fig. 7.—Astrocytes at the border of a focus of softening in the right frontal lobe. Silver diaminocarbonate stain.

proliferation, and no thrombosis of any vessel was observed. Within the softened areas were rather numerous newly formed capillaries.

Preparations of the destroyed regions stained for reticulum by the methods of Achucarro and Perdrau demonstrated clearly the reticulum of the walls of the vessels, but there were no intercapillary connections or other signs of proliferation of reticulum fibers into the lesion, even in the lesions that appeared to be the oldest, judged from the density of the glia scar.

Organisms. No organisms were found in numerous sections stained with methylene blue (methylthionine chloride, U. S. P.) and by Gram's method.

Although some differences existed in the relative proportion of glia fiber proliferation and scavenger cells in the lesions from different parts of the white

matter, still, on the whole, their general appearance was so uniform that they must be considered of approximately the same age.

No special attempt was made to establish a relationship between the affected regions and the distribution of blood vessels. Small precapillary vessels were often observed in the centers of the smaller foci of myelin damage. The larger areas of softening apparently bore no relation to the anatomic patterns of blood supply. Many of them appeared to develop from the coalescence of smaller lesions.

Cerebral cortex. The cellular architecture of the cortex was everywhere undisturbed, and no significant changes were seen in the microscopic appearance of ganglion cells or neuroglia. Except in the portions of the deeper layers of the

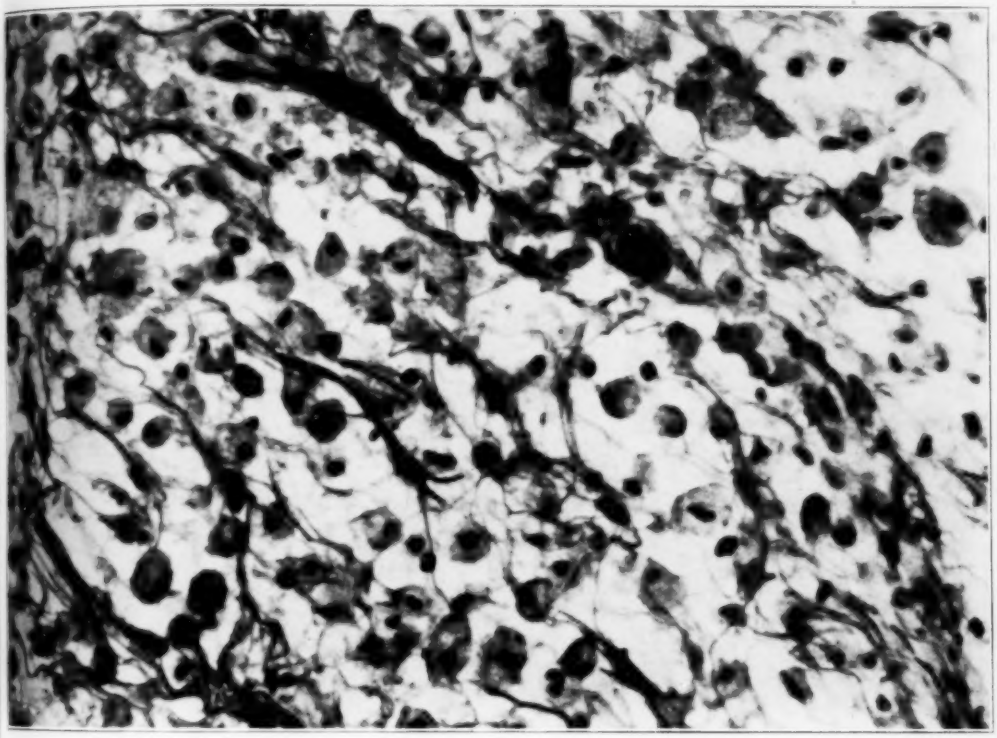

Fig. 8.—Area of softening in the right frontal lobe, showing a meshwork of neuroglia fibrils and included gitter cells. Holzer stain.

cortex where the demyelinization of the subjacent white matter extended up to the corticomedullary junction, there was no involvement of cortical myelinated fibers, and none of axis cylinders.

In the fat stains it appeared that the perivascular spaces of many of the cortical vessels were utilized as pathways for the transport of lipoids, since they contained appreciable numbers of fat-bearing cells. But only a few of the vessels in the fifth and sixth cortical layers presented small perivascular infiltrations of lymphocytes and plasma cells.

Central gray nuclei. Within the lenticular and caudate nuclei, thalamus and corpus subthalamicus there were no regions of softening or of demyelinization, and

no noteworthy changes of ganglion cells or neuroglia. The essential pathologic changes in these parts were those in and about the vessels. These were found in all parts of the brain in question and consisted of venous dilatation and engorgement, perivascular exudation and hemorrhage. The perivascular infiltrations were on the whole, rather mild, and were of the same character as those described in the white matter except that they were made up chiefly of lymphocytes and plasma cells with very few fat-granule cells. The hemorrhages were seen only in the globus pallidus and corpus subthalamicus, mostly in the latter. Most of them occurred around moderate sized veins. The largest did not exceed a high power field in diameter.

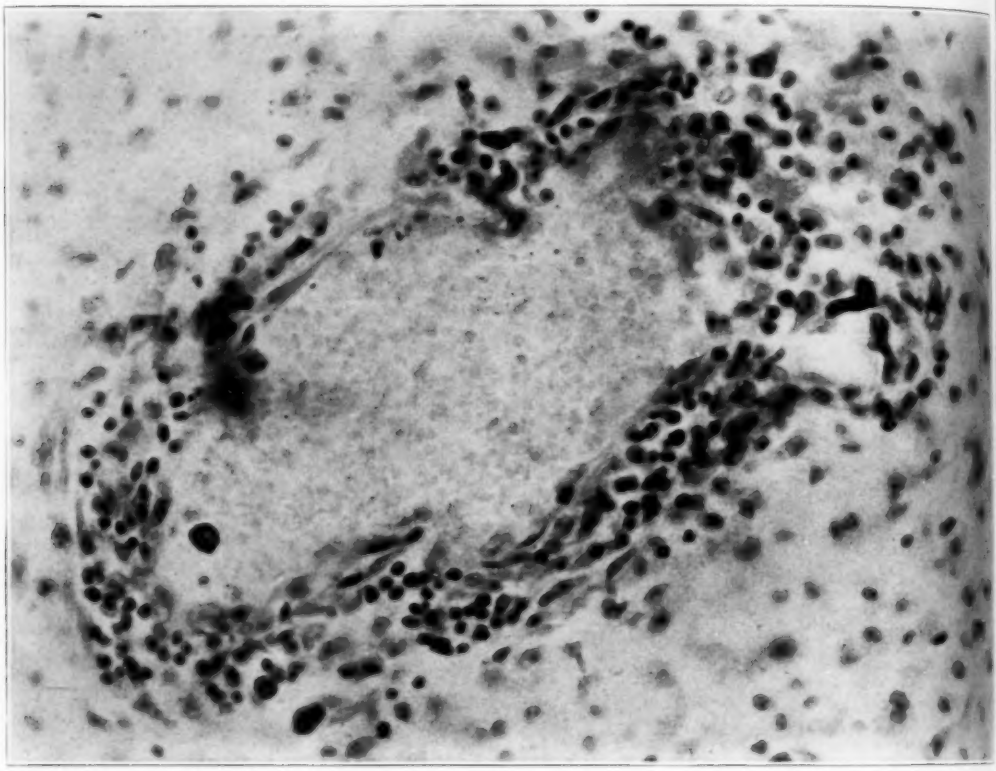

Fig. 9.—Perivascular infiltration in the white matter of the right frontal lobe. Thionine stain.

Usually the vessels about which hemorrhage had occurred exhibited no mesodermal exudate. The ganglion cells in the immediate neighborhood of such hemorrhages had suffered rather advanced retrogressive changes, but there was no glial reaction.

A number of the vessels in these sections contained within their walls and in their lumina a large amount of dark brown pigment, some of it sprinkled in fine dustlike granules, but much of it collected into larger rounded compact bodies as if taken up in phagocytic cells. The ganglion cells adjacent to such vessels in many instances were heavily laden with the same pigment granules. A few of the granules were seen also in proximity to the glia nuclei, but by far the greatest inclusions were within the ganglion cells themselves (fig. 10). The degree of

pigmentation in these cells decreased with their distance from the vessel. All of the hemorrhagic regions presented such pigmentation, and it was in such places that it tended to be most marked, but the same changes were seen about many vessels where no hemorrhage could be found. Similar granules were contained in appreciable numbers in many of the ependymal cells lining the third ventricle. Sections stained for iron by the Prussian blue method did not yield corresponding pictures.

Cerebellum. No areas of softening were found. The Purkinje and other ganglion cells of the cerebellar cortex of both hemispheres and those of the dentate

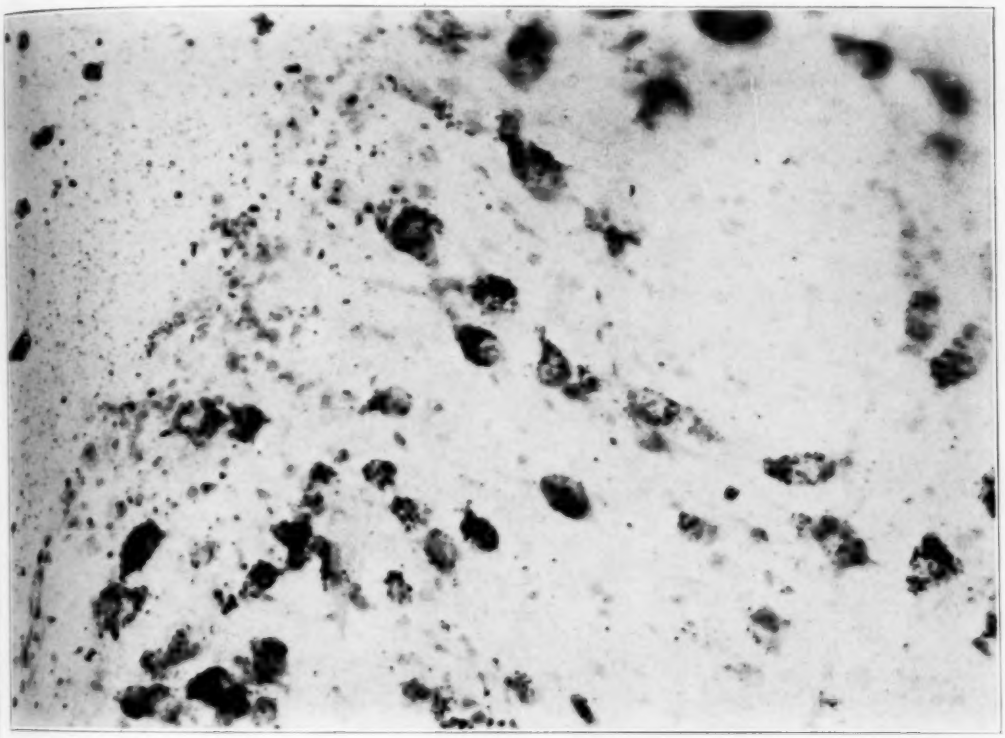

Fig. 10.—Wall of a vessel from the left side of the pons, showing pigment granules within the wall and lumen and in the surrounding ganglion cells. Thionine stain.

nuclei were normal. Occasional perivascular infiltrations occurred in the medullary substance, and around a few of the vessels was the pigmentation already described.

Brain stem. Examination of serial sections of the brain stem from the upper pons through the medulla revealed no foci of softening, and no demyelinization, either in patches or as secondary descending degeneration. The ganglion cells of the cranial nerve nuclei were intact. Here again the essential changes were limited to the vessels. There was marked vascular dilatation, and infiltrations of lymphocytes and plasma cells were fairly numerous and in some places intense. Such exudation did not appear to be more marked at one level than at another. Hemorrhages were limited to the extravasation of a few red blood corpuscles about some

of the infiltrated vessels of the medulla. Accumulations of pigment like those described in relation to vessels in the basal ganglia were seen commonly, especially in the pons. Pigment was also present in the ependymal cells of the fourth ventricle, in more than customary amount. Marchi preparations from the first cervical segment of the cord revealed no fields of degeneration.

Optic chiasm. There were no areas of demyelinization in Weigert-Pal staining of serial sections of the chiasm.

Meninges. The leptomeninges of all parts of the brain examined were densely infiltrated in places by lymphocytes and plasma cells. In addition there were

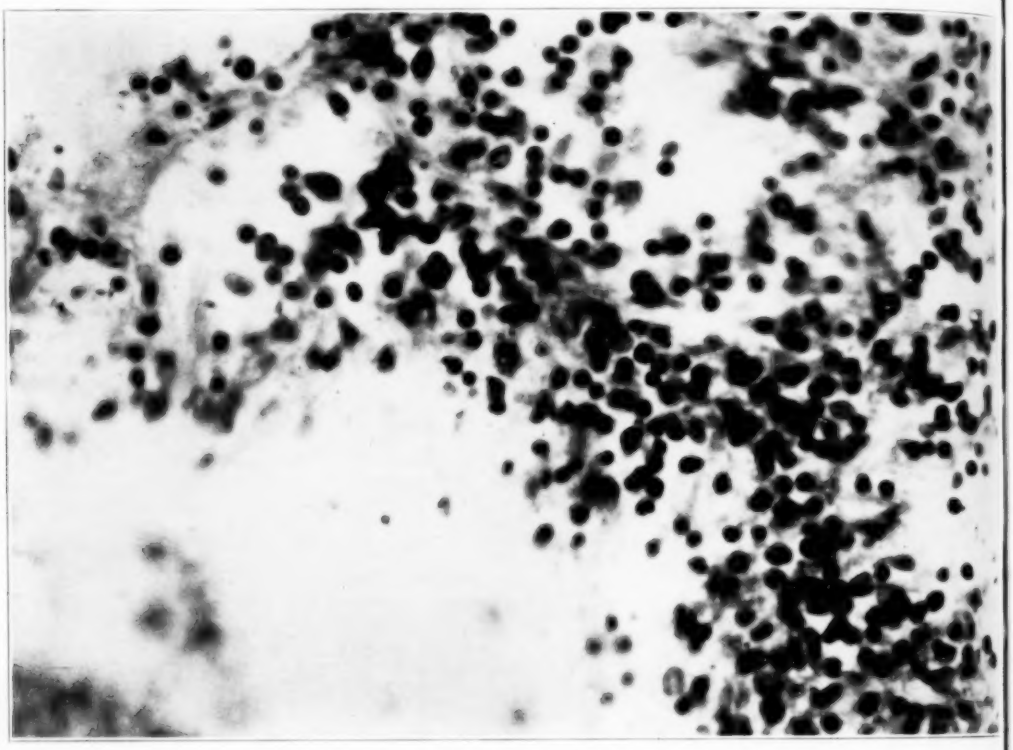

Fig. 11.—Infiltration into the leptomeninges covering the right postcentral convolution. Thionine stain.

numerous areas of hemorrhage (fig. 11). In places the dark pigment granules mentioned heretofore were abundant, appearing both in a scattered apparently free form in the pia-arachnoid, but found chiefly in the vessel walls and lumina, free or contained in large phagocytic cells. The choroid plexus was normal.

COMMENT

The anatomic diagnosis of encephalitis disseminata is made in this case because of the widespread inflammatory changes throughout the brain and meninges leading to the formation of multiple foci of enceph-

alomalacia which are discontinuous and sharply delimited, both grossly and microscopically. That the essential morbid process is a primary inflammation, there can be no doubt, mixed as it is in places with the pictures of secondary inflammation, so-called, dependent on the taking up of the products of nerve fiber degeneration and the transport of this material. The three cardinal changes of inflammation formulated by Lubarsch, viz., alteration (retrogression), exudation and proliferation, are all outstanding in this brain. Nor can the infiltrations of lymphocytes and plasma cells, occurring as they do exclusively in young lesions and in sites removed from places of myelin damage or of sclerosis, be interpreted simply as "small, round lymphocyte-like cells, common to all chronic processes," as did Dawson [1] for the mesodermal infiltrations he described in his analysis of multiple sclerosis.

We are further of the opinion that the inflammatory changes in this brain are the consequence of the presence of living micro-organisms within it. We are aware of the hazards of making etiologic deductions from anatomic appearances, a danger sufficiently emphasized by Spielmeyer,[2] who spoke explicitly against the all too easy use of the presence of plasma cells as a criterion of infectious causation. Our conclusion in this case is drawn from the presence of a combination of morbid changes, each of which is frequently found in diseases of the central nervous system of known infectious etiology. These changes are: widespread vascular dilatation and engorgement, cufflike perivascular infiltrations of lymphocytes and plasma cells in regions of the brain showing no other essential alterations, perivascular hemorrhages in the brain and infiltrations and hemorrhages into the meninges.

In regard to the unusual pigment inclusions, described particularly in the ganglion cells of the brain stem and central ganglia and in the cells of the ependymal lining, we have no comment to make, except to point out that the accumulations tend to be greatest in the vicinity of visible hemorrhages, and therefore we consider it most likely that the pigment is hematogenous. We have found no similar pictures described in the literature.

The views of various writers concerning the nature and pathogenesis of multiple sclerosis, in particular its relationship to disseminated encephalomyelitis, remain most divergent and unsettled. They run the gamut from those who, like Hassin,[3] regard it as a purely degenerative disease to those who consider it impossible to distinguish

1. Dawson, J. W.: The Histology of Disseminated Sclerosis, Tr. Roy. Soc. Edinburgh **50**:517, 1916.

2. Spielmeyer, W.: Die Diagnose Entzündung bei Erkrankung des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **25**:543, 1914.

3. Hassin, G. B.: Report of Association for Research in Nervous and Mental Disease, 1921, vol. 2, p. 144.

between what has been called multiple sclerosis and what is known to be disseminated encephalomyelitis, a position that for some observers is tantamount to a denial of the existence of multiple sclerosis as a special disease. Thus, Pette [4] concluded that multiple sclerosis is a disseminated encephalomyelitis caused by a virus closely related to, if not identical with, that of vaccinal encephalitis. With more moderation Spiller [5] stated that, "The distinctions between encephalomyelitis disseminata and multiple sclerosis at present cannot be drawn." Symonds,[6] speaking of the pathologic findings from a case of indubitable multiple sclerosis clinically, said: "The type of cellular reaction is that met with in all diseases of the central nervous system which are known to be due to micro-organisms, and it may be deduced that the cause of disseminated sclerosis is in all probability of a similar nature." Still other writers have reported a number of cases of disseminated encephalitis in which the anatomic characteristics of multiple sclerosis were apparent, contenting themselves simply with pointing out the close relationship in the disease pictures of the two conditions. Among these is the recent case of Marcus,[7] who nevertheless was unwilling to abandon the concept of multiple sclerosis in a chronic, insidiously developing form as formulated by Charcot, and who considered also that acute multiple sclerosis is an established entity. Others include the second case in a recent contribution on disseminated encephalomyelitis by Bassoe and Grinker,[8] and a case reported by Jakob [9] because of its bearing on this question. Even Dawson,[1] the spirit of whose monograph is to establish multiple sclerosis as an entity histologically, when speaking of the differentiation between disseminated encephalomyelitis and multiple sclerosis, particularly with reference to acute multiple sclerosis, expressed himself as follows: "—the pathological and clinical concepts of the two diseases pass into each other: the differential diagnosis must rest, clinically, on the further course of the disease and anatomically on data which differ only in degree."

4. Pette, H.: Klinische und anatomische Studien: Ueber der Pathogenese der multiplen Sklerose, Deutsche Ztschr. f. Nervenh. **105**:76, 1928.

5. Spiller, W. G.: Encephalomyelitis Disseminata, Arch. Neurol. & Psychiat. **22**:647 (Oct.) 1929.

6. Symonds, C. P.: The Pathologic Anatomy of Disseminated Sclerosis, Brain **47**:36, 1924.

7. Marcus, H.: Encephalitis lethargica-Sclérose en plaque, Acta psychiat. et neurol. **5**:129, 1930.

8. Bassoe, Peter; and Grinker, R. R.: Disseminated Encephalomyelitis: Its Relation to Other Infections of the Nervous System, Arch. Neurol. & Psychiat. **25**:723 (April) 1931.

9. Jakob, A.: Zur Pathologie der diffüsen infiltrativen Encephalomyelitis in ihren Beziehungen zur diffüsen und multiplen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:290, 1915.

We think that in this case there are sufficient similarities to some of the essential features of multiple sclerosis to justify the assumption of a close alliance between them. Complete remission with recrudescence of symptoms, a point stressed particularly by almost all writers who attempt to draw a hard line between multiple sclerosis and disseminated encephalomyelitis, is no less striking in this patient. Indeed, this feature seems to us to be an extremely artificial one on which to base a distinction between a degenerative or toxidegenerative process and an infectious one. Epidemic encephalitis and syphilis, to mention only two undoubted infections of the nervous system, both attest to the long latent periods and extreme fluctuations possible in infectious disorders. We are not, therefore, surprised to find a case of nonepidemic encephalitis presenting this type of clinical course. On the anatomic side, the resemblances consist in the insular arrangement of the majority of the lesions, in the presence in many places of discrete foci of partial demyelinization with relatively intact axis cylinders and little or no cellular infiltration, identical in appearance with such lesions in classic multiple sclerosis, and in a neuroglial sclerosis. It is true that the neuroglia fiber proliferation of this sclerosis does not have the compact, orderly appearance seen in the usual sclerotic patch of multiple sclerosis. But Dawson [1] pointed out in his material, accepted by him as that of multiple sclerosis, areas of sclerosis in which the arrangement of the glia fibers was loose and areolar ("areolierte Herde" of the Germans), and in these, he observed, the myelin destruction was intense and the axis cylinders were not merely damaged, but destroyed. Bearing these similarities in mind, we think it entirely possible to regard this case as one of acute multiple sclerosis without unduly straining the term: an extremely acute case, to be sure, and one, therefore, of relatively short duration, with an unusually intense exudation and unusually severe damage to nerve fibers to the point of extensive axis cylinder destruction and softening, and, finally, without the typical variety in the lesions due to differences in their ages.

In searching the literature for cases similar to this one, we found three very much like it. It is significant that each of them was reported under a different name. One was the case of encephalomyelitis of Jakob, already referred to, one a case of neuromyelitis optica reported by Marinesco and his co-workers [10] and the other a case of Schilder's disease reported by Schaltenbrand.[11] The gross appearances in the last

10. Marinesco, G.; Draganescu, S.; Sager, O., and Grigoresco, D.: Sur une forme particulière anatomo-clinique d'ophtalmo-neuromyélite, Rev. neurol. **2**:193, 1930.

11. Schaltenbrand, Georg: Encephalitis Periaxialis Diffusa (Schilder), Arch. Neurol. & Psychiat. **18**:944 (Dec.) 1927.

case, judging from both the description and the photographs, were practically identical with ours. And it can be said that the macroscopic appearance of Schilder's disease is as characteristic as anything of the anatomic syndrome of that disease. Massive, diffuse destruction of white matter localized to the cerebral hemispheres, but sparing, relatively, the arcuate fibers, is described in all the cases reported, without exception, be that destruction in the form of a dense glial sclerosis with little or no sign of activity as in the case of Marie and Foix [12] or in the form of large spongy areas of softening as in that of Schaltenbrand.[11] Although the lesions in our case are on the whole focal, yet in many places the myelin destruction is also diffuse, and, because of the great number of large contiguous regions of encephalomalacia, massive. We do not find it difficult to imagine that if the disease had lasted longer, the element of diffuseness would have become outstanding through the fusion of more and more areas of softening. The characteristic selective localization to the subcortical white matter with relatively little implication of the U fibers is clear.

When one comes to consider the microscopic findings in Schilder's disease as they are given in the reported cases, one is struck at once with the great variability in the essential changes of nerve fiber destruction, cellular infiltration and glial reaction. The periaxial character of the nerve fiber degeneration, considered so distinctive by Schilder that he incorporated it into the name "encephalitis periaxialis diffusa," has been found to be most inconstant. Many of the recorded cases exhibit marked destruction of the axis cylinders as well as of the myelin. To be sure, there is a growing tendency among neuropathologists to deny that differential involvement of myelin is a pathologic mark of any decisiveness, an attitude that gains support from this case, in which in the same brain the relation between the degree of myelin and of axis cylinder dissolution is so variable. Likewise, the alterations of the glia differ considerably in the individual cases, particularly as to the presence of certain regressive forms such as the large globoid cells described by Collier and Greenfield,[13] but, on the whole, the usual changes consist in the formation of fat-granule cells from the mesoglia with clearing of the demyelinated fields, the development of "gemästete" glia and other hyperplastic forms, and of a glial scar—in a word, the identical neuroglial reactions observed in this brain. Perhaps the greatest differences between the recorded cases of Schilder's disease relate to the presence and character of infiltrations around the vessels. In

12. Marie and Foix: Sclérose intracérébrale centrolobaire et symmétrique, Rev. neurol. **22**:1, 1914.

13. Collier, J., and Greenfield, J. G.: Encephalitis Periaxialis Diffusa, Brain **47**:489, 1924.

some of the cases such changes are minimal, or the infiltrations are made up of scavenger cells only, while in others exudative pictures with lymphocytes and plasma cells are abundant. This has led Bouman [14] to separate the cases into two general classes, the degenerative and the inflammatory.

We have, then, in this case a brain in which the gross anatomic manifestations are compatible with a diagnosis of Schilder's disease, and in which all of the histologic findings, with one exception, are those that have been recorded in accredited examples of this disease. The exception in question is the presence of diffuse perivascular infiltrations in parts of the brain which do not contain areas of nerve fiber degeneration. Of the cases on record in the literature, that of von Stauffenberg [15] alone hinted at a similar finding, and he merely mentioned that he found perivascular infiltrations in tissue that was apparently normal. He stated that no changes of any sort were found in the pons, but did not refer to other parts of the brain specifically. This point is crucial and leads us to look on this case as one that represents a morbid picture intermediate between that of infectious disseminated encephalitis and Schilder's disease.

A case that straddles nosological fences in the way this one does, of course, raises the question of the essential identity of the several conditions it so strongly resembles. We may say here that we do not think that we have proved any such identity or that it is susceptible of proof on the grounds of pathologic anatomy. But we do believe that the material presented points to an interrelationship so intimate that actual identity is quite possible. It seems to us that much of the confusion in the current views on this problem arises from confounding the whole with its parts. In this connection, it is suggestive that in the working schema of infections of the central nervous system put forward by Bassoe and Grinker,[8] as lucid a classification as any yet proposed, disseminated encephalitis is placed as an example under three of the six subdivisions of inflammation of the central nervous system.

It cannot be denied that when most of the cases of multiple sclerosis, of disseminated encephalomyelitis and of Schilder's disease are examined, it is apparent that there are great differences between them. In general, they are entities. This is also evidently true for that group of encephalitides occurring in association with vaccinia (Perdrau [16]) and certain infectious diseases, as variola, influenza and measles (Green-

14. Bouman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:453, 1924.

15. von Stauffenberg: Ein Fall von Encephalitis periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **39**:56, 1918.

16. Perdrau, J. R.: The Histology of Post Vaccinal Encephalitis, J. Path. & Bact. **31**:17, 1928.

field [17]). But the frequent nuances that exist between the various syndromes, exemplified by the present case, suggest that they are perhaps entities only in the sense that tabes is an entity within neurosyphilis. What determines the likenesses and differences in the anatomic features of these cases must be left an open question. Conceivably this might depend equally on the action of quite different causative viruses, on the tempo of the pathologic process, on the potency and amount of any given virus or on the susceptibility of the host. This point of view is, of course, in no sense new or original. On the contrary, it is one that has been adopted by numerous contemporary investigators.

CONCLUSIONS

1. The probabilities are that disseminated encephalomyelitis, multiple sclerosis and Schilder's disease all belong to the class of nonsuppurative infectious encephalomyelitis.

2. The decision as to the mutual relationships of this group of disorders and their ultimate classification into diseases in the true sense of the word must wait on the isolation and study of the etiologic agent or agents.

ABSTRACT OF DISCUSSION

Dr. Peter Bassoe: At the time Dr. Gill asked me to see the patient, there was quite a discussion as to whether the case was a vascular lesion or encephalitis. The patient was too young for arteriosclerosis. At the time the pathologist was inclined in favor of multiple emboli, and if it had not been for the microscopic examination the case might have passed for one of embolism or thrombosis.

Dr. Victor E. Gonda: Was the cortex examined, and were pathologic changes found?

Dr. Richard Richter: In a few vessels in the cortical layer there were insignificant perivascular infiltrations of lymphocytes and plasma cells; the ganglion cells were not changed.

17. Greenfield, J. G.: Acute Disseminated Encephalomyelitis as a Sequel to Influenza, J. Path. & Bact. **33**:453, 1930; The Pathology of Measles Encephalitis, Brain **52**:171, 1929.

POSTHEMIPLEGIC ATHETOSIS

REPORT OF A CASE: RÔLE OF CORTICOSPINAL PATHWAYS IN PRODUCTION OF CHOREIFORM AND ATHETOID MOVEMENTS

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The literature pertaining to the causes of choreiform and athetoid movements contains almost as many hypotheses as there are authors writing on the subject. The writings of Kahler and Pick,[1] Monakow, Horsley,[2] Bonhoeffer,[3] C. and O. Vogt,[4] A. Jakob, Foix and Hillemand,[5] Wilson, Foerster, Minkowski, Spiller,[6] Cobb,[7] Niessl von Mayendorf [8] and others illustrate the disharmony of the conceptions concerning the anatomic structures participating in the development of these involuntary movements. The nature of this paper will not permit a detailed review of the various opinions offered. Briefly, it may be said that there are those who relegate these movements to the corticospinal pathways (Wilson, Monakow, Spiller, Niessl von Mayendorf), and others (C. and O. Vogt, A. Jakob, Foerster, Minkowski, Bonhoeffer [3]) who attribute them to the perverted activity of systems of basal ganglia.

The following case is of interest because it manifests certain pathologic findings that bear a significant relationship to this unsettled question—whether choreiform and athetoid movements are caused by lesions

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From the Boston Psychopathic Hospital.

The material presented in this report is from the anatomic laboratory of the late Professor A. Jakob, Staatkrankensanstalt, Friedrichsberg, Hamburg, Germany.

1. Kahler and Pick: Lokalisation der posthemiplegischen Bewegungserscheinungen, Vrtljsschr. f. prakt. Heilk. **1**:1, 1878; quoted by Monakow: Gehirnpathologie, Vienna, A. Hölder, 1905, p. 554.

2. Horsley, V.: Brit. M. J. **2**:125, 1909.

3. Bonhoeffer, K.: Ein Beitrag zur Lokalisation der choreatischen Bewegung, Monatschr. f. Psychiat. u. Neurol. **1**:1, 1897.

4. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systeme, J. f. Psychol. u. Neurol. (Ergnzgshft., iii) **25**:627, 1919-1920.

5. Foix and Hillemand: Les syndromes de la région thalamique, Presse méd. **33**:113, 1925.

6. Spiller, W. G.: Acquired Double Athetosis, Arch. Neurol. & Psychiat. **4**:370 (Oct.) 1920.

7. Cobb, Stanley: Electromyographic Study of Chorea, Bull. Johns Hopkins Hosp. **30**:35, 1919.

8. Niessl von Mayendorf: Chorea und Linsenkern, Monatschr. f. Psychiat. u. Neurol. **74**:273, 1930; Ueber die Bedeutung der Linsenkernschleife für das choreatische Phänomen, ibid. **68**:802, 1928.

that pervert the normal activity of the corticospinal pathways or occur as a result of lesions of the basal ganglia which do not necessarily call into play the corticospinal tracts.

REPORT OF CASE

History.—H. B., a gardener, aged 65, was admitted to the St. Georg Hospital in Hamburg on Oct. 20, 1925, following a severe convulsion and subsequent mental confusion and restlessness. The family history was essentially without significance. The patient was married at 31; three children died soon after birth; three are living. One suffers from asthma and a cardiac disorder. Between the ages of 10 and 12, the patient began to have generalized convulsions which were described as follows: There would be a drawing of the mouth, sometimes for twenty-four hours before the attack started; as the attack began, the patient would issue a loud cry and fall unconscious; violent clonic convulsive movements followed for approximately five minutes. During the convulsion the patient bit his tongue and sometimes passed urine involuntarily. After the convulsion he slept, and later he complained of headache. He was restless and on several occasions ran about the house in an excited manner. At the age of 17, following a convulsion, the patient could not speak and lost the use of the left arm. Two months later, speech and the function of the arm returned. Convulsions continued to recur.

At the age of 34, while under the influence of whisky, the patient was struck by a trolley car. Following the accident he lost the use of the right arm and leg. Later, involuntary movements (athetoid) occurred in the right arm and hand, and he began to have difficulty in speaking. The convulsive seizures continued to occur, though somewhat altered in appearance after the paralysis of the right side. After many years it was noticed that his memory was gradually failing. The paralysis of the right side persisted, and the difficulty in talking became more noticeable. There were times when he was free from involuntary movements in the right arm, but they recurred at irregular intervals.

The patient was not under a physician's care again until Oct. 17, 1925 (at the age of 65), when he had a violent convulsion. Following the convulsion there appeared involuntary (athetoid) movements of both arms, the right leg and the right foot. The movements were most marked in the right hand. The patient became restless and mentally confused. He was admitted to the St. Georg Hospital on Oct. 20, 1925, under the care of Professor Trommer.

General Examination.—The heart rate was irregular, and the sounds were of poor quality. Bronchopneumonia was present in the lower lobes of both lungs. The abdomen was essentially normal.

Neurologic Examination.—The intellectual functions were impaired: mental confusion rendered many tests inaccurate and unreliable.

Cranial Nerves: There was a history of defect in the sense of smell. Sight was impaired in both eyes; tests of the visual fields were not reliable. There was no papilledema. The pupils were constricted and reacted poorly to light. There was no nystagmus. The right side of the face was weak. The tongue protruded in the midline, with marked tremor. There were definite dysarthria and pronounced aphasia.

Reflexes: The biceps, triceps, supinator, patellar and achilles jerks were increased on the right side. The abdominal reflexes were present, but were stronger on the left. A Babinski sign was present on the right. The sphincters functioned normally.

Extremities: Both arms and the right foot manifested characteristic involuntary (athetoid) movements. The index finger of the right hand was partially

flexed at the metacarpophalangeal joint and was held against the thumb. The three lateral fingers of this hand, when at rest, were extended. When the patient was asked to touch the left ear with the right hand the right upper limb abducted slowly, the forearm flexed at the elbow and the extremity moved slowly in a purposeless manner behind the head, without touching the ear. At the same time there were weak involuntary flexions and extensions of the fingers. Movements of these fingers were more pronounced than those of the fingers of the right hand. Tone was increased in both upper limbs. There were involuntary extension of the right great toe and a slow drawing inversion of the foot. Tone was increased in both legs but more in the right leg.

Course.—The patient remained confused mentally; he died four days after admission.

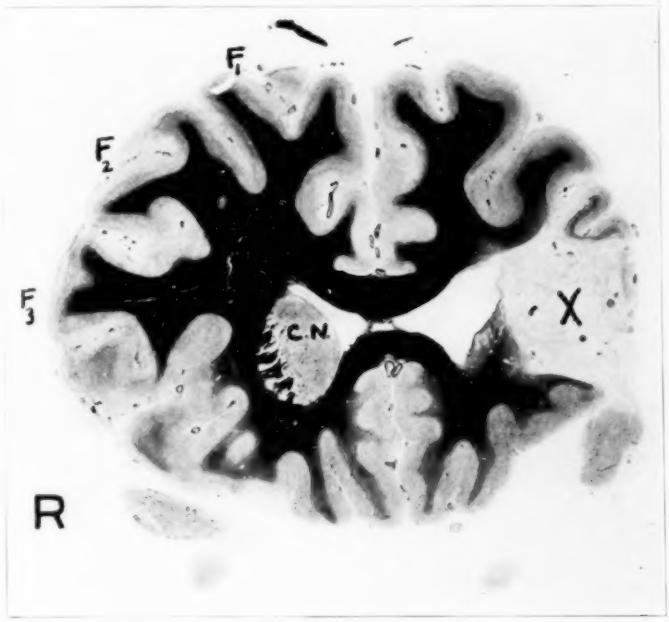

Fig. 1.—Section passing through the anterior end of the caudate nucleus. *X* marks the site of the cystic cavity.

Postmortem Examination (Professor Wohlwill of the St. Georg Hospital).—Macroscopic Findings: The dura was free; the pia was strongly injected, but smooth and glistening. On the left, near the sylvian fissure, there was a large cyst containing clear fluid; it extended the entire length of the sylvian fissure and involved the frontal, parietal and temporal lobes, but was most prominent in the region of the operculum and the anterior central gyrus. The gyri near the cyst were narrow, and here the pia was distinctly thickened. Another cyst, about the size of a small plum, was present in the right parietal lobe. It involved the postcentral gyrus and extended across the rolandic fissure into the anterior central gyrus. The brain substance in the neighborhood of this cyst showed no changes.

The unsectioned brain was sent to Professor Jakob's laboratory in the Staatkrankensanstalt at Friedrichsberg where modified Kulschitzky preparations were made through the entire brain and brain stem. Sections were cut at 60 microns, and

every tenth section was mounted. It is to be regretted that cell stains were not made, but since attention is focused primarily on the corticospinal pathways this omission is not important.

Microscopic Observations: Figure 1 is a photograph of a section passing through the anterior end of the caudate nucleus. There are a distinct widening of the anterior horn of the left lateral ventricle and a destructive lesion of the anterior portion of the left caudate nucleus. The greater portions of the second and third frontal gyri in this area have undergone degeneration, and the most anterior of the fibers radiating into the internal capsule have been interrupted. Succeeding sections confirm the presence of lesions in the localities mentioned.

Figure 2 portrays a section, slightly posterior to that shown in figure 1, passing through the lenticular and caudate nuclei. The cyst here is of greater dimensions, and only a narrow wall separates its cavity from that of the lateral

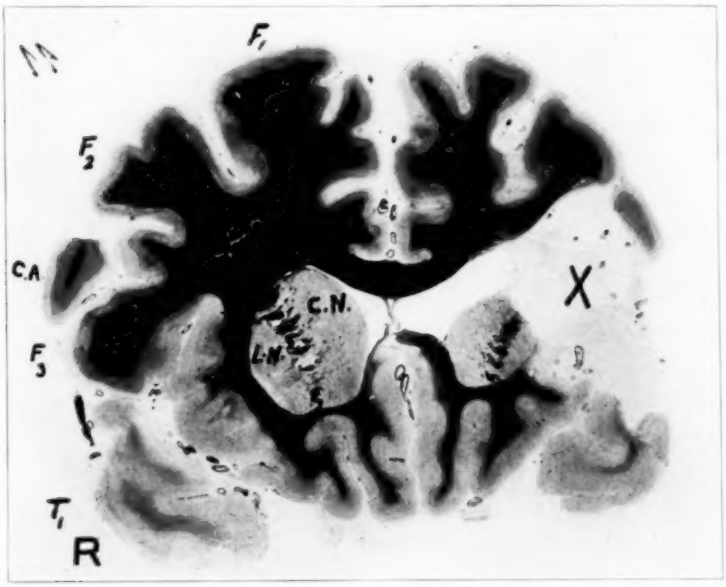

Fig. 2.—Section through the anterior ends of the caudate and lenticular nuclei showing marked destruction of the frontal cortex.

ventricle. There is a definite diminution in the size of the bodies of the left caudate and lenticular nuclei. This becomes evident from a study of successive sections. The fibers passing into the internal capsule from the anterior portions of the second and third frontal gyri have been interrupted. There is also involvement of the operculum and the superior portion of the temporal lobe.

Figure 3 portrays a section through the optic chiasm and anterior commissure. At this site the cyst has destroyed a portion of the anterior central gyrus, the insula and portions of the first and second temporal gyri. The left caudate nucleus, the putamen and the pallidal nuclei show greater destruction. Only a few fibers from the anterior lobe pass uninterrupted through the internal capsule.

Figure 4, which represents a section passing through the mammillary bodies, shows destruction of a considerable portion of the left anterior central gyrus, with destruction of portions of the first and second temporal gyri, but some fibers

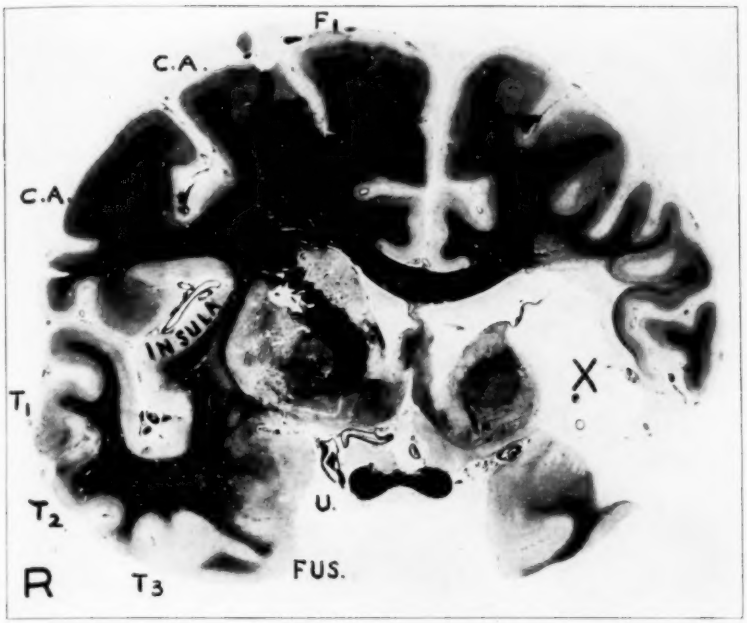

Fig. 3.—Section at the level of the optic chiasm.

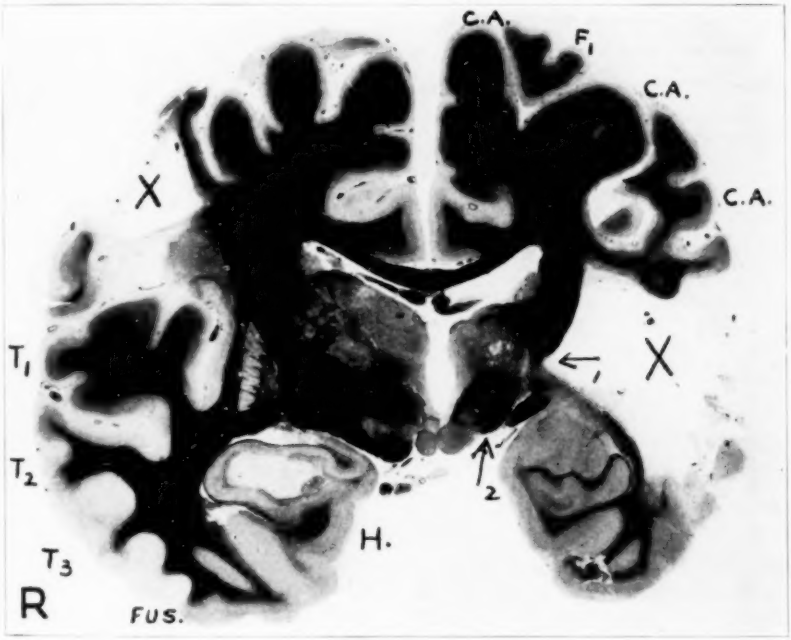

Fig. 4.—Section through the mammillary bodies. *X* marks degenerated areas of the right and the left motor cortex.

radiate into the internal capsule. However as can be seen from the photograph, the insula and the lenticular nucleus have been destroyed by the cyst, leaving the fibers of the internal capsule to form the medial wall of the cavity. Fibrous tissue has severed almost all fibers passing through the internal capsule (indicated by arrows in figure 4). The thalamus on the left is greatly reduced in size, and

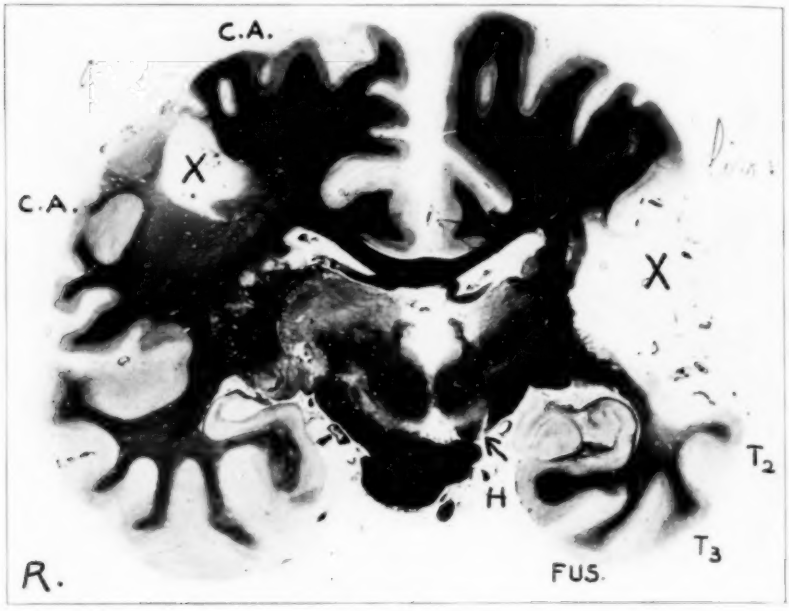

Fig. 5.—Section from a cut passing through the anterior portion of the pons.

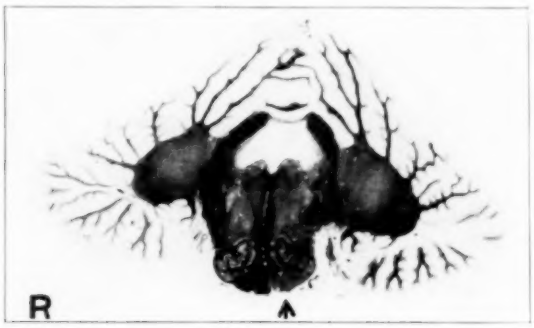

Fig. 6.—Section through the brain stem and cerebellum. The pyramidal tracts show a great difference in size.

its nuclei show definite areas of degeneration. The corpus luysii has also undergone changes. Arrow 2 (fig. 4) indicates the site of the degenerated pyramidal fibers in the middle two fifths of the left peduncle. On the right, another cyst has destroyed a portion of the right anterior central gyrus.

Figure 5 exhibits further involvement of the left anterior central gyrus, and an extension of the lesions of the operculum and of the second and third temporal gyri.

The left thalamus and substantia nigra show further degeneration. At the site where the pyramidal tract passes through the peduncle there is a definite area of degeneration on the left (indicated by the arrow in figure 5). The cyst on the right has destroyed a portion of the right anterior central gyrus.

In figure 6, the extent of the degeneration of the pyramidal tract can be seen.

COMMENT

Since Hammond's original contribution to the problem of posthemiplegic athetosis appeared, the literature has abounded with descriptions of lesions that were thought to be responsible for the production of choreo-athetoid movements. A variety of locations, ranging between the medulla oblongata and the cerebral cortex, have been incriminated. Some authors have attempted to link the lesions directly with the involuntary motor phenomena. For example, as early as 1878, Kahler and Pick emphasized the frequency of lesions in the parts of the thalamic and lenticular nuclei bordering on the internal capsule. These writers, with Kolisch,[9] Nothnagel[10] and others, suggested that lesions in the proximity of the corticospinal fibers as they pass down through the internal capsule act as irritants to these fibers and cause them to discharge impulses that give rise to choreo-athetoid movements. Charcot spoke of a special hemichorea bundle. Monakow also was of the opinion that the corticospinal tracts participate in the production of these movements but was not inclined to think that such involuntary phenomena originate as a result of direct irritation of these pathways. He stated:

> The source of the stimulus (perhaps only an improper distribution of physiologic stimuli) for the excitement of the motor zone, in the sense of athetoid movements, lies in the diseased midbrain (in the region of the thalamus or regio subthalamica, perhaps in the red nucleus or in the reticular substance) for which the majority of postmortem findings speak. From here flow abnormal centripetal waves of stimulation, concomitantly exciting neuron complexes, that is to say, nervous mechanisms adapted to the innervation of composite movements, and it is these which, possibly in connection with other subcortical centers, are the cause of at least the purely athetoid movements. Of course, the pyramidal tracts must also participate in the carrying out of these movements, as when they contain motor components in the sense of isolated movements. They would not be capable of doing so if pressure from the focus was exerted on them.

Monakow[11] stated further:

> Und da in keinem der bisher zur Sektion gekommenen Fällen die Pyramidenbahn vollständig unterbrochen befunden wurde, so darf man meines Erachtens mit

9. Kolisch, R.: Posthemiplegische Bewegungsercheinungen, Deutsche Ztschr. f. Nervenh. **4**:14, 1893; quoted by Monakow: Gehirnpathologie, Vienna, A. Hölder, 1905, p. 554.

10. Nothnagel, H.: Zur Diagnosis der Sehhügelerkrankungen, Ztschr. f. klin. Med. **16**:424, 1889; quoted by Monakow: Gehirnpathologie, Vienna, A. Hölder, 1905, p. 554.

11. Monakow, C. V.: Gehirnpathologie, Vienna, A. Hölder, 1905, p. 553.

ziemlicher Bestimmtheit annehmen, dass vom Cortex aus die Erregungswege für die athetotischen Bewegungen teilweise wenigstens, mit der Pyramidenbahn zusammenfallen.

(And since in none of the cases that so far have come to postmortem examination was the pyramidal tracts found to be completely interrupted, it is my opinion that one may assume with considerable certainty that going out from the cortex the pathways of stimulation for the athetoid movements coincide, at least partially, with the pyramidal tracts.)

Many writers have stressed the similarity between spontaneous choreo-athetoid movements and movements executed as a result of volition. Jackson,[12] in 1873, commented on the kinship of these movements, and, of late, Wilson [13] has placed great emphasis on their resemblances. Like Monakow, Wilson stated that he had never seen a case of chorea or athetosis occurring in the presence of complete corticospinal paralysis, and in his "Modern Problems of Neurology" he offered the following hypothesis:

> Athetosis and chorea are exteriorized via the corticospinal paths, and behind their appearance is an afferent disorder of regulation, producing choreiform and athetoid characters in movement, ataxia, or incoordination and hypotonia. This afferent disorder or derangement of regulation is attributable to lesions of the cerebello-mesencephalo-thalamo-cortical system. As a consequence, voluntary movements via the corticospinal tracts may exhibit characters corresponding to the functional defects; and these tracts are, continuously or intermittently, usurped also by spontaneous movements of choreiform or athetoid character, movements in many ways closely resembling voluntary movements.

In the light of this hypothesis, Wilson [14] has described a hemichorea occurring in a woman aged 88. Autopsy revealed only a circumscribed atrophy of the contralateral postcentral gyrus and a "clinically unimportant" small area of softening in the thalamus. Wilson attributed the chorea in this case to a disturbance of the afferent cerebellocerebral impulses which, suffering from a derangement of regulating components, caused the pyramidal tracts to function in a perverted manner. He attached great significance to the contralateral postcentral atrophy and suggested that it was of primary etiologic importance in the production of the hemichorea. It is difficult to think of a woman, aged 88, suffering from hemichorea with no ganglion cell changes other than those described by Wilson. Moreover, one hesitates to consider with indifference the small area of softening in the thalamus, regardless of its dimensions.

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12. Jackson, Hughlings, quoted by Wilson: Modern Problems in Neurology, New York, William Wood & Company, 1929.

13. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood & Company, 1929; Croonian Lectures on Some Disorders of Motility and of Muscle Tone, Lancet **2**:1, 53, 169, 215 and 268, 1925.

14. Wilson, S. A. K.: Die Pathogenese der unwillkürlichen Bewegungen mit besonderer Berücksichtigung der Pathogenese der Chorea, Deutsche Ztschr. f. Nervenh. **107**:28, 1928.

Choreo-athetoid movements have been interpreted in a somewhat different manner by Bonhoeffer, A. Jakob, Foerster, C. and O. Vogt, Minkowski and others. These authors stated that lesions at various levels between the dentate nuclei and the thalamus may lead to disturbances that result in the motor phenomena recognized as choreo-athetoid movements. They do not, however, think that a participation of the corticospinal pathways is necessary before these movements can occur; that is, that the altered afferent waves of stimuli must proceed to the cortex and there, through either a functional deficit or a pure release phenomenon, pervert the normal activity of the corticospinal tracts in the sense of Wilson.

In 1897, Bonhoeffer reported his well known case of *"Bindearm"* chorea, and in a more recent article [15] he emphasized the frequency of lesions in the thalamic, subthalamic and substantia nigral regions in cases exhibiting choreo-athetoid movements. He expressed the belief that lesions in any of these localities may result in a shunting of centripetal waves of stimulation (cerebello-mesencephalo-thalamo-cortical pathway) into centrifugal pathways, thus interrupting at least the normal flow of these centripetal excitations to the cortex, and in this manner set up choreo-athetoid movements, without the participation of the motor cortex. Into which pathways these afferent stimuli are shunted Bonhoeffer was not certain, but, like Minkowski, he suggested that they may travel by way of the rubrospinal, tectospinal and other tracts not yet known.

Minkowski [16] destroyed the motor area in cats and later elicited movements of a choreo-athetoid nature in the parts deprived of their corticospinal connections. On the other hand, Wilson [17] made experimental lesions in the thalamus but was unable to elicit choreo-athetoid movements afterward. Though extremely interesting, these results, like those of other animal experiments, have proved somewhat disappointing when viewed in the light of clinical material.

Indeed, when one reviews the literature pertaining to choreo-athetoid movements, the explanations offered for the production of such involuntary motor manifestations seem to fall within two major groups. One group maintains that choreo-athetoid movements bear a great resemblance to movements executed as a result of volition, and that they cannot occur without at least a partially intact corticospinal system. The other attributes choreo-athetoid movements to the perverted activity of

15. Bonhoeffer, K.: Klinische und anatomische Beiträge zur Pathologie des Sehhügels und der Regio subthalamica, Monatschr. f. Psychiat. u. Neurol. **77**:127, 1930.

16. Minkowski, M.: Experimentelle und anatomische Untersuchungen zur Lehre von der Athetose, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:650, 1926.

17. Wilson, S. A. K.: An Experimental Research into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1913.

some basal ganglionic system and is opposed to the idea that the corticospinal pathways are necessary prerequisites for the production of these movements. It is in the light of these divided opinions that the case under discussion is of singular interest.

So far as I can determine, the literature contains only one case of athetosis occurring in the presence of complete interruption of the corticospinal fibers for the parts involved. Haenel,[18] in 1902, reported such a case in a youth, aged 20, who had suffered from early infancy with a left-sided paralysis and atrophy of the upper and lower left limbs. For some time before death, marked athetoid movements were noted in the entire left arm. The patient died of pulmonary tuberculosis, and at autopsy it was found that an old focus had destroyed the left peduncle, thereby completely interrupting the corticospinal tract for the contralateral side. Monakow commented on this case in a footnote in his "Gehirnpathologie." He was inclined to believe that what Haenel referred to as an abnormal bundle of fibers or *Faservermehrung* might well have been fibers of the corticospinal tract which had escaped destruction by the focus. Because of the uncertainty concerning Haenel's findings and the relationship that his case bears to the one under discussion here, it seems appropriate to present Haenel's own comment [18] on the abnormal fibers that were found in the vicinity of the focus.

Die übrigen hypertrophischen Faserbündel der Haubenetage haben sich nicht zu bekannten Bahnen in Beziehung bringen lassen. Sie ziehen theils mit dem Bindearm nach dem Kleinhirn, theils stellen sie abnorme Verbindungen zwischen der r. und l. Hälfte, besonders in der Gegend der hinteren Vierhügel dar, theils verlieren sie sich in der Gegend der Hirnnervenkerne, einige reichen bis in die Umgebung des Centralkanals des obersten Halsmarks. Sie werden wohl am ungezwungensten ebenfalls als Bahnen aufgefasst, die vicariirend für durch den Herd unterbrochene eingetreten sind und sich in Folge dessen stärker entwickelt oder selbst neu gebildet haben.

(The other hypertrophic fibers of the reticular substance could not be brought into relation to known pathways. In part they pass with the *Bindearm* [decussation of the superior peduncles of the cerebellum] toward the cerebellum; in part they produce abnormal connections between the right and left halves, especially in the region of the posterior corpora quadrigemina; in part they lose themselves in the region of the nuclei of the cerebral nerves, and some reach up into the area of the central canal of the uppermost portion of the cervical spinal cord. They are probably most simply explained as pathways that substitute for those which have been interrupted by the focus, and as a result have become stronger or have even been newly formed.)

These remarks suggest that Haenel himself was in some doubt concerning the significance of the *Faserbündel der Haubenetage* (fibers of the reticular substance). Moreover his photographs do not completely

18. Haenel, H.: Zur pathologischen Anatomie der Hemiathetose. Deutsche Ztschr. f. Nervenh. **21**:28, 1902.

dispel the doubt as to whether all the corticospinal fibers were destroyed by the focus before they crossed into the pons and medulla. They do, however, show that the corticospinal pathway on the right had undergone serious damage.

With respect to the case reported, close examination of figure 5 reveals extensive degeneration of the motor cortex of the left hemisphere. Some fibers succeed in passing down through the internal capsule, but those fibers radiating from the cortical area that sends motor impulses to the right forearm and hand have undergone complete interruption. Of course, as one studies the sections serially, one notes that motor areas for other parts have been involved, but not to such an extent that some fibers did not succeed in escaping interruption. However, the cyst was so located that the entire motor area of the cortex for the right forearm and hand was destroyed. This was borne out by the whole series of preparations when they were studied carefully under the microscope.

This degeneration was not a complete interruption of the entire corticospinal tract, but the corticomotor area for a particular part manifesting athetoid movements was destroyed (figs. 4 and 5). This leads one to assume that the impulses responsible for the development of the involuntary movements traveled over some system other than the corticospinal pathways.

No one will argue that the region destroyed by a lesion can ever produce signs that are as positive in nature as athetoid movements. I agree with Wilson that some intact, or partially intact, system must initiate these involuntary movements, but the findings in this case speak against the idea that the corticospinal pathways are the ones to be incriminated. Choreo-athetoid movements were noted in the forearm and hand even in the presence of an interruption of corticospinal connections for these parts. This is sufficient evidence to show that some other system is responsible for these movements.

The findings in this case are of interest primarily with regard to the divided thought concerning the rôle of the corticospinal system in the development of choreo-athetoid movements. However, one must bear in mind the lesions seen in the thalamus, caudate and lenticular nuclei, corpus luysii, substantia nigra and peduncle, and must remember that these sites are intimately connected with each other, and that there are other descending pathways the functions of which may be altered so as to result in involuntary movements. These facts then render the picture in this case, at least partially, in keeping with the striopallidal theory of Jakob.[19]

19. Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923; The Anatomy, Clinical Syndromes and Physiology of the Extrapyramidal System, Arch. Neurol. & Psychiat. **13**:596 (May) 1925; personal communication to the author.

Jakob attributed athetoses of adult life (with some cases of torsion spasm and cases occurring during adolescence) to disturbances of coordination having a pallidal origin. In some instances of perverted activity of pallidal functions, alterations in the static and kinetic coordinating mechanisms of the midbrain and brain stem are particularly prominent clinically, in the form of athetoid movements. In other disturbances of pallidal function, conditioned by an *Ausfall* of small receptive ganglion cells of the striatum, interferences with the static and kinetic coordinating mechanisms are manifested objectively as choreiform movements. This means that Jakob regarded chorea as a striatally localized disorder and athetosis (of adults) as a pallidally localized malady. However, he stated specifically that lesions in other localities of the midbrain and brain stem may produce either of these clinical pictures, because neither the striatum nor the pallidum functions independently. The midbrain and brain stem centers are subject to a double regulating influence. They are influenced by the efferent tracts of the cerebellum and, concomitantly, are subjected directly to the influences of the extrapyramidal system, especially by fibers to the red nucleus and the posterior commissure, through which both pallida exert homolateral and contralateral action. In this manner, numerous influences are brought to bear on the functional mechanisms of the brain stem and insure its functional balance. According to Jakob, a disturbance of this balance at any point may result in incoordination of the functions of the brain stem and produce a disruption of the extrapyramidally influenced automatism. Choreiform movements result from conditions having a predilection for the small ganglion cells of the striatum, thus disturbing the coordinating function of these ganglia. On the other hand, athetoid movements occur as a result of disturbances of coordination having a pallidal origin. Of course, lesions in these ganglia might produce a disturbance in the functional components of the afferent cerebellocerebral stimuli, in the sense of Wilson, but, according to Jakob, it is not necessary for the corticospinal pathways to be called into action before these alterations can result in choreo-athetoid movements. Jakob suggested that the rubrospinal tracts and the pallidorubro-olivary and pallidorubroreticular connections may be utilized in the production of these movements, but there is little evidence (clinical or experimental) to confirm such assumptions.

There is no doubt that the case reported showed lesions in both the lenticular and the caudate nuclei (this can be noted in figs. 2 and 3), but the thalamus, corpus luysii, substantia nigra and peduncle, and possibly the red nucleus, also underwent changes (fig. 5), some of which were no doubt serious enough to disrupt the functional components of these and other subcortical centers, particularly those traveling by way of the

fibers emanating from the dentate nuclei. In keeping with Jakob's hypothesis, one can say with certainty that there was a disturbance of the coordinating functions of these subcortical centers, but whether or not the involuntary movements noted can be attributed to the alteration of mere pallidal and striatal components I am unable to say because of the multitude of lesions involving so many other intimately connected centers. It may be that the falling out of functional components from these other centers (thalamus, red nucleus, dentate nuclei and others) could produce the movements, even though the pallidal and striatal functions were left undisturbed. Thus, unfortunately, one can utilize the findings in this case for an understanding of the production of choreo-athetoid movements only so far as they show that choreo-athetoid movements can develop in the absence of corticospinal connections for the parts concerned.

CONCLUSIONS

Athetoid movements have been observed in parts of a limb deprived of corticospinal tract connections. This observation leads to the conclusion that choreo-athetoid movements can develop without participation of the corticospinal tracts.

ACTION CURRENTS IN THE CENTRAL NERVOUS SYSTEM

I. ACTION CURRENTS OF THE AUDITORY TRACTS

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The primary function of the nervous system is apparently to transmit and to integrate nerve impulses. It seems clear that in neurologic and psychiatric diseases the crux of the difficulty is a disorder of function of the central nervous system—a disordered transmission or interplay of nerve impulses. In the psychoses chiefly the higher levels seem to be implicated. It would be of great interest and of importance to have direct quantitative information as to the transmission of impulses within the central nervous system, especially in the suprasegmental structures. A method that appears to be capable of yielding such data is available[1] and will be described.

This method depends on the modern neurophysiologic technic for the detection of action currents in nerves.[2] When a nerve transmits an impulse, an electrical disturbance is intimately associated with it. These electrical disturbances, or action currents, can be directly detected, recorded and measured quantitatively as to size, frequency and rhythm. The action currents are led off from the nerve or muscle that is being studied by the application of a fine silver needle to the region and the placing of a large, grounded electrode elsewhere on the body to complete the circuit. The action currents thus enter an amplifier where they are magnified to sufficient size to operate ear-phones or a recording instrument, such as a string galvanometer. Minor adaptations of the technic

1. Another paper on this subject has previously been published. Davis, H., and Saul, L. J.: Action Currents in the Auditory Tracts of the Midbrain of the Cat, Science **74**:205, 1931.

2. Gotch, Francis, and Horsley, Victor: On the Mammalian Nervous System, Its Functions, and Their Localisation Determined by an Electrical Method, Phil. Tr. Roy. Soc. London **182**:267, 1891. Forbes, A.; Miller, R. H., and O'Connor, J.: Electrical Responses to Acoustic Stimuli in the Decerebrate Animal, Am. J. Physiol. **80**:363, 1927. Adrian, E. D.: The Basis of Sensation, New York, W. W. Norton & Company, 1928.

evolved for peripheral nerves enable one to study similarly events in the living, functioning pathways within the central nervous system. Similar methods have already been used by Wever and Bray [3] on the eighth nerve and by Bartley and Newman [4] and Travis and Dorsey [5] on the cortex.

TECHNIC

Cats were employed in all of these experiments. Under full ether anesthesia a tracheal cannula leading from a bottle of ether is inserted. The carotid arteries are then tied. The skin of the scalp is incised from ear to ear, and the pinnae are removed by quick cuts, about 1 cm. of cartilage being left projecting from the bony canals. While the vertebral arteries are held, decerebration is performed with the Sherrington guillotine, and the ether tube is disconnected. Everything anterior to the tentorium is thus shorn away, giving a section between the anterior and the posterior colliculi. The basilar artery, which usually retracts, is pinched with small forceps for several minutes until firmly clotted. In the later experiments the decerebration was done just cephalad to the anterior colliculi. Section was then made with a scalpel at the desired level between the anterior and posterior colliculi, the cut being stopped just before it reached the ventral surface. A ligature encircling this remaining tissue included all the bleeding vessels. The preparation is then kept warm and quiet for at least an hour to allow recovery from the ether and the shock of decerebration.

Other operations employed in particular experiments are:

1. Exposure of the sciatic nerve, which is then stripped of its sheath and separated into its peroneal and popliteal divisions. These are ligated and cut at the level of the knee.

2. Immobilization of the hind leg. The muscular attachments to the greater trochanter are cut, as well as the nerve to the hamstrings. By an incision in the groin the crural nerve and psoas muscles are severed.

3. Exposure of the medulla and upper segments of the spinal cord, by laminectomy and careful incision of the dura.

4. Exposure of the auditory nerves, by cutting away of enough of the bony tentorium to remove the portion of the cerebellum that overlies them.

5. Exposure of the ventral surface of the brain stem, including the trapezoid body, by removal of the basilar portion of the skull back almost to the foramen magnum, and, when necessary, part of one or both bullae. The jaw and tongue may be tied back or removed.

A cat-board holds the preparation. The head fits firmly between two movable brass posts, curved to avoid the auditory canals. The projecting sides of the skull fit into slots, and brass screws through the posts fasten the skull with absolute rigidity, so that chance movements of the body cannot disturb electrodes applied to the head. When working on the ventral surface of the brain stem, with the preparation supine, it is more convenient to hold the head with long clamps, extending from upright posts, which grip the protruding arch of the skull.

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3. Wever, E. G., and Bray, C. W.: Auditory Nerve Impulses, Science **71**:215, 1930.

4. Bartley, S. Howard, and Newman, Edwin B.: Studies on the Dog's Cortex, Am. J. Physiol. **99**:1, 1931.

5. Travis, L. E., and Dorsey, J. M.: Mass Responsiveness in the Central Nervous System, Arch. Neurol. & Psychiat. **26**:141 (July) 1931.

The board, with the animal so mounted, is then placed on a glass plate which rests on a sheet of galvanized iron. Perpendicular to the latter is a panel which holds the electrical control switches and binding posts. A galvanized iron cage with screened top, balanced by a counterweight, slides down so that, with the panel as one wall and the sheet of iron as the bottom, a complete box envelops the preparation. The box is grounded for electrical shielding.

The recording electrodes are made of silver wire, the size of ordinary sewing needles, moderately sharpened and insulated to within 0.3 mm. of the tip with de Khotinsky cement. They are attached to fine, flexible copper wire insulated with enamel. The tips are cleaned and coated electrolytically with silver chloride. The grounded diffuse electrode is a flat plate of silver about 1 cm. square, chlorided and covered with cotton soaked with Ringer's solution. The recording electrodes are held rigidly in position in the nerve tissue by small bulldog clips which fasten by brass toothed clamps to the skull.

The stimulating electrodes used on the popliteal nerve are of the tubular shielded type [6] built with two cathodes, one near each end, to reduce the spread of stimulus.[7]

The control panel enables us to put in place several electrodes and to record from one or another by the turn of a selector switch. The panel also holds a variable air condenser. This couples the stimulating circuit directly to the input of the amplifier and thus provides a signal of controllable size for the recording of the exact instant of stimulation. The coreless induction coils and the remainder of the circuit are those employed by Forbes, Davis and Lambert.[6]

For acoustic stimulation, a stethoscope with glass tips is fitted to the auditory canals. Tubing of large caliber (in recent experiments 16 mm. in inside diameter) reduces sound distortion. Clinical ear specula make convenient stethoscope tips. The center arm of the stethoscope reaches into a sound-proof box which holds the stimulating apparatus. In the later experiments, a slide valve on the arm provided a ready means of adjusting the intensity of the sound stimuli. A Jacquet clock taps the diaphragm of the Bowles bell of the stethoscope five times a second. A more satisfactory device is the clockwork of an ordinary Maelzel metronome removed from its box and mounted to tap the Bowles bell instead. A side arm of the stethoscope with a funnel can be unclamped to receive the voice or other sounds. Clamping one or the other arm of the stethoscope suffices to direct the sound to one or the other ear. For experiments on the limits of pitch, variators were used to give pure tones from about 30 to 1,500 vibrations per second. More recently, we employed a General Radio beat frequency oscillator, type 413-B. With the output amplified and delivered through a Baldwin loud speaker, all pitches of from 0 to 10,000 double vibrations per second are obtained continuously by the turning of a single dial. The intensity is also continuously variable over a wide range. With everything carefully shielded electrically and acoustically, there is no direct pick-up by the recording apparatus except at far greater intensities than those employed in the actual experiments.

Two amplifiers were used. The one, described by Forbes and Thatcher,[8] amplifies the action currents approximately fifteen times and actuates a Hindle

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6. Forbes, A.; Davis, H., and Lambert, E.: The Conflict Between Excitatory and Inhibitory Effects in a Spinal Center, Am. J. Physiol. **95**:142, 1930.

7. Werigo, B.: Ueber die Reizungen des Nerven mit dreiarmigen Elektroden, Arch. f. d. ges. Physiol. **76**:517, 1899.

8. Forbes, A., and Thatcher, Catherine: Amplification of Action Currents with the Electron Tube in Recording with the String Galvanometer, Am. J. Physiol. **52**:409, 1920.

string galvanometer which records photographically on motion picture film. Recently an additional stage (now two tubes) has provided an optional maximal amplification of about 100.

The other amplifier, six stage, resistance-coupled, magnifies approximately ten thousand times, sufficient to make the action currents clearly audible in ear phones. A microphone attached to an alternate input lead serves as a control on the amplifier.

Precautions are taken as to electrical shielding and soundproofing. Listening on the phones is usually done behind closed doors in a separate room not immediately adjacent to the room containing the cat and the stimulating apparatus.

At the end of each experiment the animal is killed by ether, chloroform, asphyxia or sectioning of the medulla while control records are being made. Autopsy is then performed, and the medulla is placed in a diluted solution of formaldehyde, U. S. P. (1:10) for gross sectioning and examination, and, when indicated, for sectioning and staining for microscopic verification of the position of the electrode.

RESULTS

In one series of experiments we stimulated the popliteal nerve and recorded action currents from the popliteal nerve itself and from the reflex discharge down the peroneal nerve (fig. 1 *A*), the motor pathway of the well known flexion reflex.[9] We then endeavored to trace the afferent impulses up the spinal cord, through the medulla to higher levels. This was done by placing the diffuse grounded electrode on or under the muscles of the skull or spine and exploring with the needle electrode. Records were thus obtained from the upper segments of the spinal cord, from the medulla and from the decerebration section through the midbrain. The electrode was placed on different points of the surfaces or penetrating to various distances into the nerve tissues. In the case of the midbrain it was inserted at least 5 mm. down the cord at right angles to the plane of decerebration in order to avoid dead and edematous tissue.

Observations on twelve cats indicate that the curves recorded from the columns and nuclei of Goll and Burdach of the side stimulated were more constant in shape and larger in amplitude and had shorter latent periods than curves obtained from the contralateral side or from other regions. Similarly curves from certain regions of the midbrain were much more definite and characteristic than from other points. Samples of the curves appear in figure 1 (*A, B, C* and *D*). We have not undertaken a detailed analysis of these curves, as this will be done by Dr. C. E. Leese, who began the study of this aspect of the problem, but the results indicate that the method is sufficiently selective to yield information regarding activity in individual tracts in the central nervous system.

Action Currents of the Auditory Tracts.—In the course of exploration of the hindbrain it was found that with the active electrode in a

9. Forbes, A., and Gregg, Alan: Electrical Studies in Mammalian Reflexes. I. The Flexion Reflex, Am. J. Physiol. **37**:118, 1915.

certain position any noise in the room would cause a deflection of the string of the galvanometer. On listening in the ear phones it was found that the intensity, timber and pitch (up to at least 1,000 per second) of the sounds applied to the ears of the cat were reproduced with considerable accuracy (fig. 1 *E*). The person singing or talking could usually be identified, and a tune could regularly be recognized. Subsequent gross

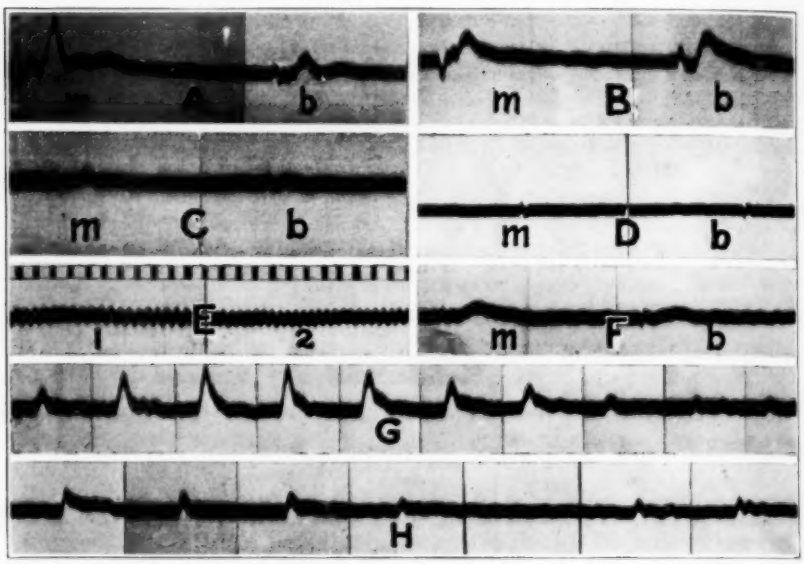

Fig. 1.—*A*, *B*, *C* and *D*, action currents obtained in a series of experiments. The action currents are the large deflections, always upright. The stimulus signals are the small deflections, and are characterized by an opposite polarity on make from that on break shocks. They are controlled as described in the text. In all cases the popliteal nerve is stimulated. The recordings are: (*A*) from the peroneal (Jan. 16) film speed, 2.8 σ per millimeter; (*B*) from the medulla, over the proprioceptive pathways (Jan. 16) film speed 2.8 σ per millimeter; (*C*) from the midbrain, 4 mm. caudal to the decerebration section (March 18), film speed 5 σ per millimeter, and (*D*) control, from the midbrain, immediately after death of the animal (March 23), film speed 5.6 σ per millimeter (in this record, from a later experiment, with a different disposition of leads, the stimulus signal is of reversed polarity from that in *A*, *B* and *C*). Time markings of 1/100 second are on the original films, but do not appear in the figures in this article. *E* and *F*, records obtained from the trapezoid body (March 23): (*E*, *1*) voice singing in a low tone to a cat's ear, and (*2*) voice singing in higher pitch (the time marker indicates intervals of 1/100 second); (*E*) recording electrodes in the same location, showing responses to induction shocks stimulating the popliteal nerve. *G* and *H*, records obtained from the trapezoid body. Stimulus: clicks of a watchman's rattles (March 23); film speed, 5.6 σ per mm.; *G* shows how moving of the recording electrode approximately 1 mm. passes it through a sharply localized position of maximum response. *H* gives an example of reversible depression of responses, obtained in this record by compression of the vertebral arteries.

section showed that the electrode had been on the trapezoid body (fig. 2). The striking experiment of Wever and Bray [3] was then repeated, and their results were confirmed. They showed, by means of well controlled experiments, that electrical disturbances led off the auditory nerve of the cat, and amplified, reproduced in ear-phones the sounds applied as stimuli to the animal's ear. In our twenty-six preparations, electrical responses have been obtained from various points along the auditory nerve and nuclei, the trapezoid bodies, the acoustic striae and the lateral lemnisci, thus tracing them from the cochlea along the specific pathways to the inferior colliculi at the plane of decerebration. In a recent experiment on the intact brain, with the left cerebral hemisphere exposed, under light avertin-ether anesthesia, similar localized responses have been obtained from the brachium, the medial geniculate body and the auditory radiations.

Comparison of responses obtained from the nerve with those from the brain stem, to identical stimuli, shows significant differences. In the first place the responses from active points on the brain stem are nearly

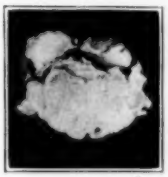

Fig. 2.—Cross-section through the hindbrain of the cat showing a lesion in the left trapezoid body, thus clearly indicating the position the electrode had occupied. Serial sections show how far caudally the electrode had penetrated.

always greater than those from the nerve. This is true even if the electrode pierces the nerve sheath, thereby giving much larger effects than when resting on the surface. This is shown in table 1:

TABLE 1.—*Results of Experiment of May 27, 1931*

Recording from:	Right Brain Stem			Left Brain Stem			Left Eighth Nerve		
Ear receiving sound:	Right	Both	Left	Right	Both	Left	Right	Both	Left
Height of excursion in millimeters:	8.5	10.0	3.6	1.9	3.6	3.2	0	3.0	2.9

The second striking difference is that, although louder, the words heard from the brain stem are much less clear and are usually not quite intelligible. Each sound begins with a rush. The words sound "bloated," "puffed up" or "mouthed." This quality is characteristic. Consonants can rarely be recognized, although vowels and musical tones evince less distortion. The fidelity of reproduction of sounds yielded by responses from the auditory nerves may perhaps be due to a cochlea

spread rather than to true action currents in the nerve. The third point of distinction between the nerve and the brain stem has not yet been completely elucidated, but our evidence thus far indicates that higher pitched musical notes may be recovered from the nerve than from the brain stem. Notes of 4,000 double vibrations per second have been obtained from the nerve, but no notes of more than 1,000 double vibrations have been detected with certainty from the brain stem. This question of the upper limit of pitch is one of great theoretical interest, but our data are as yet not sufficiently conclusive to warrant discussion of the issues involved. The technical difficulty is that the responses are masked or augmented to some extent by electrical spread from the cochlea or auditory nerve. This condition can be greatly reduced by using stimuli of very low intensity, but this in turn requires a high-powered very quiet amplifier for detection of the action currents. Recent experiments show that the frequencies of more than 1,000 double vibrations are almost certainly due to "spread," and are not true action currents.

Sharpness of localization is characteristic of the effect in the brain stem. A movement of the electrode of a millimeter or less suffices to pass through a maximum and frequently to lose the response, which returns on restoration of the electrode to its optimal position (fig. 1 *G*). These active points have been shown by subsequent gross section to lie invariably on auditory paths. With the string galvanometer and an amplifier that is not sensitive enough to detect the diffuse spread, no other regions have yielded such responses. With a more sensitive amplifier and ear-phones, the active points give sharp, strong maxima. When very strong sound stimuli are used, such as hard blows on the diaphragm of the stethoscope, responses in the nervous system may be caused by pain and pressure as well as by the sound, thus involving other tracts. Evidence of purely reflex responses to acoustic stimuli was noted by Forbes and Sherrington [10] in 1914. It is noteworthy that in the first experiment strong induction shocks to the popliteal nerve gave action currents at the same position of the electrode on the trapezoid body that yielded strong auditory responses (fig. 1, *E* and *F*). It must also be recognized that when loud acoustic stimuli are applied to the ears there is an electrical "broadcast," probably from the cochlea, as described by Adrian.[11] This electrical spread is of such intensity that, with a sensitive amplifier, the effect can easily be picked up from any

10. Forbes, A., and Sherrington, C. S.: Acoustic Reflexes in the Decerebrate Cat, Am. J. Physiol. **35**:367, 1914.

11. Adrian, E. D.: The Microphonic Action of the Cochlea: An Interpretation of Wever and Bray's Experiments, J. Physiol. **71**:28, 1931. Adrian, E. D.; Bronk, D. D., and Phillips, G.: The Nervous Origin of the Wever and Bray Effect, J. Physiol. **73**:2, 1931.

tissue in the region of the head, bone and muscle, as well as nerve tissue. But by decreasing the intensity of the stimulus and adjusting the amplification accordingly, responses are obtained that are highly localized in the auditory tracts. Some idea of the difference in the threshold of these effects is given by the experiment of Nov. 23, 1931. The stimulus was a continuous range of musical tones (beat frequency oscillator). At the amplification employed, the thresholds were as follows, in terms of dial readings on a potentiometer, 180 degrees being maximum:

	Degrees
20,000 ohm non-inductive resistance instead of preparation (i .e., direct pick-up of stimulus by amplifier)	22
Electrode on petrous bone	6
Electrode piercing left eighth nerve	1

Moreover, in the ear-phones, the spread is always heard as clear and metallic and the words are intelligible. The localized effect in the brain stem produces in the phones the characteristic puffiness and unintelligibility already described.[12]

It is probably the failure to discriminate between the true action currents and the diffuse spread in all the adjacent tissues that has led to recent revolutionary theories as to the "mass responsiveness" of the nervous system.[5] In most of the papers dealing with action currents of the brain that have come to our attention we do not find convincing evidence that artefacts, such as the spread of electrical effects from more distant regions and mechanical vibration of electrodes, have been adequately controlled.

The contralaterality of the responses agrees well with the known anatomy of the auditory tracts. An electrode placed on a crossed tract, such as the lateral lemniscus, is more sensitive to stimuli applied to the opposite ear than it is to those applied to the homolateral ear. This is clearly illustrated in the protocol of June 3, to be presented. If the electrode is placed on the nucleus of the eighth nerve or proximal parts of the lateral lemniscus, it is more sensitive to homolateral stimulation. The data are not yet adequate for a more detailed quantitative statement.

Narcotization of parts of the brain stem by injection of 5 per cent or 10 per cent procaine hydrochloride in Ringer's solution near the electrode obliterates responses on the string galvanometer. The responses return after from one to three hours. If procaine hydrochloride is injected on one side of the brain stem between the electrode and acoustic nerve, responses from that ear disappear while those from the other ear persist. It is much easier to cause a decrease in the size of a response

12. It may be added that in a recent experiment highly localized responses were obtained from optic tracts upon shining a light in the eyes, and also from just below the surface of the cortex in the hind leg area on pinching the left foot. In this experiment avertin anesthesia was used.

than to obliterate it entirely. The contralaterality and the reversible effects of the injection of procaine hydrochloride are illustrated in table 2, which represents the most definite of four narcotization experiments.

TABLE 2.—*Summary of Experiment of June 3, 1931* *

Recording from:	Right Brain Stem			Left Brain Stem		
Ear receiving sound:	Right	Both	Left	Right	Both	Left
Time						
6:13	3.0	4.4	4.0	3.0	3.3	1.5
6:14	A few drops of 5 per cent procaine hydrochloride injected into right brain stem near tip of right electrode. Quieter base line					
6:14¼	2.0	3.9	3.8	1.5	2.5	1.0
6:16	More procaine hydrochloride injected into right brain stem					
6:17	0.0	0.0	0.0	1.0	1.6	1.0
6:20	0.0	0.0	0.0	0.0	1.5	1.0
6:30	0.0	0.0	0.0	0.5	1.3	1.3
6:45	0.0	0.0	0.0	0.5	1.2	0.9
8:15	0.0	1.0	1.0	2.1	2.4	1.1
9:12	0.0	1.0	1.0	2.0	2.3	1.1
	Control after death of cat					
11:40	0.0	0.0	0.0	0.0	0.0	0.0

* Figures represent size of action currents as measured by heights of deflection in millimeters of the film.

Application to the auditory nerve of procaine hydrochloride or alcohol causes a decrease in the responses from both the nerve and the brain stem. Urea (10 per cent) and diluted solution of formaldehyde (10 per cent) injected into the nerve cause irreversible loss of response. Six of these experiments were done. An example is shown in table 3:

TABLE 3.—*Summary of Experiment of April 15, 1931*

Stimulus: Clicks of watchman's rattle, 6 inches above skull	
Action Currents on Film in Millimeters. Accuracy of Measurement ±0.2 Mm.	
From Right Brain Stem	From Left Brain Stem
4.5	3.1
Procaine hydrochloride crystals on left eighth nerve, 10 minutes	
3.0	3.0
Cut left eighth nerve	
2.8	3.1
Pithed right cochlea	
0.0	0.0

It would appear that the right cochlea was in this case responsible for all of the responses on the left and for most of those on the right. Cutting of the left nerve produced no greater effect than the injection of procaine hydrochloride. In other experiments one nerve was cut at the beginning of the experiment, and attention was focused on the narcotization of the other. Diminution in the size of responses was obtained.

Ethyl chloride sprayed onto the trapezoid body (exposed by removal of the basilar portion of the skull) causes a reversible loss of responses. Respiration is sometimes depressed for a moment or so. Full ventilation may then be maintained artificially. This method of narcosis is open to criticism because it freezes the tissue.

The effects of ether, asphyxia and diallylbarbituric acid are summarized by the curves shown in figure 3. These may not represent entirely pure action currents, but a combination of true action currents with a very small amount (certainly not over 10 per cent) of "spread" such as was described. These records were all made with the active electrode in the same position. With the basilar portion of the skull removed, the electrode was placed on the right trapezoid body by causing

TABLE 4.—*Experiment of Nov. 2, 1931* *

	Sound Delivered		
Time	Right Ear	Left Ear	
9:31	7.0	2.3	
9:32	Ethyl chloride sprayed on		
9:33	3.2	1.0	Respirations barely perceptible, artificial respiration started
9:35	Spontaneous respiration resumed		
9:36	7.0	0.5	
9:47	6.0	2.5	
9:58	4.2	Clamped	
9:59	More ethyl chloride sprayed		
10:00	2.0	Respiratory panting	
10:01	2.2	Respirations almost normal	
10:02	3.0		
10:03	4.5		
10:04	4.5		
10:05	4.5		

* Size of action currents in millimeters on film. Recording from right trapezoid body.

it just to penetrate the pyramidal tract on that side. There is a gradual decrease in the size of the responses, reversible except with diallylbarbituric acid, a huge overdose of which was given intentionally.[13] Ether depresses the knee jerk, muscular tone and respiration rate without obliterating the acoustic response, whereas diallylbarbituric acid obliterates the response before the knee jerks or respirations. Rebreathing causes cessation of respirations without loss of auditory responses.

When the cat dies in the course of an experiment the responses from the brain stem are lost as soon as the heart stops beating, and sometimes a few minutes before. The responses from the auditory nerve persist after those from the brain stem are no longer detectable, and sometimes

13. Forbes, A., and Miller, Richard H.: The Effect of Ether Anesthesia on Afferent Paths in the Decerebrate Animal, Am. J. Physiol. **62**:113, 1922.

for several minutes after the heart beat is no longer perceptible. Pithing of the cochlea or cutting of the nerve obliterates the response. Compression of the vertebral arteries diminishes it reversibly (fig. 1 *H*). These results confirm those of Wever and Bray.

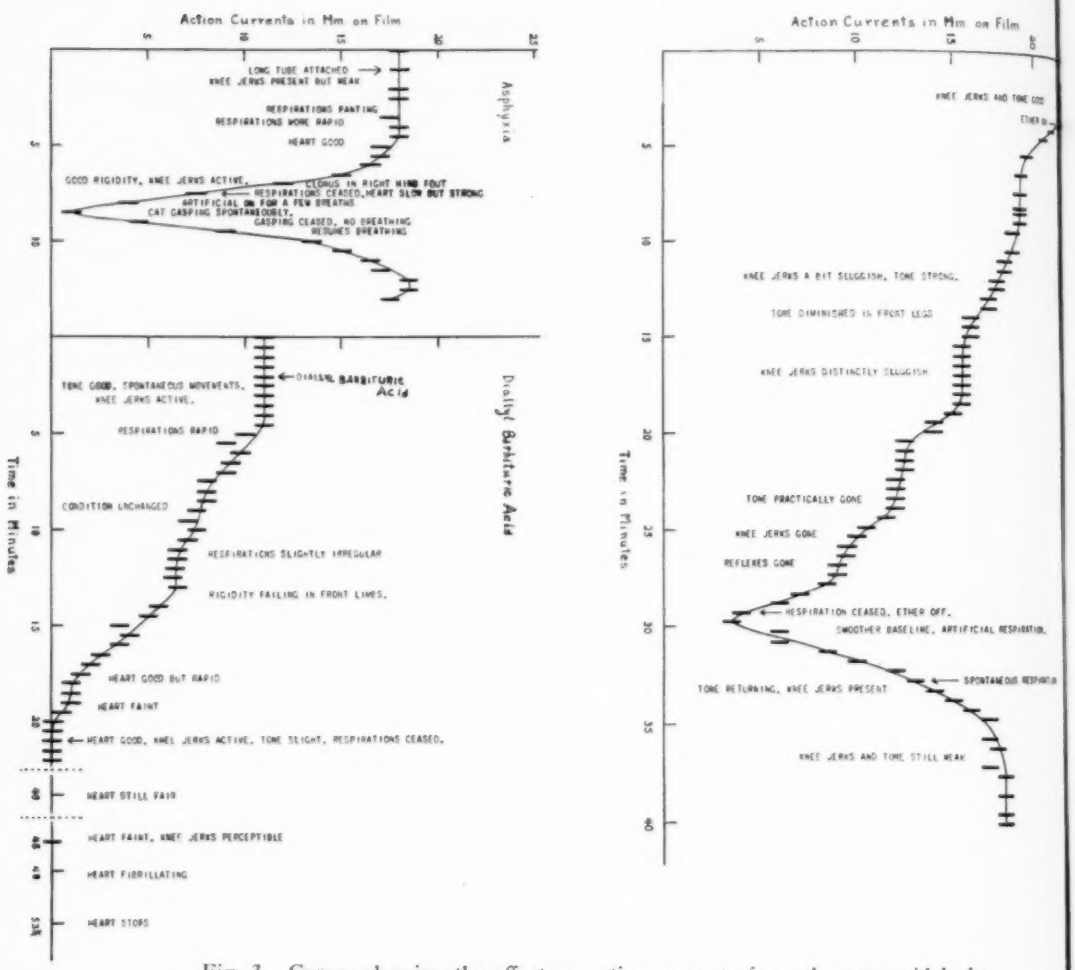

Fig. 3.—Curves showing the effect on action currents from the trapezoid body (ordinates, height in millimeters on film) produced by administration of ether (curve 1) and of diallylbarbituric acid (curve 2) and by rebreathing (curve 3). The stimulus was the click of a metronome, constant in rate and intensity.

COMMENT

We conclude that we are dealing with a complex response which represents at least three components: 1. True action currents from regions close to the tip of the electrode. If the electrode is in an active

region this factor dominates the picture. 2. Microphonic effects. These refer to the direct pick-up of the sound by the apparatus, i. e., by the tubes or connections of the amplifier or by the vibrations of the electrodes themselves. With the amplifications used in these experiments the microphonic effects are readily controlled and are rendered imperceptible. Care must be taken to eliminate them in every experiment. 3. Spreading electrical effects from more distant parts of the auditory mechanism, such as the cochlea. With loud stimuli such diffuse spread permeates all surrounding tissues, nerve, bone and muscle. It is greatest in the region of the cochlea and the auditory nerve. As pointed out on page 1110, it can be eliminated by using less intense stimuli without too much amplification. With the one stage amplifier and string galvanometer used in these experiments, this diffuse spread is not detectable. (Some idea of the extent of such diffuse spread may be obtained by recalling that electrocardiograms can be recorded from the extremities. A quantitative study of this electrical spread in the case of muscles has been made by Forbes and Barbeau.[14])

More difficult to rule out is the possible presence of a more localized type of electrical spread, originating perhaps in the cochlea and following the auditory paths selectively, as an electric current flows in an insulated wire, and masking the true action currents in these paths. Against this effect three important phenomena play a noticeable part: First, procaine hydrochloride dissolved in Ringer's solution reversibly obliterates the response without, so far as we know, materially changing the electrical conductivity of the tissue. This is the familiar effect of procaine on nerve action currents. Second, responses from the brain stem are larger and of different quality than those from the nerve. Spread would be expected to show only a decreased intensity with increasing distance from the source, without change of quality. Third, clearcut contralateral responses have been obtained. It is extremely improbable that a diffuse electrical effect could spread so selectively across nuclei, synapses and decussations of the tracts.

Theoretical discussion of the various questions raised by these observations is reserved for the future when more data are available. For the present we merely call attention to the fact that a considerable degree of the original pattern and pitch (frequency) of auditory stimuli is still maintained in the action currents from regions that anatomically are separated from the ear by at least one and perhaps as many as three or four synapses.

14. Forbes, A., and Barbeau, Antonio: The Question of Localizing Action Currents in Muscle by Needle Electrodes, Am. J. Physiol. **80**:705, 1927.

SUMMARY

1. A method is described for the study of action currents within the central nervous system. It is essentially identical with the familiar neurophysiologic technic developed for the study of action currents in peripheral nerves.

2. Responses can be obtained selectively from individual tracts in the central nervous system. Localized responses have been obtained from the auditory pathways of the cat, tracing from the eighth nerve to the acoustic radiations.

3. In the case of the auditory pathways the amplified action currents reproduce in the ear-phones, with varying accuracy, sounds, musical tones and words applied to the animal's ear. At least three effects contribute to this reproduction: (1) true action currents; (2) spreading electrical effects, which can be controlled and usually eliminated; (3) microphonic effects, which are usually negligible.

4. These auditory responses have the following characteristics, all of which indicate that they are predominantly true action currents: (*a*) sharp localization in the auditory tracts; (*b*) contralaterality in crossed tracts such as the lateral lemniscus; (*c*) reversible diminution or disappearance on anesthetization, either local (procaine hydrochloride, ethyl chloride) or general (ether, diallylbarbituric acid), and on rebreathing; (*d*) obliteration on pithing of the cochlea or cutting of the eighth nerve, and on the death of the animal; diminution on compression of the vertebral arteries; (*e*) clearness of words from auditory nerve (the words are louder if the electrode pierces the nerve sheath); (*f*) the fact that words from the brain stem are slightly louder but much less distinct than those from the eighth nerve, and (*g*) evidence that higher pitched musical notes may be detected in the nerve than in the brain stem.

This method appears to be an effective instrument for exploring the central nervous system.

THE NONSPECIFICITY OF THE HISTOLOGIC LESIONS OF DEMENTIA PARALYTICA

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There is a remarkable contrast between the amount of investigation that has been done on comparative anatomy and histology and that on comparative histopathology of the central nervous system. A great body of knowledge is available on the structure and course of fiber tracts in the different animal species. But only fragmentary data are available concerning the finer nature of pathologic processes in the central nervous system of animals, even though such knowledge is of the greatest importance for neuropathologic problems in man.

Those who are versed in histopathologic technic and in observation of human material have frequently not been inclined to systematic experimental investigations. The occurrence in animals of spontaneous diseases that are difficult to diagnose *intra vitam* has had an equally dampening effect on investigative initiative. On the other hand, those who have experimented a great deal with the central nervous system in animals have often lacked sufficient experience with the finer methods of pathologic histology and their interpretation. It should not be the endeavor of physicians today only to produce experimentally in animals diseases that occur in man, in order to study the anatomic picture of different stages of the disease, the effect of therapy and the like. Of equal interest is the investigation of neuropathologic processes in animals in order to learn what types of histologic syndromes and symptoms occur there without intervention, and what light they throw on neurohistologic processes similar to them in man.

In this way one may learn to understand isolated histopathologic symptoms as parts of broader physiopathologic processes or biologic reactions. Not a few of the histologic signs that have been used to characterize neuropathologic diseases in man are such isolated phenomena, which are used semeiologically without explanation or correlation. Such, for example, are the histologic criteria that are regarded today as characteristic for dementia paralytica.

From the department of Professor Jahnel at the German Research Institute for Psychiatry.

The present study began with an investigation of the effect of Spirochaeta gallinarum on the central nervous system of chickens. Spirochetosis gallinarum is a disease of chickens which is transmitted by insects,[1] but which can easily be produced experimentally. The spirochete responsible for the condition was first described in 1890 by Sacharoff, who found it in an epidemic disease of geese in the Caucasus.[2] Later epidemics of spirochetosis were observed in chickens, first in Brazil, then in many other countries. Spirochaeta anserina and Spirochaeta gallinarum are morphologically indistinguishable, and by some authors are considered to be identical.

Owing mainly to the recent investigations of Jahnel,[3] experimental spirochetosis gallinarum in its relation to the nervous system is parasitologically and histoparasitologically well known. About the first or third day after the inoculation, spirochetes can be seen in the blood. In the course of the disease, usually several days after the spirochetes first appear in the blood, there is a definite crisis, after which the organisms disappear from the blood. The animals either die or recover completely. During their stay in the chicken, the spirochetes penetrate to the inner organs and, as Steiner [4] was the first to show, also to the central nervous system. Jahnel has demonstrated that after the spirochetes have disappeared from the blood they can still be found for a short time in the inner organs; they remain longest in the central nervous system, but no longer than one or two days after they have disappeared from the blood and inner organs. Death usually occurs during the crisis; but it may also occur later, after the spirochetes have disappeared from the blood and inner organs and even from the central nervous system. It can happen, therefore, that an animal dies at a time when spirochetes can no longer be demonstrated—a fact that has apparently not been sufficiently considered in the differential diagnosis of diseases of chickens. Therapeutically, the condition can be influenced by arsphenamine and bismuth and gold preparations. Investigators of the anti-

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1. Clinical data may be found in von Heelsbergen, T.: Handbuch der Geflügelkrankheiten und der Geflügelzucht, Stuttgart, Ferdinand Enke, 1929.

2. Soberheim, G.: Geflügelspirochaetose, in Kolle, Kraus and Uhlenhuth: Handbuch der pathogenen Mikroorganismen, Jena, Gustav Fischer, 1930, vol. 7, p. 691.

3. Jahnel, F.: Spirochaeten und Nervensystem, Naturwissenschaften **17**:587, 1929; Untersuchungen ueber die Hühnerspirochaetose mit besonderer Berücksichtigung der vergleichenden Pathologie der Spirochaetenerkrankungen, Zentralbl. f. d. ges. Neurol. u. Psychiat. **54**:413, 1930; Ueber das Verhalten der Geflügelspirochaeten zum Zentralnervensystem, Ztschr. f. Hyg. u. Infectionskr. **112**:613, 1931.

4. Steiner: Das Zentralnervensystem bei der Hühnerspirochaetose. Ein Beitrag zur vergleichenden Pathologie der Syphilis des Zentralnervensystems, Arch. f. Psychiat. **57**:284, 1917.

spirochetal properties of various chemotherapeutic agents have made extensive use of experimental spirochetosis gallinarum.

Spirochetes can be demonstrated in histologic preparations in the nerve parenchyma, in the meninges and in the plexus choroideus. Steiner described spirochetes in ganglion cells. He also saw small pigment granules in ganglion cells which he took for disintegrating spirochetes. These observations have not been confirmed by Jahnel, who worked with his own spirochete stain. Steiner used the Levaditi method, which has the disadvantage that, as Jahnel has demonstrated in an as yet unpublished work, it may also stain the so-called Golgi apparatus. It has been proved by Jahnel that the chicken spirochetes never penetrate into ganglion cells. They behave, therefore, in this respect like all other pathogenic spirochetes.

While the distribution of the spirochetes themselves in the central nervous system is thus well known, the histologic effect of the spirochetes on the nerve tissue of chickens has so far not been investigated. The brains of chickens that had been inoculated by Professor Jahnel were made available by him as material for the first part of the present investigation. By further inoculations and transmissions new material was also obtained, so that altogether chickens that died or were killed in every stage of the disease from several days to one year were available.

METHODS

The brains of the chickens were removed immediately after death. A few were placed entirely in alcohol, a few entirely in formaldehyde. Most of them, however, were dissected and fixed as follows. The optic nerves were removed back of the chiasm and put in formaldehyde. The median cerebellum was dissected off and cut through the midline, and half was put in alcohol and half in formaldehyde. Then the brain was cut in frontal sections, which were laid alternately in formaldehyde and alcohol. In practically all cases the spinal cord was examined in the cervical and lumbar regions (both formaldehyde and alcohol material) and in some cases the peripheral nerves and the aorta were also examined.

A few charactertistics of the central nervous system of the chicken brain may be mentioned here, based mainly on the presentation of Papez.[5] The most distinctive features of the bird brain to be kept in mind for orientation in pathologic studies are the great development of the striatum in the forebrain, the median cerebellum and the laterally placed tecta or optic lobes. The tecta are very large, and there is a complete crossing of the optic nerves, so that the right nerve goes to the left tectum and the left nerve to the right tectum. The optic fibers spread over the entire surface of the optic lobes as a superficial fibrous envelop. The arrangement of the gray matter in the tectum gives the appearance of a definitely laminated cortex.

The forebrain has no true cortex. Its dorsal medial wall has a rudimentary hippocampal formation. The striatum, which fills the posterior part of the forebrain, is divided into four parts: the central or paleostriatum, the posterior or

5. Papez, James W.: Comparative Neurology, New York, Thomas Y. Crowell Company, 1929.

archistriatum, the middle or mesostriatum and the dorsolateral or neostriatum, the ventral part of which is spoken of as the ectostriatum.

The cord extends the entire length of the vertebral canal; there is no cauda equina. The lumbosacral region is characterized by a broad dorsal rhomboid sinus. The ventral horns of the gray matter project laterally into the white matter, except in the thoracic region, where there occurs the typical H-form of man.

Orientation concerning these structures and concerning the nature of the nerve cells was obtained by serial sections on embedded material stained for cells (Nissl stain) and for myelin sheaths (Kulschitsky-Wolter). The usual present-day survey and analytic methods were used in examining the material. Thirty-three chickens with experimental infection with Spirochaeta gallinarum were studied. There were marked variations in the degree of the changes found. As already explained, all chickens had shown spirochetes in the blood. Some died or were killed while the organisms were still in the blood, others immediately after these organisms disappeared from the blood or at varying periods up to a year later. The different types of observations will be discussed first.

RESULTS

Macroscopically, nothing unusual was observed. Nissl stains of embedded material were made of all the main areas in each case. It was found that the usual sections of 20 microns did not give a satisfactory picture, as the cells of the chicken brain lie so closely packed together. All observations mentioned here, therefore, were made on sections cut 12 microns thick. The meninges in some cases showed slight infiltration with lymphocytes and plasma cells. This could also be seen in embedded sections of the cord, but was not pronounced. In some cases there was marked ependymitis resembling ependymitis granularis, such as occurs for example in dementia paralytica (fig. 1). The plexus was frequently markedly changed. There were no definitely inflammatory reactions, but in some places the plexus contained circumscribed regions in which the stroma was swollen. These areas were sometimes symmetrical on both sides. Some of the changes found in the chicken's plexus choroideus were of the same nature as the changes described by Monakow and Kitabayashi in schizophrenic patients.

In a general survey of the fields, one was struck with various degrees of nerve cell changes. Since it was not possible to demonstrate any clear correlation between the occurrence or the distribution of these cell changes and the intensity or the duration of the infection, the changes are described without reference to individual cases. Such changes occurred both locally and in diffuse distribution, and might be roughly classified in two types. One type occurred mostly at the periphery of preparations (influence of fixation?). These cells were shrunken and pyknotic, stained very deeply and had no clearly visible nucleus. The beginnings of the processes were fine, but sharply etched. The other type of nerve cell change resembled the "severe cell change" of Nissl. The cell protoplasm was apt to be clear and lightly stained,

with the material of the Nissl bodies at the periphery or completely absent. The nucleus was dark and sometimes was eccentrically placed (fig. 2).

What seems to be a characteristic of disintegration of the nerve cells of chickens was observed in various degrees and stages of changes. This was the formation of vacuoles in the protoplasm, giving pictures in all stages of transition from cells with only one or two vacuoles in the protoplasm (which was then usually rather deeply stained) to large, faintly stained, completely vacuolated cell remnants. In one case all such stages were clearly illustrated in one of the tectal

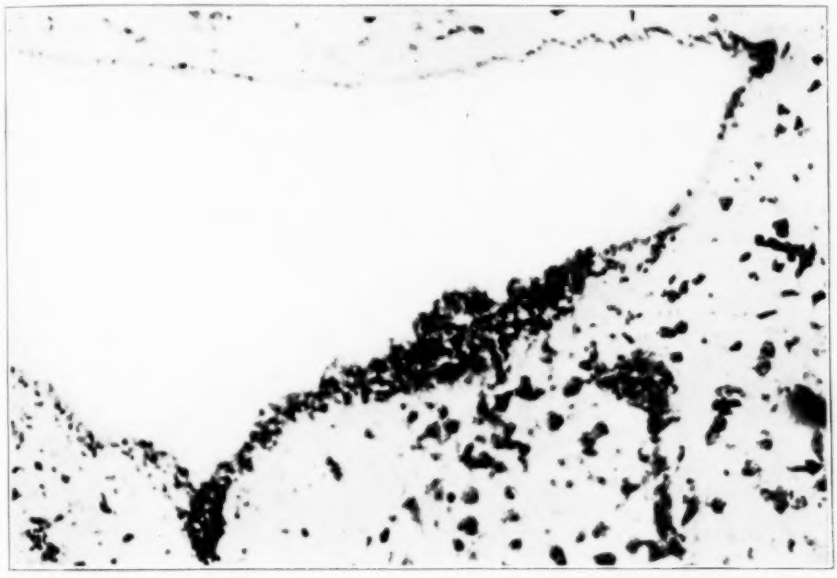

Fig. 1.—Section from a chicken showing ependymitis; Nissl stain.

nuclei, where all the cells were affected. Some of the cells there were merely deeply stained, unclearly delimited reticular masses, with no observable characteristic cell structure. Others showed only as lightly staining, vacuolated, disintegrating remnants. In some instances the development of the vacuoles could be clearly followed in the cell processes to a considerable distance from the cell body (fig. 3). The cell nucleus was usually either invisible or in various stages of regression.

Postmortem disintegration of nerve cells in animals, as Ostertag has also pointed out recently, is apt to occur quickly after the animal dies. But since in a large part of this material the brain was removed and fixed immediately after death, it is questionable whether these cell changes can all be referred to postmortem changes.

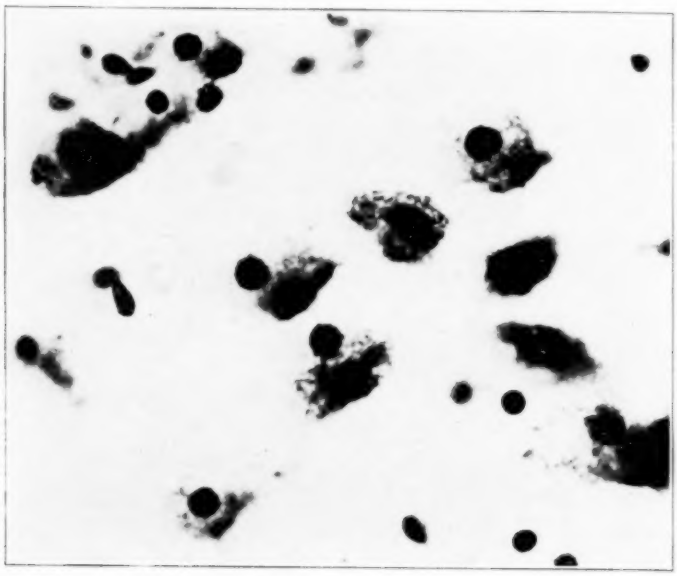

Fig. 2.—Section from a chicken showing "severe cell change;" Nissl stain.

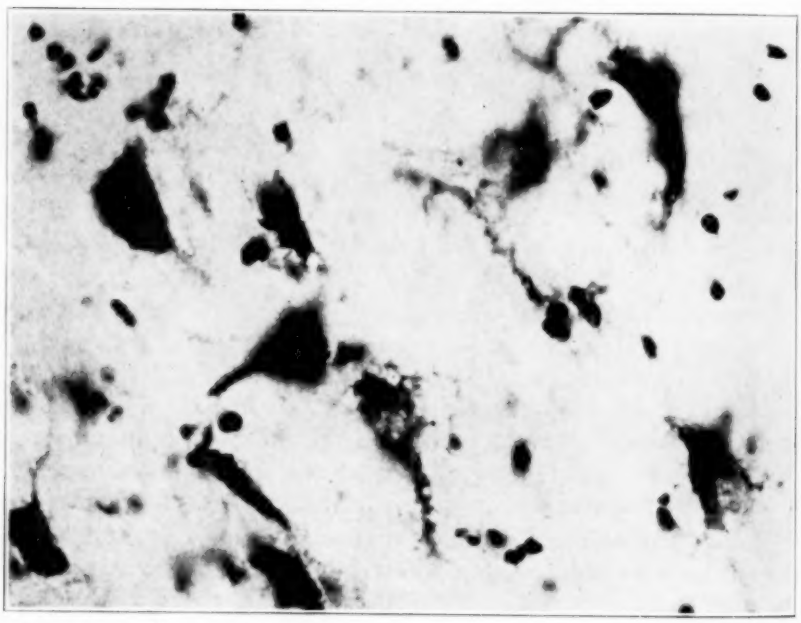

Fig. 3.—Section from a chicken showing severely changed nerve cells with vacuolization of cell body and processes; Nissl stain.

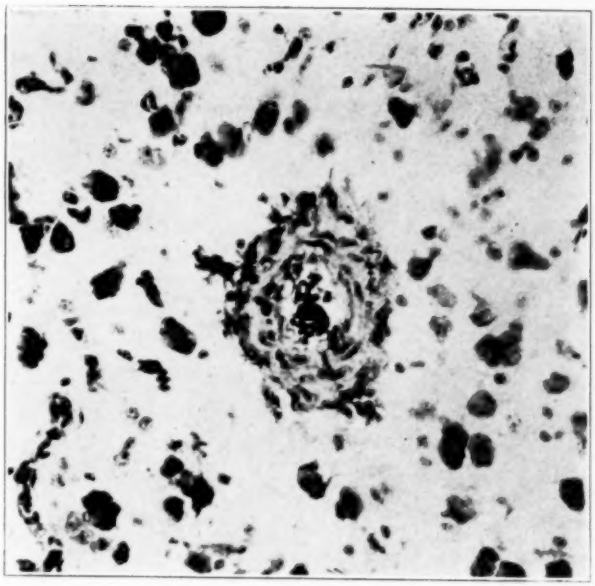

Fig. 4.—Section from a chicken: blood vessel with thickened adventitia.

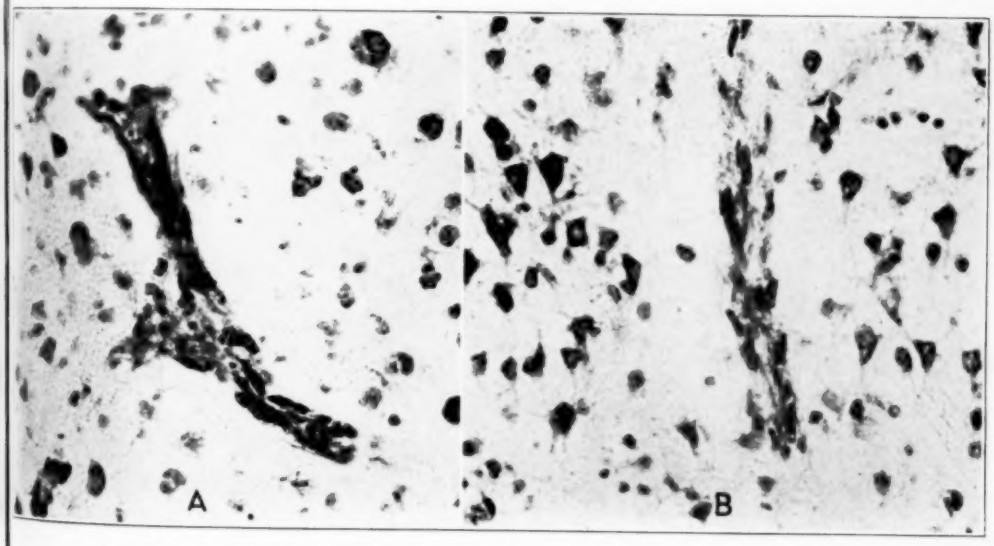

Fig. 5.—Small blood vessels walled with plasma cells: *A*, chicken; *B*, dementia paralytica; Nissl stain.

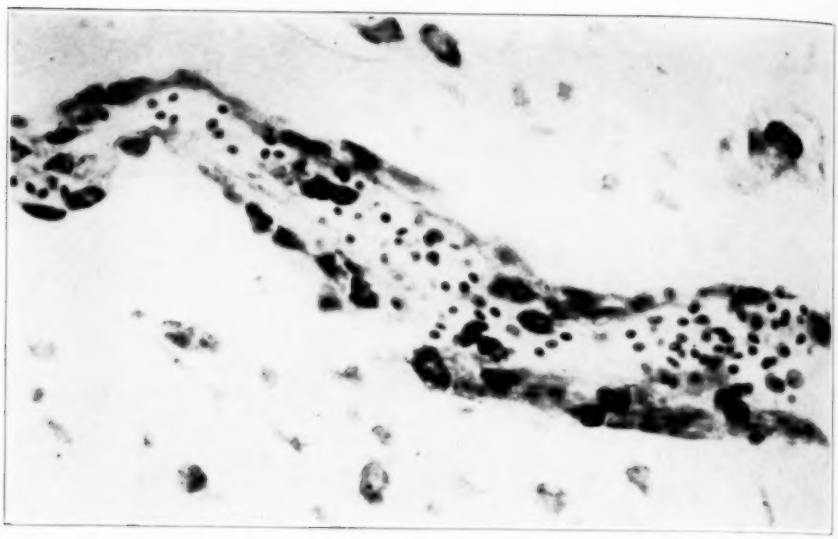

Fig. 6.—Section from a chicken: small vessel with plasma cells along its walls; Nissl stain.

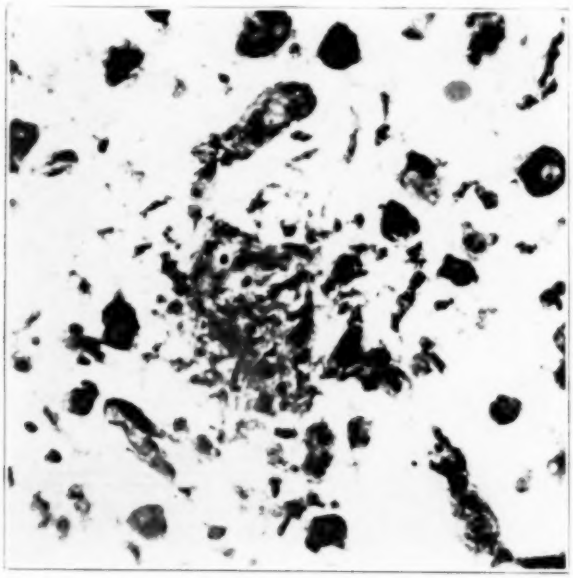

Fig. 7.—Section from a chicken: small glia cluster in the forebrain; note the Hortega cells at the periphery of the focus; Nissl stain.

In many cases the vessels showed enormous hyperemia. Even the smallest vessels were distended and filled with blood corpuscles. It should be mentioned in this connection that the red blood corpuscles in the chicken have nuclei that stain with all nuclear stains. This is apt to be confusing, since in lower magnifications the vessels are likely to appear infiltrated. It is possible that statements in the literature about infiltrated vessels should be considered with this point in mind.

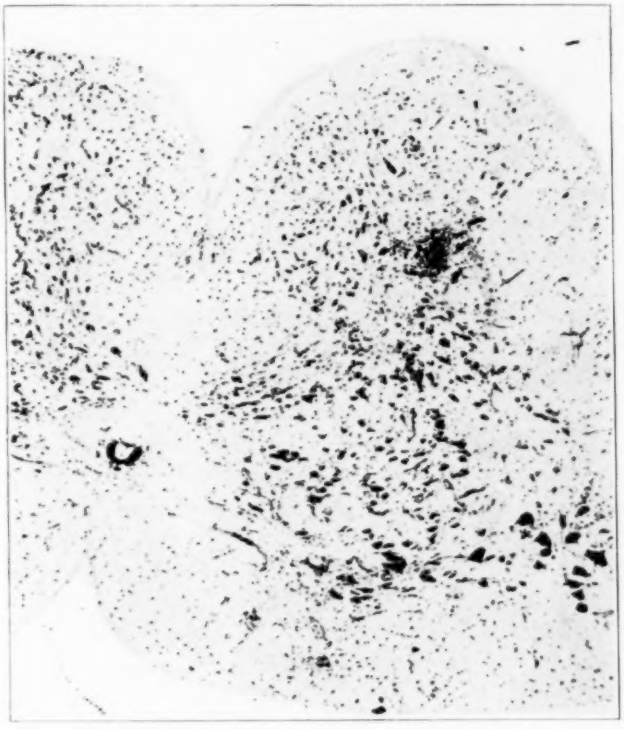

Fig. 8.—Section from a chicken: small glia custer in the gray matter of the dorsal horn of the spinal cord; diffuse increase of glia in the dorsal column as compared to the ventral columns; Nissl stain.

In some cases the walls of the vessels were very much thickened. This was chiefly due to a loosening and thickening of the adventitia, and may be spoken of as a kind of periarteritis (fig. 4).

In the smaller vessels there was frequently an infiltration with plasma cells (figs. 5 *A* and 6). This was sometimes so marked that the vessels were completely walled with these cells, which were often very large. The presence of the plasma cells was controlled with the Unna-Pappenheim stain for such cells.

As a reaction of the glia, the focal occurrence of glia clusters or nodules must be mentioned. Their distribution in the brain was ubiquitous. They occurred also in the spinal cord at various levels, in both the white and the gray matter (figs. 7 and 8). In the so-called optic cortex of the tectum they were practically absent. Only one small glia cluster was observed there in all cases. The clusters were seen frequently in the cerebellum, in the medulla and in all the various sections through the forebrain. Their number varied from a few or none at all to eight or ten in one low power field. They resembled in nature the glia clusters observed in man, first described for spotted fever but now recognized as a reaction occurring frequently in infectious, toxic and degenerative conditions. In some instances they were large and occurred perivascularly. There was occasionally a slight glial proliferation around the ventricles. But, as I have pointed out in my study of purulent meningitis, it is important to keep in mind that in the angles of the lateral ventricles there is normally, not only in children but also in adults, a conglomeration of glia cells that might be (and has been) mistaken for evidence of ependymitis.

On the basis of the Nissl stain alone, no definite statement with respect to proliferation of glia could be made with any certainty. Spatz has pointed out for the human brain that one cannot get from the Nissl stain an adequate picture of the sometimes enormous proliferation of Hortega glia in dementia paralytica. In the chicken, too, I have found that it is almost impossible to derive any clear impression of Hortega cell proliferation with this method. A special Hortega cell method is therefore indispensable. In some cases small blocks of material were fixed directly in a bromide formaldehyde mixture and stained by the original Hortega method. Other blocks, however, which had previously been fixed in formaldehyde were stained for microglia with the Kanzler modification of Hortega's method. The results obtained in this way were so satisfactory that the rest of the cases were examined for microglia only by this method. In some instances a Hortega cell proliferation was found which can be described only by referring to the well known picture of dementia paralytica in man (fig. 9). The cells were numerous and in some places were markedly elongated—typical rod cells. They were arranged in such regions in a parallel formation, as is also well known from the typical picture of dementia paralytica in man. In other cases Hortega cell proliferation was less marked.

The most striking findings were brought out with the elective stains for iron. The Spatz method revealed large amounts of iron along the vessels. With the Turnbull stain the distribution of this iron was investigated more thoroughly. In many cases the intra-adventitial iron deposits in the small vessels were relatively large. While most of this iron was free in the adventitial spaces, some also occurred in the adven-

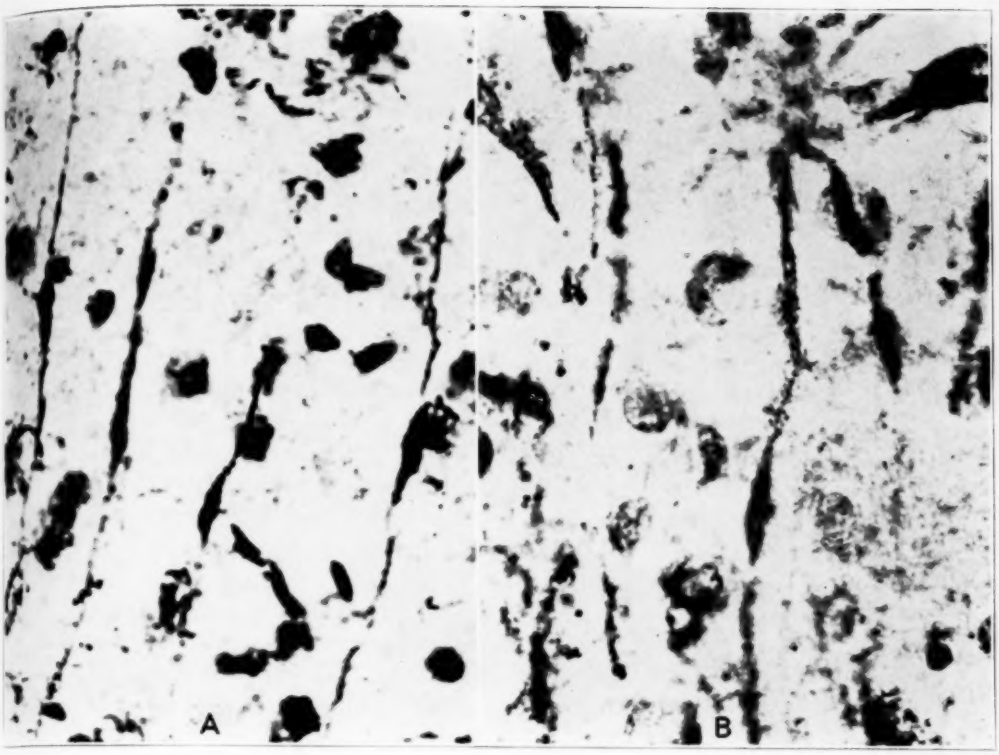

Fig. 9.—Rod cells: *A*, chicken; *B*, dementia paralytica. Kanzler stain.

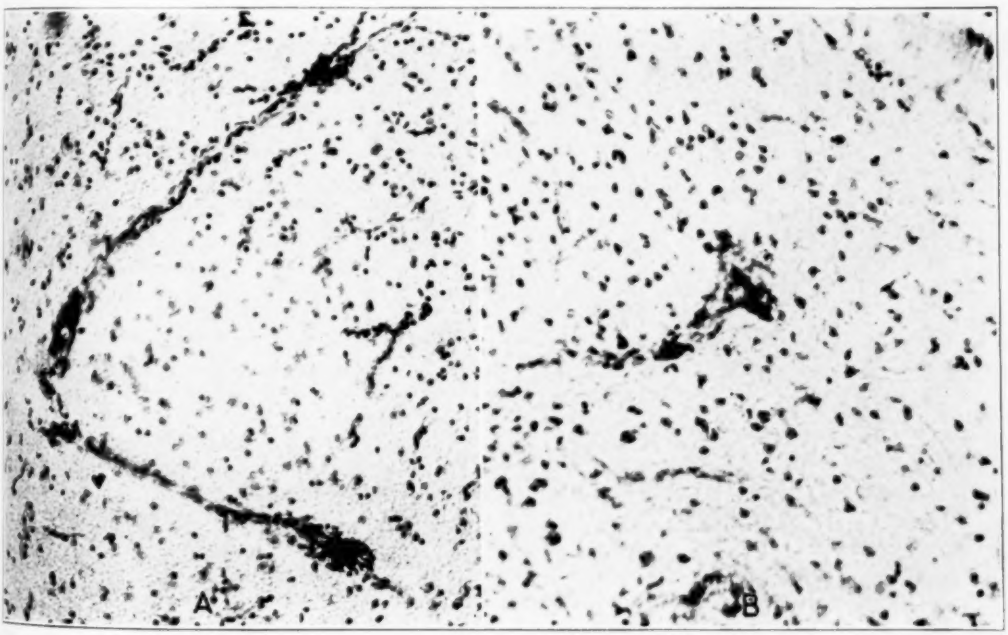

Fig. 10.—Intra-adventitial iron deposits (Paralyseeisen of Spatz): *A*, chicken; *B*, dementia paralytica. Turnbull stain.

titial cells. The blue-coated vessels standing out so clearly in the Turnbull-stained material were impressive (figs. 10*A* and 11). To a much less extent iron was also found in Hortega cells. In other types of glial elements practically no iron was seen. The quantity of the iron varied in different cases. Sometimes there was very much iron. The chief region where much iron was found was the forebrain, especially in its frontal part. Less iron was contained in the cerebellum, but there also it was striking. Small amounts of iron were also noted in the meninges, perhaps more in the cerebellum than in the forebrain (fig. 12). In the cord and medulla there was very little iron. It is especially noteworthy that the optic lobes (tecta) were practically free. This type of iron corresponds exactly in nature and distribution to that found in dementia paralytica (fig. 10). Spatz has called it dementia paralytica iron (*Paralyseeisen*), a term that has been generally accepted in neuropathology, for, with the exception of small amounts in a few isolated cases of trypanosomiasis, this type of iron deposit has never been found in man or in animals except in dementia paralytica. It is generally regarded as specific for this condition.[6]

It is not generally known how this type of iron was discovered in dementia paralytica. Lubarsch had noted that in the aorta and in some inner organs there were iron deposits in dementia paralytica. He then proceeded to examine the central nervous system for iron deposits, and made the discovery of this new addition to the pathologic anatomy of dementia paralytica. Later authors confirmed his observations. Hayashi's discovery of iron-coated vessels in dementia paralytica was made independently of Lubarsch. After I had found that this same type of iron can occur also in animals, I proceeded in the opposite direction from that of Lubarsch, and examined the aortas of the chickens. Large amounts of iron could be seen in the aorta perivascularly, and there was a fine line of iron at the junction of the media and adventitia. Marked infiltration with plasma cells was also noted.

The cord was examined at various levels. With the Nissl stain, besides the existence of circumscribed glia clusters already mentioned, there was noted a questionable increase of glia nuclei in the dorsal columns (fig. 9). It should also be mentioned here that a peculiar phenomenon frequently occurred in the Nissl stain: Both the axis cylinders and the myelin sheaths were clearly stained. In a number of cases the cord was examined with the myelin sheath stain. Small foci of demyelinization occurred, chiefly in the white matter, but also reaching into the gray matter. They were sharply delimited and occurred mainly in the anterior and lateral columns. Fat stains of corresponding sec-

6. For further details about iron findings see Wertham: Zur Frage des Eisenbefundes bei der Dementia paralytica auf Grund vergleichend histopathologischen Untersuchungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:62, 1931.

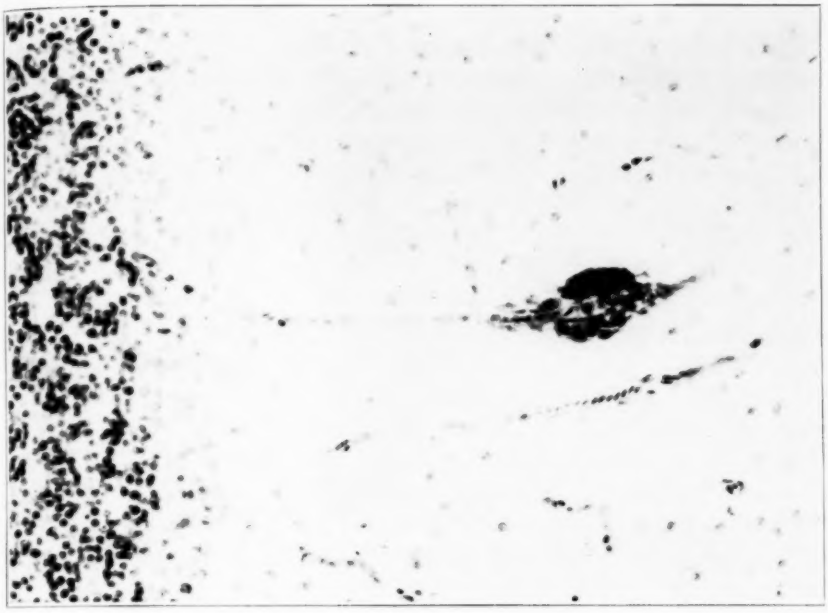

Fig. 11.—Section from a chicken; iron deposit-coated vessel in the molecular layer of the cerebellum ("dementia paralytica iron"). Turnbull stain.

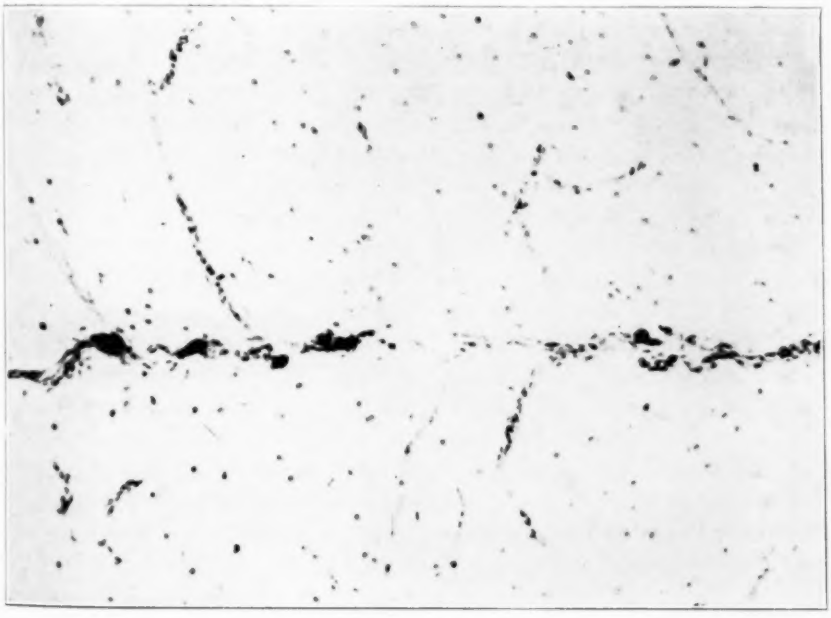

Fig. 12.—Section from a chicken: iron deposits in the meningeal spaces and small blood vessels of the cerebellum. Turnbull stain.

tions gave practically negative results, showing only very slight amounts of fat in the meninges. These stains were done with gelatin-embedded material, and the possibility that these small lesions are artefacts cannot be ruled out with certainty.

Myelin sheath and fat stains of the nervus opticus gave negative results in the cases examined except for very slight amounts of fat in the sheaths of the opticus. Samples of peripheral nerves showed no abnormal findings.

COMMENT

Of the total observations, three changes seem to stand out as having significance: the accumulation of iron in the intra-adventitial spaces and, to a lesser degree, in Hortega cells; the proliferation of Hortega cells, with the formation of rod cells, and the occurrence of plasma cells in the small vessel sheaths. The combined occurrence of these three features constitutes a definite histopathologic syndrome. The other features mentioned have, in comparison with these outstanding signs, less neuropathologic significance. Part of them, e. g., the nerve cell changes, the ependymitis granularis, etc., would fit with this syndrome, but their value is only secondary. The pathologic worth of glia clusters has been much overrated. The small lesions of demyelinization in the cord cannot be given any weight because of the possibility that they were due to artificial influences.

The features stressed as significant varied in degree in different cases. In some they were marked. The plasma cells were very large and on occasion formed a wall along the vessels. The iron was so plentiful that it could sometimes be seen in Hortega cells with only a low magnification, and the vessels in Turnbull preparations often seemed iron-coated to a marked degree. Hortega cell proliferation was especially striking when it took the form of very elongated rod cells in parallel formation. Other cases were studied in which plasma cells had to be sought, in which the Hortega cell proliferation was less marked and the amount of iron was less or relatively small. No correlation could be established between the variations in these observations and the clinical data presented by the chickens.

The syndrome represented by these observations will immediately suggest the picture of dementia paralytica. The histologic picture of dementia paralytica has varied greatly since the first valid anatomic changes in this disease were reported. Without discussing more fully this interesting historical development, it can be stated that the histologic diagnosis of dementia paralytica rests today on the combined occurrence of four cardinal signs. Three of these are the three features already mentioned: plasma cell infiltration (fig. 5 *B*), Hortega cell proliferation (fig. 10 *B*) and accumulation of iron in the intra-adventitial spaces of vessels and in Hortega cells (fig. 10 *B*). The fourth sign of

dementia paralytica, the demonstration of spirochetes in the tissue, is not, strictly speaking, a histologic but is rather a histoparasitologic sign. It is interesting that in chickens killed or dying during the crisis or a brief period after it, Spirochaeta gallinarum could be demonstrated with absolute regularity (Jahnel).

The finding of iron in the intra-adventitial spaces and in Hortega cells in the chicken must be especially emphasized, for this so-called "dementia paralytica iron" is considered today as absolutely pathognomonic for human dementia paralytica. Hayashi and Lubarsch discovered that this charactertstic occurrence of iron is one of the most specific signs of the disease, for plasma cells, although always present, are in some cases so sparse that it requires considerable search to find them. Spatz confirmed these results and in extensive investigations found this type of iron in no condition other than dementia paralytica and three cases of human trypanosomiasis. On his observations he based a new method of rapid histologic diagnosis of dementia paralytica. In chickens examined in this investigation this test gave the identical iron reaction on which today is based the rapid diagnosis of dementia paralytica with fresh human material.

There are, of course, other valuable histologic symptoms of dementia paralytica in addition to the four cardinal signs mentioned; but they must be definitely considered as secondary and not obligatory. Frontal atrophy, for example, so valuable a sign in the diagnosis of dementia paralytica, cannot be expected in every case, especially in early ones. Nor is diffuse or focal demyelinization of the cortex always present. Nerve cell changes belong to the picture of dementia paralytica, but they are not characteristic, and all attempts to see anything specific in them have so far failed.

It is interesting that some of the other features in the chickens do not disagree with the general picture of dementia paralytica. The small circumscribed foci of demyelinization that occurred in two chickens resemble very much the lesions that occur in dementia paralytica. The character of these lesions has been fully discussed in a previous paper.[7] The uncharacteristic nerve cell changes found in the chickens would not disturb the picture. Ependymitis granularis also is frequent in dementia paralytica.

One detail of the general distribution of the lesions in the chicken has some significance from the point of view of a comparative study of the central nervous system. The so-called optic lobes of the chicken were found to be remarkably free from any pathologic changes. An interesting parallel may be drawn between this fact and the fact that

7. Wertham, F.: Small Foci of Demyelinization in the Cortex and Spinal Cord in Diffuse Sclerosis: Their Similarity to Those of Disseminated Sclerosis and Dementia Paralytica, Arch. Neurol. & Psychiat. **27**:1380 (June) 1932.

in dementia paralytica the optic cortex is infrequently involved in the paralytic process, and then only to a much less extent than the more anterior parts of the cortex or the striatum.

The most conspicuous of the other features are the glia clusters. Their pathognomonic significance is slight and has been much exaggerated in animal pathology. This type of lesion occurs in all sorts of infectious and toxic and also degenerative conditions. I have depicted it in acute phosphorus poisoning.[8] It seems from the literature on the pathology of chickens that in these fowls, and perhaps also in other animals, this is a type of reaction that occurs easily.

The changes in the plexus, the marked hyperemia and the indication of endarteritic changes seem to have little pathologic importance.

In summarizing, one may say that if one considers the chickens in which the changes are most pronounced and regards the rod cell proliferation, the plasma cells and the iron-coated vessels, any observer ignorant of the source of the material would pronounce the picture to be that of dementia paralytica (figs. 6, 10 and 11). In fact, I have tried this experiment successfully with persons familiar with the histopathologic picture of dementia paralytica. The question arises, therefore, whether one can draw the conclusion that by inoculation of chickens with Spirochaeta gallinarum one can produce the histopathologic picture of a disease closely paralleling dementia paralytica in man.

CONTROL OBSERVATIONS

In order to come nearer to a solution of this question, the second part of this investigation was carried out, namely, the study with identical methods of a series of normal chickens. These chickens were of different breeds and came from different sources. Altogether thirteen control chickens were examined. The findings in the normal chickens were decidely unexpected and can be briefly described. The iron stains were positive, in some cases markedly, in other cases in lesser degree. Plasma cells were found in the smaller vessels. The Hortega cells were proliferated, in some instances with markedly elongated forms. All the other lesions described for the previous series of chickens occurred in the controls, in varying degrees, with the exception only of the small foci of demyelinization in the cord. Since the cords were not examined with the myelin sheath stain in all cases, no emphasis can be laid on the negative observation.

There were only three differences between the "normal" chickens and those inoculated with Spirochaeta gallinarum. In one chicken, which died eight days after inoculation and which had very positive findings

8. Wertham, F.: The Central Nervous System in Acute Phosphorus Poisoning, Arch. Neurol. & Psychiat. **28**:320 (Aug.) 1932.

of spirochetes in the blood with marked agglomeration, iron in the typical distribution occurred in a marked degree, more than in any of the other chickens. (In this chicken there was also a definite malformation of the forebrain.) In another chicken, killed five days after the inoculation, at the height of the crisis, the exaggerated rod-shaped form of the microglia was conspicuous. A third chicken, which was killed ten months after the inoculation, showed a great number of the glia clusters described, as many as eight or ten in a low power field. This chicken was also the one with the most marked lesions in the cord.

These three differences would seem to carry little weight. First, they are only quantitative, since the same type of lesions occurred in other chickens. Quantitative significances cannot carry much weight here because the number of the inoculated chickens examined was so much greater than the number of the controls. In a larger group of controls, similar quantitative accentuations might easily have been found.

Comparison of the chickens with experimental spirochetosis gallinarum with the "normal controls" shows, therefore, that in both there is either indicated or fully fledged a histologic picture bearing the closest resemblance to the histologic syndrome of dementia paralytica in man. It can therefore be demonstrated that this histologic picture occurs spontaneously in chickens. Even if Spirochaeta gallinarum, as is unlikely, produced this encephalitis in the experimental chickens, the condition is the same as that which occurs spontaneously in the control chickens.

Does the type of disease here described correspond to any of the known diseases of chickens? Histologic examinations of the central nervous system in chickens with the finer analytic methods are scarce. Systematic investigations of chickens suffering from diseases involving the central nervous system, with the Hortega strain for microglia or with the iron stain for example, have not been made. Even investigations with the Nissl stain seem to have been made only in rare instances.

One may rule out cyanolophia, or chicken pest,[9] for, apart from its definite symptoms, in an epidemic of this disease many chickens would have died, and not merely some of those studied in this investigation. A diffuse encephalomyelitis has been described as occurring in cyanolophia.[10] A great deal of stress has been laid on the occurrence of circumscribed clusters of glia, but it is known from human neurohistology that they have little significance for the evaluation of pathogenic processes. About the involvement of the central nervous system

9. Gerlach, F.: Geflügelpest, in Kolle, Kraus and Uhlenhuth: Handbuch der pathogenen Mikroorganismen, Jena, Gustav Fischer, 1929, vol. 9.

10. Seifried, O.: Pathologie der neurotropen Viruskrankheiten der Haustiere, Ergebn. d. allg. Path. u. path. Anat. **24**:554, 1931.

in leukosis (Ellermann and Bang) or leukemia [11] no adequate data are available. In human leukemia the central nervous system may be affected.[12] Whether chicken leukosis belongs to the group of leukemias found in man has been questioned by F. Henschen,[13] who regarded it as a special disease. These leukemias of chickens may be very similar to the tuberculosis of chickens with which from 7 per cent to 15 per cent of the fowls in Germany are said to be affected.[14]

An interesting neuropathologic disease in chickens is the so-called fowl paralysis first described by Marek. In this condition the animals show a paralysis of the legs and wings. Death may occur suddenly; in some cases recovery has been observed. Whether all the cases described as cases of "fowl paralysis" belong to one group seems doubtful. Pappenheimer, Dunn, Cone and Seidlin [15] have recently given a full description of this condition with a comprehensive consideration of the literature.[16] They give the main clinical characteristics as partial paralysis of the wings, the legs and rarely the neck, and gray discoloration of the iris with blindness. The condition affects mainly the peripheral nerves, which show marked infiltrations. Infiltrations were also found in the cord and, to a much smaller degree, in the brain. The circumscribed proliferations of glia, glia nodules, occurred abundantly. Only the involvement of the peripheral nerves is held responsible for the paretic symptoms. It is interesting that these authors also found "perivascular infiltrations" in the brain and cord in many normal chickens. These chickens were seemingly healthy and came from unaffected sources. Pappenheimer and his co-authors stated that they

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11. Ellermann, V.: Die uebertragbare Hühnerleukose (Leukämie, Pseudoleukämie, Anämie), Berlin, Julius Springer, 1918. Warthin, S. A.: Leukaemia of the Common Fowl, J. Infect. Dis. **4**:369, 1907. Knuth, P.: Leukaemie der Säugetiere und des Geflügels, in Kolle, Kraus and Uhlenhuth: Handbuch der pathogenen Mikroorganismen, Jena, Gustav Fischer, 1928, vol. 9.

12. Fried, B. M.: Leukemia and the Central Nervous System, Arch. Path. **2**: 23 (Jan.) 1926.

13. Henschen, F.: Zur Frage der Hühnerleukämie, Arch. f. Tierheilk. **43**:203, 1917.

14. Klimmer, M.: Die Uebertragung der Geflügeltuberkulose auf Menschen und das Vorkommen von Tuberkelbazillen in Hühnereiern, Berl. tierärztl. Wchnschr., 1930, p. 702; abstr. Internat. Rev. Poultry Sc. **3**:44, 1930.

15. Pappenheimer, A. M.; Dunn, L. C., and Cone, V.: Studies on Fowl Paralysis (Neurolymphomatosis Gallinarum): I. Clinical Features and Pathology, J. Exper. Med. **49**:63, 1929. Pappenheimer, A. M.; Dunn, L. C., and Seidlin, S. M.: Studies on Fowl Paralysis (Neurolymphomatosis Gallinarum): II. Transmission Experiments, ibid. **49**:63, 1929.

16. Compare also McGaughey, C. A., and Downie, A. W.: Preliminary Report on an Outbreak of Fowl Paralysis in England, J. Comp. Path. Therap. **43**:63, 1930; The Prevalence of Fowl Paralysis in England, Vet. Rec., Dec. 13, 1930. Doyle, L. P.: Neuritis in Chickens, J. Am. Vet. M. A. **21**:622, 1926.

would have regarded these slight infiltrations as normal if they had not also found in material received from Edinburgh that such infiltrations were completely absent. Seifried [10] has described a condition closely resembling mild forms of Marek's "fowl paralysis" in which the peripheral nerves macroscopically show no changes, and in which the infiltrations were not of such a marked degree. He also emphasized the occurrence of little glia clusters in the brain.

In "fowl paralysis" the involvement of the peripheral nerves is entirely in the foreground. Dobberstein and Haupt [17] classified the condition, therefore, with nutritional neuritis among the group of forms of epidemic polyneuritis. In the cases of the present study no involvement of the peripheral nerves was found.

Changes in the cord described by McGowan [18] in primary anemia and a cerebellar disorder in chicks reported by Pappenheimer and Goettsch [19] are of interest in a consideration of the histopathology of birds, but have less direct bearing on the present discussion.

The condition described in the present study is evidently not identical with any of the conditions described in the literature. In the attempt to compare it with these diseases, the fact must be taken into account that none of the latter were systematically investigated with a combination of the necessary analytic methods of neurohistology, such as the Nissl stain, selective glia stains and the iron stain. It seems that the histopathologic condition of the central nervous system here considered is evidence of a hitherto undescribed form of spontaneous disease in chickens which need not cause clinically observable symptoms.

Concerning the etiology of this encephalitis no statement can as yet be made. So far, with different staining methods, I have not found any structures in the tissue that were similar to any known microorganisms and could be considered as the etiologic factor of this disease. Further investigations will have to show whether some such structures may be found in some animals. Experiments in which brain substance from chickens with this spontaneous disease was transmitted to canaries have not been successful. Here is evidently a task of neuropathologic and general pathologic interest. It is necessary to investigate other species of birds with appropriate methods and young chickens in different stages of development. In a series that is entirely free from the changes described, attempts should be made to find out,

17. Dobberstein, J., and Haupt, H.: Ein Beitrag zur Polyneuritis des Geflügels, Ztschr. f. Infektionskr. **31**:58, 1927.

18. McGowan, J. P.: Subacute Combined Degeneration of the Cord in Primary Anaemia of the Fowl, Brit. M. J. **2**:204 (Aug. 9) 1930.

19. Pappenheimer, A. M., and Goettsch, M.: A Cerebellar Disorder in Chicks, Apparently of Nutritional Origin, J. Exper. Med. **53**:11, 1931.

by way of transmission experiments, whether these chickens are susceptible to infection by Spirochaeta gallinarum. Only then can the effect on the central nervous system of this parasitologically and histoparasitologically so unusually well known and easily produced infection be determined.

The question may be raised whether a special spirochete is responsible for this disease of chickens. Just as it is known that in man different types of spirochetes occur, such as the spirochetes of recurrent fever and the spirochete of syphilis, so it is not impossible that in addition to the epidemic spirochetosis of chickens another kind of disease due to spirochetes comparable to syphilis may occur in chickens. Jahnel has examined the central nervous system of chickens extensively for spirochetes. He has never found in chickens in which there was no evidence of Spirochaeta gallinarum, any evidence of organisms that might have been interpreted as another kind of spirochete. Altogether, it does not seem probable that some kind of spirochete is responsible for this spontaneous disease in chickens. It would be unjustifiable to assume from the identity of the iron tests alone that there is an etiologic-biologic relationship between this spontaneous disease in birds and dementia paralytica.

CONCLUSIONS

Ever since a pathologic anatomy of dementia paralytica has existed, attempts have been made to produce in animals or to find there histopathologic processes of the central nervous system comparable to the picture of dementia paralytica. Among these must be mentioned in the first place the spontaneous encephalitis of rabbits, which Nissl first described at the beginning of the century, pointing out then the similarity of the condition to dementia paralytica. Nissl's observations seem to have been forgotten, for later in experimental studies on inoculation with Spirochaeta pallida in rabbits the spontaneous encephalitis of rabbits was mistaken for an experimentally produced effect of Spirochaeta pallida. In experiments on the transmissibility of encephalitis epidemica this spontaneous encephalitis of rabbits played the same rôle of joker.

Nissl mentioned also a spontaneous encephalitis in dogs which resembled in some respects the picture of dementia paralytica. A further disease of animals that was compared with dementia paralytica is the trypanosome infection that has been investigated by Spielmeyer. Recently, Bodechtel [20] described a spontaneous encephalitis in a monkey which he compared to dementia paralytica. But the iron deposits found

20. Bodechtel, G.: Spontanencephalitis bei einem Affen, Ztschr. f. Hyg. u. Infektionskr. **111**:331, 1930.

were of an entirely different nature from those in dementia paralytica. They occurred only locally in places where there was a definite proliferation of vessels. There was also an intensive local degeneration in the white matter, with fresh phenomena of dissolution demonstrable with the fat stain. This would be an unusual lesion for dementia paralytica.

All other observations of the diseases of animals mentioned that have been compared with dementia paralytica date back to a time when the modern analytic methods, with the aid of which the findings in the chickens of this study were demonstrated, were not known or not applied in neurohistology. Moreover, the essential features of the histologic picture of dementia paralytica have changed considerably since then. From the point of view of the conception of the essential histologic characteristics of dementia paralytica here outlined, it can be stated that at present the disease of chickens described in the present study bears the closest resemblance to dementia paralytica of all the animal diseases that have ever been compared with it.

The histologic picture of dementia paralytica has had to be considered as something specific, which seemed without any parallel in pathology. The iron deposits in the central nervous system had to be regarded as an isolated phenomenon, the study of which remained entirely on a descriptive level. It has been shown in the present study that the essential histologic features of dementia paralytica, including the iron deposits, constitute a reaction of the central nervous system that may exist under totally different biologic circumstances, namely, as the expression of a new form of spontaneous disease in chickens which need not cause any clinical symptoms. This opens the way for a closer study of some of the histologic symptoms of dementia paralytica on animal material, which is more open to investigation than material from human cases, which can usually be examined only in the end-stages of the disease.

SUMMARY

1. A description is given of the histologic lesions of a new spontaneous disease in chickens, the etiology of which is not yet determined.

2. The three chief histologic signs of this condition are infiltration of small vessels with plasma cells, proliferation of Hortega cells with formation of rod cells and iron deposits in intra-adventitial spaces and in the Hortega cells.

3. It is pointed out that these correspond to what must be considered the three cardinal histologic signs of dementia paralytica (the changes of the nervous parenchyma in dementia paralytica are diagnostically less significant because they are uncharacteristic and may be inconspicuous in early cases).

4. The demonstration of this spontaneous disease in chickens shows that the essential histologic lesions of dementia paralytica are unspecific, and that they constitute a pathologic reaction of the central nervous system possible under totally different biologic and etiologic conditions.

5. It seems likely that lesions in the brain that have been ascribed to infectious or nutritional diseases in birds are at least in part due to the spontaneous disease described here.

6. The evidence given here that the so-called "dementia paralytica iron" which has been regarded as specific for dementia paralytica occurs also in animals opens a path to the closer study of the development of this important neuropathologic phenomenon which is as yet only descriptively known.

7. In the present study, the central nervous system of birds is for the first time histopathologically examined with a combination of all the pertinent modern methods used in human neuropathology.

INJURY AND REPAIR WITHIN THE SYMPATHETIC NERVOUS SYSTEM

II. THE POSTGANGLIONIC NEURONS

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The postganglionic sympathetic nerve fibers can regenerate. First, Tuckett,[1] in 1896, and later, Machida,[2] in 1929, demonstrated this clearly, with the fibers leaving the superior cervical ganglion for the eye. Observations on the return of vasomotor and sudomotor function after section and suture of a peripheral nerve, made in the experimental animal by Kilvington and Osborne,[3] in 1907, and on man by Head,[4] in 1920, and by Trotter and Davies,[5] in 1909, indicate that the postganglionic fibers are, indeed, among the fastest growing of the fiber components of such a nerve. Recently, however, a new method has become available by which the state of sympathetic function in surfaces relatively free from hair can be studied. By the determination of the presence or absence of action currents in the skin, either spontaneous waves in the electrical potential of the skin or the reflexly elicited galvanic skin response, the presence or absence of sudomotor innervation may be established. Furthermore, the resistance offered by the skin to the passage of a small constant current provides a more or less quantitative measure of sympathetic activity in the part involved. That these phenomena afford a most sensitive index to the effect of lesion and the course of repair of preganglionic sympathetic fibers has been shown in the first part of this study.[6] It was found that section

From the Anatomical Laboratory of the Johns Hopkins University and the Department of Psychiatry of the Johns Hopkins Hospital.

1. Tuckett, J. L.: J. Physiol. **19**:267, 1896.

2. Machida, K.: Bull. Johns Hopkins Hosp. **45**:247, 1929.

3. Kilvington, B., and Osborne, W. A.: J. Physiol. **35**:460, 1907.

4. Head, H.: Studies in Neurology, New York, Oxford University Press, 1920, p. 288.

5. Trotter, W., and Davies, H. M.: J. Physiol. **38**:134, 1909.

6. Tower, S. S., and Richter, C. P.: Injury and Repair Within the Sympathetic Nervous System: I. The Preganglionic Neurons, Arch. Neurol. & Psychiat. **26**:485 (Sept.) 1931.

of the preganglionic rami to the stellate ganglion produced a great, but transient, increase in the resistance of the skin, amounting to from ten to one hundred times the maximum of normal resistance. Both the spontaneous waves and the galvanic skin reflex disappeared temporarily. In a few weeks, however, resistance was down again, and on the twenty-eighth day, on an average, the spontaneous waves reappeared. The reappearance of these currents was taken as evidence of the reconstitution of connection between the central nervous system and the periphery. The reflex response returned a day or two later. The present research was designed to extend these methods to the study of lesion and repair of the postganglionic neurons.

METHODS AND MATERIAL

The technic of measuring the skin resistance and of determining the presence or absence of the galvanic skin currents has already been fully described.[6] The galvanometer leads are attached, one to the central pad of the forepaw, the other to the pinna over the site of a skin puncture. The resistance offered to the passage of a small constant current is determined by the use of a potentiometer and a string galvanometer. The action currents in the skin are led off to the galvanometer string and its movements are photographed on bromide paper.

Eighteen young adult cats were used for the experiments. The right stellate ganglion was selected as the point of attack on the postganglionic neurons supplying a paw pad. When the ganglion had been exposed, under ether anesthesia, in the vertebral end of the first intercostal space, the branches leading from it were identified and cut—the visceral rami, the two strands forming the ansa subclavii, the vertebral nerve (gray rami communicantes to the lower cervical nerves) and the gray and white rami to the first and second thoracic roots. Thus all the nerve fibers leaving the ganglion, both preganglionic and postganglionic, were cut and the ganglion was left in situ, in connection only with the thoracic sympathetic trunk.

The white rami of the first and second thoracic nerves were, of necessity, included in the section of the corresponding gray rami. However, the first part of this study has shown that these white rami are not utilized to transmit the spontaneous waves and galvanic skin reflex to the forepaw pad, and that they are of negligible importance in maintaining the skin resistance of the pad at a normally low figure. Hence, section of these white rami in conjunction with the gray is without significance for this study.

Control.—The normal left forepaw pad afforded control of observations made on the partially denervated right. In a healthy cat the skin resistance of a normally innervated forepaw pad ranges between 2,500 and 30,000 ohms. Readings above the last figure may be obtained after ether anesthesia, in general infections or with a local infection near the pad. But even in the severest of these disorders, 200,000 ohms is a very high figure. The skin action currents are less reliable. In the great majority of cats the galvanic skin response never fails in a normally innervated paw pad. On the other hand, the spontaneous waves are quickly suppressed by infection or anesthesia. The first paper of this study[6] presented the figures on which these statements are based.

OBSERVATIONS AND INTERPRETATION

Skin Resistance.—The effect on the skin resistance of the sectioning of the postganglionic sympathetic fibers for the paw pad was qualitatively similar to the effect of preganglionic section, but quantitatively far greater. Resistance started to rise at once, mounting in twenty-four hours to from ten to fifty times the 30,000 ohm maximum of normal resistance. During the next three to five days, the increase continued

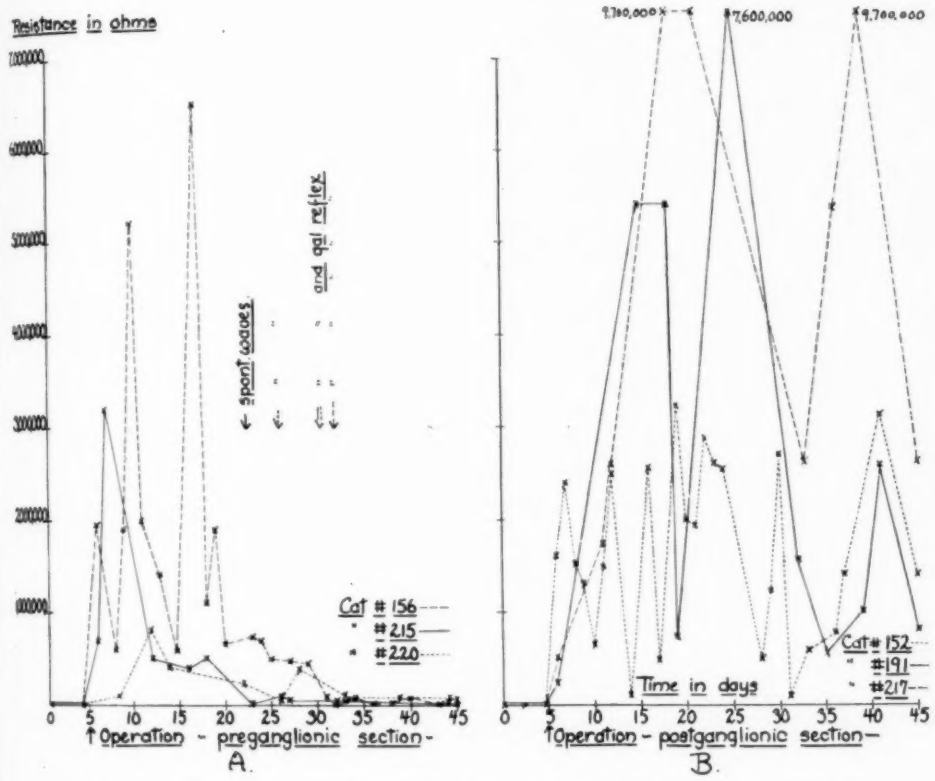

Chart 1.—Data on skin resistance for the first six weeks after operation: (*A*) from three cats after preganglionic section, and (*B*) from three cats after postganglionic section. The resistance in ohms is given on the ordinates, and the duration of the experiment, in days, on the abscissas. The arrows in (*A*) indicate the reappearance of spontaneous waves and the galvanic skin reflex after preganglionic section. After postganglionic section these did not reappear.

until an average of nearly 3,000,000 ohms had been reached, a figure one hundred times the normal limit. At this level the average resistance was stabilized for a period of months, although the daily records showed enormous fluctuations. At this time also, peaks of resistance

(shown in chart 1), readings above 5,000,000 ohms, began to appear. In the series of eighteen cats there were but two exceptions to this characteristic postoperative course; two animals, sickly at the time of operation, showed maximum resistance readings on the first day and died of pneumonia shortly thereafter. As was the case after preganglionic section, the individual cats responded quantitatively differently to the lesion. There were animals whose skin resistance was persistently high, and those whose resistance was low, with the usual reaction somewhere between. Chart 1 presents records illustrative of each type of response for the first six weeks after operation. These

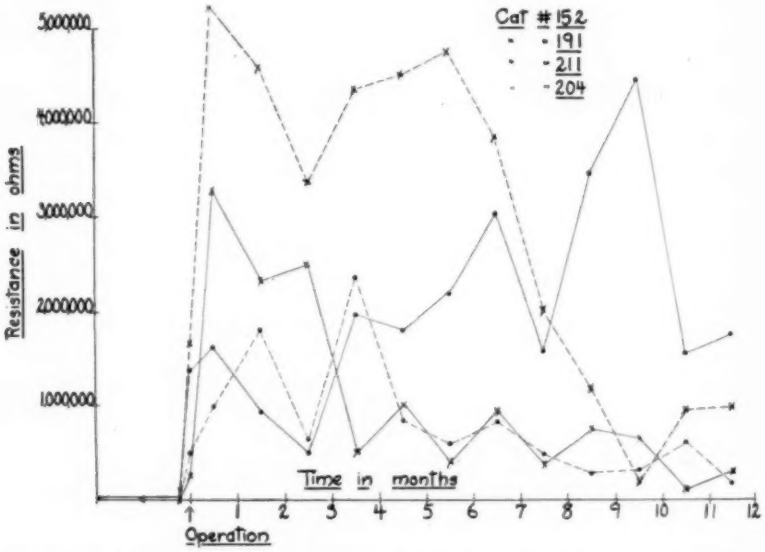

Chart 2.—Data on skin resistance from four cats for the first day after section of all the nerve fibers leaving the stellate ganglion, and averaged month by month for a year thereafter.

are placed, for comparison, beside similar records of preganglionic lesion, reproduced from part I of this study.[6]

Four cats of the series were kept from a year to a year and a half after operation. Chart 2 presents data on the skin resistance of each of these animals on the first day after sympathetic denervation, and the average month by month for a year thereafter. Three of the animals (cats 191, 204 and 211) had postoperative courses that were roughly similar. The resistance shot up on the first day, and continued to mount during the first week until a level from fifty to two hundred times the normal maximum had been reached. Then the steady rise stopped, and for a period of from three to six months the resistance oscillated

above and below this stabilization figure. After this phase, the resistance rapidly declined again. Then, in the last four to eight months of the year, resistance was again stabilized, but at levels comparable with those of the first day, 1,000,000 ohms or less. Even when the records were continued to the fifteenth month (cats 204 and 211), this level was not further reduced. Readings within the range of normal were not at any time obtained.

The daily and weekly variations in skin resistance so clearly shown in chart 1 were unfortunately suppressed in chart 2 by the averaging of the eight or ten readings constituting a month's data. None the less they were characteristic of the whole middle phase of the postoperative course. These fluctuations had a certain form. The resistance rose during a period of days or weeks to 5,000,000 or 10,000,000 ohms and subsided again. Crudely cyclic, these waves appeared and reappeared for months in seemingly normal animals and with no corresponding increase of resistance in the control paw pad. Then at the time when the high average level of skin resistance began to be finally reduced, they disappeared and did not recur. Eleven million ohms was the maximum figure for such a crisis in a healthy animal. However, resistance readings of between 20,000,000 and 25,000,000 ohms were obtained in animals with local or general infection.

Although three of the cats (cats 191, 204 and 211) presented records similar in their postoperative course, the fourth (cat 152) was in almost every respect an exception. This animal showed indeed the usual reaction to sympathetic denervation on the first day, but little subsequent increase of resistance until the sixth month. Then, when resistance was falling in the other cats, in this animal it reached unprecedented levels. And for the last year of the animal's life (this cat was kept the longest of the four) the skin resistance maintained an average of 2,500,000 ohms. At this time the other cats were registering a million ohms or less.

Skin Action Currents.—On the skin action currents postganglionic sympathetic section had exactly the effect of preganglionic section. Both the spontaneous waves and the reflexly elicited galvanic skin response were immediately and completely abolished. In contrast, however, with the course after preganglionic section, after postganglionic section the skin currents never reappeared. To be sure, the usual high level of skin resistance prevented routine examination for these functions, but whenever the resistance dropped below 400,000 ohms, the currents could be and were tested for. In four of the series of eighteen cats, this condition never obtained, but in the remaining fourteen the examination was possible. In the group of animals surviving operation for a year, and especially in the later months, resistance was frequently low, some-

times for weeks, and the skin currents were repeatedly sought. But never in any animal was there trace either of the spontaneous waves or of the galvanic skin response, even a year and a half after operation.

However, to make additionally certain that small action currents were not being obscured, drugs were used to lower the level of skin resistance. Pilocarpine, in doses of $\frac{1}{20}$ grain (0.003 Gm.), and bulbocapnine (55 mg.) markedly reduce resistance, causing it to drop from levels of 1,000,000 ohms and more to 100,000 ohms or less. These drugs were given several times to each of the animals still alive a year after operation without at any time bringing out the slightest trace of the galvanic skin currents.

Finally, during the last month or two of life, the ulnar and median nerves were laid bare in these same animals, and the skin currents were sought by direct stimulation (tetanizing current from a Harvard inductorium, the secondary coil at from 10 to 8 cm., two cells in the primary circuit). Under these conditions a normal paw pad yielded marked action currents, but when connected with a pad affected by the lesion, the galvanometer string was entirely quiet.

Sweating.—Similarly to the loss of the skin action currents, sudomotor function was also completely and permanently abolished on the forepaw on the side of lesion. The drugs used (pilocarpine and bulbocapnine) and direct stimulation of the ulnar and median nerves failed to bring out the faintest trace of moisture on the toe or paw pads. Yet the normal left forepaw pad, under the same stimulation, poured out sweat in large droplets.

From the evidence so far presented we may now consider the effects of postganglionic sympathetic lesion as of two degrees of severity. On the one hand, the suppression of sudomotor activity and of the skin action currents was immediate, complete and permanent. For as long as a year and a half after operation there was no sign of recovery in either of these functions. On the other hand, skin resistance showed a progressively changing postoperative course in which three phases may be distinguished. There was an initial period, of a week or less, during which the resistance continued to rise. This was followed by a second period of months, during which the resistance maintained a fairly constant high average level, with enormous daily fluctuations which are at present inexplicable. Finally, in three of four cats, after an abrupt decline, the skin resistance reached stability at a level comparable with the readings of the first day after operation, but the range of normal was not encroached on.

Reoperation.—To discover, if possible, the mechanism behind the lowered skin resistance of three of the four long-surviving cats, a second series of operations was performed. First, in three cats (152, 204 and

211) the right stellate ganglion was excised in the fifteenth or eighteenth month after the initial operation. Surprisingly, the effect on skin resistance was in each case slight, no more than etherization would occasion. Indeed, the only apparent effect of removal of the stellate ganglion was to reestablish the Horner's syndrome from which each of these animals had recovered five or six months after the first operation. One week after the excision of the stellate ganglion, two of the animals (152 and 204) were again operated on. This time the spinal nerves, from the sixth cervical to the first thoracic, were exposed on the right side as they issued from the muscles covering the vertebral column, and each was cut. The immediate effect of this operation was different in the two animals. Cat 204, one of the three in which resistance had been low for many months, showed a temporary reaction in which the resistance rose from an average of 350,000 ohms for the week elapsing between the stellate ganglion and brachial plexus operations to 2,350,000 ohms for the week following, and to 5,400,000 ohms for the second week, readings equaling the highest ever given by this animal. But by the fourth week, the resistance was again below half a million ohms, and stayed there. In contrast, section of the brachial plexus in cat 152 was as lacking in effect on the skin resistance as removal of the stellate ganglion had been. In this animal the skin resistance, which was still very high, was apparently totally independent of any nervous influence.

HISTOLOGIC OBSERVATIONS

The long-surviving cats were finally examined histologically. The animals were killed with ether, and the blood vessels were washed out with physiologic solution of sodium chloride. The middle third of the paw pad was excised and dropped into Bouin's fluid.[7] Lastly, the whole body was fixed by vascular injection of 80 per cent alcohol. The stellate ganglia removed at operation had previously been fixed in alcohol.

The results of histologic study were illuminating. Nissl preparations of the stellate ganglia all showed marked degeneration and fibrosis. Complete serial sections of the ganglia removed at operation from cats 152 and 211 contained, indeed, not a single recognizable nerve cell. The specimen from cat 204 showed perhaps half a dozen cells in each 5 micron section. The ganglion from cat 191 contained, by estimate, about one-tenth the number of cells of the left control. However, in this ganglion, which was the only one of the four fixed by injection, the cells present were large and the Nissl substance was normal in

7. Solution of formaldehyde, U. S. P., 500 cc.; distilled water, 1,500 cc.; glacial acetic acid, 100 cc., and trinitrophenol to the saturation point.

appearance. On the other hand, the sweat glands of the paw pads, stained by iron hematoxylin, though atrophic, were not actually degenerated.

When we integrate the histologic observations and the physiologic findings, the condition of the sympathetic innervation to the forepaw a year or more after section of the gray rami communicantes to the brachial plexus becomes clear. In the first place, there is no indication, in any animal, of the return of sudomotor fibers to the paw. The pad did not sweat, and the skin action currents, so closely associated with activity on the part of the sweat glands, never returned. Finally, the sweat glands themselves, though not degenerated, were much atrophied. Furthermore, although there is clear evidence of the reestablishment of some form of control over skin resistance in three of four animals months after the operation, the negligible reaction to resection of the stellate ganglion rules out the possibility of regeneration of the cut postganglionic fibers. Furthermore, histologic examination confirms the failure of regeneration by the complete degeneration of the nerve cells in two of the stellate ganglia and their scarcity in the other two.

There is, then, every indication that the lesion of the postganglionic sympathetic fibers produced in these experiments led to virtually complete degeneration of the postganglionic neurons. Two factors probably contributed to this result: The point of section was very near to the cell bodies, and the blood supply to the ganglion was, of necessity, interfered with, both initially by section of the vessels passing to the ganglion along the rami and secondarily as the ganglion became involved in the cicatricial process in the field of operation. The observations presented in this paper are, then, of the effect of lesion, but not of the course of repair of postganglionic neurons.

COMMENT

Physiologic and histologic evidence has been presented to show that, after section of the gray rami communicantes to the brachial plexus, the postganglionic sympathetic neurons to the paw do not regenerate. In the failure of regeneration the loss of the sudomotor function and of the skin action currents is complete and permanent. Yet the postoperative course of skin resistance points to the reestablishment of some form of control. Months after the initial operation, skin resistance was reduced to a final, very low, stable level, and the enormous daily and weekly fluctuations were suppressed. The temporary effect of section of all the peripheral nerves to the part indicates a readjustment entirely non-nervous in mechanism. It seems most probable that the final low resistance expresses the capacity of the epithelial tissues to compensate

for sympathetic denervation. However, there was evidence, too fragmentary to merit detailing, of a possible vascular factor in this process.

Regardless, however, of the tissue involved, epithelial or vascular, if the conclusion reached is valid that the reduction of skin resistance to a low stable level is a matter of peripheral readjustment and not of nervous control, then two factors operating in the regulation of resistance must be recognized. The prime importance of the activity of the sweat glands in maintaining the exceedingly low level of normal skin resistance is firmly established. To keep resistance below the normal limit (30,000 ohms for a cat) the function of the sweat glands would seem to be essential. But when the activity of the sweat glands is eliminated, a new control of resistance is brought to light. This control comes into effect slowly, and is totally inadequate to hold resistance within the range of normal. Nevertheless, it operates not only to moderate the excessive resistance at first prevailing in a sympathetically denervated region but also to restrain the enormous daily fluctuations, that is, to stabilize resistance.

This twofold control of skin resistance presents a contrast with the entire dependence of the galvanic skin currents on sudomotor function. Therefore, of the electrical phenomena in the skin, the action currents are the specific indicator of sympathetic function, for which the skin resistance provides the quantitative measure. The present study confirms the conclusion arrived at in the first paper of this series,[6] that the electrical phenomena in the skin, action currents and resistance, offer a more sensitive and sure index to sympathetic function in the skin than any other activity available for study in the intact animal. Yet further study must clarify our understanding of the influence of vascular conditions and of the state of the epithelial tissues on skin resistance before the significance of all the variations in resistance can be evaluated. It is hoped, however, that the application of these methods to the investigation of sympathetic disorders, for example, to clinical entities such as Raynaud's disease, may yield both new insight into these conditions and further knowledge of the mechanism of skin resistance.

SUMMARY AND CONCLUSIONS

The nerve fibers leaving the stellate ganglion were cut on one side in a series of eighteen adult cats. For as long as a year and a half after this operation, observations were conducted on the electrical resistance and the action currents in the skin of the paw pads, and on sweating. Finally, the ganglia and the paw pads were studied histologically.

The results of operation were in part permanent, in part transient. The galvanic skin currents and sweating were abolished, and did not return. On the other hand, the postoperative course of skin resistance

showed three phases. During a short period, several days, the resistance mounted steadily. Then for months it continued high. Finally, by a rapid decline, a stable low level of resistance was established, but the normal range was not intruded on.

The conclusions drawn from this study are four: 1. The effect of the postganglionic sympathetic lesion is qualitatively similar to the effect of preganglionic section, but quantitatively far greater. 2. Lesion of the gray rami communicantes is not repaired. 3. In the absence of sympathetic regeneration peripheral structures recover some degree of control over the skin resistance. 4. The skin resistance and skin action currents provide not only a more sensitive but a more quantitative index to sympathetic function in the skin than does any other single function.

INJURY AND REPAIR WITHIN THE SYMPATHETIC NERVOUS SYSTEM

III. EVIDENCE OF ACTIVITY OF POSTGANGLIONIC SYMPATHETIC NEURONS INDEPENDENT OF THE CENTRAL NERVOUS SYSTEM

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Investigators have long been intrigued with the idea that the sympathetic ganglia may constitute centers for integrative activity outside the central nervous system. For the most peripherally located ganglia, those in the viscera (the myenteric and submucous plexuses, the plexuses of the bladder and heart), the importance of this concept to an understanding of the activities of the organs is equaled only by its obscurity. Morphologic studies have contributed minute details of cells and fibers, and physiologic analysis, equally clearcut facts concerning function. But the two lines of work have not, as yet, come together.

For dealing with the more centrally placed and isolated ganglia of the paravertebral and prevertebral chains, more complete data are, however, available. To begin with, only the thoracolumbar portion of the sympathetic outflow from the central nervous system enters these ganglia. The parasympathetic division has no recognized share. Furthermore, the synapses in these ganglia are on the efferent path from the central nervous system to the periphery and, seemingly, they constitute the only synapse in this pathway. The sensory fibers passing to the central nervous system by way of the sympathetic are generally conceded to have their cell bodies in the dorsal root ganglia, and to pass through the sympathetic ganglia without interruption. Clear evidence, anatomic or physiologic, of a reflex arc in the ordinary sense contained within the sympathetic ganglia and postganglionic connections, is still wanting.

The axon type of reflex arc is, however, another matter. Langley and Anderson [1] (1894) showed beyond reasonable doubt that there are nerve fibers passing through the inferior mesenteric ganglion into the hypogastric plexuses that, in passage, give off collaterals to synapse

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1. Langley, J. N., and Anderson, H. K.: J. Physiol. **16**:410, 1894.

with the postganglionic neurons in this ganglion. These fibers could be made to serve a species of axon reflex. They also demonstrated in sympathetic ganglia, the general evocability of a reaction of axon reflex type, involving the preganglionic axon, synapse and postganglionic neuron. Axon reflexes utilizing only postganglionic neurons have been much sought after, but never clearly found. Certain peripheral vascular reactions belong, perhaps, in this category, but it is difficult to discriminate between direct reaction to an exciting agent on the part of blood vessels and their reaction to excitation through short peripheral nerve pathways. Even granting, however, the existence of a mechanism for axon reflexes, their possible import for normal function is still another problem, and one as yet unsolved. Involving as they do more or less antidromic conduction, and often sensory reception on the part of an otherwise motor neuron, the concept challenges the most severe criticism. It is altogether possible that the reaction is a phenomenon only of laboratory physiology.

Yet, in the absence of central nervous system connections, the sympathetic system can exert a very real control of peripheral activities. The excellent studies of Goltz and Ewald [2] (1896) of the activities possible to an animal with considerable portions of its spinal cord destroyed showed clearly that, after the period of shock has passed, the blood vessels recover tone; micturition and defecation take place regularly, and even the processes of parturition and suckling can be carried through. Characteristically, however, these functions seemed to be imbued with less energy than in the intact animal.

The experiments reported in the first and second papers [3] of this study of injury and repair within the sympathetic nervous system seem to bear on the problem of the independent activity of the sympathetic ganglia and their peripheral connections. That the central nervous system controls the skin resistance is amply evidenced by the immediate rise in resistance on interruption of the pathway between the spinal cord and periphery at any point. But that this is not the total mechanism of control of resistance is equally demonstrated by the nonequivalence of preganglionic and postganglionic section of this pathway. Chart 1 in the second paper of this series places, side by side, records of skin resistance during the first six weeks after preganglionic and after postganglionic section. The chart here presented, shows, as a composite curve for a group of cats, the average skin resistance on the first day, and week by week for six weeks after each of these sections. The

2. Goltz, F., and Ewald, J. R.: Arch. f. d. ges. Physiol. **63**:362, 1896.

3. Tower, S. S., and Richter, C. P.: Injury and Repair Within the Sympathetic Nervous System: I. The Preganglionic Neurons, Arch. Neurol. & Psychiat. **26**:485 (Sept.) 1931; II. The Postganglionic Neurons, this issue, p. 1139.

average reaction in skin resistance during the first week after operation was twice as great after postganglionic as after preganglionic section. Furthermore, 3,000,000 ohms, which was nearly the maximum of resistance shown by a healthy cat after preganglionic section, was the average figure maintained for many months after postganglionic section in a series of cats. The maximum resistance for a healthy cat after postganglionic section was more than three times this figure, 11,000,000 ohms.

The evidence seems conclusive, therefore, that a moderating influence is exerted on skin resistance by the intact postganglionic mechanism,

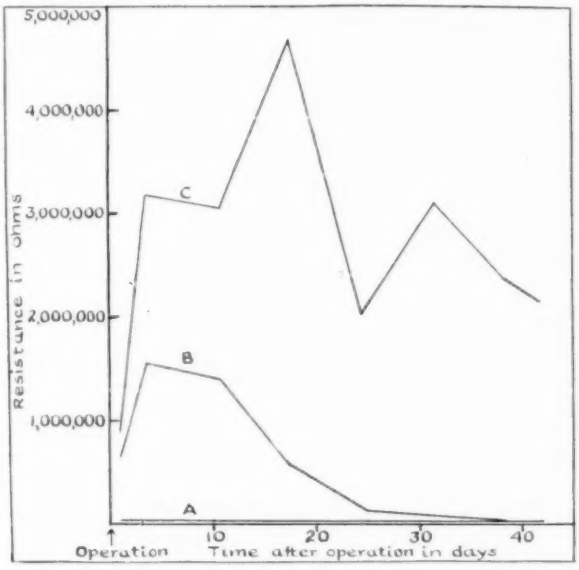

Chart presenting in composite curves the data on skin resistance for a number of cats on the first day after operation, and averaged week by week for six weeks thereafter. Two or three readings from each cat made up the week's average, giving from ten to twenty or more readings for each point on a curve. *A*, resistance on the normal left forepaw; eleven cats. *B*, resistance on the right forepaw after section of the preganglionic fibers entering the right stellate ganglion; six cats. *C*, resistance on the right forepaw after section of the postganglionic fibers leaving the same ganglion; five cats.

independent of the central nervous system. What the nature of this influence is, the evidence does not show. There are, however, several possibilities. A reflex mechanism may be implicated. No true reflex arc, utilizing afferent nerve fibers through the ganglion, could be involved, because afferent fibers, having cells of origin in the dorsal root ganglia, would be degenerated. But an axon type of reflex taking

place entirely in the periphery is possible; or a humoral influence may be at work, acting on the postganglionic neurons either at the cell in the ganglion or at the nerve ending; or, lastly, by a species of so-called trophic control, the mere physical integrity of innervation, deprived of function, may serve to prevent degenerative changes in the peripheral tissues and so modulate the skin resistance.

The first two parts of this study [3] emphasized the instability characteristic of skin resistance after decentralization. Normally the secretory activity of the sweat glands maintains resistance at a low level (from 2,500 to 30,000 ohms). But when these glands are put out of commission by denervation the skin resistance fluctuates enormously, dependent on a number of factors, the most important of which seem to be changing conditions in the vascular bed. Perhaps the discrepancy in the reaction of skin resistance to preganglionic and postganglionic section is to be ascribed to a difference in the effect of these lesions on the blood vessels. The matter needs further investigation. However, regardless of the mechanism of the effect, the conclusion is valid that by the study of skin resistance we have arrived at new evidence of activity of the postganglionic sympathetic neurons independent of the central nervous system.

SUMMARY

The evidence contained in the literature for independent activity on the part of postganglionic sympathetic neurons is summarized and evaluated.

New evidence bearing on this problem is presented, contributed from an investigation of injury and repair of preganglionic and postganglionic neurons that employed the new methods made available in the study of the electrical resistance and the action-currents in the skin.

The conclusion is reached that the postganglionic neurons in connection with peripheral tissues are capable of some variety of activity independent of the central nervous system.

PANIC

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In contrast to older psychiatry, the present day tendency is toward a study of the individual, his pathologic reaction and the situations that cause it (this is not true of German psychiatry, in which the tendency to nosologic systematization still prevails). Even so, there is still too marked a tendency to look for disease entities and to neglect the various phases. Due attention and interest directed to the phases in the setting of the whole illness will allow one to study the patient more carefully and to deal with him more intelligently.

One of the developments of considerable importance is that of panics. Although the term panic is frequently used in daily life as well as in psychology and psychopathology, its definition is somewhat vague. In the study of fear and panic reactions I arrived at the conclusion that panic is not merely a high degree of fear, but a fear based on prolonged tension, with a sudden climax which is characterized by fear, extreme insecurity, suspiciousness and a tendency to projection and disorganization. The projections are delusions of persecutions and auditory hallucinations; the disorganization may lead to a schizophrenic picture.

It is essential that one distinguish between the individual panic and the panic reaction of a whole group. The latter is different in nature, for it is produced by mass suggestion; it therefore rapidly subsides when the individual person is transplanted into another group. During this whole discussion it is necessary to keep in mind the distinction between fear and anxiety. Fear is the emotion that is caused by a danger or threat and has therefore a definite content. Anxiety is more vague and not linked to anything definite. It is relatively contentless. This distinction is accepted in German psychiatry but is not clearly made in this country.

Prolonged tension and slight panics as a climax are frequently observed. The recognition is important for an intelligent treatment that will succeed in reestablishing security. The following case may serve as an illustration.

REPORT OF A CASE

An intelligent, unmarried woman, aged 28, had been treated for several months for hyperthyroidism, which had been diagnosed because of high pulse rate (100

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to 120) and a basal metabolic rate of around + 20. She complained of physical fatigue, which was more marked in the morning and when she had to work hard, irritability and tension. Sleep was not disturbed; appetite was good; the weight remained steady, and the bowels moved well. The tension increased, and an operation was therefore contemplated. The patient's symptoms grew rapidly worse. Sleep became broken and was disturbed by annoying dreams of being confronted with tasks which she could not solve. Difficulty in concentration developed ("my mind wanders") and in "thinking." In the morning, before getting up, she had a "detached, far-away feeling" with regard to people. "I felt as if I were answering rather mechanically and hearing rather mechanically." These symptoms usually improved when she was up and distracted by visitors, but became especially trying when she was ordered to remain in bed and rest. The restlessness increased, and she "felt panicky" when thinking of the impending operation on the thyroid gland, knowing that she would have to stay in bed afterward and could not get away even if she should feel panicky. "It is the feeling of being caught in a situation" describes her reaction well. When this fear became marked, the patient had to rush out of bed. She felt a tightening in her throat, palpitation, nausea and a fear that "here is something I do not know anything about," a fear of "mental disease." She had "no idea of mental disease—people being put in cells, in straight jackets—they look frantic in state hospitals." When she heard that a psychiatrist had visited the patient in the next room, she became afraid of being transferred to a psychiatric clinic. In the evening she became panicky, anticipating that she might not be able to stand being alone in her room after the nurse had gone off duty. She tried frantically to read in order to forget her fears, which became more predominant, and she became afraid of the return of these fear states. She described this by "I got in a panic about having panics." Her difficulty in sleeping increased, although she received large doses of a barbital derivative.

Two days before the scheduled operation, I saw the patient in consultation. She related the facts mentioned, dating the onset of the tension about eight months back—when she was forced to take a position in another city and had to break away from the physician who had analyzed her during the preceding year because of homosexuality, which had been a topic of concern and occasional fear to her since the age of 15. When she left her physician, she developed a slight panic lest she would not be able to control her sexual desire without his help. After a few days she adjusted herself to her new life, but again became tense when she fell in love with another woman. At the same time work increased. Emancipation from another love affair seemed impossible.

On the basis of these data I felt justified in advising against an operation, explaining the high pulse rate and increased metabolic rate, as well as other symptoms, as due to fear, which had reached the degree of a slight panic. Under the influence of divided doses of barbital and occupational therapy, which took into account the patient's thinking difficulties and restlessness, and with the reassurance gained by brief interviews in which her problems were discussed in only a preliminary way, her fear soon disappeared, and the pulse rate gradually lowered to normal. After about one and a half weeks, the patient's confidence and ease had been sufficiently restored so that a more thorough discussion of her difficulties could be undertaken, which led to a good adjustment.

The patient was a cheerful person, but one whose mood and thinking were easily affected by her surroundings; she anticipated pleasure and displeasure intensely. Her anticipation imaginations were increased by impending situations in which her marked self-consciousness or conscientiousness might play a rôle. Being sociable and having a need for social contact, she was well liked and, due to her self-assertion,

always a leader in social and club life, although she felt ill at ease, concerned about the impression she made on others and anxious for approval. Her homosexual interests worried her greatly, not because she disapproved of them, but because she pictured social disgrace and a thwarting of her ambitions if they became known. She also suffered from inability to form lasting homosexual relations.

The need of feeling that a decision was never final was intensified by her conscientiousness and inability to distinguish easily between the important and the more negligible factors in a situation. Situations in which she felt caught were extremely painful and made her feel "panicky"; for instance, when she had to sit on a platform after having introduced a speaker. The same feeling was far less marked when she had to deliver a lecture. Action relieved the tension (this feature is usually observed in similar situations).

At 16, she had had her first slight panic, when she was at a party and unable to return home on time because of tire trouble. This panic was due to conscientiousness and not to fear of punishment. At 18, she experienced a more serious panic during a minor train accident in a subway, when she felt caught in a situation in which she was unable to do much about it. The same factor had caused a minor panic one year before the present writing, and recurred during the treatment, when she had to decide about a new position from which retirement on impulsive notice would have been impossible.

In the past five years, her personality difficulties, and with them slight tension, had increased. She felt incapable of handling her life; she felt that she did things only because of others, and a recurring fear of mental illness or that people might consider her queer developed. (The former refers to the fear of being caught in a situation and of being frantically afraid, the latter to her need of social approval and to her father relationship—he was a querulous person who suffered from many obsessions and compulsions and who made family life unbearable. The patient hated and loved him. Her apparent devotion to her domineering mother concealed a marked underlying antagonism and a wish for complete emancipation, which she had never been able to achieve.)

The patient gradually obtained a better understanding, which allowed her to view and balance her assets and difficulties differently. Constructive aspects of conscientiousness and self-consciousness became apparent. The habit of indulging in anticipation was largely corrected. In many ways, e. g., in her perfectionistic attitude, the patient became more lenient. She began to substitute more constructive imagination for homosexual preoccupations, and to avoid creating opportunities for homosexual infatuations. A heterosexual salvation (several flirtations had led to physical pleasure but also to intense fear of these sensations) became less important. During the whole treatment, self-confidence and self-reliance were considered as the goal, and by this means dependence on the physician was prevented. For a year now the patient has been well adjusted in her new position, and has been able to analyze constructively current minor difficulties without the help of a physician.

This patient's illness was characterized by prolonged tension, with occasional panic outbursts as a climax. Depressive features were practically absent. Occasionally, the patient felt blue in the morning and had difficulty in getting started, but this affect description is given more as an incidental complaint. The various tension episodes can always be explained by recurrent or persistent situations that are trying to this constitutional make-up. The last tension reaction was caused by having to rely on herself instead of on her physician, by being confronted with

new work, which was especially difficult to a perfectionistic make-up, and by a new homosexual infatuation which caused concern because of possible social implications. The panic was due to fear of an operation and was characterized by a fear of insecurity.

Tension and its accompanying features of jerking sensation of various muscles, stiffness, abdominal or cardiac pressure, is frequently the personality reaction to strain (what constitutes strain depends on the personality involved). It does not necessarily belong to the group of affective psychoses (depressions), although depressive affect may be described as a more incidental feature. If not dealt with properly, such a tension state may lead to a chronic invalid reaction. When insecurity is one of the factors producing the tension, brief panic reactions may form the climax.

Kempf is the only author who has tried to analyze the situations that cause panics. He found homosexual factors as the fundamental cause but did not distinguish whether homosexuality is a leading or merely an incidental factor. In the case cited, homosexuality was present and one of several important factors. In other cases homosexual features are merely part of a general sex upheaval. I have noticed in several panic reactions homosexual, heterosexual and auto-erotic tendencies. Homosexual panics, i. e., panics in which homosexuality is the leading factor, are frequent, but I also find masturbation panics and panics due to unmanageable heterosexual desires, as well as many other situations that are unbearable to certain make-ups and from which the subjects see no escape either by mastery or flight. A great variety of factors and situations may produce a tension in certain constitutional make-ups. Panic is the climax of this tension.

Not infrequent are recurrent panic reactions in the setting of prolonged tension, thus indicating clearly the constitutional factor. In one instance I treated the sister for a sexual insecurity panic and ten years later her brother for a homosexual panic.

A more marked panic reaction, characterized by tension, leading to great fear with general insecurity, suspicious and paranoid delusions, is seen in a teacher, aged 33, who was brought to our hospital in his fifth panic reaction.

This intelligent, reserved and seclusive man had always felt ill at ease in crowds and concerned about the impression he made on others. He was ambitious and pushing, very conscientious and had a high sense of duty, but afraid of responsibilities. Such a make-up will be unable to stand uncertainty, especially when ethical difficulties and responsibility are involved.

From 14 to 16, he worried greatly over masturbation and religious scruples. At 18, after his only extramarital sex experience, he worried greatly whether he had destroyed the girl's chastity and was in a panic. This recurred a few months later, when he worried for some time concerning whether he had impregnated the

girl. Slight panics occurred in periods of worry and tension when he married at 24, when his first child was born (at 28), and when he was joining the Episcopal church (at 30). Each period lasted from six to twelve months and was characterized by worries over responsibility which he took, inability to carry it, tension and some slight depression.

The present illness was the climax of two years' hard work for promotion and publication of a book, with increasing tension and irritability and a tendency to be suspicious that difficulties were put in his way. For two months he had been in charge of a committee, which task he took very seriously. For the past three weeks he had appeared weary and slow. During the meetings of his committee there was considerable disagreement among the members, and the patient felt that they were trying to oust him. Three days before admission, he thought he was considered a stool-pigeon for the college administration. The next day he telephoned several friends and talked about having wronged them as Masonic brothers, and wanted their forgiveness and begged for their protection against the order which he felt was seeking his death. He would not eat as he feared that the food was poisoned. He did not sleep at night, and throughout the day he was tense, tearful and sought reassurance without being able to accept it. After this state of panic had lasted three days, his wife was able to persuade him to enter the clinic.

Under our observation the patient was tense and restless, suspicious of everybody and everything. He misinterpreted occurrences in the ward and had many ideas of reference. He felt constantly watched, and was afraid he was going to be killed or "doped." The dominant mood was fear, and he also stated that he was "worried" and felt "pretty bad," "afraid and depressed on account of the fearful content." He had wronged some Masonic brothers unknowingly and feared that he had broken his fraternity obligations and that he would make a slip of the tongue and divulge Masonic secrets. In the evening there was an increase of tension and of these fears. He talked agitatedly about his fears and delusions, with frequent reiteration. He asked for reassurance and begged to be protected from the Masons. At times he wept childishly and pleaded for his life. His sensorium was clear, but he complained of thinking difficulties and felt "perplexed." His hands were cyanotic, cold and clammy; his pulse varied between 70 and 100; the reflexes were exaggerated.

Responding well to barbital medication, the patient felt more at ease after five days and showed little fear, but still had a tendency to hold the physician's hand and asked for reassurance (due to the great insecurity, such a patient needs frequent sympathetic reassurance). He was also frequently indecisive, but at the same time self-assertive. After a visit from his wife, ten days after admission, the patient became again more restless. She had told him that the physician had asked her about sex relations and wondered whether he had thought withdrawal caused his illness. The patient talked of having lived beyond his means, and about masturbation worries and sex relations in adolescence with the daughter of a Mason. (We were again able to reassure him by a formulation which took care of his present sexual worries, but avoided discussing the topic too thoroughly. The thoughtless remark of his wife had clearly shown the present great instability and the danger of stirring up more than the patient or the physicians could handle at the time.) He asked that a tonsillectomy be performed, which had been advised previously, but he had been afraid that he might die (this indicates how any additional insecurity may aggravate the condition and ought to be avoided). After the operation he went through a normal convalescence, seemed less tense and denied delusions of any type. Three days after the operation, i. e., fifteen days after admission, the patient talked about Masonry with another Masonic patient. His

uneasiness, fear and suspicions returned. An unfortunate remark by a visitor that his physician probably thought that sexual factors were the basis for his illness, and hearing that this physician to whom he had confided sexual relations with a Mason's daughter (at 18) belonged to a Masonic order, destroyed the confidence which had increasingly developed. His panic rapidly increased, and transfer to another hospital was advised. He left after about three weeks' hospital stay. In the new environment he again soon felt at ease and was able to leave, recovered, after about a month, to resume his professional duties. In this second hospital the patient was reassured, and discussion of personality difficulties avoided. As no constructive analysis had been tried when the patient was well enough and had established enough security he is not aware of the dynamic forces of his illness. The present adjustment can therefore be considered as only temporary, and with similar difficulties new panic reactions must be expected. The importance of various factors is well seen in the recurrence of panics in his past life.

The patient is an intelligent, reserved and seclusive man, who always felt ill at ease in crowds and was concerned about the impression he made on others. He was ambitious and pushing, but feared responsibilities. His thinking and actions were characterized by conscientiousness and a high feeling of responsibility. Such a make-up will be unable to stand uncertainty, especially when ethical difficulties are involved. At 14, he was worried over masturbation and religious scruples. This lasted about two years. At 18, after his only extramarital sex experience, he worried greatly whether he had destroyed the girl's chastity (a Mason's daughter) and was in a panic. This lasted a few days but recurred a few months later when he worried for some time as to whether he had impregnated the girl. At 24, another period of worry and tension occurred when he married, then again at 28 when his first child was born and at 30, when he joined the Episcopal Church. During this period he worried whether he had committed the unpardonable sin. The various episodes lasted from 6 to 12 months, characterized by the worries over responsibility which he took and felt unable to carry, tension and some slight depressed feelings, but no behavior disturbance or sleep disturbance.

The personality make-up and hereditary factors (maternal grandfather suicide, paternal grandmother depression) are the important dynamic forces that cause tension and panic whenever the patient is confronted with a situation which thrusts responsibility and uncertainty upon him.

This type of panic leads over to the recurrent reactive depressions that frequently occur in persons with a similar make-up and are often initiated by a panic in difficult situations. Similar factors cause "promotion depressions" (Adolf Meyer), i. e., depressions with which conscientious people with lack of confidence in themselves may react to promotion to positions for which they feel inadequate.

Recurrences of panics do not necessarily occur in patients with a hereditary factor for depressions; they occur more frequently in personalities that are not well balanced. They are therefore frequently observed in persons who are unable to control their sex desires according to their code. To this group belonged the minister who reacted with panics to sexual tension on a heterosexual basis and to religious scruples and the young college woman previously mentioned who had homosexual panics. In the first case there were ethical conflicts, in the second a fear of social contempt if the patient's homosexuality were known.

These panic reactions are of a much milder type and are therefore grouped with psychoneuroses. They are not anxiety neuroses. In the latter the definite fear content, which characterizes panics, is missing. The climax of an anxiety state is without special content and without projections and is more like a temper tantrum. On the other hand, even slight panics are attempts at escape, with despair if escape seems impossible or self-assertion. Marked panics cause either disorganization or paranoid reactions, of which the second case is an example. The panic reactions that I have discussed are the climax of a tension state, which may or may not be accompanied by a more or less depressed mood. The whole group can be designated by "tension states leading to panic," or panics in the narrower sense of the term. They can be separated from panics that occur as a climax of the depressions, which are characterized by anxiety and often form a prolonged phase of the illness.

In a married woman, aged 51, there developed, in April, 1929, a gradually increasing depression with agitation, apprehension and hypochondriacal ideas. She feared that she suffered from cancer and syphilis. At her admission to the clinic (May 14, 1929) she presented a similar picture during the first four weeks but also complained of choking and burning in her throat. This she elaborated into the delusion that radium was burning up her throat. Voices were calling her name or vile names. There was increasing tension to hallucinations and marked sensitiveness to noises, which she frequently interpreted as voices. At times she talked of war going on between Catholics and Protestants, or blacks and whites, or dry and liquor people. She might be the cause of it. At other times she wanted to be a martyr to save the people. She had a disease that would spread over the whole world. Occasionally she mentioned delusions of poverty. These delusions were present in the beginning (May, 1929), but she did not mention them again till February, 1930, when they became more dominant.

In June, she had short-lived panics, hearing her cousin calling for help, and hearing he was murdered in the cellar. In July, she was afraid of food, medicine and the tub and showed increasing suspiciousness. She complained of "filthy food," tasting "ground glass and gravel" and smelling a bad odor of garbage and later of poison (a few weeks previously she had complained of a bad odor coming from her). She therefore objected to treatment and frequently became panicky and combative when forced to eat, to take medicine or to bathe in tubs.

Kempf has pointed out that disturbances of sensation are caused by the erotic affect. The patients complain of these sensations as visions, voices, electric injec-

tions, "dopy feelings," "poison" and "filth" in the food, etc. In this patient there was obviously a great deal of sexual tension, which was recognized by the patient, and Kempf's explanation might be applicable. There are, on the other hand, sensations which are caused by the panic and fear affect, as I shall discuss later. One has, therefore, to be rather guarded in applying the same theory to similar symptoms in different panic settings.

The patient became preoccupied with the fear of animals being put in her bed, for instance, while she was asleep, and was afraid of going to bed. (In May, voices had told her that she might give birth to a dog, and in June she felt she might be turned into a horse.) In the tub she felt animals crawling over her; later, she felt this also when up. First, there were paresthesias ("I feel very large bugs crawling all over me"); later, she heard the animals scream and saw them in her room, due to illusions. ("Look at those shadows. Sure I see them—they keep on changing all the time. I am so afraid," or "At night I feel as though this place is full of rats, and I am scared of rats and that I am having sexual intercourse with animals. I cannot look at anything but it seems queer and distorted." "If I look at a thing long enough, it begins to look like a rat or animal.") Her own voice was hoarse and "sounds like that of an animal." The voices of patients (hallucinations) "are so loud that they sound like animals' voices." There were many statements that "I feel them," and of insight in her illusions. At times she talked of the animal hallucinations as "an obsession of mine." In the tub she felt "somebody tries to drag me down" and was afraid. The sheets in the bed felt "as if there is red pepper in them." The patient admitted sex tension, which we tried unsuccessfully to relieve by sitz bath and dialacetin.

She complained of "awful tastes." She constantly thought of all these tortures and walked agitatedly around: "How can I sit down and do anything when I think of the tortures ahead of me"? In August, she barked like a dog to scare animals away at night. She constantly begged to be killed instead of tortured. When her hair was washed she felt that her "scalp is burned with acids." Frequently she begged the nurses to stay with her and to reassure her. At other times she scorned reassurance ("I don't want any of that damn reassurance"), and mocked and mimicked nurses. Most of the time she was sarcastic and antagonistic. This was marked in the period from August to February, during which she had daily panics to the situations mentioned. After the panic she frequently had insight ("I know those awful things I saw aren't true. They are all deformed and out of proportion"). She heard people "hiss at me from all sides," "every one is shouting 'Edna,'" and got very tense; "why are they killing them (relatives)"?

After November, she frequently had unreality feelings ("every one's voice seems so different. . . . I have never heard it like that. It sounds like animal voices." "Nothing is the same, everything has changed and is being changed around"), and feelings of familiarity ("I cannot read anything because it seems to me that as if I had written all the stories I read or as if I had read them all before"), and misidentification of people. There was a great deal of concern about her looks ("It's awful to be an old woman"), and she asked for an operation, "something is wrong with my organs."

In February and March the patient was free from panics; this seemed to be due to a general improvement and subsiding of the delusions, and she was able to accept food and medicine (tubs had been omitted long ago because of her fear of them and the increase of sensations). During this time she showed marked agitation but no panics, because the situations did not arise in the same frightful degree.

The patient had three agitated depressions, which lasted ten days at 20, one month at 33, and one year at 45. All occurred at the time of some strain and ended

abruptly. The patient never wanted help during her illnesses, and showed marked suspiciousness in her third depression. When well she is an active, cheerful, outgoing person, enjoying athletics, ambitious to lead and direct and desiring praise. Her father was an alcoholic addict.

When transferred to another hospital the patient remained depressed and agitated with many delusions of poverty and self-depreciation but no panic outbursts. She is improving very slowly. Her depression has now lasted two years, but we still believe that ultimate recovery will occur.

Many of the features in this agitated depression are intelligible from her constitutional make-up. It must be extremely difficult for a self-assertive person, who has a need to lead and who has never been willing to accept advice, to be guided by others in a state of unhappiness, distress and dread. The feeling that others could not understand and therefore could not help her made bending impossible. Sometimes during tension, therefore, her reaction was anger, at other times antagonism.

In each of the four depressions the patient showed aversion to advice and to interference with her way of managing her illness. This type of aversion is due to some special self-assertion features in the constitutional make-up. Persons with aversion depressions, as Adolf Meyer calls them, are inclined to react with panics when they are unable to adjust to situations such as threatening hallucinations.

No doubt one might argue that I overstretch the fear and panic concept when I include fear reactions to hallucinations, as the term fear should be applied only when the reaction is to actual threatening situations but not to delusions and hallucinations. Such a distinction, however, would not be justified. To the patient, delusional and hallucinatory dangers are real. Reality has to be taken "as if" it were so. One sees the same in other panic reactions. The patient reacts, e. g., to "insanity" and "death" as if they were terrible.

The last case described belongs to the group of anxiety psychoses. This term was used by Wernicke, who meant by it a special type of depression, characterized by marked and extreme anxiety, which dominated the whole picture, with many threatening delusions and hallucinations. Anxiety is the leading affect, which directs the patient's activity, and, in case of overproductivity, leads to overtalkativeness and even to flight of ideas. Because of the latter symptoms Kraepelin grouped anxiety psychoses with the mixed affective psychoses (Weygandt), insisting that anxiety as the depressive affect, plus the manic features of flight of ideas and increased motility forms the picture of anxiety psychoses and agitated depression. Others call it active productive melancholia.

These types of depressions occur frequently in late life. They are often considered ominous, but in most of our cases recovery occurred;

no presenile or early arteriosclerotic symptoms were found. The duration may be of from two to three years.

A careful analysis of the symptoms proves Kraepelin's conception of mixed manic-depressive illness erroneous. The increased motility cannot be compared with manic overactivity. It is due to the tension, restlessness and agitation, which accompany anxiety and fear. Despair and fear, not elation, are the driving forces. Flight of ideas may occur as a relaxation symptom in panics. This relaxation may be in striking contrast to the patient's previous fearful behavior. He may be observed singing and humming. It is not a pure elation but euphoria. In daily life one notices that relaxation follows tension, and it is therefore not surprising that an increased relaxation may follow as great a tension as that which occurs in panic. After the earthquake of Messina many persons who had been in great panic previously were unconcerned and euphoric (Stierlin).

COMMENT

The more frequent panics can be grouped under "incidental panics." They are then merely an incident in the course of a psychosis. They may occur in any setting as a reaction to an unbearable, threatening situation to which the patient is unable to adjust himself.

The symptoms of a panic are those of extreme fear, but, in addition, owing to the state of more or less extreme insecurity, one notices suspiciousness, projections, misinterpretations, ideas of reference and delusions of persecutions that may or may not be self-depreciatory, according to the setting in which the panic occurs.

The behavior is often bewildering because of the many apparently contradictory features, which can be explained by the patient's inability to decide to whom he should turn or where to find his enemies. He may yell for help and cling to people, or he may hit anybody who tries to interfere with him, even with obviously the best intentions, and abuse everybody. The patients rush around, stand immobile in a corner or toss around in the bed, staring or looking wildly about, the muscles of the body jerking, the face quivering and the eyes protruding from fear. The pupils are dilated; the skin is pale and covered with clammy perspiration; the mouth is dry; constriction of the throat makes swallowing difficult. The voice is often husky.

In the interval between these outbursts of panic the patients may be quiet or restless, in good rapport with their environment or on suspicious guard. The high and extremely variable pulse rate is one of the best indications of the still persistent tension, which can also be recognized from other sympathicotonic symptoms.

Knowledge of the bodily changes in panics is rather meager, partly due to the lack of cooperation in states of extreme fear and insecurity,

partly because a methodologic approach to the somatic aspects in personality disorders has never been established. Most investigators group their findings according to textbook classifications and neglect to study the various phases in an illness and to compare them with similar reactions. The result is a statistical accumulation of confusing and contradictory findings.

The higher psychobiologic symptoms have been studied more successfully. Projections are frequent and not seldom akin to illusions. Voices are usually little elaborated, and convey the threats by which the patient feels surrounded. They predict disaster or may be the voices of friends calling for help. In depressive settings they are self-depreciatory or self-accusatory. Acuteness of hearing is one of the earliest symptoms, leading to sensitiveness to noises which may even cause disturbance of sleep and misinterpretations. Visual hallucinations are elaborations of illusions that occur easily, due to blurred vision in states of extreme fear. Shadows and spots on the wall may change into threatening animals. The patient frequently hears the animals bark and howl. In case 3 this was elaborated into the fear that she might turn into an animal and behave like one. Paresthesias are misinterpreted as animals crawling over the body. Acuteness of smell can lead to various hallucinations. Disturbances of taste are the basis for complaints of having "ground glass and gravel" in the food. In one of our cases the sense of equilibrium was disturbed, when the patient felt like flying through the air. The content of the hallucinations depends on desires and strivings of the personality involved.

The sharpening of all senses in the state of external insecurity seems to protect the individual from all possible danger. In strange contrast to this psychobiologic mechanism for self-preservation are the difficulties in thinking, which the patients describe by "bewildered," "haze," "perplexed," "puzzled" or "confused." These difficulties increase indecisiveness, which the panicky patient feels because he does not know the direction of the danger. Indecision is often a sign of fear of action, fear of doing something.

Occasionally there occur feelings of unrealty and depersonalization. Distorted hypochondriacal ideas are due to paresthesia. Obsessions and obsession-like fears are not unusual. Sleep is disturbed by fearful dreams, which frequently recur.

Insecurity demands self-assertion, which leads to paranoid projections and impulsive acts. In milder degrees, or when the fear is subsiding, the patients are arrogant, sarcastic, uncooperative or evasive, especially when pushed with questions. This seems an important self-protection, as patients react frequently with severe panics when a zealous physician pushes through this defense and forces the patient into a realization of the leading threatening factors.

In some patients we have observed peculiar convulsion-like attacks, with jerky movements of certain muscles and a respiratory rate of 12, lasting about an hour, during which the patient did not speak; no content was obtained later. Other patients had attacks of stiffness of the whole body and slow breathing. These attacks are caused by extreme fear and correspond to the immobility that occurs in sudden fright. They are altogether different from catatonic attacks.

The grouping of panics that I have proposed is based on a dynamic formulation of the whole illness. Instructive is a situational grouping which includes:

1. Sexual Insecurity: The most discussed factor is homosexuality. It is necessary to distinguish between the panics of patients who are aware of their sexual strivings and those of patients who are not aware of these strivings and where they were stirred up. Constitutional instability may cause more difficulties. Masturbation and emissions, especially in adolescence, not infrequently cause panics. Sex tension and desires, especially desire for philandering in married people, are frequent factors. A fear of impotency produced a panic in a young man shortly before his marriage. More rare are sodomitic experiences and masochistic and sadistic desires.

2. Financial Insecurity: Certain make-ups cannot stand this strain. The possibility of being caught in an unbearable situation looms over them.

3. Conscientiousness and Inadequacy Panics: To this group belong all the cases of persons who are incapable of carrying responsibilities; these people react with panics, e. g., to marriage and to promotion. The panic is frequently due to a feeling of being inadequate to the requirements of a situation.

4. Philosophic Insecurity: This includes the person's reaction to the problems of death and eternity, which frighten certain people because they feel unable to cope with situations that are unintelligible and mystical to them. Insanity panics are reactions to a similar vague threat. Insecurity of the self and loss of freedom are the important factors.

Less vital situations may produce incidental panics; for example, psycholeptic attacks favor the development of panics. It is not the sudden threatening, unintelligible experience but the fear of its recurrence. Many panics are reactions to involved situations. The panic due to an impending operation is usually complex, as the analysis of several cases showed. The fear of the recurrence of a panic often produces a new panic. Impaired judgment increases the possibility of panic. Less difficult or vital situations may then seem to be of unsurmountable danger.

An analysis of situations proves that situational factors are not leading in producing a panic, but that the constitutional make-up has to be considered preeminently.

Panic reactions can also be grouped from a more formal point of view into paranoid and disintegration panics. In the first form the personality remains more or less intact, although deeply involved, as seen by systematization of the delusions, which may last several months. In most cases the delusions change frequently, according to new situations, and the patients have transient insight. In the disorganization panics a schizophrenia-like picture results. Most of these cases are diagnosed as depressions with schizophrenic features. What impresses one as schizophrenic features can be traced to the disintegrating effect of the panic. I have seen cases of schizophrenic excitement and delirium-like or stuporous reactions that had to be explained on the basis of a panic. The stupor was caused by fear of action in a state of complete insecurity, or was the expression of great aversion. Unexplained laughter, which suggested schizophrenic incongruity, was a relaxation feature. These patients utilize the situation rather than dwell on fantastic topics and their elaboration, as is characteristic of schizophrenic reactions. Vague passivity feelings were occasionally mentioned.

These disintegration features are part of the fear and panic influence and disappear with the clearing up of the panic reaction. In all these cases complete recovery resulted and has in some cases lasted for fifteen years. Situations that these patients were unable to manage caused the illness.

To gain a complete understanding of any psychobiologic reaction, one must study not only the form and content but also the situational factors and the personality involved. Without this one would remain on the level of descriptive psychiatry. Persons who are apt to react with panics are those who have a high feeling of responsibility with a lack of genuine belief in their ability to deal well with a certain type of situation. They need full security to feel at ease. Certain make-ups require financial or physical security; others often need security of a more ethical and philosophic nature. The frequency of sexual panics would be expected because of the importance that a satisfactory individual management of the sexual instincts plays in almost everybody's life. The urge of instinctive desires also confronts one with the problem of having to give in frequently against one's wish. Social considerations aggravate the conflict in homosexual difficulties.

Interesting are cases of panics or tension depression reactions to promotion. Conscientious persons feel inadequate to the new position, but feel under obligation to themselves to carry on. Their already

insufficient confidence in their ability is undermined, and insecurity increases. Many have successfully hidden their lack of confidence behind apparent self-assertion and aggressiveness. The failure of achievement in such a person leads to paranoid projections in the state of insecurity.

These features may occur in a shut-in as well as in an outgoing personality. A dualistic grouping of personalities, and especially their correlation to certain psychoses (I refer here to the fashionable schizoid and syntonic or introvert and extrovert types, which are so closely connected with schizophrenic and manic-depressive psychoses), is more a hindrance than a progressive aid in psychiatry. Typology (i. e., classification in types) has to be replaced by a characterology that occupies itself with the study of the individual personality. It is helpful to try to get order out of the innumerable varieties of human personality by grouping persons with similar features in types, but one has to be constantly aware of the fact that a type is an artificial product of a desire for classification.

The study of reaction, situation and individual personality is an approach that leads to a careful treatment of the patient. It requires analysis of the disturbing and helpful minor situations of the twenty-four hours as well as of the major situations that precipitated the illness, and it forces one to attempt to adjust the past and future situations in the patient's life. On such a basis an individual and active treatment is possible in all psychoses and psychoneuroses and their various phases.

The treatment of panic reactions must be carefully planned. Protection against suicidal attempts, which may be impulsive and violent, due to the fear and insecurity, or carefully planned, is exceedingly important and makes hospitalization in the more marked conditions necessary. Because of the patient's suspiciousness and insecurity, the adjustment to the hospital is a difficult task. A frank attitude on the part of the physician and of whoever comes in contact with the patient is necessary. Admission and every step of routine must be carefully explained and considered, with such modifications as may be necessary. It is, for instance, important that rectal temperatures be omitted in homosexual panics, and that homosexual attachments to other patients be prevented. One ought not to expect more from a patient than seems wise according to his make-up. His conscientiousness and feeling of inadequacy ought to warn one against giving him tasks that are difficult for him at a time of fear and of difficulty in thinking. Premature transfer to a better ward or sudden withdrawal of sedatives may precipitate an increase in insecurity or cause a panic outburst. Divided doses of small amounts of barbital (2½ grains [0.1625 Gm.], four times a day) and hydrotherapy decrease the tension and make the patient

appreciate the treatment. One is thus able to establish the basis for cooperation and confidence. A discussion of the more fundamental factors must be delayed until the patient feels able to face his shortcomings and can also give due appreciation to his assets. Interviews must be short and end with a reassuring formulation.

The patient's dramatic and frequently childish behavior is the expression of despair; sarcasm and aversion are symptoms of self-assertion. When the self-assertive defense prevents the patient from gaining confidence in his environment, a transfer to another hospital may prove helpful.

Fear and panic belong to the group of impure affects. The study of impure affects has been greatly neglected in psychiatry. On the insistence of the Kraepelin school, they have been considered as mixtures of the pure affects of elation and depression. Panic reactions are therefore found in the group of mixed manic-depressive psychoses. Other impure affects are classified among the schizophrenic symptoms. They are frequently part of a schizophrenic picture, but this does not justify the use of them for a diagnostic evaluation, except in relation to all the other symptoms and to the development of the whole illness. The observation of some authors that panic reactions without adjustment lead to a schizophrenic end-reaction is correct only for some cases.

Theoretical contemplations on fear and panic and other impure affects are instructive and necessary, but, as I deal with the whole topic more thoroughly in another article, I shall omit them here. I shall stress only that marked degrees of fear may lead to disorganization. One must, on the other hand, distinguish between nonorganization and disorganization of a personality. Many persons, especially those of psychopathic make-up, who are too loosely organized, and immature people, react easily under strain, with certain features that in the better organized personality would indicate disintegration. They also seem to react more easily with impure affects.

Panic is maximal fear, but, owing to its intensity, the subjective and objective symptoms change. Symptoms of projection and disorganization appear. This corresponds to Bleuler's observation that beyond an upper intensity limit, which changes according to individuals and situations, affects change.

It is necessary to distinguish between fright and panic. Fright is the fear reaction to sudden disaster. The only escape seems to be flight. If this can be accomplished, fright usually passes away quickly. Fright plays, therefore, a minor rôle in psychiatry. Fright psychoses are usually found after accidents and in war time. (English authors erroneously call them "shock psychoses." The German term, "Schreckpsychosen," is correct, but includes mostly the individual reaction in

crowd panics.) Fright and fear have a far-reaching psychobiologic effect and can even lead to death in certain make-ups, as several publications prove.

Anxiety climax is different from a real panic. It is characterized by a discharge of the tension that has accumulated and is therefore more temper or tantrum-like, without special content and lasting only a short time. Anxiety and fear features are frequently observed together, and a clear distinction is not always easy. In organic anxiety, i. e., anxiety due to heart disease, an object is often found (e. g., fear of death), and anxiety changes into fear.

Impure affects occur frequently on the basis of fatigue and exhaustion but seem to reach a high degree only in certain constitutional make-ups.

The two groups of leading panics, which I described in tension depressions and depressions with uneasiness and anxiety (anxiety psychosis of Wernicke), are important psychiatric reactions. Although some lead to definite schizophrenic disorganization, panics must be viewed differently. In most cases they belong to the affective reaction type. Those of less marked degree impress one often as psychoneurotic reactions. Further studies on impure affects will broaden the approach to the problem of what constitutes the characteristics of schizophrenia. Panic is a whole phase of an illness, with well defined symptoms. The motor symptoms of marked fear are not the essential symptoms, but the prolonged tension, leading to a climax with fear, marked insecurity and paranoid reaction or disorganization, is.

In most cases the patient recovers after a few weeks or months, but the illness may last more than a year and end in a final adjustment. Some panics are only the initial phase of a serious schizophrenic illness. The duration and final adjustment depend much on intelligent treatment.

The concept of panic and tension allows one to deal with a group of symptoms that previously were frequently bewildering. Realizing that these are insecurity reactions, treatment has to try to reestablish security; constructive analysis, which will produce a fundamental adjustment, must be delayed until the patient has enough self-confidence to view his difficulties.

A COMBINATION THERAPY OF INDUCED NARCOSIS AND FEVER

ITS EFFECT ON THE "AFFECTIVE SYNDROME"
A PRELIMINARY REPORT

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In a series of ten psychotic patients subjected to a combination therapy—prolonged narcosis and artificial induction of fever—the clinical results were specific in six patients presenting a decidedly affective symptom complex. The addition of this form of therapy to the neuropsychiatrist's armamentarium in the treatment of the affective states is deserving of further consideration and investigation.

Since its introduction into the continental clinics by Kläsi [1] in 1920, prolonged narcosis has been used considerably in the treatment of schizophrenia with variably reported results, but in only a few instances is it reported as effective in the affective states. Kohra [2] and Beyerman [3] reported favorably on the results obtained in the manic-depressive psychoses; Beyerman [4] even advocated it as a specific remedy. The concept as to what constitutes schizophrenia and a manic-depressive psychosis, of course, varies in individual psychiatric clinics. Not only that, but the same patient on successive reentries in the same clinic may be labeled with a diagnosis of schizophrenia at one admission and with that of a manic-depressive psychosis at the next. Campbell [5] called attention to this fact in his report of two cases illustrating the combination of affective and schizophrenic symptoms; the type of symptoms dominating the clinical picture at any given admission led to the corresponding diagnosis of either schizophrenia or an affective psychosis.

This work was done at the Pennsylvania Hospital, Department for Mental and Nervous Diseases, Philadelphia.

1. Kläsi, J.: Ueber die therapeutische Anwendung des Dauerschlafmittels Somnifen bei Schizophrenen, Ztschr. f. d. ges. Neurol. u. Psychiat. **74**:557, 1922; Eigenes über Schizophreniebehandlung, ibid. **78**:606, 1922.

2. Kohra, Takehisa: Die Dauerschlafbehandlung des manisch-depressiven Irreseins mit Sulfonal, Zentralbl. f. d. ges. Neurol. u. Psychiat. **53**:638, 1929.

3. Beyerman, W.: Die Behandlung manisch-depressiven Zuständen mit Somnifen, Zentralbl. f. d. ges. Neurol. u. Psychiat. **51**:848, 1929.

4. Beyerman, W.: Die Behandlung der manischer-depressiven Psychosen mit Somnifen, Zentralbl. f. d. ges. Neurol. u. Psychiat. **52**:767, 1929.

5. Campbell, C. MacFie: Two Cases Illustrating the Combination of Schizophrenic and Affective Symptoms, Am. J. Psychiat. **6**:243, 1926.

A study of the literature on the treatment of schizophrenia with prolonged narcosis impresses one with the fact that in most of the cases in which a cure or improvement is reported, the patient suffered from a psychosis with a dominant affective element in the foreground. Von Horânsky [6] stated: "The delusional and hallucinatory content of the formulations, the catatonia and the negativism are not influenced by the narcosis. The patients with an affective element present have shown the best results, which were permanent." An analysis of the cases presented in the report of Lutz [7] in the greater number of instances corroborates this observation. On the other hand, the more or less definite cases of dementia praecox showed the least clinical improvement. Furthermore, from an experimental point of view, Pavlov [8] found that in certain types of dogs an "acute neurosis" developed in the course of the experiment (objectively certainly simulating the affective syndrome in the human being) which was persistent and prolonged, and even after termination of the experiment for many months these dogs showed no tendency to improve. However, after the application of a bromide narcosis for from ten to eleven days they made an immediate lasting recovery. That a moderately severe infection may alter the course of these psychoses in the direction of early convalescence or complete recovery is well known. Menninger [9] has already pointed this out and reviewed the literature. This phenomenon seems especially striking in the manic patient with such complications, in whom sedatives are administered to avoid exposure and conserve energy.

Therefore, on the basis of these facts I concluded that patients suffering from the affective types of psychoses are the most desirable for a form of therapy embodying the artificial induction of fever and a prolonged narcosis. With a few exceptions the therapeutic results in the patients to be described, so selected and treated on this basis, would justify this assumption. The type of psychosis, then, in which this type of therapy offers a fairly specific relief, I wish to designate as the "affective syndrome"; I shall include the manic-depressive psychoses and the so-called acute schizophrenic reactions; the latter usually show a predominant affective element in their clinical picture.

TECHNIC OF TREATMENT

Since I knew of no published technic when this work was undertaken, the routine here briefly outlined had to be developed cautiously.

6. von Horânsky, Ferdinand: Ueber einige neuere Behandlungsmethoden der Schizophrenie, Arch. f. Psychiat. **84**:181, 1928.

7. Lutz, Jakob: Ueber die Dauernarkosebehandlung in der Psychiatrie Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:91, 1929.

8. Pavlov, I. P.: Conditioned Reflexes, translated by G. V. Anrep, New York, Oxford University Press, 1927.

9. Menninger, Karl A.: The Amelioration of Mental Disease by Influenza, J. A. M. A. **94**:630 (March 1) 1930.

Of course, the results were more specific as experience and confidence were gained.[10]

Each night, the patient is given orally from 3 to 6 grains (0.19 to 0.39 Gm.) of soluble phenobarbital sodium (Abbott), depending on the desired depth of the narcosis. Each following afternoon, gradually increasing doses of typhoid vaccine are given intravenously for the production of a temperature reaction, usually for five days; the initial dose is 120,000 bacilli. The vaccine is then discontinued and the prolonged narcosis begun. The drug is preferably given intravenously in from 4 to 3 grain (0.26 to 0.19 Gm.) doses three or four times in twenty-four hours. Scopolamine hydrobromide, $\frac{1}{100}$ grain (0.0006 Gm.), is added when indicated. The patient must be kept in a natural even sleep and frequently observed. Food in the form of a liquid diet is given twice daily, just before the morning and evening medication. If the patient is too drowsy at the stated meal time, gastric gavage or even the rectal administration of a 10 per cent solution of dextrose may be necessary. Determinations of pulse rate, temperature, respiration and blood pressure, twice daily, are the best criteria of the progress of the narcosis. The pulse rate ranges between 70 and 50, the temperature between 99 and 97 F. (rectal), and the blood pressure between 110 systolic and 80 diastolic, and 90 systolic and 50 diastolic. Deviation from these limits in either direction or the appearance of early signs of a phenobarbital reaction (difficulty in voiding urine to a mild retention, a bulbar type of speech, marked nausea and the development of fever) call for precautionary measures in the administration of the drug. Usually the optimum state of narcosis at such moments may again be attained by either decreasing or omitting several doses of phenobarbital and correspondingly reenforcing or replacing the drug with some other form of sedative. (The appearance of the menstrual period in the female patient is not a contraindication to the normal continuation of the treatment.) After from eight to twelve days, the narcosis is discontinued and the patient is removed to a convalescent ward, started again on graded doses of typhoid vaccine and left alone. Any form of psychotherapy and visitors are to be avoided. It is usually found that the patient reacts gradually and by the seventh day is cooperative.

REPORT OF CASES

Case 1.—W. M. G., aged 44, a housewife, was admitted on Feb. 3, 1930, in an acute affective state: exalted, symbolic, destructive and talkative. There was a definite family history of psychopathy. The patient had been neurotic as

10. Since this manuscript was submitted a slight modification of the technic, incorporating certain principles in use at the Heilanstalt Burghölzli, has been developed. The initial injections of typhoid vaccine are omitted. Instead, the patient is given a cleansing enema the preceding evening and again the next morning, followed by the administration of 1,500 cc. of weak tea. The patient is then narcotized, nourishment being given by protoclysis in the form of 2,500 cc. of from 5 to 7 per cent dextrose plus 500 cc. of physiologic solution of sodium chloride. From the second to the fourth day a slight rise in temperature may develop which responds favorably to the administration of from 0.1 to 0.2 Gm. of quinine added to the dextrose solution. Experience has shown that this initial rise may be disregarded, provided it responds to the quinine and no other signs of marked vegetative depression are in evidence. Otherwise the technic remains as described. This technic has an advantage in that the patient cannot aspirate vomited food and the narcosis remains uninterrupted. Its disadvantage is that loss in weight of from 4 to 6 Kg. is registered within the average ten day period of treatment, and patients already in a poor state of nourishment do not react well.

a child, and gave an abnormal marital sex history. There had been a previous attack, of seven months' duration, at the age of 32. The diagnosis was manic-depressive psychosis of manic type. The present illness began in December, 1929.

Course.—Treatment was administered from March 11 to March 27, 1930. There was an immediate recovery of the mental state, but the patient remained in the hospital until May 24 because of her poor physical condition. At the time of discharge she had gained 20 pounds (9.1 Kg.) in weight and up to the last report, about January, 1931, had remained well.

Comment.—Though this patient's psychosis was again classified statistically as manic-depressive of manic type, her personality background was schizoid. However, during the attack the affective element was predominant and the therapeutic results of the special treatment were good.

Case 2.—R. T. B., a single woman, aged 37, a clerk, was admitted on March 17, 1930, in a confused state, with periods of excitement and a set of systematized delusions. There was a family history of psychopathy. Two previous attacks had occurred in 1919 and 1920, respectively, and were of a few weeks' and six months' duration. The diagnosis was manic-depressive psychosis of manic type. During the interval she had shown a decline in the social and economic level; during the last five years she had revealed an ever-expanding set of delusions accompanied by intermittent swings of mood. The present illness developed in December, 1929, and at the time of admission was complicated by a secondary anemia and a mild nephritis.

Course.—The special treatment was given from March 29 to April 14, 1930, but was discontinued several times for short periods because of general poor health. The patient made a temporary improvement in the affective state, but relapsed and deteriorated rapidly. She was committed to a state hospital on July 2 as having paranoid schizophrenia.

Comment.—The poor physical health, plus the paranoid delusions of at least five years' standing, made this patient an unfavorable risk. With each attempt at special treatment she made a temporary improvement in the affective sphere; the delusions remained unaffected.

Case 3.—T. H. S., aged 30, a housewife, was admitted on Feb. 22, 1930, in an agitated and confused state, with inappropriate mood, delusions and auditory hallucinations. There was a family history of psychopathy, and the patient had shown an eccentric personality. The present illness began in May, 1929, and up to the time of admission the patient had attempted suicide four times.

Course.—The special treatment was attempted several times during the interval from April 4 to April 14, 1930, but had to be interrupted each time because of reactions to phenobarbital. There was no improvement.

Comment.—Though the patient presented a clinical picture of a markedly agitated depression, the special treatment not having been carried through to completion because of the risk involved, no conclusions can be drawn. Up to the last report in January, 1931, the patient was still in the hospital.

Case 4.—F. O. T., aged 24, a single woman, a stenographer, was admitted on March 11, 1930, in a confused state with depression, a feeling of unreality

regarding the environment and relative insight. The past history was negative for earlier attacks. The present illness began acutely on Feb. 14, 1930, following the death of both the mother and the fiancé of the patient within a space of two days.

Course.—The special treatment was begun on May 5 and ended on June 4. The depression and confusion resolved, and the patient was discharged after a short period of rehabilitation in the hospital.

Comment.—The central picture in case 4 was a depression and confusion; no clear-cut distortions of relations to the environment in the nature of delusions, hallucinations or ideas of reference were ever established. It was the only case of depression in this series, and the patient made a good response to the special therapy.

Case 5.—R. A. D., aged 24, single, a professional man, was admitted on Oct. 4, 1929, in a state of confused excitement; he was resistive, irritable and occasionally very impulsive, and presented periods of catatonic phases. There was a family and personal history of psychopathic tendencies. The present illness began on Sept. 26, 1929, with an acute onset.

Course.—The special treatment was given from April 18 to May 2, 1930, and the patient was discharged on May 16, 1930 to return to his professional duties.

Comment.—Case 5 was classified as catatonic dementia praecox, but was considered for the special treatment because of the affective elements at the onset of the illness as well as at later periods in the course of the illness. This case illustrates that the outcome cannot be postulated, in the borderline diagnoses between schizophrenia and affective psychoses, from the descriptive level.

Case 6.—T. W. S., aged 25, a single man, whose last occupation was that of clerk, had suffered from a chronic hypomanic state with emotional instability since the initial attack at the age of 22. The diagnosis was manic-depressive psychosis of manic type. The present readmission occurred on Feb. 24, 1930.

Course.—The special treatment was given from April 18 to May 2. The patient made a rapid recovery, and according to his family was back to a normal state for the first time since the original attack three years before. He had remained well up to the last report, in January, 1931.

Comment.—This case illustrates that the manic-depressive psychoses may go over into a chronic hypomanic state and incapacitate the patient for long periods.

Case 7.—G. T. N., aged 56, married, a business man, in September, 1929, following a reversal in business, showed tendencies to overactivity, was irritable, suffered from insomnia and poor memory and made poor investments. He was admitted in October, following an attempt at suicide. In the hospital he presented a labile temperament, and was destructive to bedding and clothing, untidy, noisy and overactive.

Course.—The special treatment was given from May 12 to June 7. The patient made an immediate recovery. He was discharged on July 3 after one month's rehabilitation of the poor physical condition. He was well at the last report, about January, 1931.

Comment.—This attack was the first in a previously healthy man, and was rather cyclic and persistent. The depressive phases were of such an extent that the patient once attempted suicide.

CASE 8.—J. G. H., aged 19, a single man, an electrician, was admitted on Dec. 17, 1929. During the period at home from Dec. 3, 1929, to the time of admission he expressed many grandiose ideas, heard people whistling and thought that they followed him. He sat about smiling inadequately and displayed many erotic tendencies. On admission he was in a state of confusion, gesticulated, was untidy and destructive to bedding and talked incoherently.

Course.—The special treatment was given from May 4 to June 7, 1930. The patient showed a decided improvement in behavior and was transferred to the convalescent ward; there he took an active interest in games, etc. However, his mood was inappropriate, and he lacked insight. He was discharged later as improved.

Comment.—This case again illustrates the combination of affective and schizophrenic symptoms in one patient. The affective element resolved following the treatment, leaving the clear schizoid pattern. However, as a result of this the patient was clinically well enough to be in a ward for convalescent patients and eventually to leave the hospital. The ultimate prognosis in this case is doubtful.

CASE 9.—W. P. R., aged 31, a single woman, an actress, was admitted on Feb. 20, 1926. The onset of the illness had been insidious over a period of years. The patient had undergone a psychoanalysis. During the four years' residence, the central picture of the patient's psychosis was one of seclusiveness, defiance and irritability, and presented many delusions of an erotic content; she showed many impulsive outbursts accompanied by violence and destructiveness.

Course.—The special treatment was given from May 7 to June 2, 1930. The psychosis remained unchanged.

Comment.—The psychosis in this case was of insidious onset and of many years' duration; the diagnosis was undisputed. The patient was included in the series to see what effect the treatment might have in an old case of long standing not showing any affective symptoms.

CASE 10.—H. W. A., aged 28, single, a salesman, was admitted on May 26, 1925, with delusions of persecution, and periods of impulsion and excitement. There were a slightly tainted family history and consanguinity of the parents. During five years of residence in the hospital the patient deteriorated considerably, sitting or lying about, displaying silly mannerisms, etc.

Course.—The special treatment was given from May 17 to June 4, 1930. There was no perceptible improvement.

Comment.—The onset was insidious over a period of years; the diagnosis was undisputed. In this case the treatment might have been of benefit when the patient was first admitted, but apparently when the patient had deteriorated to a vegetative level, the psychosis was no longer amenable to treatment.

COMMENT

In all ten cases here reported, the patients suffered from a major type of psychosis, in each case for practically four months or more. In all the cases the usual forms of treatment had been tried without any striking results.

In three cases a diagnosis of manic-depressive psychosis and in two of schizophrenia was fairly clear. The remaining five cases, however, fell into that borderline group which in psychiatric nosology has been variously labeled acute schizophrenic reaction, katatonischer Schub, manic-depressive, manic, etc. However, the cases of what I have chosen to call the "affective syndrome" present in their clinical picture some points in common: The episode is usually of rather acute onset; frequently there is present a history of previous attacks; usually, accompanying deviations away from the normal autonomic physiologic functions (to be reported eleswhere) can be demonstrated; in the center of the mental picture stands a predominant affective element. From a clinical standpoint hair-splitting classifications in diagnosis have really very little practical value.

The special treatment here reported on proved satisfactory in this type of psychosis when it could be carried through to completion. Just what is the modus operandi and what rôle, if any, the induction of fever plays in bringing about this definite improvement or recovery needs further investigation. That the type of drug employed was not the responsible factor is shown by the good results obtained with other forms of sedatives. However, it is true that most of the drugs employed successfully thus far fall into the group designated by Pick [11] as having a specific action on the brain stem; hence the point of therapeutic attack must be on the central part of the vegetative nervous system. It is of further interest in this connection that the various autonomic physiologic dysfunctions repeatedly demonstrated by various authors [12] are usually reversed while the patient is under the influence of the narcosis. That is, if the patient shows a gastric hyperchlorhydria he will show an

11. Pick, E. P.: Pharmacology of the Vegetative Nervous System, Arch. Neurol. & Psychiat. **23**:582 (March) 1930.

12. Pavlov (footnote 8). Cannon, Walter B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton and Company, 1929. Farr, Clifford B., and Lueders, Charles W.: Gastric Secretory Functions in the Psychoses, Arch. Neurol. & Psychiat. **10**:548 (Nov.) 1923. Henry, George W.: Some Roentgenologic Observations of Gastro-Intestinal Conditions Associated with Mental Diseases, Am. J. Psychiat. **3**:695, 1925. Westburgh, Edward M.: Psychogalvanic Studies of Normal and of Abnormal Subjects, Arch. Neurol. & Psychiat. **22**:453 (Sept.) 1929. Reiman, Emil: Ztschr. f. Heilk. **23**:1, 1902. Folin, Otto, et al.: Some Observations on Emotional Glycosuria in Man, J. Biol. Chem. **17**: 519, 1914. Henry, George W., and Mangam, Elizabeth: Blood in Personality Disorders, Arch. Neurol. & Psychiat. **13**:743 (June) 1925.

achlorhyria, and vice versa. With recovery these functions again return to their physiologically accepted norm.[13]

This theory breaks down, however, when one considers that very good results have been obtained with the use of chloral hydrate, morphine, scopolamine hydrobromide and other drugs known to have a specific action on the cerebrum. However, when one considers the dynamics of the therapeutic action from the standpoint of the pathogenesis of the "affective syndrome," all these observations seem to fit into a pattern. As a result of the many afferent stimuli, conditioned reflexes are established. In the cerebrum, integration of these reflexes takes place according to definite laws, as shown by Pavlov.[5] Analogous to the observations on his dogs, in certain human constitutional types these delicate mechanisms are easily disturbed, and a cycle of heterogeneous disorganized reactions follows. As Pavlov has shown, these reflex reactions express themselves objectively through the medium of various autonomic functions: salivary secretion or inhibition, emotional states, gastric secretion, etc. Hence, there arise the accompanying autonomic dysfunctions in these psychoses. To effect a recovery, this cycle must be broken, and rest, that is, a reduction in the afferent stimuli, is the best agent. The use of a drug the therapeutic attack of which breaks this cycle at any point, in either the brain stem or the cerebrum, producing absolute rest, is the goal of this therapy.

In this type of psychosis one presumably, then, deals with a physiopathologic process, the psychologic signs and symptoms forming merely a part of the symptom complex. That this process originates on a psychogenic basis as the result of the interaction of these various stimuli is plausible; but, the illness once established, the approach in therapy must be a different one from psychotherapy. Contact with these patients is absolutely lost. This pathologic derangement of the normal physiologic reflex integration, analogous to any other disease process, must run its natural course, resulting in either recovery or death of the organism, or remain in a chronic state, unless an objective form of treatment is offered to aid in the healing. And again, like any other disease process, when it has reached the chronic state it is more difficult to effect a cure.

SUMMARY AND CONCLUSIONS

1. In reporting the specific results of a combination of induced fever and narcosis on six patients presenting an "affective syndrome" out of a series of ten psychotic patients subjected to this form of therapy, no panacea for the treatment in mental diseases is offered. Nor is it

13. Westburgh, Edward M.: Psychogalvanic Studies on Affective Variations in the Mentally Diseased, Arch. Neurol. & Psychiat. **22**:719 (Oct.) 1922. Hackfield: Studies to be reported elsewhere.

claimed that after recovery the patient is guarded against further recurrences, but the induced remissions do compare favorably in duration with those obtained with other forms of treatment. However, the apparent specificity of this therapy in the affective syndrome suggests its application in suitable cases, because affective types of psychoses may thus sometimes be terminated within three weeks or less which otherwise might be protracted into months or years, or even become chronic.

2. A suggestive concept as to the pathogenesis of the "affective syndrome" is offered.

3. No specific therapeutic claim is made for any form of sedative. The most probable mode of therapeutic action of any of the sedatives employed is the production of absolute rest, resulting in an either directly or indirectly induced break in a cycle of deranged conditioned reflexes.

4. That the "affective syndrome" does not constitute a psychopathologic entity, but rather a psychophysiopathologic process, though probably of psychogenic origin, is attested by the other accompanying autonomic dysfunctions during the illness and their return to the physiologically accepted norm with recovery from the psychosis.

Heilanstalt Burghölzli.

Clinical Notes

CRITICAL STUDY OF A CASE OF APHASIA

HAROLD W. LOVELL, M.D.; RAYMOND W. WAGGONER, M.D., SC.D.
AND
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Much has been written about the various manifestations of aphasia and their significance. At the present time there is no completely accepted theory in regard to the physiologic and psychologic manifestation of this condition. Therefore we believe that every case that may bear on the interpretation of such disorders should be carefully studied and reported. Consequently, we are presenting the following case.

REPORT OF A CASE

History.—The patient, R. S., a man, aged 31, was admitted to the University Hospital on May 25, 1931, complaining of difficulty in expressing himself in speaking and in writing. It was said that three years before, while loading sheep into a truck, he was accidentally struck on the chin in a manner which threw his head sharply backward. There were no immediate symptoms, but within an hour or two it became impossible for him to understand what people said to him. There was no loss of hearing, but words were meaningless to him. At first there was a little difficulty in speech, such as a tendency to mix words that sounded alike but were spelled differently. During the time prior to admission to the hospital, he became progressively worse. He always knew what he wanted to say, but usually found himself unable to say it. On occasions, however, he could speak almost normally. Three months before admission to the hospital, while attempting to lift a box of groceries, he suddenly became unconscious for a few minutes; this attack was followed by partial deafness in both ears and some mental confusion which lasted for approximately one week. The patient had frequent headaches, some of which were severe and some of which were only moderately severe. There was a slight progressive impairment of vision, but never vomiting, vertigo or tinnitus.

The patient had always been healthy, and was considered to be of average mental capacity. He completed the tenth grade in high school at the age of 17 years, at which time he stopped school to work on a farm. He had always been right-handed until the age of 10, when he lost his right hand at the wrist. The patient then learned to write with the left hand. At no time was there evidence of difficulty in speech.

The family history was carefully investigated, and it was found that one uncle and two cousins on the mother's side were left-handed. One cousin died during an epileptic attack. Other than this, the family history was irrelevant. The patient was married and had five children. His wife and children were all living and well.

From the Departments of Neurology and Surgery, University of Michigan Hospital.

Examination.—The patient was well nourished and well developed, though he appeared somewhat older than his stated age. There were no atrophies or deformities, except that the right hand had been amputated at the wrist. Station and gait were normal with the eyes open and closed. The pupils were round, regular and equal; the left reacted somewhat better to light than the right; both reacted in accommodation. The extra-ocular movements were normal. There was no nystagmus. Bone conduction of sound was better than air conduction on the right. Otherwise, the cranial nerves were normal. The upper teeth had all been removed. The tendon reflexes were active, equal and normal. Plantar stimulation resulted in plantar flexion on both sides, although there was an occasional delayed extension of the great toe on the left. The cutaneous reflexes were active and normal. There were no sensory changes anywhere on the body. Ophthalmologic examination gave entirely negative results, and the visual fields were normal. A Bárány examination revealed the fact that the right side was stimulated in thirty seconds, the left in twenty-five seconds.

The patient manifested numerous anxiety symptoms and was rather irritable and easily distracted, although he attempted to cooperate in all respects.

He could understand spoken conversation when it was slowly and distinctly enunciated, but if the conversation or speech became rapid he became confused. He was well oriented as to time, place and person. There was no impairment of memory except that he was unable to spell. He could recognize coins, but was unable to count correctly, and calculation was impossible. He could read short sentences and understand their meaning, but it was impossible for him to comprehend the meaning of longer sentences. He could not write from memory, and he could copy only brief, simple phrases, usually omitting several letters in each word. As a rule, he could not carry out complicated commands, but after considerable hesitation he was able to carry out the Marie paper test. It was impossible for him to repeat or recite the alphabet. He was unable to write the alphabet from memory and could copy it only with great difficulty. He could not recognize common abbreviations which he had formerly known, such as Y. M. C. A.

Roentgen examination of the skull gave essentially negative results. The Kahn test of the blood was negative. The spinal fluid pressure was 130 mm. of water. The fluid was clear, containing 3 lymphocytes per cubic millimeter and no increase in solids. The Kahn reaction on the spinal fluid was negative, and the colloidal gold solution and mastic curves were flat. Urinalysis gave negative results. Examination of the blood showed 83 per cent hemoglobin; 4,700,000 red cells, and 8,900 white cells per cubic millimeter.

An encephalogram was made, at which time 180 cc. of fluid was removed and 160 cc. of air introduced. The postencephalographic convalescence was short; the patient was able to be up and about on the day after the injection of air was made.

There was a moderate uniform dilatation of the lateral ventricles with some enlargement of the third and fourth ventricles. There was no deviation of the ventricular system from the midline. There was a marked increase in the amount of subarachnoid cortical air, particularly on the right side. There was a well defined collection of air in the region of the right angular gyrus, which was interpreted as a right-sided cortical cyst in this region.

Operation.—On June 24, 1931, the patient was operated on (by Dr. Kahn) for a right postparietal cortical cyst. The cyst as exposed appeared to be about 3 by 2 cm. The arachnoid was thickened and discolored. The cyst was opened and found to extend under the convolutions but was not adherent to them. At the base of

the cyst there appeared to be some creamlike softened brain. The cyst was excised, and the softened brain was removed down to what appeared to be healthy brain tissue. The dura was closed, and the bone flap was replaced without decompression. Microscopic study of the tissue removed showed a mixed connective tissue and glial proliferation with numerous giant astrocytes. The pathologic diagnosis was "old traumatic lesion of the brain."

Course.—The patient made an uneventful recovery, although on two occasions it was necessary to aspirate serosanguineous fluid from beneath the bone flap. On the day following the operation, the patient was able to speak almost normally. On the next day there was some retrogression in the ability to speak, but from that time on the condition gradually improved. At the time of discharge from the hospital, three weeks after operation, he was able to carry on a conversation if allowed to speak slowly. He could spell correctly his own name and other words of not more than six letters. He could write simple sentences fairly well from dictation and could read aloud easily. He read with understanding, and was able to relate to the examiner the contents of that which he had read. He carried out complicated commands much more rapidly than he had been able to do prior to the operation, and could repeat complex sentences with only slight difficulty. He was able to count correctly forward and backward.

The patient has been reexamined from time to time since discharge. He is now able to do farm work. His weight has increased. Headaches have occurred only rarely. He is no longer irritable and, though his aphasic manifestations have not completely disappeared, there has been a constant progressive improvement.

Summary.—The patient was born right-handed, learned to write well with the right hand and, if the history is correct, was also right-eyed. At the age of 10 the right hand was injured, necessitating amputation. He soon learned to write well with the left hand and did this without difficulty in speech. Several years later, following an injury, a right-sided cerebral lesion associated with sensory and motor aphasia developed which, when surgically corrected, resulted in marked improvement of symptoms to the point where he is almost entirely recovered.

COMMENT

This case is of decided interest for several reasons. It suggests that cerebral dominance is not fixed even after the age of 10 and that it is possible that cerebral dominance is more closely related to that part of the body that is most used, thereby making it a secondary characteristic rather than a primary one. It is stated that as a child, before the injury to the right hand, the patient always used the right eye in aiming a gun. Since the injury he has been compelled to use the left eye in aiming a gun, and on examination at the present time it is obvious that the patient is left-eyed. In the interpretation of the tests for aphasia it will be noted that he showed evidence of difficulty in understanding spoken and written words, as well as difficulty in saying and writing words and sentences. It would seem, therefore, that from the older type of terminology one might call this a mixed motor and sensory, auditory and visual aphasia.

Operative intervention was employed only at the region of the angular gyrus, and yet following operation the patient has shown a steady improvement until at the present time he is practically free from gross defects either in understanding written or spoken words or in the motor manifestations of speaking and writing.

From a purely mechanical standpoint, the case is also exceedingly interesting. An encephalogram was made which showed the ventricles to be in the midline and without deformation. However, there was evidence of a cortical cyst on the right side in the region of the angular gyrus, which was found on operation. Such a diagnosis might not have been made if a ventriculogram had been taken.

In view of the history of right-handedness before the injury and the lack of lateralizing findings other than the aphasia, we should probably have been tempted to investigate the left cerebral cortex if it had not been for the encephalographic findings.

Realizing that any generalization from interpretation of the findings in a single case would be of little value, we are merely making a record of the facts in this case.

Obituary

EDWARD WYLLYS TAYLOR, M.D.
1866–1932

In the death of Edward Wyllys Taylor, Aug. 17, 1932, after an illness of many months' duration, American neurology loses one of its outstanding figures and Boston one of its most esteemed practitioners and teachers. Few physicians have been more respected or admired; as an instructor in the difficult technic of neurologic diagnosis to a generation or more of students, he will be long remembered. His patients, also, quickly grasping his essential kindness, came to him repeatedly for advice; physicians, knowing his sound knowledge of nervous disease, depended on him in consultation.

Born in Montclair, N. J., May 7, 1866, the son of Alfred and Jane Brown Tucker Taylor, he attended public schools and entered Harvard College in 1884. During his four undergraduate years he made many friends, particularly a number of men who later practiced medicine in Boston. He made philosophy his major subject, received honorable mention as a student, and wrote a dissertation for his commencement in 1888. He entered the Harvard Medical School the next year and obtained the Boylston Medical Society prize in February, 1891, with an essay entitled, "The Mental Element in the Treatment of Disease," published the same year.

After his graduation he went back to his home and then left for study in Europe spending the time from October, 1891, until September, 1893, in Germany, at Berlin and Freiburg. He became a student of Prof. Hermann Oppenheim in Berlin and showed so much promise that he was appointed assistant in Professor Oppenheim's department, serving there from September, 1892, until August, 1893. During this period he was largely concerned with the anatomy and pathology of the nervous system. There were at that time few laboratories devoted to neuropathology, either in this country or in Europe. It was, therefore, a rare opportunity to study under the leading clinical neurologist in Europe. The stains then used in the preparation of sections were less elaborate than at present, although several of them at least have persisted unchanged. The methods of staining particularly in vogue then were those of Weigert and a modification by Pal, in which the gray matter was completely decolorized. These stains were, and are, invaluable in determining myelin degeneration and in tracing fiber tracts, both normal and degenerated. Golgi's silver preparations were just appear-

ing, and there were then no adequate means of staining the neuroglia, about which, in fact, little was known. The ample material at one's disposal in Oppenheim's laboratory and the close association which he always maintained between clinical manifestations and pathologic changes constituted valuable material for an ardent student.

In the autumn of 1893, he began the practice of neurology in Boston and soon became associated with the Harvard Medical School. As the

EDWARD WILLYS TAYLOR, M.D.
1866-1932

result of his work with Oppenheim, he had become interested in the pathology of the nervous system, and his first connection with the school was in this department, under Prof. W. T. Councilman. On his first visit to Councilman, he showed him some very large and beautiful slides of the brain which he had cut and stained in Oppenheim's clinic. Such slides had never been seen here before and did much to recommend

Taylor for the school position he sought. A small laboratory was, therefore, established as adjunct to general pathology with Taylor in charge of the very moderate amount of teaching which was considered sufficient for that day. The importance of neuropathology was recognized, however, by J. J. Putnam and W. N. Bullard, and soon after a separate department was created; E. E. Southard became the Bullard professor of neuropathology when Taylor gave up the laboratory for clinical neurology.

In 1906, Taylor officially began his career as teacher of neurology as assistant to Professor Putnam, succeeding him in 1912, and continuing as the James Jackson Putnam professor of neurology until 1926, when with the regrets of all he resigned on his sixtieth birthday to become professor emeritus. It was as a teacher of clinical neurology that Taylor undoubtedly made his greatest reputation. With the individual student he was sympathetic and stimulating, with a small group he was lucid in his discussion, but before a large class his presentation was at its best. Such a clinic was seldom prepared in advance. He carried no notes. He often did not know about the patient to be presented, but by a few rapid, well-worded questions he obtained the essential symptoms and, with this as a start, he then developed with skill the clinical picture. His talk would be filled with reference to similar and contrasting conditions and illustrated with diagrams on the blackboard, always drawn by him during the lecture. Although giving full credit to others, he disliked the pedantic method, and so omitted references, long words, dates, figures and complicated prepared diagrams in his effort to simplify his exposition. In this manner he brought neurology before the student as a vivid, intelligible subject, understandable even to the least interested of the class. It is not without reason that he was considered by many a student as the best clinical lecturer in the school. His clearness and simplicity also appealed to many graduate students in his successive years as "the chief" at the Massachusetts General Hospital. His enthusisam for neurology was strongly appreciated by Dr. Harvey Cushing, a "house pupil" 1896-1897; they worked together, both dissatisfied with neurosurgery as it was practiced at that time. It is probable that Taylor's influence on the younger man was not inconsiderable.

At the Massachusetts General Hospital he was an enthusiastic advocate for the importance of his department, and it was a pleasure for him to watch it grow from a small outpatient group to a well established unit, with its own ward in the general hospital and with multiple ramifications into the other departments. But his interests within the hospital were not confined to his own department, and he served for a number of years as chairman of the General Executive Committee.

Taylor established many connections with hospitals in cities near Boston. One of his particular interests was the Long Island Hospital, a city institution for chronic disease in Boston Harbor. Here he did his earliest pathologic work after returning from Berlin. Up to the time of his death, he served as secretary of the Board of Visiting Physicians. In his earlier days he did much of his teaching at this institution, and some of his best papers result from long clinical observation of chronic cases with correlated necropsy reports. His interests were also broadened by membership on the Massachusetts State Board of Insanity, and later as consultant at the Riggs Foundation in Stockbridge, in both of which capacities he served for a number of years.

In practice, he soon gained the respect of his brother physicians. His friendly spirit endeared him to many. This was clearly shown by the unusual spontaneous enthusiasm of his medical colleagues at his sixtieth birthday, May 7, 1926, when a complimentary dinner, largely attended, was given in his honor.

From the time of his graduation from college he was always interested in the literary side of medicine. He served on the staff of the *Boston Medical and Surgical Journal* as assistant editor (1899-1912) and finally as editor (1912-1914, inclusive). Other activities included positions on the editorial board of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, the *Journal of Nervous and Mental Diseases*, and the *New England Quarterly*. For many years he edited the Collected Reprints, department of neurology, Harvard Medical School.

Taylor became a member of the American Neurological Association in 1895, vice president in 1912, president in 1917, and councillor from 1918 to 1922. He was a member of many societies, serving as secretary of the Boston Society of Medical Sciences; president of the Boston Society of Psychiatry and Neurology in 1913; president of the Boston Society for Medical Improvement in 1912-1913; president of the Boylston Medical Society in 1911-1912; chairman of the medical section of the Suffolk County Medical Society, and vice president of the Association for Research in Nervous and Mental Disease in 1921. Other memberships included the American Academy of Arts and Sciences, the American Medical Association, the American Psychopathological Association, the Association for the Study of Internal Secretions, the Massachusetts Medical Society, the New England Psychiatric Society and the American Association for the Advancement of Science. From 1899 to 1901 he served, also, as professor of neurology at the University of Vermont. He was granted an A.M. degree by Harvard University in 1899.

His medical contributions consisted of nearly one hundred papers, many of them, before publication, being read before local or national societies. Particular interest was shown along two lines of thought:

multiple sclerosis, which occupied his attention from the time of his earliest medical work in Oppenheim's clinic up to the latter years of his life, and psychotherapy, which was always prominent in his mind. In 1894, he published, in German, a paper on the pathology of multiple sclerosis. This was the beginning of his interest in the disease; a second paper, in 1906, contained some of the best illustrations of pathologic tissues published in this country up to that date; another on the location of lesions with respect to symptoms was presented at a meeting of the Association for Research in Nervous and Mental Diseases, 1921, and chapters on the same subject were contributed to "Nelson's Loose-Leaf Living Medicine," 1920, and "Cecil's Text-Book of Medicine," 1927.

In 1906, psychotherapy in its newer applications was considered, and, the next year, the whole subject was reviewed. Strongly of the opinion that simple methods have a place in psychotherapy, he published his views from time to time. These papers, published during the height of the freudian controversy, served a double purpose, for they not only tended to draw together the extremists, but served to emphasize the importance of psychotherapy in the minds of the medical practitioner at a time when such clearcut, logical exposition was greatly needed. "My only present contention," he wrote in 1917, "is that it is our duty to make the far-reaching principles of the newer psychological methods as universally applicable as possible, and to accomplish this it is essential that they should be made usable under the conditions which actually confront us in dealing with our patients. This is worth striving for, even at the risk of being charged with superficiality."

Other papers of more than usual interest were on the following subjects: adiposis dolorosa (an early account); miliary aneurysm of the brain; diffuse degeneration of the spinal cord; senile trepidant abasia; injuries to the spinal cord; a new syndrome, progressive vagus-glossopharyngeal paralysis with ptosis, and neuroglia (a very early paper). In the last study he used the Mallory stain, which at that time was just coming to be recognized, to demonstrate fibrils. In addition, the passing of one of his colleagues always called forth a biographic notice, written in a charming style, not often equaled in medical literature.

Outside of his medical work, Taylor had many interests. He wrote a number of papers on witchcraft, especially the medical aspect of the problem. In his later years he became a devotee of chess, and established an informal club in Boston which met frequently in his house. On the grounds of his summer home at Ipswich he built a small stone building, known as the "chess house," ingeniously devised in the shape of a chess "castle" where he could play a quiet game surrounded by pine trees which he himself had planted many years before. He particularly enjoyed the quiet friendship of medical colleagues and others, and for many years he was a member of a small medical dinner club. He was

a popular member of his class in Harvard College and often spoke at the reunion dinners. On Oct. 14, 1897, he married Elsie Brewster Howe, in New York. She and two daughters survive him.

Such in brief outline is the medical life of Taylor—a persistent worker, almost exclusively in his chosen field of neurology. Much good original work stands under his name, but without doubt his greatest contribution was of a personal kind. He was one of a rare group who knows not the meaning of jealousy; on the contrary, generosity and honesty were his outstanding characteristics, endearing his associates to their chief in a manner not often attained. His was never the hand of the task-master. Though his love of his profession was great, his life was conspicuously balanced, for his participation in games and sports and his interest in even the trivial affairs of his friends were vital to him. Even-tempered, optimistic, alert, often humorous, these are some of the characteristics which come to mind when we think of Wyllys Taylor, not as a doctor, but as a friend.

J. B. A.
H. R. V.

Abstracts from Current Literature

PROGRESS IN THE TREATMENT OF TABES. B. DATTNER, Fortschr. d. Neurol., Psychiat. **2**:516, 1930.

In tabes, reports of favorable therapeutic results must still be accepted with great reserve, since, more than in dementia paralytica, the course of the disease tends to spread over many years. A large series of successfully treated patients is still required to help support the reliability of a given therapeutic method. In a statistical evaluation of therapeutic results, tabes does not present as imposing results as does dementia paralytica (based on the malarial treatment). The question of diagnosis in tabes also makes any evaluation of therapeutic results in this disease difficult. The symptomatology of tabes is not as specific as that of dementia paralytica and a larger number of cases of pseudotabes are encountered than of pseudodementia paralytica. The results of serologic tests are more often completely negative in tabes than in a stationary case of dementia paralytica, which, of course, speaks just as strongly for the presence of an arrested process as against the assumption that a tabetic process is present at all. The fact that not all the symptoms of tabetic disease have equal value must also be considered in evaluating a therapeutic method and its results. Results are difficult to estimate because of the difference of opinion among authors as to the so-called "residual symptoms" (Restsymptome).

Statistics of the results obtained by various authors in the treatment of tabes with malaria cannot be compared with those obtained in similar treatment of dementia paralytica. A large number of therapeutic results are conceded by nearly all authors. Disagreement among the various writers prevails insofar as many of them are of the opinion that malaria can be highly recommended only when other methods have failed, while others advise malarial therapy at the outset, since it not only removes therapeutically receptive clinical signs of the tabetic process, but also manifests an excellent influence on the serologic syndrome.

The reports of Jakob and Vohwinkel speak favorably of combined bismuth, malaria and neoarsphenamine in the treatment for tabes. In their thirty-five cases they noted an improvement in the crises and other painful manifestations, in the bladder and rectal symptoms, in the ataxic gait and visual disturbances and in other tabetic manifestations as well. They frequently noticed an increase in weight and in two instances a return of the patellar reflexes. Paulian, in thirty-eight cases, reported improvement in the ataxia and lancinating pains in 65.7 per cent. The serologic findings also shared in this improvement. Of the twenty-five cases of Jakob and Vohwinkel that before treatment showed positive serology, after treatment only three remained positive, whereas nine were negative, thirteen showed improvement and only one became aggravated. A similar effect on the spinal fluid was observed by Wüllenweber, who, examining the spinal fluids in nineteen of his thirty cases after treatment, obtained normal or much improved findings in fourteen cases (82 per cent).

The treatment of tabes with African recurrent fever has received such scant attention in the literature that one is unable to orient himself concerning its therapeutic position. Since recurrent fever unquestionably makes less demands on the resistance of patients than does malaria, Steiner recommends its use in tabetic patients who display marked physical reduction.

In order to avoid the heroic method of making use of an infectious disease as a form of therapy, other methods of treatment for both tabes and dementia paralytica have been developed for the purpose of releasing, by artificial means, fever reactions of shorter or longer duration. In the treatment of metasyphilis, Siemerling recommended pyrifer (a member of the B. coli group obtained from milk and made apathogenic), and this treatment has many adherents. The injection, which is increased from 50 to 5,000 units, provokes a fever of varying degree and duration in from one-half to one hour. After two years' experience

with pyrifer therapy, Siemerling reported that of sixty-four patients treated with this method, no less than fifty-six, or 87 per cent, showed improvement. Mandl, Sperling, Jehn, Meir and Eskuchen also reported favorable effects from pyrifer on lancinating pains, gastric crises and ataxia.

In recent years, American authors have been using typhoid vaccine to produce fever in the treatment of metasyphilis. Some French authors use a streptococcus vaccine, known as dmelcos of Nicolle (Deecrey bacillus) to produce fever. An Italian report of Artom, based on fourteen cases of tabes, in which six patients received malaria and eight dmelcos, stated that the favorable effects on the subjective complaints as well as on the gastric crises is the same with both methods. There is nothing new to report on the use of other fever-producing substances.

Schroeder uses a 1 per cent suspension of pure sulphur in olive oil. Even small doses, which are gradually increased from 0.5 to 10 or 12 cc., by intramuscular injection, provoke high temperatures from eight to fourteen hours later. According to Schroeder, ten injections constitute a series. Two weeks later another series follows. A complete course of treatment usually requires from two to three series, which, however, may be increased. In six tabetic patients whom Schroeder treated with a combined therapy of sulphur in olive oil and antisyphilitic remedies, a decided improvement was seen in four. As patients with cerebrospinal syphilis and a positive serology treated exclusively with sulphur in olive oil showed a return to a normal cell count, this preparation actually seems to have an important place in the system of pyretotherapy.

Methods of producing fever by physical means are also in vogue. Two American authors, Mehrtens and Pouppirt, employ hot baths (based on Egyptian, Greek and Roman medicine), with temperatures ranging from 104 to 105 F. The temperature of the water is increased to 110 F., and the bath prolonged for one hour. The patient is then wrapped up and placed in bed with hot-water bottles. This procedure is repeated each day. A course of treatment consists of fourteen baths. In twenty cases of tabes with lancinating pains and gastric crises, Mehrtens and Pouppirt observed improvement in all. In one case with severe gastric crises, in which all relief seemed fruitless and morphine was required, and in which the crises would last for several days, the pain disappeared within twenty minutes. These improvements were not always lasting. Recurrences frequently occurred after intercurrent infections; the attacks, however, appeared less stubborn. In addition to hydrotherapy, in ten cases antisyphilitic therapy, which was not described, was administered, and better results seemed to be obtained.

A new therapeutic principle was expressed in the suggestions of Schrottenbach who recommended cutaneous injections of ponndorf B and cutivaccine Paul, preceded by intravenous injections of an iodine preparation. Immediately after the first intravenous injection of this preparation the first cutaneous vaccination is given, and after about five more injections another cutaneous vaccination follows. In all, about four vaccinations and twenty intravenous injections are given, the latter about every second day. Only mild elevations of temperature are produced (generally to about 38 C.), which recede within about from twelve to twenty-four hours. In any event, an ample local and general reaction to the cutaneous vaccination must be obtained. If this does not occur, a new vaccination must be undertaken within from two to four days. Schrottenbach obtained definitely favorable results in a patient with nervous gastric symptoms, in one with intestinal crises, in one with radicular pains in the back and in three with lancinating pains.

In hitherto untreated patients, Reid preferred to administer intensive specific treatment, from three to four courses of neoarsphenamine, supplemented by injections of mercury and bismuth. Thomas recommended a mixed preparation of bismuth and arsphenamine known as bismarsen, which is easily absorbed by intramuscular administration. Solomon and Viets considered tryparsamide superior to arsphenamine or intraspinous therapy, but were not decided on the method most suitable because of the danger of injuring the patient's vision, which cannot be avoided in all cases, and because headache, nausea and states of confusion often follow injections of typarsamide. Reese, who believed in an individualized treatment, recommended from 4 to 5 Gm. of tryparsamide in gastric crises and lancinat-

ing pains, given at intervals of two weeks for twelve weeks, the patient having first been prepared by inunction therapy and iodine for from four to six weeks.

The various intraspinous methods of treatment are still in vogue despite the objections of men like Wagner-Jauregg and Nonne, and Kissóczy and Woldrich, who produced aseptic meningitis by introducing air into the spinal canal so as to increase the permeability of the meninges and thus facilitate the passage of chemicals from the blood serum into the spinal fluid, and who reported that they obtained favorable results in ten cases of tabes with crises and lancinating pains. In one case the ataxia was markedly improved. Every fourth day, in fractional doses, they drained about 20 or 30 cc. of spinal fluid and introduced from 15 to 25 cc. of air. They repeated this procedure from five to seven times and the course of treatment from two to three times. One hour later, they administered from 0.3 or 0.45 Gm. of neoarsphenamine. There were no unpleasant sequelae, except a slight elevation of temperature about five hours after the operation. Lafora claimed to have successfully used intraspinal injections of sodium bismuth tartrate in patients with tabetic arthropathy.

Dattner then considers the problem of treating patients with special tabetic symptoms — optic atrophy, arthropathies and osteopathies, ataxia, lancinating pains and gastric crises. He cautions against evaluating the results of treatment for optic atrophy, because the spontaneous termination of tabetic optic atrophy rests on the influence of unknown factors. It is important to remember that the number of patients with optic atrophy, compared with figures for 1905, 1910, 1920 and 1925, shows no reduction despite modern methods of antisyphilitic therapy. Meesmann and Roggenbau reported their observation in treating optic atrophy by intraspinous therapy. Their work is based on twenty-one cases that have been followed since March, 1927. In twenty of the twenty-one no aggravation of the ocular symptoms occurred; in nineteen the rapidly progressing tabetic process was impeded, and in two cases an arrest of the condition was observed for two and one-half years. Winkler reported success in treating optic atrophy with sulphur. He used a sulphur preparation in doses of from 0.1 to 0.2 Gm. injected intramuscularly and combined with bismuth; this provokes fever, an increase of intermediary metabolism and more rapid elimination of the products of metabolism. Ten such injections are given within a period of ten weeks. Of seven patients so treated, five showed an increase in the field of vision and a return of color sensation. Mauksch used a rhinologic method of treatment for tabetic optic atrophy. In order to influence the circulation of the optic nerve, he first opened the ethmoidal cells and the sphenoid sinus, thereby causing a wound in the mucous membrane which did not heal by primary intention. In this manner he produced hyperemia of the surrounding tissue and adjacent periosteum, which, in his opinion, is transferred to the nearby optic nerve. Then he introduced a tampon saturated with epinephrine in the region of the ethmoid, whereon first blanching and later hyperemia of the mucous membrane set in, which was increased by the stimulation of the tampon. With this method, Mauksch claimed to have obtained an improvement of vision as well as of the visual field in four of five patients thus treated. Dattner emphasizes the necessity of early treatment and laments the fact that treatment is so often started after the disease is well under way.

Treatment for the arthropathies and osteopathies received slight consideration in the literature. Lafora's method of treatment is based in part on the trophic theory of Charcot (lesion of the medullary centers) and in part on Volkmann's and Virchow's theory of trauma. It aims, by means of irritating the meninges, blood vessels and nerve parenchyma, to set the trophic-medullary centers into a state of stimulation and thereby to usher in a restoration of function. He reported on a case of tabes of over sixteen years' standing, with arthropathy of the knee joint, paresthesias, ataxia, sphincter disturbance and impairment of potency, epileptiform attacks, reduction of vision on account of bilateral optic neuritis, a history of two spontaneous fractures and areflexia. The serologic findings were almost negative. With two intraspinal injections of tartrobi (Roche) plus intramuscular injections of bismuth and later a course of neoarsphenamine, the patient

showed an almost complete restoration of the knee joint, improvement of vision and a recession of the ataxia.

In the treatment for ataxia, there was no progress beyond mechanical methods of treatment.

Real progress was made through the unusually fruitful conception of Wagner-Jauregg of the character of lancinating pains and gastric crises. The observation that sometimes, despite continued pain, no progression was seen in a tabetic process led Wagner-Jauregg to the theory that lancinating pains and crises are in some manner the result of irritating noxae which act on a structurally changed nerve tissue. He compares this condition to polyneuritis, in which the process is mainly focused on the medullary sheath and, on the one hand, causes it to atrophy, while, on the other, it may often merely cause segmental decay, which may finally lead to a destruction of the nerve fibers, though not necessarily. He also compares this situation to the manifestations that are present at the central stump of severed nerve trunks. Whenever the continuity of a nerve is destroyed by trauma, thereby causing a central stump, painful irritations analogous to lancinating pains are observed. Wagner-Jauregg believes that the point of attack for such irritants that may release lancinating pains is the peripheral neuron. He believes further that the changes that provoke the nerve to react in this manner are similar to those found in polyneuritis and in so-called retrograde degeneration, which experience shows may remain stationary in old nerve stumps. Evidence for this notion, in his opinion, seems to be indicated by the fact that in an advancing case of tabes, lancinating pains often become reduced. Irritants that tend to release the lancinating pains Wagner-Jauregg divides into: (1) meteorologic, e. g., coldness, dampness, marked barometric fluctuation, heavy winds, sultry weather, rain and snow, wherein individual sensitiveness plays a prominant rôle; (2) disturbances of the alimentary tract, constipation, dyspepsia, etc., in which toxic products of digestion may possibly be important, and (3) infectious-toxic conditions, because by experience rhinitis, angina and even every febrile reaction associated with nonspecific therapy tend to aggravate lancinating pains. Sensitiveness to pain is dependent on a constitutional factor. The faculty of feeling stimuli as pain is as a rule individually graduated. It is clear that in line with this conception, treatment must aim to exclude first of all the irritants that may release pain; and in cases in which this is impractical one must use methods that are capable of raising the patient's threshold of stimulation to a considerable degree. To exclude meteorologic irritations, Wagner-Jauregg recommends wearing deerskin underwear during cool or cold seasons. Following his observation that a diet rich in sugar tends to release lancinating pains, Kogerer recommends injections of insulin for both lancinating pains and gastric crises. Acidity of the tissues caused by articles of food that tend to produce acidity provokes painful sensations, whereas alkaline measures, dietetic or pharmaceutic, often bring immediate relief.

The expectations anticipated from surgical treatment for gastric crises, which, like lancinating pains, represent a crux medicorum, have generally not been fulfilled, according to Mandl, one of the best informed men on operative methods in this field.

Marinesco believes that a disturbance of the acid-alkali balance may lead to an alkalosis-vagotonia affecting especially the fifth to the tenth dorsal segments. The result is an increase of gastric tonus, increased peristalsis, pains and vomiting, as well as a local vagotonia. He obtained excellent results in these patients with intraspinous injections of from 1 to 2 cc. of a 25 per cent freshly prepared sterile solution of magnesium sulphate. Pain and vomiting disappear in about thirty or fifty minutes after treatment.

BOLTZ, Binghamton, N. Y.

A STATISTICAL STUDY OF MULTIPLE SCLEROSIS. OTTO MARBURG, Jahrb. f. Psychiat. u. Neurol. **48**:303, 1932.

Five thousand neurologic patients observed since the World War constitute the basis of this study. There were 152 cases of multiple sclerosis among them (3.2 per cent); if one considers only the number of organic cases among the

5,000, the percentage of multiple sclerosis is almost 10 per cent. In a similar study undertaken before the war the percentage of cases of multiple sclerosis was only 6 per cent of all organic cases. The disease affected 102 females and 50 males. Marburg points out that in his postwar material the percentage of females affected with dementia paralytica and other syphilitic diseases has shown a marked increase over that of males, as compared with the material before the war.

Judging by the time of onset of the first symptoms, the ages of incidence are as follows: first decade, 2 cases; second, 23; third, 30; fourth, 48; fifth, 25, and sixth, 3. One patient was too psychotic to be able to give his age. The figures as to racial incidence are not given in detail because Marburg states that most of the 80 patients who said that they were Viennese were not. One fact, however, was striking, that among the Japanese the disease is unusually rare, while it is unusually prevalent among Jews. As to occupation, whereas most statistical reports seem to show that the largest number of cases occur in laborers and farm hands, Marburg could find only 5 patients with these occupations in his series; the remainder had no occupation, did housework, were intellectuals or were factory workers. It would seem, then, that the generally prevalent idea that the disease spares those engaged in intellectual occupations will have to be revised.

Although constitutional factors are supposed to play no rôle in multiple sclerosis, Marburg found in his series 3 cases of familial incidence. In 1 case, that of the mother, the disease developed relatively late in life (at 36) while it developed in her daughter at the age of 18. In the second case the disease affected 3 generations (all patients being female), and in the third case, a mother and 2 daughters. Marburg also calls attention to the fact that most of the females with the disease showed a skin with poor circulation and unusually narrow cutaneous veins.

Another etiologic factor discussed is trauma. Psychic as well as somatic traumas are considered. The former seem to be effective through the vasomotor system and the latter through the same system and, in addition, by direct injury to a previously predisposed nervous system. A history of psychic trauma was found in 3, and somatic trauma in 12, cases. Marburg cautions that before one attributes multiple sclerosis to trauma it is essential that the trauma be adequate and that the symptoms or an aggravation of the disease appear immediately after the receipt of the injury.

To establish a reasonable etiologic relationship between the infectious diseases of childhood and multiple sclerosis is still more difficult, because most persons have had measles, scarlet fever and diphtheria in childhood. These diseases then play no etiologic rôle, and need never be seriously considered in this connection unless they appeared late in life, when the symptoms of multiple sclerosis or their aggravation became manifest immediately after the infectious disease has run its course. Marburg could find only 1 such case in his entire series; it occurred in a woman, aged 47, in whom, at the age of 33, a few months after an attack of scarlet fever, a left-sided paralysis developed. This disappeared after five months; the next year there appeared diplopia, vomiting and disturbances in gait; these symptoms improved but soon returned and were associated with bladder disturbances; there have since been several remissions, and there is no question that the patient is now suffering from typical multiple sclerosis. In another case the symptoms of multiple sclerosis appeared immediately following an attack of grip, complicated by pneumonia.

In 56 cases the first symptom of the disease was referred to the lower extremities, at first with a feeling of "tiredness," which was soon followed by definite pareses. Most of the patients also complained of vague pains, especially in the back and calves. These symptoms, however, were not isolated but were initially associated with bladder disturbances, visual defects, diplopia and sensory irritative phenomena. In 21 cases, sensory disturbances were an isolated initial manifestation; these consisted of pains (in 1 case a genuine trigeminal neuralgia) and

paresthesias, often in 1 extremity and occasionally in one half of the body or in several extremities. The next early symptom in the order of frequency was disturbances referable to the optic nerve; these were observed in 19 cases, in most of which retrobulbar neuritis was the first symptom. Paralysis of the ocular muscles giving rise to diplopia was noted in 8 cases, in most of which (6 cases) it was due to a paralysis of the abducens nerve.

Symptoms of increased intracranial pressure are not at all rare initial symptoms. Headache, nausea, vomiting and papilledema were the first symptoms in 8 cases. One case presented, in addition to these symptoms, also cerebellar signs, and in the absence of evidences of multiplicity of lesions the patient was subjected to an operation for tumor of the brain. Six months later the true nature of the condition was recognized.

Pareses of the upper extremities are, in contrast to those of the lower, much less common as initial symptoms. Great care must be taken in the evalution of this symptom; it is not infrequently confused with clumsiness, ataxia and even astereognosis. When the paresis affects the right upper extremity a disturbance in the ability to write may be the first symptom in those engaged in intellectual pursuits.

The following symptoms were also noted as initial manifestations: vestibular attacks (Ménière) in 4 cases; cochlear disturbances in 3 (annoying tinnitus with sudden deafness); peripheral facial paralysis in 3, and disturbances in deglutition in 3. It is noteworthy that genito-urinary symptoms as an initial manifestation were noted in only 2 cases, and fecal incontinence in 1. Epileptiform seizures were initial symptoms in 2 cases; loss of speech was the first manifestation in 1, nystagmus associated with tremor in 2, nystagmus of the head in 1 and tremor alone in 1.

Another misleading initial symptom is hemiplegia; it occurred in 6 cases. In the absence of multiple lesions the hemiplegia could not be distinguished from the hemiplegia due to a cerebral vascular accident. Bradyphasia was the first symptom in 1 case, and lightning-like pains during movement in another. One case began with paralysis of the ulnar nerve, but the diagnosis was readily established, because the ulnar paralysis was soon followed by diplopia. Another case began with a sensation of a sudden loss of tone—"collapse with sudden giving way of the knees"—and 1 case began with a peculiar melancholia which was soon followed by the appearance of somatic symptoms of multiple sclerosis.

Charcot's symptom triad was conspicuous by its absence in most of the cases. In 51 cases the abdominal reflexes were absent; these cases do not include those with relaxed abdominal walls in which on repeated examinations, especially when the patient's attention was distracted, these reflexes could be elicited. In 8 of the 51 cases there was no plantar response. In 6 cases the abdominal reflexes were absent on one side only, or the uppers were present and the lowers absent, or vice versa. Repeated reexaminations occasionally revealed that after a lapse of some days a previously unobtainable abdominal reflex would be present and perhaps be unobtainable again at the next reexamination. The plantar reflex was absent in 12 cases and the cremasteric in 3. The Babinski sign was bilateral in 33 cases and unilateral in 3. In only 7 of the cases with a positive Babinski sign could a positive Rossolimo sign be obtained. In most cases the loss of abdominal reflexes was associated with a positive Babinski sign. In several cases a Babinski sign could be obtained only by stimulating the sole of the foot in the anterior portion of the metatarsal pad; in these cases there was also a positive Rossolimo sign. Not infrequently a patient would show patellar clonus, a normal ankle jerk, a positive Babinski and a Rossolimo sign on the same side. Such antagonism of reflexes is, according to Marburg, one of the important criteria for the diagnosis of disseminated sclerosis.

Clinical types of multiple sclerosis: The initial symptom may be the only symptom and may persist throughout the entire disease. Marburg designates these cases as oligosymptomatic. The entire series includes 18 such cases. In this group are also included such combinations as retrobulbar neuritis, a positive Babinski sign and somewhat diminished abdominal reflexes; paresthesias in the

upper extremities and a positive Babinski sign; a slight paresis in one of the lower extremities, absent abdominal reflex and the presence of ankle clonus, and pains in the back, difficulty in walking and lively tendon reflexes. Only 15 cases presenting the Charcot triad were found in the entire series. These cases are designated as belonging to the classic form of multiple sclerosis.

In 8 cases the disease presented at the onset the clinical picture of tumor of the brain. Six cases presented the picture of hemiplegia for a long period and 2 of these began in apoplectiform fashion. Among the rarer forms of the disease were 2 cases with the picture of tabes, 1 vestibular, 2 sensory and 1 bulbar. Three patients belonged to the spinal type and showed a Brown-Séquard paralysis. In 1 case the predominating clinical feature was a psychic disturbance. Eight patients began with "ophthalmic" manifestations, which persisted later in the disease. Four cases ran an acute course, and 112 a chronic progressive intermittent-remittent course. Two were stationary. No case presented a purely chronic progression without remissions. In the remaining cases the history is too indefinite to enable one to classify them. Although there occur many cases of multiple sclerosis without progression of symptoms and with long remissions that may last for decades, Marburg doubts whether one is justified in speaking of benign forms, and this in spite of the fact that he found in his series 2 cases that had remained stationary for many years.

KESCHNER, New York.

HISTOPATHOLOGY OF THE SYMPATHETIC GANGLIA IN ACUTE INFECTIONS. C. G. CHODOS, Ztschr. f. d. ges. Neurol. u. Psychiat. **135**:358, 1931.

Relatively few studies have been made on the pathology of the sympathetic ganglia. There are two schools of thought concerning the interpretation of the pathologic findings; one looks on them as specific for the disease under investigation and as explaining the syndrome in question, and the other looks on them as merely a part of a complicated series of changes unexplained by the pathologic condition in the sympathetic ganglia.

Chodos investigated all the cervical sympathetic ganglia, the semilunar ganglion of the solar plexus, the second and third ganglia of the thoracic chain and the rami internodal ganglia in the cervical chain in forty-three patients. The cases studied were distributed as follows: scarlatina, eighteen; diphtheria, seven; measles, three; typhus abdominalis, two; typhus exanthematicus, one; lobar pneumonia, two; sepsis, six; tuberculous meningitis, two; anthrax, one; rabies, three; cerebral tumor, one, and Little's disease, one.

There are certain normal variations in the structure and connections of the ganglia in persons of the same age, which Chodos points out. Some authors have tended to speak of sclerosis of the ganglion in cases in which the ganglion is smaller than normal. This is really a normal variation in size. The confusion as to the normal is seen in the measurements given for the upper cervical ganglion by three authorities: Spalteholz, 2 cm.; Ranvier, from 25 to 30 mm., and Hovelacque, 5 cm. Chodos has seen a superior cervical ganglion that was one and a half times as large as that of the opposite side. There are some cases of complete union between the superior cervical ganglion and the ganglion nodosum of the vagus. It has been known for a long time that these two ganglia are connected, but it has not been pointed out that they may sometimes be one complex. This was true in seven of thirty-five cases seen by Chodos.

There can be no doubt that there are changes in the sympathetic ganglia in general infectious diseases. This has been reported by a number of authors. The only questions to be settled now are: How frequently in these diseases are the sympathetic ganglia involved? How severely are they affected, and what is the significance of the changes? Analysis of Chodos' material shows that the sympathetic ganglia often show severe pathologic changes, which may be inflammatory or degenerative, and that in the majority of cases with fatal result the nerve parenchyma and the stroma of the ganglion are so severely affected as to make the changes assume a great significance in the rôle of the disease.

Chodos divides the changes seen in the sympathetic ganglion cells according to Nissl's classification — swelling, shrinking and liquefaction of cells. Acute swelling was not seen in a single case. Nevertheless, swelling of the ganglion cell is not uncommon and is characterized by solution of the stainable substances, homogeneity of the cytoplasm and enlargement of the nucleolus. Often there is dissolution of the Nissl substance without other changes in the cell nucleus or cytoplasm. Shadow cells are not common.

Cell shrinkage is not often seen in sympathetic ganglia, but some of the characteristics of this process are seen here and there in different cells. One often sees an intensive staining of the cell body and diffuse coloring of the nucleus, without any evidence of shrinkage of the cell. At times there is a picture like Nissl's chronic cell disease — dark staining of the nucleus, which has an angular outline, diffuse, intense staining of the cytoplasm, a large nucleolus and marked visibility of the processes, but no evidence of cell shrinkage.

Liquefactive processes in the cells are common and assume many different forms. Vacuolization of the cytoplasm is extremely common and has been remarked by a number of observers. The liquefaction is shown by a disease of the nucleus with relative intactness of the cytoplasm, by a hyperchromatic nucleus with a dirty appearing cytoplasm or by a granular disintegration of the cell.

Often there are changes in the sympathetic ganglion cell that belong to no definite group. Silver methods show changes in the intracellular neurofibrils and in the shape and size of the nucleus, the nucleolus and the cytoplasm. Often there are swellings of the cell processes as well as shrinkage. In the latter instances the cell processes become tortuous and thinner.

There have been some observations on changes in the nerve fibers of sympathetic ganglion cells in acute infectious diseases. Mogilniezky found that changes in the nerve fibers were much less constant than those in the ganglion cells. He found myelinated fibers that were severely affected in cases of diphtheria, with loss of myelin and pathologic changes in the axis-cylinder. Terplan has found no definite changes in the nerve fibers in these diseases. Herzog said that degenerative changes in the myelinated and unmyelinated fibers are rare. Chodos found proliferation of the cells of Schwann in six cases. Elzholz bodies were often found and, not infrequently, true wallerian degeneration. Definite changes in the nerve fibers were found in fifteen cases; five times in scarlet fever and dysentery and once in measles, typhoid, typhus, pneumonia and rabies. In most instances the changes involved only small groups of fibers or only isolated fibers. They were characterized by a granular disintegration, fragmentation, swelling and tortuosity of the axis-cylinders. The changes in the axis-cylinders in acute infections of the sympathetic ganglia correspond to those seen in the peripheral nerves.

The vessels in the ganglia in acute infections are often dilated and filled with blood. Hemorrhages are not usually seen. A marked hyalinosis of the vessel walls was found in people with arteriosclerosis and twice in children. At times the vascular endothelium was swollen and desquamated. The question whether there is increase in the intercellular tissue in the sympathetic ganglia in disease conditions is hard to settle. Age causes an increase in this tissue, and the determination of an increase in the stroma is largely subjective. Chodos found it in only three of his cases.

The infiltration in the ganglia was variable, in some cases all the vessels showed infiltration, and in others only scattered areas of infiltration were found. The same was true of the tissue among the ganglion cells, which was diffusely infiltrated. In the cases of scarlet fever and sepsis the infiltration was chiefly around the vessels, but in some cases was diffuse in the stroma. In typhoid, in addition to perivascular foci, there were areas of diffuse infiltration in the ganglia. The infiltrate was chiefly polyblasts and lymphocytes, with plasma cells present in some cases. In scarlet fever, diphtheria and pneumonia there were vessels that were infiltrated entirely with plasma cells and that looked much like the picture in dementia paralytica. In two instances Chodos found a plasma cell within the capsule of the ganglion cell. He believes that the presence of plasma cells is

not alone due to the slow course of the infection, but that they occur in definite diseases, as, for example, those mentioned.

Chodos investigated the presence of glycogen in the sympathetic ganglia. In the central nervous system there is no glycogen normally, except in the hypophysis, choroid plexus and rods and cones of the retina. It is found in infections of the nervous system, but not constantly. It is most commonly found in the adventitia of the vessels, less frequently in the glia cells, and still less often in the ganglion cells and their processes. Munzer, in 1928, found glycogen in the peripheral nerves in two cases and in the gasserian ganglion in a case of pneumonia in a girl, aged 16. Chodos found no reference to the presence of glycogen in the sympathetic nervous system in the literature. He found it in the ganglia in one case each of scarlet fever, measles, rabies and typhus. The glycogen may lie free in the stroma beside the vessels or in the capsule or ganglion cells as fine or coarse granules.

Chodos believes that the sympathetic nervous system is involved as part of the disease process in acute infections. The changes are not specific for any one disease, however. There must be some clinical effect of all this on the patient. What this is, Chodos is unable to say.

ALPERS, Philadelphia.

DIFFUSE SCLEROSIS AND MULTIPLE SCLEROSIS. MAX BIELSCHOWSKY AND OTTO MAAS, J. f. Psychol. u. Neurol. **44**:138, 1932.

The authors report the case of a man, aged 35½, who, except for two generalized seizures within two months before admission to the hospital, had always been in good health. The seizures were associated with loss of consciousness, urinary incontinence and pupillary rigidity. During the next six months the convulsions became more frequent, and it was noted that the patient's behavior became somewhat peculiar; he began to laugh without provocation. There were no evidences of organic nervous disease till two years after the first convulsive seizure, when there appeared right homonymous hemianopia, partial mixed aphasia, dyspraxia and a slight right hemiparesis which included the face. The hemiparesis gradually increased, so that eight years after the onset of the illness he was completely hemiplegic, and both optic nerve heads showed temporal pallor. He remained practically in this condition for the next five years when he died during an epileptic attack. The illness lasted thirteen years. The clinical diagnosis was: cerebral tumor (?) and encephalitis of the left frontal lobe (?).

Necropsy revealed two types of lesions throughout the brain and cord: (1) sharply limited foci characteristic of multiple sclerosis and (2) diffuse alterations in the cerebrum—sclerosis of almost the entire white substance of both hemispheres. The thalamus showed lesions that appeared as if they had originally been small foci that later became confluent. Whether or not the lesions in the cerebrum were of the same nature could not be determined. The glia, which was the basis of the sclerosis, was not of the same density throughout the affected areas. The changes in the white substance were not like those in multiple sclerosis; the demyelination was much less marked. This was also true of the demyelination of the fibers in the convolutions. The process was one of atrophy with sclerosis rather than of demyelination. In other words, the process was one of diffuse sclerosis without corresponding demyelination.

On superficial examination the numerous plaques in the cerebral cortex resembled those usually observed in multiple sclerosis and in dementia paralytica. Detailed histologic examination revealed that the lesions were not characteristic of either of these two conditions.

The authors point out that the phenomena of productive reaction in the macroglia, especially of those that develop by formation of fibers, were more marked than in the case reported by Kufs. It is for this reason, as well as because of the unusually extensive dissemination of isolated foci of sclerosis, that they believe their case to be unique. According to Kufs, the occurrence of transitional lesions between the mildest forms of multiple sclerosis and the

severest forms of diffuse sclerosis does not justify the establishment on clinico-pathologic grounds of special groups of these two diseases. Similar difficulties are encountered in attempting to draw definite conclusions as to etiology from morphology. The potentiality of reaction of the organism is limited, so that noxae of an entirely different nature may produce reactions that are similar. This is especially exemplified when one compares the lesions of diffuse encephalitis with those of "pure" polysclerosis. The lymphocytic and plasmocytic infiltrates in the sheaths of the blood vessels and in the parenchyma adjacent to them have been generally assumed as evidences of an infectious process. This, however, is by no means always the case. Spielmeyer has recently called attention to the fact that infection of the central nervous system may manifest itself in various ways. According to him, "it is as difficult to deny in some cases the possibility of an infectious genesis in degenerative processes and in lesions due to circulatory interference as it is to establish it in processes which appear definitely inflammatory, for inflammations may be produced by all sorts of poisons, and some may even represent secondary or symptomatic reactions of endogenous processes." In this connection it must also be borne in mind that in the present state of knowledge it is impossible to state what rôle exogenous factors may possibly play in the production of the characteristic lesions of diffuse encephalitis and of poly-sclerosis. The problem becomes further complicated because no one can deny the possibility that in these two diseases the deleterious effects of the exogenous factors may be activated or enhanced by endogenous factors based on constitutional and hereditary influences.

Bielschowsky and Maas believe that no final classification and separation of the various forms of scleroses will be possible until more and better knowledge of their pathogenesis is available.

KESCHNER, New York.

EPIPAPILLARY TISSUES. BERNARD SAMUELS, Arch. Ophth. **6**:704 (Nov.) 1931.

This paper is based on the microscopic study of 300 eyes, the major portion of which were adult eyes. Seventy sections were from eyes with congenital defects or defects present at birth, the defects in the other cases being the results of pathologic conditions in the optic nerve or in the tissues immediately contiguous to it. Under congenital defects, Samuels discusses the remains of the hyaloid artery, voluminous connective tissue in the pit of the papilla and connective tissue in relationship with other intra-ocular anomalies. With reference to remains of the hyaloid artery, the congenital tissues can be grouped into four general classifications: (*a*) strands of connective tissue of varying length and thickness; (*b*) clumps of pure glia cells, representing a more advanced stage in the involution of the artery than that of those just mentioned; (*c*) membranes of pure glia cells spread over the medial aspect of the nerve head, and (*d*) cellular masses in the pit of the papilla. The other congenital defects are 6 in number, occurring in cases showing connective tissue ensheathing the retinal vessels.

The remaining 230 cases were examples of acquired defects. These are grouped under: (*a*) Neuroglia alone, which originate from the proliferation of the neuroglia in the anterior layers of the nerve. Glia cells remaining from the involution of the hyaloid artery may also proliferate. (*b*) Connective tissue alone. The sole source of this tissue is the walls of the vascular system. (*c*) Mixed tissues. A simultaneous growth of connective tissue and of neuroglia is frequent. (*d*) Tissues derived from the extension of abnormal tissue on or from the surface of the retina. (*e*) Tissues acquired by traction. The adjoining retina may be drawn into a pathologic excavation with the recession of the cribriform fascia.

Under neuroglia cells, Samuels discusses the proliferation of glia cells, which are of frequent occurrence in old iridocylitis of mild degree and of many deep glaucomatous excavations.

Connective tissue alone is most interesting in its behavior. Exudates on the nerve head most frequently organize into the form of membranes. The connective tissues are stimulated to proliferate under the influence of toxins of severer intensity

than those causing a growth of the neuroglia alone. They apparently may extend beyond the nerve head and do not confine themselves to it. They also were seen to lie over on the retina, frequently detaching themselves completely from the retina though still adherent to the papilla. Glaucomatous excavations also showed membranous formations with a pronounced tendency for these membranes to detach themselves from the papilla. Some of the membranes had a cordlike structure. The mixed tissue membranes are a simultaneous growth of connective tissue and of neuroglia. In some of the sections one could see that the two tissues, while proliferating at the same time, were separating one from the other. Thus, in a glaucomatous excavation of a highly myopic eye, a mass of glia cells was present on the nasal side under the scleral spur (a favorite site for the growth of neuroglia), and on the temporal side of the papilla was a mass of connective tissue. Where the two tissues intermingled, the connective tissue alone survived; the neuroglia, being more delicate, appeared to be choked out.

The tissues derived from the extension of abnormal tissues on the surface of the retina and those acquired by traction were instances of a condition that may be called retinitis proliferans.

The article is illustrated by photomicrographs showing the various types of epipapillary tissues. A most interesting portion of the paper is that in which the author correlates his histologic observations with ophthalmoscopic pictures and findings.

The author's conclusions, in abstract, were: 1. Strands of tissue lie on the nerve head and in the horizontal meridian. 2. All delicate transparent veils on the nasal side of the nerve head are of pure glial origin and should be referred to as neuroglial membranes. The walls of cystic spaces in front of the nerve are of the same origin. 3. The mass of cells at the bottom of the pit is both connective tissue and neuroglia. 4. The pure white areas observed in the center of many nerve heads represent the only connective tissue of congenital origin ever present. Any congenital connective tissue remanants are extensions from such a mass. 5. So far as glial membranes are concerned, they cover the medial aspect of the nerve; so the lateral half is the part always free from membrane.

With reference to acquired tissues, the following conclusions were drawn: 1. A proliferation of glia cells is more likely to be found on the papilla in glaucomatous excavations than in any other condition. 2. Inflammatory reactions have no relation with remnants of the hyaloid artery. 3. It is possible to distinguish clinically (with a fair measure of certainty) the various types of congenital membranes, and to distinguish congenital types from those of an acquired nature.

SPAETH, Philadelphia.

THE BRAIN IN PREHISTORIC AND RECENT RACES. C. U. ARIËNS KAPPERS, Acta psychiat. et neurol. **6**:505, 1931.

In this paper Kappers compares the brains of prehistoric and modern man and the brains of various present-day races. He first compares the frontal lobes of the chimpanzee and Pithecanthropus erectus, concluding that, although the frontal fissuration of Pithecanthropus is rather chimpanzoid, it comes nearer to the human brain by the wider curve of the inferior frontal and by the reduction of the fronto-orbital to a small subfrontal sulcus, such as is present in man. Nevertheless, the relief of the Pithecanthropus frontal lobes is not like that found in the human being. This is especially true of the field underneath the inferior frontal sulcus, which is too narrow for a human brain. This same region in the Neanderthal man shows certain differences from that in the Pithecanthropus erectus just described and from that in the superior paleolithic man and in his direct successor—present man. In the Neanderthal man the frontal sulci are human, but with these differences: 1. The midfrontal fissure, corresponding frontally with the frontomarginal, has shifted slightly more dorsad, so that the second convolution, especially the so-called foot of the second convolution, is larger than in the ape man from Java. 2. In contrast to the present human brain, the midfrontal fissure is not interrupted

and seems to keep a connection with the inferior precentral sulcus. 3. A greater difference from the Pithecanthropus is shown by the inferior frontal sulcus, the curve of which has become much wider, so that a large part of it has a horizontal course, dipping down only at its frontal end. A single frontal branch of the sylvian fissure is always found. Two anterior branches have not been observed, which is of interest, considering their obvious occurrence in the superior paleolithic Predmost race. The lunate sulcus of the occipital lobe in the ape and Pithecanthropus erectus corresponds to, or lies in front of, the lambda suture, while in the Neanderthal and present man it always lies behind.

Kappers then discusses some racial differences in the form of the brain. In his researches he has advised a number of measurements and indexes which are given in full in the original article. He found that the brachycephalic, hypsicephalic brain form shows a distinct similarity to the early postnatal form. The Chinese brain shows the following peculiarities: a pronounced concavity of the orbital surface with an orbital rostrum; round shape of the frontal lobe; inward curvature of the lower part of the blunt temporal pole; depressed occipital lobe, with a strongly pronounced medial concavity for the cerebellum and a narrow fossa interpeduncularis; a bulging parietal lobe; a hooklike calcarine; a steep callosomarginal fissure, and a steep uncus, often indented by a small groove, probably caused by the anterior petrosal edge of the tentorium. Characteristic for the highly brachycephalic Armenian brain is the great parieto-occipital angle. A consequence is the wedging in of the precuneus underneath the posterior part of the callosomarginal gyri, which therefore has a more oblique course. The ratio of cortex to total brain weight is the same for all races.

In regard to the ratio of brain weight to body weight, the Neanderthaloids, Japanese and Eskimos have average skull capacities but smaller bodies than the Europeans, while Australians, Hindus and perhaps also some Negro races have a relatively small skull capacity compared to the large size of the body. This, however, probably has to do not so much with differences in intellect as with differences in muscular skill. Other authors have stated that people with short and strong extremities and a strong musculature generally have a greater relative brain capacity as compared with peoples who have slender, long extremities and less well developed muscles, and ascribe this to a better innervation and higher coordination of the muscular apparatus and of the proprioceptive sense. This seems to be the reason why the brain weight as compared to the body weight is proportionately larger in the chimpanzee than in the orang-utan. A number of authors have found that in all domesticated animals (rabbits, cattle, ducks) the cephalization coefficient is smaller than in their nondomesticated relatives, and Kappers believes that, as domestication generally leads to a deterioration of natural skill, it does not seem improbable that similar differences, such as occur in animals on account of their lesser pragmatic endowments, may be brought about gradually in the human race by the deteriorating influence of unnatural or domesticated life, which cannot but lead one to expect a smaller, rather than a higher, cephalization in those human races that for ages have been subject to domestication.

PEARSON, Philadelphia.

THE TRANSFORMATION OF BENIGN GLIOMAS INTO MALIGNANT SPONGIOBLASTOMAS. J. H. GLOBUS, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:325, 1931.

It is assumed that benign tumors may become malignant at one time or another in their growth. This transformation is seldom observed in tumors of the brain, though it probably occurs with relative frequency. Globus reports such transformation in five gliomas. His studies show that these tumors repeat one or another phase of the primordial cells from which they spring, and he emphasizes that a careful study will reveal the nature of the primordial cell of which the tumor is composed. Its discovery will permit one to determine whether a glioma is benign or malignant, but often there are transitional forms which predominate,

so that Globus has come to designate certain gliomas as "transition forms of gliogenic growths."

In 1918, Globus and Strauss described a type of tumor composed of undifferentiated glia cells, which were derived from spongioblasts, and which they named spongioblastoma. These tumors had been designated giant cell glioma because of the large number of giant cells within them; adenoglioma because of the alveolar arrangement which they often assume; neuro-epithelioma gliomatosum to designate the undifferentiated nature of the glial elements; glioma ganglionare to indicate the presence of the giant cells which looked like ganglion cells; glioma telangiectatum to designate the rich vascularity of the tumor, or, most frequently, gliosarcoma, because of the small, round, dark, undifferentiated cells. A few months after the publication of Globus and Strauss, there appeared a report of a series of gliomas by Ribbert with the same characteristics as those described by Globus and Strauss.

In 1924, Globus and Strauss designated their tumor spongioblastoma multiforme at the suggestion of Cushing, in order to indicate the varied aspects of the cells and to differentiate it from a group of tumors which Cushing and Bailey called spongioblastomas, a name later changed to medulloblastoma.

Globus reports five cases of benign types of glioma which were followed through transition stages into spongioblastomas, or malignant gliomas. Case 1 showed an astrocytoma. On the reappearance of symptoms months later another tumor was removed from the original area. This corresponded to what Globus terms a transition form of glioma. A third biopsy on the same area showed a definitely malignant growth of the type spongioblastoma, with giant cells predominating. In the last biopsy, the cells were more numerous and were definitely identified as spongioblasts. Case 2 is not so clear, the original biopsy diagnosis being "a piece of brain tissue, apparently from a glioma." After the second biopsy, the tissue was found to contain areas of necrosis and infiltrated foci, glia cells, giant cells and spongioblasts. The second specimen was diagnosed spongioblastoma. In case 3, the original biopsy was diagnosed as a transition form of glioma with islands of spongioblasts. The second biopsy showed definitely a malignant growth, giant cells and spongioblasts. The tumor was diagnosed a spongioblastoma. Case 4 showed a transitional form of glioma with transformation into a spongioblastoma. In case 5 the original diagnosis was spongioblastoma, but even this growth showed evidences of progress toward greater malignancy at the second operation.

There has been some objection to the term spongioblastoma multiforme. The term glioblastoma multiforme has been suggested, but Globus objects to this because of the inference that the cell elements composing the tumor are well differentiated rather than embryonic in type. The objection to the term spongioblastoma lies in the fact that there are other elements than spongioblasts within these tumors. Globus has shown, however, that the mixing of cell types, all of which are derived from a parent cell, is typical of tumors of the nervous system.

The transformation of benign into malignant tumors in the nervous system has been observed previously. Tooth reported two such cases, and thought that surgical intervention was responsible for a greater activity of cells, with overgrowth and the bringing out of a latent malignant tendency. Irradiation does not help.

ALPERS, Philadelphia.

THE PSYCHOSES AND PSYCHONEUROSES IN THE INVOLUTIONAL PERIOD OF MEN. E. JACOBI, Arch. f. Psychiat. **93**:358, 1931.

The studies reported in this paper form a sequel to a previous report on the mental disturbances in the involutional period of women which appeared in the *Archiv für Psychiatrie und Nervenkrankheiten* **90**:595, 1930), reviewed in the ARCHIVES OF NEUROLOGY (**26**:414 [Aug.] 1931). The material was studied at the same clinic and during approximately the same length of time. The problems especially emphasized by the author are: 1. Are the psychoses occurring at this age

in men in any way similar in sympatomatology and course to those in women? 2. Do the disturbances in men show any definite relationship to involutional or climacteric factors? Are these relationships so important that one can speak of them as causes? 3. Are there any essential symptomatologic differences between psychoses at this period of life and similar psychoses at other periods?

The subject is introduced by a thorough investigation of the literature, and this is followed by a brief presentation of the histories and clinical pictures in representative cases. On the basis of the opinions expressed by others and of his own material the author reaches the following conclusions:

1. During the involutional period (from 40 to 60) there seems to be an increased tendency toward mental disease. In men one must discount mental diseases due to syphilis, alcohol and other organic causes, which form a high proportion of the psychoses at this age. Even after discounting these factors, however, there is a definite increase in the incidence of mental diseases at this age, although it is not so marked in men as in women.

2. The question of how much climacteric factors are responsible for the development of these diseases is preceded by the more fundamental question as to whether there is a climacterium in men. This question is answered in the negative; that is, there is no sharply outlined climacteric period in men as there is in women. The author agrees with Hoche in the opinion that the climacterium in men is really represented by a very gradual, at times almost imperceptible, change, which later blends with the involution and senile changes of the rest of the body. Consequently, the influence, if any, is indefinite.

3. The psychoses occurring most frequently at this stage of life are depressions. The next in frequency are paranoid states with more or less marked depressive colorings. Next to these in frequency are the so-called psychogenic mental disturbances, clearly related to some mental and physical incident of a depressing nature. They resemble most closely the psychoneuroses and are frequently connected with insurance and pension claims. The least frequent of all are the schizophrenia-like diseases, and the other especially stresses the point that, unlike women, men do not show the so-called "late catatonias."

4. All the mental disturbances, no matter what their type, show certain characteristically involutional peculiarities. The most important of these are anxiety states, hypochondriac complaints, depression and agitation. The increase in psychomotor activity, although present in a great number of cases, is not so frequent as in women. The prognosis is poor, and feelings of hopelessness and inadequacy accompany practically all of these conditions.

5. The intimate relationship that exists between the sexual life of the patient and the occurrence of these disturbances is not as evident in men as in women. There may be a lessened sexual activity with the psychosis, but it is most usually the resultant of the psychosis, especially of depression, rather than the cause. Similarly, there does not seem to be such a marked relationship between the prepsychotic personality and the symptoms as there is in women. The hereditary influence is marked.

MALAMUD, Iowa City.

ANGIOMATOSIS RETINAE WITH CEREBELLAR CYST (LINDAU'S DISEASE). WALTER S. ATKINSON, Arch. Ophth. **7**:510 (April) 1932.

The association of angioma of the retina with angiomatous and cystic lesions in other parts of the body, particularly with a cerebellar cyst, and its familial tendency are not generally recognized by ophthalmologists. This is evident from the statement made by Cushing and Bailey in reporting a case of this condition. In spite of many examinations made during the life of their patient (by at least eight observers), the presence of an angioma was not detected.

The diagnosis in the case that Atkinson reports was verified by histologic examination during the life of the patient. The patient is still alive and well. Examination of the fundus showed that the superior temporal retinal artery was

enlarged to at least three times its normal size, and along its course there were many aneurysmal swellings, varying in size, some twice the diameter of the enlarged artery; on a terminal branch, rather far into the periphery, were several aneurysms that were quite large, compared with the small branches of the artery. The superior temporal vein was of much the same color as the artery but was considerably larger; toward the periphery it increased enormously in size, becoming more and more tortuous, until in the periphery it disappeared in a vascular tumor mass having the appearance of a tangled coil of enlarged vessels. The other retinal vessels appeared normal, except that the veins were possibly slightly enlarged. In the left eye, the media were clear, the disk was normal, and the veins were a little full. There was a large, irregular, pigmented, whitish, chorioretinal patch, extending vertically between the superior and inferior temporal retinal vessels, at a distance of about 2 disk diameters from the temporal side of the macula lutea and about 1 disk diameter in width, with a fringe of pigment around the edge.

Further, a provisional diagnosis of cerebellar tumor was made on the basis of choked disk in the right eye and optic atrophy in the left eye, weakness of the occipitofrontalis muscles, exaggeration of the left knee jerk and suggestive Gordon and Babinski signs. An operation was performed, and a cystic tumor was found protruding from below the lower surface of the left cerebellar lobe; it had been pushed downward toward the midline. The top of the cyst was cut off for microscopic examination.

The author's conclusions are: The enormous vein with an angiomatous tumor mass in the periphery, the white patches of exudate in the retina and the enlarged artery with aneurysms present a rather typical picture of angiomatosis retinae, often referred to as von Hippel's disease. This, together with the cerebellar cyst and the angiomatous areas in the cyst wall, seems sufficient evidence to warrant a classification of Lindau's disease.

That no other members of the patient's family have been found to have the disease does not preclude this diagnosis. Moller, in a recent communication regarding Lindau's disease, stated: "There should be a cerebral tumor plus familial incidence, or retinal angiomatosis plus cerebral tumor, with or without familial tendency to make a diagnosis of Lindau's disease."

This is the second case of Lindau's disease in which the histologic diagnosis of the cerebellar lesion has been verified during the life of the patient.

SPAETH, Philadelphia.

INFLUENCE OF HYDRIC NOURISHMENT ON BODY DEVELOPMENT AND GENESIS OF GOITER AND THYROID DYSFUNCTION. R. COLELLA, Riv. di pat. nerv. **37**:355 (March-April) 1931.

The author, who has investigated the origin of goiter and thyroid dysfunction from both a clinical and an experimental standpoint in relation to hydric nourishment, reaches the following conclusions: 1. Goiter, bodily development and thyroid dysfunctions are directly correlated with the use of certain goiter-producing waters. 2. The use of such water from birth and thereafter for a long time produces in mammals under experiment hypertrophy of the thyroid and morphologic changes of the body as represented by a retarded bodily development associated with a precocious somatopsychic development. 3. The goiter-producing water produces in man an enlargement of the thyroid gland that occurs in endemic form among the population, and especially among the women. 4. In the more advanced stage, from the simple hypertrophy of the thyroid the exophthalmic type of goiter may develop. Besides, other thyroid dysfunctions may be observed with particular reflection on the menstrual period, pregnancy and the menopause. It follows that simple goiter and its exophthalmic type (Flajani-Basedow disease) may represent the first, and the last link of a chain of intermediary pathologic conditions which seem to uphold the conception of unity of the so-called hyperthyroid syndromes. Various intermediate stages of such conditions may acquire a familial character, developing

in various members of the family. 5. The mental disturbances which may accompany the various types of exophthalmic goiter, and which in the typical form of the disease are represented by elementary mental disorders, involve more the emotional side of mental life. Rarely, typical manic or depressive attacks or acute confusional hallucinatory stages or schizophrenic manifestations, though atypical in type, occur. For the development of such mental conditions, however, the hydric factor is not the only one to be taken into consideration. 6. Concerning the pathogenesis of the condition, the author believes the thyroid to be the fundamental element. In the thyroid, infectious or toxic elements may determine the modification of the quality of the colloid substance, which, therefore, would influence abnormally the nerve tissue, especially of the sympathetic system. 7. In regard to the active principle of the goiter-producing water, the author believes that it contains specific germs, or a toxic substance liberated by germs, which directly affect the thyroid tissue. The experiments of the author do not allow him to establish definitely the exact nature of the toxic or infectious agents. 8. The hydric type of thyroid involvement is only one type of goiter-producing condition, as the author believes that hypertrophy of the thyroid and exophthalmic goiter may be due to more than one pathogenic element. 9. Along therapeutic lines, the author advises the removal of a certain group of waters which he has particularly studied and which he considers to be goiter-producing. He advises the use of opotherapy (serum of thyroidectomized animals), diathermy and galvanization of the thyroid, and finally radiothermy and surgical removal.

FERRARO, New York.

THE EXTRADURAL VENTRAL CHONDROMAS, THEIR FAVORITE SITES, THE SPINAL CORD AND ROOT SYMPTOMS THEY PRODUCE AND THEIR SURGICAL TREATMENT. CHARLES A. ELSBERG, Bull. Neurol. Inst., New York **1**:350 (June) 1931.

The author calls attention to the fact that, in addition to the large cartilaginous growths derived from the bony part of the vertebral column, another type of chondroma is rather frequently found. These tumors are usually, if not always, derived from the cartilaginous intervertebral disks, small in size, situated in front of the dural sac and not revealed by roentgenograms. They usually take origin from the posterior border of the vertebral disk and occupy space within the vertebral canal. In the author's last series of one hundred spinal tumors such ventral chondromas (ecchondroses), composed 14 per cent of all, and 36 per cent of the extradural growths, as compared to one case in his first series of one hundred spinal cord tumors. This difference is explained by the assumption that in former times the small tumors were not recognized. Locations of these tumors were as follows: cervical, nine; lumbar, four; thoracic, two. Age incidence is chiefly early or advanced middle age; 80 per cent occurred in males. The question is raised whether these small outgrowths are new growths or localized hyperplasias. The microscopic structure is similar to that of cartilage from normal intervertebral disks, and it is considered questionable if they can be termed neoplasms in a strict sense.

The clinical history is frequently one of long periods of vague symptoms before definite evidence of localized compression of the spinal cord can be recognized. Occasionally, the duration of symptoms was remarkably brief, from two to five months. Attacks of twitching of muscles, numbness and sudden loss of power were frequent and were often followed by periods of apparent normality. The clinical picture is that of anterior cord compression and cutaneous sensory loss, with little disturbance of tactile sensibility. Vibration and position sense are usually intact. Sphincteric disturbance is rare. There is less tendency to subarachnoid block and protein increase than in other tumors causing cord compression. Operative technic is discussed in some detail. Exposure by bilateral laminectomy with incision of the dura is advocated. Removal is best accomplished by a transdural method, although in some instances in which

the growth is in the lumbar region an extradural approach may be preferable. The operative results are listed as follows: complete recovery, four; marked improvement, two; moderate improvement, five; no improvement, two, and unknown, one.

KUBITSCHEK, St. Louis.

MOTOR ELEMENTS IN AGRAPHIA (DISTURBANCES OF WRITING AND FORCED GRASPING). L. BOUMAN and A. A. GRÜNBAUM, Monatschr. f. Psychiat. u. Neurol. **77**:223, (Nov.) 1930.

The generally accepted conception of agraphia does not include disturbances of writing caused by purely motor defects. Nevertheless, the authors believe that careful examination of patients with agraphia will reveal motor disorders of a compulsive nature. In support of their view, a detailed investigation of a case is reported. It was that of a patient with cerebrospinal syphilis who showed signs of multiple lesions of the brain. One of the most prominent features of the clinical picture was complete agraphia. The usual tests of motor function of the fingers of the right hand yielded normal results. By the use of block letters, however, the following abnormalities were brought out: compulsive turning of the hand toward the object observed and forced grasping of objects that stimulated the sense of touch in the hand. These disturbances led to difficulty in forming letters, for as soon as the fingers touched the paper they tended to cling to one spot. The increased effort necessary to overcome this resulted in the production of heavy strokes. Furthermore, the first letter acted as a visual stimulus which hindered the hand from moving onward. Consequently, there was a marked tendency for succeeding letters to encroach on the space occupied by previous letters. At times the writing of the patient showed motor perseveration. This owed its origin to the fact that the compulsive phenomena could be overcome only by impulses that were so strong that they frequently caused a repetition of the required motor act.

In order to test the validity of the view that agraphia may be based on compulsive motor phenomena, the authors investigated a case of encephalitis in which forced grasping was a prominent symptom. The examination was undertaken only when the compulsive symptoms were beginning to disappear. The handwriting of the patient then showed changes similar to those found in the first case. Furthermore, it closely resembled the writing of a patient reported by Erbsloh to have isolated agraphia. According to Bouman and Grünbaum, a careful analysis of many of the symptoms described by other authors in cases of agraphia indicates that these symptoms are produced by purely motor phenomena of a compulsive nature.

ROTHSCHILD, Foxborough, Mass.

AN EPIDEMIC OF THE BULBAR TYPE OF POLIOMYELITIS. W. G. S. BROWN, Lancet **2**:1287 (Dec. 12) 1931.

An epidemic of the bulbar type of poliomyelitis was observed in an English school during the months of May and June, 1929. It was thought to be an outbreak of pharyngitis until signs of involvement of the brain stem appeared in the patients affected. The school housed 85 persons; 15 were stricken. One case, apparently unrelated, was observed in a town six miles away. There was no case of spinal poliomyelitis during the epidemic. A search of published papers revealed an increase in the number of cases of bulbar poliomyelitis in recent years, but no epidemic consisting of bulbar and abortive cases had been described.

The clinical features of the prodromal or abortive cases were not such that a diagnosis of a sporadic case could be made. The most typical features were nausea and vomiting followed by fever and slight cough. Pharyngitis was present in every case; the patient did not feel particularly ill and appeared to have recovered by the third day. On the fourth day, as a rule, the cough became more pronounced and the child now looked ill and apprehensive. Palsy of the cranial

nerves developed on from the third to the ninth day of illness, usually on the fourth or fifth day.

In each case the diagnosis was confirmed experimentally in monkeys by the neutralization test. Control tests were made with saline solution and serum. As a result of the experimental work, immunity was shown to have developed in the patients with abortive cases and in several contacts. Evidence in favor of a spread from case to case is suggested by the authors. The incubation period would appear to be from seven to nine days in the cases in which a contact infection can be assumed.

An observation not emphasized in the paper, but appearing to be of importance to the abstractor, was the diagnostic help that could be obtained by examination of the spinal fluid. The spinal fluids examined showed definite pleocytosis in the presence of a normal chloride content. In many cases the differential diagnosis between the bulbar form of this disease and meningitis is in question. The normal chloride content in the presence of an increase of cells in the spinal fluid would seem to be almost diagnostic of infantile paralysis.

BECK, Buffalo.

SUPPURATION IN THE CEREBRAL VENTRICLES, COMPLICATING CHRONIC OTORRHEA. LOUIS H. LEROUX, Rev. d'oto-neuro-opht. **9**:760 (Dec.) 1931.

A man, aged 35, was admitted to the clinic complaining of occipital headache, insomnia, vertigo, repeated vomiting, constipation and diplopia. A chronic otorrhea in the left ear had existed for twenty years. Examination revealed signs of mastoiditis, spontaneous nystagmus to the right and deviation of the arm to the left. There were no cerebellar signs, and the eyegrounds were normal. Mastoidectomy revealed that the lesion was localized at the tip and behind; the lateral sinus and the dura over the cerebrum and cerebellum appeared healthy. The spinal fluid was normal in all respects. Two days after operation, headaches, left facial paralysis, chills and wide fluctuations of temperature announced the presence of a thrombophlebitis. This was operated on, and the cerebellum was explored for an abscess but none was found. Improvement followed, but the facial paralysis persisted and the temperature remained somewhat elevated. During a period of three weeks, examination of the eyegrounds and of the cerebrospinal fluid gave constantly negative results. At the end of this period, headaches and fever returned, and nystagmus, this time to the left, reappeared. The cerebrospinal fluid now showed cloudiness and numerous polymorphonuclear cells, but no increase of pressure or bacteria. Death occurred three days later. At autopsy, both lateral ventricles were found to be filled with pus under tension, but there was no abscess in the substance of the brain.

In this case the clinical problem was to determine the nature of the intracranial complication. The diagnosis of cerebellar abscess was most probable, on account of the occipital headache, nystagmus to the left, sinus thrombosis and facial paralysis. The true condition, meningitis of the ventricles, was not thought of, because the characteristic signs of ventricular hydrops (hypertension and convulsions) were absent. The abnormal localization of the meningitis, secondary to an otitic infection, is not explained. No such case has been reported previously.

DENNIS, Colorado Springs.

CYTOPLASMIC STRUCTURES IN THE GANGLION CELLS OF CERTAIN ORTHOPTERA, WITH SPECIAL REFERENCE TO THE GOLGI BODIES, MITOCHONDRIA, "VACUOME," INTRACELLULAR TRABECULAE (TROPHOSPONGIUM), AND NEUROFIBRILLAE. H. W. BEAMS and ROBERT L. KING, J. Morphol. **53**:59 (March 5) 1932.

The Golgi bodies in the ganglion cells of the grasshopper consist of isolated elements, composed of an osmiophilic and an osmiophobic portion. The osmiophilic portion can be dissolved away, leaving the mold of which the Golgi mate-

rial forms the cast. When seen in face the Golgi bodies appear ringlike, semicircular, or banana-shaped.

The mitochondria are composed of granules, short rods, and filaments. They were not observed to hypertrophy and give rise to the Golgi bodies, nor to anastomose giving rise to the "Golgi net." The neurofibrillae are composed of anastomosing threads of fibers which surround the nucleus.

Neutral-red bodies ("vacuome" of Parat) may be caused to appear in the ganglion cells of the grasshopper following the injection of the dye into the living animal. These vary in size and number in the cell, depending to some extent on the amount and concentration of the solution injected, and the time it is allowed to act. These bodies are considered new formations in the cell evoked by the neutral red injected, and it is concluded that there are no preformed red-staining granules or vacuoles in the nerve cell of the grasshopper.

The intracellular trabeculae (trophospongium of Holmgren) emerge from the fibrous capsule of the cell and penetrate the cytoplasm about one third the distance to the nucleus. These are interpreted as fibrous structures which form a supporting framework for the nerve cells. No Nissl bodies like those found in vertebrate nerve cells were found in the nerve cells of the grasshopper.

WYMAN, Boston.

ACUTE ABDOMINAL SYNDROME IN TRANSVERSE MYELITIS. L. CORNIL and F. BLANC, Rev. neurol. **1**:781 (June) 1931.

Disease of the thoracic portion of the spinal cord is often associated with profound visceral alterations. In the case reported, although the etiology is unclear, the first phenomenon noted was priapism for six days. Following this, the patient suffered pain in the lumbar and abdominal region and retention of urine developed. Progressive weakness in the lower limbs then followed, and on admission to the hospital, forty-eight hours after the onset, the abdomen was distended and the bladder contained 500 cc. of urine. The lesion in the spinal cord was in the neighborhood of the eighth thoracic segment, as judged from the sensory changes. The spinal fluid contained 80 lymphocytes per cubic millimeter and gave a negative Wassermann reaction. A few days later there was hemorrhage from the intestine and from the kidney. The progress of the illness was steady to the point of complete paraplegia, with total anesthesia and rather marked vasomotor, pilomotor and sudorific manifestations in the lower limbs, with the development of decubitus ulcerations and finally of atrophy of the muscles in the lower limbs.

The authors point out the salient features in the abdominal syndrome, which is characterized by intense vasodilatation leading to intestinal and urinary hemorrhages, cessation of intestinal motility with meteorism, renal hyposecretion, fever and tachycardia, in the absence of pulmonary, urinary or cutaneous complications and peripheral sympathetic disturbances. In this case they noted no gastric hypersecretion.

FREEMAN, Washington, D.C.

MENTAL DISEASE AMONG THE JEWS. BENJAMIN MALZBERG, Ment. Hyg. **15**:766 (Oct.) 1931.

In spite of the emotional instability commonly ascribed to them, and in spite of the widespread belief that insanity is disproportionately prevalent among them, the Jews actually have a lower rate of mental disease than non-Jews. In New York, in 1927, the rates of first admissions to hospitals for mental disease were 42 for Jews and 75 for non-Jews. (These rates are all computed on the basis of admissions per 100,000 population of the racial group). In Massachusetts, in the same year, the rates were 31 for Jews and 74 for non-Jews, while in Illinois the 1927 incidences were 30 and 64 for Jews and Gentiles, respectively. To eliminate the influence of urbanization, Malzberg analyzed the data on admissions from the city of New York and found rates of 40 for Jews and 78 for non-Jews.

The two leading functional disorders, manic-depressive psychosis and dementia praecox, accounted for 59 per cent of Jewish admissions and 33 per cent of Gentile admissions. On the other hand, the organic and toxic group, especially dementia paralytica, alcoholism and senile dementia, represented a much smaller percentage of Jewish than of non-Jewish admissions. Malzberg's conclusion is that the belief concerning the peculiar tendency of Jews to mental disease is a superstition that should be relegated to oblivion.

DAVIDSON, Newark, N. J.

PARENTERAL USE OF LIVER EXTRACT IN TREATMENT OF PERNICIOUS ANEMIA. JOSEPH E. CONNERY and L. J. GOLDWATER, J. A. M. A. **98**:1060 (March 26) 1932.

A series of fourteen patients with pernicious anemia in relapse were treated by Connery and Goldwater with varying amounts of a parenteral liver extract. In all the patients there occurred prompt hematologic and clinical improvement. In general the factors that influence the clinical and hematologic course in patients treated with whole liver or with liver extract by mouth operated in those treated parenterally. A plan of treatment is suggested. There is some evidence that smaller dosage may be adequate. Nothing in any way suggestive of an allergic reaction of any type was noted in more than 500 intramuscular injections. A group of patients previously treated with other forms of liver therapy were changed to treatment with weekly intramuscular injections of the material derived from 100 Gm. of liver. Two of these showed red cell counts below 4,000,000 when the treatment was changed. All the patients showed clinical and hematologic improvement, and remained in a state of satisfactory remission during the period of observation. Special indications for the use of parenteral liver extract are enumerated. A miscellaneous group of patients suffering from various forms of secondary anemia were treated with parenteral liver extract. In none of these was hematologic or clinical improvement noted.

EDITOR'S ABSTRACT.

XANTHOMATOSIS. H. B. METTELL, Am. J. Dis. Child. **42**:858 (Oct.) 1931.

The most frequent findings in xanthomatosis are: (1) irregular "moth eaten" defects in the bones, especially of the skull and of the pelvic and rib bones; (2) the presence of diabetes insipidus, especially if there is a deposit of cholesterol around the region of the sella turcica; (3) exophthalmos, if there is a disturbance of the bony roof of the orbit; (4) increase of the blood cholesterol; (5) loss of teeth; (6) jaundice, and (7) retardation of skeletal growth. In 1928, Rowland reported that the condition was due to a disturbance of the lipoid metabolism of the body.

Mettel reports one case, in a child aged 5, the youngest of three children, all of whom presented some developmental pathologic abnormality. Roentgen examination revealed a defect in the right frontal bone of the skull which followed five months after a trauma in that region. The condition was first thought to be due to melanoma or syphilis. Antisyphilitic treatment had no effect in retarding the progress of the disease. The patient was then treated by radium, with marked improvement, as was shown by the regeneration of bone demonstrated in the x-ray films. The case exhibited no findings indicative of diabetes insipidus and no increase in the blood cholesterol, nor was there any exophthalmos.

The report is incomplete, and the author considers the presentation a preliminary one.

LEAVITT, Philadelphia.

THE NORMAL PRESENCE OF A AND Y EXCITABILITIES IN THE NERVE-MUSCLE COMPLEX. W. A. H. RUSHTON, J. Physiol. **72**:265 (July 6) 1931.

During the past twenty years there has been some difference of opinion as to whether the chronaxia of a muscle is the same as that of its nerve, or is quite

different. Lucas obtained evidence for the latter conclusion, while Lapicque maintained that the chronaxia of a muscle is the same as that of its motor nerve (isochronism). Rushton's results as here described confirm those of Lucas in that they show that there are two excitabilities, γ and α, in the nerve-muscle complex, of which γ is isochronous with nerve, and α has a chronaxia many times longer. The two excitabilities are not confined to the sartorius and sternocutaneous muscles previously investigated, for they may be equally obtained in a dozen other muscles in the frog.

This matter is of importance from two aspects: (1) The simple technic of chronaxia measurement as set forth and practised by Lapicque and his followers is inadmissible if there is more than one excitability present with different chronaxias. (2) The physiologic concept of isochronism, and therefore the theory of curarization, cannot be maintained in the present form if a nerve the chronaxia of which is at least twenty times greater can supply the α excitability.

ALPERS, Philadelphia.

STUDIES IN MULTIPLE SCLEROSIS: I. HISTOGENESIS OF EXPERIMENTAL SCLEROTIC PLAQUES AND THEIR RELATION TO MULTIPLE SCLEROSIS. TRACY J. PUTNAM, JOHN B. MCKENNA and L. RAYMOND MORRISON, J. A. M. A. **97**:1591 (Nov. 28) 1931.

The authors produced disseminated areas of myelin loss with perivascular infiltration and reactive gliosis in dogs by the injection of minimal doses of tetanus toxin. The lesions resembled those seen in some cases of human encephalomyelitis. The myelin loss was permanent up to a year from the time of inoculation. The gliosis appeared to be progressive. Areas of myelin destruction with reactive gliosis may be produced in dogs by carbon monoxide poisoning. The myelin shows no sign of regeneration within two months. Similar areas of demyelination and gliosis may be produced by embolism with cod liver oil emulsion. Destroyed myelin is not regenerated at the end of five months, but gliosis is progressive. Vascular obstruction appears to play a part in the production of lesions of the two latter types and perhaps in the first also. All three types of lesion resemble closely the "early" plaques of multiple sclerosis. From their observations the authors conclude that it is not necessary to postulate a specific virus, toxin or ferment to account for the histologic appearances seen in multiple sclerosis.

EDITOR'S ABSTRACT.

A CONTRIBUTION TO THE PATHOGENESIS AND HEREDITY OF THE LAURENCE-BIEDL SYNDROME (DYSTROPHIA ADIPOSOGENITALIS, RETINITIS PIGMENTOSA, MENTAL DEFICIENCY AND POLYDACTYLISM). REPORT OF THREE CASES IN ONE FAMILY. A. M. ORNSTEEN, Am. J. M. Sc. **183**:256 (Feb.) 1932.

The literature on the subject of the Laurence-Biedl syndrome is reviewed, and forty-two reports of cases are found, with mention of the etiology in most instances as hereditary and familial and of the pathologic process as dysfunction in the region of the hypothalamus. In a family of six children, three were found by the author to be affected with the disorder. Recent studies in relation to the functions and pathology of the hypothalamus are discussed. It is argued that the adiposogenital dystrophy of the Laurence-Biedl syndrome is an embryonal defect involving the diencephalon. In discussing the embryology, the author states that the ventral segment of the ectopic zone of Schulte gives origin to the infundibulum, the optic chiasm and the retinal fibers. The general conclusion is made that the adiposogenital dystrophy, retinitis pigmentosa and mental deficiency are related to a genetic defect of the ectopic zone in its cephalic and ventral segments, a cerebral genotypic unit character.

MICHAELS, Boston.

CORTICAL HERNIATIONS. CURTIS T. PROUT, J. Nerv. & Ment. Dis. **74**:468 (Oct.) 1931.

Multiple herniations of the brain were noted first by Cruveilhier in 1835 and later by von Recklinghausen in 1870. They consist of small mushroom-like masses of brain tissue on the external surface of the dura. Though caused by increased intracranial pressure, they are not always present with such a condition, being dependent not only on its duration, but also on its severity and rapidity of onset. In the author's twenty-five cases, the herniations were found most commonly in the presence of tumor of the brain. Age is not an important factor, except that in advanced age there is a greater tendency to increased blood pressure and to temporary episodes of increased intracranial pressure. The herniations are of importance from the standpoint of roentgenologic diagnosis, because they must be distinguished from malignant tumors, which erode the inner plate of the skull. Their situation is not important in localizing lines of pressure. They seem to follow the villi, but do not necessarily follow them in the presence of other dural weaknesses.

HART, Greenwich, Conn.

UNILATERAL TROPHIC DISORDERS OF THE FACE (HEMIATROPHIA FACIEI). W. S. SURAT, Monatschr. f. Psychiat. u. Neurol. **77**:202 (Oct.) 1930.

Although the etiology of facial hemiatrophy is still much disputed, disturbances of the sympathetic nervous system undoubtedly play a part in its origin. Various observers have suggested that facial hemiatrophy may be produced by a lesion located in the cervical sympathetic chain or in the sympathetic centers of the midbrain. In a certain number of cases facial hemiatrophy appears to be based on involvement of the trigeminal nerve. Since this nerve contains sympathetic fibers, a lesion of the former may also affect the latter. Hence, trigeminal neuralgia of long duration might be expected to cause chronic irritation of the trophic fibers, with a subsequent disturbance of their function. Surat reports two cases of facial hemiatrophy of this type, in which the neuralgic symptoms were confined to the middle division of the trigeminal nerve. Both cases showed definite signs of sympathetic involvement. The hemiatrophy was probably not directly dependent on the disease of the trigeminal nerve but on a concomitant lesion of the sympathetic fibers.

ROTHSCHILD, Foxborough, Mass.

SUBNORMAL ACCOMMODATION. AVERY DE H. PRANGEN, Arch. Ophth. **6**:906 (Dec.) 1931.

The relative infrequency of subnormal accommodation is perhaps the reason for its being so easily overlooked. Actual determination of the accommodative nearpoint is necessary, because refraction fundamentally is an accommodative problem, and this matter of subnormal power of accommodation is a not infrequent cause of asthenopia: it is often encountered in members of the same family.

This problem of subnormal accommodation seems likely to afflict asthenic persons, who are deficient in their reserve of nerve energy. They often have accommodative power that is persistently below the normal for their age, and this low power is still further depressed by the incidence of some intercurrent infection or debilitating condition, with resultant acute asthenopic symptoms. It seems according to the author that focal infection, especially dental infection, is a major cause. The article discusses in great detail etiology, symptomatology and the details of twenty illustrative cases.

SPAETH, Philadelphia.

ARACHNOIDITIS OF THE OPTIC CHIASM. VINCENT, PUECH and DAVID. Rev. neurol. **1**:760 (June) 1931.

The authors report seven cases in which an operation on the chiasmal region disclosed arachnoid adhesions about the optic nerve and chiasm. They point out certain phenomena that will distinguish arachnoiditis clinically from tumor. These

are: (1) rapid onset of blindness, without changes in the fundus, but progressing toward primary optic atrophy; (2) frequency and precocity of central scotomas, without bitemporal hemianopia, and (3) signs of a mild infection, with steplike progress. Corresponding negative signs are: normal sella and spinal fluid and absence of adjacent glandular or tuberal symptoms, as well as of definite indications of acute meningitis, tuberculosis or syphilis. Of the seven patients, three were benefited by the operation, although, as the authors point out, the underlying infectious process was not cleared up. The operation consists in freeing the optic nerve and chiasm from the investing membrane.

FREEMAN, Washington, D. C.

HUNTINGTON'S DISEASE. KURT SCHROEDER, J. f. Psychol. u. Neurol. **43**:183, 1931.

Schroeder describes a case of Huntington's chorea, which, he states, is unusual because of the transition into progressive rigidity. Histologic examination showed predominatingly degenerative changes, not only in the cerebral cortex and basal ganglia, but in the midbrain, pons, medulla oblongata and spinal cord. Myelin sheath and cell preparations from the corpora quadrigemina, pons and medulla showed no appreciable changes, but sections taken from these areas stained with the Holzer method revealed a striking increase in glia fibers; this was not a mere secondary reactive phenomenon, but was a replacement of parenchyma. Another noteworthy feature was the severe myelin sheath changes in the cerebral cortex, which were accentuated in some areas giving the sections a peculiar "patchy" appearance. Schroeder states that he has been unable to find in the literature on Huntington's chorea the report of any case with this peculiar type of cortical involvement.

KESCHNER, New York.

AN ATYPICAL SYNDROME OF THE NASAL NERVE. CARLOS CHARLIN, Ann. d'ocul. **168**:808 (Oct.) 1931.

The syndrome of the nasal nerve previously reported on by Charlin (*Ann. d'ocul.* **168**:86 [Feb.] 1931) is now considered by him in its atypical form. In this paper he states that neuritis of the nasal nerve may occur in an incomplete and atypical form. In some cases the symptoms are primarily ocular; in others, the nasal symptoms predominate. In the latter type there is unilateral, oculo-orbital pain, and the most careful examination of the eye is required to detect tenderness of the eyeball, slight hypotension or superficial keratitis. In some cases a mild cyclitis is discernible only with the slit-lamp. The nasal mucous membrane is hypersensitive, congested and moist in the areas supplied by the nasal nerve. Applications of cocaine and epinephrine to the nasal mucous membrane in this area bring about rapid amelioration. The diagnosis is often facilitated by palpating the cutaneous distribution of the nasal nerve. If these points are painful, a nasal examination should be ordered.

BERENS, New York.

THE RELATION OF TONSILS AND ADENOIDS TO INFECTIONS IN CHILDREN. ALBERT D. KAISER, Am. J. Dis. Child. **41**:568 (March) 1931.

After studying almost 5,000 children before and after tonsillectomy, Kaiser observed that chorea developed more frequently in children who had undergone this operation than in those who still retained tonsils and adenoids. The incidence of chorea among tonsillectomized children was 1 per cent and among those not operated on, 0.6 per cent. However, chorea in a tonsillectomized child is less apt to be followed by a cardiac complication than in a patient who has not undergone the operation. Tonsillectomy favorably influenced the incidence of cold in the head, sore throat, otitis, lymphadenitis and acute rheumatism. Bronchitis, pneumonia and sinusitis were more common in children whose tonsils and adenoids had been removed. From Kaiser's study it would appear that chorea is not an indication for the removal of healthy tonsils.

DAVIDSON, Newark, N. J.

PRIMARY JUVENILE PARALYSIS AGITANS. LUDO VAN BOGAERT, Rev. neurol. **2**:315 (Sept.) 1930.

Van Bogaert presents a clinicopathologic study of a case of primary paralysis agitans beginning at the age of 7 years. This progressed slowly, and was characterized more particularly by tremor, without hypertonus but with rather marked dysarthria and retropulsion. There were no definite indications of hepatic disorder; the patient died at the age of 30 of an intercurrent disease. The most striking feature in the brain was degenerative atrophy of the globus pallidus, with partial involvement of the corpus subthalamicum and locus niger. The neostriatum seemed relatively uninvolved. There was atrophy of the connections between the striate body and the corpus subthalamicum and substantia nigra, and more markedly of those between the lenticular nucleus and globus pallidus. There were no cortical, thalamic or cerebellar lesions.

FREEMAN, Washington, D. C.

TREATMENT OF DEMENTIA PARALYTICA. CLARENCE A. NEYMANN and MICHAEL T. KOENIG, J. A. M. A. **96**:1858 (May 30) 1931.

The authors present the results of a comparative study of therapeutic results obtained in a series of clinically similar cases of dementia paralytica treated with malaria, sodoku, and diathermy. They state that the remission and improvement rate of diathermy exceeds that of malaria and sodoku. The death rate with the diathermy method is nil. Diathermy offers a hope of remission in types of dementia paralytica which seemed to be unamenable to treatment of any kind. The serologic changes produced by any form of hyperpyrexia do not coincide with the clinical changes. Diathermy permits the treatment of patients for whom the use of malaria or sodoku would be contraindicated. The use of this method is easily accessible to any physician, trained in the technic. In many cases the treatment can be given ambulantly.

EDITOR'S ABSTRACT.

BLOOD SUGAR DETERMINATIONS IN PATIENTS WITH SO-CALLED "PRIMARY MYOPATHIES." G. C. BOLTEN, Monatschr. f. Psychiat. u. Neurol. **78**:213 (March) 1931.

Blood sugar determinations were performed in five cases of progressive muscular dystrophy. The results obtained in a fasting condition were within normal limits. Dextrose tolerance tests yielded rather low curves. Similar results were obtained in a case of myotonia congenita. One case of myasthenia gravis was investigated. In spite of the fact that there were definite clinical signs of insufficiency of the chromaffin system, the fasting blood sugar and sugar curves were essentially normal. The author concludes that a chromaffin insufficiency cannot be regarded as a primary factor in the etiology of progressive muscular dystrophy, myotonia congenita or myasthenia gravis.

ROTHSCHILD, Foxborough, Mass.

PROGRESSIVE LIPODYSTROPHY. FRANZ POLLAK, Ztschr. f. d. ges. Neurol. u. Psychiat. **127**:415, 1930.

Lipodystrophy, preeminently a disease of the vegetative nervous system, begins with lipatrophy of the upper half of the body, which is followed by the second stage of lipohypertrophy, chiefly involving the lower half of the body. In the causation of this malady the endocrine glands, particularly the hypophysis and gonads, are involved. During the first or atrophic stage the diencephalic vegetative nervous system is involved, according to the author, and the blood is filled with lipase. In the second stage, the endocrine system is in control, and thereby a storage of the free fat is brought about. The disease, according to the author, is really due to an abiotrophic process of the vegetative centers, a nuclear weakness.

HART, Greenwich, Conn.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Secretary*

March 17, 1932

E. W. TAYLOR, M.D., *in the Chair*

THE VALUE OF LUMBAR PUNCTURE IN THE DIAGNOSIS OF SUSPECTED TUMOR OF THE BRAIN. DR. FRANK FREMONT-SMITH and DR. TRACY J. PUTNAM.

The dangers of lumbar puncture in the presence of an expanding intracranial lesion were disclosed soon after the procedure was introduced. A study of the literature shows, however, that there was a gross neglect of ordinary precautions in the earlier fatal cases. The reports of seventy-one cases were collected from the literature in 1915, and only four reports have been published since. The hazards of lumbar puncture can be greatly reduced by proper technic; however, occasional accidents doubtless occur in spite of all safeguards. In many cases of suspected tumor of the brain the value of the information obtained outweighs the slight risk involved, particularly when signs of pressure are dubious. Careful weighing of the manometric, chemical and cytologic data may serve to rule out tumor or to make the diagnosis before symptoms or changes of the eyegrounds are definite. A series of cases was reported showing the value of lumbar puncture in the differential diagnosis of tumor of the brain.

DISCUSSION

DR. T. J. PUTNAM: I came to the City Hospital ready to scoff at the diagnostic value of spinal fluid observations and remained to puncture. A survey of the literature is surprising. Dr. Fremont-Smith has already spoken of the large number of cases collected by Schönbeck. In most of these cases a 12 to 14 gage needle was used, and many of them showed a high grade of choked disk before puncture. One half of the fatalities occurred in cases without tumor, such as meningitis and apoplexy. Since Schönbeck, the only long series is that of Masson whose only fatality is questionable. Two deaths have been all that I have been able to discover since, one in a case of abscess starting from mastoiditis and the other in a syphilitic case in which pressure was not elevated, both instances in which one should not hesitate to make a puncture. A long series is also reported by Puussepp—eighteen cases of tumor of the posterior fossa in which puncture was made without an accident. This means that the technic of lumbar puncture has been improved. Certainly, punctures are performed with much greater frequency. It probably also means that fatalities are not reported now because the general subject is no longer controversial. Unquestionably, deaths have occurred and unquestionably many more than Schönbeck reported. In regard to the diagnosis of tumor of the brain, one is on another basis than one was before 1915. The great problem then was to make a diagnosis ante mortem, and now one hopes to make a diagnosis in the early stages, because that is the time when treatment is more helpful. For this reason this refined method of diagnosis should not be overlooked. We do not advocate promiscuous puncturing in all cases of cerebral tumor. Certainly the fatalities would then mount. Our plea is that those in specialized clinics should not overlook the possibility of gaining more information by this method.

DR. GILBERT HORRAX: I agree with Dr. Fremont-Smith that the danger is slight with a low grade of choking. I cannot speak of detailed information because I have none. Would it not be as simple to take a ventriculogram provided one

was prepared to proceed with an operation. It is in patients who have to wait after ventriculograms that accidents occur. Dr. Cushing is so thoroughly against lumbar puncture because of experiences in the past. I have heard him recall two or three deaths at Johns Hopkins which were attributed directly to lumbar puncture.

DR. J. B. AYER: I think that Dr. Fremont-Smith's problem and the problem at the Massachusetts General Hospital is different from that at the Brigham Hospital. We have many more patients without than with a tumor. We cannot make ventriculograms when there is definitely not a tumor. We make a lumbar punture. Dr. Horrax's suggestion is not applicable to many cases. Multiple sclerosis, syphilis of the central nervous system and cerebral hemorrhage are 1, 2 and 3 on the list. In such cases lumbar puncture is indicated. The best general guide is choked disks. I think that, using precautions, one seldom has trouble. I do not remember that any deaths have occurred since the procedure has been performed in this way. I remember one case that occurred not long ago in which a decompression was performed for a known tumor of the brain but subsequent lumbar punctures were required for relief from pressure. On the seventh puncture the patient succumbed. Within a week I was called to see another patient. This patient died of lumbar puncture, and at autopsy it was found that he had a flattened medulla and pons and a herniation of the cerebellum. A lumbar puncture was made six hours prior to death, but there was no choked disk two days before when examination was made by an excellent ophthalmologist. There was a pneumococcus abscess occupying the whole of the left temporal lobe. One or 2 cc. of fluid was removed at lumbar puncture. Of course patients with cerebral abscess sometimes die of respiratory paralysis. We are more willing to perform puncture in patients suspected of having tumor than we were three years ago. It is usually true that in cases of large tumor of the brain there are some pathologic changes in the spinal fluid, but as patients are seen earlier this is not always true. Dr. Taylor and I saw an epileptic patient a year ago. Roentgen examination gave negative results. The initial pressure was 130; cells, 1, and total protein, 35, and the colloidal gold and Wassermann tests were negative. Within three months a large spongioblastoma was found at operation. We had made a diagnosis of epilepsy, probably not tumor of the brain. On the other hand, a patient who had intracranial pressure increased to 240, a total protein value of 220 and symptoms which every one thought were evidence of tumor of the brain, but which looked somewhat like a picture of hypothyroidism, proved to have a very low rate of basal metabolism and responded to treatment. He recovered, and the spinal fluid on examination was normal. Therefore these tests are not pathognomonic, but are often helpful. Lumbar punctures ought to be performed more frequently.

DR. C. A. MCDONALD: I saw a girl a little while ago who had been suffering with headache, involvement of coordination and moderate hypertension for some time. While she was drinking an ice-cream soda she fell. I saw her shortly afterward and was of the opinion that she had had a hemorrhage. I almost thought that I saw the disks swell. I made a puncture and obtained clear fluid at a pressure of 340. She died in four hours. I believe that the condition was something else, but I performed a puncture and hastened death. In regard to lumbar puncture in general, we feel rather free in advising and performing lumbar puncture when there is no or only slight choking of the disks. If I have any evidence that the tumor is not subtentorial, I not only perform a puncture but advise the introduction of air, too. In cases of syphilis of the brain with choked disks and a high pressure, would it not be worth while to perform a decompression to save vision?

DR. J. B. MCKENNA: In corroboration of Dr. Fremont-Smith's statements, I recall a case at the City Hospital of a man who was admitted to one of the surgical services. He had had a slight accident to the head some days before, and during a period of about three days he showed progressive symptoms, including increasing headache, falling pulse rate and rising blood pressure. Shortly before admission he became unconscious. In the surgical service a spinal puncture was made immediately and, although the pressure was not recorded, the intern reported that the fluid spurted out from the needle, and 12 or 15 cc. was collected. The resident

neurosurgical service was called in consultation, and although there were no localizing neurologic signs I suspected a midmeningeal hemorrhage because of the progressive symptoms. The patient was transferred to the neurosurgical service, and Dr. Munro was informed. He agreed with the tentative diagnosis, and preparations were made to operate. In the course of these preparations the patient suddenly stopped breathing; artificial respiration was performed while the man was being supported to the operating room to be put into a Drinker respirator. The right side of the cranium was opened; this revealed tremendous intracranial pressure but no hemorrhage. The patient did not resume normal breathing, but continued to be alive in the respirator. The next morning a similar exploration was made on the left side, with similar results—tremendously increased intracranial pressure and no hemorrhage. The man died twenty-four hours later, and subsequent autopsy revealed an extensive tumor of the brain.

DR. E. W. TAYLOR: I have a case in mind which occurred before Dr. Cushing pointed out the dangers of lumbar puncture when intracranial pressure was present. In this instance, obviously that of a tumor of the brain, the pain was so great that the then new method of lumbar puncture was used for its relief, with the result that the patient forthwith stopped breathing and died after the usual protracted period of artificial respiration. The warning coming from such a source was heeded, and possibly the pendulum swung too far in the direction of conservatism. I should like to ask Dr. Horrax whether lumbar puncture is now used at the Cushing clinic more freely in cases of obviously increased intracranial pressure.

DR. G. HORRAX: We perform lumbar puncture provided tumor is not suspected, but not in cases of choked disk; occasionally it is done in arachnoiditis as a therapeutic measure. I think, as does Dr. Ayer, that every clinic has its own criteria in view of its own problems.

DR. F. FREMONT-SMITH: In regard to Dr. Horrax's suggestion that ventriculography should be done instead of lumbar puncture, I should point out that Dr. Solomon has shown clearly that ventricular fluid may have a negative Wassermann reaction when the lumbar fluid is positive in cases of syphilis of the central nervous system. A ventricular tap in no way rules out syphilis. One has to have lumbar fluid. To secure lumbar fluid in cases with high grade choked disk it is perhaps wise to perform a combined ventricular and lumbar puncture. I am grateful to Dr. McKenna for bringing this case to my attention. The amount of fluid removed is less important than the rate of removal; the fluid should be taken out very slowly. The abrupt dropping of pressure is one of the real dangers. I should suggest the value of the three-way stop-cock attachment; with these not a drop of fluid is lost. Some physicians have felt that if little or no fluid is removed there is less danger. The fact is that in cases of high pressure, fluid will continue to leak through the needle hole in the dura for several hours. It is more sensible to collect slowly into a test tube sufficient fluid for adequate examination than to have this fluid leak into the tissues of the back after the needle is withdrawn. I wish that Dr. Putnam would answer the question in regard to decompression to save the sight. In the case with a pressure of 500 I did not wish to indicate that decompression was not necessary.

DR. T. J. PUTNAM: I have not much to add as to the saving of vision. If repeated lumbar puncture does not do this, then decompression is indicated. Perhaps Dr. McDonald's patient was suffering from uremia as well as from tumor of the brain.

SOME NEWER TRENDS IN PSYCHIATRY AND THEIR APPLICATION AT THE MCLEAN AND MASSACHUSETTS GENERAL HOSPITALS. DR. K. J. TILLOTSON.

This article deals with the progress of psychiatry and the changes that have taken place at the McLean Hospital as a result of the program of reorganization. A closer affiliation between the Massachusetts General Hospital and the McLean Hospital has been established. This means a closer relationship of psychiatry to general hospital work. It brings into the psychiatric hospital the services of

internists, surgeons and other specialists, so that psychiatric patients are being studied more thoroughly from a general medical as well as from a psychiatric point of view. The McLean Hospital facilities have been materially increased, so that we are now dealing with a large number of acute psychotic cases, together with an increasing number of psychoneurotic ones. Intensive work on the individual patient from the psychobiologic point of view is being stressed.

At the Massachusetts General Hospital a psychiatric clinic has been established by the McLean group. The work of this clinic, together with the psychiatric consultation service that it affords, is leading to the emphasis and importance of the psychiatric point of view in relationship to general medical problems. In many instances psychiatry can offer little specific data to the problems that it is called on to solve, but it does offer a great deal in methods of approach, from a different point of view, and in the formulation of the problem as a whole. Through the closer cooperation of psychiatry and general medicine, I believe there are greater possibilities for the development of psychiatry and that it will become increasingly useful to the general hospital needs.

DISCUSSION

DR. G. L. WALTON: I rise as a relic of bygone days. Every time I attend a medical meeting I realize the need of an interpreter and guide for the mazes of a science with the nomenclature of which, at least, I once fancied myself familiar. Of late I have been awakening to the realization that the department with which I have been associated for over fifty years has been undergoing an important change inaugurated and carried out by friends and colleagues who have been busy during my intellectual dormancy.

In former times, when the aid of a psychiatrist was needed, a call was sent for Dr. Jelly, usually regarding the question of custodial care. Now the psychiatrist is already at hand to help in the solution of problems having to do also with social, familial, occupational and other adjustments bearing on prophylaxis and the guidance of the convalescent. With the details of this new phase I have not the familiarity to justify discussion, but I can readily see that such problems can be best worked out by this collaboration, not least among the advantages of which must be the opportunity for the psychiatrist to study the early development, personality and character traits of the potentially psychotic patient.

I hope that I may be pardoned for a rambling reminiscence accentuating the change of conditions. Within my memory the neurologic department of the Massachusetts General Hospital was limited to a single room, run, with the assistance of one student (I think I was the first — in 1879), by Dr. Putnam, whose eminence in the profession would doubtless have entitled him to more sumptuous quarters had neurology as a specialty then received the respectful attention it deserved. It was a small three-cornered affair in which loomed large a somewhat complicated electrical apparatus designed for the use of two operators at the same time. With the intricacies of this instrument Dr. Putnam was so familiar that I always assumed he had a hand in its construction; he certainly did in its repair. On the table was a big ledger in which were inscribed the names of the patients together with such notes as it interested the head of the department to make in shorthand, illegible to the other member of the staff.

The "nervous room" has long since disappeared, to make way for numerous departments, some of which were then almost, if not entirely, unknown. Such, for example, was the room for the x-rays, at its inception deemed worthy of an exposition in which the lecturer explained that, while an interesting phenomenon, it was doubtful whether the x-rays would ever be of any practical value.

DR. A. H. RUGGLES: An important step forward has been dealt with in Dr. Tillotson's paper, namely, the introduction of the psychiatric point of view in the wards and outpatient departments of a general hospital. One must realize that there is a great deal in mental medicine that is not yet thoroughly understood. There is still a great opportunity for research in the field of mental diseases. Until every hospital for mental disease collaborates and cooperates, we must wait a long

time for much scientific advance. We are still searching for etiologic factors. I wish to emphasize the need of fundamental, scientific research in this whole field. I should like to see child guidance brought back to the hospital. It has become rather well socialized, and I should like to see it kept under the direction of the medical sciences.

DR. DONALD GREGG: Dr. Tillotson has mentioned the Mental Hygiene Movement in a way to justify comment. Those of us who are interested in this work recognize and readily admit that so far as cure is concerned, the enthusiasm, particularly that of lay workers, has outrun the facts. There is such a tremendous field for proper education and prophylaxis and amelioration in the field of mental abnormality that the overenthusiasm, particularly of nonmedical laborers in the field, should not arouse condemnation of the whole movement.

DR. J. B. AYER: The success of the method of peaceful penetration of the Massachusetts General Hospital by the psychiatrists is gratifying. There have been two general proposals: one was to raise a large sum of money and have a psychiatric institute, and the other was to bring in the psychiatrist and see what he could do with the patient first. We felt that the best way was to bring the psychiatrist into the department of the hospital for nervous diseases. There are six regular psychiatrists with an equal number of organic neurologists, and so far there has been only success with the project. I can vouch for the fact that the psychiatrist has penetrated the pediatric service, and I know he has penetrated the medical service. The climax came today when the senior surgeon said that he wanted a psychiatrist. A year and a half is a short time in which to attain such a triumph.

DR. O. J. RAEDER: I was glad to hear Dr. Tillotson mention the psychiatric social service. That element of it is so important. It is here that the psychiatric social work—a new development since the war—plays a very important rôle. Dr. Campbell at the Psychopathic Hospital has called attention to the help that we can derive from psychiatric social service in both diagnosis and treatment.

DR. K. J. TILLOTSON: I appreciate all the nice things that have been said. I realize that our job has only begun. One sees as much psychiatric material in the general hospital as in that for mental disease. I think that in the future our research work is going to take entirely different lines, through closer cooperation with general medicine. There is a great opportunity for physiologic and thorough chemical researches in the mental hospital. In reply to Dr. Gregg: I certainly do not want in any way to condemn mental hygiene, but since I have met people who ask me embarrassing questions that I cannot answer I think that the general hospital clinic may demonstrate what early diagnosis means and what actually can be done. I think, for instance, that the pediatricians are offering us a challenge. They say: "Here is our problem; what can you do about it"? The psychiatrist has the problem, and we must decide in the future what to do. Here is an opportunity for us to work it out together. It is all right to overcome the stigma which psychiatry has had, and having done that we must formulate some definite methods that we can apply. This can be done only by close contact and cooperation with the general practitioners.

TRACY J. PUTNAM, M.D., *Secretary*

Regular Meeting, April 21, 1932

STANLEY COBB, M.D., *in the Chair*

THE BIO-ANALYSIS OF THE EPILEPTIC REACTION. DR. A. KARDINER, New York.

The attempt was made in this paper to reconstruct the epileptic reaction from a series of reaction types subsequent to traumatic experiences. In the latter it was found that, irrespective of the nature of the presenting symptoms of the ensuing neurosis, whether it is autonomic disturbance, sensory motor disorders or epilepti-

form phenomena, the remaining psychologic picture of the neurosis was the same in all cases. From the point of view of an instinct psychology, this similarity must be based on the fact that the conflict must be the same in all cases, and that the difference in the clinical manifestations is a purely quantitative matter. Comparison with the essential epilepsies shows that the psychologic picture of the traumatic neurosis is present in the "epileptic character," in many instances long before the onset of the seizures themselves.

The study of the traumatic neurosis shows that the effect of a trauma is to inhibit unsuccessful modes of adaptation. Substitutive gratification such as we find in the psychoneuroses is difficult to establish, owing to the special character of the development of those appendages of the ego that have as their executives the sensorimotor apperceptive apparatus. There is, however, regression to earlier forms of mastery, oral and destructive. These forms of mastery are, however, very difficult to maintain with the same economy as regressions in the domain of psychosexuality.

The principle of abandoning an unsuccessful mode of adaptation is universal in all neuroses and can be experimentally verified by the work of the conditioned reflexologists. However, in the case of epilepsy, the traumatic factor operates from an impediment to the execution of ego functions on somatic bases, chiefly in the central nervous system.

The relation of the organic and the psychologic is then studied from the point of view of ontogenesis, the most important factor influencing development being the slowness with which the process of myelinization is completed in the human being. This is the anatomic fact which confers a high degree of plasticity to the human being as regards possibilities of adaptation, and also defines the regressive paths.

From this approach the epileptic reaction proves to be a contractile process, which has many lesser forms in the traumatic neuroses. It shows itself, moreover, to be a specific form of repression.

DISCUSSION

DR. S. COBB: Dr. Kardiner brought out well that in traumatic neurosis and epilepsy there is a great psychologic element accompanying the organic lesion. In the study of these two conditions, there is an excellent example of how impossible it is to draw the orthodox line between "functional" and "organic" diseases. To my mind such a distinction is no longer tenable. "Mind and body," "physical and psychologic" are too often misused as contrasting words. There are now so many authenticated examples of emotional stimuli causing physical changes in the organism that no neurologist or psychologist can reasonably deny the fact. A recent experience of my own is perhaps illuminating: A child of 7 and his mother were consulting me. The child was waiting outside my office while within the mother was telling me how on four occasions he had reacted with a convulsion when scared by dogs, the first occasion having been a severe fright when surrounded by hounds in the woods. Suddenly a cry outside caused me to rush to the door, where I met my laboratory assistant who urged me to hurry to the animal room where the child was having an attack. Seeing the child waiting, she had thought that she would amuse him by showing him the animals; on entering the room the dogs had jumped up and barked, and he had fallen in a fit. I found him in the middle of a typical grand mal seizure, and, stripping off his shoes and stockings, demonstrated Babinski's sign in each foot. Fear had been the stimulus that precipitated an "organic" reaction (in this case possibly cerebral vascular spasm) resulting in unconsciousness, convulsion and Babinski's sign. Where can one draw the line between "functional" and "organic" in such an episode? I believe that it is a useless distinction, and that we should cease bothering about a line that does not exist.

DR. W. HERMAN: Dr. Kardiner's interesting and daring paper stimulates many questions. I am much interested in his linking together of the traumatic neuroses and epilepsy. As I understand it, the main basis for this linking is the similarity of the almost total reaction of recoil in both conditions against attack on the body ego. The specific differences in the reaction of the traumatic neuroses and of the transference neuroses is extremely interesting and gives again an objec-

tive sense of factors in describing the special entity of the traumatic neuroses. It is difficult for me, however, to differentiate so clearly in thinking of the total reaction of the traumatic neuroses and that of the transference neuroses. Certainly, in all neuroses the organism recoils to a certain degree. I was surprised at Dr. Kardiner's definite characterization of epilepsy as an organic disease. Of course, we are all agreed that the convulsive symptom can be instigated by demonstrable organic lesions. But many typical epileptic convulsions, as he states, suggest no other organic basis than an emotional stimulus acting on the autonomic nervous system. In one of my cases, a man, aged 21, with a difficult birth lasting twenty-four hours and a high forceps delivery, suffered a trauma at the age of 2 years when left alone in a chicken coop. He was told to play with the chickens and succeeded in frightening them. One flew past and hit him in the face. He shrieked, became obviously panic stricken and tried to get out. The door was shut, and his mother was outside. Following this panic he began to stammer as soon as he began to talk, at the age of 2½. Between 3 and 4 years of age he had three convulsions associated with childhood diseases. He was then free from them and led a healthy and normal life, except that he was constantly driven to excel in competitive sports by tense and overambitious parents. All his attacks but one followed severe competitive events in which his efforts were partially frustrated. Certainly, in these attacks one sees the reaction of recoil and a complete dissolution of the ego in the unconscious event. There is here, however, unlike all other neuroses, a total reaction of recoil destroying the body ego, as though the attack symbolized both recoil and aggression toward the outer world and the ego.

Dr. M. B. Hodskins: My experience with epilepsy differs a good deal from the experience of the men who have spoken. I consider the epileptic convulsion a physical condition that cannot be explained on a psychogenic basis. I wonder about the diagnosis in these cases: What criteria were used to establish whether or not these patients had epilepsy?

Dr. F. Alexander: I do not think that Dr. Kardiner intended to hold a brief for the psychogenesis of the epileptic attack. I think that the great problem in the field of epilepsy is the establishment of the relations between the organic and the psychic. Dr. Kardiner cited three cases in which a lesion of the brain or local mechanical irritation were the basic factors. Anatomic or physiologic lesions cannot be discovered in the others. One can assume different possibilities. We know that rage can influence clinical changes. Rage can influence the physiologic process that influences the muscles of the extremities. That a psychic stimulus has a direct approach to the center of motility is well established; therefore we do not need special theoretic proof. The question is whether or not this is the case in epilepsy. It is interesting that in the epileptic person and in the epileptic character aggressiveness and destructive tendencies play a great rôle. Their relation to extreme acts of violence is a nuclear problem of the syndrome. From the point of view of the psychoanalyst, neurotic reaction types were found to be due to instinctual frustrations in the outer world. The results that ensue follow a well known path—introversion and regression. In Dr. Kardiner's cases we see a new factor, the relation of the individual to his own body. There he also demonstrated to us regressions. There is established a new relationship to the world, one that prevailed in early childhood. Children's technic of handling things that cause pain is to cast them out. They give up a certain psychic level which they have already reached. The regressive phenomena in traumatic neurosis take forms not seen in other neuroses. These patients change their relations to their own bodies, not only to their environment. In studying hysterical phenomena one sees also such renunciation of organic functions. An extreme case is that of a woman who lost her vision. Psychologic investigation showed that this blindness was provoked by a powerful wish to deny something. She saw her husband in an intimate relation with a chorus girl. Her reaction was: I do not want to see him any more. She did not content herself with not seeing her husband, but she did not wish to see any one else. We see that in the development of the individual, the first reaction of the child is to deny everything except those in which the child finds some kind of gratification. At the beginning the child loves only himself, and only gradually begins to build up posi-

tive relations, love for the environment. This is not a self-evident fact. The first reaction to physical injury is to withdraw, and there remains only aggressiveness. He can love himself again. We can see that even the body is not loved if it does not give gratification. The body is also a nucleus of ego, so that if an organ becomes a cause of pain its function is inhibited. This explains the defense attitude. In epileptic patients we see also such an aggressive attitude, especially in idiopathic epilepsy. The psychogenic theory is one in which the psychologic stimulus is the one that irritates the motor centers. The theory must account for the great amount of aggressiveness that is released. Sometimes epileptic persons hurt people; at other times they only overcompensate their injury. Powerless rage is a common content of the epileptic seizure. We cannot explain everything ourselves, we need the cooperation of the neurologist. Therefore, I agree with Dr. Cobb that the future destiny of epileptic etiology is best worked out on such a cooperation. There must be physiologic or biologic factors which make certain people react to a psychic stimulus with a convulsion.

DR. A. KARDINER: I am grateful to those who discussed my paper. I had hoped in presenting this paper to take you out of the airtight compartments of organic versus psychologic and to show a way in which the gap can be bridged. Heretofore the methods employed by both have been mutually exclusive. My feeling is that heretofore we could study the organic only in terms of its completed functions. I have in this paper attempted to outline a method that gets a little behind the function, which we understand only from the point of view of utility. From the point of view of instinct the end-function looks different from what it does according to standards of physiology. From this angle, a physiologic function can be analyzed to have certain definitely recognizable components. When the function is disturbed by a disorder in the somatic portions through whose agency they take form, or by external factors which render it useless, we find certain products of the disintegration, and these in turn are clinically recognizable. As to Dr. Herman's question: What is the difference between a transference neurosis and epilepsy? The difference is in the nature not of the reaction but of the material on which it is enacted. In transference neurosis the cachectic processes are characterized by a free mobility and displaceability. In the unconscious they are exactly the same. That is why, by means of regressive substitution, the individual is able to maintain a more or less constant and continuous relationship with a given source of gratification. The regressive process is an extremely economical one in the transference neuroses. The neuroses I described, the traumatic neuroses and the epilepsies, involve cachectic processes whose qualities are specific and not interchangeable. One cannot see with the ears. The utility value of the eye is highly specific, and its function cannot be taken over by any other organ. The means by which the ego is able to establish relations with the world are fixed. The very act of repression is exactly what takes place when a limb is injured—its functions are inhibited. The traumatic neurosis is the simplest of all neuroses. It illustrates the same principles as the transference neurosis, only what is inhibited is an organ. The case of Dr. Herman is of great interest. The repeated illnesses of this child should be stressed. Illness has an important significance in increasing the quantity of destructiveness and influencing its direction. On that account I believe that many of these cases show either a long history of parental or after-birth illnesses. As Dr. Alexander emphasizes, I did not come to you with a brief on psychogenesis of epilepsy. Another point of Dr. Herman's: in theory I have described only the nuclear scheme of the disease; the uses to which it is put and the secondary elaborations vary widely. This theory need not materially alter our therapeutic attitude. The uses can vary, but always there is a distinct gain of purpose, if only flight. In a conversion hysteria the aim is always the result of certain punitive influences or effort to deny repressed cravings. The epileptic attack is rather an infantile effort to inhibit certain influences in the outer world. For my thesis to prove valid, it must give standards that will account for the difference between epilepsy and hysteria. It does not suffice to say that in epilepsy we are dealing with "narcissism" or with an increase in aggression. Compulsion neurosis and schizophrenia have the same factors at work. The differences are to be found in the origin of this aggression and the secondary libido regressions that it makes necessary.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, March 17, 1932

A. B. YUDELSON, M.D., *President, in the Chair*

SPASMODIC TORTICOLLIS. Presented by DR. MEYER SOLOMON.

This woman, aged 50, with the exception of mild arthritis of the left shoulder for several months fifteen years before presentation and constipation for years, has been in unusually good health until one year ago. In the first half of 1930, the menses were of shorter duration and of lessened amount, but regular, until the last menses in June, 1930. One month later, the patient noticed, while speaking, that her head involuntarily turned toward the left. This recurred thereafter at irregular intervals, at times being of a ticlike motion. The condition varied in severity and frequency. There were good and bad periods. The condition improved when the patient lay down and was worse when she stood, and especially when she walked. While at a movie she would be unaware of the condition, or it was much improved. She had received various types of treatment — including the administration of bromides, phenobarbital, hyoscine, massage and therapy with ultraviolet and infra-red rays. For three weeks before presentation she had had constant tonic spasmodic torticollis to the left, which is much worse when she is standing or walking. The head is supported with the left or right hand under the left side of the neck, jaw and chin. The patient sleeps on the right side of the face, supporting the head well with pillows. The chin can be moved forward only with difficulty toward but not fully to the midline, and it returns immediately to its position to the left. The right sternocleidomastoid stands out rigidly. There is pain on the left side of the neck (posteriorly and laterally) and less pain over the pectoral muscles below. The patient is left-handed, except for writing. Neurologic examination gives negative results otherwise. General physical examination revealed no abnormality. Roentgen examination of the region of the neck gave normal results, except for a rudimentary cervical rib from each side of the seventh vertebral body. Laboratory observations, including Wassermann tests of the blood, were negative. No examination has been made of the spinal fluid. Roentgenograms of the teeth show one definite abscess; two teeth have slight cavities, not invading the dental pulp. No other foci of infection are discoverable.

The patient is dissatisfied in marriage. Her husband is a traveling salesman and is away most of the time. She is sexually not satisfied, and her husband has neglected her otherwise, but this situation is of many years' standing, and she says that she has accepted the situation and can control herself sexually. Otherwise, her home and family life, as I have had occasion to observe, are happy. Although never definitely occupied, she spends her leisure agreeably, and is well poised and pleasant. No other sources of emotional upset have been discovered as possibly causative or superimposed.

I present this patient because in a recent review of the literature on spasmodic torticollis I have found that improved surgical therapy is being used in an increasing number of cases. If further study shows that the condition is definitely not psychogenic and the abscessed tooth is removed and the dental cavities are looked after, but no improvement occurs, how long should one wait before advising surgical intervention in the most advanced type? Dandy recently reported eight cases in which the patients were treated by his special surgical technic, five patients being entirely relieved and two improved; one died of pneumonia a few weeks later. In a study of thirty-nine women and forty-three men at the Mayo Clinic, treated by medical methods, it was found that 19 per cent recovered completely and 27 per cent were improved. Of those who had foci of infection removed, 51 per cent improved or recovered.

DISCUSSION

DR. G. B. HASSIN: I think that it would be well to wait for a time before advising surgical measures. My impression is that the majority of cases of spasmodic torticollis are of organic origin. I have seen a number of patients during eighteen years of service at the Cook County Hospital, and none of those who were treated nonsurgically recovered.

DR. MEYER SOLOMON: I agree with Dr. Hassin that one can wait for a time, but I think that it will be necessary to operate eventually. Dandy is of the opinion that he can get good results in such cases without cutting the sensory roots.

CRIMINAL CONFESSIONS UNDER NARCOSIS. WILLIAM F. LORENZ (by invitation).

The topic to be discussed is the application of a method of examination that has been found particularly useful in the psychoneuroses and psychoses to persons charged with crime to obtain a confession or statement of fact. The main interest has been to induce a state of narcosis by means of certain drugs and to attempt a psychoanalysis with the aid of the narcotic state. In our hands this method has demonstrated definite value. Many psychoneurotic patients reveal experiences and complexes during a state of narcosis which sometimes cannot be obtained during a state of consciousness or which, if obtained by the usual methods of psychoanalysis, require a tremendous amount of time and effort. During the state of narcosis it is possible to make direct suggestions, which operate subsequently in a manner not unlike posthypnotic suggestions. In the psychotic cases it has been possible to break down barriers such as dominant moods, particularly depressions, mutism and negativism, and the patient has become accessible, giving a vast amount of information, much of which seems to have an etiologic bearing. By this method of psychoanalysis the operator or physician is not prominent in the picture; transfers do not occur; the patient is definitely amnesic for the entire period of the examination, and disagreeable personal practices or experiences are related without the patient's having to censor his own past conduct. In the psychotic cases this method of examination has permitted us to separate the patients who can recover from those who cannot; in the benign types of depression, excitement or schizoid reactions; the abnormal mental reactions do not manifest themselves while the patient is under narcosis. In other words, in conditions that are less amenable to treatment, the psychosis is almost as evident during the narcosis as it is during the state of wakefulness. These psychoses have been found to be much less amenable to suggestion and treatment, and constitute the malignant type of mental reaction.

The same method of examination applied to persons charged with crime has been used with a varying degree of success. Up to the present we would conclude that the method is satisfactory and successful in the case of innocent people charged with crime. In the cases of guilty persons, we have not always been successful in obtaining a confession and therefore believe that the method does not supplant the so-called lie detector, which apparently, judged from reports, is a highly successful procedure in the presence of guilt that is denied by the subject.

In several cases of persons charged with murder the use of narcosis thoroughly satisfied prosecutors, special investigators and detectives as to the innocence of the one charged. There are certain ethical considerations covering the practice. It is suggested that the physician should act only in the capacity of a physician, that is, to induce the mental state, to be certain that the proper state of narcosis has been obtained and to be certain as to the physical condition of the patient, and then that he should stand by, concerning himself mainly with the physical and mental condition of the patient; the matter of questioning should be left in the hands of the prosecuting attorney or special investigator, and some one interested in the subject's welfare, a lawyer or friend, should also be present.

After a rather lengthy experience with various narcotics, namely, scopolamine, scopolamine and morphine and sodium amytal, it was found that the last named when properly used gives the best results. The technic of administration is as follows: dissolve 1 Gm. of sodium amytal in 20 cc. of sterile distilled water; inject by the intravenous route; the rate of injection should be 1 cc. per minute, controlled by a stop watch. Usually after 10 or 12 cc. has been administered the average adult relaxes and gradually falls into slumber. Injection is continued until the corneal reflex disappears. Administration is then stopped, and after ten or fifteen minutes the subject is aroused by the means of talking or the use of cold wet towels to the face. From then on for a variable period, ranging from two to three hours, the subject can be interrogated. Usually there is a spontaneous talkativeness, and all that the operator needs to do is to introduce a topic and to permit the subject to talk without interruption. After the examination is completed the subject usually sinks into sleep again and after a variable period of from three to four hours awakens. At this subsequent return to full consciousness the subject has a hazy, vague recollection of what transpired during the period of examination.

DISCUSSION

DR. A. B. MAGNUS: My experience with the use of diallylbarbituric acid in the production of hypnosis was unlike that presented by Dr. Lorenz. A case that was particularly illuminating was that of a man, referred to me by Dr. Krumholz, who became acutely despondent after an extensive loss in the stock market. The patient was subjected to the "*Schlafkur*" for eight days, and while coming out of the state of narcosis and before full consciousness was regained volunteered to relate a life experience which was not borne out by the facts. He persisted in saying that he had been using morphine hypodermically for years, and even told the source from which he was getting it. Dr. Krumholz and a priest who was interested in the case and I made searching inquiries to determine the accuracy of the statement. Our efforts were futile. The man was a responsible business man, and we failed to elicit a history of a drug habit.

Another case was that of a physician who during a postnarcotic and preconscious interval insisted that he was not in the hospital to which he had intended to go and was at a loss to explain how he had found his way to our hospital. When admitted, he had been in the administration building; just prior to the "*Schlafkur*" he was transferred to a different building for the treatment. This impression was apparently firmly embedded and was revealed in his subconscious state in a somewhat modified or clouded interpretation of an occurrence.

Of late I have used sodium amytal to some extent. It would appear to differ somewhat from diallylbarbituric acid, but the difference is slight, as both drugs belong to the same family of barbituric acid derivatives. I have had no experience with the drug with criminals, but I should like to ask Dr. Lorenz to explain why the drug should be given to obtain confessions from criminals who have committed minor offenses rather than from those who have committed more serious crimes, if it has the merit ascribed to it.

DR. MEYER SOLOMON: The question comes to mind whether there is an increased suggestibility in a condition such as this artificially induced mental state and whether, if the examiner used a bull-dozing technic and elicited a fear reaction, a man would confess things he had not done. Would a patient in such a state, as in the case just mentioned of the patient who confessed using morphine but who had apparently never used it, construct a fabrication and persist in it? Another question is whether in selected cases, even without the consent of the patient, the drug could not be used by prison physicians and given to the patient by mouth, disguised in fluid or food, to see whether confessions could be obtained. This could be done without the consent of the patient or his family and without telling him what he would be subjected to in order to put him off his guard. That would be an abuse of the physician-patient relationship. Also, one would be unearthing facts that the patient would not confess otherwise. In psychoanalysis

suppressed material is often mentioned; it is often not suppressed. The patient knows all about it, but he does not wish to speak of it or does not see the relationship. It is not necessarily hidden by critical consciousness. Those who have kept in touch with the work of Prince and others know that Prince has claimed for years that there is a coconsciousness. One may distinguish between reflex, passive, onlooking, uncritical consciousness and reflective, active, critical consciousness. Really all one is doing here is releasing the control of critical consciousness, just as occurs in dream states.

This method seems to be an added technic of tapping the subconscious and of bringing more of this work into the more definitely controlled experimental field.

DR. CHARLES F. READ: Does Dr. Lorenz find that in the ordinary catatonic patient he secures more definite information and reaches deeper levels of consciousness by this technic than by talking with him after he wakes up naturally from sleep? Dr. Lorenz has discussed only those persons who were innocent. We know that it is commonly accepted that the hypnotic subject cannot be forced to do things contrary to the instinct of self-preservation and his accepted code of morals. Has Dr. Lorenz found that those who are actually guilty will make confessions that will incriminate them, at least so far as the major crime is concerned?

DR. ALFRED SOLOMON: Does Dr. Lorenz lay any stress on the fact that patients are given prior instructions as to what will be done and on whether those instructions have any determining value on what happens during the period of narcosis? In other similar psychotherapeutic measures, such instructions are taken into account.

DR. JOHN A. LARSON: I have been following this method of narcosis with confessions for about ten years. It was my privilege to watch Dr. House in several of his experiments. In connection with the statement made by Dr. Lorenz that he did not know the source of the newspaper publicity and where the statement "truth serum" came from, I might mention that this arose through statements made by Dr. House himself. Up to the time of his death, Dr. House had read papers at several medical conventions. In his article he stated definitely that at a certain stage of the narcosis the patient was unable to lie. I had occasion to see one of his experiments during which a murderer definitely did lie throughout the whole test and have proof of this. It must be remembered that one cannot compare psychologically subjects who volunteer for experiments for purely experimental purposes with actually guilty persons.

Since Dr. Lorenz stated that he worked chiefly with the problem of clearing innocent men, I wish to ask just how many such experiments he has performed and what his results were and should like to check them, not by the opinion of district attorneys or police officials, but by actual authoritative facts that would be undisputed as evidence.

SPONGIOBLASTOMAS OF THE BRAIN. DR. PERCIVAL BAILEY.

A great deal of controversy about gliomas is concerned only with the terminology used. The names that I have used I created because there were no suitable ones available when I published my monograph on the gliomas. No one, so far as I know, has ever protested the validity of a single pathologic entity described in that monograph. However, clinicians are worried because it is too complicated for them; if the classification is simplified pathologists complain because they know that the structure of the tumors is more complicated than the terminology used. I am therefore apt to change the classification depending on my audience. If I am talking only to clinicians I do not bother about distinguishing between a pinealoma and a pineoblastoma, but in talking to pathologists it is necessary to do so. The same is true with the ependymomas in which two or three distinct types of structure may be shown to occur in tumors composed of ependymal cells. This is especially true in the spinal cord, as Kernohan has recently pointed out.

In regard to the tumor which I have described tonight, the cells composing it resemble more closely the spongioblasts of the developing nervous system than those of any other tumor. For that reason I prefer to call it a spongioblastoma. Germans refer to it as neurinoma centrale, a term that I do not like because, contrary to the peripheral neurinomas, the cells of the tumor do not form reticula. Penfield calls this spongioblastoma polare. That term is satisfactory to me, but the adjective seems to me superfluous. At any rate, this tumor is of a fairly benign type; it has a predilection for the brain stem and optic chiasm and has certain peculiarities of structure and characteristic degenerative changes which distinguish it from other gliomas.

DISCUSSION

DR. LOYAL DAVIS: Though pathologists may continue to discuss the terminology employed in describing the various types of gliomas, their controversies should not be allowed to hide the value of the fundamental classification that Bailey and Cushing proposed. The correlation of the type of tumor encountered at operation and the clinical course of the patient affords a principle on which neurologic surgery may progress.

DR. G. B. HASSIN: I understand that Dr. Bailey considers his studies of gliomas finished. Attempts to classify different types of gliomas were made by others before Dr. Bailey, who utilized the unusual opportunities of his association with Cushing and is mainly responsible for the new classification of these tumors. Before the appearance of Bailey and Cushing's monograph, pathologists were happy when they could recognize a tumor of the brain to be a glioma. In the monograph of Bailey and Cushing more than twenty types have been outlined. As I understand it, the number was gradually reduced to about eight or ten. I also understand that there is no agreement between the experts on spongioblasts as to the proper classification of the so-called spongioblastomas. At a meeting in New York I heard two of them discuss this topic. One remarked that spongioblastoma multiforme is not a tumor, to which remark the other expert objected. I should like to hear the opinion of Dr. Bailey as to whether the tumor he described as a spongioblastoma differs from that described by Globus and Strauss, and if so, what the differences are; also, how does he classify the spongioblastoma multiforme of Globus and Strauss? I wish also to ask Dr. Bailey what is the reaction, if any, of the blood vessels to the tumor cells and whether this reaction is the same in spongioblastomas, astrocytomas and astroblastomas.

NOTE.—Dr. Bailey's replies have been included in the abstract.

RECOVERY OF SENSATION IN DENERVATED PEDICLE AND FREE SKIN GRAFTS. DR. J. P. EVANS and DR. F. E. KREDEL (by invitation).

Recovery of sensation is described in a series of denervated pedicle flaps and free cutaneous transplants. Recovery is more rapid and more complete in pedicle flaps of full thickness than in Wolfe, Thiersch or Reverdin grafts. There is a temporal dissociation in the return of pain, touch and temperature discrimination. In pedicle flaps pain returns in from three to six months and touch in nine months or later, while temperature discrimination returns last. There is apparently no relation between the course of the original neurilemmal sheaths of a flap and the ingress of new nerve fibers. Recovery of sensation begins at the periphery of a flap at the point of proximal nerve supply. Cicatrization about a flap is an unfavorable field for the invasion of new nerve fibers.

DISCUSSION

DR. LOYAL DAVIS: Since my association with Dr. Allen B. Kanavel in 1920, I have observed several cases in his and Dr. Sumner Koch's service. We have records of eighty-three cases of pedicle and full-thickness grafts. Our observations are essentially the same as those reported. We believe that the sensation returns to the flaps from the horizontal plane. I wish to know whether Dr. Kredel has

made observations in relation to the presence of a protopathic response to pin prick stimulation? Early in the recovery of sensibility to pin prick there is a protopathic response which makes the patient withdraw defensively. There is no response to touch stimuli at this early date, but later, when this painful response has disappeared, tactile sensation is present. We believe, and I think that it has been shown by Dr. Kredel, that in full-thickness skin grafts sensation is recovered much sooner than in pedicle grafts. We believe that this is due to the thickness of the two types of flaps.

We are now interested in removing small portions of these flaps at various intervals to study the nerve endings in the skin and to correlate these with the sensory findings that have been charted. As yet we have come to no conclusion regarding the types of sensory endings that are present. Regarding the point that Dr. Kredel mentioned concerning flaps on bony surfaces, we have found a return of sensation in these flaps, which should prove that the sensation comes into the flap from the periphery and not from the underlying tissues. We believe also that the polarity of the flap bears no relation to the pattern of the return of sensation.

DR. D. B. PHEMISTER: I do not believe that Dr. Kredel emphasized sufficiently the fact that this work contradicts the statement that regenerating nerve fibers must find the old degenerated nerves of the denervated portion and grow along them. The flap in this case (case 1) had its original nerve supply coming in from below. There must have been some branches that were not connected with others and that did not reach the cut surface of the flap above or on the sides. Consequently, there was no opportunity for invasion of these fibers, as in its new position the trunk of the nerve was at the lower margin of the lip. I believe that the restoration of sensation in the entire flap indicates that the nerve merely grew into it from the margins, independent of the old fibers.

DR. ROY R. GRINKER: I have no preconceived reason for believing that nerves could grow along the old neurilemma sheaths, but this work has not disproved this belief. The nerve fibers probably have a plexiform arrangement, so that the neurilemma sheaths would be distributed in every direction. Nerve fibers are probably capable of penetrating tissue for some distance without sheaths to guide them, but obviously within a short distance would be affected by the tropism of the pathways of the old fibers. I should like to see added to this clinical demonstration a histologic demonstration showing the relation between the neurilemma sheaths and the old fibers. According to the clinical data presented, I do not think that the conclusion can be drawn that the newly formed fibers grew along new pathways.

DR. F. E. KREDEL: In reply to Dr. Davis, a protopathic type of response to pin prick was not obtained in most cases. Enough tests for discrimination of temperature were performed to demonstrate a lag behind the recovery of touch. Reports on several biopsies performed on these flaps will be given subsequently.

I rather agree with Dr. Grinker that we have not proved that new nerve fibers do not follow the old neurilemma sheaths. This question can be settled only by a histologic demonstration. Some experimental work on the rabbit is being done which may give the answer.

Regular Meeting, April 21, 1932

A. B. YUDELSON, M.D., *President, in the Chair*

COMBINED DEGENERATION WITH LHERMITTE SIGN: PRESENTATION OF PATIENT. DR. D. M. OLKON.

This patient is presented to demonstrate the Lhermitte symptom in a case of subacute degeneration of the cord with pernicious anemia. M. M., aged 50, a carpenter, was well up to two years before presentation. The previous personal history gave no incidents of disease. Two years ago the patient had digestive

disturbances. He was then treated at the Cook County Hospital, and apparently fully recovered. In November, 1931, he felt tingling and creeping sensations in the arms and legs, with numbness of the hands and fingers and some staggering. In December, he noticed a shooting sensation down his spine and legs when he bent the head downward and then upward. The sensation that followed this movement of the head he described "as like an electric shock" that went down his legs.

Physical examination gave entirely negative results. The eyegrounds are normal; the pupils react promptly to light and in accommodation. There is a fibrillary tremor of the tongue. All of the deep reflexes are present. The reflex of the left knee is 3 +. There is no nystagmus or foot-clonus. The Rossolimo sign is 1 + on the left. The Babinski sign is also suggested on the left. Vibration sense is lost in the lower limbs. The Wassermann reactions of the blood and spinal fluid are negative.

Examination of the blood, on April 4, 1932, showed: hemoglobin, 60 per cent (Dare); red cells, 5,100,000; white cells, 7,300; polymorphonuclears, 42 per cent; large monocytes, 3 per cent; lymphocytes, 51 per cent, and eosinophils, 4 per cent. The fragility test showed that hemolysis began at 0.45 per cent and was complete at 0.32 per cent. Analysis of the gastric contents showed that fifty minutes after digestion of an Ewald test meal there was still a large residue of undigested food. The total acidity was 20 degrees. Free hydrochloric acid was absent. Combined hydrochloric acid was 20 degrees. Lactic acid was absent; there was a trace of occult blood, and mixed bacteria were present, with a few epithelial cells. A roentgenogram to determine whether there was a malignant condition was normal.

The patient is being given liver therapy; hence the masked blood picture.

The greatest discomfort of which the patient complains now is that the "electric shock" he gets when moving his head downward and upward leaves him in a weakened condition, and that his limbs feel shaky after the "shock." After careful consideration of the differential points of diagnosis, I am of the opinion that this is a case of the Lhermitte symptom in subacute degeneration of the cord on a substrate of severe anemia.

DISCUSSION

DR. PETER BASSOE: Am I correct in my impression that the lymphocyte count was 51 per cent? I did not hear the total leukocyte count. There might be a question of a lymphatic leukemia. Has the patient ever had a high leukocyte count, and have several counts been made?

DR. D. M. OLKON: Many leukocyte counts have been made; the highest was 7,300.

DR. P. BASSOE: In leukemia there is sometimes a normal total leukocyte count while the differential count remains abnormal. In leukemia there may be a combined degeneration in the cord or a leukocytic infiltration in the meninges.

DR. D. M. OLKON: The lymphocytosis is the only abnormal observation on the blood at this time. When the patient came to the clinic a month ago he had a spastic gait, but today that condition is much improved.

BILATERAL FACIAL SPASM (PARASPASME BILATÉRAL OF SICARD). HARRY L. PARKER, Rochester, Minn. (by invitation).

In 1910, Meige described a series of cases in which the outstanding feature was a more or less continuous spasm of all the muscles of the face. In this spasm the eyelids were tightly shut and the muscles around the eyes contracted in a synergic, orderly, tonic fashion, with short periods of relaxation. The spasms of the other muscles of the face were asynergic and less orderly, but none the less continuous. The condition was continuous during the day but disappeared during sleep. Lying down relieved the spasm. Most of Meige's patients were persons beyond middle age. In 1925, Sicard described more cases and coined the

name *parasp asme bilatéral* for the condition. Since then, other patients who were somewhat younger have been described, and it is possible that there are two groups of cases, one of senile origin and one due to encephalitis with or without parkinsonism. Two illustrative cases are described. The disease is apparently allied to the ordinary facial hemispasm, but it is present bilaterally and must be differentiated from tics, athetoses, myoclonias and choreas. It differs from the so-called blepharospasm only in degree. Further cases are shown illustrating the different types of blepharospasm, more especially the cases of this condition occurring during the course of epidemic encephalitis. Both in bilateral facial spasm and in blepharospasm, regardless of origin, there are some curious subterfuges and tricks attempted by the patient to relieve the spasm. Both in this fact and in the stubborn persistence of the disease the condition is rather similar to spasmodic torticollis. Up to date the pathologic basis of the condition is unknown.

DISCUSSION

Dr. G. B. Hassin: Can Dr. Parker suggest any physiologic or pathologic explanation for the various cases of the type of spasm he demonstrated? Were psychologic factors instrumental in their causation, and did any patients come to necropsy?

Dr. Lewis J. Pollock: It might be well to point out that, as Dr. Parker has shown, the so-called spasm is not limited to the seventh nerve. In one case he described, the contraction of the platysma would have been insufficient to produce a spasmodic opening of the mouth and the movement of the jaws. Many of the cranial nerves may have been involved in the spasm. I recall the case of a woman, aged 45, in which the condition began with a so-called bilateral blepharospasm and in which a periodic spasmodic closure of the palate developed. The palate was suddenly released, making a snapping sound, and then the patient made swallowing movements. She, too, was influenced by restraining gestures and also by cocainizing of the conjunctivae. It is notable that the movements are not due to stimulation of the seventh nerve alone. The use of the word spasm in such cases makes it a little more difficult to evaluate properly what is commonly understood as facial spasm.

Dr. A. B. Yudelson: Were any of these so-called spasms accompanied by pain at any time during the tonic or the clonic phase? In one of the cases it was noted that the patient moved his head from side to side and forward. Did Dr. Parker think that these movements of the head partook of the form of torticollis?

Dr. Harry L. Parker: Replying to Dr. Hassin, no particular basis has as yet been found to explain this condition. In all the literature dealing with the subject, no cases in which necropsy was performed have been recorded, and therefore the pathologic condition is unknown. It is probable that these conditions are of the same order as spasmodic torticollis, and that they behave in a somewhat similar fashion.

Dr. Pollock brought up a good point in mentioning that nerves other than the seventh are involved in the case that I have just presented. However, on studying such cases it is difficult to disentangle the primary spasms of the muscles supplied by the seventh nerve and the antagonistic movements made by the patients, more or less voluntarily, to overcome the spasm. In one case the movements of the tongue and jaw were presumably performed in an effort to open the eyes. An interesting case has been described by Laignel-Lavastine, similar in many respects to the case Dr. Pollock mentioned. The patient had severe spasms of the eyes, face, soft palate and pharynx, and during these spasms thrust his head forward, with the chin depressed on the chest, and made movements as if to swallow a large bolus of food which had become impacted in his pharynx. Laignel-Lavastine found some polyps in the nasopharynx, and thought that removal of these polyps ameliorated the spasms.

In answering Dr. Yudelson, I stated that these spasmodic movements are somewhat allied to spasmodic torticollis. They are more or less continuous, are absent during sleep and are relieved by lying down, and the patients resort to many tricks

to relieve them. I suppose that they are on the same basis, and if I could be told the pathologic basis of spasmodic torticollis, I probably could say what the basis of these facial spasms is.

THE ETIOLOGY OF MONGOLISM. DR. R. L. JENKINS (by invitation).

The reported cases of mongolism occurring in twins indicate that in the case of dizygotic twins only one member of the pair is affected, while in the case of monozygotic twins both members are mongols. Any familial tendency to mongolism is extremely slight. The incidence of mongolism varies widely as a function of the age of the mother, increasing rapidly with advancing maternal age. After the age of 30, it behaves as a logarithmic function of maternal age. There is a 30,000 per cent increase in the incidence of mongolism between the children born to mothers aged from 15 to 19 and the children born to mothers aged from 50 to 55. The relation between the incidence of mongolism and the age of the father is a result of the correlation between the ages of parents. The reproductive history of the mothers of mongols shows that they have borne fewer children than mothers of the same age who bear normal children. The birth of a mongol is much more frequently preceded by a long gap than is the birth of a normal child, even when allowance is made for maternal age. None of the existing hypotheses concerning the etiology of mongolism avoids conflict with some of these facts. A new hypothesis concerning the etiology of mongolism is presented. The etiology of mongolism is ascribed to a diminished viability of the ovum. This hypothesis adequately explains all of the recorded facts. It is compatible with the occurrence of mongolism in both members of pairs of monozygotic twins and in one member of pairs of dizygotic twins and, at the same time, with its lack of familial tendency. It harmonizes with the increasing incidence of mongolism as fertility diminishes with advancing age of the mother and with the association of mongolism with diminished fertility as evidenced by the fact that mongols occur in families smaller than the average, and that they are more frequently preceded by a long gap than is the birth of a normal child.

DISCUSSION

DR. A. B. YUDELSON: In the study of this subject and the survey in this country was any geographic distribution observed by those making the survey? Further, was there any relationship between cretinism and a modification of the real mongolism?

DR. HARRY A. PASKIND: In the statistics, were the stillbirths and miscarriages taken into account? Was a count made of the type of births preceding the birth of mongols?

DR. R. L. JENKINS: In regard to geographic distribution, I am not able to give any data, except that, so far as we know, mongolism occurs everywhere. There are differences in the rate reported among patients admitted to homes for the feebleminded, but I think that these differences cannot be taken as indicating the actual differences in population because of the lack of agreement as to when a child is fit for placement in such institutions.

I do not believe that there is any relation between mongolism and cretinism, and what I judge to be the better material I have read gives the same opinion.

The United States statistics used were those of births of white infants, including stillbirths and miscarriages. The inclusion of stillbirths would not alter the statistics, for they are sufficiently infrequent in relation to normal births not to alter the curve. The statistics for the Netherlands were for total births. I am not able to state in what percentage of cases the mongols are preceded by miscarriages or stillbirths. I think that this would be an interesting study, but material is not available at present.

FLEXION PARAPLEGIA AND LHERMITTE SIGN IN SUBACUTE COMBINED DEGENERATION OF THE CORD. DR. G. B. HASSIN.

This article will be published in full in a later issue.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, March 8, 1932

S. PHILIP GOODHART, M.D., *President, in the Chair*

SOME PRINCIPLES IN THE THERAPY OF MULTIPLE SCLEROSIS. DR. RICHARD BRICKNER.

During the two and one-half years in which the treatment for multiple sclerosis with quinine hydrochloride has been in progress, more than forty patients have been treated. Of these, thirty-three have continued with the drug, without significant intermission, for periods ranging from four months to two and one-half years. The theoretical foundation of treatment with quinine has been described in previous communications (Brickner, R. M.: ARCH. NEUROL. & PSYCHIAT. **23**:715, 1930; *Bull. Neurol. Inst., New York* **1**:105, 1931; *New York State J. Med.* **31**:885, 1931, and ARCH. NEUROL. & PSYCHIAT. **28**:125, 1932). In cases of multiple sclerosis, characterized as they are by spontaneous remissions, the difficulty in evaluating therapeutic effects is great. There is additional uncertainty from the fact that, in any particular patient, some of the lesions may be of much longer duration than others. The possibility that healing will occur may therefore vary considerably for the different lesions in the nervous system of a single

Total Number of Symptoms Observed in All Patients Who Have Taken Quinine Continuously and Who Have Been Followed

Duration	Number of Symptoms		
	Improved	Not Improved	Regressed
Came on during treatment	1	..	..
6 months' or less	21	5	..
6 to 12 months'	24	8	1 (1 ?)
12 to 18 months'	15	0	..
18 to 24 months'	12	2	..
Not long; exact duration unknown	12	1	..
2 to 3 years'	14	8	..
3 to 4 years'	4	13	3
4 to 5 years'	1	9	.. (3 ?)
5 to 6 years'	1	4	..
9 to 10 years'	0	1	..
10 years' or more	1	3	..
Many years'; exact duration unknown	0	6	..
Duration entirely uncertain	2	1	..
	108	61	4 (4 ?)

patient. Hence, in evaluating the results of therapeutic measures it has seemed best to consider the course of each symptom rather than to think of the patient as a whole.

The present outcome in the total number of patients who have consistently taken quinine for a considerable interval and whom it has been possible to follow throughout the period of treatment is given in the accompanying table.

The table shows that in the majority of instances improvement has occurred in symptoms of not more than two years' duration. No symptom has been listed as improved unless uninterrupted improvement was maintained as long as the patient remained under treatment, so that the table also shows that few symptoms have regressed during treatment. The outcome of episodic regressions is of particular interest. Eight of the patients have, at some time during treatment, suffered from severe relapses of all their symptoms. In four of these, the relapse was definitely associated with an acute febrile illness. Quinine therapy was continued throughout the regression, and the symptoms of multiple sclerosis returned to their former levels in from four to six weeks in every instance.

Certain points deserve emphasis. Relapses should not cause the treatment to be abandoned, since up to the present no relapse has lasted longer than from four to six weeks when treatment has been continued. The therapy should be continued indefinitely, with no prolonged interruptions, because the theory on which it is grounded does not point to cure, only to continued relief. Hope of arresting the progress of the disease is a valid reason for giving treatment in cases in which the symptoms may be sufficiently fixed so that no actual improvement can be anticipated. As much quinine should be given continuously as the patient can tolerate without the development of cinchonism. Cinchonism, however, should always be an indication for only temporarily interrupting the administration of the drug, as most symptoms — spasticity in particular — regress with the use of the drug. The drug should be given again three or four days later, usually in a smaller dose. In every case it has been possible to find a dose that the patient could tolerate. The treatment should not be considered a failure unless the symptoms make no regression of several months' duration while the correct administration of quinine is continued.

DISCUSSION

DR. HENRY ALSOP RILEY: I do not think that this is a proper time for any extended discussion of the technic developed by Dr. Brickner in his experimental investigation of multiple sclerosis; neither do I believe that the time has come for any definite conclusions to be drawn in regard to either the pathogenesis or the treatment of this disease. Dr. Brickner's results will have to be corroborated by others and his conclusions substantiated by them before any definite judgment can be reached in regard to these difficult problems. A number of dissimilar conclusions in regard to this disease have been published during the past three or four years, and in view of certain recent unfortunate developments in connection with the investigation of the cause and treatment of multiple sclerosis it is essential that conservatism be maintained. We should, therefore, do everything in our power to support Dr. Brickner's conservative attitude toward his own investigation and avoid any attempt to push this matter to a premature conclusion or to force his hand in any way. The results of treatment with quinine must be obtained in a large number of cases with an adequate group of control patients over a considerable period before any definite judgment can be reached in regard to its efficacy. So far as my personal experience with quinine in my service at the Neurological Institute and in private practice is concerned, I can state that remissions have occurred more frequently after the institution of quinine therapy, and improvement has been better sustained and more satisfactory than with any other form of therapy that I have followed.

It would seem to me from these early results that quinine therapy is a hopeful and promising method of treatment. Whether the results of therapy will bring us much further in the appreciation of the true cause of multiple sclerosis can be decided only by the passage of time. The obvious course at present is to apply this method of treatment carefully and conservatively, and to watch and report the results without prejudice.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, April 5, 1932

S. PHILIP GOODHART, M.D., *President, in the Chair*

PRIMARY ATROPHIC MYOPATHY. DR. WILLIAM D. SHERWOOD.

I present three cases of primary atrophic myopathy occurring in one family — in a father, aged 54, in a daughter, aged 22, and in a son, aged 18. The family and past history in each case is negative. None of the patients had ever been

able to pucker the lips or to whistle. The father had had a bilateral footdrop from the age of 20; it had developed so slowly that he had paid no attention to it. When first seen, the daughter had just observed footdrop. While the son has no definite footdrop, one foot slaps the floor more sharply than the other; he is nearing the age when his father first observed the condition in himself. The father shows scoliosis, dorsal to the right, winging of both scapulas, myopathic facies and tapir mouth. He cannot walk on his heels. The daughter shows scoliosis, dorsal to the left, inability to stand on the left heel, atrophy and weakness of the facial muscles, giving the myopathic facies and tapir mouth, and winging of the right scapula. Both achilles jerks are absent. The son has slight winging of both scapulas, the free border of the right trapezius muscle being less prominent than the left. Myopathic facies and tapir mouth are present. Equilibratory tests of each patient are fairly well performed.

On reexamination, after fourteen months, the father showed definite progress in the existing atrophies; the muscles of the pelvic girdle show atrophy. He experienced difficulty in going up stairs. There was involvement of the anterior and posterior muscles of the thighs. Six months later, definite increase of the atrophies was noted, with lordosis of the lower dorsal and lumbar spine, prominent abdomen, bilateral pes cavus, atrophy of the pectoral muscles and those of the lower part of the back and more marked weakness and atrophy of the deltoid muscles. Muscle tendon sense is reduced in the fingers and toes. The daughter was seen fourteen months after the first examination, during which time the disease had progressed; marked atrophy of the muscles of the shoulder girdle was evident. The small muscles of the hand were involved, and there was a bilateral pes cavus; right foot and wrist drops were noted. Six months later, weakness of the internal rotators of the right thigh was found. Six months after the first examination, the son showed slight gain in weight. The biceps, triceps and patellar jerks were obtainable only on reenforcement; there was active plantar flexion on stimulation of the soles. No fibrillary twitchings were present in any of these patients. The laboratory findings in all three cases were negative, except for the presence of fairly large amounts of creatine and creatinine in the urine. The electrical reactions were similar in the three patients, namely, a quantitative reduction in electrical irritability; the faradic response was obtained in all muscles; no polarity changes were noted on galvanic stimulation.

DISCUSSION

DR. BERNARD SACHS: It is unusual for three members of one family to be shown with this condition. I presume that they are presented as typical examples of the Landouzy-Dejerine type of progressive muscular dystrophy. These are as clear examples of that type as I have ever seen, showing all the cardinal symptoms. The absence of the muscular fibrillation helps to differentiate them from the Aran-Duchenne type, which is definitely spinal. All of these patients have shown weakness of the anterior tibial muscles.

THE CONDUCTION OF LABYRINTHINE IMPULSES TO THE CORTEX IN EXPERIMENTAL EPILEPSY. DR. LOUIS S. ARONSON.

Departing from the usual methods of provoking epileptoid muscular contractions. Bagleoni, Clementi, Amantea, Dusser de Barenne and others have shown that one can produce a hyperirritability of the sensory centers in the cortex by localized applications of strychnine to the sensory areas in cats and dogs. Further stimulation of the corresponding limbs evokes muscular twitching of several groups of muscles, notably those of the skull. The explanation of these authors for these phenomena is that impulses are conveyed from the periphery to these oversensitive centers and thence radiated to motor centers. After strychninizing such animals, Spiegel produced labyrinthine cortical irritation by rotating the animals on a Bárány apparatus, after they came out of the anesthesia. He found that these twitchings of the nose, eyelids and mouth recurred, and that the

muscular clonic spasms would extend to the limbs and the rest of the body, so that the animal was convulsed. I repeated these experiments and found that there was always a latent period before the onset of the convulsions during which the animal would either partly or entirely lose consciousness. The pupils would dilate, the convulsion would start as a local twitch, and then spread in irregular muscle groups, thus simulating convulsions in human epilepsy. Sometimes status epilepticus would result. Fits would arise without further strychninization of the cortex or rotation. One had to differentiate generalized strychnine rigidity from an epileptiform convulsion. In strychnine poisoning, the animals always went into spasms, during or immediately after rotation, with no latent interval and no unconsciousness. The spasms were tonic, not clonic, involved the extensor muscles in greater degree, were of short duration, and invariably could be elicited by sudden jarring of the animal. Moreover, they were always fatal.

I studied the pathways in Spiegel's experiments by strychninizing the cortex and then extirpating one labyrinth, first of the same side as that on which the cortical operation had been performed, then of the opposite side, and found that in either case impulses could reach the cortex through the remaining labyrinth and produce convulsions. If destruction of the remaining healthy cortex was carried out, impulses could still produce convulsions. Stimuli from the labyrinths to the cortex were both crossed and uncrossed. Similarly, I obtained convulsions by extirpation of the eighth nerve near the internal auditory meatus.

Spiegel extirpated the cerebellum in such cases and found that impulses from the vestibular apparatus could still reach the cortex and cause convulsions. I cut the fibers of the posterior longitudinal fasciculus, and found that though the convulsions were greatly reduced in volume and intensity, they could be elicited. The result of this work seems to show that neither the cerebellum nor the posterior longitudinal bundle, which can carry vestibular impulses to the cortex, are essential, and that the blocked impulse may elect another path, which may be ipsolateral or contralateral to the strychninized cortex. This is much like the pattern of conduction of cochlear nerve impulses, and is in agreement with the observations of Lorente de No and Spiegel, who observed that with bilateral extirpation of the posterior longitudinal fasciculus, nystagmoid jerks could be elicited in animals by rotation. It seems likely that vestibular mesencephalic tracts in the formatio reticularis carry impulses to the eye muscle nuclei in the midbrain. Possibly these tracts are used by the labyrinthine impulses to the thalamus, as Held believed. In either event, neither the cerebellum alone nor the posterior longitudinal bundle alone is essential for such conduction. The anatomic studies of Winkler, confirmed by Waldenberg, showed that these impulses can also travel up via the cochlear nerve.

DISCUSSION

Professor E. Spiegel, Vienna and Philadelphia (by invitation): A cortical center of the labyrinth has been postulated in very different areas of the cortex, viz., in the parietal, in the temporal and in the frontal lobes. But no evidence has substantiated these suppositions. Local poisoning with strychnine seems to be a method by which to study this question. Labyrinthine impulses seem to enter the temporal lobe. That there are so many pathways conducting the vestibular impulses to the cortex may seem surprising. But the conditions hold for other centripetal impulses, for instance, pain. It seems that especially such sensory impulses as are of biologic significance have these manifold pathways at their disposal to reach higher centers, viz., one main pathway and beside it secondary pathways, the latter being used if the main pathway is destroyed.

Experimental Toxic Approach to Mental Diseases (The Reaction of the Brain Tissue to Subcutaneous Injection of Enterogenous Toxic Substances — Indole and Histamine). Dr. A. Ferraro and Dr. J. E. Kilman.

We have attempted to prove the existence of pathologic changes in the central nervous tissue due to the action of toxic substances present in the gastro-intestinal

tract. Among the various agents we have considered especially are indole and histamine. For many years histamine has been considered responsible for the onset of mental conditions, whereas indole has recently been neglected.

The experimental work was carried on in cats, which received various doses of histamine or indole, or both. The action of small as well as of large doses of histamine and indole has been investigated. In order to bring about the death of the animals, daily doses of histamine and indole were administered in a large series of animals; it was found that those receiving from 3 to 5 mg. of histamine could live for over a year. Animals receiving 100 mg. of indole could also live for over a year. Cats receiving a dose of 150 mg. of histamine could live as long as ninety-five days; those receiving progressive doses of histamine, from 5 to 50 mg., could live twenty-eight days, having received a total amount of 705 mg. of histamine.

If indole and histamine are combined, length of life is considerably shortened; in one instance, 100 mg. of indole associated with 3 mg. of histamine produced death in forty days; in another, the combination of the indole with 150 mg. of histamine produced death in eleven days.

We therefore conclude that the association of indole and histamine is an important one and in the experiment corresponds to what really happens in the normal person in whom both histamine and indole can be detected in the gastro-intestinal canal.

Experiments were also carried out with potassium cyanide, which is supposed to diminish the oxidizing power of the cells. It was found that potassium cyanide could be administered for over fifty days, starting from 1.5 mg. of the drug daily up to 35 mg.; when indole was combined with potassium cyanide in a dose of 150 mg. of indole and 2.5 mg. of potassium cyanide, death of the animal occurred in a much shorter time.

From the histopathologic standpoint the lesions produced by indole and by the combination of indole and histamine are of the severe type of degeneration. Nerve cells all over the cortex appear acutely swollen, undergoing a gradual process of liquefaction. The astrocytes also undergo severe degenerative changes, leading to clasmatodendrosis and disintegration of the elements. Not only the brain but also the liver, the kidney and the intestines show pathologic changes. The pathologic changes in the liver consist in fatty degeneration; in the intestine they consist in a hyperplasia of the lymphoid tissue and degeneration of the epithelial covering of the villi. The involvement of the liver and of the intestine, organs which serve in part to detoxicate indole and histamine, seems therefore to play a rôle in the damaging effect of the aforementioned substances on the central nervous tissue.

In conclusion, we recall the fact that mental disorders are often accompanied by gastro-intestinal disturbances, and that the injection of indole and histamine in normal persons produces some of the manifestations present in the psycho-neuroses. This seems to substantiate our contention that in one group of mental diseases the source of origin is undoubtedly gastro-intestinal toxemia. The importance of histamine intoxication has already been emphasized by Buscaino and his co-workers in Italy; we emphasize the importance of indole, and more especially of combined indole and histamine intoxication.

Book Reviews

Ritual: Psychoanalytic Studies. By Theodor Reik. With a Preface by Sigmund Freud. Translated by Douglas Bryan. Price, $5. Pp. 367. New York: W. W. Norton & Company, Inc., 1931.

The four studies reported in this volume deal with the psychology of religion as studied by the psychoanalytic method. The subject is approached through a consideration of religious ritual, which was chosen as the point of departure because it has already proved a sound starting point for the scientific analysis of religion, the first analytic comprehension of religious phenomena having started from the ceremonies of believers, which Freud has compared with the obsessive acts and religious ceremonials of neurotic persons. Also, the character of action, which is such a marked feature of ritual, may be more profitably investigated psychoanalytically than the ideas, commands, prohibition, dogmas and complicated sentiments, which have later become the chief content of religion.

Four examples of religious ceremonial have been selected, and the author attempts by means of analysis to throw light on the operation of unconscious factors, the mechanisms of affects and the significance of conscious influences in the origin and development of the rituals concerned. He selected religious customs that are still practiced in order to show that in the latest forms of reaction-formation the same mental forces develop their activities in accordance with the same laws as in the earlier stages of development, and that by psychoanalytic methods it is possible to reconstruct the nature of the original impulses from which the ritual is derived by working back from the forms of expression and the hidden tendencies which the ritual still presents.

The four religious ceremonies he discusses are: (1) the couvade, (2) the puberty rites of savages, (3) Kol Nidre and (4) the Shofar (the ram's horn). The last two Jewish ceremonies have been selected because it is recognized that the founders of the Christian religion based their feelings and thoughts on Judaism; i. e., religions of the Church represent both the continuation and the transformation of the Jewish religion. An analytic understanding of the religious questions of Judaism should, therefore, throw light on the unconscious factors which have determined the nature and origin of Christianity, and also the analysis of the fundamental stages in the development of Judaism may have a special value and significance for the pychology of religion in that it may explain the psychogenesis of the claim of the Jews to be the chosen people and to stand in a peculiarly intimate relationship to the Deity.

In the first section is discussed the couvade. After a detailed description of the ritual and a discussion of the various theories that have been advanced to explain it, Reik applies the psychoanalytic method to two parts of the ritual: the pseudomaternal couvade and the dietetic couvade. Both ceremonies seem to be based on the same psychic mechanism. The new-born child stands to the prehistoric father and to the unconscious of the primitive father as a person who has come between him and his sexual partner, i. e., as a reincarnation of the grandfather, the fear of whom separated the father as a young child from enjoying the entire love of the grandmother. Consequently, the father's hate and fear of the grandfather (resulting from the expectation that the grandfather and his reincarnation — the new-born son — would retaliate on the father for his hostility) comes into conflict with the father's love for his son (and his father). The ceremony of the couvade is a prohibition placed on the father's hostile desires, e. g., the prohibition in the dietetic couvade against killing and eating animals is the repetition of the totem prohibition against eating and killing the grandfather, or the child as his reincarnation. Also, the displacement of the birth from the mother to the father corresponds to the fantasy of the father having given birth to the child and is equivalent to a nullification of the child's birth from the mother. The affective basis of this fantasy lies in the unconscious incestuous fixation of

the child on the mother which was created by the birth, and on this basis also rests the father's striving to detach this libido fixation from its object and to transfer to himself the child's love. This nullification of incestuous attitude can have no more radical enforcement than by the denial of its first and most essential cause; it is not the mother who has given birth to the child, but the father; to him, therefore, the child's love must go. The couvade denotes a definite advance in civilization, the victory of the tender impulses for his wife and child on the part of the man. The unconscious identification of the man with his own father now begins to be a lasting one, and his affection for him has so successfully suppressed the fear of retaliation that his concern about the new generation now becomes the central point in his emotional life as a parent. This signifies, however, a partial renunciation of the gratification of his impulses, a necessary condition in the advance to each higher stage of civilization.

In the second section, puberty rites of savages are discussed. A consideration of them leads to the conclusion that they are based on the same mechanism as the couvade; they are the effects of the same unconscious attitude of feeling expressed in different forms, in which the ambivalency toward the son stands out with special prominence. Through his discussion of puberty rites the author comes to consider the development of religion and considers the bond which the primordial fathers of the Jews concluded with their god as a glorified and emended account of an initiation ceremony. In this section, however, he passes over the Jewish ritual to discuss the replacement of father gods by son gods. Christianity is culturally the most significant instance of such a radical replacement. The part played by an oppressive sense of guilt as well as by defiance in the son is clearly recognizable in these later forms of religion. All of the son gods — Tammuz, Adonis, Attis, Osiris and Christ — have in common death, mourning by the mother and other women and resurrection of the killed god. Their sacrificial death is an attempt at expiation; it has the character of a compromise, for it ensures the attainment of the son's most urgent wish, namely, his own enthronement at the side of his father. Looked at in this way, the myth of the suffering, death and resurrection of the Savior, i. e., the account of the passion, can be denoted as a complex of the puberty rites. The son gods are also redeemers and bringers of culture because they took on themselves the primordial guilt, the hereditary sin, and thereby freed humanity from the burden of its guilty conscience. Out of the puberty rites and constructed in the same theme — the defiance and rebellion of the son against the father, and the former's death as an expiation for his crime — has arisen also the drama. As Reik states, "It may be well in reviewing all that our psychological analysis of the puberty rites of savages has contributed to our knowledge of the development of mankind, to repeat Freud's dictum, that 'the beginnings of religion, morality, society, and art converge in the Oedipus complex.'"

The section on the Kol Nidre is extremely interesting. The Kol Nidre is the melody sung at the commencement of the service on the Day of Atonement. The words of the melody in brief are as follows: "All vows, obligations, oaths, and anathemas, which we may vow, or swear, or pledge, or whereby we may be found, from this Day of Atonement unto the next, we do repent. May they be deemed absolved, forgiven, annulled, and void, and made of no effect; they shall not bind us nor have power over us." The marked contradiction between this and the sanctity in which Jewish people hold all vows serves as the point of departure for Reik's study. He develops the thesis that the original oath or vow was a mutual agreement among the brothers of the primordial horde because of their guilt and contrition following the slaying of the loved, yet hated and feared, father, that they would never repeat the crime. The wish to do so, however, still remained and remains but has been repressed. The overconscientiousness of the Jew in regard to vows is in reality a reaction formation against the wish to repeat the crime. But, as occurs in obsessional neurosis, this type of repression usually results in a return of the repressed, so that the Kol Nidre in effect says, "We confess our sins, we really desire to again slay and devour our God (the primordial father)," while the deeply affecting melody is justified,

since it is not related to the present wording but to the secret feelings which have become unconscious. This music brings adequately to expression the revolutionary wish of the congregation and their subsequent anxiety; the soft broken rhythms reflect their deep remorse and contrition. Thus the song is really full of terror and mercy.

In the section on the Shofar, the ram's horn blown on certain solemn occasions, the author discusses in detail the episode of Sinai and considers in this connection also the statue of Moses by Michelangelo (which has been discussed earlier by Freud). He concludes that the essence of the events of Sinai is the suppression and rejection of rebellious tendencies against God, and is the victory of the conscious impulses of love over the unconscious feelings of hate and rage. Moses is only a representative of the Jewish people; in him they recognized themselves with all their virtues and weaknesses. It is therefore reasonable that the people should be prepared to take over the guilt of the leader, since they have actually cooperated in the crime; they have burdened themselves with guilt through unconscious impulses of hostility and rebellion against God. The first Greek drama and the Sinai myth, besides definite differences, have much in common. In both cases a hero, or God, burdens himself with heavy guilt; but whereas the Greek chorus appears only in the rôle of the spectator bewailing the suffering hero, the Jewish people take his tragic guilt on themselves so that the hero may be freed from it. The guilt, however, is the same, a monstrous offense against the Deity. If the development of the Greek drama had lasted longer, it would perhaps have resembled the Jewish tradition, in which the return of a repressed situation is secured by the guilty conscience of the people. Perhaps, however, constitutional and historically determined peculiarities account for the difference between the mental attitude of the two peoples toward their mythical heroes.

Another factor which greatly facilitated the association of Moses' deed with the people, namely, the masochism which is concealed in the assumption of the guilt, must not be overlooked. This important factor in the psychology of the Jewish people, whose misunderstanding has led to far-reaching error, early began its activity and has persisted into present times. Perhaps none of the modern civilized people have so great a sense of guilt as the Jews, who in the course of thousands of years have sought and attained again and again the gratification of masochistic and self-punitive tendencies. An element of archaic mental life, which in other peoples has long since given place to a more stable mental condition, has persisted in Judaism and contributed essentially to its isolation. The covenant between Jahve and the Jews, with which the peculiar fate of the Jews and their belief that they are the chosen people was to be bound up, was founded on the repression of the strongest unconscious affects. Without a knowledge of these basic factors there can be no understanding of the problems of the Jewish religion.

Although the reviewer has attempted to give a bird's eye view of the contents of this book, it is impossible to deal adequately with it. It is a mine of valuable anthropologic and historical data concerning religion and its psychoanalytic interpretation. Many of the primitive customs cited have their counterpart in certain social situations in civilized communities, e. g., the desertion of his family by the husband each time the wife becomes pregnant. This desertion seems to be a kind of couvade. Only by an understanding of the mechanisms underlying the couvade can adequate social therapy be developed for such situations.

But not only is it of value in this connection; the clear presentation of the relation between religious ritual and the obsessional neurosis and the mechanisms underlying both make the book one of extreme importance to those who are interested in the problems and attempts of human beings to free themselves from their own unconscious desires and strivings and their inner sense of guilt.

Reflex Activity of the Spinal Cord. By R. S. Creed, D. Denny-Brown, J. C. Eccles, E. G. T. Liddell and C. S. Sherrington. Price, $3.75. Pp. 183. New York: Oxford University Press, 1932.

In this book there is presented in compact form a digest of the work of the Oxford school of physiology on reflexes at the spinal level. Professor Sherring-

ton and his associates have been working in this field for many years. They have developed a technic that has not been equaled elsewhere, have shown remarkable originality and insight in planning their experiments and have contributed most of what is known about spinal reflexes. Those who have followed fairly closely the large number of highly technical papers which they have published on this subject will welcome this brief digest, interpretation and authoritative summary of their work, and those who have not had time to read the individual papers will find in the book an account of the reflex activity of the spinal cord which is clearly stated and easily understood.

The book differs from the "Integrative Action of the Nervous System," published by Sherrington in 1906, in that relatively less attention is paid to the biologic significance of the reflexes, or, in other words, to their meaning as parts of animal behavior, while much more information is presented as to what is going on in the spinal centers during reflex activity. The improved method of recording the responses simultaneously in electrograms and isometric myograms, which has been used in the later investigations, has added much to the precision of the results. Several new topics, not even formulated in 1906, receive considerable attention in this new book. As among the more important of these there may be mentioned the following: the "stretch reflex," the response of an extensor muscle to the stimulation of certain of its own afferents by passive stretching, which plays an important rôle in reflex standing and in the production of decerebrate rigidity; the "motor unit," an individual motor neuron with the muscle fibers, sometimes as many as 150, that it innervates, which motor units represent the divisions into which a reflex fractionates its muscle, and the activation of which as units sets the limits of fineness of gradation in muscle contraction; and the "central excitatory state" and "central inhibitory state," representing, respectively, the alteration in the reflex center produced by excitatory and inhibitory impulses and serving as a basis for an explanation of many central phenomena such as facilitation, summation and inhibition.

The scope of the book is indicated by the headings of the seven chapters as follows: the reflex arc, the spinal gray matter, the flexor reflex, the stretch reflex, reflexes in extensor muscles other than postural reflexes, central inhibition and lower reflex coordination.

It is of interest that the muscle proprioceptors are no longer regarded as the only source of the afferent impulses maintaining muscle tonus and decerebrate rigidity. It is recognized that the impulses from the labyrinths play a large rôle in decerebrate rigidity, especially in that exhibited by the forelimbs.

The bibliography of 209 references naturally includes the papers published by the Oxford school, but it is unfortunate that it is not more representative of the world literature. The small number of citations of French and German papers is explained as for the "convenience of students who are accustomed to consult work written in English." As an example of the points at which discussion of the work of others would have been helpful, one may mention the account of the pseudo-affective reactions in thalamic preparations in which the studies of Cannon and Bard are not mentioned.

After-discharge, the continued firing of nerve impulses from the center for several seconds, or perhaps minutes, after the cessation of the stimulation which caused the response, remains as mysterious a phenomenon as ever. It now appears that a piling up of a central excitatory substance at the synapses of the motor neuron cannot be offered in explanation. The authors suggest the "delay paths" of Forbes as the most probable explanation, although Fulton has called attention to the fact that these paths would have to be a quarter of a mile in length to explain the observed results.

Nowhere in the book is there an adequate statement of the variability of spinal reflexes. It seems clear that the reactions of an intact animal cannot be built up of a series of rigidly fixed and stereotyped responses. Herrick has said, "We want to see the physical machinery of integration in action and to have an intelligible account of it. The rigidity of the reflex arc concept disqualifies it as

an adequate statement." It is to be regretted that the authors of this book have presented their results in a way which might be interpreted as tending to support this conception of rigidly fixed reflex arcs, although their own results have given abundant evidence of variability of response. Much could have been done to eradicate this false idea of absolutely stereotyped responses at the spinal level if adequate space had been given to the discussion of the excellent work of one of Sherrington's former students. There is no adequate discussion of Graham Brown's observations on rebounds and reversals nor of his theory of mutually antagonistic half centers which permit the alteration of reflex responses with changes in neural balance.

Medical Psychology: The Mental Factor in Disease. By William A. White, M.D. Nervous and Mental Disease Monograph Series, No. 54. Price, $3. Pp. 141. Washington, D. C.: Nervous and Mental Disease Publishing Company, 1931.

The trend of psychiatric literature, as well as that in other fields, is dealing with human beings as individuals having definite relationships to their environment. The concept of the "organism as a whole," although not a new one, is receiving much attention and study. This book adds to these studies and discussions in an excellent way and elaborates especially in the field of medical education, emphasizing the fact that "disease no matter of what part of the body or how caused has in every instance a psychological aspect."

The work of C. M. Child, which shows how the process of integration became structuralized along the lines of dynamic gradients, and the researches of G. E. Coghill, who has shown how integration manifests itself in total behavior patterns, have been used extensively by the author as foundation material for this book. He has developed it and correlated it beautifully, as should have been done long before. Through the function of integration the important function is that of the whole rather than that of the sum of the functions of the parts. In chapter 4, on "the nature of the mental functions," this thesis is carried through to the end, that "the unique character of the mental reaction is that it is a total reaction." Later, the author states "that organism and environment are verbal distinctions, that the problems which these two terms usually indicate are what I call pseudo-problems quite in the same way as the body-mind functional-organic problems."

The mind is considered to be something which is not necessarily new and "not something which has been added at a given point in the course of evolution, but in its present form is an elaboration and final expression of the supremacy of the head end." The correlation here with Child's gradient theory is obvious. Each individual organism is shown to be a place where "certain forces have been nucleated and where they have developed in a peculiar way but not in a way out of relation to the forces that surround them." "Therefore the psyche is a built-in bit of introjected environment." Medicine in the past has not considered the organism in this light, and the prophesy is made that great possibilities will open up in the future by reincorporating the mind in medical thinking. It has only been through the development of psychoanalysis that the "past of the psyche now becomes of greater significance and of use in medicine."

Throughout the book there is an active correlation between biologic and psychologic fields. In chapter 11, "The Psychological Factor in Disease," this correlation of the mental factor as it is seen particularly in somatic diseases is presented clearly. No attempt is made to go further, and the statement is given that to make proper advance not only in medicine but in other associated fields the psychologic factor must be taken into consideration and the very acceptance of such a factor only opens up more difficult problems in medicine.

This book has a psychoanalytic basis of a practical sort. It represents a step toward the correlation of psychoanalytic theories and knowledge with organic facts, and will undoubtedly be joined by similar works later. It is not essentially a book for a medical man, but for an interested student in any field who deals with individual organisms.

Criminals and Criminal Justice. By Nathaniel F. Cantor. Price, $3.50. Pp. 470. New York: Henry Holt & Company, 1932.

If criminology is a science, it is certainly an immature one. This is evident alone from the fact that criminologists generally do not seem to deal with any well defined subject matter. Authors on criminology often feel called on to discuss the foundation and theories of psychology, the elements of practically all the social sciences, the data and justification of economics and the like. The present volume, which undoubtedly belongs to the best type of books on criminology, is no exception. The author has assembled with great industry an enormous amount of data from the literature. He discusses the psychologic, sociologic, legal, political, philosophic and penologic aspects of crime. He covers a tremendous field, and while his book is perhaps not one which is to be read easily from beginning to end, it serves as a useful reference book.

The author has given full attention to the field of experimental psychology and psychiatry in relation to crime. He thinks that psychiatry has an important part to play in the rational treatment of crime. Like most criminologists, he does not make a sharp enough distinction between the sound, scientific part of psychiatry and the more speculative, however ingenious, theories to be found in the literature. A quotation by Kempf notwithstanding, there is after all a great deal of agreement among psychiatrists about the diagnosis of the essential forms of psychotic conditions. A psychiatric examination that lasts five or ten minutes (mentioned on page 130) is not a psychiatric examination, whether the subject is a criminal or a patient. The psychoanalytic statements quoted by the author to the effect that the search for the causes of antisocial attitudes, even at the time of the school period, is already hopeless (page 426) have to be taken with more than a grain of salt.

There are a few important contributions made by psychiatrists and psychologists to the problem of crime to which the author does not do sufficient justice. It was a psychiatrist, Kraepelin, who made one of the best and early pleas for the indeterminate sentence. In the discussion on the bearing of the relationship of experimental psychology and crime, the important work of Marbe should be mentioned. On the other hand, writers on mental hygiene have taught practically nothing valid about crime that was not already well known before. The author discusses well the difficulties that stand in the way of psychiatric work in connection with crime. He quotes a prosecuting attorney who opposed the introduction of a psychiatric service with the classic statement: "The next step will be to furnish golf links to these criminals."

It is, perhaps, inevitable that in a book of this scope the author should be a little indiscriminate in quoting the literature of the different specialized fields with which he treats, but as a general survey of crime, with special reference to the recent American literature on the subject, it deserves the highest recommendation. It has a good index of subjects. There is a brief introduction by Professor Moley.

Growth and Development of the Child: Part IV. Appraisement of the Child. Mental Status. Physical Status. Report of the Committee on Growth and Development, White House Conference on Child Health and Protection. Kenneth D. Blackfan, M.D., Chairman. Price, $2.75. Pp. 344. New York: Century Company, 1932.

That the White House Conference on Child Health and Protection was of great value is evidenced by the publications which have followed. So far there have been four. The fourth, which is here reviewed, concerns itself with the mental status and physical status. These volumes are under the general editorial direction of Dr. Kenneth D. Blackfan.

The present volume is divided into two parts; the first, on the mental status, takes up two thirds of the volume. Most of the contributors are psychologists.

There is only one neurologist, Bronson Crothers. It is by all odds the sanest and best presentation of this subject that the reviewer has had the pleasure of reading. After the general introduction, there is an interesting chapter on "Mental Growth in the Infant and Child," followed by a short but excellent presentation of the intelligence tests. Their exact value is well put forth. Some of these tests are given in detail. The chapter on "Mentally Superior Children" is particularly interesting. Such children are the "products of heredity but nature and personality determine in large measure the extent to which they achieve. Geniuses have practically all shown unmistakable signs of superiority in childhood, but not all gifted children become geniuses. Other causes of deterioration of ability usually explain the failure of those who do not."

The chapter on motor skill in the development of the child is of great value. The discussion of the "Development of Language" is short but to the point. So it is with the whole of that part of the book which deals with mental growth.

The second part, which concerns itself with physical status, is equally well done. The contributors are mostly pediatricians. The discussion concerns itself with "Normal Growth," then the "Growth of Subcutaneous Tissue and Muscle" and "Socio-Economic Factors Influencing Growth." There is an interesting chapter on the "Roentgenographic Appraisement of Developmental Growth in the Skeleton." This is followed by "Vital Capacity of the Lungs as Related to Physical Status," and, finally, an "Appraisement of Physical Status of the Child."

Not only should this book be in the hands of all pediatricians and neurologists, but it is so well and easily written that it would serve as a textbook for parents.

Cerebral Injury in New-Born Children Consequent on Birth Trauma: with an Inquiry into the Normal and Pathological Anatomy of the Neuroglia. By Erik Rydberg. Pp. 247. Copenhagen: Levin & Munksgaard, 1932.

This monograph is divided into two parts, one dealing with the anatomy of the neuroglia in the infant brain and the other with the study of the brain after trauma sustained at birth. Particular attention is given to the characteristics of the matrix tissue, a portion of the infant brain which requires still further study. Rydberg differentiates unorthodoxly between small and large spongioblasts. He comes to the conclusion further that the microglia is of ectodermal rather than of mesodermal origin as proved by Hortega. Rydberg claims that it is derived from the ependyma mainly, but in part also from the vascular elements or the leptomeninges. He also favors the concept of a glial reticulum in which "the astrocytes appear as widely ramified cells with an extensive plexiform extension of the expansions, and a dense reticulum becomes visible which is connected with the expansions of both the astrocytes and the oligoglia cells, forming a direct continuation of them." This is in opposition to the present generally accepted concept of the neuroglia. Rydberg takes up also the question of the identity of the embryonic fat granule cells. He found that most of the fat was extracellular, surrounding astrocytes, oligodendroglia and microglia. In only a small percentage of cells was the fat found within the microglia. This fat presumably has something to do with myelinization.

The study of the matrix tissue is well founded in response to an actual need. The author has made a serious attempt to unravel its characteristics. His conclusions concerning the microglia and the glial reticulum cannot be accepted without better proof. The contrary evidence is too convincing.

The second portion of the monograph is the report of a study of a hundred fetuses dying at birth at term or within ten days after birth. Gross hemorrhages were found in fifty-eight cases. Meningeal hemorrhage was present in fifty-six cases, cerebral hemorrhage in twenty-eight and subependymal hemorrhage in eleven. Some attempt is made to trace the clinical characteristics of these cases of hemorrhage. The mechanism of production of the hemorrhages is not entirely

clear. Rydberg attributes them to "a primary circulatory obstruction in the brain, due to local brain pressure." Compression of the head causes an increased intracranial pressure, causing a secondary rise in blood pressure. So long as equilibrium between these two pressures is maintained, all is well. If there is a sudden fall in intracranial pressure, causing a marked difference between intravascular and extravascular pressure, hemorrhage results. "This may happen at the moment of the cessation of a pain, if the fetal blood pressure is raised to a high level."

The monograph is written in English. It is well illustrated. The first portion dealing with the nature of the matrix tissue is more valuable than that part of the monograph concerned with cerebral birth trauma. The conclusions reached by the author are open to question.

Brain and Personality: Studies in the Psychological Aspects of Cerebral Neuropathology and the Neuropsychiatric Aspects of the Motility of Schizophrenics. By Paul Schilder, M.D., Ph.D. Price, $3. Pp. 136. Washington, D. C.: Nervous and Mental Disease Publishing Company, 1931.

The subject of this book is based on two sets of lectures delivered by the author, the first before the Washington Psychoanalytical Association on "Studies in the Psychoanalytical Aspects of Cerebral Neuropathology," and the second before the staff of the Phipps Psychiatric Clinic of Johns Hopkins Hospital, Baltimore, on the "Relation Between the Personality and Motility of Schizophrenics." Much of the material has already appeared in the German literature. The work is divided into two parts, the first being subdivided into seven chapters, and the second part into six. It would be impossible to review a book of this kind, for the subjects are of such great variance as, for example, the problems of consciousness, tone, speech disturbances, psychic and organic apparatus, catalepsy, actual causes and regression in neurosis and psychosis, and so on. The book is well worth perusal, for it contains an interesting and refreshing point of view.

Six Theories of Mind. By Charles W. Morris, Ph.D. Price, $4. Pp. 337. Chicago: University of Chicago Press, 1932.

This is an interesting book in which the author has examined critically in successive chapters the six dominant types of theories of mind. In addition, Laird, Lovejoy, Strong, Russell and John Dewey have read and edited the material in which their views are given. In comparing and analyzing the various theories of mind, the author has done a real service.

The Commoner Nervous Diseases for General Practitioners and Students. By Frederick J. Nattrass, M.D. Cloth. Price, $4. Pp. 211. New York: Oxford University Press, 1931.

This book of 211 pages is interesting chiefly in that it essays to give fundamental information required by general practitioners in the diagnosis of the commoner nervous diseases. After an exposition of the methods of diagnosis, which takes 32 pages, the author discusses disseminated sclerosis and follows this with chapters on syphilis of the nervous system, subacute combined degeneration of the spinal cord, and so on. In order of discussion, epilepsy is treated in chapter 11, vertigo in chapter 17, chorea in chapter 19 and the psychoneuroses in the twentieth and last chapter. There is no indication anywhere in the preface that these various subjects are selected because of their frequency, but nevertheless such inference cannot help but be drawn. Neurologists who have practiced for some years will at once agree that they are consulted most frequently by psychoneurotic persons. It is rather difficult to see how any general practitioner or student could get an adequate conception of the diagnosis of intracranial tumors in 11 pages, or of the psychoneuroses in 8.

Encephalitis Lethargica. Its Sequelae and Treatment. By Constantin von Economo. Translated by K. O. Newman, M.D. Cloth. Price, $6. Pp. 200. New York: Oxford University Press, 1931.

The neurologic profession is indeed fortunate to have had Professor von Economo write his own conception, particularly of the discovery of epidemic encephalitis, before his untimely demise, which occurred a few months ago following the meeting of the First International Neurological Congress held in Berne in the summer of 1931. There is no question that von Economo deserves credit for the original description of this disease. This is brought out clearly in the text. The book as a whole gives an excellent conception of this now well known disease. The references at the end of the book are of great value, but a complete reference can best be obtained in the book on this disease published by the Matheson Commission. The translation has been well done.

The Bell Witch of Middle Tennessee. By Harriet Parks Miller. Cloth. Price, $1. Pp. 72. Clarksville, Tenn.: Leaf-Chronicle Publishing Company, 1931.

This small book calls attention again to a neighborhood phenomenon that caused considerable exitement in middle Tennessee a little over a hundred years ago; it was the presence of the so-called "Bell Witch" in those parts. This book gives a general outline of what generally was supposed to have occurred, and abstracts references to the phenomenon from newspapers and letters of the period. This book should be in the possession of any one interested in endemic psychopathology as it is found in different regions of America, or any one who is interested in witchcraft and demonology in general. Outside the place where it occurred the interesting story of the Bell Witch is hardly known in the United States. References to it are rarely found in the international books on witchcraft, and it has been the subject of only one book, now practically unobtainable: "The Bell Witch" by M. V. Ingraham, published in 1894. (Copies of the book may be obtained from the author, Mrs. Harriet Parks Miller, Adams, Tenn.)

Mental Nursing (Simplified). By O. P. Napier Pearn. Price, $2. Pp. 304. New York: William Wood & Company, 1932.

This is a very good and informative book on the nursing of mental patients written by the superintendent of a hospital for mental diseases in England. If a nurse were able to master all of the knowledge contained therein, she would probably know much more than the average physician. For example, figure 11 denotes the level of activities such as the cortical, basal, midbrain, medullary, spinal and so on, and while voluntary movements are rightfully placed in the cortex, instinctive movements are put in the basal ganglia, and postural in the midbrain.

What has all this to do with nursing? Apparently the English authorities who ordain the type of knowledge needed for mental nursing are just as stupid as they are in this country. What is really needed is more common sense and less learning.

The Anatomy of the Nervous System. By Stephen W. Ranson, M.D. Fourth Edition. Price, $6.50. Pp. 478. Philadelphia: W. B. Saunders Company, 1931.

The fourth edition of this well known work is a considerable improvement over the third, which appeared in 1927, in that there has been added a series of serial sections through the brain stem and basal ganglia. This in itself adds considerable value to the book from the standpoint of the student, for it obviates the necessity of an additional book on anatomy that contains such material. Besides, the book has been considerably revised and brought up to date, and many new illustrations have been added. Altogether the present edition more nearly fills the need of what a textbook on the anatomy of the nervous system should be than any other book in the English language.

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