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THE CEREBELLUM

ITS FUNCTIONS, DISEASES AND ENCEPHALIC INTERRELATIONS *

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One of my earliest clinicopathologic publications was an article concerning a large hemorrhage into the thalamus in which, besides giving the symptomatology of the disease, I also recorded the macroscopic observations found at necropsy. A well marked tract of degeneration extended from the thalamus to the inferior olive.[1]

Tilney [2] and others have shown the connections between the inferior olive and the cerebellum.

The parietal lobe is of importance in any consideration of the symptomatology of the cerebellum, as one of the mistakes occasionally made is that of confusing conditions of this lobe with disease of the cerebellum.

By a neurophysiologist as able as Lewandowsky,[3] the cerebellum has been described as an organ of muscular sensibility. The reason for this and similar mistakes is not hard to see. Loss of muscular sense from disease of the parietal lobe or of the thalamus or from the sensory tracts coming from the spinal cord to the cerebellum or the thalamus gives motor symptoms which at first sight resemble cerebellar disorders of motility. A patient with disease of the parietal lobe uses his arm and leg in an ataxic or disorderly manner, because he does not comprehend the position of the limbs, whereas in cerebellar ataxia, no loss of sensation is present. I shall not, however, go in detail into the well settled question of the differential diagnosis between parietal and cerebellar disease.

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* Read at the Fifty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 24, 25 and 26, 1927.

1. Mills, C. K.: Hemorrhage into the Right Optic Thalamus and Small Cyst in the Right Corpus Striatum; Also in the Same Case, a Large Cyst in the Left Corpus Striatum, Phila. M. Times **9**:268 (March 1) 1879.

2. Tilney, Frederick: The Relation of the Inferior Olive to Cerebellar Activity, Proc. Assoc. for Research in Nerv. & Ment. Dis., December, 1926. Also Tilney and Riley: Form and Functions of the Central Nervous System, ed 2, New York, Paul B. Hoeber, 1923, p. 422.

3. Lewandowsky: Die Functionen des zentralen Nervensystems, Jena, 1907.

In 1882, I became a visiting member of the staff of the Pennsylvania Training School for Feeble Minded Children at Elwyn. My attention was soon called to a boy known in the school as the "whirling dervish." A few years after I made my first examination of the boy, he died of what was supposed to be tuberculous meningitis, but unfortunately necropsy was not made.

Many, if not most of us, have at times seen a dog or perhaps a cat, engaged in the interesting experiment of pursuing his tail. In doing this it is noticeable that his body assumes a curved or crescentic appearance, the incurvature being toward the side of the movement. In this effort the animal's movements become faster and faster.

To the ordinary observer such a procedure is probably an object of amusement, but to the student of brain phenomena it calls to mind the labyrinthine mechanism and the medipeduncle of the cerebellum of which the animal seems to be able to make use, not only without any disturbance of his animal mentality and without any physical inconvenience, but with a certain amount of pleasure in the sport.

The spectacle also calls to mind to one familiar with the literature of the East, the stories of Mohammedan whirling dervishes or fakirs. These dervishes, it is said, pirouette or revolve on one heel used as a pivot. They probably attain great facility in their performances through training from their early childhood to adult life. The whole performance is after all a cerebrocerebellar one.

It is not improbable, although by no means certain, that the Elwyn boy who died of tuberculous meningitis may have had a small tuberculoma in the pons or cerebellar medipenduncle.

Tilney and Riley,[4] in their book on the "Forms and Functions of the Central Nervous System," report the case of a boy, 4 years of age. In this case, there was paralysis of the left internal and right external recti muscles of the eyes giving rise to left lateral gaze, which produced a right conjugate deviation. The symptoms in the whirling boy to whom I referred were different, and I refer to the case only because Tilney and Riley found on necropsy a tuberculoma the size of a pea on the right side of the pons as the one lesion to account for the pontocerebellar symptoms.

At the meeting of the American Neurological Association of June, 1881, at which I was elected a member, I presented a paper recording a case of tumor of the pons causing conjugate deviation of the eyes and rotation of the head.[5] The tumor was situated in the left upper quarter of the pons. It was in the body of the pons the anterior and posterior surfaces of which retained their integrity.

4. Tilney, F., and Riley, H. A.: Forms and Functions of the Central Nervous System, ed. 2, New York, Paul B. Hoeber, 1923, p. 397.

5. Mills, C. K.: Tumor of the Pons Varolii with Conjugate Deviation of the Eyes and Rotation of the Head, J. Nerv. & Ment. Dis. **8**:470 (July) 1881.

Conjugate deviation of the eyes and of the head is an early symptom in many cases of apoplexy of the cortex or subcortex of the cerebrum producing hemiplegia. In these cerebral cases, as shown by the studies of Vulpian,[6] Flourens,[7] Ferrier,[8] Priestly Smith [9] and others, the conjugate deviation is usually toward the side of the lesion in the hemiplegic cases. If, however, the lesion is irritative causing convulsion, for instance, the conjugate deviation will be away from the side of the lesion or, in other words, toward the side of the convulsions. In pontile cases, the conjugate deviation is toward the side of the paralysis if the lesion is situated in the cephalic portion of the pons. In pontile cases also, conjugate deviation is away from the side of the lesion and toward the side of the paralysis if the lesion is in the caudal portion of the pons, but deviation does not invariably occur.

In a paper by me, contributed to *Brain* in 1880, was included the account of a case of tumor of the pons, in which rotatory movements toward the left took place during a convulsive attack.[10] I witnessed one of these seizures in which, although the spasmodic attack was general, the patient's right side was more affected than the left. With the patient lying on his back the spasm had the effect of lifting up the right side of his body and causing him to work over toward the left as if the patient were trying to get on his face in this direction, but before getting altogether on his left side, he would fall backward again, when the same curious lifting rotatory movement would be repeated.

This case had a number of other interesting features, but I dwell on the rotatory movements because of the situation of the tumor, and the associated softening were such as to involve the pontile nuclei and medipeduncle of the cerebellum on the left.

The case recalled the experiments by Schiff [11] in which he cut the left cerebellar medipeduncle which resulted in causing the animal to exhibit a rotatory movement toward the side of the lesion as in the case of the tumor I recorded.

I have recorded a number of cases, clearly indicating the part played by the pons in the interrelations of the cerebrum and the cerebellum and

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6. Vulpian: Leçons sur la physiologie du système nerveux, 1866, cited in Ferrier: Functions of the Brain, ed. 2, London, Smith, 1886.

7. Flourens: Recherches expérimentales sur les propriétés et les fonctions du système nerveux, ed. 2, 1842.

8. Ferrier, D.: The Functions of the Brain, ed. 2, London, Smith, 1886.

9. Smith, Priestly: Reflex Amblyopia, Ophth. Rev., May, 1884; cited in Ferrier's Function of the Brain (footnote 8).

10. Mills, C. K.: Five Cases of Disease of the Brain, Studied Chiefly with Reference to Localization, Brain, January, 1880.

11. Schiff, M.: Lehrbuch der Physiologie des Menschen, Lahr, Schauenburg, 1858-1859.

emphasizing the thesis that in order to understand the cerebellum it is necessary to comprehend the evolution of as well as much else concerning the various regions of the brain. The frontal, parietal, occipital and temporal lobes all have anatomic connections with the cerebellum which is also intimately associated in its activities with both the mesencephalon and the diencephalon.

On Feb. 23, 1882, I exhibited at the Philadelphia Pathological Society the brain of a negro who had died in my wards.[12] The negro had committed a murder nearly thirty years before. He was tried, convicted and sentenced to death, but the governors of the state would not sign the warrant for execution. He was pardoned five years before his death, two or three years subsequent to the appearance of paralysis of the left side.

The right hemisphere of the cerebrum, especially in the motor region, was much atrophied as was also the left hemisphere of the cerebellum. A hard, brownish-black nodule or small tumor was found isolated in the upper portion of the pons to the right of the median line. This probably involved not only the pontile nuclei but also by compression or directly, the pyramidal tract.

I presented a paper at the meeting of the College of Physicians of Philadelphia, May 4, 1910.[13] This paper included the record of a patient whom I saw in consultation. About six months before she came under observation, she had had an attack which rendered her right side somewhat paretic. She had a continuous coarse tremor in the right arm which she held slightly flexed at the elbow. She had lost the sense of position and passive movements in the right arm and leg. Tactile discrimination and the spatial sense were also markedly affected, and she had astereognosis in the right hand. The right pupil was somewhat larger than the left.

I concluded that the lesion was near the nucleus ruber, where the superior cerebellar peduncle passes into the brain stem. It is probable that the loss of muscular sense and of astereognosis were due to lesion of the tracts entering the thalamus from below.

The case was an example of the so-called Benedikt's syndrome. It might be said, in connection with the report of this case, that the region of the cephalic ends of the superior cerebellar arm and the floor of the sylvian aqueduct is a fruitful eponymic soil. Besides the name of Benedikt, names like those of Weber, Millard-Gubler, Westphal, Perlia,

12. Mills, C. K.: The Brain of a Negro Murderer, Phila. M. Times **12**:575 (May 20) 1882.

13. Mills, C. K.: Hemichorea, Hemiataxia, Hemiparesis, and Dilated Pupil Probably Due to a Lesion of the Superior Cerebellar Peduncle, Tr. Coll. Phys. Phila. **32**:136, 1910.

Spitzka, Siermerling, Kahler and Pick, Spiller and others are associated with particular syndromes occurring in this limited area.

The floor of the aqueduct is a continuation of the floor of the fourth ventricle, and therefore, in Hughlings Jackson's scheme, it belongs to the lowest or spinal level. In this floor or just cephalad of it are located the nuclear representations of the subdivision of the movements of the third and fourth nerves. It therefore follows that restricted lesions may give a variety of symptom pictures.

Perlia located a nucleus in the middle line in the floor of the iter, which nucleus acts in the control of convergence of the eyes. The center of convergence has been the object of particular study by Dr. W. G. Spiller,[14] who not long since presented a paper on this subject.

At the meeting of the American Neurological Association in 1912, I reported a case with necropsy of which I had previously recorded the clinical symptoms.[15] The symptoms were ataxia of the upper and lower extremities on one side and on the other side deafness and paralysis of the emotional expression in the face and loss of the senses of pain, heat and cold over the entire half of the body.

At the necropsy the macroscopic examination revealed a destructive lesion involving the left dentate nucleus and the cerebellar cortex above this nucleus including also the superior cerebellar peduncle. Degeneration was also evident to the naked eye in the right nucleus ruber which body was much smaller than the left ruber.

At this meeting a detailed record of the microscopic observations was made by Dr. Spiller. These conditions threw light on the functions of the cerebellum and its physiologic relations both to the cerebrum and to the spinal cord. Branches of the superior cerebellar artery supplying the dentatum, cerebellar folia, and superior arm were obliterated. Tracts of degeneration proceeded in both directions through the brachium conjunctiva.

This case was of importance as showing the relations of the superior region of the cerebellum to the nucleus ruber and spinal cord, and also the relation of the cerebellum to the thalamus by way of the prepeduncle.

An article on "The Diagnosis of Tumors of the Cerebellum Especially with Reference to Their Surgical Removal" was contributed by me to the *New York Medical Journal*, Feb. 11 and 18, 1905.[16] The

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14. Spiller, W. G.: Ophthalmoplegia Internuclearis Anterior; A Case with Necropsy, Brain **47**:345 (Aug.) 1924.

15. Mills, C. K.: Preliminary Notes on a New Symptom Complex Due to Lesion of the Cerebellum and Cerebello-Rubro-Thalamic System, J. Nerv. & Ment. Dis. **39**:73 (Feb.) 1921.

16. Mills, C. K.: The Diagnosis of Tumors of the Cerebellum Especially with Reference to Their Surgical Removal, New York & Phil. M. J. **81**:261 (Feb. 11) and 324 (Feb. 18) 1905; also in the Phil. Hosp. Rep. **4**:15, 1905.

article also appeared in the *Philadelphia Hospital Reports,* volume 4, 1905, accompanied by contributions of Drs. Frazier, de Schweinitz, Weisenburg and Lodholz on various aspects of cerebellar disease and cerebellar physiology. This article was republished as a small monograph entitled "Tumors of the Cerebellum" [17] and was followed by another volume on "Tumors of the Cerebrum." [18]

My paper in the cerebellar volume was founded largely on personal experience in the wards for nervous disease in the Philadelphia General Hospital and in the neurological and surgical department of the hospital and in the neurological and surgical department of the hospital of the University of Pennsylvania. At this time I did not altogether recognize that synergy was the one great function of the cerebellum, a fact which soon became apparent to me.

In recent years, the cerebellum as the particular organ or subdivision of the brain concerned with synergy has been most emphasized by Babinski,[19] Babinski and Tournay,[20] and Rothmann,[21] although this idea really goes back many years.

Ferrier in his work on "The Functions of the Brain" traces the history of the knowledge of the physiology of the cerebellum as first determined by Magendie,[22] Flourens, Vulpian, Weir Mitchell [23] and others. The experiments of these investigators indicated a loss or disturbance of the power of coordinating or harmonizing movements when the cerebellum or a large part of it was experimentally extirpated.

In determining that synergy is the special function of the cerebellum, the use of moving pictures has proved of convincing value.

I first became aware of the value of moving pictures for the demonstration of nervous phenomena, normal and abnormal, by the oppor-

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17. Mills, C. K.: With Drs. Frazier, de Schweinitz, Weisenburg and Lodholz; Tumors of the Cerebellum, Philadelphia, E. Pennock, 1906.

18. Mills, C. K.: With Drs. Frazier, de Schweinitz, Spiller and Weisenburg: Tumors of the Cerebrum, New York, A. R. Elliot, 1905.

19. Babinski, J.: De l'asynergie cérébelleuse, Soc. de Neurol. **7**:684 (Nov. 15) 1899; Hémiasynergie et hémitremblement d'origine cérébello-portuberantielle, ibid. **9**:422 (April 30) 1901; Asynergie et inertie cérébelleuse, ibid **14**:685 (July 15) 1906.

20. Babinski, J., and Tournay, A.: Les symptomes des maladies du cervelet et leur signification, Tr. 17th International Congress of Medicine, London, sect. 11, part 1, p. 51, 1913.

21. Rothmann, M.: The Symptoms of Cerebellar Disease and Their Significance, Tr. 17th International Congress of Medicine, London, sect. 11, part 1, p. 59, 1913.

22. Magendie, F.: Mémoire physiologique expérimentale et pathologique, 1828, cited in Ferrier's Function of the Brain (footnote 8).

23. Mitchell, S. Weir: Researches on the Physiology of the Cerebellum, Am J. M. Sc. **57**:320 (April) 1869.

tunities which I had in 1888 of observing the experiments made by Muybridge and Dercum on locomotion in the lower animals and in man. This work of Muybridge undoubtedly laid the foundation of kinematography.

Professor Edward Muybridge,[24] who was an enthusiastic student of the subject of animal locomotion, was engaged in 1888 by Dr. William Pepper, then Provost of the University of Pennsylvania, to pursue a research on animal locomotion under the supervision of a commission appointed by the trustees of the University. A small book was published comprising articles by Professor W. Dennis Marks on "The Mechanisms of Instantaneous Photography," by Dr. Harrison Allen on "Materials for a Memoir on Animal Locomotion" and by Dr. Francis X. Dercum "A Study of Some Normal and Abnormal Movements Photographed by Muybridge."

With Dr. T. H. Weisenburg I began a series of investigations which finally led to the publication of the paper on "Cerebellar Symptoms and Cerebellar Localization, Including Kinematographic Observations on Cerebellar Phenomena." [25] It became clear to me that moving pictures could be used not only for teaching purposes but as a method of investigation. The opportunities to enlarge the views of the motor disturbances and the time given to dissect more thoroughly the luminous picture presented, enabled the observer to obtain a truer idea of the character of cerebellar symptoms.

The outcome of the kinematographic studies of cerebellar cases was the adoption of the theory previously expressed by Ferrier, Babinski and others that synergy was the fundamental function of the cerebellum and that cerebellar symptoms local or general, simple or compound were expressions of asynergy.

I have carefully read several of Hughlings Jackson's papers on the cerebellum, but from these it seems to me impossible to arrive at a satisfactory conclusion regarding his views.[26] In one of the cases reported, owing to the closure of the sylvian aqueduct, extensive hydrocephalus resulted, causing enormous enlargement of the head and even

24. Muybridge, E.: Animal Locomotion—The Muybridge Work at the University of Pennsylvania, Philadelphia, J. B. Lippincott Company, 1888.

25. Mills, C. K., and Weisenburg, T. H.: Cerebellar Symptoms and Cerebellar Localization, Including Kinematographic Observations on Cerebellar Phenomena, J. A. M. A. **63**:1813 (Nov. 21) 1914.

26. Jackson, J. Hughlings: Cases of Tumor of the Middle Lobe of the Cerebellum; Cerebellar Paralysis with Rigidity and Occasional Tetanus-Like Seizures, Brain **29**:435, 1906; Case of Tumor of the Middle Lobe of the Cerebellum, Cerebellar Attitude; no Tetanus-Like Seizures, General Remarks on the Cerebellar Attitude, Brain **29**:440, 1906. Jackson, J. H., and Russell, Risien: A Case of Cyst of the Cerebellum, Weakness of Spinal Muscles; Death from Failure of Respiration, Brit. M. J., Feb. 24, 1894; also in collected papers.

separation of the sutures. As revealed by necropsy, the case was undoubtedly one of disease of the base of the middle lobe, but the symptoms present resulted from both the primary involvement of the cerebellum and the secondary effects of the lesion.

The second case was also a tumor and cyst of the inferior surface of the vermis, which must have exerted great pressure on the pyramidal tracts. Jackson speaks of the resulting condition as one of paralysis. It was in reality a mixture of asynergy from destruction of the cerebellar folia and paralysis from pressure on the pyramidal pathway. Jackson seems to recognize this fact in the reference which he makes to the investigations of Ferrier and Turner,[27] the practical outcome of which was that synergy was the primary cerebellar function.

In one case reported by Jackson and Risien Russell,[28] the patient placed face downward was unable to lift his body from the floor hardly more than one half as far as a normal person of about the same age and strength. The account of this case reminds me of a moving picture of one of the patients on whom a similar experiment was tried. The inability exhibited in such an experiment is due to the loss of power to regulate the movements required and not simply to the loss of energy or paralysis in its technical sense.

At the neurological research meeting in New York in December, 1926, some valuable records were made of experimental lesions of the cerebellar nuclei and the tracts of degeneration produced by these lesions. A tendency was shown, following Horsley and Clarke,[29] to hold that it is necessary to determine only the reactions of the deep nuclei to obtain the key to the functioning of the cerebellum. Investigations of the deep nuclei are, of course, of much importance, but one must search the cortical folia of the cerebellum to obtain a knowledge of its specific functions just as one must look to the convolutions of the cerebral cortex if one would unravel the functions of the cerebrum.

The main deep nuclei of the cerebellum—dentate, emboliformis, globosus, fastigial and vestibular—are places of anatomic and physiologic concentration and integration of the centers of the cerebellar cortex. I do not believe it is correct to infer as Horsley and Clarke and MacNalty and Horsley[30] have done, that the large volume of

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27. Ferrier, D., and Turner, A.: A Record of Experiments Illustrative of the Symptomatology and Degeneration Following Lesions of the Cerebellum and Its Peduncles, Phila, Tr. Roy. Soc., 1895, vol. 105; cited in Ferrier's Functions of the Brain (footnote 8).

28. Jackson and Russell (footnote 26, third reference).

29. Horsley, V., and Clarke, R. H.: Structure and Functions of the Cerebellum Examined by a New Method, Brain **31**:45 (May) 1908.

30. MacNalty, A. S., and Horsley, V.: On the Cervical Spinobulbar and Spino-cerebellar Tracts and on the Question of Topographical Representation in the Cerebellum, Brain **32**:237 (Nov.) 1909.

purely cerebellar tissue known as the folia has no distinct function except that of receptors. It is not beyond likelihood that the cerebellar laminae, evidently arranged so as to increase the amount of functional material, are designed to receive, transform and transmit the impressions conveyed by the spinocerebellar tracts to the cerebellar nuclei.

The theory of Horsley and Clarke and their followers calls up a memory of many years ago. When Hughlings Jackson, Ferrier and others were beginning to present a train of phenomena which indicated the existence of centers in the motor cortex, Brown-Séquard [31] at first challenged this view, and asserted that the phenomena of motion produced by the electrical irritation of the cortex were the result of transmission of the current to the spinal and bulbar centers of the neuraxis. This view was supported by Dupuy [32] and others but soon had to give way to the overwhelming evidence in favor of centers in the cortex.

It is true that a relatively stronger current is required to produce cerebellar cortical phenomena than one for the elicitation of cerebral response. I am as firm a believer in cerebellar localization as I am in the localization of centers and areas in the cerebrum. Cerebellar centers, however, have distinct points of difference from those of the cerebrum. The synergic movements of the cerebellum are compound and therefore a little more difficult to elicit.

In one of my cases in which operation was performed I faradized the exposed folia in order to determine positively whether the operation was on the correct side of the brain, some doubt having arisen regarding this matter. The faradization with a weak current produced movements in the limbs on the side on which the operation had been performed.

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31. Brown-Séquard: Entre-croisements des conducteurs servant aux mouvements volontaires, Arch. de physiol. norm. et path. **1**:218, 1889.

32. Dupuy, E.: The Rolandic Area Cortex, Brain **15**:190, 1892.

ACUTE TOXIC ENCEPHALITIS IN CHILDHOOD

A CLINICOPATHOLOGIC STUDY OF THIRTEEN CASES *

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Nonsuppurative encephalitis includes all inflammations of the brain not characterized by the formation of an abscess and therefore a number of unrelated diseases: polio-encephalitis, epidemic encephalitis, encephalitis secondary to a contiguous meningitis and a vague, indefinite condition called toxic encephalitis. The first three types have been carefully studied clinically; they reveal specific pathologic changes and are probably due to invasion of the brain substance by a specific virus even though it has not yet been demonstrated.

Little is found in the literature to prove that toxic encephalitis is anything but a clinical designation. According to some textbooks, however, such an involvement of the brain is not uncommon. Dana,[1] for example, speaks of a secondary or toxic encephalitis and of an encephalitis due to influenza, by which he does not mean the epidemic type.

In 1884, Strümpell [2] and later Leichtenstern described an encephalitis characterized, aside from the acute general symptoms, by hemiplegia. This disease was assumed to be polio-encephalitis with pathologic changes in the cortex similar to those commonly found in the cord in acute anterior poliomyelitis. It was later disclosed that the Strümpell-Leichtenstern type was only an acute syndrome which may be caused by polio-encephalitis, by sudden vascular lesions or by hemorrhagic encephalitis as a sequel to influenza. Wernicke's [3] type of encephalitis, characterized by external ophthalmoplegia, was also found to be a midbrain syndrome of varying etiology.

In 1895, Putnam,[4] in discussing the rôle of infectious processes in the production of diseases of the nervous system, mentioned cases of

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* From the Otto Baer Fund for Clinical Research, the Neurological Service, and the Sarah Morris Hospital for Children of the Michael Reese Hospital, the Nelson Morris Institute for Medical Research, and the Department of Neurology of the Northwestern University School of Medicine.

* Read before the Chicago Neurological Society, November, 1927.

1. Dana, C. L.: Disease of the Nervous System, New York, William Wood & Company, 1920.

2. Strümpell, A.: Ueber die acute Encephalitis der Kinder, Jahrb. f. Kinderh. **22**:173, 1885.

3. Wernicke: Lehrb. d. Gehirnkrankh., Berlin, 1881.

4. Putnam, J. J.: The Relation of Infectious Processes to Diseases of the Nervous System, Am. J. M. Sc. **109**:254, 1895.

encephalitis following influenza. He said that the symptoms characteristic of cerebral involvement following infectious processes are due for the most part to the toxic substances which are elaborated during the course of the bacterial action rather than to the micro-organism itself. He believed that acute primary hemorrhagic encephalitis occurred after various forms of acute infections or without known infection, although even then dependent on a toxic cause.

In 1897, Putnam [5] again wrote of encephalitis following influenza and remarked concerning the greater susceptibility of young children to this condition. He quoted a case reported by Nauwerch. A girl, aged 14, who had not had any signs of the infection during an epidemic of influenza, developed fever, hemiparesis, vomiting and convulsions. Necropsy revealed a soft, friable brain with small foci of hemorrhagic softening.

Oppenheim [6] reported clinically three cases of encephalitis following influenza and considered the Strümpell-Leichtenstern type as influenzal. Later, in his textbook,[7] he quoted many clinical reports of encephalitis following scarlet fever, measles, mumps, pneumonia, typhoid, erysipelas and pertussis. He described the disease as an "acute hemorrhagic encephalitis." He used this vague term, often misused to describe macroscopic petechial hemorrhages, to designate an acute inflammatory process associated with hemorrhages, ganglion cell and axonal destruction, and perivascular infiltration of round cells, leukocytes and plasma cells.

In 1906, Abt [8] discussed encephalitis and revived the view that it may follow any acute infectious disease, but especially influenza. He also described the disease as a hemorrhagic encephalitis.

Marsh's [9] consideration of acute nonsuppurative encephalitis in children is of great value. He believed that there is an acute encephalitis of infants with cerebral symptoms, not unlike those of acute meningitis, which ends fatally. Autopsy reveals an extensive inflammation of the brain with necrosis, atrophy of the white matter, disappearance of ganglion cells and marked proliferation of the neuroglial tissue. The condition is particularly prone to attack premature and atrophic infants; in most cases, the seat of the inflammation is in the cerebral hemispheres,

5. Putnam, J. J.: A Contribution to the Clinical History of Nonsuppurative Acute (Hemorrhagic) Encephalitis with a Report of a Case Following an Attack of Mumps, J. Nerv. & Ment. Dis. **22**:1, 1897.

6. Oppenheim, H.: Die Prognose der acuten nicht-eitrigen Encephalitis, Deutsche Ztschr. f. Nervenh. **6**:397, 1895.

7. Oppenheim, H.: Lehrbuch der Nervenkrankheiten, ed. 7, Berlin, S. Karger, 1923.

8. Abt, I. A.: Acute Nonsuppurative Encephalitis in Children, J. A. M. A. **47**:1184 (Oct. 13) 1906.

9. Marsh, N. P.: Four Cases of Acute Nonsuppurative Encephalitis in Children, Brit. J. Child. Dis. **7**:241, 1910.

less often in the basal ganglia and rarely in the pons. In older children, the course of the disease is more favorable, and the process tends to be more localized. The disease is believed to be secondary to some septic process, and the most frequent causes are infectious diseases, especially measles, mumps and influenza.

An apparently new type of nonsuppurative encephalitis in children was reported by Anderson [10] and later by Brown and Symmers [11] in 1925. In their cases there was rapid onset of irritability, anorexia, vomiting, diarrhea, sore throat, irregular respiration, ptosis, nystagmus, hemiplegia, coma and convulsions, with fever of from 105 to 106 F. and death in from twenty-four to forty-eight hours. Autopsy revealed a large, wet, friable brain with engorged pial vessels, flattened convolutions and narrowed sulci. Microscopically, every capillary was crowded with red blood cells. There were marked perivascular and pericellular edema, acute cloudy swelling of the ganglion cells, and focal collections of glia cells, round cells and a few leukocytes. Anderson stated that it was first thought that these cases were of toxic nature; later this conception was discarded, and the designation "actue serous encephalitis" was given because of the pronounced interstitial edema.

Without quoting many articles concerning encephalitis following the exanthematous diseases, the foregoing are all that we were able to find in the literature concerning that type of encephalitis which is associated with acute infectious diseases. It is evident that such a condition has as yet a poorly understood pathologic basis and is almost purely a clinical concept of infrequent occurrence. Excluding the exanthematous diseases and the exogenous poisons, influenza is apparently the only condition which is known to produce a toxic encephalitis. Its importance is evident when one scans reports describing, without necropsy, cerebral symptoms in infectious diseases and in the exanthems as "encephalitis."

We have been able to study thirteen cases of encephalitis in children associated with infections both of a local purulent and of a generalized character; these we will describe under five general groups.

TOXIC ENCEPHALITIS WITH SEVERE NEUROLOGIC SYMPTOMS AND A DEFINITE FOCUS OF INFECTION

CASE 1.—*History.*—A boy, aged 7, was admitted to the hospital on Feb. 14, 1926. He had been well until three days prior to admission, when apparently he caught cold and suffered from a nasal discharge and cough. The temperature rapidly rose to 104 and 105 F., and he became irrational and delirious. The child held his neck stiffly and resisted passive head movements.

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10. Anderson, A. I.: Report of Five Cases of Acute Encephalitis, Boston M. & S. J. **189**:177, 1923.

11. Brown, C. L., and Symmers, D.: Acute Serous Encephalitis, Am. J. Dis. Child. **29**:174, 1925.

Examination.—The child was acutely ill and was in an opisthotonic position. The pupils were small and irregular but reacted to light. The tonsils were large, and red with white specks on the surface; the submaxillary glands were enlarged. The abdomen was distended and tympanitic. The right knee jerk was not obtained, the left was decreased; both achilles reflexes were absent. A Kernig sign was present with a suggested Babinski sign on the right and marked cervical rigidity, but no Brudzinski sign was noted (?). Localized twitchings of the right hand were later recorded. The leukocyte count was 15,000. Hemolytic *Staphylococcus albus* was cultured from the blood. The spinal fluid was cloudy, probably because antimeningococcus serum had been given in another hospital. On admission, the temperature was 105.4 F. and rose before death that evening to 108 F.

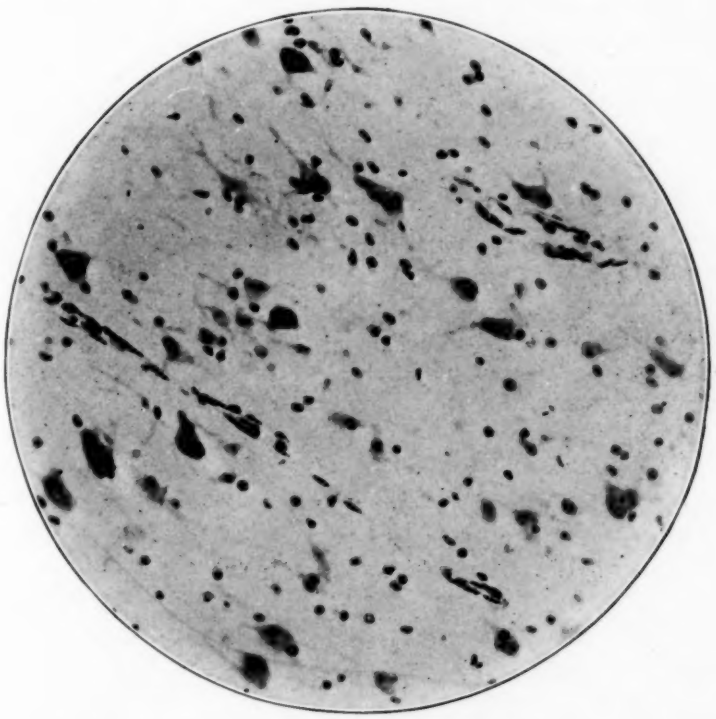

Fig. 1 (case 1).—With a hand lens, ganglion cells in the cortex in various phases of degeneration may be seen including swelling, "Umklammerung" by neuroglia, neuronophagia and shadow cells. The blood vessels have an excessive number of pyknotic endothelial cells. Toluidine blue stain; × 230.

Clinical Diagnosis.—Acute meningitis, acute pharyngitis and tonsillitis were diagnosed.

Anatomic Diagnosis.—The diagnosis was acute fibrinous pleurisy; right otitis media (organism, hemolytic *Staphylococcus albus*); acute splenic tumor, and hyperplasia of the lymph nodes and splenic follicles.

The Brain.—Gross Examination: The surfaces of the brain were deeply congested. The larger vessels were prominent and distended with blood; the smaller

ones also were distinctly visible. The brain substance was firm, and there was slight flattening of the occipital and temporal lobes. The only noteworthy change on the cut surfaces was an increase in stippling and a pinkness in the color of both gray and white substance.

Microscopic Observations: The meninges were slightly thickened throughout and somewhat excessively cellular. The cells, for the most part, were macrophages, with a few leukocytes and fibroblasts, which were also present in clumps. An occasional vein plugged with leukocytic thrombus was seen. Throughout the brain there was extensive new vessel formation. Activated endothelial cells were present in the young capillaries. Tortuous capillaries with budding and branching

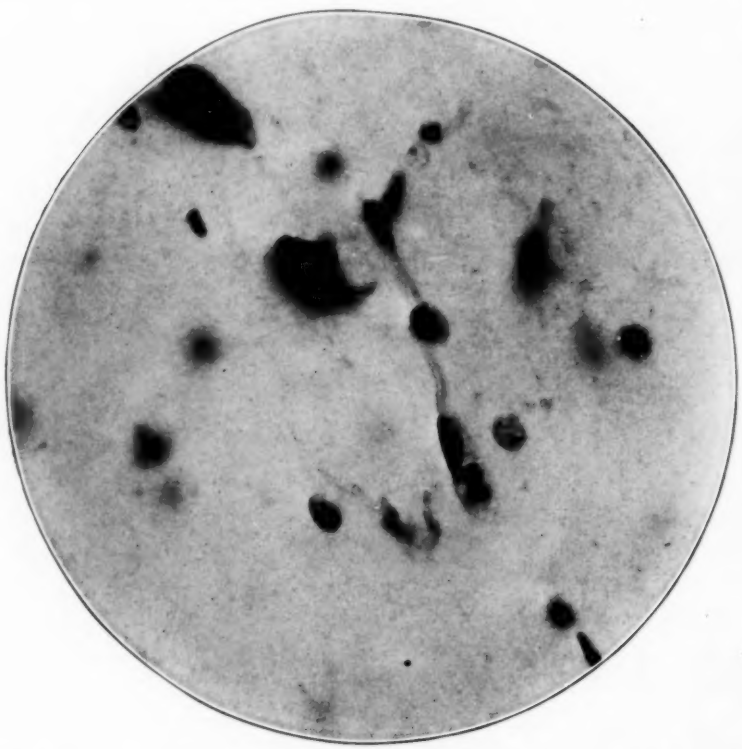

Fig. 2 (case 1).—The capillary contains a solitary leukocyte within its lumen. The endothelial cells are pyknotic and swollen. Budding is present at two points of the vessel. Toluidine blue stain; × 800.

were frequent. Many capillaries dilated to four times the normal size were seen and resembled tissue spaces; they contained no blood cells. A few round cells were found in the adventitial spaces of the arterioles, and there was a moderate amount of perivascular edema. The subpial layer was thickened with glia fibers, and in this area there was an increase in the large fibrous glia. Collections of oligodendroglia, in layers often three deep, were seen about the capillaries, and beside most of the vessels there were streams of oligodendroglia. This type of glia cell was frequently swollen and poor in chromatin, which was sometimes present only at the periphery of the nucleus. Many of the nuclei were frag-

mented. There was marked increase in all forms of glia cells, but the predominating forms were the cytoplasmic glia, which were greatly enlarged, frequently forming collections and rosets. Few Hortega cells only were present; there were no free, rounded gitter cells and no lipoid within the glial cytoplasm. There was a most profound change in the ganglion cells. Most of them were enormously swollen, the processes were distinctly visible, and the cytoplasm was a homogeneous blue or granular. The nuclei were greatly enlarged, eccentric, often fragmented, and possessed an irregular membrane. This type of cell change was found in all parts of the brain substance. Many completely degenerated cells with only a few chromatin granules, an extruded nucleus and bare shadowy outlines were undergoing neuronophagia in the midst of glial rosets. Coarse ringlets were present in the cytoplasm of many ganglion cells. The architectonic structure was well preserved, except for a great increase in glia cells in all layers.

CASE 2.—*History.*—A boy, aged 2 months, was admitted to the hospital on July 12, 1926. Three days earlier he had vomited, appeared ill and as if in pain. A physician diagnosed the condition as otitis media, and two days later punctured the right ear drum obtaining only a little pus. Since the onset, the patient had been stuporous and had vomited all food.

Examination.—The infant was pale, stuporous and critically ill, with a temperature of 104 F. The anterior fontanel was depressed. There was a suggestion of a Brudzinski sign, with ptosis of the left upper eye lid and bilateral nystagmus. The child vomited all feedings and had marked diarrhea. Cyanosis developed on July 15, and signs of pneumonia were found at the pulmonary base of the right lung. On July 16, after intravenous injection of blood, respirations became labored and the infant died. The spinal fluid was entirely normal, including a negative culture, and contained only six cells. A blood culture remained sterile. Urinalysis revealed a slight amount of albumin, sugar and acetone.

Anatomic Diagnosis.—Right otitis media (organism, *Staphylococcus albus* and *Bacillus coli*) was the diagnosis.

The Brain.—Gross Examination: There was a slight amount of recent hemorrhage about three recent fontanel punctures, and the brain was sunken beneath the dura. The subarachnoid space was distended with an excess of spinal fluid. The cortical blood vessels were all conspicuously injected, but there was no exudate in the meninges. The cut surfaces of the brain were pink, and stippling was greatly increased.

Microscopic Observations: The blood vessels of the meninges were engorged with fresh blood, but there was no infiltrate about them or in the tissues. There were small localized areas of thickening composed of endothelial cells and a few large, free macrophages. About the blood vessels, a small amount of brownish-green pigment was lying free in the tissues and also within the macrophages. The intracerebral capillaries were all dilated and filled with blood. A few activated endothelial cells were seen, but there was no budding of the vessels or marked proliferation of the capillaries. The glial elements were increased, especially the oligodendroglia. The ganglion cells were moderately swollen; some revealed severe central chromatolysis, while other cells contained fine dustlike chromatin at the periphery. There was great increase in satellites. Much ganglion cell degeneration was present, especially in the basal ganglia and pons. These cells were swollen and chromatolyzed; the nucleus was pyknotic and its membrane often indefinite. Neuronophagia was frequently seen, and there were many completely degenerated cells. No gitter cells or intracellular fat were found. Only an occasional round cell or a leukocyte was found in the walls of the blood vessels;

many capillaries, however, were plugged with leukocytes. A slight amount of recently extravasated, fresh blood lay free in the pons. The adventitial layer of the blood vessels throughout the brain was moderately thickened, even the capillaries containing several layers of endothelial cells. Some of the capillaries were markedly thickened, and the lumens were almost obliterated.

CASE 3.—*History.*—A boy, aged 8 months, was admitted to the hospital on Feb. 15, 1927; his parents said that diarrhea and persistent vomiting had been present for three weeks and convulsions for ten days. The onset was sudden, with cough, and at the time it was thought that the child was developing whooping cough. Diarrhea began the next day and was marked for about one week, when it decreased in severity. Severe diarrhea recurred only one day before admission. Vomiting began with the onset and continued after the cough had ceased; it was not of the projectile type. For a few days previous to admission, the child had had almost continuous clonic movements of the right arm; the left arm was kept tightly flexed. Two days later, with cessation of the convulsions, the body became generally flaccid and the eyes sunken. The child then remained quiet, except that he screamed at times.

Examination.—The child was apathetic, acutely ill and pale. The anterior fontanel was depressed. The pupils were equal and reacted to light; the corneas appeared glassy. There was no glandular enlargement, but the posterior fauces were somewhat red. The heart and lungs were normal except for an occasional gruntlike type of respiration. The lower edge of the spleen was palpable. The left arm was held flexed, while the other extremities were flaccid; the knee jerks were equal and lively. The spinal fluid was clear, under moderately increased pressure, and contained from 30 to 40 lymphocytes per cubic millimeter; globulin was absent.

Course.—On February 17, the eyes were fixed in downward rotation, the right pupil was larger than the left, which was pinpoint in size. Both ear drums appeared dull and injected; the throat was acutely inflamed and dry. The extremities were still flaccid, except that the left arm was spastic and held tightly flexed against the chest. The knee jerks later were elicited with great difficulty. Babinski and Oppenheim reflexes were present on the right side. The leukocyte count was 27,000; 70 per cent of the cells were of polymorphonuclear type.

Examination of the fundi on February 16 revealed slight papilledema of the right disk, advanced papilledema of the left disk and clouding of the left vitreous body. The right ear drum began to discharge on February 17; it was then thought that the cerebral symptoms were secondary to otitis media.

Reexamination of the spinal fluid revealed a strongly positive Pandy test, and a cell count of 42, 10 of which were leukocytes. The spinal fluid sugar was 15 mg. per hundred cubic centimeters. The urine on February 17 contained albumin (+++), acetone (+) and was loaded with coarsely granular casts, many white blood cells and a few epithelial cells. The urinary condition was essentially the same on February 18. The temperature was 104 F. on admission and varied thereafter from 100 to 105 F. The child died on February 18.

Anatomic Diagnosis.—The diagnosis was right otitis media; generalized lymphoid hypoplasia.

The Brain.—Gross Examination: In the subarachnoid space, clear fluid was greatly increased. The vessels of the convex surface were all markedly engorged. The convolutions of the surfaces of the upper part of the brain were normally prominent, but around the temporal and under surfaces they seemed to be slightly compressed. The brain tissue everywhere seemed firmer in consistence than

normal, particularly about the cerebellum and the base. There was a slight foramen magnum pressure groove of the cerebellum. On the cut surfaces of the brain the cortex was of a deeper red than usual and contrasted rather sharply with the white matter; stippling was greatly increased.

Microscopic Observations: The leptomeninges were not thickened, but contained distended blood vessels. A few leukocytes were present in the lumen of some vessels. In certain areas, the pia-arachnoid had a meshlike structure and was lifted away from the cortex as if distended by fluid; it was infiltrated with a few round cells and fibroblasts.

The glial elements, particularly the cytoplasmic glia, were moderately increased in number, and many of the glial nuclei were degenerated and fragmented. There was marked swelling of the oligodendroglia. No rod cells were found. Proliferation of blood vessels was not noted, but there was a severe endarteritic obliteration of many capillaries. The endothelial and adventitial layers were markedly thickened in the small vessels. A few round cells were found scattered

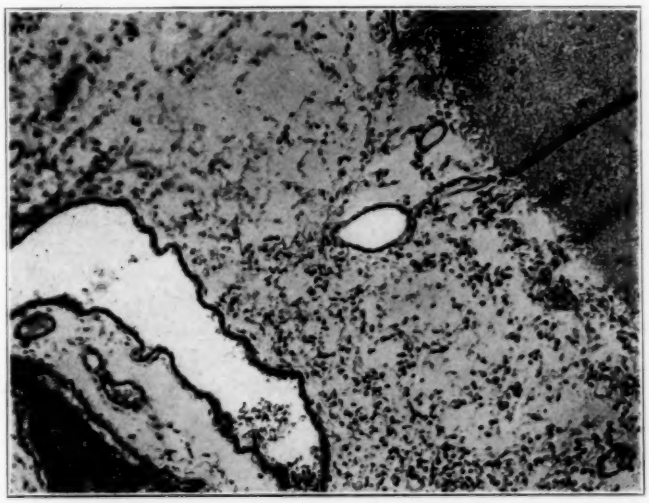

Fig. 3 (case 3).—There is a marked increase in cells in the cortical leptomeninges consisting of macrophages, large round cells and fibroblasts. The reticular appearance suggests distention with fluid. The large vein contains a small leukocytic thrombus. Hematoxylin and eosin; × 50.

in the adventitial spaces. The ganglion cells were all severely altered; many were swollen and exhibited central chromatolysis; others were mere shadows with chromatin absent and invisible nuclei, and were undergoing neuronophagia. Some cells contained so little chromatin that it was difficult to see the cell membrane; the nuclei were relatively enlarged and frequently were fragmented. Other cells were pyknotic and shrunken.

Case 4.—*History.*—A girl, aged 3½, was admitted to the hospital on March 5, 1926, and died the same day. Three days before admission the child fell ill; she had a running nose and a cough, and complained of sore throat. Vomiting was frequent and blood was said to have been seen in the vomitus. The day before admission the child became comatose and cyanotic, had five generalized convulsions with rigidity and loss of consciousness, and developed fever of 104 F.

Examination.—The child was comatose with dyspnea. The pupils were pinpoint in size and unresponsive to light. Blood crusts and frothy fluid were present in the nostrils and about the lips, and the chest was full of bubbling râles. The deep reflexes were normal, and no pathologic reflexes were elicited. The leukocyte count was 36,000. The spinal fluid was clear and a culture remained sterile.

Clinical Diagnosis.—Fulminating meningeal or respiratory disease was the diagnosis.

Anatomic Diagnosis.—Bilateral purulent otitis media; acute bronchopneumonia; generalized lymphoid hyperplasia; hyperplasia of the splenic pulp and necrosis of the malpighian bodies, and subacute interstitial hepatitis were diagnosed.

The Brain.—Gross Examination: The cortical vessels were engorged, and the brain was hyperemic. The cut surfaces were reddened; stippling was pronounced, and the ependymal vessels were engorged.

Microscopic Observation: The leptomeninges contained no infiltration or thickening. The capillaries of the brain were distended with blood but not thickened, infiltrated or proliferated. The ganglion cells were profoundly altered. The most marked changes were found in the cortical cell layers. The basal ganglia were less affected, and the Purkinje cells of the cerebellum were normal. The ganglion cells did not contain normal Nissl substance, but the cytoplasmic chromatin was in a finely divided state. Most of the cells contained several small vacuoles occupying the entire cytoplasm; others contained one or two large clear vacuoles, which were most pronounced at the periphery of the cell. Some cells were shrunken, angular and stained an irregularly deep, glassy blue. The nuclei were relatively enlarged and of a deep homogeneous blue. The nuclear membrane was frequently indistinguishable and often ruptured; the nucleolus was pyknotic and frequently fragmented. Many of the cells were swollen enormously, contained only a remnant of chromatin, and were undergoing neuronophagia. There was a moderate increase in glial cells of the cytoplasmic type and of the astrocytes. The oligodendroglia cells were not proliferated but were swollen.

Case 5.—*History.*—A boy, aged 2½, was admitted to the hospital on Feb. 23, 1927, with the complaints of sore throat, fever, convulsions and inability to speak, which had been present for the preceding two months. The child had been well until he contracted a cold and sore throat which led to the present illness and developed a temperature of 103 F. Two days after the onset he had a convulsion, in which consciousness was lost, the eyes were rolled and he stared into space. He became cyanotic, bit his tongue and was stuporous for five minutes. The next night he had three similar spells, each lasting a minute. Inability to speak nad been present for three weeks prior to admission. The left ear drum was punctured five days after the onset of the cold, and a purulent material exuded from it. There was a rash on the body a few hours before admission.

Examination.—The boy was drowsy and apathetic; he was unable to talk but could cry. He was pale and had a staring expression. The pupils were equal, regular and reacted to light. There was slight redness of the throat with some cervical adenopathy, and the left ear was discharging pus. There was definite paresis of the left upper extremity, and the right lower extremity was more rigid than the left. All deep reflexes were lively, except those of the upper right extremity. The abdominal reflexes were absent.

The leukocyte count was 23,700. The urine contained a slight amount of albumin. Spinal puncture revealed a normal fluid; the spinal fluid sugar was 59 mg. per hundred cubic centimeters; the Lange curve was of the meningitic type. The Wassermann reaction with the blood was negative.

Course.—Mastoidectomy was performed on the right side and was followed by an uneventful recovery, but the neurologic symptoms did not improve.

It was suspected that the child had an abscess of the brain, and therefore ventriculography was performed. Two hours after the operation the temperature rose to 105 F., and the eyes became fixed in a position upward and to the right. The next morning the temperature was 108 F., the child was pale and toxic, and the respirations were rapid and shallow. There was generalized rigidity, more marked on the left side, and all deep reflexes were exaggerated. The pulse rate was about 160 and the respiratory rate 60; death occurred that afternoon.

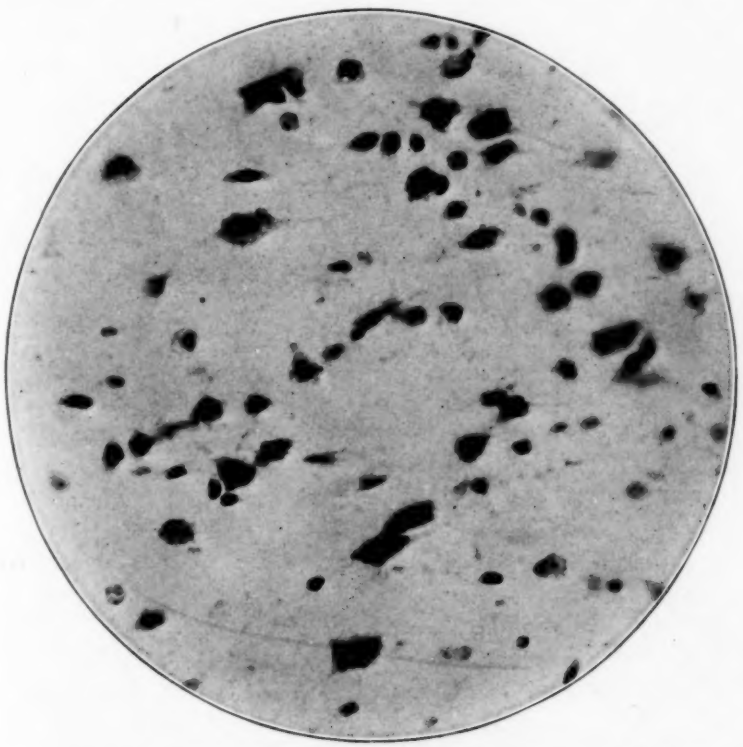

Fig. 4 (case 5).—Ganglion cells in the cortex in various stages of acute degeneration. The protoplasmic ringlets are well marked. Toluidine blue stain; × 325.

Anatomic Diagnosis.—Right mastoiditis and mastoidectomy; bilateral otitis media, and trephine opening of the right frontal region were diagnosed.

The Brain.—Gross Examination: Aside from the local reaction to the ventriculography, no external abnormality was seen. The cut surfaces of the brain did not show any change in the vascularity of the gray and white matter, but the ependymal vessels of the entire ventricular system were tremendously engorged with blood. The ependymal lining was pinker than normal.

Microscopic Observations: The leptomeninges were only slightly thickened with fibroblasts. The blood vessels were distended with blood. There was no infiltration and no abscess of the brain. The blood vessels of the subependymal tissues were widely distended and engorged with blood; for some distance beneath

the ventricular surface, there was marked proliferation of astrocytic glia. The vessels of the choroid plexus were distended with blood, and there was a moderate amount of recent hemorrhage. The glia cells were universally proliferated; most of them were of the cytoplasmic type and astrocytes. The former were large, often forming focal collections, but were not filled with lipoid. Many oligodendroglia cells were present in the white matter and about the blood vessels. In the deep white matter there were small nodule-like collections of oligodendroglia cells. These were swollen and had deeply stained coarsely granular nuclear chromatin. There was marked increase in the capillary network. The larger

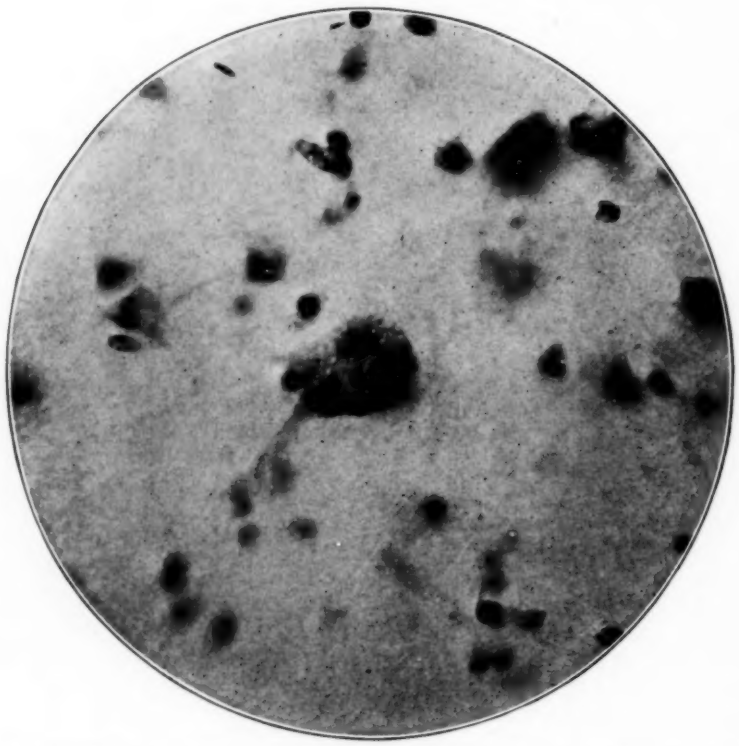

Fig. 5.—Higher power magnification of specimen in figure 4 showing a swollen vacuolated ganglion cell containing a large pyknotic nucleus, the membrane of which is irregular in contour—the acute cell degeneration of Nissl. Toluidine blue stain; × 700.

vessels were greatly thickened with adventitial cells, the lumen often being obliterated.

The ganglion cells were severely damaged. Many were undergoing neuronophagia, and some areas were seen in which cells were completely absent. Shadow cells were abundant. Many cells contained ringlets in the cytoplasm. Most of the cells were swollen and distorted and had a homogeneous cytoplasm.

Summary.—The foregoing five cases present a fairly uniform group in that all of the patients had a demonstrable focus of severe infection

with neurologic symptoms developing rapidly in from two to four days after the onset of the first sign of infection. The children ranged in age from 2 months to 7 years and were, according to the history obtainable, in perfect health until the onset of the illness. In all, the onset was manifested by complaints pointing to the primary infection: the nasopharynx in four, the middle ear in one. In case 3, along with the infection of the upper respiratory tract, there was an alimentary intoxication. With the onset there was a rapid rise in temperature to between 103 and 105 F. It is noteworthy that in all patients rapidly increasing drowsiness and stupor developed and led to coma in two cases before admission.

General examination in all cases disclosed the primary infection; in only two cases was there renal involvement. The leukocyte count varied between 15,000 and 23,700.

The neurologic observations pointed clearly to a diffuse cerebral involvement in all the children. Meningeal symptoms predominated in two cases, and in two children clonic movements of a single extremity suggested cortical pathologic changes. Nystagmus and strabismus suggested a localization in the brain stem only once; it is remarkable that no other cranial nerves were involved except when papilledema, in case 3, suggested cerebral edema. Aphasia was noted in case 5, in which ventriculography was performed for a suspected abscess of the brain. This was the only case in which life was prolonged for more than ten days after the onset of the neurologic symptoms. The course of the disease was usually rapidly fatal, with early development of drowsiness and then coma.

The observations on the spinal fluid were negative except in one case in which forty-two cells, mostly lymphocytes, were found. Even when meningeal symptoms were pronounced, the fluid was devoid of globulin or an excess of cells, while the case in which pleocystosis was found did not present meningeal symptoms.

The microscopic observations in each case were of varying severity, but on the whole presented a uniform picture. In the meninges a moderate excess of fluid and moderate increase in cellular elements (particularly macrophages, adventitial cells and a few round cells) were the only abnormalities. In the brain substance itself no evidence of microbic invasion was present; no organisms were found, and there was no localizing mesodermal reaction nor anything suggestive of a polio-encephalitis or of epidemic encephalitis.

The stress of the toxic agent was directed against both the vascular system and the ganglion cells. In all cases, there was marked increase in the cellularity of the capillaries, frequently leading to obliteration of the lumen. In case 5, in which the patient survived longest, this thickening extended to the larger vessels. Only a few round cells were found

here and there in the vessel walls. In each case leukocytic thrombi were found in the smaller vessels—evidence of an infectious process somewhere in the body.

The ganglion cells were profoundly damaged. They were acutely altered, with swelling, chromatolysis, nuclear damage and vacuole formation. Many either were undergoing neuronophagia or had degenerated completely into shadow cells. In case 5, in which the process was of two months' duration, many cells had completely disappeared.

A profound proliferation of both cytoplasmic glia and oligodendroglia cells had taken place, giving an excessively cellular appearance to the sections. The glia cells were increased diffusely; besides the proliferation, they showed retrogressive changes such as nuclear fragmentation and swelling.

TOXIC ENCEPHALITIS WITH SEVERE NEUROLOGIC SYMPTOMS AND A FULMINATING SEPTICEMIA

CASE 6.—*History.*—A girl, aged 6 months, entered the hospital on Feb. 16, 1926, and died the same day. The child had been well except for an acute sore throat two months before. The day before admission, she cried a great deal, became drowsy and shortly afterward had a series of convulsions lasting six hours. These convulsions were generalized, with foaming at the mouth, rotation of the head, nystagmus and finally stupor. The temperature rose to 105 F.

Examination.—The child was in coma. The right pupil was larger than the left; both reacted to light. There were slight nystagmoid movements of the left eye. The left upper and lower extremities seemed rigid, and on that side the deep reflexes were markedly exaggerated. Kernig and Brudzinski signs were not obtained, but there was a bilaterally positive Babinski sign. On opening the mouth, which was done with great difficulty, the pharynx was seen to be greatly congested. Convulsive movements of the right arm were observed, and soon spread into generalized convulsions. The spleen was palpable. The spinal fluid was clear and gave a negative reaction for globulin or cells. Blood cultures revealed *Staphylococcus albus* and *Streptococcus nonhemolyticus.*

Anatomic Diagnosis.—Pulmonary congestion and enlarged thymus were diagnosed.

The Brain.—Gross Examination: The brain was hyperemic, all cortical vessels being engorged. The subarachnoid space was filled with clear spinal fluid. The cut surfaces of the brain were red.

Microscopic Observations: The leptomeninges were thickened, certain cortical areas being covered by a pia-arachnoid from two to three times its normal size. There were many large macrophages containing no intracellular material, a moderate number of large round cells and an occasional leukocyte. A few fibroblasts were seen. The blood vessels were distended with fresh blood. This same type of cellular reaction was found in the pia dipping down into the sulci, with meshlike interwoven connective tissue strands containing a moderate number of macrophages.

The cortical architectonic structure, on the whole, was well perserved, but in many areas it was difficult to identify the various layers; this was due to increase of the cellular elements, which on close examination were seen to be glia cells.

The ganglion cells were universally profoundly altered; practically no normal cells were seen. The cells were swollen to various degrees and contained no clearly defined Nissl substance. The cytoplasm was usually of a homogeneous, glassy blue. In many cells there were small cytoplasmic ringlets, and in a few of the large striate and thalamic cells there was a single large vacuole at the periphery of the cell. In many cells the chromatin substance had a fine dustlike appearance. The cell processes were visible for long distances and at times were tortuous and corkscrew-like. A few shrunken, angular cells were visible. The nucleus was displaced to the periphery, and the perinuclear chromatin was lighter than that about the periphery of the cell, which often formed a dark ring. The

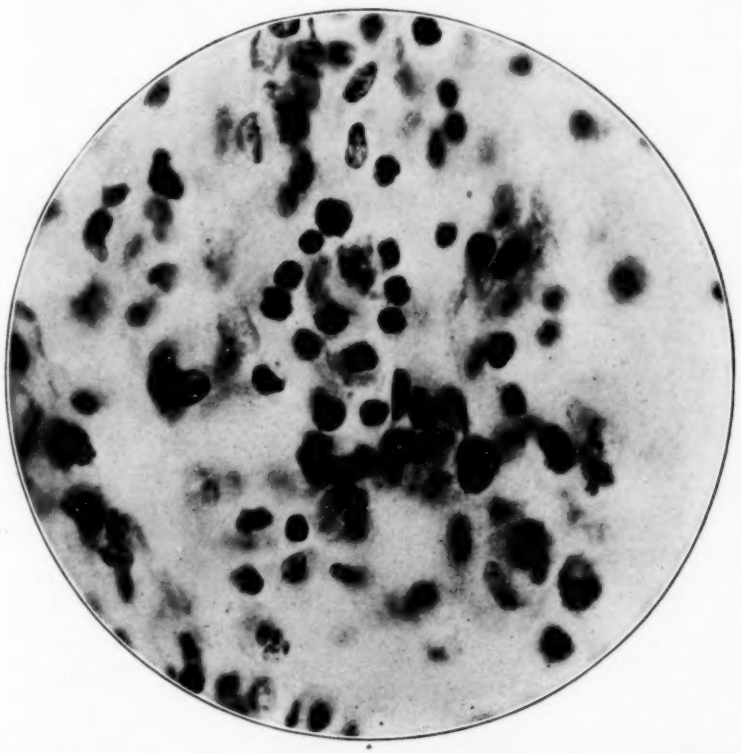

Fig. 6 (case 6).—The cellular increase in the leptomeninges consists mostly of macrophages, a few round cells, fibroblasts and adventitial cells. Toluidine blue stain; × 800.

nucleus was swollen, its membrane frequently irregular and indefinite. Many nucleoli were fragmented and irregular in shape. The cytoplasm of many cells had faded, leaving a bare cell outline with perhaps only a remnant of the nucleolus or a few small chromatin granules. The smaller or central cells contained pyknotic nuclei. Occasionally, the cell outlines were ragged. The large substantia nigra and supra-optic nucleus cells were obviously swollen, and presented a picture of axonal reaction with central chromatolysis. There was much neuronophagia in all stages. A degenerating cell might be surrounded by several glia cells indenting the cell wall, and many glia rosets were present

around degenerating ganglion cells, of which only the nucleolus could be definitely identified. Most of the ganglion cells were surrounded by several glial satellites. Fatty changes were not found within the ganglion or glia cells.

Examination with a low power lens revealed at once the diffuse proliferation of neuroglia. It was most marked, however, in the deeper cortical layers, the white matter and the basal ganglia. All forms of glia cells were proliferated, the true glia most strikingly. Many large astrocytes with definite sucker feet were present. The majority of the glia cells were of the cytoplasmic variety. They formed glia rosets, took part in the neuronophagia and were found in streams about the blood vessels. They possessed a large, deeply staining, chromatin-rich nucleus with a large cytoplasm. Often they attained a size reminiscent of a giant glia cell. A large number of the glia cells were degenerated and had large, swollen, pale nuclei which were often fragmented and extruded. Oligodendroglia and some Hortega cells were present in pathologic numbers. No free rounded

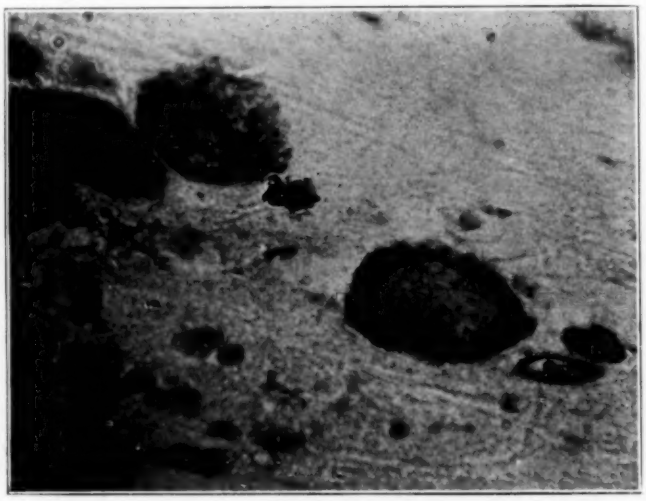

Fig. 7 (case 6).—The ganglion cells in the supra-optic nucleus are swollen, the nucleus is displaced to the periphery and there is central chromatolysis. Toluidine blue stain; × 450.

gitter cells were seen. Occasionally, a glia "Rasen" was found. The myelin sheaths and axis cylinders did not show any change.

The vascular system was profoundly affected. The arterioles were cellular, having several layers of adventitial cells. The capillaries were dilated but empty, and about many of the capillaries a few cytoplasmic glia cells were found. Occasionally, a few small round cells or macrophages were present in a vessel wall. There was marked activation of the endothelial nuclei; budding and new vessel formation was pronounced; a section seemed to be filled with capillaries. Occasionally, a vessel packet was seen. Many of the capillaries were profusely rich in cells, the lumens being almost obliterated by endothelial cells. A few leukocytes plugged some of the capillaries.

Case 7.—*History.*—A boy, aged 3 months, entered the hospital on Feb. 24, 1927, and died within twelve hours. He had been well until that morning at 6 a. m., when the mother noticed that he was staring and that the breathing was rapid

and shallow. The body was hot and was wet with perspiration. Marked twitching of the facial muscles, with a tendency to throw the head back and severe clonic movements of the whole body were noted. There was no rigidity and no vomiting, but the child would not nurse.

Examination.—The infant was apathetic, and the breathing was stertorous and suggestive of a Cheyne-Stokes type. He soon became cyanotic and moribund. The anterior fontanel was somewhat tense, but depressed; the posterior was closed and the suture lines were not separated. The nose was normal. The left ear drum was dull; the right was slightly hyperemic. The eyes were glassy and staring. The pupils were contracted and equal, but did not respond to light;

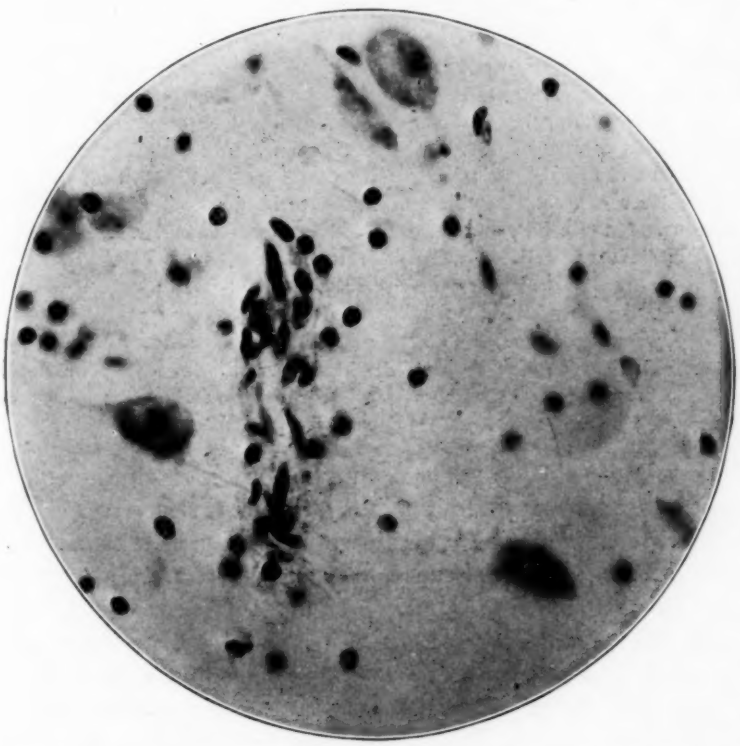

Fig. 8 (case 6).—The blood vessel in the pallidum is rich in endothelial and adventitial cells many of which are degenerating. The absence of infiltrate should be noted. Toluidine blue stain; × 600.

there was rotary nystagmus of the right eye. The tongue was moist; no Koplik spots were present. The throat was somewhat congested and edematous. The neck was not rigid, and there was no Brudzinski sign. The chest and heart were normal except for a faint systolic blow at the base. All extremities were spastic and rigid. The knee jerks were not elicited; ankle clonus was present on the left. Babinski, Oppenheim and Brudzinski reflexes were present on both sides. The red blood cells numbered 4,000,000, and the hemoglobin was 70 per cent; the white blood cells numbered 18,000; a differential count revealed 47 per cent of polymorphonuclear cells.

Anatomic Diagnosis.—The diagnosis was large thymus with several minute petechial hemorrhages; petechial hemorrhages in the visceral pleura of each lung; cloudy swelling of the liver; phlebolith in the cortex of the left kidney and bacteremia (*Streptococcus hemolyticus* cultivated from the heart blood).

The Brain.—Gross Examination: The subarachnoid space contained a moderately increased amount of clear cerebrospinal fluid. The blood vessels in each sylvian fissure were moderately congested; the vessels elsewhere did not show any evidence of congestion. Areas of hemorrhage were not demonstrable. The brain was soft and friable and held together with difficulty. The cerebral convolutions were not flattened.

Microscopic Observations: In a few areas of the leptomeninges there were accumulations of large, pale-staining macrophages. The blood vessels of the meninges and brain were not distended. A few vessels of the brain were slightly thickened with adventitial cells. Much of the vascular endothelium revealed degenerative changes with swelling of the nuclei, which contained most of the chromatin in a faint peripheral ring. An occasional leukocyte was seen within the lumen of a capillary. The ganglion cells were all severely damaged. They were swollen and had pyknotic, homogeneous blue cytoplasm with a frayed periphery. On closer examination this was found to be due to the presence of many fine ringlets. Many cells contained several large clear vacuoles. The nuclei were enlarged and the nucleoli fragmented. Many of the ganglion cells were present only in bare outline, being completely devoid of chromatin or nucleus. These cells were undergoing neuronophagia. There was profuse proliferation of all forms of neuroglia, particularly of the oligodendroglia. Many of the latter cells were degenerating and were swollen, their nuclei containing only a faint peripheral chromatin ring. Others exhibited progressive changes, the nuclear chromatin being intensely stained and coarsely granular.

Summary.—Two cases presenting close similarities have been described in which apparently healthy children were stricken with a fulminating condition causing death within twenty-four hours. In both children, severe generalized convulsions and a rapid rise in temperature precipitated the condition. Increasing stupor and coma soon followed.

Inequality of the deep reflexes, which were generally exaggerated, a bilateral Babinski sign, nystagmoid movements of the eye and convulsions were all clinical evidence of a diffuse encephalitis. Meningeal symptoms were absent. The throat was red and edematous. Blood cultures were positive in both cases.

Necropsy in both cases revealed brains that were extremely hyperemic; microscopic examination disclosed engorgement of all blood vessels. The ganglion cells were diffusely and severely altered, with swelling, serious damage to the cytoplasm and nuclei and, frequently, complete degeneration. Intense proliferation of neuroglia cells was found. In both cases increased cellularity of the capillaries was noted, often leading to obliteration with only an occasional round cell in the vessel walls. In case 6, new vessel formation was most striking.

In classifying these cases under septicemia, it was not forgotten that a hyperemic throat was discovered on examination. We considered this

as a possible portal of entry for the invading organism, not sufficient in itself to harbor the infection.

The pathologic symptoms in the brains were again not indicative of an actual microbic invasion but suggested strongly a brain reaction as part of a severe toxemia.

TOXIC ENCEPHALITIS WITH SEVERE NEUROLOGIC SYMPTOMS OF UNDETERMINED ORIGIN

CASE 8.—*History.*—A colored boy, aged 5, was admitted to the hospital on March 22, 1926, and died within twelve hours. Six hours before admission to the hospital, he was supposed to have swallowed a little "moonshine." Several adults had partaken of the same material without ill effects. He became dizzy, staggered and finally vomited. Twenty minutes before admission, he became stuporous and could not be aroused.

Examination.—The child was comatose and was having repeated generalized convulsions. The eyes were turned to the right. The pupils were small and inactive to light. The jaws were fixed and the lips dry. Cervical glands were palpable on both sides. All extremities were in extension and were rigid. The knee jerks were exaggerated, and there was cervical rigidity, but pathologic reflexes were not elicited. The child had repeated convulsions until death. The temperature ranged from 104 to 106 F. Gastric lavage brought forth no evidences, material or odor, of alcohol. The spinal fluid was clear, and under increased pressure. The leukocyte count was 16,000.

Anatomic Diagnosis.—Bilateral bronchopneumonia; acute splenic tumor; cloudy swelling of the liver and kidneys, persistent thymus, and generalized lymphoid hyperplasia were diagnosed. (The pathologist could not find any evidence that alcohol was the cause of death.)

The Brain.—Gross Examination: The subarachnoid fluid was not increased. The pial vessels were markedly engorged; the convolutions were flattened, but no exudate was present. The cut surfaces of the brain were pinker than usual, with marked increase in stippling.

Microscopic Observations: The leptomeninges were thin, but the blood vessels were distended with blood. There was a small amount of blood pigment free in the tissues, about which were small accumulations of macrophages. There was considerable blood pigment in the cytoplasm of these large macrophages. No exudate was present. The intracerebral vessels were all conspicuously distended; the capillaries appeared ready to rupture. There was no vascular proliferation or perivasal infiltration. There was no marked glial increase. Only occasionally were a few glia cells seen clumped together close to a blood vessel. No round cells or leukocytes were noted. The essential pathologic change was found in the ganglion cells, most of which were greatly swollen and had undergone complete chromatolysis. The cytoplasm was of a homogeneous, glassy blue. The nuclei also were swollen. Most of the ganglion cells were surrounded by a clear vacuole-like tissue space. Neuronophagia was not evident.

Summary.—After supposedly imbibing a little "moonshine," a child, aged 5, developed severe generalized convulsions and coma, with cervical rigidity and high fever; death rapidly ensued. The pupils were pinpoint in size; this would be unusual in alcoholic poisoning, and neither

clinically nor at postmortem examination was evidence of alcohol obtained.

The brain revealed pericellular edema with acute cloudy swelling of the ganglion cells. There was severe vascular congestion.

This case is classified as a toxic encephalitis of undetermined origin. We are of the opinion, in spite of the history of alcohol, that it may be of endogeneous (septicemic) origin, but in either case the pathologic changes were those of an intoxication.

TOXIC ENCEPHALITIS WITH FOCUS OF INFECTION WITHOUT SEVERE NEUROLOGIC SYMPTOMS

CASE 9.—*History.*—An apparently normal girl, aged 12 days, was admitted to the hospital on June 30, 1926, for feeding. On July 15, the throat became infected and the left eye began to discharge pus containing gram-positive cocci. The next day the pharynx and tonsils were extremely red. The child took feedings poorly, vomited frequently and developed diarrhea. On July 20, the temperature was 101 F.; both ear drums were opened and pus escaped. On July 26, the child was emaciated and dehydrated, and died. The leukocyte count was 7,700; the urine was normal.

Clinical Diagnosis.—The condition was diagnosed as septicemia.

Anatomic Diagnosis.—The anatomic diagnosis was left otitis media.

The Brain.—Gross Examination: Slight hyperemia was noted.

Microscopic Observations: The leptomeninges were not thickened; no unusual cellular elements were found in them, save that in a few areas the pia was lifted off the cortex by a small amount of blood. The entire brain contained a large excess of glia nuclei which obscured the architectonic structure in many areas. Many of the arterioles and a few of the capillaries were plugged with leukocytes. The blood vessels were greatly increased in number, the capillaries branched and budded frequently, and contained darkly stained, activated endothelial cells. There was marked increase of the adventitial and endothelial nuclei of all blood vessels; in the capillaries, this had frequently resulted in complete obliteration of the lumen. A few round cells were seen occasionally in the wall of an arteriole. There were areas of atrophy surrounding a few of the arterioles in which no cellular elements were visible.

Glia elements were diffusely proliferated; these comprised only a few rod cells, many cytoplasmic cells and oligodendroglia. The latter were most abundant in the white matter, forming streams about the blood vessels; at times they were seen within the vessel walls. The cytoplasmic glia cells were abundant both in the cortex and in the white matter. They were the elements concerned in the neuronophagia, but were also diffusely proliferated, being found in clumps apparently not in relation to ganglion cells.

The ganglion cells were all profoundly affected in various ways. Many of the large basal ganglion cells were swollen, with the nuclei at the periphery of the cell, and the central cytoplasm had undergone chromatolysis, leaving only a peripheral ring of Nissl substance. This axonal reaction was the least severe type of change found. Most of the cells were surrounded by three or four glia cells; many were completely degenerated and surrounded by a clump of glia cells, a glial roset; others were undergoing neuronophagia, and glia cells had penetrated into the cytoplasm. Some of the cells were swollen; the Nissl substance was

absent and was replaced by a cytoplasmic reticulum; the nucleus was large, irregular and faded, or was sharply defined, angular and darkly stained. In many cells the chromatin material was in the form of ringlets; in others, it was dustlike. The nucleus was frequently disintegrated.

CASE 10.—*History.*—An infant, aged 1 month, was admitted to the hospital on Feb. 15, 1927, with a statement by the Children's Home and Aid Society that the child had fever of unknown duration and that food did not agree with it.

Examination.—The child, a poorly nourished boy, did not look acutely ill. The left ear drum appeared reddened and bulging; the right ear drum was difficult to examine because of the presence of blood either from the wall or from rupture of the drum itself. The pharynx was slightly reddened. There was no adenopathy or rigidity of the neck. The knee jerks were diminished.

Course.—February 17: Left otitis media was present; the Kernig sign was absent.

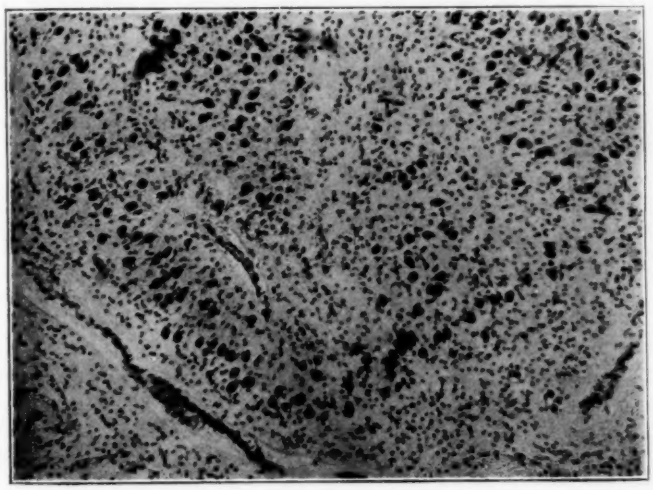

Fig. 9 (case 9).—There is a massive proliferation of glia cells in the inferior olive. The capillaries are excessively cellular but contain no infiltrate. The ganglion cells are swollen. Toluidine blue stain; × 65.

February 19: The temperature was 101 F. The left ear drum opened spontaneously and drained pus. The right drum and canal, which were red, were opened by paracentesis and yielded blood only.

February 27: Both ears were draining; there was no Kernig sign and no rigidity of the neck. The temperature was normal.

March 3: The body weight had remained stationary. There had been two or three bowel movements daily. The child appeared acutely ill and had poor turgor of the tissues. The anterior fontanel was distended; the veins of the cranium were prominent. There was a profuse discharge from both ears. The profuse nasal discharge was diminishing.

March 5: Mastoidectomy was performed on the right side; pus was not obtained.

March 10: The mastoid wound was discharging foul-smelling, yellow pus in large quantities. The child was cyanotic at times with periods of dyspnea. The

hemoglobin was estimated at 85 per cent; the red blood cells numbered 4,100,000, and the white cells 16,000. The urine was normal. Death occurred on this date.

Anatomic Diagnosis.—Mastoiditis and mastoidectomy on the right; otitis media, right bilateral congenital renal hypoplasia, and hydronephrosis were diagnosed.

The Brain.—Gross Examination: The vessels of the pia were diffusely injected, the finest branches standing out plainly, but the congestion was most marked over the surfaces of the right temporal, parietal and occipital lobes. The cut surfaces of the brain were distinctly pinker than normal; the blood vessels stood out plainly and were filled with freshly clotted blood. This was especially true of the vessels in the distribution of the basilar branches of the middle cerebral artery. The striking fact, however, was that the large basal ganglia and internal capsule of the right side were much redder than the left, and that the deep white matter of the right hemisphere in the temporal and parietal lobes was somewhat softer than that of the left. There were a few petechial hemorrhages in the striate body

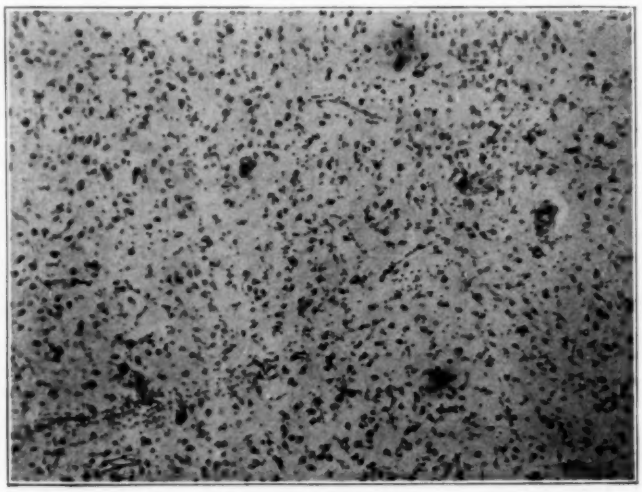

Fig. 10 (case 10).—With the use of a hand lens, the large number of young capillaries in the corpus striatum can be seen excessively rich in endothelial cells leading in some to an obliteration of the lumen. There are streams of oligodendroglia along the capillaries. Toluidine blue stain; × 65.

of the right side. The cut surfaces of the cerebellum on the right side revealed in the dentate nucleus a few small bright red areas, apparently recent hemorrhages. The white matter of the right cerebellar hemisphere was considerably pinker than the left.

Microscopic Observations: The blood vessels of the leptomeninges were distended with blood cells. No infiltrate was seen about them. The meninges were moderately cellular, containing many fibroblasts and macrophages. The latter were scattered through the pia-arachnoid but were also present in clumps in a few areas. The intracerebral blood vessels were dilated but empty save in the cerebellum, where they were filled with blood cells. In the right cerebellar white matter, there were a few areas of blood recently extravasated. In the walls of many capillaries and precapillaries, occasional round cells were present. The capillary endothelium was activated, the cells pyknotic and swollen and amitotic

division was noted. New blood vessel formation was frequent. Many of the blood vessels were thickened, with an excess of adventitial cells, often obliterating the vessel lumen. On examination with a lower power lens marked cellular richness was seen consisting of an enormous diffuse proliferation of cytoplasmic neuroglia and oligodendroglia. The latter cells were increased especially in the white matter and about the vessels, in which they formed streams. Often they appeared to be two or three layers thick about a small blood vessel. These cells were undergoing degeneration, their nuclei consisting often of only a membrane with a few dots of chromatin. The cytoplasmic glia formed a large part of the glial increase. They were often found in small nodule-like collections. The ganglion cells for the most part were swollen, with chromatolysis of the cytoplasm; the nucleus was usually enlarged and eccentric. Many of the cells were undergoing neuronophagia, and the nuclei were barely visible within the glia rosets.

Summary.—Two infants, aged 12 days and 2 months, respectively, were admitted to the hospital primarily because of disturbances in feeding; both were atrophic. In one, an infection of the upper respiratory tract developed after three weeks in the hospital; as a sequel, a bilateral otitis media appeared, followed by death in eleven days. The other child had otitis media on admission; three weeks later this necessitated mastoidectomy, and death occurred in five days.

In neither case were objective neurologic observations recorded on the pediatric service; examination was not made by a neurologist. Spinal punctures were not performed.

The pathologic observations were almost identical in the two cases. There was slight cellular increase of macrophages in the leptomeninges, and the pial vessels were crowded with blood cells. Leukocytic thrombi were noted in the vessels. Capillary proliferation with endothelial activation and proliferation were present, often to the point of endarteritis. Severe degeneration of the ganglion cells and neuronophagia with proliferation of the cytoplasmic glia and oligodendroglia cells were diffuse.

In case 10, the white matter on the same side as the mastoiditis, both grossly and microscopically, was more hyperemic and contained petechial hemorrhages.

TOXIC ENCEPHALITIS WITH SCARLET FEVER

CASE 11.—*History.*—A girl, aged 16 months, was admitted to the hospital on Oct. 22, 1925, and died on the following day. Three weeks before admission she had developed a diffuse rash, had become irritable, had vomited and had had high fever. The day before entrance, she had had a hemorrhage from the right ear, and the left ear also had discharged a small amount of blood. The mother said that the child had also bled from the nose and throat.

Examination.—A serosanguineous discharge was coming from the nose, throat and ears. There were edema of the right eyelid and periorbital tissues and profuse epistaxis. The pupils were equal, regular and reacted to light. Desquamation of the skin of the neck, shoulders and back was noted. Petechiae, purpuric spots

and ecchymoses were present in the skin of the abdomen, chest, back and extremities.

Course.—On October 23, more hemorrhagic spots were present in the skin of the extremities. The temperature was 100 F.; the pulse rate was 136, and respiration 46. A blood count revealed 3,400 monocytes.

Anatomic Diagnosis.—The condition was diagnosed as bilateral suppurative and hemorrhagic otitis media; postscarlatinal scaling of the skin; cloudy swelling of the parenchymatous organs; subcutaneous, subserous and subconjunctival petechial hemorrhages.

The Brain.—Gross Examination. Marked engorgement of the vessels in the leptomeninges and edema of the brain were noted. There was no exudate. The cut surfaces were a deep pink, and all the vessels stood out prominently as bright red points.

Microscopic Observations: The blood vessels of the meninges were distended with unclotted blood. There was moderate increase of endothelial cells, in certain

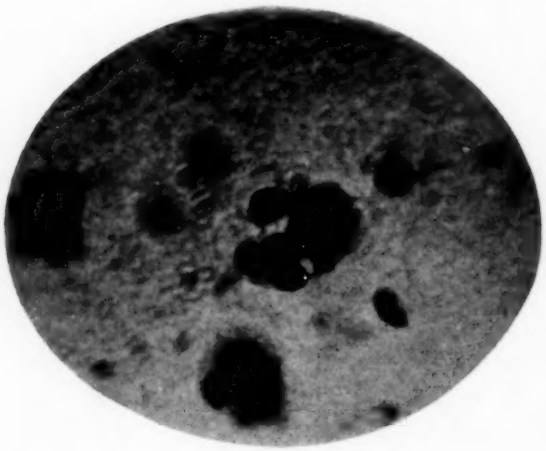

Fig. 11 (case 11).—Neuronophagia in the cortex; a glial roset completely surrounds a degenerated ganglion cell. Toluidine blue stain; × 450.

areas intermixed with large macrophages. The cerebral vessels were not distended; there was, however, an infiltration of their walls with small and large round cells in a single or a double layer. In the capillary walls were a few round cells. The capillaries were undergoing proliferation and budding frequently; they showed an activated endothelial lining. A moderate amount of perivascular edema was present. There was profuse proliferation of glia cells, including the true glia, the oligodendroglia and the Hortega cells. Gitter cells were not found. The ganglion cells were diffusely affected. Their cytoplasm had undergone chromatolysis; the cell periphery was frayed and contained many small vacuoles. Many ganglion cells revealed only cloudy swelling. A large amount of severe degeneration was present, with neuronophagia in all stages.

Summary.—Three weeks before admission, there was the onset of scarlet fever, of which remnants in the form of desquamation were still present when the patient entered the hospital. On the day preceding

admission, multiple hemorrhages occurred from the ears and nose, and into the subserous, subcutaneous, and subconjunctival tissues. No neurologic symptoms were recorded. The temperature was 100 F.

Pathologically, there was severe hyperemia of the meninges with a moderate increase of macrophages. The cerebral vessels were dilated, contained a few round cells within their walls, and were surrounded by edematous spaces. Diffuse glial cell proliferation, severe degeneration and cloudy swelling of the ganglion cells were found.

TOXIC ENCEPHALITIS WITH NEUROLOGIC SYMPTOMS AND A FOCUS OF INFECTION WITH RECOVERY

CASE 12.—*History.*—A boy, aged 5, was admitted to the hospital on July 4, 1927, with headache and fever. Six days prior to admission, he had been hit on the nose and had suffered a headache, but in a day was entirely well. The severe headache and fever present on admission had begun the day before and were associated with pain in the eyes and malaise.

Examination.—The boy was flushed and perspiring, the temperature being 100 F. The tonsils were enlarged and extremely red. There was moderate cervical rigidity. There was a bilateral Brudzinsky sign but no clonus or Babinski sign. All deep reflexes were brisk.

Neurologic Examination.—On July 7, one of us (R. R. G.) noted: left facial paresis; deviation of the tongue to the right; absent abdominal reflexes; decrease of the left cremasteric and of the deep reflexes. The spinal fluid was under increased pressure; it was clear and contained 95 cells, of which 90 per cent were lymphocytes. A culture remained sterile.

Course.—The temperature gradually receded, and the throat became less red. The cervical rigidity and neurologic signs disappeared, and on July 10 the child was discharged well.

Diagnosis.—The condition was diagnosed as acute tonsillitis, with toxic meningo-encephalitis.

CASE 13.—*History.*—A boy, aged 10, was seen by one of us (R. R. G.) because of neurologic complications attending a frank lobar pneumonia. The child had been doing well, with a temperature of from 103 to 104 F., when he became delirious, apparently with hallucinations.

Examination.—There was marked cervical rigidity, with a Kernig sign and bilateral Brudzinsky sign. The cranial nerves were normal. There were bilateral ankle clonus and a Babinski sign. The abdominal reflexes were not obtained. The spinal fluid was clear, free from globulin, and contained six cells.

Course.—A diagnosis of toxic encephalitis was made. In two days resolution took place, the child became quieter and gradually recovered strength. The neurologic signs receded completely, and the child was discharged apparently well.

Diagnosis.—The diagnosis was toxic meningo-encephalitis.

Summary.—The cases of two children with toxic encephalitis and recovery are reported. The primary infection in one was tonsillitis and pharyngitis; in the other, pneumonia. Diffuse cerebral involvement with severe meningeal symptoms was manifested by the objective signs in both. In the case with infection of the throat, ninety-five cells, mostly

lymphocytes, were found in the spinal fluid; in the other case, there were no cells. With subsidence of the primary infection, the neurologic signs gradually cleared, and the patients were discharged with apparently no physical remnant of the inflammation.

COMMENT

The postmortem observations in the cases studied, although varying in severity, form, on the whole, a fairly uniform group.

The macroscopic appearance of the brains was usually that of hyperemia. The leptomeninges were engorged, the subarachnoid space was slightly distended with fluid, and the cut surfaces were reddened and studded with visibly dilated vessels. This engorgement, however, was not constant, since several brains did not show much gross change.

That the macroscopic appearance of hyperemia is not pathognomonic of encephalitis was clearly demonstrated to us in a recently studied case. The patient had a moderately severe mastoiditis, with unusually profound general symptoms, increasing stupor and death. The cut surfaces of the brain were intensely pink and the blood vessels dilated. Much to our surprise, histologic preparations revealed only vascular engorgement and no more change in the ganglion cells than could be accounted for by the pyrexia.

We have encountered several reports concerning brains from children who had had a severe infectious disease in which the author stated that there was a "severe hyperemia of the brain: hemorrhagic encephalitis." As Spielmeyer [12] states, this term is limited to those infections which produce actual evidence of an inflammatory reaction of the brain together with involvement of the wall of the vessel leading to its rupture. This type of encephalitis was common after an attack of influenza, as reported in the older literature, and is still seen after the exanthematous diseases as exemplified by the postscarlatinal case reported by Toomey, Dembo and McConnell.[13]

Microscopically, we did not find any resemblance to epidemic encephalitis or polio-encephalitis. Infiltration with mesodermal elements was noticeably absent. This important fact differentiates the so-called toxic encephalitis from actual invasions of the brain substance by a virus such as is found in polio-encephalitis or in epidemic encephalitis. Mesodermal infiltrations are also characteristic even of parasitic invasion of the brain, as has been described by Hassin and Diamond [14] in trichina

12. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

13. Toomey, I. A.; Dembo, L. H., and McConnell, G.: Acute Hemorrhagic Encephalitis: Report of a Case Following Scarlet Fever, Am. J. Dis. Child. **25:** 98, 1923.

14. Hassin, G. B., and Diamond, I.: Trichinosis Encephalitis: A Pathologic Study, Arch. Neurol. & Psychiat. **15:**34 (Jan.) 1926.

encephalitis. The severe infiltration in general paralysis, in which spirochetes are present, is well known. One of us (R. R. G.) has recently studied a case of encephalitis caused by a mold, in which leukocytic infiltrations were found. Torula encephalitis also calls forth the same type of reaction.

In all cases there was profound destruction of the ganglion cells. This took the form of swelling, chromatolysis, ringlet formation in the cytoplasm, severe nuclear damage, complete degeneration and neuronophagia. Both cloudy swelling and the severe ganglion cell degeneration of Nissl are included in these changes, which Spielmeyer states may be found in intoxications and in acute septic processes.

The local vascular system was also severely affected. In some cases, striking new vessel formation was present; in others, there was stimulation of the vascular endothelium, often leading to obliteration of the lumen of many capillaries, an endarteritis productiva which Jacob [15] states may develop acutely in various intoxications.

There is little doubt that the severe reactions on the part of the nerve elements and of the vascular system are in response to a bacterial toxin rather than to a microbic invasion. The changes resemble closely the encephalopathies described in lead, arsenic and manganese poisoning and in dysentery and other intoxications.

Perhaps the work most applicable to our consideration of the encephalitis which we here call toxic is that of Hassin [16] in his study of the contrast between lesions of the brain produced by lead and arsenic and those caused by epidemic encephalitis. He reports a case of acute lead poisoning with proliferative and hyperplastic leptomeningeal reaction, proliferation and progressive glial cell changes, degeneration of the ganglion cells and proliferative vascular changes. Hassin states, "It seems permissible to claim that vascular infiltrative phenomena are indicative of an infectious type of encephalitis, while the proliferative phenomena denote a toxic condition." It is remarkable how closely the pathologic changes in our cases of toxic encephalitis resemble those in cases of acute lead encephalitis in the nature of the vascular, glial and meningeal reactions.

Through the kindness of Douglas Symmers we were privileged to examine slides from a case of acute serous encephalitis. The pericellular and perivascular edema and the cloudy swelling of the ganglion cells described by Brown and Symmers are evident in the celloidin preparations. We have no case which resembles the several he reported and

15. Jacob, A.: Anatomie und Histologie des Grosshirns, Vienna, Franz Deuticke, 1927.

16. Hassin, G. B.: The Contrast Between the Brain Lesions Produced by Lead and Other Inorganic Poisons and Those Caused by Epidemic Encephalitis, Arch. Neurol. & Psychiat. **6**:268 (Sept.) 1921.

which occurred almost in epidemic form. Dr. Symmers states in a personal communication that in New York he has not encountered any more of these cases. As he says, one cannot be sure that his cases form a new clinical entity. In the histories of four of the patients there was some reference to a possible focus of infection.

The marked proliferation of the glia cells which has formed such a constant feature in our cases consisted mainly of cytoplasmic glia and oligodendroglia. Few Hortega cells were seen. With the advent of the specific glial stains originated by Hortega, it has been possible for Penfield[17] to show experimentally that the Hortega or rod cells are of mesodermal origin and are the cells which become mobile, rounded, and form the so-called gitter cell or phagocytic glia. The stimulus which he used to cause glial proliferation resulted in what Spielmeyer would term a mixed gliogenous and mesodermal repair.

In our cases, free mobile glia cells were not found. The toxin stimulated a proliferation of the fixed type of glia, the true glia. Neuronophagia was carried on by the cytoplasmic glia. All types of progressively changed glia cells, degenerating cells and dividing cells, were found. In the type of repair, or Abbau, with which we have been dealing, the cytoplasmic glia and oligodendroglia play the important rôle. Further and detailed studies of this fact will be reported later.

The focus of infection in most instances made itself known as the initial complaint; the micro-organism recovered from that focus or from the blood was a staphylococcus or a streptococcus. It is known that each of these groups of organisms may produce a toxin; whether it is an endotoxin or an exotoxin matters little in the effects it produces on the brain. How this toxin reaches the brain cannot be definitely decided, but in view of the simultaneous damage to the kidneys, spleen and other parenchymatous organs, it is natural to assume a hematogenous route. This explanation is even more logical in the two instances of septicemia. In our cases the effect has been more drastic on the brain, while in other infections the kidneys or cardiovascular system may suffer the most damage. In those cases in which our patients died, death was probably caused by the overwhelming toxemia, although in the first two groups at least the lesions within the brain, severely affecting the vital centers, played an important part in the production of a lethal outcome.

Clinically, meningeal symptoms predominated in several cases, and yet, with one exception, the observations on the spinal fluid were entirely negative. Microscopically, the meninges were greatly engorged and were somewhat infiltrated with macrophages and round cells; occasionally there was edema and moderate thickening of the pia-arachnoid. Hassin,

17. Penfield, W.: Microglia and the Process of Phagocytosis in Gliomas, Am. J. Path. **1**:77, 1925.

whose observations so closely resembled our own, believes that the condition of the subarachnoid space in acute lead encephalitis, is evidence of a reaction against an irritating substance.

There is no reason why the same toxin acting on the brain substance may not have its effect also on the meninges, producing a toxic meningitis. This is termed, clinically, meningismus. We do not believe that we have dismissed the mystery of all meningismus by these pathologic observations, but we do believe that the meningeal symptoms of our patients can be explained on the basis of a toxic reaction in the meninges.

We are unable to establish a new syndrome and label it toxic encephalitis. The clinical picture in our cases is too fulminating and indefinite. However, the rapid development of stormy neurologic symptoms, drowsiness, hyperpyrexia, and convulsions in the presence of a focus of infection or septicemia should suggest that diagnosis. With such a syndrome it may be difficult to differentiate polio-encephalitis clinically except by the absence of definite bulbar involvement in the toxic type and the normal observations on the spinal fluid. Lethargic encephalitis, now not epidemic, is, at present at least, not attended by such a fulminating course.

In case 5 and in one other which need not be reported in detail, an abscess of the brain was suspected. We have learned that with mastoiditis or otitis media and a clear spinal fluid, symptoms in themselves significant of an abscess of the brain when associated with evidence, however slight, of more diffuse involvement, mean toxic encephalitis.

The sequel to ventriculography in case 5 is of interest; the blame for death cannot be placed, as is usually done, on the altered cerebrospinal dynamics resulting from a tumor. Death took place quickly after ventriculography with fever mounting rapidly to 108 F., dyspnea and tachycardia. This was a fatal reaction purely to air within the ventricles. It was evidenced microscopically by the tremendous engorgement of the ependymal vessels and the acute hyperemia of the ependymal and subependymal tissues and of the choroid plexus. Probably these changes in the fourth ventricle resulted in the hyperpyrexia and respiratory and cardiac disturbances which led to death.

From the varying degree of change in the nerve elements, it can be seen that the damage was not always irreversible. If recovery can take place from the general toxemia, life may be prolonged. In other types of encephalitis, residual symptoms have frequently been described. In fact, the classical Little's disease is assumed to be due often to a previous encephalitis. It is difficult, when death takes place long after the acute infection, to state definitely from pathologic evidence that an encephalitis has been present.

We have as yet not observed any cases in which recovery occurred from a toxic encephalitis with evidences of cerebral defects. With these

cases in mind, however, we have recently studied the history of children who have apparently progressed normally for some years and have then developed convulsions or have been classified as mentally deficient. In some of these cases, the mothers have said that the children were entirely well until the advent of an acute disease of the upper respiratory tract or an infection of the ear associated with high fever. After the infection, they were never normal.

We are not sure that we can rely on such indefinite histories or that the infection did not call attention to defects previously not obvious. But we think that toxic encephalitis may prove capable of producing grave organic neurologic sequels as well as mental deficiency.

CONCLUSIONS

In acute infections of varying kinds, including those of the upper respiratory tract, acute otitis media, acute mastoiditis, pneumonia, scarlet fever, and septicemia, severe neurologic symptoms were observed clinically, and an acute toxic encephalitis was revealed on histologic examination.

A fairly uniform clinical course was followed: rapidly developing symptoms of diffuse cerebral involvement, often associated with meningeal symptoms; early stupor; hyperpyrexia, and death in from three to four days. The spinal fluid usually was entirely normal. In two atrophic infants, neurologic symptoms were not noted. Two cases with recovery are reported.

Pathologically, evidence of actual microbic invasion of the brain was not found. The symptoms resembled those described in lead and arsenic encephalitis. The leptomeninges were hyperplastic and rich in macrophages; the ganglion cells were in various stages of acute degeneration; there was marked proliferation of the glial cells, and the vascular system was stimulated to new vessel formation and to endarteritic obliteration. The stress of the toxic agent was directed against the ganglion cells and the vascular system. It is believed that the toxin exerted its influence by a hematogenous route.

One mechanism of postventriculographic death was revealed in a case in which there was an immediate rise of temperature to 108 F. with the pathologic symptoms of marked hyperemia and extravasation of blood into the subependymal tissues and the choroid plexus.

The proliferation of the glia cells in these cases of endogenous toxemias was mostly of the cytoplasmic and oligodendroglia types and represented the fixed type of Abbau.

It is suggested that severe neurologic sequelae may develop from acute toxic encephalitis associated with acute infections if recovery occurs, and that more attention should be directed to encephalitis as an etiologic factor in these sequelae.

DISCUSSION

DR. BERT I. BEVERLY: Anyone seeing children who are acutely ill and who present neurologic symptoms is impressed with the apparently increasing frequency of conditions that can be explained only on the basis of an encephalitis. The majority of cases studied since the epidemic have a clinical and pathologic picture that differs from the lethargic or other previously described types of encephalitis and are similar to the cases demonstrated by Dr. Stone and Dr. Grinker. Studies of this type of case have been made at the Children's Memorial Hospital in the past four years with the help of Dr. George B. Hassin, who has made pathologic studies of some of the brains. Patients with a toxic encephalitis usually present the following clinical picture: The disease is secondary to a respiratory infection, a mild infection of the throat or a complicating pneumonia or an infectious diarrhea. The neurologic symptoms may appear at any time during the illness. The onset is acute and of varying severity. Change in the sensorium is an outstanding symptom; deep coma (not lethargy) is often the first symptom to appear and is sometimes present long after all other neurologic symptoms have disappeared. The patients often appear to be toxic. Every conceivable combination of cranial nerve and deep reflex changes may be present. Another characteristic of the disease is the rapidly changing neurologic picture. One pupil may be larger than the other at one time, and a few minutes or hours later the opposite condition may be found. A convergent strabismus may be seen to change to a divergent strabismus, etc. As in other forms of encephalitis, the evidence of meningeal irritation is variable, and usually not great. Examination of the spinal fluid shows it to be apparently the same as it is in other forms of encephalitis. A low or high temperature may be present. The course of the disease is usually stormy. It may be fatal in a few hours or may go on for days—one of our patients was comatose for twelve days. Marked irritability is often present for several weeks, followed by complete recovery from the acute illness at least. In some cases there is a severe sequela in the form of intelligence change; idiocy resulted in one of our cases. I think that the majority of these patients get well.

DR. HASSIN: In pediatrics one encounters cases in which death follows the acute onset and course of a group of disease symptoms of the brain, such as convulsions, unconsciousness and vomiting. Data obtained at necropsy are generally meager. They usually show as cerebral edema with flattened convolutions and obliterated sulci. In a number of such cases, studied mainly through the kindness of Dr. Beverly, I found a marked glia reticulum as a manifestation of stasis of the fluids of the brain tissue and no structural changes. The absence of the latter may be explained by the fact that the duration of the illness is usually too short (two or three days) for manifest changes to show. If present, as outlined by Dr. Grinker, they might be designated toxic encephalitis, a term I readily use, though the German authors prefer the name toxic degenerative states.

DR. GRINKER (closing): I find a great deal in the German conception that similar pathologic manifestations should be designated as toxic degenerative states. I had a great deal of difficulty in choosing between the two terms. This lies in the fact that the definitions of inflammation and degeneration are not sharply differentiated from each other. An analogous situation occurs in the kidney and the tendency lately is to consider the toxic reactions as degenerative phenomena. But who can say exactly where the division is between nephrosis and nephritis? The important point is not the label that one attaches to a condition found in fact but rather the study of its significance in relation to pathogenesis. Realizing the pathologic condition as dependent not on an invasion of the brain by micro-organisms but as a reaction to a circulating toxin, one should perhaps designate the condition a toxic brain reaction.

Dr. Hassin points out an edema of the glia reticulum. That is evident in the photomicrograph of the subependymal hemorrhage after ventriculography

and is dependent on the acute changes in fluid exchange in the tissue about the hemorrhage. It is absent elsewhere and in other cases.

It is interesting that Dr. Beverly has observed cases clinically in children associated with pneumonia; the sequelae he observed are what one would postulate from the pathologic changes. It might be well to state that we have observed similar changes in the brain associated with amyloidosis of the liver and spleen in an adult.

One clinical point deserves mention, and that is the frequency of this encephalitis associated with acute otitis media and the possibility of confusion with an abscess of the brain, as occurred in one of our cases.

COMPRESSION OF THE SPINAL CORD DUE TO VENTRAL EXTRADURAL CERVICAL CHONDROMAS

DIAGNOSIS AND SURGICAL TREATMENT *

BYRON STOOKEY, M.D.
NEW YORK

Within the past few years an unusual group of tumors of the spinal cord, not heretofore recognized as a definite clinical entity, has come under observation. They are discrete, sharply circumscribed, ventral, extradural chondromas lying in the midline or slightly to one side of the midline, usually in the region of the fourth, fifth or sixth cervical vertebrae. The more typical of these tumors present sufficiently defined clinical signs to permit recognition before operation. The most characteristic picture is that of marked unilateral spasticity, with atrophy and weakness of the muscles of one or two cervical segments at the level of the tumor and on the side of the spasticity, and changes in pain and temperature sense on the opposite side. Muscle, joint, vibratory and discriminative sensations are unaltered. The upper limit of the sensory changes is usually several segments lower than the atrophy and motor weakness, which, as has been said, are at the level of the tumor. Such is the clinical picture when the chondroma is sufficiently small to exert unilateral pressure on the ventral columns of the cord. When the tumor is large enough, however, to exert bilateral pressure sufficient to displace the cord as a whole, the picture is indistinguishable from other forms of extradural compression of the cord. On the other hand, if the growth is somewhat more lateral, compression may be exerted primarily on a nerve root and the only neurologic signs be those referable to involvement of the isolated nerve root, as in one of the cases here reported. The ventral and extradural position of these growths, their relatively small size and their tendency to lie from two to three segments higher than the sensory level would suggest make it easy for one to overlook them.

Among the seven tumors here reported, three were so placed and of such size as to exert unilateral pressure on the ventral column of the spinal cord. These gave rise to the characteristic picture of spasticity, focal atrophy and changes in pain and temperature on the opposite side, with no other alteration in sensation. In two of these I was able to make a preoperative diagnosis of extradural chondroma. Three tumors were

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* Read at the Fifty-Third Annual Meeting of the American Neurological Association at Atlantic City, N. J., May 25, 1927.

* From the Department of Neurological Surgery, Neurological Institute, and the Department of Neurological Surgery, Bellevue Hospital.

of sufficient size to give rise to bilateral signs and cause dorsal angulation of the cord. One, situated somewhat more laterally, yet still ventral, gave rise to nerve-root signs only. There are, then, three main locations, all ventral, yet varying slightly in their position and in their

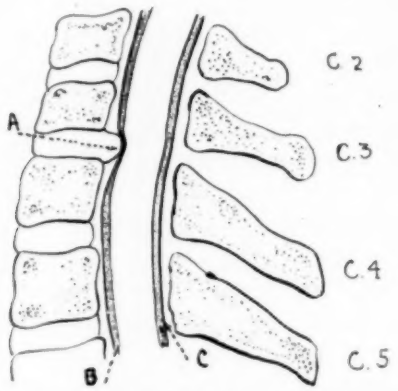

Fig. 1.—Schematic drawing showing origin of extradural ventral chondroma. The tumors are sharply circumscribed and exert discrete pressure on the spinal cord. *A* indicates chondroma; *B*, spinal fluid buffer, and *C*, dura.

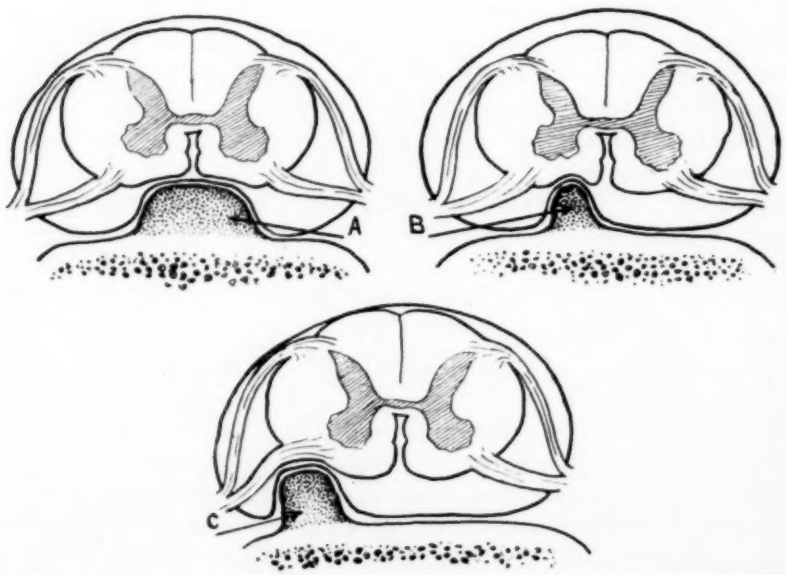

Fig. 2.—Schematic drawing to show variation in the position of the tumor; *A*, syndrome of bilateral ventral pressure; *B*, syndrome of unilateral ventral pressure; *C*, syndrome of root pressure.

relation to the spinal cord, with three main syndromes, the syndrome of bilateral ventral pressure, the syndrome of unilateral ventral pressure and the syndrome of root pressure (figs. 1 and 2).

All the tumors occurred in men, the youngest, aged 44, and the oldest 68, with an average age of 53. The tumors were found to lie either between the fourth and fifth, fifth and sixth or sixth and seventh cervical vertebrae, the positions between the fourth and fifth and fifth and sixth being the more common. Because of their ventral position and nearly constant level, it was at first thought that these growths might be an embryologic form of tumor derived from the notochord. The histologic appearance of the tumors, however, left little doubt as to their cartilaginous nature without sufficient evidence to suggest origin from the notochord.

In a review of the literature on tumors of the spinal cord, a description of this particular type of growth has not been found except those reported by Adson [1] (1925). Bruns [2] (1908), in his thorough study of tumors affecting the nervous system, Lubarsch and Ostertag [3] (1904) and Schlesinger [4] (1898) do not refer to similar tumors. Paravertebral chondromas of rather large size, usually in the lumbosacral region and invading the vertebral canal secondarily, are reported, but these differ materially from the group under discussion. The tumors here reported arise primarily in the vertebral canal; they are discrete and sharply circumscribed, somewhat resembling the intracranial chordomas described as small midline tumors derived from the notochord, varying in size from minute structures to 2 or 3 cm. in diameter, and situated in the region of the sella turcica and the basisphenoid. These intracranial tumors may remain as small benign tumors or undergo malignant change, becoming malignant chordomas. According to Bruns, mixed forms may coexist, with some areas showing simple chondroma structure and other areas showing chordoma structure.

It is significant that the tumors in the present series should appear in relation to the more freely movable vertebrae of the cervical region, and those most liable to injuries. No history of trauma or of any special occupational activity requiring continuous movements or strain on the cervical vertebrae could be established.

The tumors measure about 1 by 0.5 cm. to 1.5 by 1 cm. in size with the axis usually transverse. The tissue readily separates into thin

1. Dr. A. W. Adson has illustrated in Northwest Medicine (**24**:309 [July] 1925) an extradural ventral chondroma at the level of the fifth, sixth and seventh cervical segments, and in a personal communication has been kind enough to send me photographs of specimens removed from five additional patients. This material, and those cases here reported, are the only similar cases of which I am aware.

2. Bruns, Ludwig: Die Geschwülste des Nervensystems, Berlin, S. Karger, 1908.

3. Lubarsch and Ostertag: Ergebn. d. allg. Pathol. u. path. Anat., 1904.

4. Schlesinger, Hermann: Rückenmarks und Wirbeltumoren, Jena, Gustav Fischer, 1898.

layers of frayed, curly, cartilaginous material somewhat resembling oyster chips. Before removal a definite ridgelike projection with discrete indentation of the cord may be seen, and after removal a small depression along the ventral wall of the vertebral canal is observed.

PRESENTING SYMPTOMS

The presenting symptom is extremely interesting when the chondroma is so placed as to exert unilateral ventral pressure on the spinal

TABLE 1.—*Average Age and Duration of Illness*

	Age	Duration
Group I		
R. R.	44	5 months
J. R.	52	6 months
G. A.	68	2 months
Group II		
J. D.	49	36 months
T. D.	50	5 months
J. S.	55	11 months
Group III		
C. D.	54	24 months
	Total 372	89 Total

SUMMARY

Age	Sex	Duration
Average.....53	All men	Average.....12 months
Youngest.....44		Shortest..... 2 months
Oldest.....68		Longest.....36 months

TABLE 2.—*Presenting Symptoms*

Group I: Ventral chondroma exerting unilateral pressure on left side of the spinal cord	
	Syndrome of unilateral ventral pressure
R. R.	Weakness of left knee, with history of transient pain in the back of the neck two years previously, followed by pain in the left arm; this lasted only a few days and disappeared spontaneously
J. R.	Stabbing pain in left side of neck, followed in a few weeks by weakness of left upper extremity
G. A.	Stiffness of neck; pain in left shoulder
Group II: Ventral chondroma exerting bilateral pressure on the spinal cord	
	Syndrome of bilateral ventral pressure
J. D.	Pain and severe cold feeling in right lower extremity, with numbness and dead feeling in right calf
T. D.	Sudden bilateral paraplegia and spasticity, with pain in the shoulder six weeks previously
J. S.	Gradual numbness and loss of power in fingers of left hand
Group III: Ventral chondroma exerting pressure on the seventh cervical root	
	Syndrome of root pressure
C. D.	Peculiar, dull, numb sensation in tip of index finger and skin over styloid process of radius

cord. In all three cases of this group a history was obtained of pain or stiffness in the neck, followed by pain or weakness of the left upper extremity. The pain and stiffness may last only a few days, disappearing spontaneously as in R. R., or may persist throughout the illness. In none of the cases, however, was there any rigidity or limitation in the movements of the neck.

Correspondence in the presenting symptoms could not be made out in the cases of the second group, in which the chondroma exerted

bilateral ventral pressure (fig. 3). This observation is all the more interesting in view of the fact that one is dealing with tumors of approximately the same size, of about the same consistency, situated at about the same segmental level and exerting pressure on the ventral aspect of the cord. In a structure in which fiber tracts carrying widely different forms of impulses are compactly arranged, as they are in the spinal cord, it is not strange that the slightest variation in the relation of tumor and cord should give rise to widely different symptoms. This is all the more likely to be true when the point of pressure is discrete and sharply circumscribed, as is the case with these ventral, extradural,

Fig. 3.—Bilateral exposure of the spinal cord showing slight dorsal angulation of the spinal cord caused by an extradural ventral chondroma.

cervical chondromas. It is because of the relatively slight differences in position of these tumors that one is justified in speaking of the syndrome of bilateral ventral pressure, the syndrome of unilateral ventral pressure and the syndrome of root pressure.

MOTOR SIGNS

In the group of cases in which unilateral pressure was exerted by the tumor, rather sharply localized atrophy and fibrillations were seen. Thus, in R. R., atrophy and fibrillations in the left triceps were outstanding signs, indicating correctly the level of the neoplasm. In J. R., atrophy and fibrillations involving the deltoid, biceps, supraspinatus and

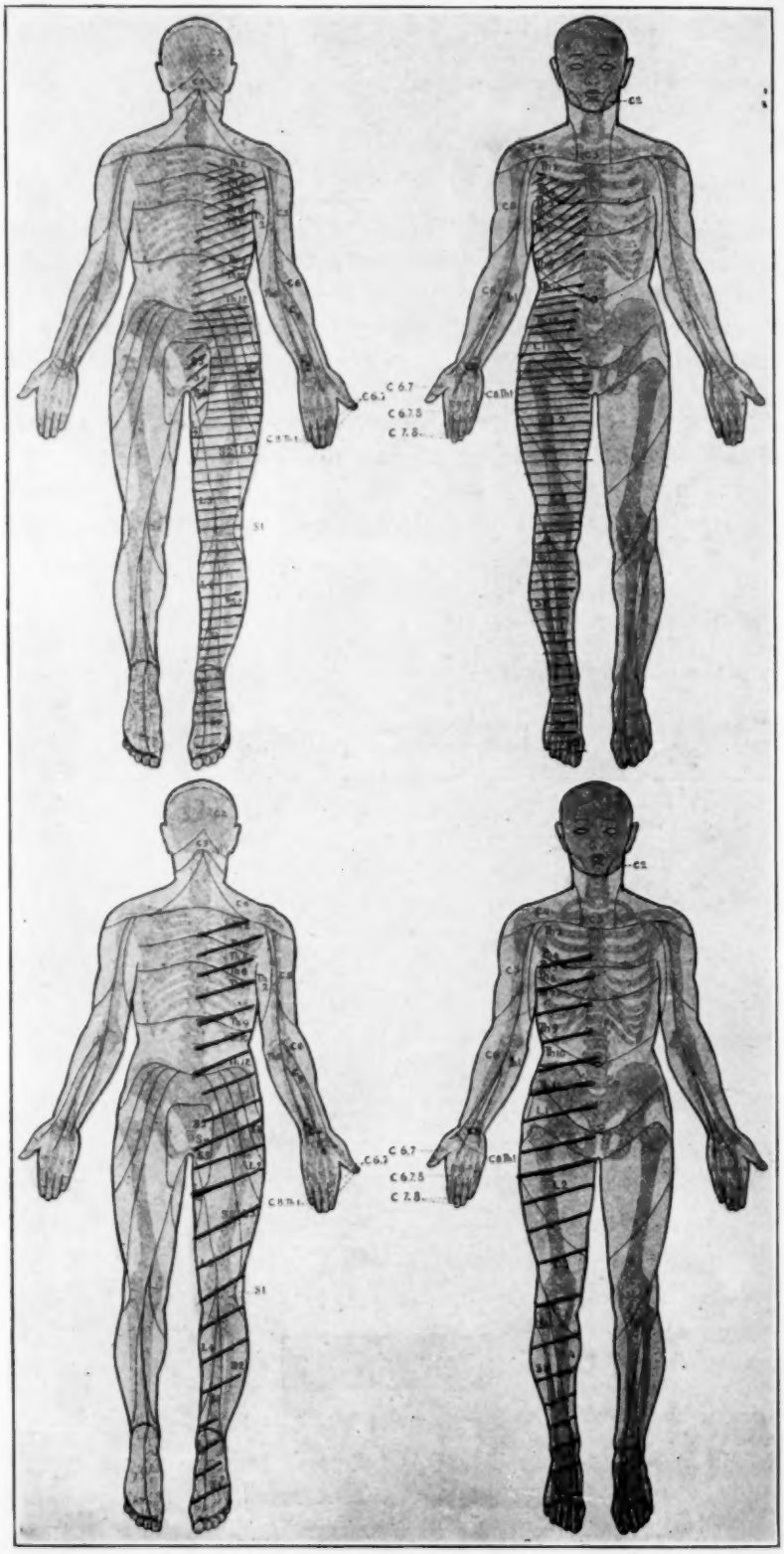

Fig. 4.—Sensory changes caused by an extradural ventral chondroma at the seventh cervical segment. Syndrome of unilateral ventral compression. It should be noted that the sensory level was three segments lower than the tumor. This is due to the fact that the tumor exerts pressure on the spinothalamic tract of the right side. The incoming pain and temperature fibers from the right thoracic third and second and the cervical eighth and seventh dermatomes cross obliquely and have not yet reached the contralateral spinothalamic tract; hence these fibers are not implicated. Cold sensation is less disturbed than pain or heat. In upper figures pain and heat sense are lost; all other forms of sensation are normal. In lower figures cold sense is moderately diminished.

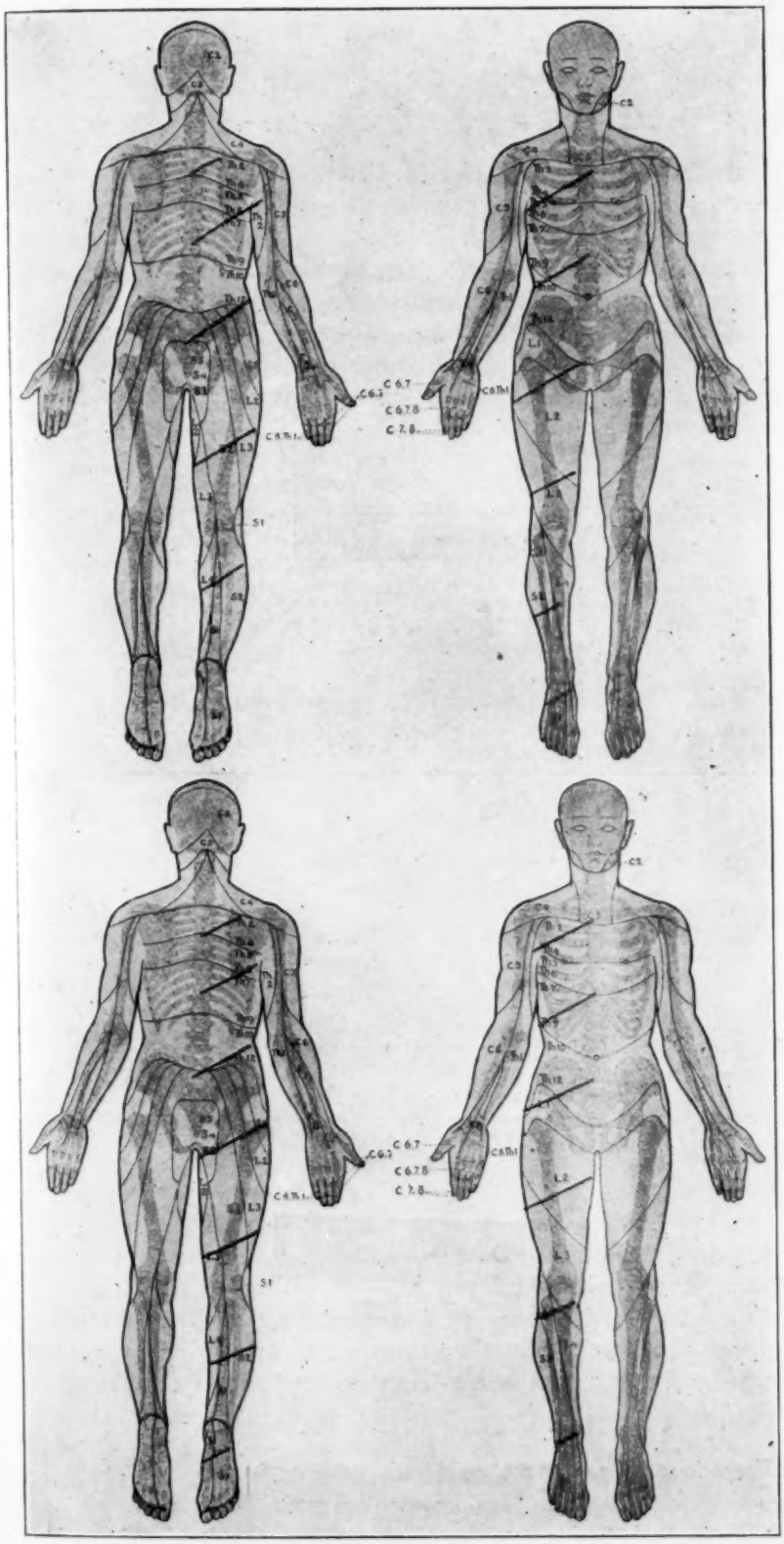

Fig. 5.—Sensory changes caused by an extradural ventral chondroma at the third cervical segment. The discrepancy between the sensory level and the level of the tumor should be noted. In this patient there was a slight diminution to crude tactile sensation but no disturbance in tactile localization or discrimination. In the upper figures there is slight diminution in tactile sensation; in the lower figures slight diminution of pain and temperature sensations.

rhomboidei were present, and in G. A., atrophy of the biceps and extensors of the wrist was found. Because of the atrophy and fibrillations, combined with dissociation of sensation, with no loss in any other modality, a diagnosis of syringomyelia is likely to be made unless the possibility of a ventral chondroma is considered.

When the chondroma was larger, making bilateral pressure on the cord (group II), and when the tumor was small and somewhat more lateral, impinging on a nerve root (group III), atrophy was also present, but fibrillations were not noted.

TABLE 3.—*Sensory Level, Motor Level and Level of Tumor*

	Sensory Level	Motor Level	Tumor Level
Group I: Ventral chondroma exerting unilateral pressure on the left side of the cord			
R. R.	Thoracic II-III	Cervical VII	Cervical VI-VII
J. R.	Thoracic I	Cervical V-VI	Cervical V-VI
G. A.	.....	Cervical VII	Cervical III-IV
Group II: Ventral chondroma exerting bilateral pressure on the spinal cord			
J. D.	Cervical IV	None	Cervical IV (midline)
T. D.	Cervical VIII	Cervical V-VII	Cervical V (more on left)
J. S.	Cervical IV	Cervical V	Cervical IV
Group III: Ventral chondroma exerting pressure on the seventh cervical root			
C. D.	No sensory changes	Cervical VII	Cervical VII

TABLE 4.—*Motor Signs*

	Atrophy and Weakness	Fibrillary Twitching
Group I:		
R. R.	Left triceps	Present
J. R.	Left deltoid, biceps, supraspinatus, rhomboideus	Present in all
G. A.	Atrophy left triceps and extensors of wrist	None present
Group II:		
J. D.	Bilateral; flexor group of forearm	None present
T. D.	Bilateral; flexor group of forearm; biceps and hand musculature	None present
J. S.	Rhomboidei	None present
Group III:		
C. D.	Sternal portion of pectoralis major and triceps	None present

Spasticity of the lower extremity is identical with that found in any form of tumor of the spinal cord: in cases in which there is unilateral pressure, the lower extremity of the opposite side may show little or no evidence of involvement of the pyramidal tract, while that on the same side may show marked involvement.

Fibrillations and atrophy are important signs for the determination of the level of the tumor, since the changes in pain and temperature may be several segments lower than the actual site of the growth.

SENSORY CHANGES

Pressure on the spinothalamic tract accounts for the sensory dissociation, with loss of pain and temperature sense on the opposite side of the body from two to three segments lower than the level of the tumor

(figs. 4, 5 and 6). The incoming pain and temperature fibers at the level of the tumor are not implicated, since these cross obliquely and do not reach the contralateral spinothalamic tract for a distance of two or three segments, entering the tract, therefore, above the level of the pressure. Involvement of the spinothalamic tract might account for the slight blunting of crude tactile sensation, which it is believed is carried in this tract. Tactile localization, muscle-joint sense and vibratory sensation carried in the posterior columns are unaffected unless the

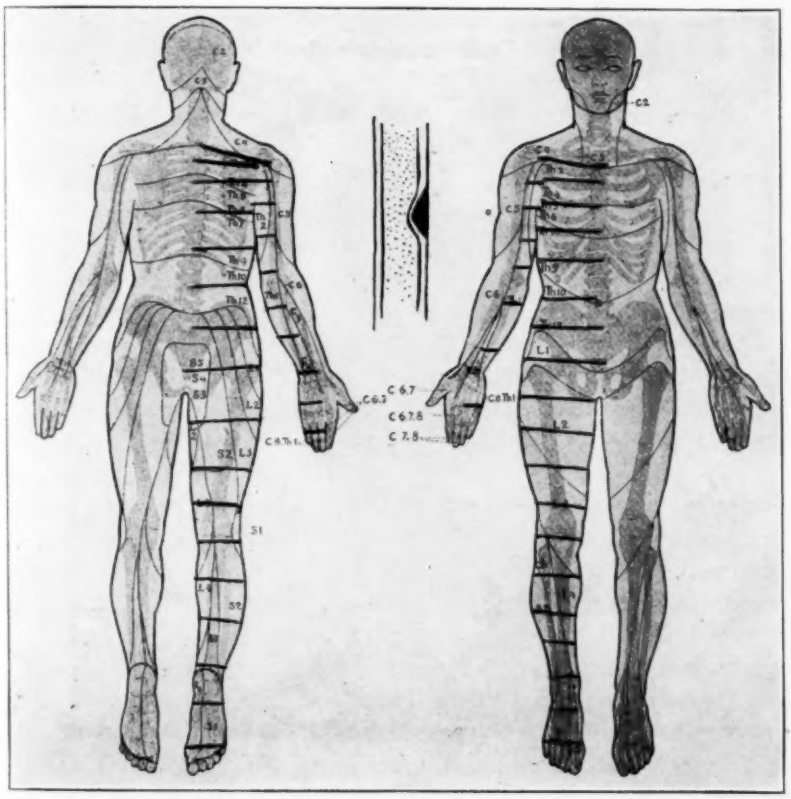

Fig. 6.—Changes caused by an extradural ventral chondroma at the fifth cervical segment. It is noted again that the two sensory levels are not in agreement. The schematic insert was made along with the preoperative diagnosis of ventral extradural chondroma and subsequently substantiated by operation. Pain and temperature sensations are lost; all other forms of sensation are normal.

tumor is fairly large. Next in order in the tracts involved are the pyramidal tracts, which give rise to the familiar signs referable to this system. I have not been able to recognize any evidence to indicate that the rubrospinal tract is involved. Probably any signs referable to this tract were overshadowed by those arising as a result of involvement

of the pyramidal tract. Pressure exerted on the ventral gray cells and emergent ventral rootlets accounts for the atrophy, fibrillations and weakness in the muscles thus directly affected. Thus, in unilateral ventral pressure such as is exerted by the tumors of group I, an exquisite anatomicoclinical study is afforded. Dissociation of sensation without loss of discriminative sensibility, combined with marked pyramidal signs and atrophy might lead to the diagnosis of intramedullary disease rather than extradural neoplasm. The unilateral character of the atrophy, however, without implication of the crossing segmental pain and temperaure fibers, and the course of the disease, together with the manometric observations of the spinal fluid, are more suggestive of neoplasm.

In the cases of group II, in which the neoplasm was larger, extending across the midline and involving both sides of the cord, the sensory observations were essentially indistinguishable from the more common forms of tumor of the spinal cord. Bilateral involvement of pain, temperature and tactile sensation, with definite blunting of discrimination as well as crude tactile sensation, were encountered. Muscle, joint and tendon sense, however, was less impaired than vibratory sensation.

Dissociation of vibratory and muscle, joint and tendon sense has been found frequently in the presence of tumors of the spinal cord, and a similar dissociation is seen after removal of tumors and during the stages of recovery, muscle, joint and tendon sense returning before vibratory sensation. Vibratory sensation carries with it a certain degree of affective, as well as discriminative sensibility. In cortical anesthesia, for example, vibratory sensation is not completely lost. The affective forms of sensation require less elaboration and simpler mechanisms than the discriminative, and for this reason, theoretically, should show return of function earlier. In order to explain the dissociation of muscle, joint and vibratory sensation, some have suggested that these impulses may be carried not only in the posterior column, but also in a separate path outside the posterior column. The cases here reported are extremely valuable in this connection; they show that vibratory sensation, at least, is probably not carried by fibers, either long or short, in the ventral reticular formation, since in three of the seven cases the ventral tracts as far as the pyramidal tracts were involved without any impairment of vibratory or muscle-joint sensation.

A difference in the resistance to the transmission of impulses along the fibers of the dorsal column may be predicated as a more likely explanation. Impulse conduction of vibratory sensation may be more easily impaired than muscle, joint and tendon sense. Such differences within the same pathway are seen in the conduction of pain and temperature sensations of pain, heat and cold not uncommonly being involved in an unequal degree. It seems more reasonable, therefore, to suppose

that differences in resistance within the spinothalamic and dorsal columns may be sufficient to account for differences in the conduction of impulse, than to predicate a multiple and scattered pathway. It is known that experimentally varying degrees of pressure exerted on the nerve in a muscle-nerve preparation may interfere selectively with impulse conduction; a similar mechanism probably holds for fibers within the spinal cord.

In group III in which the tumor was lateral, impinging primarily not on the spinal cord but on one of the nerve roots, the symptoms were predominantly those of involvement of the nerve root (fig. 7). In this case sensory signs referable to the spinal cord could not be made out,

Fig. 7.—Unilateral extradural chondroma compressing the seventh cervical root. Discrete pressure against the root was found with little or no pressure on the cervical root.

and had it not been for the lumbar manometric test, laminectomy would not have been performed. The sensory disturbances were purely subjective, described as burning, gnawing and tingling sensations, increased by movement of the extremity. Pain was constant, growing progressively worse, so that the patient finally had to give up work because of the suffering.

PARESTHESIAS

Some form of paresthesia was present in all the patients. In group I, in which the tumor was unilateral with pressure on the left spinothalamic tract, there was a spontaneous burning sensation or cold

sensation "as if the leg were on ice" in the opposite lower extremity, and in one instance a severe sensation of cold and one of burning were felt simultaneously. The patient in group III felt "as if ice had been held in the hand a long time." Paresthesias of this type, as Elsberg and Stookey have pointed out, are more commonly observed in ventral tumors than in tumors in any other position, probably owing to pressure exerted on the spinothalamic tracts. It is well known that lesions of these tracts may give rise to central pain and vague diffuse paresthesias.

EFFECT OF LUMBAR PUNCTURE

The diagnostic value of the accentuation of symptoms on the withdrawal of spinal fluid by lumbar puncture was first called to attention by Elsberg and Stookey [5] (1922), and lately confirmed by Dandy [6] (1926). Elsberg and Stookey pointed out that the withdrawal of the spinal fluid buffer between an extramedullary tumor and the cord disturbed the mechanical relations between the two, permitting the tumor to exert direct pressure on the cord, and thus causing a sudden accentuation of pressure signs and, in some instances, the appearance of new signs. When a tumor is fixed to the bony wall, displacement is not so likely to occur—thus, in five of the cases here reported no change was noted after lumbar puncture. However, removal of the fluid between the tumor and the spinal cord may allow the cord to impinge on the tumor and thus give rise to signs. This occurred in two instances: in one incontinence, followed by cramplike pains in the abdomen, appeared for the first time after lumbar puncture, and in another pain in the legs became so severe that the administration of sedatives was necessary.

In these cases mention was not made of the effect of straining. Pain, however, was made worse by exertion. In the patient with a chondroma beneath the seventh cervical root and the nerve root stretched over the tumor, neither straining nor sneezing caused any accentuation of the symptoms. However, swinging movements of the arm caused pain, while raising the arm brought relief. This relation of pain to the position of the arm is frequently observed in cases of pressure of the cervical rib on the brachial plexus, and is more likely to be considered a sign of a peripheral lesion than of a central lesion.

ROENTGEN-RAY EXAMINATION OF THE VERTEBRAL COLUMN

Due to their soft cartilaginous structure, their small size and their position, the chondromas are not seen in roentgenograms. Examination of the vertebral column gave negative results in all the cases in this series.

5. Elsberg, C. A., and Stookey, Byron: The Mechanical Effects of Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **8**:502 (Nov.) 1922.

6. Dandy, W. E.: A Sign and Symptom of Spinal Cord Tumors, Arch. Neurol. & Psychiat. **16**:436 (Oct.) 1926.

VERTEBRAL TENDERNESS

Vertebral tenderness did not prove of diagnostic value, as an indication either of the presence of a tumor or of its level. It was present in two of the cases, and in each instance three vertebrae were tender. In spite of the subjective complaint of pain in the neck, rigidity was not present.

LUMBAR MANOMETRIC EXAMINATION

This test has been most valuable in differential diagnosis of intrinsic disease of the cord and neoplasm. Had it not been for the lumbar manometric test, four of the patients in this series would in all probability not have been operated on. In this connection, it is interesting to note that in the only case of this series in which iodized oil was tried, it failed to show an obstruction, whereas the change in the character of the manometric responses indicated an incomplete obstruction.

OPERABILITY AND RESULTS

The operative results in this group of tumors of the spinal cord are not encouraging, though, usually, removal of a neoplasm of the spinal cord is followed by rapid return of function and, on the whole, rather brilliant results. Removal of ventral extradural tumors is, perhaps, the most difficult of operations on the spinal cord, owing essentially to the inaccessability of the growths and to hemorrhage from the extradural venous plexuses. Possibly, if the results in this series were compared with the results in other forms of ventral extradural tumors, there would be less disparity. Tumors firmly adherent to the underlying vertebrae are more difficult to remove than soft tumors without firm attachments. In one case ossification made removal impossible, but in the others the tumor could be removed. However, recovery took place more slowly than is usual, and was not as complete as is often the case following the removal of tumors of the spinal cord.

Having tried both combined and hemilaminectomy in the approach to the ventral surface of the spinal cord, I feel that hemilaminectomy, as introduced by Alfred S. Taylor[7] (1910), is the operation of choice, especially when the tumor lies somewhat to one side of the cord, as in the group exerting unilateral pressure (figs. 8 and 9). In hemilaminectomy the arches are removed farther ventrolaterally than in a bilateral laminectomy, and a more direct approach to the ventral surface is thus offered. Because of the bleeding encountered when an approach is made between the dura and bone this approach is avoided; the dura is opened and the vertebral bodies are approached transdurally. With the dura thus opened and the cord brought into view, two or three dentate liga-

7. Taylor, A. S.: Unilateral Laminectomy, Ann. Surg., April, 1910.

ments are grasped with fine mosquito forceps and cut. The spinal cord is then rotated, the ventral aspect of the dura being brought into view. A paramedian incision of from 1 to 2 cm. over the protruding tumor is made through the ventral surface of the dura. The tumor can then be removed in pieces, usually appearing as thin layers of frayed, cartilaginous tissue. After removal, a depression having a relatively smooth base can be seen on the ventral surface of the vertebral bodies.

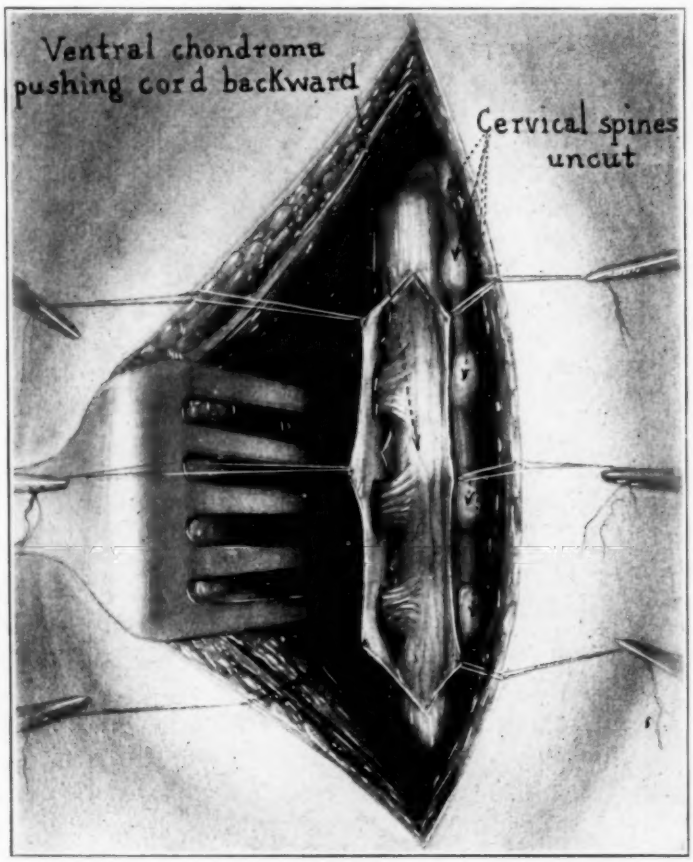

Fig. 8.—Hemilaminectomy with exposure of the cervical cord, according to the technic of Alfred S. Taylor. This is the operation of choice for the extradural ventral chondromas. The arches on the left side of the vertebrae have been removed as far as the articular processes. The vertebral spines, the intraspinous ligaments and the vertebral arches on the right side have not been disturbed. The dura has been cut and retracted. The dura on the right has been pulled up beside the spine and on the left over the cut surface of the laminae, exposing the spinal cord. When this exposure is properly effected the dorsal roots of the opposite side can readily be seen. A slight dorsal angulation of the spinal cord due to a ventral chondroma is noted.

If the tumor is large and extends across the midline, the opposite arches of one or two vertebrae immediately overlying the growth can be removed, the hemilaminectomy being converted into a bilateral laminectomy. Another paramedian incision is made in the dura on the opposite side, after rotation of the cord, and the tumor is removed in the same manner. An approach from the opposite side will seldom be necessary.

Before the recognition of cervical ventral chondromas as a definite clinical entity, it is possible that they may have been overlooked because of their extradural position, their small size and the rather unusual

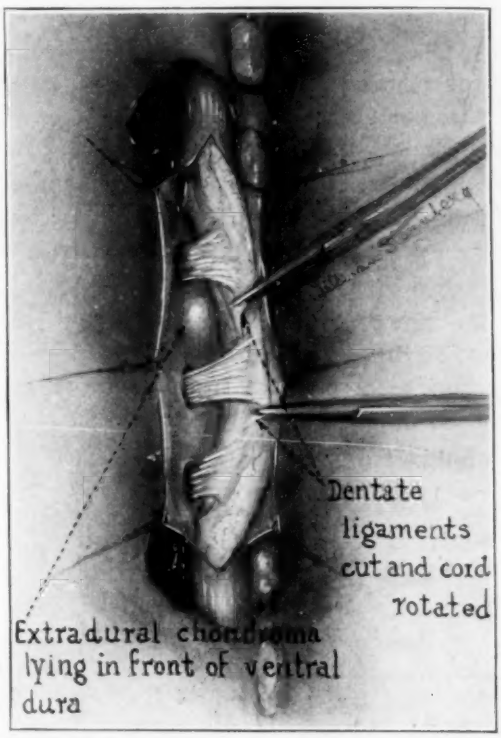

Fig. 9.—Same as figure 2. Two dentate ligaments have been cut and the cord has been rotated, the ventral surface of the dura being brought into view. A ventral chondroma is seen beneath the dura. A longitudinal incision in the dura should be made over the tumor and the tumor removed in layers.

clinical symptoms which they present. Since the sensory level is sometimes two or three segments lower than the actual position of the tumor, the segments immediately above the presumed level should be investigated by exposure of the ventral surface of the dura after rotation of the cord. A probe or soft catheter will pass by them, and unless the ventral surface of the dura is actually brought into view, they may easily be missed.

CONCLUSIONS

1. A group of primary extradural ventral chondromas producing compression of the spinal cord were found to present a definite clinical entity which heretofore has been unrecognized.

2. The more typical and recognizable forms give rise to unilateral spasticity, focal atrophy and fibrillary twitchings in the homolateral muscles of one or two segments at the level of the neoplasm with changes in pain and temperature on the opposite side of the body. Other modalities of sensation are unaltered.

3. According to the position of the tumor three syndromes can be made out: syndrome of bilateral ventral pressure, syndrome of unilateral ventral pressure and syndrome of root pressure.

4. The lumbar manometric test may indicate partial or complete obstruction. Iodized oil may pass the tumor and not give any indication of its presence.

5. The extradural cervical chondromas arise from the intervertebral disks, usually in the midcervical region, are about 1.5 by 0.5 cm. in size, elastic and sharply circumscribed and cause discrete though definite pressure on the ventral column of the spinal cord.

6. Because the tumors are small, are extradural and are from two to three segments higher than the sensory level they are readily overlooked, unless considered as a possible cause of compression of the spinal cord at the time of operation.

7. On removal, the tumor appears as thin frayed layers of cartilaginous material leaving a definite depression along the ventral surface of the vertebral canal.

8. Hemilaminectomy and a transdural approach is considered the operation of choice.

Drs. Charles A. Elsberg, Foster Kennedy, Walter Timme, Frederick Tilney and Edwin Zabriskie, chiefs of service at the Neurological Institute, and also Drs. Foster Kennedy and Alfred S. Taylor, chiefs of service, Bellevue Hospital, have permitted me to use this material.

DISCUSSION

DR. TEMPLE FAY, Philadelphia: Is there any roentgen-ray evidence either of displacement of the bodies of the vertebra or of an increasing of the intervertebral space that would tend to be useful preoperatively as a sign that could be checked? I am sure that these cases have probably been missed previously, not so much, perhaps, since the manometer came into use.

DR. CHARLES A. ELSBERG, New York: The chondromas which Dr. Stookey has described are interesting tumors of which I have seen a considerable number during the past few years. The first growth of this kind I found at an operation many years ago. The growths are usually small and can be easily missed unless the dura is open. They lie in the midline or more to one or the other side, and

the projection of the anterior dura can be felt with a probe and can be seen when the cord is drawn to the side by traction on a divided slip of the dentate ligament. It was the first case of this kind that led me to do and to recommend the transdural operation for the exposure of ventrally placed extradural growths.

I would suggest that those who make postmortem examinations should carefully examine the posterior surfaces of the bodies of the cervical vertebrae and intervertebral cartilages in all autopsies on the bony spine. It may well be that slight enlargements of the vertebral disks occur much oftener than they are thought to occur. Such localized enlargements might exist without causing any symptoms, or the symptoms might be so vague and indefinite as to make one suspect an intramedullary disease of the cord. There may not be any signs on physical examination nor any changes from the normal in the manometric tests.

Dr. Stookey has called attention to an interesting group of cases with a characteristic pathologic condition.

Dr. Byron Stookey: Roentgen-ray evidence indicating the presence of these tumors could not be produced.

CEREBELLAR SYMPTOMS PRODUCED BY SUPRATENTORIAL TUMORS

A FURTHER REPORT *

FRANCIS C. GRANT, M.D.
PHILADELPHIA

That the accurate localization of tumors of the brain is often a matter of extreme difficulty is well recognized. False localizing signs, particularly in relation to cranial nerve palsies, have been the subject of a number of communications, but it has rarely been emphasized with what frequency a mass lesion in one area may give definite symptoms of a lesion elsewhere in the brain. Apparently, statistics covering a large number of cases, which have betrayed how often a mistaken localization between a supratentorial and a subtentorial lesion has led to a cerebellar exploration when the neoplasm actually lay in the cerebral hemispheres, have not been compiled from any clinic.

An opportunity to assemble a group of cases in which this error in localization was made has been afforded by a recent study by Lehmann [1] of the results of cerebellar operations in Dr. Cushing's clinic. In the course of this study, which entailed the reperusal of the clinical histories of about 575 cases in which suboccipital explorations were performed, it was found that in twenty-seven instances a supratentorial lesion was subsequently verified.

It has seemed worth while to analyze these cases and to attempt to offer an explanation for the error. A particular interest is added to this analysis when it is remembered that these patients were all observed in one clinic, the records checked and the symptoms interpreted by the same observers. For this reason it seems certain that the false localizing signs noted were actually present, and that the same significance was placed on them in each instance. The personal equation—as to whether or not certain symptoms exist and the stress laid on them in diagnosis which is always confusing in the analysis of any series of reports of cases collected from the literature—is reduced to a minimum under these conditions.

It is difficult for the subsequent reviewer with a case history before him and aware of the ultimate diagnosis to put himself in the position of those who were called on to come to some conclusion as to localization from the physical signs at the bedside. Before the situation of the lesion

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* From the Neuro-Surgical Clinic of the Peter Bent Brigham Hospital, Boston.

1. Lehmann, Walter: Arch. f. klin. Chir. **143**:552, 1926.

has been verified, it may at times be exceedingly difficult to determine what are true and what are false localizing symptoms. Unquestionably, in the other 548 cases in this cerebellar series there must have been many in which there were comparable difficulties of diagnosis, and considering the fact that many patients with tumors of the brain enter a surgical clinic at a late stage of the disease, it need perhaps not be a matter of surprise that a gross error in localization should have been made in approximately one of every twenty-one cases. However, it is through the analysis of errors that chief progress is made.

In these twenty-seven cases of mistaken localization the ataxia, dysmetria, nystagmus, positive Romberg sign, suboccipital tenderness, marked intracranial pressure, etc., were present to such an extent that they held the center of the stage and drew attention away from other localizing signs of positive value. Nine of these patients were either blind or so uncooperative that the neurologic examination was incomplete or unsatisfactory. In retrospect, disregard or gross misinterpretation of existing cerebral symptoms was obviously the cause of the faulty localization of the lesion in only six cases. In these instances, although the cerebellum seemed clearly implicated, a review of the history shows that the facts at hand should have afforded a proper conception of the position of the tumor.

It is striking how widely distributed throughout the cerebral hemispheres these tumors proved to be, as shown in the accompanying table. Thirteen lay roughly in the anterior half of the supratentorial space; fourteen were in the posterior half. That tumors of the frontal lobe often simulate lesions of the posterior fossa has become a tradition in neurology. But that tumors of the motor cortex and temporal lobe could so closely imitate cerebellar lesions in symptomatology is startling. In a former communication from this clinic [2] dealing with defects in the visual field produced by neoplasms of the temporal lobe, the frequency with which confusion may occur between mass lesions in this region and in the cerebellum and the importance of perimetry in distinguishing them are clearly set forth. When the occipital, parieto-occipital and thalamic tumors are considered, the factor of a sagging tentorium with direct pressure on the cerebellum is regarded in this clinic as sufficient mechanical cause for the presence of cerebellar symptoms. A satisfactory explanation for the production of such signs by involvement of the tract from anteriorly placed tumors has never been offered.

All these cases have one factor in common: a marked increase of intracranial pressure. In only four instances was a choked disk of less than 3 diopters recorded, clear evidence of the high degree of tension that existed. Owing to its position at the base of the brain, the cere-

2. Cushing, Harvey: Tr. Am. Neurol. A., 1921, p. 374.

Cerebellar Symptoms in Cerebral Tumors *

Position of Tumor	Case Number	Diagnosis Warranted (16)	Ventricular Tap Positive (19)	History Suggestive of Cerebellar Tumor (16)	Onset, Purely Pressure Symptoms (14)	Time Onset From 1 to 6 Months (16)	Nystagmus (14)	Ataxia or Dysmetria (13)	Romberg Sign Positive (19)	Tinnitus or Deafness (7)	Occipital Headaches (6)	Suboccipital Tenderness (15)	Choked Disks (27)	
Frontal (5)	1	1	1	1	..	1	..	1	1	..	..	1	1	3 diopters
	6	6	..	..	6	6	..	6	..	..	..	6	6	5 diopters
	7	..	..	7	7	7	..	7	..	..	..	7	7	4 diopters
	8	..	8	..	..	..	8	8	8	..	..	..	8	4 diopters
	24	24	24	24	24	..	..	..	..	..	..	24	24	6 diopters
Motor cortex or temporal (6)	2	2	2	..	2	2	2	2	..	..	..	..	2	4 diopters
	3	..	3	3	..	3	3	3	3	3 tinnitus	..	3	3	2 diopters
	10	10	10	..	10	10	..	10	10	10 bilateral	..	..	10	5 diopters
	12	..	12	..	..	12	12	..	12	deafness	..	12	12	5 diopters
	23	23	23	23	23	23	..	..	..	..	23	23	23	6 diopters
	25	..	25	25	..	..	..	..	..	25 tinnitus	..	..	25	5 diopters
Parieto-occipital (4)	11	11	11	11	11	11	11	11	11	..	..	11	11	3 diopters in right eye, ½ diopter in left
	15	15	15	..	..	15	15	15	15	..	..	15	15	4 diopters
	18	..	18	18	18	18	18	..	..	..	18	..	18	5 diopters
	21	..	21	..	..	21	..	..	..	..	21	..	21	4 diopters
Occipital (4)	13	13	13	13	..	..	13	..	13	..	..	..	13	5 diopters
	14	14	14	14	..	..	14	..	14	..	14	14	14	5 diopters
	17	17	17	17	..	..	17	..	17	17 tinnitus	..	..	17	3 diopters
	19	..	19	..	19	..	..	..	19	and deafness	..	19	19	5 diopters
Midline, anterior (3)														
Suprasellar.....	4	4	4	..	4	4	4	..	4	4 tinnitus	..	4	4	2 diopters
Suprasellar.....	16	..	..	16	16	16	..	16	16	..	..	..	16	3 diopters
Suprasellar.....	26	26	..	..	..	..	..	26	26	..	26	..	26	4 diopters
Midline, posterior (5)														
Thalamic.....	5	5	..	..	5	5	5	..	5	5 tinnitus	5	..	5	7 diopters
Pineal.....	9	9	..	9	9	9	9	..	..	..	..	9	9	2 diopters
Thalamic.....	20	20	..	20	20	..	20	20	20	20 tinnitus	..	20	20	5 diopters
Thalamic.....	22	..	..	22	..	..	..	22	22	and deafness	..	..	22	6 diopters
Basal ganglia....	27	..	27	27	..	..	..	..	27	..	..	27	27	2 diopters

* The case numbers are listed in the left column and by following them across one may note the occurrence in each case of symptoms which led to the error in localization.

bellum is readily affected by changes in intracranial tension. The base of the posterior fossa is roughly funnel shaped with the apex below at the foramen magnum. This foramen is the largest aperture in an otherwise rigidly enclosed cavity. As tension rises within this cavity, its contents are forced downward and tend to herniate into the foramen; the cerebellum becomes crowded into the posterior fossa and is squeezed between the pressure from above and the bone beneath.

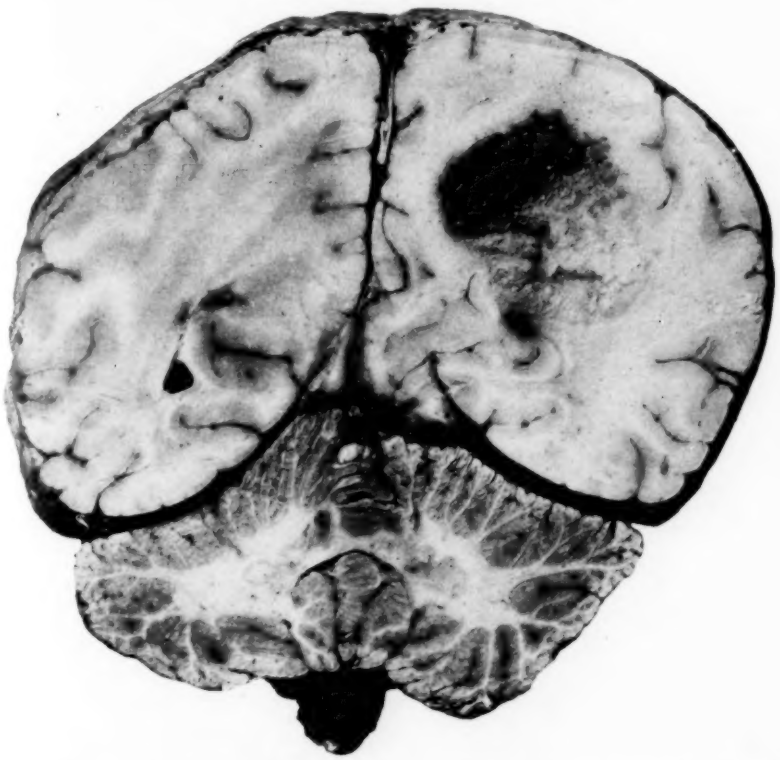

Fig. 1.—Section through the brain in case 1, showing a tumor in the right temporoparietal lobe. Note complete obliteration of the right lateral ventricle and the definite sagging of the tentorium allowing pressure on the cerebellum from above.

Not only may this direct pressure on the cerebellum interfere with its function and cause confusing symptoms, but it is to be remembered that a supratentorial tumor may lead to herniation of the margins of the cerebral hemispheres through the incisura tentorii just as the cerebellum may be forced downward into the foramen magnum. It is conceivable that the superior cerebellar peduncles may thereby become compressed and the cerebrocerebellar pathways be interrupted.

That the falx and tentorium are not rigid membranes which can withstand pressure without dislocation may be realized by inspection of almost any of the accompanying illustrations. A large cerebral tumor may push the falx far to the opposite side, and as the intracranial pressure increases, a definite sag of the tentorium with consequent pressure on the cerebellum is produced.

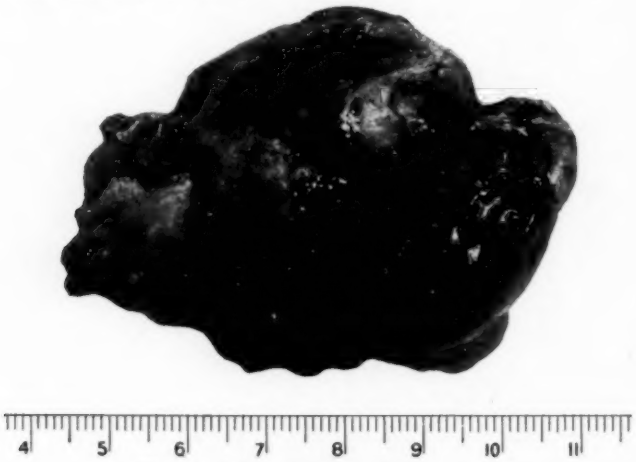

Fig. 2.—Tumor removed in case 2.

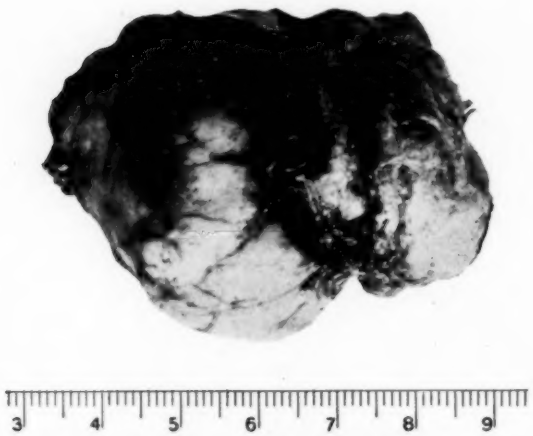

Fig. 3.—Tumor removed in case 4.

In this connection it should be noted that in the majority (sixteen) of the cases the history indicates that symptoms of pressure were relatively acute, having been present for less than six months. This of itself suggests a subtentorial lesion in which the secondary hydrocephalus may abruptly precipitate pressure symptoms in a previously quiescent lesion.

That a sudden increase in tension from a rapidly growing tumor with or without hydrocephalus may produce cerebellar symptoms and mask localizing signs pointing to other areas is borne out by the fact that of these sixteen cases in which the abrupt onset of pressure symptoms—headache, vomiting, and choked disk—were the earliest manifestations of the lesion, clinical evidence of involvement of the posterior fossa predominated in fourteen. In many instances a positive Romberg sign, staggering gait and suboccipital tenderness were noted, while twelve showed, in addition, nystagmus, ataxia and dysmetria.

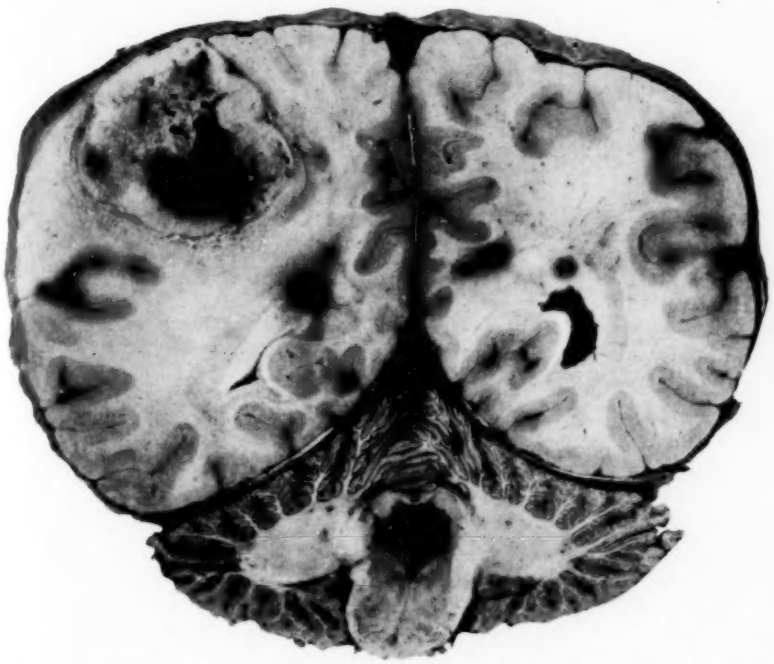

Fig. 4.—Section through the brain in case 5, showing a tumor in the left parietal lobe with obliteration of the left lateral ventricle and sagging of the tentorium, permitting pressure on the cerebellum from above.

In only six of the remaining eleven cases in which the development of pressure symptoms occurred more slowly did the evidence of cerebellar involvement predominate and obscure localizing signs of positive value. In sixteen of these twenty-seven cases, the localization of the lesion in the posterior fossa seemed clearly warranted from the evidence at hand. The following cases may be given as illustrations.

REPORT OF CASES

CASE 1.—*Right parietal tumor with cerebellar symptoms. Cerebellar exploration with ventricular tap which demonstrated undilated ventricles. Death; necropsy.*

History.—A. B., an American housewife, aged 50, was admitted to the hospital on Dec. 19, 1923, complaining of headache, weakness and vertigo. Two months before, frontal and suboccipital headaches had been noted. Six weeks before she developed marked failure in vision with great unsteadiness in gait and tremor of the hands. A definite alteration in mentality was obvious.

Examination.—On admission, the patient was fairly intelligent and cooperative. Suboccipital tenderness and pain on flexion of the neck were demonstrable. Retinoscopic examination revealed choked disk of 3 diopters on the right and 1 diopter on the left. There was a concentric contraction of the visual fields. Roentgenograms of the skull were normal. Weakness of all extremities, especially the left arm and leg, with hypesthesia of the left side of the face and body, was present. The family reported a definite change in mentality. Horizontal nystagmus to the right and left, marked hypotonia, dysmetria and ataxia of all extremities, especially on the left, with adiadokokinesis of the left arm, were present. The Romberg sign was positive, with a tendency to fall backward. The gait was markedly reeling with a wide base. The reflexes were all reduced slightly, more on the left than on the right. A questionable Babinski sign was noted on the left.

Impression.—The condition was thought to be cerebellar tumor.

Operation.—On Jan. 5, 1924, Dr. Cushing made a cerebellar exploration. In the course of this procedure, a ventricular tap was attempted to relieve pressure. It was impossible to reach either ventricle. The operator then suspected that the localization might have been incorrect. The exploration did not reveal evidence of a lesion in the posterior fossa. Death occurred forty-eight hours later.

Necropsy.—The brain was removed after fixation in 10 per cent liquor formaldehydi by carotid injection. Coronal section through the pons revealed a cystic cavity in the upper and outer portion of the right occipital lobe about 2 cm. in diameter. The tumor was fairly well circumscribed and extended forward into the center of the right hemisphere. The posterior horn of the right ventricle was completely obliterated, while the posterior horn of the left ventricle was practically obliterated and pushed to the left. A definite sagging of the tentorium with pressure on the cerebellum from above was clearly manifest.

Pathologic Diagnosis.—The tumor was diagnosed as spongioblastoma multiforme.

Comment.—The sudden onset, high degree of choked disk, suboccipital headache and tenderness, alteration of gait, positive Romberg sign, ataxia and dysmetria with nystagmus seemed certain evidence of a cerebellar lesion, showing clearly how easy it may be to place undue emphasis on misleading clinical evidence. The increased weakness of the left arm and leg with a questionable Babinski sign on the left—the important symptoms of a right cerebral tumor—were thought to be of cerebellar origin due to pressure on the motor pathways in the posterior fossa.

Failure to reach the lateral ventricle which should have been dilated had the tumor been in the posterior fossa gave the first dependable clue to the importance of the unilateral weakness and the true position of the tumor.

CASE 2.—*Right parietal tumor with cerebellar symptoms. Cerebellar exploration. Ventriculogram. Right frontoparietal exploration with extirpation of deep encapsulated glioma. Recovery.*

History.—H. B. C., an American school boy, was admitted to the hospital on March 29, 1924, complaining of headache, vomiting and failing vision for the preceding four months. At the age of 11 months the child contracted a right otitis media with rupture of the ear drum. The previous history was essentially unimportant until four months before, when pain was again noted in the right ear for a day and was accompanied by severe headache and vomiting. The headache and vomiting persisted and increased. Definite failure of vision, with difficulty in walking and inability to use the left leg as well as the right, then developed.

Examination.—On admission, the boy was fairly bright and cooperative. A cracked-pot note on percussion of the head, definite enlargement of the head presumably due to hydrocephalus and suboccipital tenderness were present. There was a bilateral choked disk of 6 diopters, with complete sixth nerve paralysis on both sides. The visual fields were normal. Some slight motor weakness of the left arm and leg could be demonstrated. This was emphasized by one observer whose diagnosis, nevertheless, was cerebellar tumor. Nystagmus in the horizontal plane, especially to the left, hypotonia, dysmetria and adiadokokinesis, especially in the left extremities were present; the Romberg sign was positive; the gait was of cerebellar type with falling to the left. The roentgenograms of the head were normal except for marked evidence of intracranial pressure.

Impression.—The condition was thought to be cerebellar tumor.

First Operation.—On April 2, 1924, Dr. Horrax made a suboccipital exploration. In the course of this procedure, a ventricular tap was performed to relieve pressure. The ventricles were found to be small and undilated. The cerebellar exploration was negative for evidence of tumor. Recovery was uneventful.

Ventriculography.—On April 12, 1924, Dr. Horrax carried through a ventriculogram. The films showed both lateral ventricles shifted to the right and the right lateral ventricle displaced somewhat downward.

Second Operation.—On April 15, 1924, Dr. Horrax turned down a large right frontoparietal flap. Inspection of the cortex revealed evidence of a deep seated tumor. A transcortical incision exposed a well encapsulated tumor which was extirpated. The child recovered and was discharged April 29, 1924, much improved.

Comment.—A patient in whom marked signs of intracranial pressure and a high choked disk developed within the short space of four months would unquestionably show dilated lateral ventricles if the tumor lay in the posterior fossa. That the ventricles were undilated was strong presumptive evidence that the tumor lay in the cerebral hemispheres. Once this conclusion had been reached, the importance of the left sided motor weakness as a localizing sign would have been appreciated.

It is disturbing to be compelled to consider the presence of nystagmus as no longer certain evidence of a cerebellar lesion, and to realize that it may be produced by intracranial pressure alone. Over one half (fourteen) of this group of patients exhibited this symptom. In five instances the tumor lay in the anterior half of the supratentorial space (three motor cortex, one frontal, one suprasellar). In the remainder it involved

the occipital poles (three), the parieto-occipital area, (three), the thalamus (two) and the pineal gland (one). That nystagmus was more frequently observed the further back in the cerebrum the tumor lay substantiates the theory that external pressure on the cerebellum or its connecting pathways may produce this symptom.

Tinnitus and deafness in conjunction with other cerebellar symptoms have long been associated as almost pathognomonic of tumor of the cerebellopontile angle. In the history of seven of the patients one or the other of these symptoms was noted—tinnitus alone four times, tinnitus and deafness twice, bilateral deafness once. Tinnitus without deafness occurred with two parietotemporal lesions, one suprasellar and one thalamic. A tumor of the occipital lobe and a lesion involving the thalamus and corpora quadrigemina were accompanied by tinnitus and deafness. A tumor of the temporal lobe produced bilateral deafness in one instance. That tinnitus and deafness may be important indications of a lesion of the temporal lobe must always be remembered. It is curious that but one of the tumors giving these symptoms actually lay wholly in this region. Again the theory of irritative pressure from without on the auditory area must be invoked to account for the presence of these symptoms.

In the case of tumor of the occipital lobe there was such a perfect history and symptom-complex of a tumor of the cerebellopontile angle that it is worthy of mention. This case also demonstrates clearly the importance of never being too sure. Had the clinical evidence not been so overwhelmingly indicative of a tumor of the angle, it seems certain that more than a rough determination of the visual fields would have been made. Accurate perimetric tests could not have failed to localize the lesion exactly. In this instance, probably direct pressure from above by the astrocytoma—a tough, firm, type of growth—produced the cerebellopontile symptoms. An outline of the case follows.

CASE 3.—*Tumor of left occipital pole with symptoms of acoustic neuroma. Cerebellar exploration negative. Ventriculogram. Left occipital exploration with removal of tumor. Recovery.*

History.—A. W. W., a housewife, aged 35, was admitted to the hospital Nov. 6, 1923, complaining of tinnitus and deafness in the left ear with vertigo, headaches, diplopia and failing vision. The initial symptom of a painful throbbing sensation in the back of the head was noted four years before. Fainting attacks with loss of consciousness occurred on two occasions. A year before admission to the hospital, tinnitus in the left ear was first noted. Three months later, she became completely deaf in this ear and suffered a great deal from attacks of vertigo. Five months before admission diplopia became apparent, the false image being always to the left of the true.

Examination.—On admission the patient was cooperative and intelligent. There was suboccipital tenderness especially on the left. The gait was cerebellar in character; Romberg's sign was present. Hypesthesia was present over the entire right side of the face, and there was paralysis of the left sixth nerve. Complete

deafness existed in the left ear. Occasional nystagmoid perks to the right and left were noted. Bilateral choked disk of 5 diopters was recorded. Perimetric visual fields were not accurately made, reliance being placed on rough hand fields which were reported as normal. Roentgenograms of the skull were normal.

Impression.—The condition was thought to be tumor of the left cerebellopontile angle.

Cerebellar Exploration.—On Nov. 10, 1923, Dr. Cushing made a cerebellar exploration. In the course of this procedure, which failed to reveal any tumor in the posterior fossa, an attempt to tap the left lateral ventricle was unsuccessful, while the right ventricle was found to be dilated. Thus ventricular asymmetry was shown to exist. An uneventful recovery followed.

Ventriculograms.—On Nov. 21, and 24, 1923, Dr. Horrax performed a ventriculogram. The plates showed the tumor to lie in the left occipital pole.

Left Occipital Exploration.—On Nov. 24, 1923, Dr. Cushing threw back a left occipital bone flap. A tumor, 3 cm. beneath the cortex of the left occipital lobe, was disclosed and removed. Recovery followed.

Pathologic Diagnosis.—The tumor was diagnosed as astrocytoma.

Comment.—While undoubtedly the omission of a determination of the visual fields was a serious oversight, it is notable that in thirteen of these cases, (six parieto-occipital, five temporal, two suprasellar) in which valuable information might have been expected from these tests, in but four would carefully performed perimetry have furnished a clue to the position of the lesion. Two patients harboring tumors of the occipital lobe who had in addition a high choked disk (5 and 3 diopters, respectively) showed merely a concentric contraction of the visual fields, a common occurrence with marked papillitis. Three other patients were blind on admission; six were stuporous or uncooperative to the point of making perimetry impossible.

That a carefully taken history is important in differentiating between symptoms due to actual cerebellar involvement and to pressure on the cerebellum from above as intracranial tension increases is not altogether borne out by this analysis. In sixteen cases the history seemed to point unmistakably to a cerebellar lesion. Thirteen gave early evidence of increased intracranial tension—headache, vomiting and visual disturbances. The intracranial pressure and the cerebellar syndrome developed together. Chronologically, it was difficult to sift out symptoms pointing to direct cerebral involvement before the factor of rising tension and its consequent cerebellar complex developed to confuse the issue. When the lesion is in a relatively silent cerebral area and when symptoms of intracranial pressure give the first warning of its presence, the differential diagnosis between subtentorial and supratentorial lesions may be extremely puzzling.

Roentgen-ray studies proved of little value in these misdiagnosed cases. Localizing evidence from this source is so positive that it is but rarely disregarded. In only one instance in which a pineal shift was

suggested could a positive diagnosis of cerebral tumor have been made. Cerebellar tumors rarely cause a lateral shift of the pineal gland. In two other instances suprasellar tumors had eroded the pituitary fossa. As the visual fields, however, did not show significant change and since cerebellar symptoms predominated, it was thought that this erosion was due to dilatation of the third ventricle from the marked hydrocephalus which commonly accompanies a lesion of the posterior fossa. That destruction of the posterior clinoids and sella may be due to this cause has been emphasized in a previous communication from this clinic.[3]

When it is realized that in more than 550 cases diagnosed as cerebellar lesions, in but twenty-seven, or less than 5 per cent, was the tumor eventually discovered above the tentorium, the conclusion must be that the differentiation between lesions in these two areas is not ordinarily difficult. It is fortunate that this is the case, for while suboccipital craniectomy in the presence of a cerebellar tumor only carried a mortality of roughly 12 per cent, if this procedure is carried out when the lesion is supratentorial the rate is more than 50 per cent.

It must be remembered in reviewing any series of errors in diagnosis that to see why the mistake was made is much easier than to prevent the error in the first instance. Once the location of the lesion is known, vague symptoms become striking because they are commonly attributed to lesions in this area and, therefore, must be present. They may have been previously overlooked and an entirely erroneous impression gained from overemphasis of localizing signs which turn out to be misleading. But once the puzzle is solved by operation or necropsy, one wonders how such apparently obvious clues had been missed.

The solution of the problem of the patient with a confusing neurologic picture, who is uncooperative or difficult to examine, may lie in a determination of the size and shape of the cerebral ventricles. This information may be obtained in two ways: ventricular estimation, or ventriculography. Almost every tumor of the brain which is sufficiently large to produce pressure symptoms causes a change in the position, size or shape of the ventricles. Cerebral tumors distort the lateral ventricle of the hemisphere in which they lie, the contralateral ventricle being less affected. Cerebellar tumors, since they impinge on the aqueduct or fourth ventricle and block the circulation of the fluid, cause a symmetrical dilatation of the lateral ventricles. If a bilateral ventricular tap is performed and if, based on the amount of fluid which can be withdrawn from each ventricle, there is found to be a marked difference in size, or if one or the other seems shifted from its normal position, this is positive evidence of a neoplasm in the cerebral

3. Bailey, P.: Cerebellar Symptoms Produced by Suprasellar Tumors, Arch. Neurol. & Psychiat. **11**:137 (Feb.) 1924.

hemisphere containing the smaller ventricle, or on the side away from which the ventricles have been displaced. But if both ventricles apparently contain a nearly equal but evidently excessive amount of fluid, the tumor probably lies below the tentorium. Since a tumor of the third ventricle or basal ganglia may also cause symmetrical dilatation of the lateral ventricles, this is not certain proof of the presence of a cerebellar tumor. But symmetrical dilatation rules out a hemispheric cerebral neoplasm just as surely as asymmetry of the lateral ventricles excludes a lesion of the posterior fossa. A careful reexamination of the symptoms should be made in an attempt to interpret them in the light of these new facts. Unless a definite localization can now be made, a ventriculogram should be attempted. But, owing to the greater risk accompanying this procedure, it should be held as a final resort for those cases in which a ventricular estimation has been inconclusive.

Nineteen of these twenty-seven lesions could have been identified as cerebellar by bilateral ventricular tap because a marked ventricular asymmetry existed (table). Of the remaining eight cases in which a tap alone would have been confusing, owing to the presence of bilateral hydrocephalus, in six instances the tumor lay in the midline (three thalamic, two suprasellar, one pineal). As has been stated, tumors in the midline will produce symmetrical dilatation. A ventriculogram may be necessary under these circumstances, for it is only in this way that the presence or absence of dilatation of the third ventricle can be determined. A ventriculogram was performed only in three of these cases. The information thus obtained was decisive and correct. The following cases and those already cited illustrate the importance of always tapping both ventricles. If the size of only one is estimated, it may be the larger of the two and may be sufficiently dilated to suggest a cerebellar tumor. Furthermore, the folly of continuing a cerebellar exploration if an undilated ventricle can be demonstrated is clearly emphasized. Once ventricular asymmetry can be proved, the suboccipital exploration should be abandoned and an attempt made to localize the lesion from the clinical manifestations, emphasizing the cerebral and not the cerebellar symptoms. The two following cases are illustrative.

CASE 4.—*Indefinite symptoms suggesting tumor in right parietal lobe. Right subtemporal decompression, right parietal flap, suboccipital decompression with ventricular tap, left occipital flap; exposure and removal of tumor. Recovery.*

History.—M. M., a housewife, aged 44, was admitted on Nov. 22, 1921, completely blind and with severe headache and vomiting. The generalized headaches had commenced a year before, when she noted slowly progressive but definite loss of vision. About three months before, the family observed that she was developing dispositional changes, becoming morose and fretful. Diplopia followed, and finally total blindness resulted. She complained of some weakness of the legs, especially on the left side, with loss of sensation of this side of her body.

Examination.—Study revealed a totally blind, morose, uncooperative woman. She was disoriented and mentally deficient. The head showed tenderness to percussion in the left parietal region. The eyes showed total loss of vision and bilateral choked disks of 5 diopters. There was weakness in the lower left side of the face. Hypertonicity was marked in the right leg, and the left leg was weak. There was apparently slight hypesthesia over the entire left side of the body except the face. Astereognosis and loss of muscle sense were apparent on the left. Roentgenograms of the skull were normal.

Impression.—The condition was thought to be intracranial tumor; its position was uncertain though it was thought that probably it lay in the right cerebral hemisphere.

Operations.—Owing to the confusing picture, on Dec. 7, 1921, Dr. Horrax made a right subtemporal decompression to relieve pressure and to attempt to restore vision. In the course of this procedure the right ventricle was tapped and found to be dilated. On Jan. 11, 1922, a right temporoparietal exploration was carried through by Dr. Horrax and confirmed the dilatation of the right ventricle but was otherwise negative. Believing that the clinical evidence and the ventricular dilatation could be explained on the basis of a cerebellar tumor, on Jan. 26, 1922, Dr. Horrax performed a suboccipital craniectomy. The exploration revealed no tumor, but in the course of the procedure an attempt was made to tap the left ventricle. The needle could not be introduced, and at a depth of 2.2 cm. from the surface of the left occipital pole a definite solid mass was encountered. Following recovery from this procedure and guided by the collapsed left ventricle, on April 4, 1922, Dr. Horrax threw back a left occipital osteoplastic flap. A meningioma was exposed in this area and successfully removed.

Comment.—If a bilateral ventricular tap had been performed earlier, the position of this tumor would have been obvious at once.

CASE 5.—*Tumor of left parietal lobe with indefinite symptoms suggesting cerebellar tumor. Suboccipital craniectomy. Death twelve hours later. Necropsy revealed a tumor lying in the left parietotemporal lobe completely obliterating the left lateral ventricle.*

History.—A. D., a housewife, aged 38, was admitted on July 18, 1922, complaining of pain in the left occipital region and vomiting. The onset of the condition was abrupt and recent, the occipital headache appearing only eight weeks previously. Projectile vomiting and progressive rapid visual loss accompanied the headaches. Within the last six weeks she had had two attacks of unconsciousness without convulsions. Definite mental torpor had been noted.

Examination.—The patient was semistuporous and uncooperative, which made examination difficult and unreliable. There were painful areas over both temporoparietal regions and some suboccipital tenderness. The cranial nerves were normal except for bilateral choked disks of 3 diopters. Nystagmus was absent. The visual fields were apparently normal to hand perimetry, accurate estimation of the form fields being impossible. It was difficult to estimate the intelligence, although aphasia was apparently not present. While there were no weakness of any extremity and no pathologic reflexes or sensory changes, the gait was definitely cerebellar with a tendency to fall to the right. Romberg's sign was marked. The roentgen-ray studies of the head gave negative results.

Impression.—The condition was thought to be cerebellar tumor.

Operation.—On July 22, 1922, Dr. Cushing performed a suboccipital craniectomy. In the course of this procedure three unsuccessful attempts were made

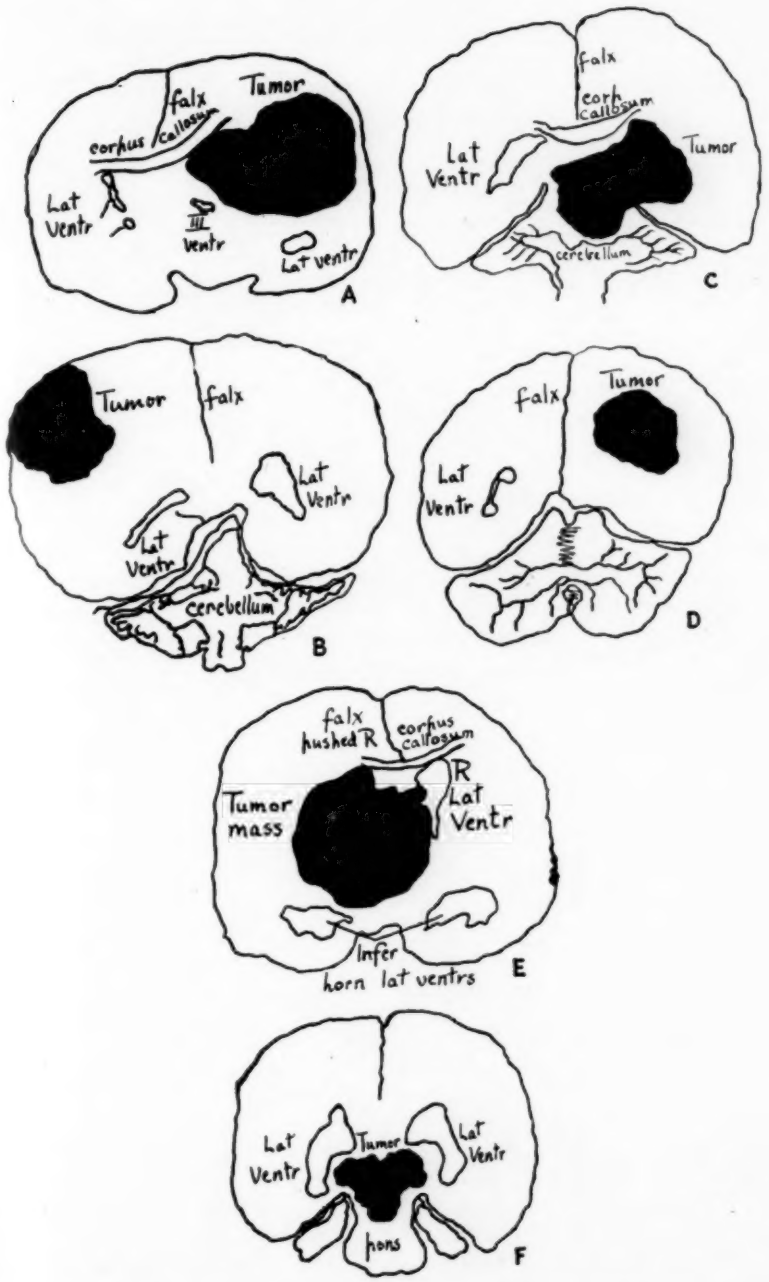

Fig. 5.—Tracings from photographs of sections of brain from material obtained at necropsy among the sixteen deaths occurring in this series. The position of the tumor and its effect on the lateral ventricles are demonstrated. Note that in all cases except *F*, a midline tumor, a bilateral ventricular tap would have shown ventricular asymmetry or the absence of bilateral hydrocephalus. In *B*, *C* and *E*, a unilateral tap would have shown a hydrocephalus and might have led to false conclusions as to the position of the tumor. Note the sagging of the tentorium in *B* and *D*.

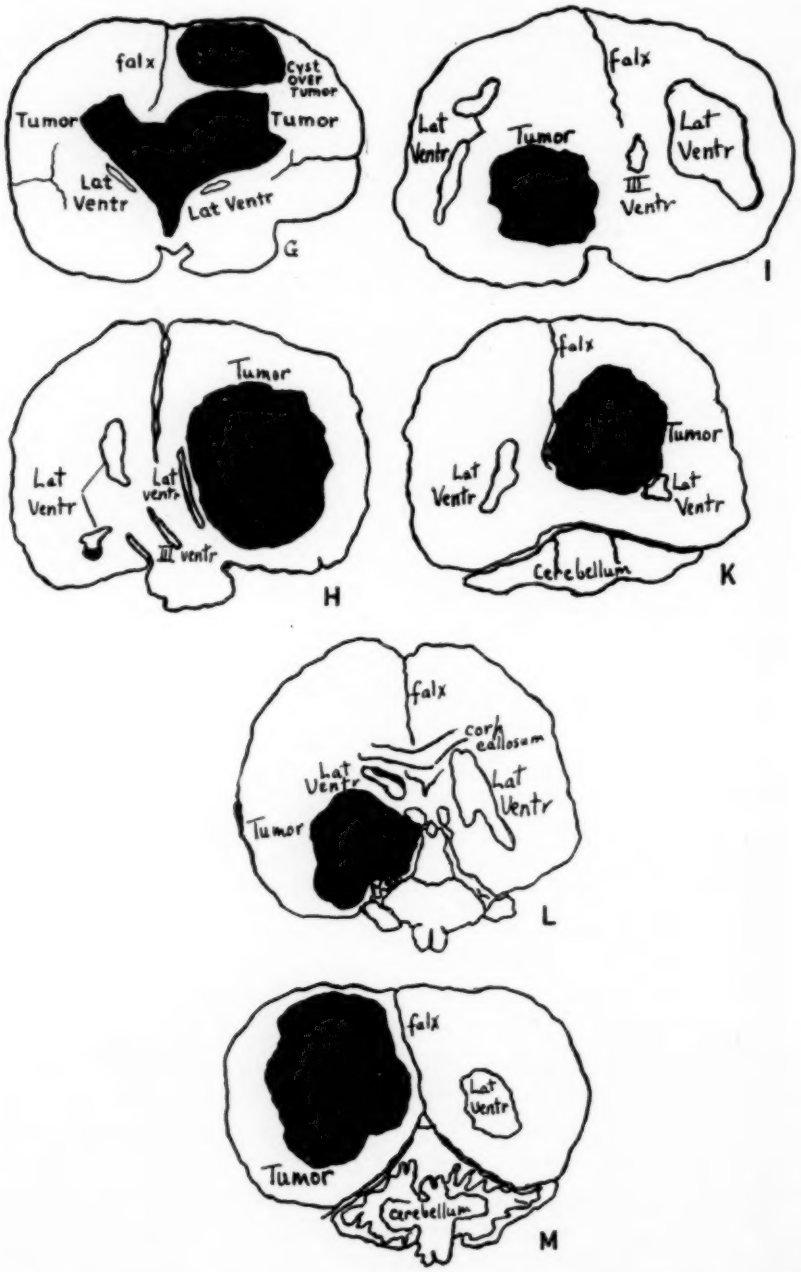

Fig. 6.—Same as figure 5. In *I*, *L* and *M*, a unilateral tap would have suggested hydrocephalus; a bilateral tap would have disproved it and localized the lesion in the cerebellum. Note the sagging of the tentorium in *M*.

to tap the left ventricle. The exploration of the posterior fossa revealed no tumor. The patient died twelve hours later.

Autopsy.—Postmortem examination revealed a large infiltrating gliomatous tumor in the left parietotemporal lobe, completely obliterating the left lateral ventricle.

Pathologic Diagnosis.—The tumor was diagnosed as spongioblastoma multiforme.

NOTE BY DR. CUSHING.—"Inability to tap the lateral ventricle should have shown that there was no posterior fossa lesion. It took two or three lessons of this kind to make me desist from pursuing a lesion in the cerebellum after a negative ventricular tap."

Although ventricular estimation may render valuable aid in the differentiation between a tumor of the cerebral hemisphere or one of the posterior fossa, nevertheless there are distinct limitations to its usefulness which must be recognized. Apparently, as pointed out by Penfield,[4] the posterior horns of the lateral ventricles may vary greatly in size, occasionally being entirely absent. This anomaly may make ventricular tap difficult and cause the operator to believe that the ventricles are either obstructed or undilated. Furthermore, certain slowly growing lesions situated lateral to the midline in the posterior fossa, for example, an acoustic neuroma, may interfere so gradually with the circulation of the cerebrospinal fluid that only slight ventricular dilatation results. Under such circumstances, if the clinical symptoms are not definite and if recourse is had to a ventricular estimation to clear up the situation, an entirely erroneous impression of the position of the lesion may be gained, for a failure to reach the ventricle should always suggest a cerebral tumor. The observations at ventricular estimation must be clearcut and positive. Definite evidence of bilateral dilatation, or unilateral dilatation with obstruction on the opposite side, should be present for this procedure to be of determining diagnostic value. If doubt as to the position of the lesion still exists after an attempted tap, a ventriculogram may be performed, although this procedure is attended by increased risk to the patient.

SUMMARY

An analysis of this group of cases in which an error in diagnosis between lesions of the anterior and posterior fossae was made seems to show definitely that in the presence of marked intracranial pressure clinical evidence commonly indicative of a cerebellar lesion may be present although the tumor lies elsewhere. Many well recognized cerebellar symptoms—nystagmus, asynergia, ataxia, a positive Romberg sign, tinnitus, deafness, suboccipital tenderness and occipital headache—may

4. Penfield, W.: Cerebral Pneumography; Its Dangers and Uses, Arch. Neurol. & Psychiat. **13**:80 (May) 1925.

under these circumstances accompany a cerebral lesion. The history of the case may strongly suggest a cerebellar tumor, since evidence of increased intracranial tension appears early in the story and with it a cerebellar response. Always beneath these cerebellar symptoms and masked by them lurk definite indications of cerebral involvement. The difficulty lies in our inability to determine on which set of symptoms to lay the most stress. Under these conditions a determination of the size, shape and position of the lateral ventricles will clear up the uncertainty. Undilated, or asymmetrical, ventricles are always indicative of a cerebral hemispheric lesion if increased intracranial pressure exists. Once ventricular asymmetry is surely demonstrated, the confusing clinical symptoms may be interpreted safely on the basis of a cerebral lesion.

CONCLUSIONS

1. A small yet significant percentage of cases of tumor exists in which it is difficult from clinical evidence alone to determine whether the lesion lies above or below the tentorium, for marked intracranial pressure from a supratentorial lesion may produce many symptoms of involvement of the posterior fossa by pressure from above on the cerebellum.

2. Consequently, if there is reasonable doubt as to the exact position of the tumor, whether above or below the tentorium, too great emphasis cannot be laid on the necessity of estimating the size and position of the cerebral ventricles.

3. In the majority of cases this can be determined by bilateral puncture of the posterior horns early in the course of an operation, although errors in interpretation of the symptoms may occur. If there is still reasonable doubt, recourse must be had to a ventriculogram. It seems safer, however, to try to derive information from ventricular tap before a ventriculogram is attempted because of the greater risk attached to the latter procedure.

4. As suboccipital craniectomy in the presence of a supratentorial tumor carries a mortality approximately four times as great as does this procedure when a subtentorial lesion is present, it is essential to be certain of the position of the tumor before the exploration is attempted.

TUMORS OF THE NERVUS ACUSTICUS

SIGNS OF INVOLVEMENT OF THE FIFTH CRANIAL NERVE*

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EXCEPTIONAL SYMPTOMS

Tumors arising from the eighth cranial nerve produce a clinical syndrome so well known as not to need further description. Cushing,[1] in his monograph on the subject, has covered the clinical symptoms comprehensively, and has established the relative constancy of the various signs and symptoms both in degree and in order of appearance. There are, however, certain interesting variations from the average law referable to involvement of the various cranial nerves other than the eighth. For example, involvement of the seventh cranial nerve usually brings about simple weakness of the muscles of expression on the side affected. In the majority of cases it is slight and indicated only by asymmetry in the lower facial muscles that is not at all conspicuous or remarkable. A rare sign of involvement of the seventh nerve is facial spasm or twitching that may appear early and dominate the whole clinical picture. This was present in only one of Cushing's thirty cases and, appearing as it did during the early stages of the disease before other signs were manifest, was a striking phenomenon. Such a variation from the common clinical picture, if not understood as a rare manifestation of the disease, may lead to error in diagnosis and some mystification as to the pathologic process at work. Just as rarely may the tumor affect the fifth cranial nerve and produce a symptom that is equally puzzling because of its unusual character. The following report of a case in which symptoms of tumor of the acoustic nerve were obscured by the syndrome of major trigeminal neuralgia illustrated this feature and led to a search for similar examples among the cases of tumor of the eighth nerve seen at the Mayo Clinic. An attempt was also made to establish the general syndrome of involvement of the fifth nerve in this group of cases.

REPORT OF A CASE

CASE 1.—A man, aged 36, came to the Mayo Clinic, Nov. 17, 1923, complaining of pain in the lower lip and jaw on the right side. Five years before, when he was examined for the army, slight deafness was discovered in the right ear. Occasional tinnitus on that side, never lasting more than an hour or two, had appeared from time to time. Three years previously the right lower third molar

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* From the department of Neurology, Mayo Clinic.

1. Cushing, Harvey: Tumors of the Nervus Acusticus, Philadelphia, W. B. Saunders Company, 1917, 296 pp.

was extracted because of aching and, although some roots were left behind, the pain was relieved. A year later sudden sharp pains appeared at the site of extraction. These were intensely severe, and the patient described them as like those caused by a "hammer" or "dental drill." Usually they lasted from thirty to sixty seconds but came in paroxysms, were aggravated by talking, eating and laughing, and were relieved when the patient lay down. After the patient had suffered for a week, the roots of the extracted tooth were removed and again complete relief was obtained which lasted for two years. Four months before the patient's first visit to the clinic the pain reappeared with increased intensity, this time in the right side of the lower lip and chin. The right lower canine tooth was extracted without any appreciable influence on the pain. The pain as before was paroxysmal, sudden in onset and rarely lasted more than sixty seconds; the paroxysms were initiated by talking, eating, and by washing and shaving the face. There was a small "trigger area" over the right lower lip and touching it immediately initiated a severe paroxysm of pain. An attack lasted about a week; the pain was worse during the activities of the day and seldom appeared at night. Pain disappeared for a few weeks; it then reappeared and persisted up to the time of examination. The day previously he had had about 200 paroxysms and had been unable to take any nourishment or even talk.

Examination.—The patient was a well developed, healthy looking young man obviously suffering from pain. His hearing was 6/15 on the right and 15/15 on the left by the watch test. There was a slight horizontal nystagmus that was unsustained; otherwise the examination gave negative results. There was no change in sensation over the face; the corneal reflex was present and equal on the two sides, and there was no motor weakness of the muscles of mastication.

Treatment and Course.—A diagnosis of trifacial neuralgia was made, and injection of the third division of the fifth nerve with alcohol was advised. Relief was obtained for six months; when the pain reappeared, a second injection was given elsewhere with relief for only three months. Pain then appeared in the second division of the fifth nerve in the roof of the mouth and upper jaw on the right side. There was the same relationship to external stimuli and activities involving the jaws, tongue and facial muscles as with pain in the third division. Several injections were given into the second and third divisions of the fifth nerve with complete relief for seven months. A mild recurrence was relieved by injection. The last injection was given five months before the second visit to the clinic when the patient was still free from pain.

The complaints on the second visit, Feb. 12, 1926, were completely different and changed the whole aspect of the case. Four months previously the patient had experienced nausea on arising in the morning and had vomited the morning meal on numerous occasions. Later, nausea and vomiting were so persistent that he became too weak to leave bed. Vertigo appeared soon after and continuous tinnitus with increase of deafness in the right ear. Headache was not present.

Second Examination.—There was horizonal and rotary nystagmus and weakness of the muscles of mastication on the right side. On that side the corneal reflex was greatly reduced. There were no subjective or objective sensory changes in the area of the fifth nerve on the right. Total deafness was present in the right ear; there was no response to caloric stimulation on that side but good response from the left side. The patient was slightly ataxic but equally so on both sides, and general weakness contributed to the ataxia. There were no

changes in the eyegrounds. The facial expression was normal, and the tendon reflexes were equal on the two sides. Tumor of the acoustic nerve on the right side was diagnosed.

Operations and Course.—A first-stage cerebellar exploration with decompression was performed Feb. 20, 1926. The patient had respiratory difficulty during the operation, and the proceedings had to be curtailed. A week later, the wound was opened and when the cerebellar lobes were elevated, a smooth oval tumor about 4 cm. in length and 3 cm. in diameter was encountered in the right cerebellopontile angle. Intracapsular enucleation was performed. Microscopic examination of the tumor showed it to be neurofibroma. The patient did not do well after operation and died on the third day from respiratory failure. Only partial necropsy was permitted, and it was necessary to remove the cerebellum and brain

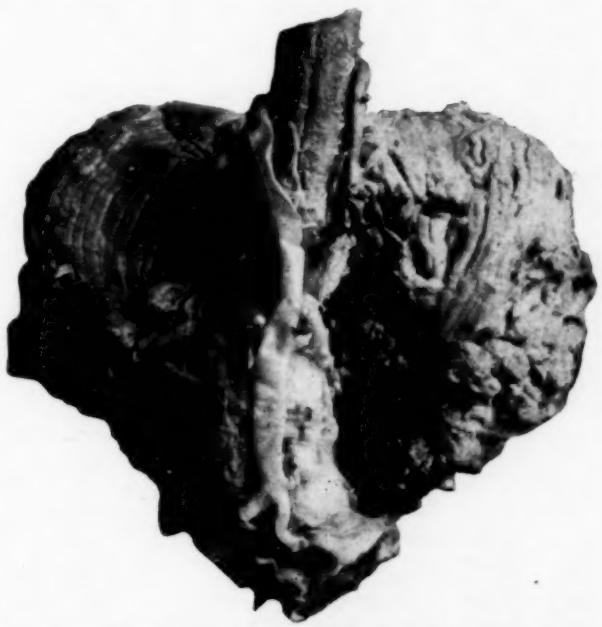

Fig. 1 (case 1).—Cerebellum and brain stem showing remains of neurofibroma of the right acoustic nerve after intracapsular enucleation.

stem through the operative wound with no opportunity to study the relationship of the tumor to neighboring structures (fig. 1). It was possible, however, to remove the petrous portion of the temporal bone on both sides; on the right side there was a marked dilatation of the porus acusticus. Histologic study of the tumor removed at necropsy verified the operative diagnosis of neurofibroma (fig. 2).

Comment.—The complaint uppermost in this patient's mind was the severe pain, for which he demanded speedy relief. Actually, there was no other complaint, since the slight degree of deafness and occasional tinnitus were matters of little concern to him, and these symptoms were elicited only by questioning. There was only slight nystagmus, and

objective signs of involvement of the sensory, motor or reflex function of the fifth nerve were not found. The signs of tumor at the time of the first examination were therefore slight and not enough in themselves to attract attention. What threw the observer completely off the track of a correct diagnosis was: (1) failure to recognize such pain as a possible symptom of tumor of the nervus acusticus, and (2) the fact that the pain syndrome was identical with that usually called major trigeminal neuralgia or tic douloureux and considered diagnostic of that disease. It was not recognized that the syndrome in all its essential

Fig. 2 (case 1).—Tumor of the acoustic nerce. A typical neurofibroma.

features could be produced by any disease other than trigeminal neuralgia. Cushing, in his series of thirty cases, has called attention to slight neuralgic discomfort in four, but in none of these was the pain like that of major trigeminal neuralgia. He did not consider this syndrome likely to occur in the course of development of neurofibroma of the acoustic nerve. The cases described by Weisenburg,[2] Krause[3] and

2. Weisenburg, T. H.: Cerebellopontile Tumor Diagnosed for Six Years as Tic Douloureux, J. A. M. A. **54**:1600 (May 14) 1910.

3. Krause, Fedor: Operationen in der hinteren Schädelgrube, Arch. f. klin. Chir. **81**:40, 1906.

Lexer,[4] wherein neuralgia pains had occurred during the development of cerebellopontile angle tumors, differed in that the tumors in question were not neurofibromas. Weisenburg's case resembled closely the one here described, but in this instance the tumor was a sarcoma and apparently did not arise from the eighth nerve.

On the occasion of the patient's second visit the general complaint and observation presented a changed clinical picture. At this time there could be no reasonable doubt that he was suffering from a tumor of the acoustic nerve. For the purpose of verification of the records, although he was free from pain, he was questioned rather closely corncerning the character of the previous suffering. The description tallied exactly with that which he had given before, precluding any doubt that the symptoms had been suggested by the examiner.

It is easy to understand why the patient suffered from pain with such a lesion, but the type of pain cannot be so readily explained. It is difficult to explain why superficial stimuli such as washing the face, eating, laughing, talking and touching the various trigger areas could evoke a paroxysm when the causal disease was central to the area stimulated. Corresponding to the noxious influence of superficial stimuli was the relief afforded by blocking their passage centrally by injecting the branches of the nerve with alcohol. Relief was only temporary but sufficiently lasting to be remarkable. It is strange that the pain caused by a tumor near the root and ganglion of the nerve could be relieved by injecting the superficial branches of the nerve with alcohol. It would be possible to theorize indefinitely concerning the mechanism of the production of pain in this case, and one is tempted to draw inferences therefrom in regard to other diseases of painful character, notably major trigeminal neuralgia. Unfortunately, however, an opportunity was not given to study the tumor and its relationships with the root of the fifth nerve, the gasserian ganglion and the brain stem. The only information that could be obtained was during the surgical removal of the tumor and from the examination of a necropsy specimen that was necessarily in poor condition.

ANALYSIS OF NEUROLOGIC SYMPTOMS

Fifty-three cases of tumor of the acoustic nerve were studied. Only those cases were taken in which the diagnosis had been established by microscopic study of tumor tissue obtained either at operation or at necropsy. In each case there had been a neurologic examination and a careful study to determine involvement of the fifth nerve or trigeminus. In fifty-one there was some sign of involvement of the fifth nerve.

4. Lexer, E.: Zur Operation des Ganglion Gasseri nach Erfahrungen an fünfzehn Fällen, Arch. f. klin. Chir. **65**:843, 1902.

Paresthesia.—In thirty-nine of the fifty-three cases some form of subjective sensory disturbance in the area of the fifth nerve was complained of, variously described as numbness or a tingling, prickling, creeping or burning sensation. One patient complained that half of her tongue felt as if it was "seared with weak carbolic." Another described a "dead wooden" sensation in the cheek and another a "frozen dead" feeling in the lower lip. Some patients spoke of a "drawing chafed" sensation as if the tongue were "scorched." In half of the cases all three divisions of the fifth nerve were involved; in the other half, either the second and third divisions or the third alone. Five patients described the paresthesia as the initial symptom of the disease, and it was only on repeated questioning that a history of deafness or tinnitus could be obtained from many of the others. The more recent paresthesia was sufficiently striking to obliterate the memory of previous trouble; this may have been true in the case of the five patients who insisted that signs in the fifth nerve antedated those of involvement of the eighth, as previous history of difficulty in hearing could not be obtained. As a general rule, once paresthesia had appeared, it persisted, grew more intense and extended to involve a larger area as the disease progressed. In only one case was the paresthesia bilateral; in another it was contralateral to the site of the tumor. In three cases, the paresthesia in the area of the fifth nerve was part of a complete unilateral paresthesia of the body on the side of the tumor.

Hypesthesia.—In contrast to the subjective phenomena, the objective signs were not marked. In twenty-eight cases there was some degree of blunting of sensation to pinprick, touch and thermal stimulation. In only four instances was there complete anesthesia in all three divisions of the fifth nerve; in the majority the hypesthesia was slight. There was no dissociation of pain, tactile or thermal sensibility, all three being equally affected. The symptoms of tumors of the acoustic nerve differ from those of the other types of neoplasms of the cerebellopontile angle in the slight degree of objective sensory change. Gliomas, by reason of direct infiltration of the brain stem and posterior root of the nerve, frequently produce marked anesthesia of the face. It is well to note, however, that this is not an absolute differential point since in four cases in this series there was a profound degree of anesthesia.

Motor Weakness.—In twenty-one cases there were signs of involvement of the motor tract of the fifth nerve. It was relatively severe in only five cases, and in the others it consisted simply in a deviation of the jaw to the side affected or in a relative diminution in tension of the temporal and masseter muscles.

Change in Corneal Reflex.—In fifty-one cases the corneal reflex on one or both sides was diminished or lost. In six cases it was the only

evidence of involvement of the fifth nerve. In seven cases the reflex was diminished bilaterally, and in the remainder it was homolateral. Therefore, change in the corneal reflex represents one of the most valuable signs in the differential diagnosis and localization of acoustic tumor.

Pain.—In only four cases in the entire series was there any disturbance of sensation which could be described as pain. In many others there was disagreeable paresthesia, but for obvious reasons it could not be included in the category of pain. Nevertheless, it is hard to know the point at which unpleasant paresthesia ends and pain begins; for example, the dividing line is notably vague in cases of thalamic lesions. One of the four cases has already been described. It is the only case in which pain was a dominant and persistent symptom and played any great part in the syndrome of the disease. In the remaining three, pain was only transitory and not conspicuous during the course of illness.

ILLUSTRATIVE CASES

CASE 2.—A man, aged 33, had been deaf for fifteen years. Nine months previously he had experienced sudden electric, shocklike pains radiating from the temporal region into the cheek and upper and lower jaws. Although momentary in duration, the pains were extremely severe. Pain could be initiated by stooping or by rubbing the beard the wrong way; the condition persisted for five months and then disappeared to be replaced by a "drawing numb" sensation in the same area.

CASE 3.—A woman, aged 46, had been deaf and had had tinnitus for eight years. Pain appeared six months before death, but lasted only four weeks and was replaced by a sensation of numbness. The pain was described as burning, constant and severe, and involved the forehead, orbit and upper jaw. It was not present at the time of examination, nor were there any marked objective sensory changes.

CASE 4.—A woman, aged 32, had been deaf for eighteen months and for as long had complained of a constant sensation of dulness and thickness in the right occiput. Occasionally, burning, tingling pains like "neuralgic toothache" would radiate from this area into the right temporal and malar regions. There was also numbness in the right side of the face and tongue. Pain was neither severe nor persistent and played a small part in the general complaint.

COMMENT

Pain, except in the few instances mentioned, was not a common symptom in this series of cases of tumor of the acoustic nerve. Likewise, in only four cases in Cushing's series was there any complaint of pain, and in none of them was pain conspicuous, persistent or at all like that in major trigeminal neuralgia. Case 1 in this series represents therefore a rare exception, but none the less one to be kept in mind.

Symptoms of irritation or compression of the fifth nerve in one form or another play a considerable part in the history of one patient with neurofibroma of the acoustic nerve. Considering how the nerve

is elongated, flattened and distorted and how deeply the pons may be indented by such a tumor, there are usually remarkably few symptoms. An attempt was made to correlate the degree of symptoms of the fifth nerve with the varying size and site of the tumor and its anatomic relation to the nerve and to establish individual peculiarities responsible for variation in degrees of dysfunction. Seven brains removed at necropsy in cases of acusticus neurofibroma and hardened in formal-

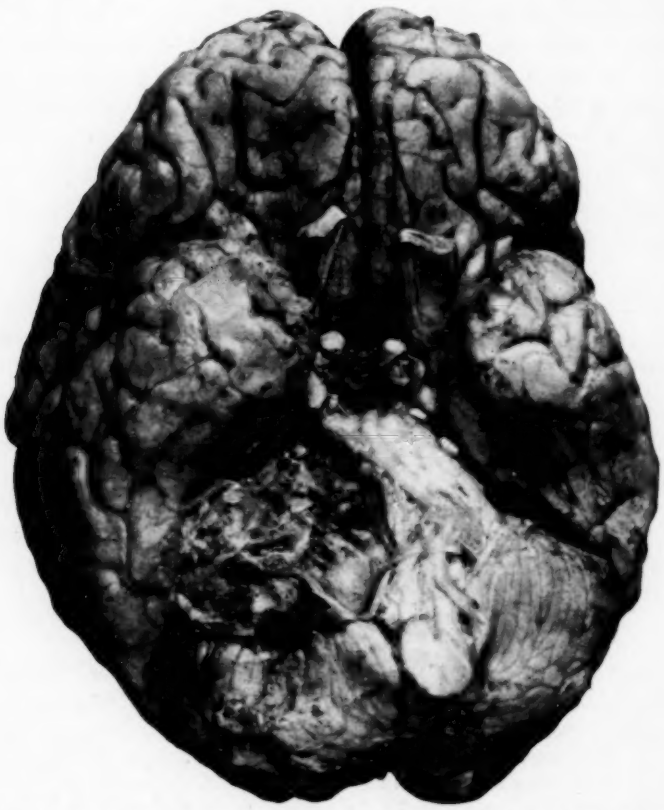

Fig. 3.—Neurofibroma of the right acoustic nerve. The patient had no symptoms referable to the fifth nerve. Objectively, there was no anesthesia in the area supplied by the nerve or weakness of the muscles of mastication. The corneal reflex was diminished bilaterally.

dehyde were examined grossly. Specimens were selected from cases in which there had been little if any antemortem intervention. It was disappointing that a definite association could not be found between the variation in the size, shape and site of the tumor and the clinical symptoms (figs. 3 and 4). In each instance the fifth nerve was elongated and flattened and pushed out of its normal relationship as shown in the diagrams in Cushing's monograph. As can be seen in figures 3

and 4, although the tumor is large and there is great distortion of the nerve and compression of the pons, there may be relatively few symptoms of disturbance in the function of the fifth nerve. The reverse holds true, in that tumors of almost identically the same size, shape and site may give rise to severe signs of injury to the fifth nerve, although the anatomic changes are apparently of the same degree and kind. Other

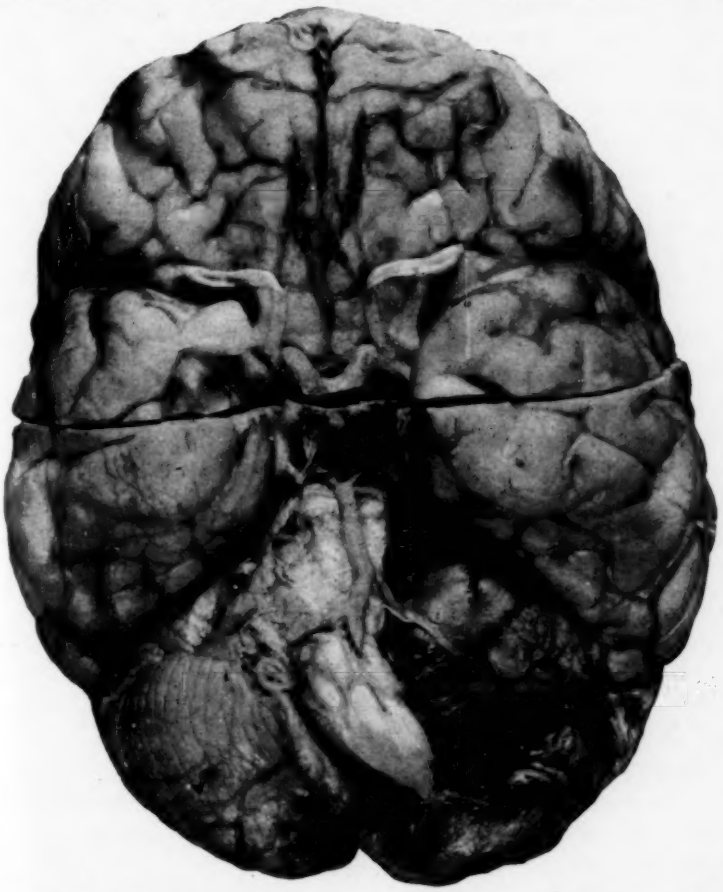

Fig. 4.—Neurofibroma of the left acoustic nerve. The tumor was about the same size as that in figure 1. There was marked sensory loss for pain, tactile and thermal stimuli over all three divisions of the left fifth nerve as well as almost complete paralysis of the muscles of mastication.

factors must therefore be present which cannot be estimated on gross examination.

The aim of the clinician is to recognize as early as possible a disease that in its later course may be irremediable. The most favorable period for surgical removal of neurofibroma of the acoustic nerve is at the earliest stage that it can be recognized. Deafness, tinnitus and vertigo

are relatively common symptoms. In many patients these symptoms may never mean anything more than that inflammatory or toxic influences are acting on the eighth nerve which, in the majority of cases, run a benign and self-limited course. On the other hand, in all of these cases there is the possibility that the symptoms represent the initial phase of a slowly growing tumor, and it is often difficult to exclude it even though there may be no other symptoms. Suspicion of the existence of a tumor is changed to certainty when the growth has reached a size sufficient to encroach on the neighboring cranial nerves or even on the brain stem. It is at this stage that signs of involvement of the fifth nerve, possibly in the form of mild paresthesia or slight diminution of the corneal reflex, begin to make their appearance and therefore become of the greatest significance in distinguishing a relatively benign condition from the more serious one of tumor. These signs appear relatively early, are easily recognized, and their correct interpretation is invaluable in making an early and correct diagnosis while there is still hope for the patient.

SUMMARY

An analysis was made of fifty-three proved cases of tumor of the acoustic nerve, especially with regard to involvement of the fifth nerve.

In all except one of these cases there was some sign of involvement of the nerve, and these signs were second in importance to those of injury to the eighth nerve.

Paresthesia was common, and in five cases it antedated the symptoms of involvement of the eighth nerve. Objective signs of involvement of the nerve such as anesthesia and weakness of the muscles of mastication were less marked. Disturbance of the corneal reflex was present in fifty-one cases.

Pain occurred in four cases, but in only one was it conspicuous. In this case the type was identical with that of major trigeminal neuralgia, pursued the same course and was temporarily relieved by the same methods as are used in that disease.

LESIONS IN THE BRAIN IN DEATH CAUSED BY FREEZING *

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CHICAGO

Death caused by freezing is thought to occur without anatomic changes. Delafield and Prudden [1] say that "while exposure of the entire body to cold may cause death there is nothing characteristic in the postmortem findings." There is "a general reduction of the activity of the body functions and cerebral ischemia with slowed respiration, low blood pressure and pulse rate, great somnolence and ultimately coma." McCallum [2] says:

> With prolonged exposure to extreme cold there is at first excitement and unrest but later the skin becomes livid and pale, blood is driven back into the interior of the body, the temperature sinks, metabolism is slowed in all of the organs and their activity consequently reduced. The respiration becomes shallow and the pulse small and weak, the temperature still sinks and when it reaches 20 to 18 C. the heart stops beating and death follows. Nothing distinctive is found at autopsy.

Stengel and Fox [3] claim:

> Freezing the body as a whole leads to death not by damage to the heart or respiration especially but by a depression of all the metabolic processes and the inability of the heat center to accommodate itself to the excess radiation. After death the only changes found are peripheral ischemia and internal congestion, at times with hemorrhage.

Krehl and Marchand [4] say:

> The postmortem findings are not characteristic although the symptoms indicate an apoplectic death which may be explained by the hyperemia of the brain and its meninges. Death is due to the slowing of the vital processes.

In a postmortem examination of the body of a man who apparently had frozen to death, I found certain lesions which seemed as though they might have been the result of freezing and might readily be one

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* From the Laboratories of the State Psychopathic Hospital, Iowa City, Director, S. T. Orton, M.A., M.D.

1. Delafield, F., and Prudden, T. M.: A Text-book of Pathology, New York, William Wood & Company, 1925, p. 11.

2. McCallum, W. G.: A Text-book of Pathology, Philadelphia, W. B. Saunders Company, 1925, p. 383.

3. Stengel, A., and Fox, A.: A Text-Book of Pathology, Philadelphia, W. B. Saunders Company, 1921, p. 28.

4. Krehl, and Marchand, F.: Handbuch der allgemeinen Pathologie, Leipzig, S. Hirzel, 1908, p. 129.

factor in causing death. Following this, I froze a rabbit and a guinea-pig and found the same lesions. This paper contains a report of these observations.

REPORT OF CASE

History.—On March 8, 1926, I performed a postmortem examination on the body of a man who had been an inmate of a county poor farm, but who had run away the previous day and had been found dead on the side of the road that morning. The body was said to have been found lying on its back with the right shoe off and the pants badly torn. The preceding night had been very cold; the body was frozen hard, and the scalp was frozen to the ground and was torn in several places when the body was moved. The patient was said to have been insane for several years and had formerly been in the Mt. Pleasant State Hospital, Iowa. It seemed probable that he was demented and had escaped from the poor farm, had bruised and scratched himself and torn his clothes, had sat down to remove the shoe from an injured foot, had gone to sleep and froze to death. He had escaped and run about in a similar manner about two weeks before and old abrasions were present, probably from injuries received at that time.

Efforts to obtain the social history of this man were not fruitful. His age was 59; he was unmarried, and there was a history of "nervousness" in the family, but no other insanity. In 1888, when he was 21, it was said that he had had a sunstroke while working in a hay field and that he had never fully recovered and had been mentally unbalanced until the time of death. He was committed to the Mt. Pleasant State Hospital in 1894. A letter from the superintendent of this institution stated that he had been committed there on four different occasions. "We found under his last commitment that the diagnosis was chronic mania, but he was referred to on a former occasion as having a case of mental deficiency, so we presume his was a case of psychosis with mental deficiency."

Autopsy Protocol.—The body was that of a white man from 55 to 60 years of age. He was well developed and well nourished. The top of the head was bald, but there was a fringe of gray hair about the ears. The body was cold but no longer frozen. There was little postmortem rigidity except in the fingers. The face, head, neck, both hands and both feet were a livid purple. There was no edema of the face, hands, genitals or feet, except in a localized area over the dorsum of the right foot, which was the one from which the shoe had been removed. The foot also presented an old ulcer measuring 2 by 3 cm. over the mesial surface of the tarsometatarsal joint of the great toe and a recent abrasion over the fourth toe. The left foot presented a small superficial abrasion over the mesial surface of the tarsometatarsal joint of the great toe and an old ulcer measuring 1 by 2 cm. over the lateral surface of the heel. There were numerous recent scratches over the shins, thighs and both lateral and mesial surfaces of both legs. The skin had been broken on the second finger of the right hand for a distance of 5 cm., and there were numerous smaller scratches on both hands. There was a superficial abrasion over the middle of the frontal area of the skull, measuring 2 cm. in diameter. Over the occiput, covering an area 10 cm. in diameter, were numerous small abrasions. This was said to be the area where the scalp was frozen to the ground. There appeared to be a depression in the midline of the skull about 6 cm. above the occipital protuberance. There had not been any bleeding from the ears, although the left one was bruised. There was no blood in the mouth, the upper teeth were missing and the lower ones were in a poor condition. There was no blood in the nares. The eyeballs were covered

with a bloodstained film. The pupils were round and equal. There was a questionable healed scar on one side of the prepuce. The lymph glands were not palpable.

The abdomen presented nothing remarkable. Both pulmonary apexes presented healed scars and were bound by adhesions to the pleural wall. There were easily torn adhesions between the right lower lobe and the posterior pleural wall and the mesial surface of the right lung and the mediastinum. There was slight congestion of the dependent portions of the lungs. The heart was not remarkable, except for slight thickening of the mitral and tricuspid leaflets and a few small plaques in the aortic valves and the base of the aorta. There was a large white area, 2 cm. in diameter, over the upper right pole of the liver, which extended into the substance of the organ for about 2 cm. Both kidneys were small; the capsules were adherent and tore the kidney substance on stripping.

An incision in the head was made over the occipital dome from ear to ear, and the scalp was pulled back from the skull. The abrasions were found to be superficial and did not extend to the underlying soft tissues. There was no hematoma. The calvarium was removed in the usual way. There was no fracture over the vertex. The depression that has been described was part of the normal contour of the skull. There was no extradural or subdural hematoma. When the dura was incised and removed, a condition presented itself which is commonly described as "serous meningitis" or "wet brain" and is ascribed to alcoholism or exposure. The pial and arachnoid tissues were distended with fluid and milky areas in the pia, common in brains of persons at that age, were lifted from the brain and gave the appearance of a fibrous exudate. As the fluid seeped out of the arachnoid tissues, the organ soon appeared normal in size, markings and all external appearance except that there was general congestion. There was no evidence of contusion. The vessels were not sclerosed. There was no fracture at the base of the skull. The mastoid sinuses and middle ears were free from infection.

Anatomic Diagnosis.—The anatomic diagnosis was: numerous recent antemortem bruises and abrasions of the head, hands, feet and legs; lividity of the head and extremities; serous meningitis; moderate senile arteriosclerosis with atheromatous patches in the aorta and slight marginal thickening of the mitral and tricuspid valves; chronic arteriosclerotic nephritis; healed tuberculosis of both pulmonary apexes; moderate fibrous pleural adhesions; scar in the liver; moderate epiploic adhesions; healed scar of the penis.

Microscopic study of the trunk tissues showed a slight amount of hypertrophy of the cells and a little brownish pigmentation of the nuclear poles in the cardiac muscle. There were a little fibrosis and a few small areas of lymphocytic infiltration. One moderate sized vessel contained a slightly granular mass described by some authors[5] as hyaline thrombi occurring in death by freezing. However, it appears to me, as it has to others,[6] that these apparent thrombi are artefacts produced by the separation of the blood cells from the serum in the larger vessels and the precipitation of the serum by the fixative. They did not show any relation to the lesions to be described, which are usually to be found in association with the smaller vessels, while the thrombi are seen in the larger ones. The lungs

5. Aufrecht: Deutsch, Arch. f. klin. Med. **117**:602, 1925. v. Recklinghausen, und Hodara: München. med. Wchnschr. **43**:341, 1896. Kriege: Virchows Arch. f. path. Anat. **116**:64, 1889.

6. Foord, A. G.: J. Infect. Dis. **23**:159, 1918. Smith, L.; Ritchie, J., and Dawson, L.: Pathology of Trench Frost Bite, J. Path. & Bact. **20**:159, 1915.

showed a patchy congestion, some areas being severely congested and showing a slight edema, while others were free. There was moderate thickening of the pleura. In the liver, the white area described in the gross protocol was seen to be an angioma. The hepatic tissue showed a little congestion and fatty changes. The spleen appeared normal, except that one vessel contained one of the so-called hyaline plugs. Some of the renal glomeruli were congested; there was some scarring, some of the glomeruli being entirely replaced, and there was a little subcapsular lymphocytic infiltration. The testes appeared normal.

Fig. 1.—A Betz pyramidal and adjacent nerve cells of the motor area of a human being who froze to death, showing the vacuolization of the cytoplasm; toluidine blue stain.

The Nervous System.—The brain was studied by the following methods: toluidine blue, eosin-methylene blue, phosphotungstic acid hematoxylin, scharlach r, and the Marchi method.

Diffuse changes were found in the precentral, postcentral, frontal, temporal, occipital and hippocampal gyri. The changes in the cortex were of both acute and chronic types. There were no chronic vascular changes. The cellular content of all layers of various parts of the cortex was good. There was, however, a definite increase in the number of satellite cells about some, but not all, of the nerve cells of the deeper layers. There was little definite neuronophagia but individual nerve cells were surrounded by a circle of inactive satellites. This

condition has been recognized by Orton[7] as characteristic of chronic psychoses without diagnostic significance for any one type. There was considerable lipochrome pigment in the larger Betz cells, which may have been associated with the age of the man as well as with the psychosis. A few of the cells stained poorly, showing only a shadow of the normal. The majority of the cells, however, had taken the stain well and had a good chromatin content. In spite of the absence of definite chromatolysis, however, the cytoplasm of all nerve cells showed a severe pathologic change. There seemed to have been vacuolization of the cytoplasm giving the appearance of large clear globules, especially at the

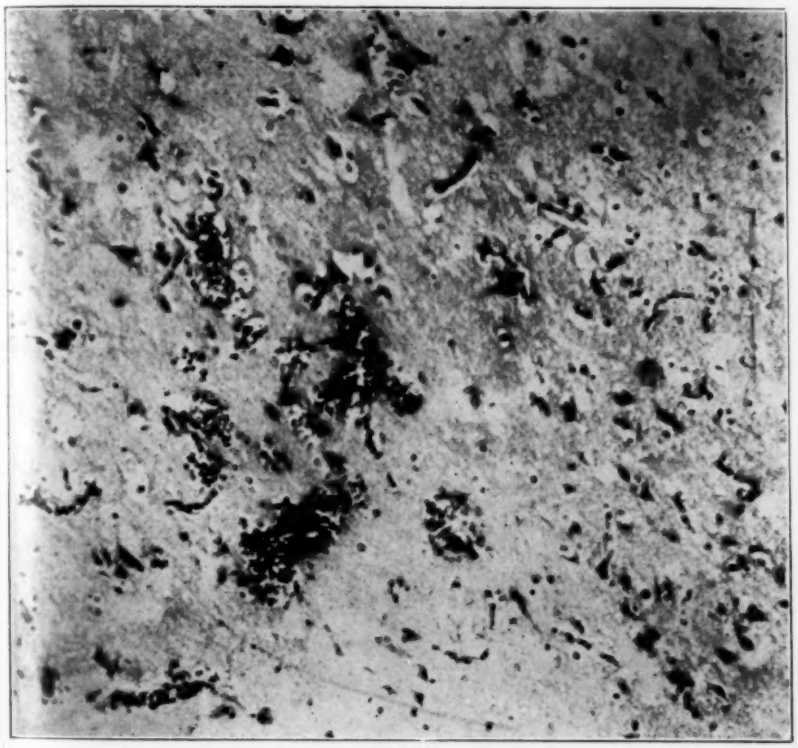

Fig. 2.—The cerebral cortex from the frontal lobe of a human being who froze to death, showing miliary hemorrhages. Phosphotungstic acid hematoxylin stain.

periphery of the cell, so that the outline of the cell body was irregular (fig. 1). These vacuoles did not stain with the fat stains. This had occurred in nerve cells of all types, from the large Betz cells to the smallest cells. In addition, the nuclei tended to be somewhat shrunken. Besides this, small hemorrhages were scattered in all parts of the cortex (fig. 2). These seldom exceeded 1 mm. in diameter; many were so small as to represent merely the seepage of a few erythrocytes from the capillaries. Occasionally, larger vessels also were surrounded by extravascular blood. These hemorrhages were very numerous, many being seen in

7. Orton, S. T.: A Study of the Satellite Cells in Fifty Selected Cases of Mental Disease, Brain **36**:525, 1914.

every section examined. They were clearly recent, as there was no reaction either by softening of the surrounding tissue, by the invasion of wandering cells, by glioses or by destruction of the blood cells themselves. Around the larger hemorrhages, the tissue appeared somewhat more compact, as it tended to stain more darkly. Thrombi were not seen. In the cerebellum, similar hemorrhages were noted in the nuclear masses but none in the cortex. Many were found also in the basal ganglia, pons (fig. 3) and medulla. Here, also, the larger nerve cells were vacuolated, but they did not show such severe changes as those in the cerebral cortex.

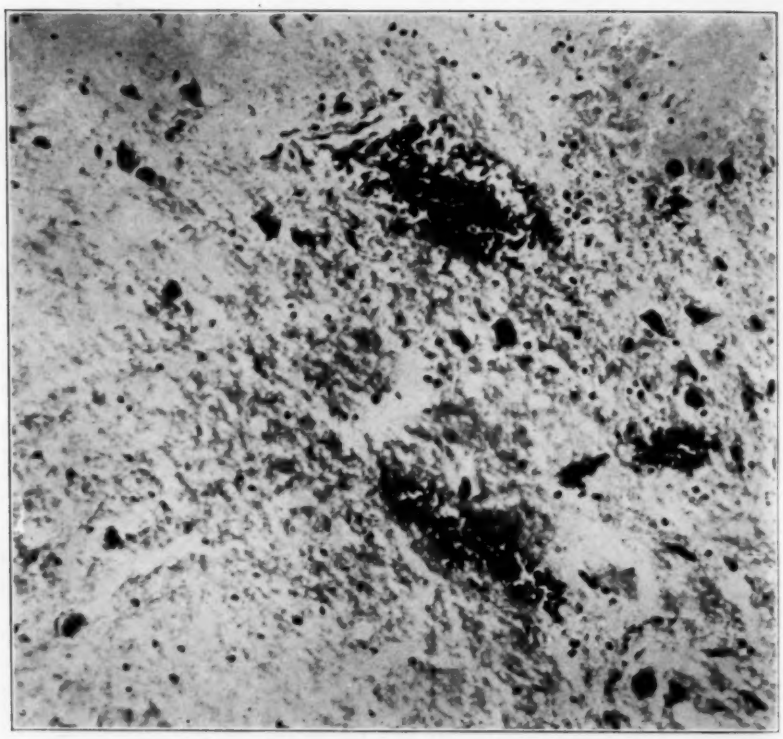

Fig. 3.—The pons of a human being who froze to death, showing miliary hemorrhages. Phosphotungstic acid hematoxylin stain.

Since such lesions had not been reported previously when death had occurred by freezing, and since multiple hemorrhages occur in certain forms of acute poisoning, such as by carbon monoxide, it seemed wise to check these observations experimentally.

REPORT OF EXPERIMENTS

A guinea-pig and a rabbit were frozen to death by packing them in a salt and ice mixture, making the necessary provision for respiration. The guinea-pig was left over night and was found the next morning nearly thawed out again, except that there were some frozen tissues deep in the abdomen. The brain had thawed

entirely. The rabbit was left in the ice and salt mixture under observation for four hours. Respiration ceased at the end of an hour and a half. When it was removed, the head, neck, chest and fore limbs were frozen solid, but the abdomen was not. The brain was removed and placed in Zenker's solution while still frozen.

Miliary hemorrhages were found in both animals in all parts of the brain. The guinea-pig also showed severe pulmonary congestion with edema and hemorrhages. All of the other tissues of the trunk appeared normal. The brain did not show other changes. The nerve cells were normal; there was no marked vacuolization.

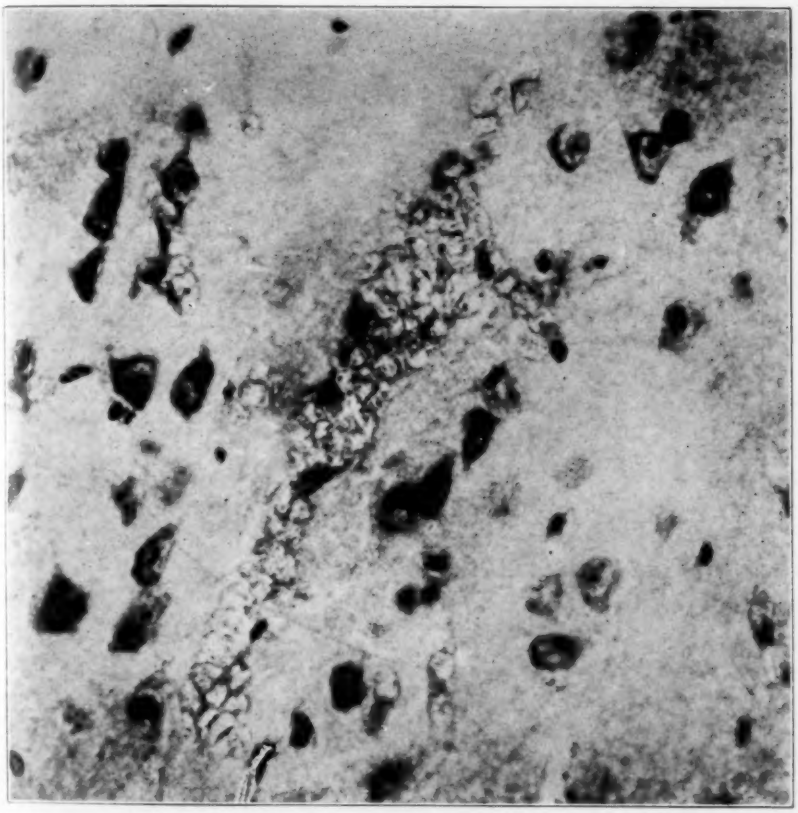

Fig. 4.—Cerebral cortex of a guinea-pig that was frozen to death, showing miliary hemorrhages. Weigert's iron hematoxylin stain.

Thrombi were not present. Small hemorrhages were found in all parts of the cerebrum (fig. 4), cerebellum and brain stem (fig. 5). In the rabbit, there were also some pulmonary congestion and hemorrhages, but this was moderate, and there was no edema. Other workers[8] in experimenting with death by freezing, especially with rabbits, have referred to pulmonary congestion and hemorrhages as the most conspicuous observations. Foord[9] claims that these hemorrhages are

8. Aufrecht (footnote 5, reference 1), Kriege (footnote 5, reference 3). Walther: Virchows Arch. f. path. Anat. **25**:414, 1862.

9. Foord (footnote 6, reference 1).

agonal and not due to the freezing. His evidence, however, is not convincing, and the agonal state in other modes of death does not commonly cause pulmonary hemorrhages. Krehl and Marchand,[4] in discussing the lesions in man, also refer to congestion in the lungs. The brain in the rabbit showed severe spontaneous encephalitis of the chronic type, which I [10] have found in nearly all experimental rabbits available in this laboratory. However, the miliary hemorrhages were identical in all ways with those seen in the brains of human beings and guinea-pigs as to their distribution, size, relation to the capillaries and absence of cellular

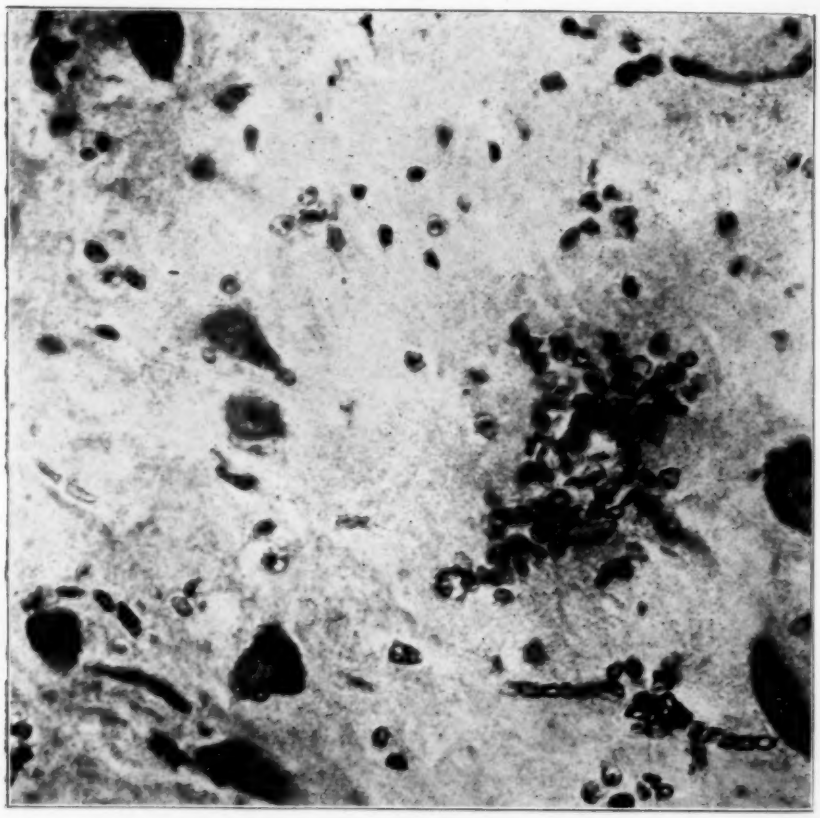

Fig. 5.—The medulla of a guinea-pig that was frozen to death, showing miliary hemorrhages. Weigert's iron hematoxylin stain.

or tissue reaction; such hemorrhages do not form a part of the pathologic picture of encephalitis.

COMMENT

The lesions of the brain here described have apparently not been observed before when death has occurred by freezing, although Krehl and Marchand [4] have stated that the "symptoms indicate an apoplectic

10. Bender, L.: Spontaneous Central Nervous System Lesions in the Laboratory Rabbit, Am. J. Path. **1**:653, 1925.

death." Lambert [11] quotes the work of Richardson (1867), who claimed that repeated freezing of a pigeon's brain produced only temporary irritative phenomena, and that a pigeon whose brain had been frozen forty-five times remained perfectly normal. Lambert points out, however, that he used ether spray on the skull in his attempt to produce a frozen condition, and it is "highly improbable that the brain was frozen at all." Jensen,[12] after being unable to account for the death of his experimentally frozen animals in any other way, claimed that it was due to changes in the nervous system, but he does not describe the nature of these changes nor does he state whether he examined the nervous system. Schack [13] claims that, aside from intracellular colloidal changes, the second most important factor in death by freezing was a disturbance in the vasomotor control of the blood vessels.

Numerous authors, especially those dealing with localized freezing, such as frostbite and trench foot, ascribe the pathologic changes and death of the parts to the vascular disturbances. Smith, Ritchie and Dawson,[14] in producing experimental trench feet in the rabbit, claim that the changes were vascular, there being a dilatation of the vessels and a seepage of the blood cells through the endothelium. Lake [15] states that in frostbite there is a "destruction of the endothelial walls of the capillaries which allows a rapid exudation of the fluids and also in some cases of the cells of the blood in the surrounding tissues." Stekelmacher found that freezing liver tissues produced the same changes as ligation of the hepatic artery: increased permeability of the cell walls, followed by similar changes in the nucleus, suggesting that the changes produced by freezing depended on the vascular disturbance.

It seems not improbable therefore that numerous hemorrhages might occur in the brain when the blood is being forced there by the peripheral ischemia. The vascular tree receives relatively little support from the soft tissues of the brain. Lambert [11] has further pointed out that:

> Morphological studies show that if a part be completely frozen all tissues give evidence of being at least temporarily injured. Shrunken nuclei and vacuolization of the cytoplasm are regularly seen and it may be stated that to cold as to other injurious agents the more highly specialized cells are less resistant.

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11. Lambert, M.: The Effect of Cold on Animal Tissues, Proc. New York Path. Soc. **12**:113, 1912-1913.

12. Jensen, H.: Einiges über den Kaltetod der Warmbluter, Deutsch. med. Wchnschr. **43**:701, 1917.

13. Schade, H.: Einzel Krankheiten der Erkaltung, Berl. klin. Wchnschr. **57**:44, 1920.

14. Smith, Ritchie and Dawson (footnote 6, reference 2).

15. Lake, N. C.: An Investigation into the Effects of Cold on the Body, Lancet **2**:557, 1917.

Since the nerve cell is one of the most highly specialized cells in the body, the severe vacuolization found in the cytoplasm of the human nerve cell is not remarkable. The fact that these changes did not appear in the nerve cells of the lower animals may be due to their smaller size, their lower grade of specialization or to shorter period of exposure to the cold.

SUMMARY

In one human being, one guinea-pig and one rabbit that were frozen to death, congestion and miliary hemorrhages were found in all parts of the brain. There was also marked pulmonary congestion. In the human brain, the nerve cells also showed severe vacuolization.

MENTAL CONDITIONS IN THE AGED*

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There is much confusion in regard to the classification of the various mental states of the senium. Terms in common use fail to define the conditions clearly and are frequently used interchangeably. In an effort to catalog these mental states, about 500 cases were reviewed from an organic standpoint, and about 100 of these were selected as a basis for this report. The vascular pathologic changes were carefully studied in the material obtained at necropsy, and it was found that all the cases fell definitely into four major groups: (1) a group in which there was sclerosis mainly of vessels of large caliber; (2) a group in which the sclerosis was mainly confined to vessels of small caliber; (3) a group in which both large and small vessels were about equally sclerosed, and (4) a group in which the vascular change was a "fibrosis" rather than a "sclerosis."

PATHOLOGIC CHANGES

The pathologic changes present in all groups can be discussed under two headings: changes in the blood vessels themselves and changes that take place in the brain tissue secondarily.

In group 1 the larger vessels are mainly involved. The usual end-result is well illustrated in figure 1, to which Marchand's designation of atherosclerosis can be applied. The lumen of the vessel is narrowed, and, as is usually the case, one part of the wall is relatively unaffected. In this vessel two atheromatous plaques are to be seen. With fat stains, it is found that a lipoidal change has already taken place, and eventually fat may entirely replace the hyperplastic tissue. In the further development of the condition, there is a breaking through of the elastic lamina, as is seen in figure 2, with marked degeneration and thinning of the media (*A*). Calcification has taken place in parts of the hyperplastic tissue (*B*). Denudation of the overlying covering of endothelial cells may occur, with resulting formation of ulcers and eventual thrombosis.

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* From the Laboratory of Neuropathology of the Philadelphia General Hospital.

† Deceased.

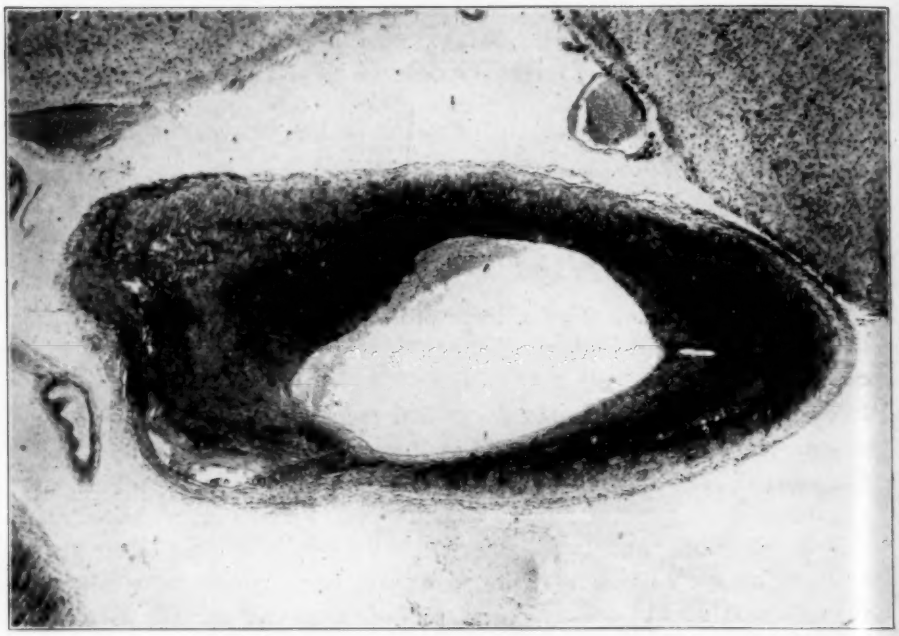

Fig. 1.—Appearance in advanced atherosclerosis.

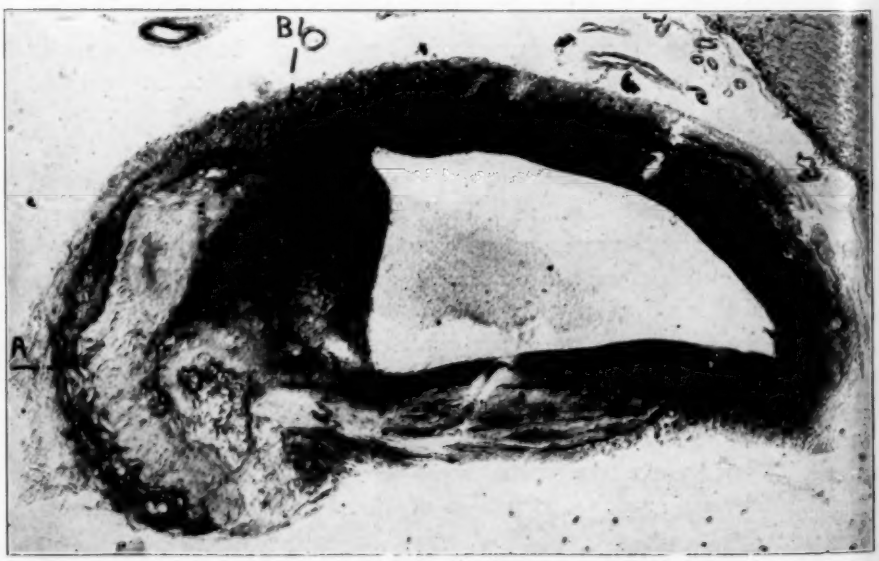

Fig. 2.—Breaking through the elastic lamina. *A* shows marked degeneration and thinning of the media, and *B*, calcification which has taken place in parts of the hyperplastic tissue.

While the primary change is hyperplasia of the subintimal connective tissue, eventually the entire wall may be involved. All this is included under the syndrome of atherosclerosis. It is in vessels of this sort that rupture or occlusion may occur and large areas of brain tissue be destroyed, with the resulting clinical picture of a "stroke."

In group 2, in which the changes predominate in the small vessels, a condition is found which has been called hyaline degeneration, or "arteriolosclerosis." This is the outstanding process in the cerebral

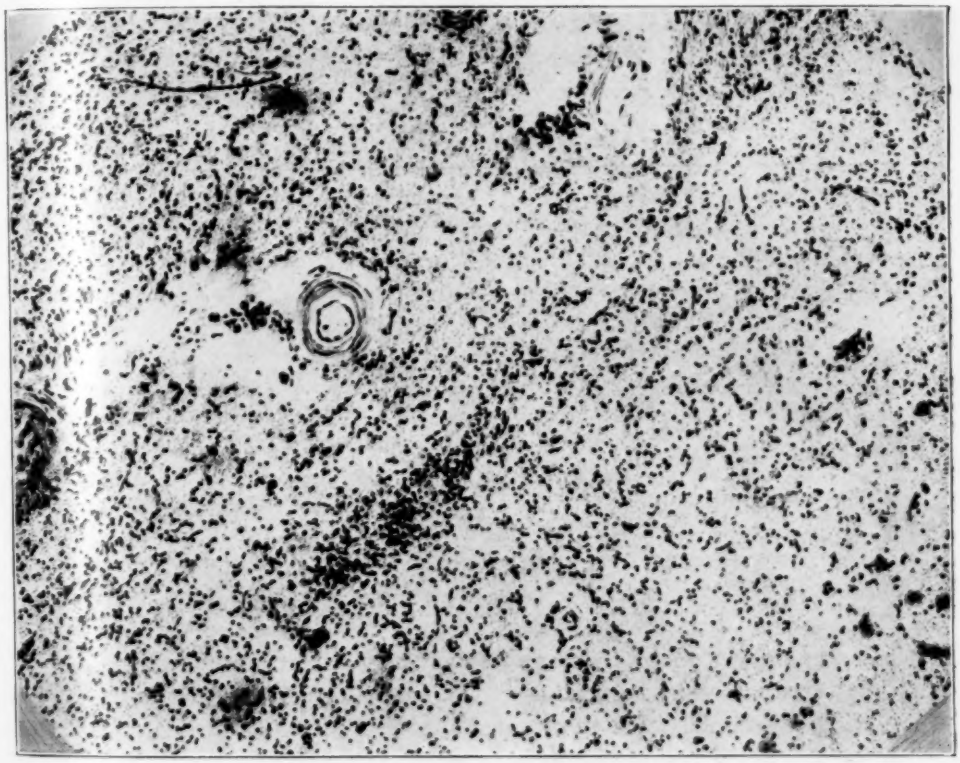

Fig. 3.—Appearance of vessels in arteriolosclerosis.

cortex and in the large gray masses at the base. The appearance of the vessels is shown in figure 3; the wall remains unstained in Nissl preparations and is highly refractile. The hyaline material is first noted under the endothelium, but gradually the whole wall becomes thickened and appears to be made up of concentric rings. The end-result is a wall without nuclei in which the individual lamellae stand out clearly.

The secondary changes that take place in the brain substance are also well shown in figure 3, in which small areas of softening with accumulations of gitter cells are noted.

After the cases were grouped according to vascular pathologic changes, the clinical features were studied and tabulated. From this analysis certain general conclusions may be drawn if one keeps in mind, however, the fact that observations on the part of relatives and friends are notoriously inaccurate and unreliable. Many details in the histories are lacking, but in spite of this the data obtained show fairly clearcut trends in certain directions and indicate sufficiently well the grouping adhered to. Many interesting tangential leads are brought to light, which must be reserved for future inquiry. For example, the fourth group, in which the pathologic change is a fibrosis of the vessel walls, includes persons who live to be very old and yet preserve their mental faculties to the end. This group lacks distinctly the clinical picture of vascular

Mental Conditions in the Aged

	Group 1 Sclerosis of Large Vessels	Group 2 Sclerosis of Small Vessels	Group 3 Sclerosis of All Vessels
Number of cases	27	13	49
Males	19	6	26
Females	8	7	23
Average age	69.6	69.9	65.3
Mental symptoms	15	10	31
Previous "strokes"	7	1	5
Onset: Gradual	6	8	7
Sudden	20	2	37
Uncertain	1	3	5
Hemiplegia: Right	13	2	18
Left	7	3	19
Blood pressure	153/96.2	145/86	174/100
Blood urea	22.5	24.6	24.3
Sclerosis of vessels: Large	27	5 slight	49
Small	1 slight	13	49
Areas of softening	24	5	35

assault, deterioration, dementia, gross anatomic changes, etc., and deserves separate consideration. It will not be included here.

The condensed table shows at a glance the most important manifestations in the first three groups.

Group 1 shows a predominance of men; this may not be of particular significance except possibly to show the results of laborious occupation. In the other two groups the sexes are about equally divided. The age incidence demonstrates a shorter life in group 3 than in groups 1 and 2. The difference in groups 1 and 2, however, is so slight as to be negligible.

The onset was sudden in 74 per cent of the patients in group 1, in 39 per cent of those in group 2 and in 75 per cent of those in group 3. The sudden onset in 74 per cent of the cases in group 1 contrasts well with the gradual onset in 61 per cent of group 2. The latter coincides roughly with the percentage of mental symptoms (77 per cent) found in group 2. Only 55 per cent of the cases in group 1 presented definite

mental symptoms, and here the manifestations of a process of deterioration developed only after the "stroke." In sclerosis of the small vessels in group 2, mental symptoms had been a part of the disease picture for a long time before hospitalization. In the histories were recorded practically a full symptom index of all the psychoses. Prior to and after admission to the hospital, such terms as the following were used to indicate the mental state: "childishness, poor memory, dementia, mental changes, senility, incoherence, confusion, instability, deterioration, hallucinations, delusions, ideas of poverty." A clearcut picture of a psychosis per se was not delineated in any history, but all patients evidenced more or less a progressive mental change of the senile type. As would be expected, the patients in group 3 show a mixture of symptoms characteristic of both groups.

Gross softening was prominent in 90 per cent of the patients in the first group, in 38 per cent of those in the second and in 69 per cent of those in the third. The blood pressure was not recorded in all cases, but in accordance with the data available it would be expected, as is shown, that the third group would demonstrate a higher average than either of the other two. The fact that the reading was higher in group 1 than in group 2 is unexplained. In regard to the estimations of blood urea, it will be noted that it was high in all cases, but highest when small vessels were sclerosed.

SUMMARY

In the cases in which the large vessels were involved, a sudden onset occurred in 75 per cent of the cases, and gross anatomic softening was found in 90 per cent. There was partial recovery with recurrent attacks in many cases. It can probably be prognosticated that either partial recovery or immediate death takes place in these cases. The mental changes found are those of a simple deterioration following the gross lesion.

In the cases in which the small vessels were sclerosed, there was a history of gradual onset in about 66 per cent, and gross anatomic softening was found in one third of them. Clinically, these patients pursue a progressive course, with few apoplectiform attacks. They have what might be termed "mental storms" from which partial recovery takes place, but which always leaves the patient a little worse than before. The mental picture is that of a true dementia.

In the patients in group 3, in whom all the vessels were sclerosed, there was a record of sudden onset in 75 per cent and gross softening in 70 per cent. There was partial recovery or a fatal issue in a short time. Recurrent attacks are recorded in only about 10 per cent. The mental changes were those of both dementia and deterioration.

CONCLUSIONS

If conclusions are based on the postmortem studies of persons with "senility," the mental changes of the aged may be divided into four groups and given a clinical appellation that coincides with the pathologic change.

The first group, in which the larger vessels showed the predominant change with a more or less uniform appearance of gross areas of softening, is to be distinguished clinically by comparatively sudden onsets of either mental or neurologic symptoms in persons who have been known to be either entirely healthy or else definitely arteriosclerotic. Hemiplegia is the commonest organic symptom, and the usual mental picture is that of deterioration. In view of these facts, it might be well to call this type arteriosclerotic deterioration, taking it definitely out of the heterogeneous group of "senile dementia."

In the second group, in which the small vessels are mainly involved, the patients are usually admitted to the psychopathic wards when they come to the hospital. They have gradually become demented, the relatives applying the term "second childhood" to the condition. While a definite history of "apoplexy" cannot be obtained, as a rule, an exhaustive anamnesis will show that there are more or less sudden attacks from which the patients make only a partial recovery. These attacks are repeated and though they are only minor the dementia progresses in steps, like going down a ladder. Anatomically, few of these cases show gross areas of softening, and even the large vessels may appear practically normal. Microscopic examinations, however, reveal multiple miliary areas of softening scattered throughout the brain. In view of the character of the onset and the clinical course, this group should be designated progressive arteriolosclerotic psychosis.

In the third group, which is a combination pathologically and clinically of the other two, there occur both deterioration and dementia, sudden apoplectiform attacks and minor mental attacks with both gross and microscopic areas of softening. This group should be called arteriosclerotic dementia.

In the fourth group, in which the vessels show only a fibrosis, the anatomicohistologic changes are comparable to the involutional changes found in other organs of the body. The patient preserves his mental faculties to the end, and death is usually brought about through some visceral disease. Marked dementia or deterioration is not found, and areas of softening are not found on gross or on microscopic examination. There may be, however, some reduction in mental energy qualitatively and quantitatively, but this is definitely proportionate to the senile changes that are found elsewhere. This condition in this group consequently should be termed senility.

The group showing marked "senile plaques" will be discussed in a later communication.

DISCUSSION

DR. DONALD GREGG, Boston: Some investigators consider three types of individuals, namely, carnivors, herbivors and mixed types. The herbivors are thought to be more prone to cardiorenal disease. In the cases studied, was there any correlation noted between the type of arteriosclerosis and the type of physique?

DR. GRAYSON P. MCCOUCH, Philadelphia: I was interested in the relation of blood pressure to the distribution of the sclerosis and would like to ask whether it is not true that in the cases in which the sclerosis is confined to the large vessels, though the mean pressure may be normal, the pulse pressure is high? That is what one would expect from a physiologic point of view. Also one would expect, of course, the high pressures in the cases in which the peripheral resistance is raised by the sclerotic process in the small vessels, assuming that that process is generalized and not merely confined to the brain. One would also expect that in the lesions in the small vessels there would be much more interference with nutrition of the tissues because of the increased peripheral resistance and consequent decrease in blood flow than in the cases in which it is confined to the large vessels, just as was found.

DR. ADOLF MEYER, Baltimore: What is the relation of the epileptic attacks in these groups? In my experience, at Kankakee and since then, I have been interested with the frequency of the occurrence of late epilepsy, particularly in the cases that show involvement of the smaller specifically cortical vessels and the intracortical small foci which create a certain amount of puckering of the cortex.

DR. ABRAHAM MYERSON, Boston: Was there any focal relation between the arteriosclerosis and the type of mental symptoms presented by the patients?

DR. MORTON PRINCE, Boston: I gathered the idea that, from a clinical point of view, Dr. Patten was meeting the gross pathologic disturbances. I was wondering if he had made a study of those minor disturbances of the heart which were not of a gross character; whether he has correlated those in the different types of arteriosclerosis?

DR. PATTEN (closing): In regard to Dr. Gregg's question, we have not attempted to make a classification according to the type of physique of the patient or his habits of life, except from the standpoint of his general physical condition.

As to the question of Dr. McCouch regarding the blood pressure, the pulse pressure is high in all cases, but highest in those cases with systolic pressure. The group in which there is sclerosis of both the large and the small vessels show a high pulse pressure as well as blood pressure.

In regard to the epileptic attacks, many of these cases show transitory attacks of various sorts, not necessarily apoplectiform attacks but states which are often characterized by the patients as "lapses of memory," almost like attacks of petit mal. These occur frequently in the group in which there is sclerosis of the small vessels. In the group showing sclerosis of the large vessels there occurs a thrombosis or a rupture, and the patients either die suddenly, or if they recover, have only a residual hemiplegia. None of them have the attacks which are common to the group in which there is so intense a sclerosis of the small vessels.

As far as focal symptoms are concerned, we have not gone into that phase of the situation nor into a study of the changes of the cortex of the brain; neither have we attempted to correlate them with our observations. Our study has been confined to the pathologic changes of the vessels and the correlation of these changes with the mental symptoms. We hope to separate these cases into groups with the vascular pathologic changes as a basis, and have reserved the more definite clinical studies for a future time.

INTRACTABLE CHRONIC PAIN IN THE LOWER SEGMENTS OF THE BODY

RELIEF BY MEANS OF SACRAL EPIDURAL INJECTIONS *

NORMAN VINER, M.D.
MONTREAL

The method of epidural injections was evolved, early in the century, separately by Cathelin [1] and Sicard; its original application was for the relief of enuresis, in which it proved of doubtful value. Some years later, the method was revived in America (in the Mount Sinai Hospital, the Mayo Clinic and in other institutions) in the treatment of intractable sciatica.

TECHNIC

The procedure is as follows:

The patient is placed in the knee-chest or knee-elbow position, though I have since found the prone position easier for the patient. The sacrococcygeal area is washed with alcohol, then painted with iodine. At the coccygeal end of the sacrum there is a small central depression between two lateral tubercles. Into this depression a preliminary injection of 2 or 3 cc. of 1 per cent procaine hydrochloride is made. A large needle—up to lumbar puncture size—is then inserted in the midline, parallel with the body of the sacrum, i.e., into the sacral canal (fig. 1), and with a glass syringe 20 cc. of 1 per cent procaine hydrochloride is injected. This is followed by the injection of from 50 to 100 cc. of sterile Ringer's solution, physiologic sodium chloride solution or liquid petrolatum, the quantity varying with the size of the patient, his build, the condition treated, and above all, with the resistance encountered to the entrance of the fluid. Three, or occasionally, four of these injections are given at intervals of one week. There is usually a certain degree of improvement with each injection.

There is practically no contraindication to the use of the method. Liquid petrolatum is frowned on by some on account of the remote possibility of its causing fat embolism. In actual use it is even more efficient than the other materials employed, but on the other hand, there is also some question of its ultimate disposal. If one misses the canal and injects dorsal to the sacrum, there is merely an infiltration of the tissues which neither benefits nor harms. The only risk—and that depends on faulty technic—is in injecting ventral to the sacrum, where important structures may be perforated or penetrated and possibly some damage done.

The basis of the favorable results obtained with this method of treatment is not well understood; different theories have been proposed

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* Read before the Montreal Medico-Chirurgical Society.

1. Cathelin, Fernand: Conférences cliniques de chirurgie urinaire, Paris, Henri Paulin, éditeur, 1909.

to account for them: (1) The anesthetic effect of the procaine hydrochloride. This is so obviously transitory that it need only be mentioned to be dismissed. (2) An erythema of the structures invaded, somewhat analogous to counterirritation, which stimulates resolution. (3) The tension on the cauda equina produced by the injected fluid pressing the cerebrospinal sac centrally and upward. This is analogous to nerve stretching and for the present seems to offer the most acceptable explanation.

Fig. 1.—Needle in sacral canal.

About four and one-half years ago I introduced this method in Montreal in the treatment of chronic intractable sciatica; I have not tried it on a single early or mild case of that condition. In fact, every patient so treated had already run the gamut of the routine methods of treatment without avail. However, in dealing with such an ill defined condition as sciatica it is wise at the outset to clear the ground by defining that term.

Dejerine, and later Sicard, after sifting a number of general medical, local surgical, traumatic, and some obviously orthopedic conditions

associated with more or less atypical sciatic pain, found that there remained a residuum of what they considered typical (sometimes called idiopathic) sciatica, for which no obvious cause could be demonstrated. They concluded that these were due to an inflammation of the structures in certain intervertebral foramens. They termed "funiculitis" the involvement of the nerve roots passing through these foramens. When the trouble was located in the second, third, fourth and fifth lumbar foramens it gave rise to lumbosacral pain, otherwise termed backache or lumbago. When the third, fourth and fifth lumbar and the first and second sacral roots were involved, the result was sciatica. Frequently there was a combination of the two.

In recent years, with the tendency to attribute the causation of so many diseases of ill defined origin to focal infection, "idiopathic" sciatica has been, probably with good reason, received into this fold. It is not unlikely that many such cases—syphilis having been excluded—may be attributed to infection in connection with the teeth, tonsils, sinuses, or even the gallbladder. Martyn,[2] in treating sciatica by the removal of such foci, claims practically 100 per cent of cures. On the other hand, Rosenheck and Finkelstein,[3] referring to their previous unsatisfactory experiences with the epidural method, attribute practically all cases of "idiopathic" sciatica to orthopedic defects, particularly to sacro-iliac disease. They follow the method of Baer and Scofield, and when the cause is demonstrably orthopedic there can be no room for criticism. In the speculative cases, however, their method is not only strenuous but cumbrous and prolonged, and its underlying basis is really a stretching of the nerve. They, therefore, lay themselves open to their own criticism of the epidural injection method "since they attack the consequences of the affection and not its origin."

The symptomatology generally agreed on includes: pain, in any position and particularly on changing position, in the lower part of the back and down the back of the thigh, sometimes going down the leg to the internal malleolus; a characteristic standing posture and gait; tender areas at the point of exit of the nerve from the great sciatic notch; pain in the back of the thigh, in the popliteal space; frequent absence of the achilles reflex; Lasègue's sign; the foot-jerk sign.[4]

The treatment obviously is to remove the cause. When this is undiscoverable or irremediable or when the pain persists in any case,

2. Martyn, George: The Significance of Lumbosacral Pain (Backache), J. A. M. A. **83**:1297 (Oct. 25) 1924.

3. Rosenheck, Charles, and Finkelstein, Harry: Sciatica: A Neuro-Orthopedic Consideration, J. A. M. A. **84**:939 (March 28) 1925.

4. Viner, Norman: Intractable Sciatica: The Sacral Epidural Injection: An Effective Method of Giving Relief, Canad. M. A. J. **15**:630 (June) 1925.

one has a choice of a vast number of procedures of greater or less avail. It is when these have failed, as they frequently do, that the epidural injection is a last, and I might almost say, unfailing resource.

REPORT OF CASE OF SCIATICA

CASE 1.—H. B., a man, aged 47, whose previous history was irrelevant except for a similar attack of a few weeks' duration five years before, was seen in December, 1923, when he complained of a dull ache in the right hip and down both legs, especially the right. The pain was generally excruciating when he made any sudden movement involving the lower part of the body. When changing from a recumbent to a sedentary or from a sedentary to an erect position, the paroxysms were sometimes intense. With the aid of two sticks he was able to stand for a few minutes, but soon became pale, broke into a cold perspiration, and felt faint from pain in the lower part of the back. This condition had persisted for two years and for the past year he had had to be lifted into and out of his car to go to the office. When there, he sat in one chair propped up with cushions, his legs stretched across another chair. He had been strapped, splinted and bandaged. He had received massage, and electrical and roentgen-ray treatment. The right leg (nerve ?) had been stretched. Several suspicious teeth and roots had been removed. He had refused tonsillectomy, which had been advised. Previous examination, which had included almost every part of the body, had not revealed any focus or locus morbi. The diagnosis made had been "sciatica probably due to rheumatoid arthritis."

Examination.—When seen by me, the examination generally gave negative results. Lumbar puncture disclosed nothing new. Neurologic examination showed tenderness at Valleix's points; Lasègue's sign and the footjerk sign were present in both legs, especially in the right. Objectively, there was some diminution in sensation to cotton and to pinprick over the fifth lumbar distribution in the right leg. There was no atrophy. The knee jerks were exaggerated and the right achilles reflex was absent.

The patient was given three treatments at weekly intervals and was kept in bed. Within a few hours after the first treatment he could lie or turn in bed with greater ease than for the preceding two years. Within two or three days after the last treatment he was allowed out of bed and found that he could get around comfortably with the aid of two sticks. A week later, he walked to his office with one stick. In the past three years he has been well, with the exception of an occasional "kink" in the back when stepping off a curb.

Impressed by the favorable results in numerous severe cases of sciatica, I decided to experiment further. There seemed no reason why chronic pain from other conditions involving nerves arising from the same general region—the cauda equina—should not be similarly benefited.[5] In experimenting with cases of pain in the lower segments of the body—coccygodynia, lumbosacral pain, traumatic neuritis, amputation stump pain, locomotor ataxia, rheumatoid arthritis, endarteritis obliterans, painful diabetic ulcer, encephalitis and supposed tumors of the spinal cord—the results have been largely favorable and occasionally surprising.

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5. Viner, Norman: The Relief of Chronic Pain in the Lower Segments of the Body by the Sacral Epidural Injection, Canad. M. A. J. **15**:1136 (Nov.) 1925.

Lumbosacral Pain.—A few patients were treated for the relief of lumbosacral pain, which occasionally darted into the leg but was by no means a typical sciatica. Except for some transitory relief in perhaps 50 per cent of the cases these may be counted among the failures.

Rheumatoid Arthritis.—A patient with arthritis of the hips and probably of the knees (as well as of the elbows and wrists) received two injections without relief. Later, another patient with arthritis of the ankles was decidedly benefited by three injections. This contrast, combined with the failure in the lumbosacral cases and the limited results obtained in the lumbosacral element of successfully treated sciatic cases, suggested that relief or failure depended on the segmental distribution of the pain. In other words, this method of what, for the present, may be called nerve stretching was effective only below the third lumbar root; pain in areas supplied by nerves originating higher up was not relieved. All subsequent experience tended to confirm this view (fig. 2).

Locomotor Ataxia.—Eight patients with lightning pains in the legs from tabes were markedly relieved, but for various reasons (four of them were treated during a visit to European clinics) only two could be followed up; in one the relief persisted for a year, when he died; in the other, the relief had persisted for five months when he disappeared from observation.[5]

Cancer of the Rectum.—Two patients with cancer of the rectum, who suffered intense pain, were enabled by this treatment to postpone taking morphine for two or three months. One patient with cancer of the rectum and lower part of the spine was not relieved.

Encephalitis.—A patient with epidemic encephalitis who had been suffering from intense shooting as well as constant pain in the legs received absolutely no relief from one injection. It was realized that this pain was of central origin and the test was purely academic.

Coccygodynia.—Two patients have been treated with marked relief.

Case 2.—J. Y. A., a woman, aged 40, suffered from severe pain, tenderness and occasional throbbing at the end of the spine. She dated the condition from some months before, when she had sat down forcibly on a stone step. The initial pain soon eased, but became far more acute and throbbing the next morning. Close questioning suggested that the patient might have been suffering from the condition since a parturition eighteen months before, but that it had become greatly intensified by the accident.

When examined on Dec. 18, 1924, she was unable to sit straight, but sat tilted or sidewise as though to relieve the coccyx from pressure. There was some local tenderness and a delayed and sluggish anal reflex; otherwise nothing abnormal was found.

One injection was given. When seen some weeks later the patient reported almost complete relief since the injection. She declined further treatment and has not been heard from since.

The second patient, treated somewhat over a year ago, received complete relief from two injections.

Amputation Stump Neuralgia.—Four patients with neuralgia of an amputation stump have been treated in the Montreal General Hospital. One had one injection, another two, and a third three treatments.[6] All professed to have been benefited immediately after the treatments, but as they never returned the duration of the effect could not be ascertained. The fourth patient was a girl who had undergone several orthopedic operations on the ankle; after the lower half of the leg

Fig. 2.—Segmental distribution; treatment is effective behind (or below) line *L3*.

had been amputated she had seven or eight resections of the nerve without relief from what she described as the most intense spasm and pain. A series of three injections gave complete relief for four months; then, another series gave relief for two months, when the patient had recourse to further resections.[6]

Traumatic Neuritis.—Two patients with traumatic neuritis, one from a severe blow across the lower part of the back and the other from

6. Since this paper was written this patient (with the three injections) has reappeared and reported complete relief for over a year so far. There have been a few other patients most of whom have been decidedly benefited.

a fall in which the upper part of the thigh was bruised, were completely relieved of pain.

Endarteritis Obliterans and Diabetic Ulcer of the Leg.—Two patients with endarteritis obliterans and one with a painful diabetic ulcer of the foot experienced no relief. As these cases were well within the required segmental distribution, the failure suggests a possible contribution to knowledge of the function and course of the sympathetic nerve. The implication, to me at least, is that the pain in these cases

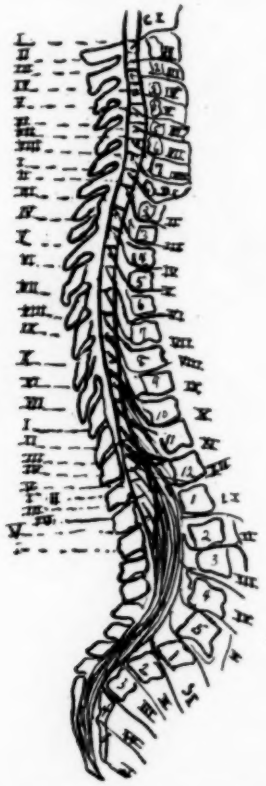

Fig. 3.—Spinal cord with cauda equina.

was conveyed by fibers in the perivascular sympathetic, and that these do not enter the cord at points corresponding to their segmental distribution but through relay stations at a higher level.

Tumors of the Spinal Cord (Supposed).—Four patients who came to me[7] with a diagnosis of tumor of the spinal cord were markedly

7. Viner, Norman: The Lipiodol Test for Patency of the Cerebrospinal Canal in a case of Sciatica (?) with Unusual Features, Arch. Neurol. & Psychiat. **13**:767 (June) 1925.

relieved, though in varying degree; the diagnoses were probably not correct. As they open fresh problems they will be left for consideration later.

COMMENT

In one treatment given in the fourth amputation stump case an attempt was made to find out how far up the vertebral canal the injected fluid passes. (I believe that it goes as far as the cervical region). It was hoped that a 10 per cent solution of sodium bromide would be sufficiently impervious to the roentgen-rays to solve this problem. Following the preliminary 20 cc. of procaine hydrochloride solution, 60 cc. of a 10 per cent solution of sodium bromide was injected and several roentgenograms were taken. This was not successful. The patient, however, secured some relief, although there was some general temporary discomfort from the substitution of the bromide for the usual Ringer's solution. Probably a 10 per cent solution of sodium iodide, being of much greater atomic weight than the bromide, would cast a shadow. It would, however, require 6 gm. of the drug—a dose too large for an academic test.

The favorable result in the cases of locomotor ataxia—especially the first patients treated—was unexpected. This result can perhaps be explained by the fact that the ganglia of the posterior roots, being partly outside the cerebrospinal sac—are capable of the same reactions to the injected fluid as are the nerves of the cauda equina.

SUMMARY AND CONCLUSIONS

A method of treatment is outlined which has proved remarkably effective in the worst and most persistent cases of sciatica, has been of decided value in tabetic lightning pains, in amputation stump neuralgia, in traumatic neuritis and in arthritis deformans, and has been of some help in cancerous and other conditions of the sacral region.

In general, it seems correct to say that this method is efficient in all kinds of chronic peripheral pain originating at or below the third lumbar segment which is not of vascular or sympathetic origin.

It should be noted that:

1. The method is not a cure-all. Effective though it may be, it is not a cover for an unsatisfactory diagnosis or a cursory examination.

2. The injection is not into the cerebrospinal canal, but into the sacral vertebral canal outside the cerebrospinal sac.

3. After the injection has proved satisfactory, the patient should not be discharged. The causal condition may appear later and may require appropriate treatment.

Many other conditions such as kraurosis vulvae, pruritus ani, and painful conditions of the bone to which I have not had access may possibly be relieved through this method. Though the series here presented is not extensive and the cases are not of long duration, the method has demonstrated such value that further investigation is indicated.

STUDIES IN EPILEPSY

V. THE FIBRIN CONTENT OF THE BLOOD *

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WITH THE ASSISTANCE OF MARGARET BELLINGER ALLEN, B.S.
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In the vital processes of the body, fibrinogen plays an important rôle. Its presence is essential both for the maintenance of normal viscosity and for the coagulation of the blood. It has been stated that in epileptic persons there is abnormality in the metabolism of protein and in the clotting qualities of the blood. For these reasons it should be known whether the blood of epileptic persons shows any marked abnormality in its fibrin content. We have not seen any direct observations of this point. Besta [1] found a decrease in fibrin ferment in all but eight of forty-five epileptic patients examined. Without presenting data, Dienst [2] states that the blood of epileptic persons is deficient in antithrombin.

MATERIAL AND METHODS

The patients examined attended the neurologic clinics of the Boston City and Massachusetts General hospitals. They were of various ages. Sixty-eight were men and thirty-two were women or girls. In the main, seizures were of unknown origin. In most instances, blood was drawn in the morning before the patient had eaten. The ingestion of food, however, causes little change in the concentration of fibrin. Blood was drawn without stasis, as Plass and Rourke [3] have shown that extreme venous stasis causes an increase in blood fibrin. Fibrin was measured by the method of Foster and Whipple.[4]

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* The expenses of this investigation have been defrayed in part by a grant from the Proctor Fund of the Harvard Medical School for the study of chronic diseases.

1. Besta, C.: Ueber das gerinnende Vermögen des Blutserums der Epileptiker, Zentralbl. f. Nervenh. u. Psychiat. **32**:459, 1909.

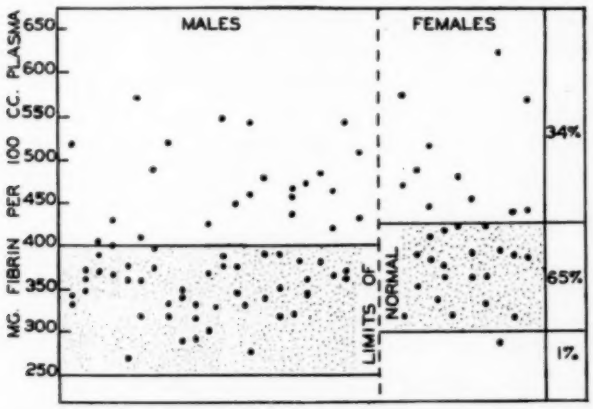
2. Dienst, A.: Das Krampfgift bindende Antithrombin in seiner Bedeutung für die Aetiologie der Eklampsie und Epilepsie, Arch. f. Gynäk. **117**:56 (Dec.) 1922; Zur Aetiologie und Pathogenese der Eklampsie und der Schwangerschaftstoxikosen, Monatschr. f. Geburtsh. u. Gynäk. **74**:1 (July) 1926.

3. Plass, E. D., and Rourke, M. D.: The Effect of Venous Stasis on the Proteins of Blood Plasma and on the Rate of Sedimentation of Red Blood Corpuscles, J. Lab. & Clin. Med. **12**:735 (May) 1927.

4. Foster, D. P., and Whipple, G. H.: Blood Fibrin Studies: I. Method for Quantitative Analysis of Blood Fibrin in Small Amounts of Blood, Am. J. Physiol. **58**:365 (Jan.) 1922.

RESULTS

One hundred and forty-one measurements were made of 100 patients. The initial measurement for each patient is shown in the accompanying chart. Concerning normal values, the largest series are by Gram [5] and by Foster.[6] The values obtained by these authors in comparison with those which we obtained in our 100 patients are summarized in table 1. The average measurements of our group—both men and women—were approximately 30 per cent above the average normal measurements given by Gram. Again 66 per cent of our men and 63 per cent of our women patients gave readings which were above the upper limit of Gram's



Concentration of fibrin in the plasma of 100 patients. Each dot represents the initial measurement of each patient. Division is made into male and female. The abscissas are without significance; the ordinates represent milligrams of fibrin per hundred cubic centimeters of plasma. The limits of normal are those given by Foster and are more liberal than measurements recorded by Gram.

TABLE 1.—*Comparison of Plasma Fibrin of Normal and Epileptic Persons*

	Total Number Examined	Male			Female			Total Average, Mg.
		Highest, Mg.	Lowest, Mg.	Average, Mg.	Highest, Mg.	Lowest, Mg.	Average, Mg.	
Normal (Gram)..	50	360	200	270	380	210	290	280
Normal (Foster).	42	446	256	332	470	255	344	338
Epileptic persons.	100	572	258	391	622	288	412	398

normal. Although Foster [6] states that there is agreement in the results obtained by his own and Gram's method, his normal values are considerably higher than those of Gram. Because we have used Foster's method of analysis, in the accompanying chart we have indicated the

5. Gram, H. C.: The Results of a New Method for Determining the Fibrin Percentage in Blood and Plasma, Acta med. Scandinav. **56**:107 (March) 1922.

6. Foster, D. P.: Blood Fibrin Studies, Arch. Int. Med. **34**:301 (Sept.) 1924.

limits of normal as stated by him. The average values for our series were 18 per cent higher for men and 20 per cent higher for women than the average values obtained by Foster. Thirty-four per cent of our patients had values which were above the upper limit of Foster's normal. In only one instance did a measurement fall below the limits of normal.

Table 2 presents certain data concerning the thirty-four patients who, on initial examination, showed increase in the concentration of plasma fibrin. The question immediately arises whether such increase in these patients could be explained by any of the recognized causes of hyperinosemia. Chief among such causes is injury of body tissues, due either to septic or to sterile processes. All the patients were ambulatory, and at the time of examination had a normal temperature. In two of the patients, however, infection probably existed. Patient 2 had a great increase in the concentration of plasma fibrin (572 mg. per hundred cubic centimeters). Subsequent measurements were still higher, and on these occasions the temperature and the concentration of leukocytes in the blood were slightly elevated. The patient had a productive cough, and although physical and roentgen-ray examination of the chest did not reveal anything abnormal, it is probable that he had an infection of the respiratory tract. Patient 4 had symptoms which suggested the presence of an infection of the gallbladder. It is possible, of course, that other patients harbored a hidden infection. Except after seizures, epileptic persons do not show a leukocytosis. Gram,[5] however, who made hundreds of simultaneous measurements of blood fibrin and of the number of leukocytes, believes that increase in blood fibrin is a more delicate indicator of toxic action within the body than is leukocytosis.

Syphilis was probably present in five of our patients who presented hyperinosis. The spinal fluid of patient 8 gave a positive Wassermann reaction. Patients 14 and 26 had a positive Wassermann reaction of the blood. In case 17, the patient had the symptoms of general paralysis without historical or spinal fluid evidence of the disease, and in case 32 the patient had a definite history of congenital syphilis but a negative serology. None of the patients whose blood fibrin was normal had any evidence of syphilis. Gram,[5] and McLester, Davidson and Frazier[7] each gave measurements for a few patients with syphilis, all of whom had high values for fibrin. It is therefore possible that syphilis accounts for the hyperinosis present in these five patients of ours. Gram[5] and Foster[6] found that blood fibrin is high in pregnancy. None of our

7. McLester, J. S.; Davidson, M. I., and Frazier, B.: Blood Fibrin Changes in Various Diseases with Special Reference to Disease of Liver, Arch. Int. Med. **35**:177 (Feb. 15) 1925.

TABLE 2.—*Thirty-Four Epileptic Patients with Increased Plasma Fibrin*

Patient	Sex*	Age	Hematocrit, per Cent	Fibrin per 100 Cc.		Seizures		Comment
				Blood, Mg.	Plasma, Mg.	Years Duration	Approximate Number per Month	
1. H. Ma.	♂	25	48	273	517	5	0-2	Severe grand mal
			49	224	438			
			49	210	409			
2. G. Na.	♂	33	53	270	572	10	2-6	Pulmonary infection present
			54	403	873			
			49	385	769			
3. F. Co.	♂	53	45	283	519	13	0-2	Alcoholic
			50	225	450			
4. L. Sh.	♂	32	46	294	547	2	0-2	Cholecystitis
			44	314	557			
5. A. Mc.	♂	22	60	195	487	3	1-5	Equivalents; occasional grand mal; basal metabolism, —10%
			52	185	390			
6. L. Mu.	♂	20	55	194	432	5	2-5	Examinations negative
7. S. Wa.	♂	..	44	238	425	10	0-2	Severe grand mal; basal metabolism, —11%
8. H. Su.	♂	23	51	235	542	2	100	Petit mal; syphilis of the central nervous system
9. H. Cr.	♂	15	46	245	459	5	0-1	Deterioration
10. F. Br.	♂	24	49	217	478	6	0-1	Jacksonian
11. C. Ra.	♂	45	55	206	458	25	0-1	
12. E. Je.	♂	21	44	265	472	1	2 in all	Hemangioma of brain
13. H. Sm.	♂	50	51	238	483	2 mo.	2 in all	
14. G. Tr.	♂	22	48	218	419	10	0-1	Wassermann reaction positive
15. F. Br.	♂	21	52	223	462	2	2-3	Horner's syndrome
			52	212	445			
16. S. Le.	♂	24	51	192	432	6	0-1	Visceroptosis; basal metabolism, —35%
17. F. Be.	♂	46	45	278	508	14	0-1	Symptoms of paresis
18. D. De.	♂	37	50	271	542	2	0-10	Having serial grand mal
19. M. Co.	♂	32	51	198	406	30	10-30	
20. D. Ud.	♂	12	47	214	401	2	0-1	Flat sugar curve; pituitary body type
21. W. Ga.	♂	23	49	207	409	5	2-5	Severe gand mal; diabetic sugar curve
22. T. Cl.	♂	36	48	244	466	½	0-1	Duodenal ulcer; caisson disease
23. A. Pu.	♂	15	49	223	437	9	0-1	
24. C. Ho.	♀	24	43	285	485	10	10-15	Severe grand mal; deteriorated; visceroptosis; high sugar curve
			43	279	488			
			45	220	401			
			46	190	353			
			45	236	433			
25. M. Wi.	♀	38	45	283	514	1	0-1	Essential hypertension
			46	274	512			
			45	266	483			
26. C. Kn.	♀	43	55	281	622	18 mo.	0-1	Wassermann reaction positive
			47	301	571			
27. J. No.	♀	49	38	291	468	3	2-10	Light seizures; diabetic type sugar curves
			34	299	451			
28. D. Th.	♀	13	45	266	479	6	1500	Short myoclonic
29. L. Ra.	♀	15	44	322	574	5	0-2	Flat sugar curves; pituitary body type
30. R. Sa.	♀	22	49	227	444	3	0-2	Visceroptosis
31. B. Mo.	♀	49	45	247	453	4	0-1	
32. J. Br.	♀	22	47	233	438	2 mo.	0-1	Syphilis of central nervous system
33. J. Le.	♀	17	48	230	441	1	0-10	Probably hysteria
34. M. Pr.	♀	11	45	313	568	6 mo.	3-4	

* In this column, ♂ indicates male; ♀, female.

patients was pregnant. The proportion of men and women or girls with hyperinosis was approximately the same.

Gram [8] found that healthy persons show fairly constant values for fibrin from day to day. In eleven of our patients with elevated values, a second test was performed. In nine, the plasma fibrin remained abnormally high, and in two it became normal.

COMMENT

Of the thirty-four patients with increased plasma fibrin, we found a possible cause in seven. Of the remaining twenty-seven patients, one had hypertension, five had abnormal blood sugar curves, three had marked evidence of visceroptosis and two had basal metabolic rates below minus 10 per cent. So far as we are aware, none of these conditions has been shown to be associated with high values for blood fibrin. On theoretical grounds, because it has been reported that venous intestinal blood contains a higher concentration of fibrin than arterial blood, it would seem possible that the presence of visceroptosis and of constipation might be of some significance. Gram,[5] however, did not find any increase in blood fibrin in patients who had disturbances of the gastro-intestinal tract. Because of high values for fibrin found in a few patients with myxedema, Starlinger [8] believed that the thyroid gland is an important factor in the regulation of blood fibrin. The basal metabolism rate was measured in twelve of our patients; in four, the metabolism was normal and the blood fibrin high; in five, the metabolism was subnormal and the blood fibrin normal, and in three, the metabolism was low and the blood fibrin high. In other words, there was no correlation between the rate of consumption of oxygen and the concentration of blood fibrin in these patients.

Can the high concentration of plasma fibrin in these twenty-seven patients be directly related to the seizures to which they were subject? Inspection of table 2 shows that the patients in this group were not the ones with the longest history of seizures, nor were they the ones having the most frequent or the most severe seizures. The blood for examination was drawn without relation to convulsions. In one instance blood drawn during a seizure contained 378 mg. per hundred cubic centimeters of plasma, whereas another sample obtained thirty minutes later contained 361 mg., a decrease which is probably without significance.

These observations might find possible correlation with certain theories concerning epilepsy which have been advanced: that in epilepsy there is an unusual degree of protein destruction, or a disturbance in the function of the liver or abnormal clotting properties of the blood.

8. Starlinger, F.: Schilddrüse und Bluteiweissbild, Wien. klin. Wchnschr. **37**:617 (June 19) 1924.

The evidence for and against these various theories has received recent critical review by Lennox and Cobb [9] and need not be repeated in detail.

The idea that there is either qualitative or quantitative abnormality of protein metabolism in epilepsy has been a favorite one. Numerous workers have measured the nitrogen content of the urine and stool without demonstrating consistent abnormalities. Observations concerning abnormal concentration of proteolytic ferments in the blood and urine have been reported by Rosenthal,[10] by Pfeiffer, Standenath and Weeber,[11] and by Frisch and Walter.[12] Wuth's [13] results were negative. More recently, DeCrinis [14] has reported an abnormally slight increase in the consumption of oxygen following the ingestion of protein food. Various authors have found abnormal reactions to the intradermal injection of protein substances in epileptic persons, or benefit from its parenteral administration. Although most of these authors have reported variations from the normal, perusal of the data presented does not give convincing evidence that the observed abnormalities are clearly beyond the limits of normal.

The results of examination of the blood for unusual concentration of nonprotein nitrogenous constituents have been equally negative. Wuth [13] obtained essentially normal values in fifty patients, and Lennox, Wright and O'Connor [15] in 123 patients. If the amount of blood fibrin is elevated, one might expect to find coincident increase in the albumin and globulin fractions of the plasma protein. Meyer and Brühl [16] concluded from examination of sixteen epileptic persons that

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9. Lennox, W. G., and Cobb, S.: Epilepsy from the Standpoint of Physiology and Treatment, Baltimore, The Waverly Press, 1928.

10. Rosenthal, S.: Das Verhalten der antiproteolytischen Substanzen im Blutserum bei der Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:588, 1910.

11. Pfeiffer, H.; Standenath, F., and Weeber, R.: Ueber den Peptidasenhaushalt unterer Versuchstieren und des Menschen mit besonderer Berücksichtigung des Epileptikers, Klin. Wchnschr. **4**:1122 (June 4) 1925.

12. Frisch, F., and Walter, K.: Untersuchungen bei periodischer Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:366, 1922.

13. Wuth, O.: Untersuchungen über die körperlichen Störungen bei Geisteskranken, Monographien aus dem Gesamtgebiete der Neurol. und Psychiat., Berlin, Julius Springer, 1922.

14. DeCrinis, M.: Ueber den Stoffwechsel beim epileptischen Symptomenkomplex, Ztschr. f. d. ges. Neurol. u. Psychiat. **99**:718, 1925.

15. Lennox, W. G.; Wright, L. H., and O'Connor, M. F.: Studies of Metabolism in Epilepsy; I. Nonprotein Nitrogenous Constituents of Blood, Arch. Neurol. & Psychiat. **11**:54 (Jan.) 1924.

16. Meyer, M., and Brühl, F.: Ztschr. f. d. ges. Neurol. & Psychiat. **75**:157, 1922. Brühl, F.: Weitere Untersuchungen über den Serum — Eiweisswert beim epileptischen Krampfanfälle und seine Beziehungen zum Blutdrück, Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:656, 1923; Weitere blutchemische Untersuchungen zur Pathologie des epileptischen Krampfanfalle, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:642, 1923.

the refractive property of their serum albumin was at fault. Their data, however, are not conclusive. Wuth,[13] on the other hand, found essentially normal values in forty patients. The method used by Wuth, the Zeiss dipping refractometer, makes it desirable that the observations should be repeated. With regard to the spinal fluid, approximately one fourth of more than 200 patients examined by us showed an abnormally high concentration of the total protein. Such increase, however, did not seem to be related to hyperinosis, for only 30 per cent of seventeen patients with elevated blood fibrin whose spinal fluid was examined had an abnormal increase of total protein in the spinal fluid.

From these various observations we do not find definite evidence that persons who are subject to seizures show abnormality in their protein metabolism. It is possible, however, that elevation of blood fibrin may be a more delicate indicator of protein destruction than the other measurements cited. The belief that circulating toxins may be the cause of seizures is so widespread that continued experimental work to prove or disprove the presence of toxic substances is desirable.

A second possible explanation for the increased fibrin values in these epileptic persons is the presence of an irritative lesion of the liver. In case 3, the patient was a confirmed alcoholic and may have had cirrhosis of the liver. Foster[6] found hyperinosis in patients who had jaundice following the intravenous injection of arsphenamine. He believed that the increase in blood fibrin was due to an irritative lesion of the liver. It is possible, however, that the presence of syphilis itself may have accounted in part for the high values obtained. It has long been known that in certain circumstances the liver may have a so-called detoxifying function, as shown by the fact that dogs in which an Eck's fistula had been produced when fed meat may have convulsions. Thom,[17] and Lalor and Haddon[18] found that the weight of the liver, when compared with that of the brain, was unusually low in epileptic persons. Lind[19] found fibrosis of the liver in 64 per cent of 259 epileptic persons at autopsy. His observations, however, need confirmation through microscopic examinations. In eclampsia, various authors have reported abnormal function of the liver as shown by retention in the blood stream of injected dye. Foster[6] found hyperinosis in patients with eclampsia, the concentration being especially high in a patient having convulsions. We have not seen any observations concerning the func-

17. Thom, D. A.: Abnormal Relation Between Liver and Brain Weights in 42 Cases of Epilepsy, J. Nerv. & Ment. Dis. **43**:422 (May) 1916; Bull. Mass. Comm. Ment. Dis. **1**:123, 1917-1918, and **2**:123, 1918-1919.

18. Lalor, P., and Haddon, G.: Toxemia in Epilepsy, M. J. Australia **1**:251 (March 20) 1920.

19. Lind, W. A. T.: Conclusions Based upon the Clinical and Postmortem Study of Epilepsy, M. J. Australia **2**:244 (Aug. 21) 1926.

tion of the liver in a group of patients with epilepsy. The question of the pathologic processes and function of the liver in epilepsy needs further study.

A third possible relationship between convulsions and abnormally high concentration of blood fibrin lies in abnormal viscosity or clotting time of the blood. The physical properties of the blood bear an intimate relationship to the caliber of capillaries and to the transfer of substances between the blood and the tissues. The nervous tissues are particularly susceptible to variation in their blood supply and nutrition. For these reasons, accurate observations concerning the physical properties of the blood are important. Measurements by Brown [20] and by Meyer [21] on the viscosity of the blood of epileptic persons are too fragmentary to be of value. Concerning the speed of coagulation of the blood in epilepsy, the observations by Besta,[22] Turner,[23] Austin,[24] Jenkins and Pendleton,[25] Spangler,[26] Fackenheim,[27] Chiola [28] and Choroschko [29] are not convincing either because of the methods used or because of the small number of patients examined. Thom [30] in 203 patients and Wuth [13] in forty patients obtained normal values by an accepted method.

The concentration of the fibrin of the blood is closely related to the speed with which red cells sink to the bottom. Wuth [13] found increased speed of sedimentation of red cells in many of the forty patients examined by him. In one patient Löwenberg [31] found an

20. Brown, R. D.: The Viscosity of the Blood in Epilepsy, J. Ment. Sc. **56**:686, 1910.

21. Meyer, Max: Serologische Studien zur Pathologie des epileptischen Krampfanfalls, Zentralbl. f. d. ges. Neurol. u. Psychiat. **41**:726, 1925.

22. Besta, C.: Ricerche sopra il potere coagulante del siero di sangue degli epilettici; analisi quantitativa del fermento fibrinoso, Riforma med. **22**:1191, 1906.

23. Turner, J.: Coagulation Rate of Blood in Epileptics, J. Ment. Sc. **53**:766, 1907.

24. Austin, M. L.: Clinical Observations on Blood Coagulability and Calcium Therapy in Epilepsy, Ohio M. J. **6**:486, 1910.

25. Jenkins, C. L., and Pendleton, A. S.: Crotalin in Epilepsy, J. A. M. A. **63**:1749 (Nov. 14) 1914.

26. Spangler, R. N.: Toxic Manifestations of Epilepsy, New York M. J. **104**:534 (Sept. 16) 1916.

27. Fackenheim: Blutbefunde bei Epilepsie, Deutsche med. Wchnschr. **40**:1086, 1914.

28. Chiola, G.: Ricerche sulla coagulazione del sangue negli epilettici, Gior. di psichiat. clin. e tecn. manic. **53**:17, 1925.

29. Choroschko, W.: Gesteigerte Blutgerinnung vor dem epileptischen Anfall als eine klinische Tatsache, J. Nevropat. i Psichiat. **18**:59, 1925.

30. Thom, D. A.: Coagulation Time of Blood in Epileptics, Illinois M. J. **26**:382 (Oct.) 1914.

31. Löwenberg, K.: Ueber die Senkungsgeschwindigkeit der roten Blutkörperchen bei Geisteskranken, Ztschr. f. d. ges. Neurol. u. Psychiat. **87**:197, 1923.

increased speed of sedimentation after a seizure. George [32] emphasized the unusual degree of flocculation which occurs when the blood plasma of an epileptic person is mixed with sodium chloride. As yet, we know little concerning the formation and disposal of fibrin in the body. We cannot say whether any increase in the blood is due to increased formation, to increased mobilization or to decreased destruction. The rôle played by fibrin in the function of the important endothelial system is obscure. Increasing knowledge along these lines may permit evaluation of such abnormalities as we have found.

If we are to look on epilepsy, that is, "seizures," as a symptom, it is possible that an abnormality which is demonstrable in one fourth of the patients examined may be of significance in these particular patients. Further investigation of the subject is needed. Besides measurements of blood fibrin in larger groups of epileptic patients and known normal subjects, there should be simultaneous measurement of the speed of coagulation of the blood, of the sedimentation of red cells and of the concentration of the other plasma proteins: albumin and globulin. Great care should be taken to exclude the presence of infections by means of leukocyte counts, by frequent measurements of body temperature and by careful physical examination.

SUMMARY

Measurements of blood and plasma fibrin have been made in 100 patients with epilepsy. The average concentration of fibrin in the plasma was approximately 19 per cent above the average concentration for normal persons obtained by Foster. The concentration of plasma fibrin was abnormally high in thirty-four of the patients. In seven the hyperinosis might be accounted for by the presence of pyogenic or syphilitic infection. In the remaining twenty-seven patients the cause for the increased concentration of blood fibrin was not apparent. The possible significance of these observations, especially as regards abnormal protein metabolism, function of the liver and physical properties of the blood, is discussed.

32. Georgi, F.: Zur Pathophysiologie der epileptischen Anfälle, Deutsche Ztschr. f. Nervenh. **83**:356, 1924-1925; Zur Genese des epileptischen Anfalls, Klin. Wchnschr. **4**:2053 (Oct.) 1925.

TUBERCULOMA OF THE CENTRAL NERVOUS SYSTEM*

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It is my purpose to record a series of cases of tuberculoma of the central nervous system and to analyze these from the standpoint of observations of possible clinical value. Incidentally, this group of twenty-seven cases represents the largest series found in the available literature in which such an analysis is made. A comparison of some of these cases with those cited in the literature is made, together with a tabulation of the cited cases as to author, sex, age and location of lesion. The case reports are not published, since all the important data are summarized in the tables.

COMMENT ON CASES

Age.—Of the twenty-seven cases, the age was known in twenty-two, which group gave an average age of 31.8 years. This refers to the age at admission, but since, except in a few cases, the stay in the hospital was not long, the different age at death is not significant. One patient was 61; another was 54 years of age. Two other patients are definitely stated to be adults, and in only three cases was the age absolutely unknown. The age study is interesting because of the frequently encountered assertions as to the extreme preponderance of tuberculous tumors in childhood, with greatly diminishing incidence after early adult life. However, the small percentage of children in the Philadelphia General Hospital must be considered in drawing any conclusions as to age incidence from this series.

Sex.—Males constitute twenty-one of the list (77.7 per cent), with only six females (22.3 per cent). Probably some consideration must be given here to the greater percentage of males admitted to the hospital.

Number of Tumors.—In approximately three fourths of the cases in this series, there were solitary tubercles (twenty cases; 74 per cent). In four others, two distinct masses were presented; three showed three or more separate lesions.

Size of Tumors.—The table of cases can hardly be simplified, in this respect, other than to say that the average dimensions approximate

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2 cm. by 2 cm. The variations ranged from 0.2 cm. by 0.2 cm. to 4 cm. by 8 cm. These figures are thus in accord with the averages found in the literature.

Location.—There was no predilection for either side of the brain. The right side was involved six times, the left eight times, and both sides in five instances. The remainder constitute either cases of the spinal cord or those, as in the cerebellum, in which distinction as to the side is not made in the description.

More interesting and important, however, is the determination of the anatomic locations. These are shown in table 1.

TABLE 1.—*Anatomic Locations*

	No. of Cases	Percentage
Frontal	7	26.0
Frontal and pons	2	7.4
Parietal	3	11.0
Parietal and cerebellum	1	3.7
Cerebellum	3	11.0
Thalamus	3	11.0
Temporal	2	7.4
Pons	1	3.7
Cauda	1	3.7
Cord proper	4	14.8

Weight of Brain.—Because of the frequent observation that gliomatous tumors tend to cause large brains, it was thought of interest to note the weights of the brains in this series. In fifteen cases in which the weight was recorded, the average was 1,390 Gm., while in sixty consecutive reports taken at random from the files the average weight of the brain was 1,350 Gm. Peculiarly enough, however, the two largest of the group, i. e., the only ones weighing more than 1,600 Gm. were those of patients who had tumors of the spinal cord. If these are excluded, the average weight of the other thirteen intracranial tumors is 1,350 Gm. —identical with the general average. The average weight of the male brains of the series was 1,415 Gm.; of the female brains, 1,255 Gm.

It is interesting to observe, however, how frequently the approximate descriptive term of "large" was used. In eight cases some variation of this term occurred, and in only one was the comment "smaller than usual" used. Furthermore, it is noteworthy that the term "large" was used several times when the weight of the brain was not above the average, so that it would appear that volume in these cases is not closely related to mass; in other words, the $\frac{\text{mass}}{\text{volume}}$ ratio is distinctly disturbed.

Meningitis.—Of the twenty-seven patients, twenty-one (77.7 per cent) were definitely stated to have had meningitis; in five, apparently no meningitis was found; in one, it was impossible to ascertain whether meningitis was present.

TABLE 2.—*Data in Twenty-Seven Cases of Tuberculoma of the Central Nervous System*

Case	Sex	Color	Age	No. of Tuberculomas	Meningitis	Size of Tuberculoma	Location	Clinical Diagnosis	Pulmonary Tuberculosis	Duration Before Hospitalization	Time in Hospital	First Symptom	Headache	Cells in Fluid	Spinal Fluid Observations	Size of Brain
1	M	?	?	1	0	1.5 × 1.5	Right thalamus	? Hemorrhage	?	?	?	?	?	?	?	?
2	M	B	3	1	+	?	Left cerebellum	? Meningitis; tuberculosis ?	+	?	?	?	?	?	?	"Large"
3	F	B	?	1	+	?	Right temporal	Tuberculous meningitis; bronchopneumonia	+	4 mo.	10 days	Pain in head	+	144 320	Colloidal gold test, 001233211	1,250 Gm.
4	M	?	Adult	1	+	1.5 × 3	Lumbar cord extradural	Tuberculous meningitis; syphilis	?	1 mo.	6 days	Headache and aching	+	40	Wassermann positive	1,650 Gm.
5	M	?	?	1	+	4 × 3 × 2	Cerebellum	?	?	?	?	?	?	?	?	"Larger"
6	M	B	29	2	0	3 × 3 1 × 1	Right frontal Left frontal	Tuberculous meningitis	+	1 wk.	8 days	Headache	+	154	Globulin, 3+; Sp pr. 290 mm. H_2O; Colloidal gold test, 0012333210	Normal
7	M	W	30	1	+	3 × 1.5 × 2	Right precentral	Pulmonary tuberculosis	+	1 yr.	4 mo. 4 days	Loss of weight	+	—	Wassermann negative; Colloidal gold test, 2234332000	1,325 Gm.
8	M	W	38	1 large m. small	+	1.5 × 1.5	Left frontal	Tuberculous meningitis	?	1 wk.	3 days	Headache	+	40	Wassermann pos.; Noguchi negative; Colloidal gold test, 0001122210; bacilli	"Slightly large"
9	M	B	4	2	+	0.5 × 0.5	Right pons Left frontal	Miliary tuberculosis; meningitis	+*	6 mo.	11 days	Lumbar pain	—	17	Trace of globulin; Colloidal gold test, 454444322	Normal
10	M	Y	41	1	0	3 × 1	Pons	Cerebral tuberculoma	Peritoneal	1 mo.	2 mo.	Gastrointestinal symptoms	—	20	Colloidal gold test, 4555554422	1,450 Gm.
11	M	B	27	1	+	1.5 × 1.5	Left thalamus	Tuberculous meningitis and empyema	+	2 wk.	11 days	Headache	+	170	Slightly increased protein	1,300 Gm.
12	M	B	34	3	+	2 × 2	Left parietal, each sylvian	Tuberculosis and tuberculous meningitis	+	1 wk.	9 days	Headache	+	42	Protein increased	"Fair size"

13	M	B	26	1	+	5 × 0.5	Cauda equina	Osteomyelitis of spine; retropharyngeal abscess	—	3 mo.	2 days	Headache	+	—	—	—
14	F	B	37	1	+	3 × 3	Left cerebellum	Toxic psychosis	0	7 mo.	4 days	Headache	+	73	Protein, 3+; Wassermann negative	1,150 Gm.
15	M	B	Adult	1	+	1.5 × 2	Frontal	Tuberculous meningitis	+	?	4 days	?	—	115	Protein increased; pellicle	1,390 Gm.
16	M	B	25	1	+	1 × 3	Left parietal	Tuberculous meningitis	+	?	2 days	?	—	9-40	Globulin negative; Wassermann negative; Colloidal gold test, 0000133210	1,470 Gm.
17	F	W	54	1	+	2 × 4	Right temporal	Chronic alcoholism	—	4 days?	2 wk.	"Nervous"	?	—	Clear, moderate protein	1,275 Gm.
18	M	W	61	1	+	0.75 × 3	Lower cord	Myelitis	—	3 wk.	2 mo. 25 days	Numbness	—	9	Globulin negative; Wassermann negative	1,635 Gm.
19	F	W	43	1	—	0.2 × 0.2	Right parietal	Intracranial pressure; scleroderma	—	4 yr.?	8 mo. 8 days	Epilepsy	—	3	Globulin, 3+; Wassermann negative; Colloidal gold test, 1233210000	—
20	M	B	25	1	+	....	Lower cord	Tuberculosis; tuberculosis of hip and spine	+	5 mo.	13 mo. 1 day	"Sinus"	—	—	Clear, no increase in protein	"Good size"
21	M	B	27	1	+	4 × 8	Right motor	Tuberculoma; tuberculosis	+	8 days	8 days	Numbness	—	5	Wassermann negative	1,550 Gm.
22	M	W	64	1	0	....	Lower cervical	Tuberculosis of spine; nephritis	+	1 wk.	20 days	Paralysis	—	—	Clear	Slightly small
23	F	B	21	1	+	1 × 1.5	Left thalamus	Tuberculosis; tuberculous meningitis	+	1 mo.	26 days	Sore foot	—	145	Wassermann neg.; Colloidal gold test, 0011110000	1,350 Gm.
24	M	W	37	1	+	1.5 × 1.5	Left precentral	Tuberculoma; tuberculosis	+	7 yr. 1 wk.	13 days	Cough, loss of voice	—	106	No bacilli, pellicle	1,420 Gm.
25	F	B	15	2	+	3 × 3	Left motor	Miliary tuberculosis; tuberculous meningitis	+	3 mo.	2 days	Headache	+	200	Marked tension, pellicle	1,240 Gm.
26	M	B	27	2	0	1.25 × 1.25 0.2 × 0.2	Right basis pontis Left upper motor	Undiagnosed	+	2 mo.	1 day	Headache	+	—	—	
27	M	B	32	Multiple	+	2.5 × 2.5 ?	Right parietal Left cerebellum, etc.	Apoplexy	—	6 yr.	23 days	Convulsion	—	—	—	

Body Tuberculosis.—Pulmonary tuberculosis was present in sixteen of the twenty-seven cases. One patient had tuberculous peritonitis; one patient without pulmonary tuberculosis had caseous tubercle of the kidney and vertebrae. In one case only was it definitely stated that no other focus was found. Inadequate information renders certainty as to the remaining group impossible.

Stay in Hospital.—The average stay in the hospital of twenty-three patients from whom these data were ascertained was one month and sixteen days.

Duration Prior to Hospitalization.—The average duration of the symptoms in twenty-two cases in which this could be determined fairly accurately was over seven months. However, it is readily admitted that this is unreliable, not only because of inadequate histories supplied by the patients or their families, but because of the insidious onset in many cases which made it impossible to determine when the nervous symptoms set in.

Spinal Fluid.—Tubercle bacilli were noted in the fluid only once in the series. They were looked for in five other cases, with negative results; mention of bacilli was not made in the other cases. In seventeen instances in which the cell count is recorded, the average was 96 cells per cubic millimeter. The extremes were from 2 to 320 cells per cubic millimeter. In a few cases, specific mention was made of the fact that these were mainly lymphocytes, with or without percentage figures.

Wassermann tests were made in seven instances; globulin tests, in six; colloidal gold tests, in nine; pellicle formation was noted in three. The pressure was noted in seven instances, but not with manometric values; hence, probably such determinations are of little real worth. In only one of the seven cases was it stated that there was no increase in pressure; in four, there was slight or moderate increase; in two, a marked increase. In only two were the Wassermann tests positive. The colloidal gold curve approached complete precipitation in two cases. In neither of these was the result of a spinal fluid Wassermann test reported.

First Symptom.—Headache is reported as the first symptom in nine cases (41.0 per cent) of the twenty-two in which such data were available. If one includes in this series another case with the term "pain in the head," the percentage is increased to 45.5 per cent. In two instances, epileptic attacks ushered in the manifestations of the disease; in two others, numbness; while in the eight remaining known clinical reports, the initial symptoms were different and consisted of: lumbar pain, loss of weight, gastro-intestinal symptoms, cough, paralysis, nervousness, "sinus trouble" and "sore foot."

Vomiting.—Only three of the cases in this report contain a definite history of vomiting. But it must again be stated that the nonfinding of certain symptoms in the necessarily inadequate histories is not to be taken at full value. Moreover, the meningitis in so many instances obscures the tumor syndrome.

Other Symptoms.—Delirium is listed as occurring in twelve cases, with no mention in fifteen. Malaise is specifically mentioned in fourteen of the series. Pain in the neck was found in five.

Clinical Diagnoses.—One of the most interesting studies on any such series of cases is the check between the clinical and the pathologic diagnoses. An examination of the table at first glance shows a poor correlation, for only three were diagnosed as tuberculomas ante mortem. It must be constantly borne in mind, however, that the usual cause of prominent symptomatology and of death is meningitis; since eleven more cases were diagnosed as tuberculous meningitis, it would seem that fourteen of the series might be considered as correctly diagnosed on the basis of the observations. Further, the complete absence of any clinical data in three cases compels one to leave them out of consideration. Hence, with fourteen of twenty-four (58.3), a fair average is maintained. Tuberculosis, pulmonary or of other extranervous type, was diagnosed in three other cases; in one, the disease was undiagnosed, while the conditions in the remaining six were as follows: toxic psychosis, alcoholism, apoplexy, myelitis, intracranial pressure and osteomyelitis (spine).

Case Incidence.—Unfortunately, this cannot be absolutely determined because of occasional uncertainties as to the hospital origin of the cases. Nevertheless, with all possible checks, an approximation is as follows: During the years 1920 to 1926, inclusive, 1,768 brains are listed as having been examined pathologically in this laboratory. Of these, about 1,550 cases came from the services of the Philadelphia General Hospital. In this series of reported cases, two definitely came from other hospitals; while of the twenty-five remaining cases, it is certain that twenty-two, and perhaps all, came from the Philadelphia General Hospital. If one considers, then, twenty-five, the percentage incidence is 1.6 per cent of all autopsied specimens; while if one takes the lesser but more certain figure of twenty-two, the incidence is 1.42 per cent. At any rate, relative numbers of this type of cases in the wards of a large general hospital are shown.

Incidence Among Tumors.—In the years 1920 to 1926, there are found approximately 175 tumors and abscesses of the brain and spinal cord among the cases studied in this laboratory. Of these, twenty-seven are tuberculomas, approximately 15 per cent.

TABLE 3.—*Case Reports from the Literature* *

Date	Author	Sex	Age	Location
1864	Steffen (Berl. klin. Wehnschr., p. 198)....	Male	3 yr.	Corpora quadrigemina
	Henoch (Berl. klin. Wehnschr., p. 125)....	Female	15 mo.	Corpora quadrigemina
1869	Foerster (Jahrb. f. Kinderh. **2**: 306).....	Male	3 mo.	Pons
		Male	2½ yr.	Cerebellum
		Male	9 yr.	Cerebellum
		Female	4½ mo.	Crus
1870	Pilz (footnotes 3 and 18).....	Female	3 yr.	Corpora quadrigemina
		Female	11 yr.	Striatum
		Male	4 yr.	Thalamus
1871	.....	Male	2 yr.	Multiple
	Fleischmann (Wien. med. Wehnschr. **21**: 191)	Male	8 yr.	Corpora quadrigemina
1881	Heubner (footnote 19).....	Male	1 yr.	Medulla
		Male	2½ yr.	Cerebellum
		Male	6 mo.	Corpora quadrigemina
1883	Smith (Brit. M. J. **2**: 821).....	Male	3 yr.	Pons
	Bristowe (footnote 20).....	.....	7 yr.	Corpora quadrigemina
		.....	4 yr.	Thalamus
		.....	4 yr.	Cerebellum
1885	Macewen	Male	36 yr.	Dura
1886	.....	Female	4 yr.	Cerebellum
	Chaffey (Tr. Path. Soc. London **37**: 63)	Female	2 yr.	Brain stem
	Ord (footnote 12).....	Male	20 yr.	Frontal
1887	Horsley (Brit. M. J. **1**: 864).....	Male	22 yr.	Cerebrum
	Bourneville and Isch-Wall (Progrès méd. **15**, tome 6, p. 118).....	Male	5 yr.	Pons
	Macewen (footnote 10).....	.....	....	Cerebellum
1888	Macewen (Brit. M. J. **2**: 302).....	Female	7 yr.	Frontal
1889	MacGregor (footnote 14).....	Female	8 yr.	Pons
	Dalton (footnote 8).....	.....	....	Multiple
	Mercanton and Combe (footnote 7).....	Female	12 yr.	Cerebrum
	Knapp and Bradford (Boston M. & S. J., p. 325)	Male	32 yr.	Cerebrum
1891	Ewald	Male	7 yr.	Corpora quadrigemina
	Roget (Lyon méd., p. 497; Am. J. M. Sc. **101**: 233)	Female	9 yr.	Corpus callosum
1892	Bradford and Bullard.....	.....	....	Cerebellum
	Knapp and Bradford (J. Nerv. & Ment. Dis.)	Male	28 yr.	Cerebellum
1893	Eisenlohr (Deutsche Ztschr. f. Nervenh. **3**: 260)	Female	8 yr.	Thalamus
	Booth and Curtis (Ann. Surg., p. 127)....	Male	35 yr.	Frontal
	Macewen (footnote 10).....	.....	....	Cerebellum
	Parry (Glasgow M. J. **40**: 35).....	Male	5 yr.	Cerebrum
	Juboulay (Arch. provinciales de chir. **2**: 74)	Female	9 yr.	Frontal
	Andeond (Rev. méd. de la Suisse Rom. **13**: 12)†	Male	40 yr.	Paracentral
1894	Bruns (Arch. f. Psychiat. **26**: 209).....	Male	9 mo.	Corpora quadrigemina
	Greiwe (footnote 6).....	Male	35 yr.	Cerebrum
	Beck	Male	23 yr.	Rolandic
	Schwartz	Male	33 yr.	Cerebrum
1895	Kroenlein (Beitr. z. klin. Chir. **25**: 251)..	Male	43 yr.	Rolandic
1896	Broca	Male	35 yr.	Rolandic
	Finlayson	Male	3 yr.	Pons
		Female	19 mo.	Rolandic
1897	Levi	Male	9 mo.	Pons
	Martin	Female	3½ yr.	Cerebrum
	Collins and Brewer (M. Rec.).....	Male	26 yr.	Cerebellum
1898	Japha (Ztschr. f. praktische Aerzte **7**: 701)	Female	7 yr.	Cerebellum
1900	Japha	Female	16 mo.	Precentral
1900	Treyer (Rev. méd. de la Suisse Rom. **20**: 229)	Female	7 yr.	Rolandic
		Male	38 yr.	Rolandic
1901	Hoppe (footnote 13).....	Male	10 yr.	Striatum
	Dercum (J. Nerv. & Ment. Dis. **38**: 451)	Male	12 yr.	Occipital
	Nissen (Jahrb. f. Kinderh. **54**: 618).....	Male	3 yr.	Corpora quadrigemina
		Male	17 mo.	Corpora quadrigemina
1903	Bovaird (footnote 9).....	Female	6 yr.	Cerebrum
	Trevelyan (Lancet **2**: 1276) 33 cases mentioned; not described			
1904	Dufour (Arch. de neurol. **17**: 82).....	Female	8 mo.	Pons
1905	Spiller (Am. Neurol. Assn.).....	Male	Adult	Pons
1906	Leignel-Lavastine (Rev. de méd. **26**: 270)	Male	52 yr.	Parietal
		Male	35 yr.	Parietal
		Male	30 yr.	Paracentral
		Male	20 yr.	Multiple

* Tuberculoma of the cord is excellently reviewed in a contribution by Thalhimer and Hassin, in 1922. None of these cases are listed here.

† This article has not been consulted.

TABLE 3.—*Case Reports from the Literature—Continued*

Date	Author	Sex	Age	Location
1907	Branson (footnote 4)	Female	3½ yr.	Occipital temporal
		Female	5 yr.	Multiple
1908	Haushalter and Lucien	.....	6½ yr.	Tuber cinereum
1909	Alger (Long Island M. J. **3**: 128)	Female	8 yr.	Corpora quadrigemina
		Female	6 yr.	Multiple
1910	.....	Male	30 yr.	Parietal
1920	Knox (Am. J. Dis. Child. **20**: 436)	Male	3 yr.	Multiple
	Souques (footnote 16)	.....	Adult	Parietal
1921	Randolph (Am. Rev. Tubere. **5**: 665)	Male	34 yr.	Frontal
1923	Harbitz and Monrad-Krohn (footnote 11)	Male	27 yr.	Optopeduncular
1925	Babonneix and Hutmel (footnot 17)	Male	35 yr.	Pons
	Pilod and Fribourg (Bull. et mém. Soc. méd. d. hôp. de Paris **49**: 1123)	.....	.....	Pons
	Gleich (footnote 15)	Female	1 yr.	Cerebellum
1927	Van Wagenen (footnote 5)	Male ?	3 yr.	Multiple
		Male	22 yr.	Cerebellum
		Female	7 yr.	Cerebellum
		Female	4 yr.	Cerebellum
		Male	27 yr.	Cerebellum
		Female	48 yr.	Cerebrum
		Male	7 yr.	Cerebellum
		Male	21 yr.	Cerebrum
		Male	30 yr.	Pons
		Male	53 yr.	Cerebellum
		Male	45 yr.	Cerebellum
		Female	34 yr.	Cerebellum
		Male	8 yr.	Internal capsule
		Female	20 yr.	Restiforme
1928	Anderson	Male	....	Thalamus
		Male	3 yr.	Cerebellum
		Female	....	Temporal
		Male	Adult	Lumbar
		Male	....	Cerebellum
		Male	29 yr.	Frontals
		Male	30 yr.	Precentral
		Male	38 yr.	Frontal
		Male	4 yr.	Pons and frontal
		Male	41 yr.	Pons
		Male	27 yr.	Thalamus
		Male	34 yr.	Parietal
		Male	26 yr.	Cauda
		Female	37 yr.	Cerebellum
		Male	Adult	Frontals
		Male	26 yr.	Parietal
		Female	54 yr.	Temporal
		Male	61 yr.	Lower cord
		Female	43 yr.	Parietal
		Male	25 yr.	Lower cord
		Male	27 yr.	Rolandic
		Male	64 yr.	Cervical
		Female	21 yr.	Thalamus
		Male	37 yr.	Precentral
		Female	15 yr.	Rolandic
		Male	27 yr.	Pons and Rolandic
		Male	32 yr.	Parietal and cerebellum

SUMMARY

Twenty-seven cases of proved tuberculous neoplasms of the central nervous system are presented and analyzed from several points of view. The following summarized statements apply:

1. The tumor syndrome may be present, but it is usually eclipsed by the signs of meningitis, rendering the diagnosis of neoplasm difficult or impossible.

2. This series is predominantly an adult group. Over three fourths of the patients are males.

3. Solitary tuberculomas constitute three fourths of the total.

4. The size of tumor range is wide, but within the limits of the usual case reports in the literature.

5. No especial predilection for certain areas is noted, cases being encountered in all parts of the brain. The frontal lobes constitute the site of greatest frequency.

6. Nothing of differential value is to be found in the weight of the brain.

7. The patients studied were hospitalized on an average of one and one half months, with an approximate previous duration of the nervous symptoms of seven months.

8. Laboratory observations are of too scattered a nature to be made into generalizations. They represent mainly secondary meningitis.

9. Pulmonary tuberculosis is the usual focus of origin.

10. Among all cases studied in this laboratory, tuberculomas constitute between 1.4 and 1.6 per cent; among all tumors studied in the same period, they constitute about 15 per cent.

REVIEW OF LITERATURE

Incidence of Tuberculomas.—The frequency with which tuberculous neoplasms occur in the central nervous systems is repeatedly commented on. Again and again reference is made to statistics compiled by Starr, in 1888, showing that of a series of 300 patients under 18 years of age with tumor of the brain, 152 were tuberculous. Some time later, thirty-five additional tumors were added, and of the total of 355, 166 were of such a nature.

Kerley [1] states that it is by far the most frequent form of neoplasm in childhood, over 50 per cent of all cases being tuberculous. Holt and Howland [2] make differentiations of age, stating that in only 2.5 per cent of their autopsies in cases in which the patients had been under 3 years of age were neoplasms found, whereas in 24.4 per cent of those in cases of children between 4 and 12 years of age was this lesion observed. They found the lesion most frequently in the cerebellum, an observation noted in almost all textbook discussions of the topic. Pilz [3] quoted Rillie and Barthez to the effect that among 312 tuberculous children they found thirty-seven cases of brain tubercle; in the same article, Ladame is quoted as having had 331 patients with tumor, including eighty-seven children under 14 years of age, with sixty-four tuberculomas. Branson [4] says: "Tuberculomatous masses form a large

1. Kerley: Practical Pediatrics, ed. 3, 1927, p. 557.
2. Holt and Howland: Diseases of Infancy and Childhood, ed. 8, 1927.
3. Pilz: Jahrb. f. Kinderh. **3**:133, 1870.
4. Branson: The Hospital **42**:550, 575, 1907.

majority of the brain tumors of childhood." Many other textbooks concur in these two fundamental points: the incidence of tuberculoma of the nervous system is high in childhood, and the commonest site is the cerebellum. Among others favoring this view are Councilman, Stengel and Fox, Oppenheim and Weisenburg.

In Starr's 152 cases, the anatomic distribution was as follows: cerebellum, 47 cases; cerebral cortex, 13 cases; pons, 19 cases; central white matter, 6 cases; corpora quadrigemina and crura, 16 cases; medulla, 2 cases; basal ganglia and lateral ventricles, 14 cases.

These figures seem to represent the current ideas of distribution found throughout studies of the subject up to the present time. Concerning the question of frequency among all tumors of the brain, however, a departure from the oft quoted statistics of Starr is made in the careful study made at Cushing's clinic in Boston by Van Wagenen.[5] He analyzed 1,000 verified tumors of the Peter Bent Brigham Hospital clinic. Of this number, 1.4 per cent were tuberculous; three others were probably, but not certainly, of this nature. Of the seventeen instances, only three were extracerebellar. Ten of the tumors were in patients over 18 years of age. It will be noted that this study of Van Wagenen harmonizes with the current idea of cerebellar preponderance, but varies markedly from the Starr statistics as to age.

Symptomatology.—Two entirely different groups of observations confront one in a perusal of the cases reported, and real harmony cannot be made of these groups. One is the usual syndrome of neoplasm, irrespective of type, and almost totally dependent on location. Many are of this type, but, since it is the second type—the syndrome of tuberculous meningitis—that usually kills, the first type is often masked or obscured by the second. In many cases in which the diagnosis is meningitis a tuberculoma is brought to light only on the autopsy table.

It has seemed worth while to present briefly a few of the cases cited in the literature as fairly typical of the group which might reasonably have been diagnosed as tumor per se. Greiwe[6] reported a case in which lameness gradually developed on one side, lasting over three fourths of a year. Later, paresthesias ensued, with weakness of the seventh and twelfth cranial nerves. A patient described by Mercanton and Combe[7] developed conjugate deviation, sensory disturbances, jacksonian epilepsy and aphasia. One of Dalton's[8] patients manifested paresis of the limbs and athetosis, dating from a fall. Other symptoms

5. Van Wagenen, W. P.: Tuberculoma of the Brain, Arch. Neurol. & Psychiat. **17**:57 (Jan.) 1927.

6. Greiwe: Neurol. Centralbl. **13**:130, 1894.

7. Mercanton and Combe: Rev. méd. de la Suisse Rom. **9**:486, 1889.

8. Dalton: Tr. Path. Soc. London **40**, 1889.

in reported cases are: loss of power of gradual development; early symptoms entirely due to tumor as such (Bovaird [9]); frequent epileptic seizures (Macewen [10]); frontal headache and impaired vision (Harbitz and Monrad-Krohn [11]); hemiplegia and headache (Ord [12]); weakness of one side (Hoppe [13]); a convulsion lasting five and one-half hours, with freedom from symptoms for fourteen months thereafter (Branson [4]), and gastric disturbances (MacGregor [14]).

Concerning the other type of clinical case, that in which meningitic symptoms are present, nothing needs be said. It seems almost a certainty that death will occur by this route. Hence, if the tumor is not operable, the main concern would be holding the meningitic onset in abeyance as long as possible. Undoubtedly there is a certain tendency for such a latency on the part of tuberculous tumors. One author (Gleich [15]) goes so far as to state that "chronicity and capacity for remaining in abeyance are characteristic of tuberculous tumors of the brain." Reperusal of the cases cited in this report gives some verification of this, although cases with a definitely long course are few.

Trauma.—Trauma is mentioned as an occasional factor in localizing the tubercle bacilli. It is especially stressed by Souques [16] and by Babonneix,[17] both of whom cite cases in which tuberculomas followed trauma. Dalton's case [8] dated from a fall, but in this instance there were three separate tumors. Bovaird's report [9] likewise dated back to a specific injury. However, the possibilities of attributing symptoms to some antecedent injury are so numerous that it seems inadvisable to discuss this further.

Meningitis.—Meningitis occurred in the vast majority of cases reported. Nevertheless, certain cases are reported without its occurrence, such as those of Pilz,[18] Heubner,[19] and Bristowe.[20]

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9. Bovaird: Proc. New York Path. Soc. **2**:97, 1902.
10. Macewen: Brit. M. J. **2**:1367, 1893.
11. Harbitz and Monrad-Krohn: Norsk. Mag. f. Laegevidensk. **84**:119 (Feb.) 1923.
12. Ord: Tr. Path. Soc. London **37**:46, 1886.
13. Hoppe: A Report of Seven Operations for Brain Tumors and Cysts, J. A. M. A. **36**:302 (Feb. 2) 1901.
14. MacGregor: Lancet **2**:1079, 1889.
15. Gleich, M.: Arch. Pediat. **42**:273 (April) 1925.
16. Souques: Rev. neurol. **36**:69, 136, 1920.
17. Babonneix, L., and Hutinel, J.: Bull. et mém Soc. méd. d. hôp. de Paris **49**:1275 (July 31) 1925.
18. Pilz: Jahrb. f. Kinderh. **4**:433, 1871 (footnote 3).
19. Heubner: Arch. f. Psychiat. **12**:536, 1881.
20. Bristowe: Brain **6**:167, 1883; Glasgow M. J., July, 1883; Rev. Clin. de Bologna **34**, 1883.

Pathologic Process.—Little need be said concerning the pathologic process of tuberculoma of the nervous system, for it is essentially that of a tubercle elsewhere. It must be remembered that what is spoken of as solitary tubercle is in reality an aggregation of many small tubercles with caseous fusion of the originally discrete lesions. Occasionally, sclerosis is observed in the vicinity of the masses, arising from a glial proliferation or from the adventitia of the blood vessels. An interesting note is the finding by Friedenwald and Greenfield of immense numbers of bacilli in the vessel walls and within the caliber of the vessels. The application of the silver fibril stains will probably prove of value in the differential study of questionable cases of tuberculoma and gumma.

Surgery.—No attempt will be made here to discuss the surgical aspects. This is excellently reviewed in the article by Van Wagenen.[5] It is evident from a perusal of many case reports that surgical procedures have had small success. The chief trouble seems to be in the development of meningitis following the operative procedure. Van Wagenen states that not more than fifty cases are reported in which extirpation has been attempted. In these cases "permanent recoveries have been exceedingly few," and with few exceptions have occurred after the removal of a cerebral lesion in an adult. This author is indeed skeptical of surgical intervention, either planned deliberately or when a tuberculoma is encountered in exploration. One of the most satisfactory cases on record is that of Elsberg,[21] in which an intramedullary tuberculoma was removed from the lower thoracic cord, with complete recovery; the patient was reported as living eight years after the operation.

21. Elsberg: Ann. Surg. **65**:269, 1917.

CENTRAL NEURITIS

ITS ETIOLOGY AND SYMPTOMATOLOGY *

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The pathologic process known as "central neuritis" involves particularly the ganglion cells and resembles the change found in the cell body of a peripheral neuron after injury to its axon. As the involvement frequently seems severe enough to interfere with function, one would expect that its presence could be detected during life. Although central neuritis is found in many different diseases, there must be a common etiologic factor. In this study, I investigated central neuritis from two points of view: (1) diagnosis during life, and (2) etiology.

HISTORICAL REVIEW

Central neuritis was first described and named by Meyer.[1] He found it in peculiar forms or end stages of depressive psychosis of the

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1. Meyer, Adolf: Demonstration of Various Types of Changes in the Giant Cells of the Paracentral Lobule, Amer. J. Insan. **54**:221, 1897-1898; On Parenchymatous Systemic Degenerations Mainly in the Central Nervous System, Brain **24**:47, 1901.

climacteric period, in alcoholicosenile and alcoholicophthisical cachectic states, in idiocy, and possibly in general paralysis. He associated the following clinical syndrome with central neuritis: After a course during which there was no suspicion of the presence of an organic disorder, there appeared, more or less suddenly, difficulty in locomotion, increasing weakness for coordinated movements, jactitations of the limbs, rigidity, disorders of the reflexes, diarrhea and occasional febrile fluctuations. The mental state of this terminal episode consisted of anxious perplexed agitation, delirium or stupor, similar to that of a protracted case of delirium tremens. In 1909, Coriat,[2] from a study of twenty-two cases, delineated a similar symptom complex and considered that it was a terminal phase of cachectic delirium or depression, and that it indicated an invariably fatal termination. Barrett[3] reviewed the question in 1913 and decided that the symptomatology was too variable for a clinical entity.

Postmortem studies have revealed the presence of central neuritis in diverse conditions. It has been reported in persons with alcoholic polyneuritis by Cole,[4] Faure,[5] Mott,[6] Spiller[7] and Turner;[8] in cachectic delirium by Faure; in cardiogenetic psychoses by Cotton and Hammond;[9] in epilepsy by Southard and Hodgkins;[10] in involutional melancholia by Wiglesworth,[11] Cotton and Southard[12] and others; in imbecility by Spiller[13] and Hirsch;[14] in insomnia and in normal per-

2. Coriat, I. H.: The Symptom Complex of Central Neuritis, J. Nerv. & Ment. Dis. **36**:227, 1909.

3. Barrett, A. M.: Presenile Mental and Nervous Disorders, in White and Jelliffe: Modern Treatment of Nervous and Mental Diseases, Philadelphia, Lea & Febiger, 1913, vol. 1, p. 676.

4. Cole, S. J.: On Changes in the Central Nervous System in Neuritic Disorders of Chronic Alcoholism, Brain **25**:326, 1902.

5. Faure: Rev. neurol., December, 1899.

6. Mott, F. W.: The Nervous System in Chronic Alcoholism, Brit. M. J. **2**:1403, 1910.

7. Spiller, W. G.: The Pathological Changes in the Neurone of Nervous Diseases, J. Nerv. & Ment. Dis. **27**:487, 1900.

8. Turner, J.: An Account of the Nerve Cells in Thirty-Three Cases of Insanity, Brain, 1903, vol. 26.

9. Cotton, H. A., and Hammond, F. S.: Cardio-Genetic Psychosis, Amer. J. Insan. **67**:467 (Jan.) 1911.

10. Southard, E. E., and Hodgkins, quoted by Cotton and Southard (footnote 12).

11. Wiglesworth, J.: On the Pathology of Certain Cases of Melancholia Attonita, or Acute Dementia, J. Ment. Sc., October, 1883, p. 355.

12. Cotton, H. A., and Southard, E. E.: A Case of Central Neuritis with Autopsy, Am. J. Insan. **65**:635 (April) 1909.

13. Spiller, W. G.: J. Nerv. & Ment. Dis., 1899.

14. Hirsch: J. Nerv. & Ment. Dis., 1898.

sons by Robertson;[15] in Landry's paralysis by Worcester;[16] in manic-depressive psychosis of the depressed type by Turner[6] and Orr;[17] in meningitis by Barker;[18] in general paralysis by Turner; in pellagra by Cormac,[19] Harris,[20] Pierce,[21] Spiller and Anderson[22] and Winkelman;[23] in acute infective polyneuritis by Bradford, Bashford and Wilson[24] and Casamajor;[25] in toxic exhaustive psychoses by Wiglesworth; in diphtheria; in fish poisoning and in typhoid. Scott[26] reported an epidemic of polyneuritis in Jamaica, which he considered to be one of central neuritis, but his pathologic protocols do not seem to substantiate his diagnosis.

THE CLINICAL CLASSIFICATION OF CASES STUDIED

The material for this study comprised all the cases presenting this pathologic change in the Pathological Laboratory of the Department for Nervous and Mental Diseases of the Pennsylvania Hospital between 1914 and 1926, and in the Neuropathological Laboratory of the Philadelphia General Hospital from 1920 to 1926. These thirty-one cases were diagnosed clinically as follows: involutional melancholia, two cases; manic-depressive psychosis, depressed type, two; manic-depressive psychosis, mixed type, two; undiagnosed, but probably toxic-exhaustive psychosis, one; psychosis with somatic disease, five; senile dementia, one; schizophrenia, paranoid type, one; chronic alcoholism, four; delirium tremens, two; pellagra, nine; probably pellagra, but diagnosed general paralysis, one, and epilepsy, one.

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15. Robertson, Ford: Textbook of Pathology in Relation to Mental Diseases, Edinburgh, William F. Clay, 1902.

16. Worcester, W. L.: A Case of Landry's Paralysis, J. Nerv. & Ment. Dis., 1897.

17. Orr, D.: Contribution to the Pathology of Acute Insanity, Brain, 1902.

18. Barker, L. E.: On Certain Changes in the Cells of the Ventral Horns and of the Nucleus Dorsalis in Epidemic Cerebrospinal Meningitis, Brit. M. J. **2**:1839 (Dec. 25) 1897.

19. Cormac, Celestin: Étude anatomo-pathologique et pathogenique sur le syndrome pellagreux, Thesis of Paris, 1902, p. 12.

20. Harris, H. F.: Pellagra, New York, The Macmillan Co., 1919.

21. Pierce, L. B.: Pellagra, Amer. J. Psychiat. **4**:237 (Oct.) 1924.

22. Anderson and Spiller: Am. J. M. Sc., 1911.

23. Winkelman, N. W.: Beiträge zur Neurohistopathologie der Pellagra, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:38, 1926.

24. Bradford, J. R.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polyneuritis, Quart. J. Med. **12**:88, 1918-1919.

25. Casamajor, L.: Acute Ascending Paralysis Among Troops; Pathological Findings, Arch. Neurol. & Psychiat. **6**:605 (Feb.) 1919.

26. Scott, H. H.: An Investigation Into an Acute Outbreak of Central Neuritis, Ann. Trop. Med. **12**:109 (Oct.) 1918.

MICROSCOPIC CHANGES OF CENTRAL NEURITIS

Histologically, the process known as central neuritis involves the cell body, the dendrons and the axon, and occurs in the medium sized and large pyramidal cells, particularly the giant cells of the motor cortex, but not in the small pyramidal and granule cells. The cell body is swollen; there is a progressive disappearance of the Nissl substance, and the nucleus is displaced toward the periphery. In the earlier stages the cell loses its pyramidal contour and becomes globular. The outline is less distinct and seems to merge into the basal substance of the tissue. Toward the final stage, the swelling regresses and the cell outline becomes irregular.

At first there is a dense accumulation of the Nissl bodies in and about the axon hillock, with a thinning out and homogenization at the center of the cell. This dissolution proceeds until the center presents a homogeneous, translucent appearance, which stains light blue in toluidine blue preparations, and the remaining Nissl bodies are clumped about the periphery, particularly in the roots of the dendrons. In cells from which most of the Nissl substance has disappeared, the remaining chromatin particles are grouped about the displaced nucleus, although sometimes a clear perinuclear space may be observed. Later, only a few masses of chromatin remain scattered here and there in the cytoplasm, and finally they disappear altogether. In some instances, when the cell body is swollen only slightly, the stratified arrangement of the Nissl bodies has been lost, but in the majority of cases, as long as sufficient Nissl substance remains, the stratification is preserved. The whirlpools described by Meyer were noted infrequently. As a general rule, the dissolution of the chromatin material is first apparent at the center of the cell.

The nucleus is displaced to one side, usually in the direction of the axon hillock. As the severity of the process increases, the nucleus evaginates the cell wall, appearing as a protrusion on the side. Later, the cell wall ruptures and the nucleus escapes. The nuclear outline is usually normal, though a mild degree of irregularity has been noted. In some cells that show severe involvement, the nucleus assumes an irregularly ovoid form, quite at variance with its normal spherical appearance. The nuclear contents are unaltered, even during the process of extrusion, though at this time the nucleolus appears larger than usual.

In Cajal and Bielschowsky preparations, Cotton and Southard, Lambert [27] and Marui [28] found a change in the intracellular neurofibrils

27. Lambert, C. I.: Notes on Pathological Material, N. Y. State Hospital Bull. **1**:3, 1908.

28. Marui, K.: Histopathologic Study on Two Cases of "Central Neuritis," Arch. Neurol. & Psychiat. **2**:1 (July) 1919.

which consisted of a variable degree of fragmentation, sometimes progressing to the point where they have dissolved into dustlike particles. This fragmentation occurred only in the parts of the cell that showed chromatolysis and, in degree, kept pace with the dissolution of the Nissl bodies.

Nearly all authors call attention to the fact that the amount of Marchi degeneration of the fibers, leading from the involved parts of the cortex, is much less than would be expected if the change in the cell was secondary to an axonal lesion. On this account, Cole considered that the alteration of the axon was not the cause of the cellular pathologic change but that the same etiologic factor affected both the cell body and the process. Marui, however, found a larger number of axons altered in Alzheimer-Mann preparations than he found in Marchi sections. This alteration consisted of an interruption of the normally blue-stained myelin sheath by nodes of unstained and red-stained material. He concluded that this degenerative change, combined with the alterations of the axons at different levels of their course, as shown by Marchi preparations, was sufficient to explain the discrepancy between the degree of change in the cells of the cortex and in the axis cylinders of the white matter.

The same author has described ameboid glia cells in central neuritis, with regressive changes in the neuroglia nuclei, consisting of swelling, homogeneity of staining and disintegration. He found the glial nuclei surrounded by small masses of greenish yellow pigment. This change was observed rarely in my cases, but satellitosis of the ganglion cells was a common occurrence.

REPORT OF CASES

Following is a brief resumé of the clinicopathologic histories of the patients:

INVOLUTIONAL MELANCHOLIA

CASE 1.—*History.*—A. M. R., a woman, aged 48, admitted to the hospital, June 4, 1915, had had measles in childhood and typhoid fever at the age of 18. For several years she had suffered from hemorrhoids complicated by anal fissure, and from hay-fever and congestive menstrual headaches. The illness began ten months before admission to the hospital with irritability, agitated depression and attempts at suicide.

Examination.—On admission, the heart was enlarged, with accentuation of the pulmonic second sound and a systolic apical murmur. The skin of the abdomen presented a brownish pigmentation, and the face was eczematous. The patient was careless of her appearance, and showed retardation and marked inertia. She talked infrequently throughout her stay in the hospital. She had delusions of jealousy and of somatic disturbances, was self accusatory and had poverty of ideas. She was depressed, agitated and, at times, noisy.

Course.—During her stay in the hospital, the blood pressure varied from 120 systolic, 84 diastolic, in 1915, to 98 systolic, 56 diastolic in 1918; the pulse rate varied from 66 to 88. Sleep and appetite were poor and, in 1916, she developed difficulty in swallowing which necessitated feeding by tube that year, in 1917

and in the early part of 1918. During this time, she was constipated. In 1915, she had peculiar manneristic movements of the hands and later developed a tremor of the head and left arm. The next year the left knee jerk was increased slightly but was normal thereafter. She lost weight gradually, until toward the end of the illness she was much emaciated. She grew weaker and during 1918 was bedridden. She developed edema of the feet and ankles, and bedsores. Toward the end of 1918, she had a delirious episode with visual hallucinations, following which she became clear mentally and remained so until death on Feb. 4, 1919.

Laboratory Studies.—At times a trace of albumin was found in the urine. Throughout the illness she had a leukocytosis of about 12,000.

Necropsy.—Degenerative myocarditis, peritoneal and pulmonary tuberculosis, chronic nephritis and fatty infiltration of the liver were found.

Neurohistology.—Sclerotic changes were found in the pyramidal tracts. Central neuritis was most marked in the precentral and postcentral areas, and in the ventral horns of the cervical and dorsal regions of the cord. It was present to a less degree in the prefrontal, temporal and occipital regions.

CASE 2.—*History.*—L. N., a woman, aged 44, who was admitted to the hospital, April 6, 1926, had an unimportant previous history. The illness began, one year prior to admission, with depression, apprehensiveness, auditory hallucinations and generalized tremor. She seldom spoke.

Examination.—On admission, she was emaciated, had mild fever, and several bedsores. There was an apical systolic murmur, and the systolic blood pressure was 120. The pupils did not react to light; the reflexes were increased slightly, and a mild tremor of the fingers was present. She was restless, depressed and apprehensive.

Course.—The temperature of 99 F. on admission dropped to 97 F. and then rose to 104.5 F. before her death. She became gradually weaker. Because the blood sugar was reported through error to be 311 she was given insulin, which reduced it to 40. Dextrose was given intravenously to combat the insulin shock, but she became worse and died the next day, April 8, 1926.

Laboratory Studies.—The urine contained albumin. The blood urea was 10.

Necropsy.—Sclerosis of the coronary arteries, diffuse fibrosis of the heart, arteriosclerosis of the spleen, fatty infiltration and passive congestion of the liver, and fatty infiltration of the pancreas were found.

Nervous System: There was mild fibrous thickening of the pia-arachnoid; the walls of the cerebral vessels were thin and stained metachromatically. A mild degree of central neuritis was present in the cortex.

MANIC-DEPRESSIVE PSYCHOSIS, DEPRESSED TYPE

CASE 3.—*History.*—H. G., a man, aged 56, who was admitted to the hospital, Feb. 1, 1918, had an unimportant previous history. The illness began, one month previous to admission, with insomnia, depression, agitation, talkativeness and the expression of a delusion that he was dead.

Examination.—On admission, he had mild fever; the blood pressure was 170 systolic; 110 diastolic, and the pulse rate, 120. He slept and ate poorly and was incontinent. Owing to difficulty in swallowing, he had to be fed by tube. A mild generalized tremor was present. He was depressed, agitated, talkative and, at times, noisy. He had auditory hallucinations and expressed ideas of self accusation.

Course.—During residence in the hospital, he developed a slight bedsore. On Feb. 12, 1918, he developed an abscess on the hand. This was followed by one

on the calf; the temperature rose, and he presented the signs of septicemia, from which he died on February 15.

Laboratory Studies.—The urine showed albumin and hyaline casts.

Necropsy.—An abscess of the calf and of the forearm, generalized arteriosclerosis and chronic nephritis were present.

Nervous System: A mild degree of "central neuritis" was present in the precentral area.

CASE 4.—*History.*—M. J., a woman, aged 43, admitted to the hospital on Dec. 8, 1916, had suffered from measles in childhood. The present illness commenced two months before admission with depression and suicidal tendencies.

Examination.—On admission an apical systolic murmur was found, with a blood pressure of 120 systolic; 76, diastolic. The pupils were irregular. She was depressed, retarded, indifferent and agitated. She had poverty of ideas and was self accusative. She expressed somatic delusions and ideas of having died.

Course.—During residence in the hospital, she had several convulsive seizures. On April 13, 1918, she suffered a sudden collapse with diarrhea, vomiting and a rise in temperature. She did not rally, but died two days later.

Laboratory Studies.—A blood count revealed: red cell, 4,496,000; white cells, 7,400; hemoglobin, 90 per cent; polymorphonuclear cells, 78.8 per cent; small lymphocytes, 11; large lymphocytes, 7.5; transitionals, 2.4, and eosinophils, 0.4.

Necropsy.—Hypostatic pneumonia, and chronic passive congestion and fatty infiltration of the liver were present.

Nervous System: Central neuritis was present in the precentral area and to a less degree in the postcentral region.

MANIC-DEPRESSIVE PSYCHOSIS, MIXED TYPE

CASE 5.—*History.*—S. R. J., a man, aged 37, who was admitted to the hospital on April 18, 1912, had an unimportant previous history. He had a first manic attack at the age of 20, which lasted three months. On discharge, he was not completely well and for the succeeding thirteen years he had mild auditory hallucinations and expressed delusional ideas. During this period he was seclusive, and his behavior showed mild paranoid trends. Two years before the second admission, the condition became more evident, increasing to a point of obvious auditory hallucinations, with mannerisms and a violent and destructive manner.

Examination.—On admission, the knee jerks were sluggish and there was a doubtful Babinski sign. He was irritable, resistive and destructive, and expressed self accusative and persecutory ideas.

Course.—During the next year, the reflexes were normal and remained so until death. During 1913 and 1914, he had to be fed by tube; he lost weight to the point of emaciation during the stay in the hospital. In 1913, he suffered a fracture of the wrist while attempting to escape. Throughout his life in the hospital he was manneristic, violent, stubborn and suffered from auditory hallucinations. On April 6, 1914, he attempted suicide by hitting his head on the floor, and produced a ventricular hemorrhage from which he died the following day.

Laboratory Studies.—The urine showed albumin and hyaline and granular casts.

Necropsy.—Degenerative myocarditis, thickening of the mitral valve, healed tuberculous lesions in the lungs and chronic nephritis were present.

Nervous System: The pia-arachnoid was congested and cloudy. A hemorrhage was found in the lateral ventricles, and the pyramidal tracts were slightly

degenerated. Central neuritis was present in the prefrontal, precentral, postcentral, temporal and parietal areas.

CASE 6.—*History.*—S. W., a woman, aged 23, admitted to the hospital on Sept. 27, 1926, had an unimportant previous history, except that she was reported as being excitable and peculiar during menstrual periods. The illness began three days before admission with hyperactivity, violence and pressure of speech.

Examination.—On admission she was mute, negativistic, made silly grimaces, laughed foolishly and sang and talked incoherently. She died the next day.

Laboratory Studies.—None were made.

Necropsy.—Beginning sclerosis of the aorta, chronic fibrous epicarditis, parenchymatous degeneration of the heart, congestion of the lungs, chronic atrophic splenitis, acute congestion of the kidneys and colloid goiter were found.

Nervous System: There was a mild degree of cortical edema; the pia-arachnoid was thickened and contained phagocytic cells. The cortical vessels were fibrotic. The precentral area showed a mild degree of "central neuritis."

UNDIAGNOSED CASE, BUT PROBABLY TOXIC-EXHAUSTIVE PSYCHOSIS

CASE 7.—*History.*—G. M., a man, aged 47, was admitted to the hospital on Feb. 4, 1926, without information concerning his past except that the complaint on admission was of cough and shortness of breath.

Examination.—On admission, he was well nourished and showed signs of a chronic bronchitis. The heart sounds were poor in quality; the blood pressure was 130 systolic, 90 diastolic. The skin showed cutaneous lesions that were suggestive of syphilis. The pupils were irregular, unequal and reacted sluggishly to light. The knee jerks were increased. He was confused, disoriented, restless and expressed persecutory ideas. Visual hallucinations were present.

Course.—During residence in the hospital, the temperature rose from 97 to 103 F. He grew weaker progressively and died on Feb. 22, 1926.

Laboratory Studies.—The urine contained albumin. A blood count revealed: red cells, 6,750,000; white cells, 12,160. The blood urea was 13 and 18, the blood uric acid 3.0 and 3.4, the blood sugar 98 and 122, at two successive examinations. Examination of the cerebrospinal fluid showed: cells, 0; globulin, negative; Wassermann test, negative, colloidal gold course, 0000000000.

Necropsy.—Acute and chronic myocardial degeneration, bronchopneumonia, and cloudy swelling of the liver and kidney were found.

Nervous System: The brain showed edema and congestion. The walls of the small cortical vessels were thickened. Central neuritis was present in the frontal area.

PSYCHOSIS WITH SOMATIC DISEASE

CASE 8.—*Progressive lenticular degeneration.*

History.—G. F. R., a woman, aged 42, who was admitted to the hospital on Nov. 23, 1914, had suffered from dysmenorrhea during adult life. For several years before the present illness, she had had an anal fissure. The illness began in August, 1914, with insomnia, loss of weight and the gradual development of choreo-athetoid movements. She suffered from auditory hallucinations, expressed expansive and persecutory ideas, and was noisy and incoherent.

Examination.—On admission there was an apical systolic heart murmur, with a blood pressure of 81 systolic, 66 diastolic, and a small liver. The pupils were unequal; the left was irregular and both reacted poorly to light. Examination of the fundus showed a neuroretinitis. Ptosis of the eyelids, weakness of the

upper facial muscles, wrist and ankle drop, absent abdominal reflexes and a positive Kernig sign were found. Marked choreo-athetoid movements were present. Cutaneous sensations were diminished in the legs. She was talkative, confused and incoherent..

Course.—During residence in the hospital, she slept poorly. Bedsores formed, and she developed a foul diarrhea. She grew weaker and died on Dec. 9, 1914.

Laboratory Studies.—None were made.

Necropsy.—Mild chronic mitral endocarditis, bronchopneumonia, mild chronic nephritis, chronic salpingitis and acute inflammatory changes in the suprarenals were found.

Nervous System: Central neuritis was marked in the prefrontal and postcentral areas and less marked in the precentral and temporal areas and the cerebellum.

CASE 9.—*Multiple septic emboli, postabortive.*

History.—A. S., a woman, aged 21, who was admitted to the hospital on Nov. 5, 1914, had had whooping cough, acute rheumatic fever and mumps as a child. At the age of 17, she developed a benign goiter. The present illness began in April, 1914, a few days after an induced abortion. She became irritable, apprehensive and restless, and suffered from auditory hallucinations. She talked continuously in an incoherent manner. She slept and ate poorly and developed peculiar movements that resembled choreo-athetosis.

Examination.—On admission, she was well nourished with a slightly enlarged thyroid and a foul vaginal discharge. The blood pressure was 140 systolic, 124 diastolic. There were jerking and twitching movements of the extremities, some of which seemed to resemble choreo-athetosis. She was talkative, incoherent and destructive.

Course.—During residence in the hospital she was constipated, slept poorly and had to be fed by tube. The toxic state increased and was accompanied by an irregular septic fever. An embolic thrombosis occurred in the left leg. She grew weaker and died on Nov. 11, 1914.

Laboratory Studies.—The urine showed albumin, hyaline casts and increased indican.

Necropsy.—Vegetative mitral endocarditis, mild aortitis, multiple pulmonary infarcts, gangrene of the leg, and chronic nephritis were found; portions of an infected placenta were retained in the uterus.

Nervous System: Central neuritis was present to a mild degree in the precentral and postcentral areas.

CASE 10.—*Diffuse cerebral arteriosclerosis (clinically diagnosed as general paralysis).*

History.—J. B. W., a woman, aged 57, who was admitted to the hospital on Aug. 7, 1923, had an unimportant previous history. The illness began in April, 1923, with dizziness, staggering, carelessness in appearance, excitability and alternating periods of depression with poverty of ideas, and of expansiveness with talkativeness and profanity.

Examination.—There was a moderate degree of sclerosis of the peripheral vessels; the blood pressure was 134 systolic, 84 diastolic; an apical systolic murmur was present and was transmitted to the axilla; a mass was present in the left vaginal vault. The left pupil was irregular, and the reaction to light was sluggish. The associated movement of the eyes upward and downward was limited in extent; the left arm was weak and spastic; the reflexes were increased, and

there was a doubtful Babinski sign. The left arm and both legs were incoordinate. The patient was careless of her appearance and talkative and expressed ideas of grandeur and of persecution. Memory was poor; she was disoriented and was frequently exhibitionistic.

Course.—During residence in the hospital, she slept poorly and had difficulty in swallowing. She developed bedsores and an irregular septic fever. During the final three weeks of life, she became much deteriorated, clouded and confused; she developed diarrhea and a vaginal discharge, and died on Oct. 11, 1923.

Laboratory Studies.—The urine contained albumin, hyaline casts and increased indican. The red blood cell count varied from 4,060,000 to 5,260,000; the white blood cell count ranged from 8,900 to 16,200, with a relative leukocytosis. The blood sugar was 105; blood urea, 15; uric acid 3.0. The cerebrospinal fluid showed: a cell count varying from 1 to 3; globulin, from a trace to none; Wassermann reaction, negative; colloidal gold curve, 0110000000.

Necropsy.—Atheroma of the aorta, acute congestion of the spleen, parenchymatous degeneration and cloudy swelling of the kidneys, cloudy swelling of the liver and an old tubo-ovarian abscess were found.

Nervous System: The brain showed chronic internal pachymeningitis, a marked degree of cerebral arteriosclerosis and a cyst in the third and fourth right frontal gyri. Central neuritis was marked in the Betz cells and in the large pyramidal cells of the precentral area.

CASE 11.—*General paralysis.*

History.—A. B. H., a man, aged 36, who was admitted to the hospital on Jan. 30, 1912, throughout life had used alcohol to excess. He contracted syphilis at the age of 24. The illness began, two months previous to admission, with talkativeness, exhilaration, irritability and insomnia. He became forgetful; usually he expressed expansive ideas, but he had short periods of depression during which he expressed delusions of poverty. He had several convulsions.

Examination.—On admission, he was emaciated. The pupils were irregular, unequal and reacted sluggishly to light. There was a fine tremor of the facial muscles; the reflexes were increased and speech was slurring. He was careless of appearance, resistive, noisy and exhibitionistic. Memory was poor.

Course.—During residence in the hospital, he slept and ate poorly. He became incontinent. Usually he was expansive with a marked feeling of well being, but this state of exhilaration was interrupted by brief periods of depression in which he expressed delusions of being poisoned. The mental condition improved and he was discharged in June, 1912, but was readmitted in November of the same year with a relapse. The physical condition had improved so that he had regained his usual weight. On Dec. 4, 1912, he complained of nausea; the following day he became comatose and had several convulsions, in one of which he died.

Laboratory Studies.—The urine contained albumin. The serology was typical of general paralysis.

Necropsy.—Mild chronic nephritis and an ulceration of the small intestine were found.

Nervous System: The arteries at the base of the brain were sclerosed. The cortex showed the pathologic changes typical of general paralysis. Central neuritis was found in the temporal area.

CASE 12.—*General paralysis.*

History.—W. E. J., a man, aged 59, who was admitted to the hospital on May 6, 1913, had an unimportant history except that he had used alcohol to excess.

The illness began at the age of 50, with slurring speech, marked intellectual deterioration and expansive ideas.

Examination.—On admission, he was moderately well nourished with a scaly condition of the skin and an enlarged liver. The pupils were irregular and reacted poorly to light; speech was slurring, and the gait was ataxic. Tremor of the face and tongue was present; the knee jerks were diminished, and there was a positive Romberg sign. The patient was irritable, restless, filthy in habits and talkative. He expressed many expansive ideas.

Course.—During residence in the hospital, he deteriorated progressively, became increasingly ataxic and lost weight to the point of emaciation. On Sept. 11, 1914, he had a series of convulsions, following which he became much weaker and bedridden; he died on Sept. 10, 1915.

Laboratory Studies.—The urine contained albumin and casts. The serology was typical of general paralysis.

Necropsy.—Hypostatic pneumonia, arteritis of the small vessels of the heart, mild chronic splenitis, chronic interstitial nephritis and chronic glomerulitis were found.

Nervous System: The brain showed pathologic changes characteristic of general paralysis. A slight degree of central neuritis was found in the precentral area.

SENILE DEMENTIA

CASE 13.—*History.*—A. C., a woman, aged 78, who was admitted to the hospital on May 25, 1914, with an unimportant previous history, had become ill three months before with persecutory ideas.

Examination.—On admission, she was emaciated and had general arteriosclerosis with an accentuated pulmonic second sound. The lower part of the left side of the face was paretic; there was tremor of the left arm; senile contractures were present in the legs. The arms were incoordinate. She was confused, disoriented and incoherent. Memory was poor and she experienced visual hallucinations.

Course.—During residence in the hospital, she was constipated and incontinent. She developed bedsores, which became infected, and for two months prior to death she was severely intoxicated and had a mild degree of irregular fever. She grew weaker and died on Sept. 15, 1914.

Laboratory Studies.—Albumin was found in the urine.

Necropsy.—Vegetative mitral endocarditis, chronic secondary nephritis, passive congestion of the liver and an adenocarcinoma of the ovary were found.

Nervous System: The pia-arachnoid was opaque, and the cerebral convolutions were atrophic. A slight degree of central neuritis was found in the prefrontal, precentral and postcentral areas.

SCHIZOPHRENIA, PARANOID TYPE

CASE 14.—*History.*—W. H. C., a man, aged 74, who was admitted to the hospital on Jan. 23, 1890, with an unimportant previous history, had become ill six months before with apprehension and auditory hallucinations. He was nonproductive.

Examination.—On admission, he presented a picture of schizophrenia.

Course.—The condition remained unchanged until 1915. Then he developed a coarse tremor of the fingers, the blood pressure was 175 systolic, 80 diastolic, speech was thick, he was disoriented, and expressed ideas of persecution and self

accusation. He experienced auditory and olfactory hallucinations. In 1916, signs of generalized arteriosclerosis were evident; the heart sounds were faint, and the reflexes were increased. During this year he had an attack of confusion with fever which lasted twenty-four hours. Throughout his residence in the hospital he had short periods of excitement at irregular intervals.

On April 9, 1917, he had a convulsion from which he appeared to recover; five days later he suddenly became cyanotic, the extremities were cold, the heart sounds weak, breathing labored, and there was twitching of the limbs and picking at the bedclothes. He died on April 16, 1917.

Laboratory Studies.—During the last year of life, albumin was present in the urine.

Necropsy.—Mild chronic myocarditis, hypostatic pneumonia, edema and congestion of the lungs, slight valvular endocarditis, slight arteriosclerosis, passive congestion of the liver, cholelithiasis and parenchymatous nephritis were found.

Nervous System: The brain showed mild subpial edema, miliary cortical hemorrhages and a cyst in the caudate nucleus. Central neuritis was marked in the precentral area.

CHRONIC ALCOHOLISM

CASE 15.—*History.*—R. H. G., a man, aged 59, who was admitted to the hospital on March 25, 1913, had used alcohol to excess. The illness began, one year before his admission, with noticeable errors in calculation; he omitted words from letters and made mistakes in his work. Four weeks before admission, he began to worry, became stubborn and obstinate, was confused and forgetful, talked in a rambling, incoherent manner, and was weak.

Examination.—On admission he had generalized arteriosclerosis, weak heart sounds, and a blood pressure of 130 systolic; 85, diastolic. The pupils reacted poorly to light; speech was slurring and the reflexes were increased. He was disoriented, confused, resistive, stubborn and destructive. Speech was incoherent; memory was poor and he replaced the lapses by fabrications. There was marked intellectual defect.

Course.—Two years later the symptoms were unchanged except that the reflexes were diminished. In 1916, the heart was weaker, the degree of arteriosclerosis had increased, and the knee jerks were normally active. During this year he developed difficulty in swallowing, which disappeared in the course of a few months. In 1917, the tremor of the fingers was more marked; he was confused and hyperactive, and the activity was aimless. During his residence in the hospital he became emaciated. He became weaker slowly and died on March 3, 1918.

Laboratory Studies.—Albumin was present in the urine.

Necropsy.—A moderate arteriosclerosis, bronchopneumonia and edema of the lungs, brown atrophy of the liver, cholelithiasis, chronic interstitial nephritis, and congestion of the gastric mucosa were found.

Nervous System: Edema of the pia-arachnoid and of the cortex were found. The cerebral convolutions were atrophied and showed irregular areas of perivascular infiltration. The spinal cord showed several punctate abscesses. A mild degree of central neuritis was present in the precentral area.

CASE 16.—*History.*—E. L., a woman, aged 53, who was admitted to the hospital on June 12, 1924, had become ill in the middle of May, 1924, with weakness, shooting pains and numbness of the legs, unsteadiness in walking in the dark and pains in the stomach after eating.

Examination.—The pupils were slightly irregular; the legs were weak and she walked with difficulty; there was ataxia of the lower extremities; the reflexes were absent and the sensations of touch, prick, heat and cold were lost below the knees. She was excited and noisy; attention was poor, and she expressed many persecutory and a few depressive ideas.

Course.—During residence in the hospital she became delirious. The temperature throughout was subnormal. On June 25, she had a cerebral hemorrhage from which she died the next day.

Laboratory.—The urine contained albumin and hyaline casts; the blood sugar was 112; blood urea, 9; blood uric acid, 2.4. The cerebrospinal fluid did not contain any cells; the globulin reaction was negative; the Wassermann reaction, negative; colloidal gold curve, 0000000000.

Necropsy.—Cloudy swelling of the heart, lungs, liver and kidneys was found; the lungs showed edema and the liver, fatty infiltration and chronic cholecystitis.

Nervous System: Thrombosis of the superior longitudinal sinus, subdural petechial hemorrhages and hemorrhagic pachymeningitis were present. The arteries at the base of the brain were sclerotic. The peripheral nerves showed degeneration by the Marchi method. A slight degree of central neuritis was present in the cortex.

CASE 17.—*History.*—A. R., a man, aged 53, who was admitted to the hospital, Sept. 25, 1925, had had a bubo in 1895, and gonorrhea five years later. Throughout life he had been alcoholic. The illness began, one month before admission, with failing vision and loss of power in the legs. During this month, he lost 15 pounds (6. 8 Kg.).

Examination.—On admission he was emaciated, with a fine tremor of the lips and tongue and a coarser tremor of the legs and arms. The peripheral vessels were sclerotic; the liver was enlarged, and there was edema of the lungs. The blood pressure was 140 systolic; 98, diastolic. Vision was poor, the legs were weak and ataxic; the reflexes were increased and there was a bilateral Kernig sign. Pain, touch and vibratory sensations were lost over the legs.

Course.—He was clear mentally on admission but rapidly lapsed into a confused state, was irrational and picked at the bedclothes. He became steadily weaker and died on Oct. 23, 1925.

Laboratory Studies.—A blood count revealed: red cells, 4,700,000; white cells, 7,200; hemoglobin, 7.2 mg. The blood sugar was 95, 105, 77 and 105 at four successive examinations; the blood urea was 13 and 18, the blood uric acid, 3.8 and 3.6. The cerebrospinal fluid contained 3 cells and a faint trace of globulin; the Wassermann reaction was negative, and the colloidal gold curve, 0000000000.

Necropsy.—The heart showed a mild degree of chronic endocarditis, coronary sclerosis and cloudy swelling. The vessels were sclerotic, particularly the aorta. The lungs showed bronchopneumonia and an old healed pleuritis. Arteriosclerotic change and chronic interstitial nephritis of the kidneys were present. The liver was congested.

Nervous System: There was thickening of the pia-arachnoid; the arteries at the base of the brain were sclerotic and the cerebral convolutions were atrophic. The Marchi method showed degeneration of the peripheral nerves. Central neuritis was marked in the precentral area and was mild in other parts of the cortex.

CASE 18.—*History.*—S. M., a woman, aged 32, who was admitted to the hospital, Nov. 27, 1925, had been healthy until two years before when she began to

drink; she had since used alcohol to excess. Six weeks before admission she had a miscarriage.

Examination.—She was delirious, and experienced auditory and visual hallucinations. The tongue and buccal mucous membranes were of a beefy red. The backs of her hands were scaly. The pulse was irregular. The pupils reacted poorly to light and did not react to distance. The reflexes were diminished.

Course.—She became weaker, developed pulmonary edema and died, Dec. 3, 1925. Throughout her residence in the hospital the body temperature was subnormal.

Laboratory Studies.—The urine contained albumin and granular casts. The blood sugar was 100; blood urea, 21; blood uric acid, 4.4. The cerebrospinal fluid did not contain any cells.

Necropsy.—The lungs showed a mild degree of edema and chronic fibrous pleurisy. The spleen was congested. Fatty degeneration of the liver, congestion of the gastric mucosa, acute parenchymatous degeneration of the kidneys, chronic cervicitis and chronic interstitial oophoritis were present.

Nervous System: The pia-arachnoid was thickened and cloudy, and there was cortical edema. The small cerebral vessels showed a mild degree of hyalinization. Central neuritis was present throughout the cortex but was most marked in the precentral area.

DELIRIUM TREMENS

CASE 19.—*History.*—J. C., a man, aged 58, who was admitted to the hospital, Sept. 28, 1926, had been addicted to alcoholism. The illness began one year before admission with tremor, dysuria and incontinence.

Examination.—He was emaciated and had hypostatic pulmonary congestion. The pupils were irregular and reacted poorly to light. He was slightly spastic in all limbs, and the reflexes were increased. He was restless and destructive and talked incoherently. Attention was poor, and he experienced visual hallucinations.

Course.—The weakness increased and he died on Oct. 5, 1926.

Laboratory Studies.—White blood cell counts revealed: 13,000 and 18,000 cells, of which the polymorphonuclear leukocytes were 55 and 74 per cent, the lymphocytes 26 and 45 per cent; the hemoglobin was 14 and 15 mg.

Necropsy.—Chronic interstitial myocarditis and fatty infiltration of the heart, bronchopneumonia, congestion of the spleen, cloudy swelling of the liver, and congestion and cloudy swelling of the kidneys were found. The pancreas showed fatty infiltration.

Nervous System: The pia-arachnoid was thickened. The basal vessels showed moderate arteriosclerosis and the small cortical vessels were hyalinized. Marked central neuritis was found in the precentral area.

CASE 20.—*History.*—C. R., a woman, aged 51, who was admitted to the hospital, May 14, 1926, had been alcoholic throughout life. The illness began five days before admission with headache and pain in the feet. These symptoms increased in severity and she became disoriented; she had hallucinations and was incontinent.

Examination.—She was obese and had a roughening of the skin on the flexor surface of the forearms. The breath sounds on the right side of the chest were of bronchial character, and râles were heard at both bases. The blood pressure was 30 systolic; 15, diastolic. She was noisy and violent, required, restraint, failed to answer questions and hallucinated actively.

Course.—The weakness increased and she died on July 4, 1926.

Necropsy.—Fatty infiltration, acute parenchymatous degeneration and coronary sclerosis of the heart, arteriosclerosis of the spleen, fibrosis of the pancreas, fatty degeneration of the liver, arteriosclerosis of the kidneys and pyelonephritis were found.

Nervous System: The pia-arachnoid was slightly thickened. The walls of the small cortical vessels were thickened and hyalinized. Central neuritis was marked in the precentral area.

PELLAGRA

Case 21.—*History.*—T. J. D., a man, aged 51, who was admitted to the hospital, Oct. 13, 1925, had been addicted to the excessive use of alcohol. The illness began two years before admission with diarrhea and loss of weight.

Examination.—He was emaciated and had a sore mouth and diarrhea. The skin showed lesions characteristic of pellagra. The heart was enlarged and the sounds were of poor quality. The pupils were unequal, irregular and reacted to light poorly. He was delirious and disoriented.

Course.—He became progressively weaker and died on Oct. 23, 1925.

Laboratory Studies.—The blood sugar was 120; blood urea, 39; blood uric acid, 4.2; blood Wassermann reaction, ++++.

Necropsy.—Cloudy swelling, hypertrophy and dilatation of the heart, aortitis and sclerosis of the peripheral vessels, bronchopneumonia, fatty degeneration and cirrhosis of the liver and chronic interstitial nephritis were found.

Nervous System: The vessels at the base of the brain showed mild arteriosclerosis; the small cortical vessels were thickened but not hyalinized. Central neuritis was present in the precentral area.

Case 22.—W. M., a man, aged 50, was admitted Aug. 5, 1926, in a comatose condition, without information as to his past.

Examination.—He was emaciated, and the tongue and buccal mucous membranes were beefy red. The skin showed lesions characteristic of pellagra. The heart sounds were poor in quality, and the peripheral vessels were sclerotic. The temperature was 99 F. The tendon reflexes were absent.

Course.—He did not improve, but died the following day.

Necropsy.—Brown atrophy of the heart, sclerosis of the peripheral vessels, bronchopneumonia, cloudy swelling of the suprarenals, fatty infiltration of the liver, arteriosclerosis and cloudy swelling of the kidneys were found.

Nervous System: A moderate internal hydrocephalus was present; the large cerebral vessels were fibrotic and degenerated, as shown by the metachromatic staining of their walls. Central neuritis was present in the precentral area.

Case 23.—*History.*—E. B., a man, aged 48, who was admitted Aug. 23, 1923, had been addicted to alcoholism. The illness began, one month before, with gastric pain and progressive weakness. This was followed by diarrhea, rapidly increasing emaciation and delirium.

Examination.—On admission he showed the mucous membrane and cutaneous lesions of pellagra, and signs of pulmonary tuberculosis. He had fever and was incontinent. The blood pressure was 100 systolic; 67, diastolic. He was delirious, experienced continuous hallucinations, and expressed persecutory ideas alternating occasionally with those of a depressive nature.

Course.—He grew weaker and died on Sept. 7, 1923.

Laboratory Studies.—The blood urea was 16; blood uric acid, 4.6 and blood sugar, 86.

Necropsy.—Healed tuberculous lesions of the lungs, congestion of the gastric mucosa and atrophy and petechial hemorrhages of the intestinal mucous membrane were found.

Nervous System: The convolutions of the cortex were atrophied; there was thickening and hyalinization of the walls of the small vessels. The large cells of the precentral area showed central neuritis; the small cells appeared to show Nissl's acute cell change. Axonal degeneration was slight in extent.

CASE 24.—*History.*—M. M., a woman, aged 42, who was admitted to the hospital, Aug. 8, 1923, had become ill eight months before with sore mouth, diarrhea, restlessness, poor memory, disorientation and rapid loss of weight.

Examination.—The skin and mucous membrane presented the lesions of pellagra. The blood pressure was 120 systolic; 80, diastolic. She had diarrhea. The pupils were irregular and reacted poorly to light; speech was slow; the reflexes were increased. She was ataxic and exhibited a Romberg sign. Pain sensation was diminished and she was astereognostic. She was confused and disoriented and memory was poor. She was depressed, experienced auditory hallucinations and expressed ideas of persecution.

Course.—She developed bronchopneumonia, the temperature rising to 107 F. before death on Sept. 4, 1923.

Laboratory Studies.—The urine contained albumin. A blood count revealed: red cells, 4,500,000; white cells, 4,800; hemoglobin, 95 per cent. The cerebrospinal fluid did not contain cells; globulin, Wassermann and colloidal gold tests were negative.

Necropsy.—Generalized arteriosclerosis, congestion of the lungs, and atrophy of the medulla of the suprarenals were found.

Nervous System: The posterior and lateral columns of the spinal cord showed a mild degree of degeneration. Central neuritis was marked in the precentral area.

CASE 25.—*History.*—H. W., a woman, aged 42, who was admitted to the hospital, May 7, 1923, had been ill for about one year with diarrhea and soreness of the mouth.

Examination.—The skin and mucous membranes presented lesions of pellagra, and a generalized edema was present. The heart was enlarged; the blood pressure was 120 systolic; 80, diastolic. She was emaciated, had diarrhea and the temperature was 99 F. The pupils did not react to light. She was delirious and, at times, drowsy and noisy and experienced hallucinations.

Course.—She grew weaker and more stuporous; the temperature rose to 101.5 F. She died, Aug. 26, 1923.

Laboratory Studies.—The red blood cells numbered 4,000,000; the white cells, 30,000.

Necropsy.—Chronic myocarditis, myocardial degeneration and brown atrophy, and chronic adhesive pericarditis, bronchopneumonia, acute splenitis, chronic interstitial pancreatitis, gastro-enteritis, fatty infiltration and passive congestion of the liver, and chronic tubular nephritis were found.

Nervous System: There was a mild degree of degeneration in the posterior columns of the spinal cord. The walls of the small vessels of the cortex were swollen and hyalinized. Central neuritis was marked in the precentral area.

CASE 26.—*History.*—C. D., a man, aged 59, who was admitted to the hospital, Sept. 14, 1922, and who had been addicted to alcoholism, had become ill two years before with the characteristic signs of pellagra. For three months he had had severe diarrhea and had noticed that his vision was failing.

Examination.—He was emaciated and had cutaneous lesions characteristic of pellagra. The blood pressure was 145 systolic; 75, diastolic. He had diarrhea. The pupils reacted sluggishly to light; the knee jerks were increased, and there was tremor of the hands.

Course.—He became weaker and died, Sept. 27, 1922.

Laboratory Studies.—The urine contained albumin, and epithelial and granular casts. The blood urea was 32; creatinine, 1.9.

Necropsy.—Chronic myocarditis and fatty infiltration of the heart, moderate arteriosclerosis, most marked in the aorta, emphysema of the lungs, chronic interstitial splenitis, pancreatitis, fatty infiltration of the liver, and chronic tubular nephritis were found.

Nervous System: The cerebral vessels were sclerosed mildly. Central neuritis was most marked in the precentral area.

Case 27.—*History.*—C. T. R., a man, aged 43, who was admitted to the hospital, July 21, 1925, had had gonorrhea and chancroid in 1900. Throughout life he had been alcoholic. Two months before admission he developed weakness, dizziness, an eruption of the skin, sore mouth and diarrhea.

Examination.—The skin and mucous membrane presented lesions of pellagra; there was a fine tremor of the tongue. He had not lost weight. He was disoriented and incoherent and hallucinated actively.

Course.—He became rapidly weaker and died, Aug. 29, 1925.

Laboratory Studies.—Examination of the blood revealed: red blood cells, 4,750,000; white blood cells, 12,200; hemoglobin, 12.1 mg.; blood sugar, 90; blood urea, 9; blood uric acid, 3.4.

Necropsy.—Endarteritis deformans of the aorta, acute purulent bronchitis, chronic ulcerative enteritis with atrophy of the intestinal mucosa, and cloudy swelling of the liver and kidneys were found.

Nervous System: Edema and atrophy of the cerebral convolutions were present. The basal vessels were sclerotic; the small cortical vessels showed swollen and hyalinized walls. Central neuritis was marked in the precentral area; it was present to a slight degree in the cells of the ventral horns of the spinal cord.

Case 28.—*History.*—G. W., a woman, aged 20, who was admitted to the hospital, April 29, 1925, had become ill four months before with severe pain in the region of the umbilicus, stupor and delirium. Three months later an exploratory abdominal operation was performed, which was followed by a fecal fistula.

Examination.—The patient was strikingly emaciated and had a chronic sinus of the abdominal wall and a stricture of the rectum. She was much intoxicated and had delirious episodes.

Course.—After admission she developed an eruption on the face that was diagnosed as pellagrous. The temperature rose; she grew weaker and died on Aug. 25, 1925.

Laboratory Studies.—The urine contained albumin.

Necropsy.—Parenchymatous degeneration of the heart with atrophy of the heart muscle, chronic fibrous epicarditis, splenitis, chronic catarrhal enteritis, fatty infiltration and passive congestion of the liver, and cloudy swelling of the kidneys were found.

Nervous System: The small vessels of the cortex were thickened. Central neuritis was present, particularly in the precentral area and the cells of the ventral horns of the spinal cord.

CASE 29.—*History.*—S. P., a woman, aged 76, who was admitted to the hospital, Nov. 3, 1925, had had a rectal abscess five months before. Eight weeks before she had had a bad cold and a "nervous breakdown." She had trouble with the left kidney. The appetite became poor.

Examination.—The skin and mucous membrane presented lesions of pellagra; enlarged heart, sclerosis of the peripheral vessels and edema of the ankles were present. The pupils were irregular. She was delirious and experienced visual hallucinations.

Course.—The temperature became subnormal, and the patient grew weaker rapidly; she died on Nov. 18, 1925.

Laboratory Studies.—The urine contained albumin; the blood sugar was 113; blood urea, 25; blood uric acid, 3.6.

Necropsy.—Fatty infiltration of the heart, congestion of the lungs, chronic hyaline perisplenitis and chronic interstitial splenitis were found.

Nervous System: The walls of the small cortical vessels were thickened and hyalinized. Central neuritis was marked in the cells of the ventral horns of the spinal cord, and was present, though to a less degree, in the cortex. The peripheral nerves did not show degeneration by the method of Marchi.

CLINICAL DIAGNOSIS OF GENERAL PARALYSIS, BUT PROBABLE PELLAGRA

CASE 30.—*History.*—J. G., a woman, who was admitted to the hospital, March 13, 1926, had been ill for two months with a cold, weakness and mental confusion.

Examination.—The patient was emaciated and had bedsores and had lesions on the skin and mucous membrane resembling pellagra. The heart rhythm was irregular. The pupils were unequal and did not react to light or distance; the extremities were spastic and the reflexes increased. She was uncooperative, retarded and depressed. Speech was incoherent; she was disoriented and showed marked intellectual defect. She experienced auditory and visual hallucinations.

Course.—She grew weaker rapidly, developed choreiform movements and died on March 25, 1926.

Laboratory Studies.—Examination showed: blood sugar, 93; blood urea, 14; blood uric acid, 2.4. The cerebrospinal fluid did not contain cells; the globulin and Wassermann tests were negative; the colloidal gold curve was 1223331000.

Necropsy.—Brown atrophy of the heart with lobular pneumonia was found.

Nervous System: The cerebral hemispheres were congested. The walls of the small cortical vessels were thickened and hyalinized. Central neuritis was most marked in the precentral area.

EPILEPSY

CASE 31.—*History.*—J. F., a man, aged 39, who was admitted to the hospital, June 20, 1926, had been an excessive user of alcohol. His wife had syphilis. In April, 1923, he had the first convulsion, and they had recurred at irregular intervals since. Three days before admission he had a severe fit, from which he appeared to recover for a short period and then became comatose.

Examination.—On admission the patient was stuporous; the heart sounds were feeble, and there were râles in the upper lobe of the left lung.

Course.—The temperature at first was 99 F., but rose rapidly to 102; he died on July 3, 1926.

Necropsy.—Myocardial degeneration and cloudy swelling of the heart, hypostatic pneumonia and hemorrhagic pleurisy, chronic passive congestion of the

spleen, fatty infiltration of the liver and chronic nephritis, with arteriosclerotic changes and cloudy swelling of the kidneys were found.

Nervous System: The brain was edematous. The vessels at the base were moderately sclerotic. The walls of the small cortical vessels were thickened. Central neuritis was marked in the precentral area.

THE SYMPTOM-COMPLEX OF "CENTRAL NEURITIS"

The symptoms of the syndrome described by Meyer and Coriat may be classified into three groups: those that indicate disturbance of function of the neurons; those that indicate some disturbance of the general systemic condition, either accompanying or producing the neuropathologic condition, and the mental symptoms.

Neurologic Symptoms.—In this group occur particularly the signs of disease of the corticospinal system, e.g., difficulty in locomotion, increasing weakness for coordinated movements, jactitations of the limbs, rigidity and alteration in the reflexes. In my series only twenty-two patients showed definite motor signs, which indicates that these symptoms are not the rule. In fourteen cases the symptoms can be explained by pathologic changes other than central neuritis. The patients in cases 2 and 3 showed mild tremor, which is not an unusual symptom in manic-depressive psychoses without central neuritis. In case 7 the reflexes were increased, but the cell change affected the frontal cortex and not the precentral area. Case 9 showed marked signs of motor irritation, but the degree of central neuritis was slight. Case 31 was one of epilepsy. Case 4 also presented convulsive seizures, but this symptom occurs so frequently in cases without central neuritis that it seems improbable that the cell change was the cause of the convulsions. Cases 1 and 5 resemble more closely the syndrome of Meyer and Coriat. Except for the central neuritis, there is not sufficient pathologic change in either case to account for the degeneration in the pyramidal tract. If these two conditions are associated, the latter being primary and the former a retrograde manifestation of axonal degeneration, the central neuritis must have remained stationary for several years to explain the symptoms which first appeared at that time. This point will be dealt with more fully later.

When one considers the definite character of the disease of the cells, it is remarkable that central neuritis does not show positive signs of disturbance of function of the corticospinal tract. They would be expected as a result of the degeneration of the intracellular neurofibrils, especially as the Betz cells of the precentral area in most of my cases bore the brunt of the pathologic process. Clinical signs of this disturbance are not the rule; therefore, the number of neurofibrils remaining intact must be sufficient to transmit impulses in a manner clinically undetectable from the normal.

Systemic Symptoms.—The symptoms of systemic disturbance (diarrhea, emaciation and fever) are thought either to accompany or to produce central neuritis. Coriat accepted the latter view and considered that the poor physical state affected the terminals of the axons, resulting in a retrograde degeneration of the cell body. Only one case in this series, case 25, showed this triad of symptoms. Diarrhea occurred in six patients with pellagra. In case 10 it was associated with sepsis and fever during the last three weeks of life. Cases 8 and 4 are similar, though in the latter instance, this terminal condition lasted only two days. Loss of weight to the point of emaciation occurred in nineteen cases, but the degree of central neuritis is the same in these cases as in those which do not show this symptom. Fever was present in ten cases, but in several of the patients a subnormal temperature persisted throughout the residence in the hospital. The systemic symptoms, therefore, are too inconstant to have any etiologic or diagnostic significance.

Mental Symptoms.—Mental symptoms—anxious, perplexed agitation, delirium or stupor—were not found consistently and when present were those of the symptom-complex in which the case belonged. Anxious, perplexed agitation was present in the manic-depressive group of cases, and delirium and stupor in the toxic conditions in which they naturally occur.

Each case in this series must be studied with regard to the syndrome to which it belongs. A difference in symptoms or course of the disease was not found when the cases in this series were compared with a number of unselected cases of the analogous symptom-complex without central neuritis. This statement does not apply to the cases of pellagra, as every case of that disease studied showed central neuritis.

When all the facts are considered there does not seem to be a group of symptoms to indicate the presence of central neuritis during life. The syndrome described by Meyer and Coriat is not characteristic of my cases.

THE ETIOLOGY OF CENTRAL NEURITIS

POSSIBLE ETIOLOGIC FACTORS

Axonal Injury.—Nissl first described chromatolysis of the ganglion cells of peripheral nerves with displacement of the nucleus as a retrograde change to injury of the axons. This has been confirmed by many observers, among whom may be mentioned Marinesco,[29] Onuf[30] and Cajal.[31] However, it rarely occurs after lesions of the intramedullary

29. Marinesco, G.: Des polynévrites en rapport avec les lesions secondaires et les lesions primitives des cellules nerveuses, Rev. neurol. **4**:129, 1896.

30. Onuf, B.: The Biological and Morphological Constitution of the Ganglion Cells, as Influenced by Section of the Spinal Nerve Roots of Spinal Nerves, J. Nerv. & Ment. Dis. **20**:597 (Oct.) 1895.

31. Cajal, S. R.: Histologie du système nerveux, 1909, vol. 1, p. 214.

axons. Penfield did not find any central neuritis of the motor cortex after section of the spinal cord. In only a few cases was it observed by Marinesco in the cells of the precentral area after a lesion of the internal capsule. When one considers the frequency of capsular lesions, "central neuritis" should be commonly found in the motor cortex of hemiplegic patients, if it were due to an axonal lesion. Only thirty-one cases of central neuritis were found among more than 1,000 necropsies, the majority of which were on hemiplegic patients; and it was not found once among such cases.

It may be argued that the pathologic picture had altered before the microscopic study was made, for the cell may recover, or when the nucleus is extruded it will disappear. Although authorities disagree concerning the duration of change in the cell after axonal injury—axonal chromatolysis having been found in the ventral horns of the spinal cord by Spiller [7] three days after, and by Kahler and Pick [32] eighteen years after amputation of a limb—the patients with hemiplegia who were studied had lived from a few days to many years after the medullary lesion; hence, if central neuritis resulted from a lesion of the intramedullary axons it should have been found among these cases.

There is some doubt whether the retrograde cell changes found years after an injury to a peripheral nerve are really due to that injury, for, in his experimental work, Nicholson [33] found that the cells of the ganglion had disappeared thirty-five days after avulsion of the nerve and that forty-four days after injury to the axons the cells were completely normal. Even if these figures are applied liberally the period is too short to account for the presence of central neuritis in cases 1 and 5 of this series, for in both instances the onset of vague signs of involvement of the pyramidal tract took place several years before death.

Reference has been made already to the paucity of axonal lesions compared to the large number of cell bodies involved. Only the terminations of the axons might be involved, but it is strange that with the wide extent of the pathologic condition Marchi sections did not show evidence of this.

Although the cell picture is similar to that found after experimental injury to the axons—i.e, with the nucleus displaced toward the axon hillock and the Nissl bodies clumped in that locality—the weight of evidence seems to show that central neuritis is not caused by lesions of the intramedullary axons.

Toxins, Endogenous and Exogenous.—Experimentally, central neuritis has been produced by a variety of methods other than mechanical

32. Kahler and Pick, quoted by Onuf (footnote 30).

33. Nicholson, F. M.: The Morphologic Changes in Nerve Cells Following Injury to Their Axons, Arch. Neurol. & Psychiat. **11**:680 (June) 1924.

injury of the axis cylinders. Dolley [34] produced it by anemia, shock and electrical, trophic, photic and chemical stimulation and concluded also that it might result from intrinsic cellular activities. Dehio [35] reported the occurrence of chromatolysis of the cells in animals poisoned by alcohol, though he does not mention the presence of nuclear displacement. Nicholson reported its occurrence following electrical stimulation, inflammations, infections, chemical poisons and fatigue. Excluding the artificial types of injury, the action of exogenous and endogenous poisons is left for consideration in human cases.

Alcohol is the only exogenous poison that figures prominently among my patients. The six cases of alcoholism reported, however, are only a few of the large number of cases in alcoholic addicts which have been studied and in which central neuritis was not found. Furthermore, at least one patient in my series had never used alcohol. Therefore, alcohol seems a negligible etiologic factor.

The blood chemistry of eleven patients in this series was studied to determine whether metabolic disturbances are a factor in producing central neuritis. In five the blood urea and blood uric acid were within normal limits; in two, the results were lower and in four were higher than normal. In none of these four cases was the degree of central neuritis greater than in those patients whose blood chemistry was normal. It is realized that laboratory tests for the retention of toxic products are a crude measure of subtle metabolic processes. The frequency of visceral pathologic changes, notably cloudy swelling, seemed to indicate that a study of the organs of metabolism might serve as a finer index of the retention of toxic products than could be obtained from the study of the blood chemistry. The visceral pathologic condition of twenty-five patients, whose nervous system did not show central neuritis, was compared with that of the patients with central neuritis. This comparison showed that such changes were at least as common in the patients without as in those with central neuritis.

Infection.—A similar negative result followed an investigation into the frequency of infectious processes in the terminal part of these patients' lives. Only ten showed signs of infection, and this number is too few to make infection worthy of consideration as a causative agent.

Type of Terminal Illness.—A study of the type of death of these patients was inconclusive also. Progressive weakness, with increasing

34. Dolley, D. H.: The Morphological Changes in Nerve Cells Resulting from Overwork, in Relation with Experimental Anemia and Shock, J. M. Research **21:** 95, 1909; The Morphology of Functional Depression in Nerve Cells and Its Significance from the Normal and Abnormal Physiology of the Cell, J. M. Research **29:**65, 1914.

35. Dehio: Experimental Investigation of the Changes Found in Ganglion Cells in Acute Alcohol Poisoning, Centralbl. f. Nervenh. u. Psychiat., March, 1895.

toxicity and the gradual failure of bodily functions accounted for death in the majority of patients, but five were an exception to this rule. The patient in case 4 suffered a sudden collapse with diarrhea, vomiting and fever and died two days after the onset of these symptoms. The patient in case 5 died within twenty-four hours after the occurrence of a traumatic ventricular hemorrhage. The patient in case 14 died of acute cardiac failure after an illness of seven days. The patient in case 16 died twenty-four hours after the onset of a subdural hemorrhage. The patient in case 31 did not have a progressive wasting illness but suffered a convulsion and sank into coma, in which he died thirteen days later. If a slowly progressive terminal illness were responsible for the production of a "central neuritis," it would be expected that a patient whose death was preponderantly of this nature would show a greater degree of pathologic change. A scrutiny of the case histories shows that the character of the terminal illness did not influence the degree of central neuritis.

Starvation.—It has been pointed out that the triad of symptoms—diarrhea, emaciation and fever—does not bear an etiologic relationship to central neuritis. If central neuritis is the result of hypercatabolism of the nutritive material of the cell, as Dolley [34] believed, marked emaciation might indicate that all the surplus food of the body had been consumed and destruction of the vital tissues was occurring in its place. Actually such does not seem to be the case, for Hassin [36] did not find this cell change in the brain of the starved person he studied.

THEORETICAL CONSIDERATIONS

So far it seems that all attempts to postulate a disturbance of metabolism with the production of a special endogenous poison as the cause of central neuritis have failed. In pellagra, every case shows this microscopic picture. Winkelman [23] recently drew attention again to the fact that pellagra presents central neuritis associated with thickening and hyalinization of the walls of the small vessels of the cortex and an excess of lipoid throughout the central nervous system. Pellagra is a condition that shows severe disturbances of metabolism. As Harris pointed out, these are: decrease or disappearance of the hydrochloric acid and pepsin from the gastric juice, decreased alkalinity and increased iron content of the blood with a decreased ability of this tissue to absorb oxygen, a decreased capacity to assimilate sugar and an increase of indican in the urine and of phenol in the blood. The latter increase also occurs in alcoholism, though there the increase of phenol is greater than the increase of indican. This summary is of interest because Cotton and

36. Hassin, G. B.: Brain Changes in Starvation, Arch. Neurol. & Psychiat. 9:551 (May) 1924.

Hammond, in their study of a case of cardiogenetic psychosis with central neuritis, theorized that the lesion in the heart might produce sufficient circulatory disturbance to diminish the supply of nutritional material to the brain and to cause an excessive production of carbon dioxide and a proportional decrease in the alkalinity of the blood.

Williams [37] advanced an interesting theory of the action of endogenous poisons in the production of polyneuritis. He noted that the French for some time have regarded alcoholic polyneuritis as due to the damage alcohol does to the liver and not to its neurotoxic action. He said that if there is decreased liver function combined with cloudy swelling of the kidney, as is frequently the case in this condition, retention of the toxic products of metabolism, notably pyridine, occurs. Pyridine produces a high degree of cloudy swelling by hydration of the cells, the hydration being a result of a variation in the acid-base equilibrium, with decreased alkalinity of the blood. The resemblance between the explanation given by Williams for polyneuritis, that given by Cotton and Hammond for central neuritis and the biochemical changes found in pellagra, points to some subtle metabolic process as the causative factor of the pathologic change in the brain in central neuritis, but in the absence of any intensive biochemical or metabolic studies on a series of cases there is no accurate knowledge of these processes. Experimental studies and the biochemistry of pellagra appear to give some measure of plausibility for the following theory:

Under certain conditions, at present unknown, there occurs a disturbance in the more delicate metabolic processes of the body, with the production of toxic products that act either directly on the cells or indirectly by altering the acid-base equilibrium of the blood and its power to combine with oxygen. These products prevent the cell nucleus from extracting nutritive material from the tissue juices and force the cytoplasm to subsist on its own chromatin.

The unassimilated nutritive material does not remain in the brain as free glycogen, for, though Casamajor [38] found this substance free in the cerebral cortex in delirious and toxic conditions, it was not found in a number of the cases of this series studied by Best's stain. Cell hunger stimulates the cell metabolism; the chromatin is destroyed more rapidly; the nucleus migrates toward the axon hillock in order that the impulse-transmitting portion of the cell may be preserved, or possibly, because starvation is felt most acutely at the extremity of the neuron. Further food supply not being available, the nucleus ceases to function, is extruded and the cell dies. If this is the process that occurs in the cen-

37. Williams, T. A.: Polyneuritis of Infectious Origin, M. Rec. **100**:1145 (Dec. 31) 1921.

38. Casamajor, L.: Ueber das Glykogen in Gehirn, quoted by Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922, p. 306.

tral nervous system, it may be a factor also in the emaciation that develops in certain of these cases, the cells of the whole body being unable to obtain sufficient nourishment. Whether this is the true explanation of central neuritis or not, it seems essential that further studies of the condition should be undertaken by biochemical methods.

A NEW NAME FOR CENTRAL NEURITIS

The names applied to this condition—central neuritis and axonal chromatolysis—are misnomers. The former term was used originally to distinguish an involvement of the intramedullary neuronic system from that of the peripheral. If the cell change was retrograde to an axonal injury, the analogy between the two processes would be striking and the term "central" or, better, "intramedullary" neuritis would be justifiable, though a more exact pathologic description would be "axonal chromatolysis." The cell change in the condition under discussion is a primary one, although eventually the whole neuron becomes diseased, so that these terms are all incorrect. Central chromatolysis, if "central" is used to describe the location in the cell in which the change is most marked, is better, but as the change following injury to the axon occurs first in the same place, this name does not differentiate this process from axonal chromatolysis. As I believe that the chromatolysis is an autolytic process due to isolation of the neuron from its food supply and is caused by some physicochemical disturbance, I would suggest the name primary cytolytic degeneration.

SUMMARY

Central neuritis is a disease of the large and medium-sized pyramidal cells of the cerebral cortex. The cell body is swollen, the Nissl substance dissolved and the nucleus displaced. In severe forms the neurofibrils degenerate, the nucleus is extruded and the cell dies. Degenerative changes are found in the axons. In some cases the glia is affected.

Thirty-one cases of central neuritis were found among more than 1,000 consecutive necropsies. These cases were distributed among the following clinical diagnoses: involutional melancholia, two cases; manic-depressive psychosis, depressed type, two; manic-depressive psychosis, mixed type, two; toxic-exhaustive psychosis, one; psychosis with somatic disease, five; senile dementia, one; schizophrenia, paranoid type, one; chronic alcoholism, four; delirium tremens, two; pellagra, nine; pellagroid syndrome, one, and epilepsy, one. Only in pellagra, however, was the pathologic change found in every patient examined. A study of the clinical symptomatology indicates that the presence of central neuritis cannot be determined during life. Central neuritis is not a prelethal condition nor does it seem to be caused by axonal injury, infection, starvation, exogenous or known endogenous toxins. There are some facts to substantiate the view that it results from some disturbance

of the finer metabolic processes, and the theory is advanced that some disturbance of the more delicate processes of metabolism prevents the cell from extracting nutritive material from the tissue juices. Autometabolism occurs, and if the process is severe the nucleus is extruded and the cell dies.

Further investigations into the etiology of the condition should be conducted along intensive physicochemical and metabolic lines. The names applied to the condition—central neuritis and axonal chromatolysis—are misnomers. A better name would be primary cytolytic degeneration.

CONCLUSIONS

1. Central neuritis does not produce a distinctive symptom-complex.

2. It is not caused by axonal injury, infection, starvation, exogenous or known endogenous toxins, nor is it a prelethal condition.

3. It seems to be the result of some subtle disturbance of metabolism that produces starvation and autometabolism of the cell.

4. The names applied to this condition are misnomers. Primary cytolytic degeneration is a preferable term.

CORRECTION

In the article, entitled "The Electivity of Disease of the Nervous System," by Dr. Friedrich Hiller, Chicago (ARCH. NEUROL. & PSYCHIAT. **20**:145 [July] 1928), the legends for figures 1 and 2, page 149, should be transposed; the legend under figure 1 should appear under figure 2, and that under figure 2 should appear under figure 1.

Clinical and Occasional Notes

A RAPID METHOD FOR STAINING MYELIN SHEATHS*

ARTHUR WEIL, M.D., NEW YORK

The disadvantage of the present methods for the staining of myelin sheaths—Weigert, Spielmeyer, Loyez, Fränkel and others—is that they require days or even weeks for the preparation of the material.

The following method can be performed within one hour and can be applied to sections fixed in formaldehyde and frozen or embedded in either celloidin or paraffin. Celloidin sections may be stained without removing the embedding material. In paraffin sections, the paraffin should be removed before staining. Frozen sections should be brought into 70 per cent alcohol for from five to ten minutes and then put back into water. Sections should be from 20 to 30 microns thick.

The agents used are: (1) 5 per cent water solution of potassium dichromate; (2) 4 per cent water solution of iron alum; (3) 1 per cent water solution of hematoxylin prepared from 10 per cent absolute alcoholic solution (at least 6 months old); (4) solution of borax, 10 Gm.; potassium, ferricyanide, 12.5 Gm.; aqua destillata, 1,000 cc.; (5) 0.25 per cent solution of potassium permanganate; (6) solution of oxalic acid, 2.5 Gm.; sodium bisulphite, 2.5 Gm.; aqua destillata, 1,000 cc.

The method of procedure is as follows:

1. Bring sections from water into solution (1) for five minutes.

2. Wash twice in tap water.

3. Mix equal parts of solutions (2) and (3) and then stain sections in the mixture at 45 to 50 C. for fifteen minutes. (Always use fresh solution.)

4. Wash sections in tap water.

5. Place sections in solution (2) and differentiate over a white background until the gray matter or degenerated areas may be recognized.

6. Wash three times in tap water.

7. Place sections in solution (4) and differentiate over white background to the desired degree.

8. Wash three times in tap water.

9. Dehydrate in 95 per cent alcohol, absolute alcohol-ether, xylene; embed in balsam.

If the differentiation in step (7) should last longer than five minutes or if sections thicker than 30 microns are used, the following additions should be made:

1 to 7. Processes 1 to 7 as above.

8. Wash sections in tap water.

9. Place them for from three to ten seconds in solution (5). (Dissolved with 2 or 3 parts water for 20 micron sections); from thirty to sixty seconds if sections are 50 microns or thicker.

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* From the Neuropathological Laboratory, Montefiore Hospital.

10. Wash in tap water.

11. Place in solution (6) until the gray matter or areas of degeneration are colorless. (Repeat 9 to 11 if differentiation did not succeed the first time.)

12. Wash in tap water.

13. Place for one-half minute in ammonia water (10 drops ammonia to 50 cc. water).

14. Wash three times in tap water.

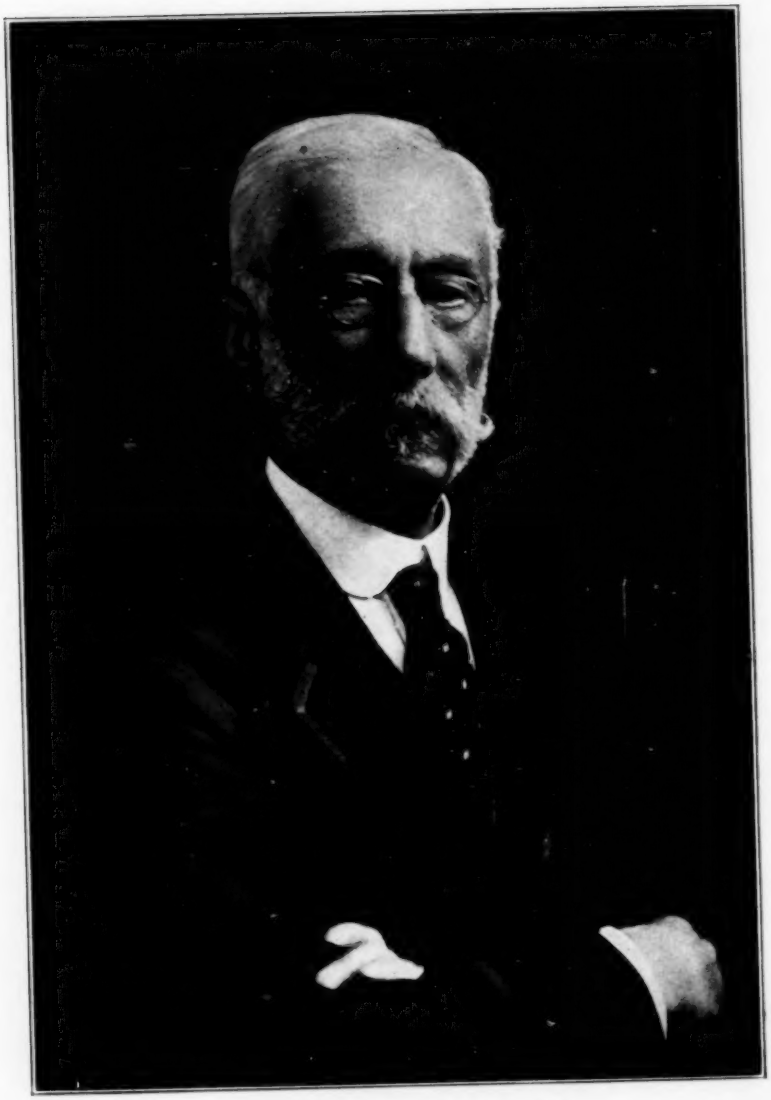
15. Embed through alcohol, xylene and balsam.

News and Comment

COMMONWEALTH FELLOWSHIPS IN PSYCHIATRY AT THE BOSTON PSYCHOPATHIC HOSPITAL

The Commonwealth Fund has created a number of fellowships in psychiatry. Five of them have been made available in the Department of Psychiatry, Harvard Medical School, with which the Boston Psychopathic Hospital is closely associated. These fellowships will be available only for workers who have already shown evidence of good work in psychiatry, who wish to prepare themselves in a well rounded way for a career in psychiatry and who are willing to devote an adequate time to this preparation. Each fellowship may be continued for three years but continuation will depend on the excellence of the work of the fellow. Each fellow will follow a program determined by his special needs and interests. The fellows will have available not only the clinical and laboratory facilities of the Boston Psychopathic Hospital but also those of other institutions, and opportunities for special work in school, industry and the general social field. A period of study in a foreign clinic might also be recommended.

Letters of application with details as to previous training and experience may be sent to Dr. C. Macfie Campbell, Boston Psychopathic Hospital, 74 Fenwood Road, Boston.



SIR DAVID FERRIER, M.D.
1843-1928

Obituary

SIR DAVID FERRIER

1843-1928

Thirty years ago, neurologic teaching in England was confined almost entirely to the National Hospital at Queen Square, London. In those days, the hospital staff comprised a galaxy of pioneers, including Hughlings Jackson, Ferrier, Gowers, Bastian, Beevor and Horsley; of these noted men, Sir David Ferrier was the last survivor. He passed away on March 19, 1928, at the venerable age of 85.

David Ferrier was born in 1843 and was educated in Aberdeen, at which university he had attained every academic honor in classics and philosophy by the time he was 21 years of age. His first intention was to devote himself to psychology; accordingly, he studied for a time in Heidelberg. In 1865, however, he again took up the study of medicine, and he went to Edinburgh. There he graduated with the highest honors in 1868, and was appointed assistant to Laycock, who was then professor of medicine in the university. But soon, like many another ambitious fellow-Scot, he migrated south. At once he began his far-reaching researches in cerebral anatomy and physiology. In 1870, he gained a gold medal for his Doctor's thesis on the "Corpora Quadrigemina." From that time onward, Ferrier settled in London and pursued his assiduous experimental studies in cerebral physiology for years until the claims of an ever increasing clinical practice withdrew him from laboratory work and made him the leading consultant in neurology of his day.

In 1874, he delivered the Croonian lectures on the "Localization of Function in the Brain." Further studies on the same subject were laid before the Royal Society in 1875; they were elaborated in his book on the "Functions of the Brain" in 1876, and formed the subject of his Gulstonian lecture in 1878. Ferrier's striking experimental demonstration of motor and sensory localization in the cerebral cortex, largely inspired, as he always said, by Hughlings Jackson, was an epoch-making contribution to the subject of cerebral physiology and will remain as an imperishable monument to his memory. Its publication gained him election as a Fellow of the Royal Society. At the International Congress of 1881, held in London, he gave a brilliant demonstration of his work before a gathering of the neurologists of Europe. Honors were showered on him. In 1878, he was elected Lauréat of the Institut de France. The Royal Society awarded him the Marshall Hall prize in 1883, the

Bird medal in 1887, and the Royal medal in 1890. The University of Edinburgh gave him the Cameron prize in 1891, and the Moxon medal in 1912. He received the honorary degrees of Doctor of Science from Cambridge and of Doctor of Laws from Edinburgh, Aberdeen and Birmingham. The Royal College of Physicians appointed him Harveian Orator, Lumleian Lecturer and Censor. In 1911, he received the honor of knighthood. He was president of the Neurological Society in 1894, and of the Medical Society of London in 1913. In conjunction with Hughlings Jackson, Sir John Bucknell and Sir James Crichton-Browne, who is still alive, Sir David was an original founder and editor of *Brain*, the journal of the Neurological Society. He was physician not only to the National Hospital, but also to Kings College Hospital.

All these positions he adorned. His alert, slight physique, his piercing eyes, his swift and accurate mentality, his modest and kindly personality, singled him out as an attractive figure in any assembly, while his generosity, hospitality and unfailing encouragement to all his colleagues, especially to his juniors, will ever be remembered by those to whom he was not only an inspiring scientific master, but a firm and loyal friend. We, his disciples, who knew him best, never heard him utter a disparaging word or an unkind expression toward any man. To the end, long after he had retired from active work, he preserved a keen interest in current scientific affairs, together with an unabated happiness in the study of classic literature. American neurologists will perhaps remember him best as president of the Neurological Section of the International Congress of 1913, held in London, where he welcomed and entertained his foreign colleagues with characteristic geniality and charm. The name of Sir David Ferrier will be worthily held in honor for generations to come, not only in England, but in America and throughout the world.

Abstracts from Current Literature

STUDIES OF POSTCHOREATIC MOTILITY DISORDERS, ESPECIALLY THE RELATION OF CHOREA MINOR TO TIC. ERWIN STRAUS, Monatschr. f. Psychiat. u. Neurol. **66**:261 (Dec.) 1927.

Systematic investigation of the physiology and pathology of the extrapyramidal motor system, stimulated by the study of epidemic encephalitis, has demonstrated that many motor disturbances, which were fomerly considered typically functional, hysterical or psychogenic in origin, have instead a definite organic basis. This has altered the former point of view as to what constitutes the criteria for differentiating the organic from the psychogenic, and is beginning to change the concept of the psychogenic. Meige and Feindel, in their studies on tic, expressed the view that the very type of movement in the tic betrays its origin as a purposive or expression movement; they considered it definitely psychogenic. But in epidemic encephalitis the development of similar tics has been observed; and it is now known that a tic may have an organic basis. Therefore, one must recognize that the character of the abnormal movement proves nothing as to its pathogenesis and will not permit its classification as psychogenic or organic.

The first step in the realinement of these motility disorders came in the study of dystonia musculorum deformans. Ziehen and Schwalbe had described the picture in 1908 under the heading "Tonic torsionsneurosis — a peculiar tonic muscle spasm with hysterical symptoms." In 1911, Oppenheim described the same syndrome under the name of dysbasia musculorum deformans, and maintained that its symptomatology and course definitely showed an organic and not a psychogenic basis. The proof of his views came a few years later when this disease was proved to be due to a chronic progressive degeneration of both cell forms of the striatum. This opened the way, and facts followed rapidly. Certain cases of torticollis were shown to be definitely organic. The same was true for tic. Reviewing the work of Meige and Feindel in the light of this knowledge, it is evident that many of their cases belong to the organic group. Their confusion was due to two factors: the status of pathologic anatomy at that time with its lack of knowledge of striatal disease, and failure to recognize the fact, which is only now being appreciated, that organic symptoms may be profoundly influenced by psychic factors. It was believed at that time that only psychogenic symptoms could be so influenced.

In 1921, O. Foerster demonstrated that a localized or generalized tic of organic origin, e. g., on the basis of epidemic encephalitis, could be exaggerated by sensory stimuli, by emotion and by voluntary movement, and that by the same token it might be diminished by quiet and by distraction, and that it might even be completely arrested for several hours by a sudden shock. Observations of this type make one shy of accepting the former sharp and clear differentiation between organic and psychogenic, and make one demand a more exact formulation of the psychogenic.

The demonstration in epidemic encephalitis that tics may have an organic basis does not prove that all tics are organic. Redlich points out that what is called tic is not always the same thing; he recognizes several types — one due to organic disease and others due to various psychic mechanisms. Bing, Potzl, Gerstmann and Schilder have pointed out the similarity of organic and psychogenic symptoms, and V. Weizsacker speaks of "a partial community of expression of organic and psychogenic disturbances."

It is difficult to study these motility disorders from the pathologic anatomic standpoint. The amount of material available is limited. For the present, one must depend a good deal on clinical studies. There is an increasing tendency to refer many of them to basal ganglion disease, and to recognize

that myoclonus, tic and chorea are all closely related. In further establishing this relationship it seemed worth while to study a series of cases in which chorea had healed, with the thought that the diffuse lesions of the acute stage might have left certain focal residual lesions capable of producing tic-like hyperkinesias.

The immediate incentive to the article was a study of two cases of negation tic, each of which followed in the wake of a chorea. Characterologically, the two patients were entirely different. One was psychopathic. The other had a stable, normal personality. One might assume for the psychopathic patient that the tic had developed on a psychogenic basis — as an habituation, an automatization of an expression movement. One could not make such an assumption for the other case. It seemed more reasonable that in both cases the tic developed as a result of the chorea, on an organic basis.

With this point in view the dispensary records were checked over. One hundred and twenty-three cases were selected and the patients were asked to report for reexamination. All had had chorea minor in childhood and had been seen in the dispensary during the attack. The interval between the attack and the present study was fifteen years, sufficient time for the patients to have reached full maturity, and sufficient time to permit the development of any late manifestations of the previous disease. Of the total group, twenty-three reported for examination and they, with two others, form the basis of this study. Of the twenty-five patients only four were entirely normal both from the psychic and from the motor standpoint. Eleven showed mild persistent psychic and motor disturbances. In all this group the psychopathic characters were marked; they were present before the chorea. Whether the chorea intensified them one cannot say. It may be that, as is true for epidemic encephalitis, an attack of chorea minor influences the later character development, intensifying constitutional peculiarities or even bringing latent ones to light. But it is more probable that the same constitutional weakness of striate and hypothalamic areas expresses itself in these psychic variations and in a disposition toward chorea, and that during the acute stage the somatic and psychic functions determined by these regions suffer most. Certain it is, however, that the motor and psychic symptoms are parallel phenomena, not the one (motor) dependent on the other (psychic).

The third group includes cases showing more marked hyperkinesias. The movements were partly choreiform, partly myoclonic and partly ticlike. All three types of movement must be closely related pathophysiologically, as they may occur in the same patient.

The patients in these groups showed only elementary tic movements. The author reports in detail a case of different type, with much more complicated motor disturbances. This is a case which conforms completely to the picture of a maladie de la Gilles de la Tourette, differing only in one point — the important point of a definite etiology, namely, a chorea which had apparently gone on to complete recovery. The boy, now aged 28, had chorea minor at the age of 6. The chorea cleared up completely in six months and he was well. Five years later he developed the present trouble — muttering sounds and slight irregular movements. The muttering developed into coprolalia. At the age of 15, in addition to the coprolalia, he had marked choreiform movements, at times of considerable violence, and sometimes an echolalia. He was irritable, had violent outbursts and occasionally showed a compulsive tendency to injure himself. Intellectually and emotionally he was normal. Even at his worst he could play the violin well after the violent spasms had stopped. At the last examination (1927) the whole picture was the same — coprolalia, choreiform movements, etc.

In this case nothing in the family or past history was suggestive; the author believes that this is to be classed as a chronic persistent chorea with the Gilles de la Tourette picture, on a definitely infectious basis. He does not believe that this observation is to be generalized to include all cases; he considers it possible that other cases, symptomatically identical, may fall

into the class of heredodegenerative diseases. In regard to the coprolalia, he considers it merely a part of a general striate motility disorder, in which the hyperkinesia of articulatory and respiratory muscles is the primary disturbance and the choice of the obscene word merely a secondary psychic process. He discusses this phase in great detail.

In view of the results of the studies on chorea cases, a number of patients with tic were brought back for investigation of possible etiologic factors, and especially the occurrence of chorea previous to the tic. Only seventeen patients came in for study. Among these, three gave a definite history of chorea, three others gave a history of repeated severe attacks of angina and one case was related to scarlet fever. An additional three cases were doubtful, and seven were entirely negative.

The cases studied justify the conclusion that a large number of tic cases, not related to epidemic encephalitis, have as their essential pathologic change damage to the subcortical motor structures on an infectious basis. Could a better history be obtained the relationship could be established more frequently; but, as in the case of certain postencephalitic disturbances, it is likely that here too the acute phase has passed unnoticed and only the late symptoms due to injury of the subcortical motor zones develop to the point of attracting attention. On the other hand, one is not justified in assuming all tics to be infectious in origin. Certain cases, like the type case in the introduction to Meige and Feindel's work, do not belong here.

SELLING, Portland, Ore.

ABSCESS OF THE BRAIN: ITS PATHOLOGY, DIAGNOSIS AND TREATMENT. E. MILES ATKINSON, Lancet **1**:483 (March 10) 1928.

This article deals in full with abscess of the brain arising secondarily to a focus of infection in the skull, usually otogenic. The blood supply of the brain comes from the circle of Willis which divides into two types of branches: central, which pass directly into the base of the brain, and cortical, which ultimately divide into short branches supplying the gray matter only and long branches which supply a thin layer of subjacent white matter. All these are end-arteries, and between the terminations of the central and cortical branches is a thin layer of white matter which is relatively avascular. It is in this zone that abscesses of the brain originate. The cortical vessels carry in with them perivascular, or Virchow-Robin, spaces which take the place of lymphatics. While, normally, spinal fluid flows outward in these spaces toward the surface of the brain, in pathologic conditions, Weed has shown that the direction of flow may be reversed, and so infection may be carried from the subarachnoid space into the brain substance.

In the pathogenesis of adjacent abscess of the brain, the osteitis by extension causes a pachymeningitis, with or without subdural abscess, then a leptomeningitis. Adhesions form, localizing the infection, and from here it spreads into the brain by one of three routes: perivascular, venous or arterial. The perivascular route is by far the most common and evidence of it was found in thirteen of sixteen specimens examined (82 per cent). Infection by the venous route was found in two of the cases (12 per cent). It occurs in the cerebellum usually as a result of the spread backward of a lateral sinus thrombosis through the pial veins, while in the cerebrum it may be the result of a pial vein being caught up in adhesions and thus infected, so that retrograde thrombophlebitis takes place (Preysing). Histologically, these cases show thrombosed veins, patent arteries and a mild perivasculitis. The abscesses are liable to track to the surface, break through and cause a generalized meningitis. The arterial route is the rarest of the three and occurred in only one of the sixteen cases (6 per cent). If a portion of clot is swept away and causes infarction elsewhere, there is an abrupt onset of symptoms.

The capsule of an abscess of the brain is no different from the limiting membrane or wall of any other abscess, except so far as the supporting tissue of the brain differs from that in other parts. In chronic cases, the wall of the

cavity is mainly of fibrous tissue. Internal to this is a layer of cerebral granulation tissue, and external to it, an encephalitis of variable degree and extent. In the subacute type, the granulation layer is thicker, the middle layer less fibrous and the encephalitis more marked. In acute abscesses, there has been no time for the development of any protective mechanism and there is no evidence of a limiting membrane. The contents of the cavity consist of necrotic brain tissue and the wall of acutely inflamed cerebral tissue. In the cerebrum, the abscess grows at the expense of white matter; it follows the vessels inward and may perforate into the ventricle. In untreated patients, the cortex may also be involved and the abscess may break through to the surface. In the cerebellum, the abscess spreads in the white matter forming the core of the lobule. The process starts from the anterior end of the cerebellum, picks out one particular lobule and tends to remain confined to it.

Cerebral abscesses in the temporal lobe are of otogenic origin, commence in the inferior temporal convolution and spread upward. They may become so large as to extend to the occipital and parietal lobes which are otherwise usually involved only by direct infection, such as wounds, or by metastatic abscesses. Those in the frontal lobe are secondary to a nasal accessory sinusitis, and are often associated with bronchiectasis. Cerebellar abscesses are secondary to infection in the ear and may be either labyrinthogenic or nonlabyrinthogenic. If the former, the infection may pass back by bone necrosis or through one of the four following preformed channels: the internal auditory canal, the aqueduct of the cochlea, the ductus endolymphaticus and the hiatus subarcuatus. Spread by the first two usually results in a meningitis; by the last is uncommon; by the ductus endolymphaticus is the usual route in this group. There may be intermediate formation of an extradural abscess. If nonlabyrinthogenic, the route of infection is through the posterior antral wall, either directly through Trautmann's triangle to the dura of the posterior fossa, or more commonly to the lateral sinus and thence to the cerebellum; in either case, with or without the formation of an extradural abscess. Because of the anatomic relationships, the postero-inferior lobule is the one most likely to be involved.

It is of great importance to diagnose a case of abscess of the brain early and to treat the patient if possible before signs of increased intracranial pressure or localizing signs have made their appearance. The presence of these indicates that the abscess is large or a wide area of encephalitis surrounds it. The stage of onset and the latent stage are the ones of great importance. The stage of onset is transient, of a few days or less, and is characterized by an initial feeling of chilliness, possibly even a rigor, headache, some rise in temperature and nausea or vomiting. When these symptoms are associated with an adjacent focus of infection, they should suggest the possibility of something serious. In some cases, especially in children and in those of vascular origin, a "fit" is the first sign and may occur when the patient is apparently well. With an associated suppurative focus, this onset of convulsions always indicates an intracranial extension. The latent stage follows the stage of onset and may last for days or weeks. The conjunction of three events—a focus of infection, a short, acute illness and an incomplete recovery—should raise strong suspicion of an intracranial extension from that focus. During this latent stage, mental changes are constant. Apathy, listlessness, inability to concentrate, drowsiness, impairment of memory, wandering attention, slow cerebration and a change in disposition may all be met with. The patient often has a grayish, unhealthy complexion and looks ill. Headache is always present to some extent, but is not continuous. The temperature shows irregularity about the normal level and the pulse rate the same. In most cases, the pulse rate does fall once in a while and becomes definitely subnormal in relation to the temperature. Any increase in pressure or in the cell count in the cerebrospinal fluid, with diminished percentage of chlorides, will be valuable confirmatory evidence. Localization at this stage may not be possible. With a focus in the ear a complaint of headache, mainly frontal or occipital, suggests a cerebellar lesion, as do also suboccipital pain or tenderness or a stiff neck. The association

of a dead labyrinth or thrombosed lateral sinus would also point to a localization in the posterior fossa. The absence of these would lead one to suspect that the lesion is in the middle fossa.

There are three indications for exploration. This should be performed: (1) when there are definite localizing signs, (2) when there are general signs of intracranial pressure associated with a neighboring focus of infection and (3) when intracranial symptoms have persisted or recurred after drainage of the primary focus. A pulsating dura, of normal appearance, is no contraindication. The best route by which to approach an abscess of the brain is via the originating focus. In the case of cerebellar abscesses, it is difficult to provide adequate drainage by this means unless the lateral sinus is thrombosed, in which case it is obliterated and exploration undertaken through its inner wall. If the sinus is intact, the author believes that it should be deliberately obliterated, as by this means the destruction of a functioning labyrinth and the danger of a tube in contact with the sinus are both overcome, and the abscess cavity can be opened up in its entire length if necessary.

The dura should be carefully exposed so that the point of entry of infection may be found. The use of antiseptics should be limited to the dura, on which they have no harmful effect. In the absence of any sign of a track, blind exploration must be resorted to. Three small incisions should be made in the dura about half an inch apart and exploration, in one direction only, carried out through each of them. In this way infection of one tract from another is avoided. Exploration by means of a cutting instrument is dangerous; by means of a cannula it is unsatisfactory because this may be blocked by thick pus. Some form of angled dilating instrument, such as aural or nasal dressing forceps or a laryngotomy dilator, is satisfactory. The direction of exploration should be toward the ventricle in the cerebrum and backward in the cerebellum. The anterior end of the temporal lobe must be remembered.

Two drainage tubes, of different bore, should be passed into the cavity to reach just above the floor and are firmly secured by stitching to the skin. The bone cavity is packed with bipped gauze and left wide open (gauze soaked in bipp, a preparation first used in the World War and consisting of bismuth-iodoform paste and liquid paraffin). Exploration by the finger or by an encephaloscope and mopping out of the cavity are wrong in the opinion of the author. Once a day, with the patient in the sitting position, the cavity is gently washed out with saline or Ringer's solution which is introduced through the drainage tube of smaller bore. The tubes are left undisturbed for about a week, until a track has formed; when removed for cleaning they should be taken out one at a time, replacing one before removing the other. Drainage should be maintained until the abscess cavity is completely obliterated.

PETERSEN, Montreal.

POVERTY, NUTRITION AND GROWTH: STUDIES OF CHILDREN IN CITIES AND RURAL DISTRICTS IN SCOTLAND. Medical Research Council — Special Report Series No. 101. D. Noel Paton and Leonard Lindlay, His Majesty's Stationary Office, London, 1926.

Although the importance of child welfare is widely recognized for "the character of the adult population of any country, its health, vigor and working capacity is determined by the development and growth of the children, and this in turn influenced not only by environment after birth, but also by factors working while the child is yet unborn," little is known accurately of the factors that make for normal development and growth of the child. It has been shown that the children of the poor of the large cities have a higher infant mortality and that those who survive are of poorer physique than those of the same social class in rural communities, but although many hypotheses — poverty, bad housing, defective feeding, lack of fresh air, inefficient maternal care, heredity, and other conditions — have been advanced in explanation, conclusive evidence, based on proper investigation, has not been advanced to support them.

This monograph reports the results of an investigation undertaken in Scotland by a number of workers in collaboration with the authors, to determine more precisely what conditions modify the growth and nutrition of the child. One hundred children of each age and sex from the slums of Glasgow, Edinburgh, and Dundee were studied and compared with a similar number in a Scotch agricultural district and in a rural coal mining area. The children were grouped into three phases of life: (1) from birth to 1 year; (2) from 1 to 5 years; (3) from 6 to 14 years; emphasis was laid on the second group — the preschool period — because it is this period that should yield the most valuable information as to the effects of conditions in the home. It was found that up to the age of 5½ years the children in agricultural districts are the tallest and heaviest and those in the districts of the slums are the lightest and shortest. There seems to be a lag in the average increase in height and weight of children of the urban districts between the ages of 6 and 18 months, and this is more noticeable among girls than boys. After eighteen months the increase in weight in boys is as rapid in urban as in rural districts, and faster among girls of the urban districts. In the same period the increase in height is quicker in the urban than the rural communities. During the first eighteen months girls of the rural districts increase in height and weight more rapidly than boys; in the cities the reverse is true. It was impossible to correlate any environmental factors with the lag in growth in the first eighteen months of the life of the slum child, but "whether environmental conditions are or are not responsible, it seems manifest that after that age the inherited growth impulse is sufficiently potent to carry it so completely on to the average size of its parents, that the influence of environment is not indicated on the curves of growth of the average of the whole number of children, and it is also evident that the average diet of the population must be at least sufficient to supply the material and energy required for growth."

A large number of the factors that were thought to influence the growth and nutrition of the child of the slums were investigated. It was found that the size of the family, health of the mother during pregnancy, the general health of the mother, the mother's occupation and the size of the income did not have any effect on the growth of the child. There was a small correlation between the total income and the calories of the diet, but the energy value of the diet depended more on the marketing than on the total income. Inadequate diets were not restricted to the low income groups, for even in families with larger incomes there existed a considerable degree of inadequacy. The relation between the diet and the growth of the children in twelve typical urban families was studied intensively. It was found that the average value of the diets was very low — 2,119 calories per person a day. There was a certain but not close correspondence between the income and energy values of the diets. The children averaged 9.1 per cent in weight and 4.8 per cent in height below the generally accepted standards. The children of families with incomes below the mean fell short of the standard in weight by 10.8 per cent and in height by 5.8 per cent, while those of families with incomes above the mean fell short by 5.5 per cent in weight and 2.5 per cent in height. When arranged in families spending more than the mean and those spending less on food, the difference was less marked; in the former the weight was 7.5 per cent below, the height 3.8 per cent; in the latter the weight was 10.3 per cent below and the height 5.5 per cent below. When the group was divided into families with a diet above the mean of calories and those below, it was found that the children of the former averaged 12 per cent in weight and 5.5 per cent in height below the standard, while of the latter were in weight 6.2 per cent and in height 4.0 per cent below. One family was studied three times in three years. The average caloric value of the diet was lower than the average of the families studied in the city in which they lived. The rate of growth of the children, however, corresponded to the mean growth of all the other children. The height and weight of the older children showed a tendency to be below the mean although that of the younger children approximated closely to it.

The results obtained from these studies were contrasted with similar studies on rural families of a similar social status, and the results indicated that even on the low intake of calories and a milk supply of about 0.4 pint a day, the child of the city slums after 18 months of age grows at the same rate as the country child who has a much greater number of calories. Age for age, the country child from 1 to 5 years was from 10 to 11 per cent heavier than the child of the slums. It would seem that the usually accepted number of 3,000 calories as the minimum requirement per person a day is excessive, and that from 2,500 to 2,700 is nearer the correct figure. The comparatively high correlation between calories in the diet and the income, and the absence of any correlation between the weights of the children and the income seemed to indicate that diet is not the all important factor in determining growth that it is supposed to be. The small size and weight of the child of the slums may be more intimately related to heredity than to diet.

Breast feeding is supposed to exert a favorable influence on the future growth of the child. It was found that the majority of mothers nurse their children during the first month and if they do not discontinue then, usually continue till from the sixth to the ninth month. There seemed a correlation between the weight of the child up to the ninth month and the duration of breast feeding, but after this age no sensible relationship was demonstrable. Breast feeding did not seem to have any effect on height. After the period of weaning, the health of a child who had not been breast fed at all was as good as that of the child who has been breast fed the whole time. This might be accounted for by the higher death rate among artificially fed infants with a consequent survival of the fittest, so that the healthiest of the artificially fed were compared with the average of the breast fed; there might be some retardation in growth from the change of feeding which would have caused recovery sooner in those that were weaned earlier.

Over-crowding and lessened air space per person did not seem to have any influence on the growth of the child under 1 year of age. Between the ages of 1 and 5 it had some influence, and during the school period it resulted in a smaller and a lighter child. The health of the mother did not appear to be affected by over-crowding, poverty or the size of the family. The efficiency of the mother was the factor most definitely related to the growth and nutrition of the child, and was related to maternal health, over-crowding, size of family, and possibly to the mental capacity, but not to income. Maternal efficiency, however, only operated as a factor during the first two years of life.

The age of the mother had a slight correlation to the height and weight of the child. Infants of young and old mothers were inferior in height and weight to those of mothers of medium age; this was noted particularly throughout the first half of the first year of life. By the last three months of the first year, the inferiority of the children of young mothers had disappeared, but that of the children of older mothers remained. The order of birth had a greater influence. Infants of the first and over the eighth pregnancy were lighter and shorter than those of the intervening ones. The inferiority of the first born was replaced at the end of the first year by a definite superiority, but that of the last born of families over eight was still apparent at the end of the year. Paternal habits were not investigated sufficiently intensively to lead to any conclusions.

Somewhat similar results were obtained from the study of agricultural families and those of rural miners. In both groups it was found that neither income, air space per person, the size of the family, nor the health of the mother had any effect on the growth or nutrition of the child. The health of the mother was dependent on the size of the family and in the former group seemed correlated with the income, but not in the latter group. Maternal efficiency seems related to the income and the size of the family.

No definite factor seems to have been discovered to account for the lag in growth and nutrition of the child of the city before the middle of the second year of life. Future investigations should concentrate on this period.

PEARSON, Philadelphia.

FRONTAL PSYCHOSES. M. ROSENFELD, Deutsche med. Wchnschr. **54**:85, 1928.

The functions of the frontal lobe remain an enticing field for study. Many neurologic and psychiatric syndromes have been ascribed to the frontal lobes, but it is still a question if these syndromes are not the result of more diffuse cortical or subcortical changes. Since Bruns first noted what he termed frontal ataxia in lesions of the frontal lobes, many varieties of ataxia have been ascribed to this area. Lately, Gerstmann has divided the frontal ataxia into four forms: ataxia, retropulsion, apraxia and atonia. Another frontal lobe syndrome is frontal akinesia or the lack of proper movements. This condition is closely allied with psychiatric disturbances and may be fundamentally psychiatric in origin. It is the author's contention that frontal lobe syndromes resulting from tumor of the brain or trauma of the frontal lobe are open to the criticism that the symptoms may be due to pressure or injury to adjacent parts. It is the writer's belief that, in cases of cerebral atrophy confined to the frontal lobes, these factors do not come into consideration. In the majority of cases reported with cerebral atrophy, the patients were between 55 and 70 years of age. Grünthal reported the cases of two brothers who became affected in the early forties.

The author reports a case which began when the patient was 38 and ran a course of four years, the last two years of which were spent under the writer's observation. This patient was well until 1921. About this time, psychiatric disturbances appeared insidiously. The relatives stated that, slowly, the patient lost interest in his usual activities. He appeared shut-in and seemed no longer able to learn. At times he would become rather irritable. He would wander the streets, whistling aimlessly. At home, he would walk up and down the stairs, talking to himself without apparent reason. At the end of two years he was placed in an institution because of his mental condition. Here he was given a thorough general and neurologic examination, including a study of the ocular fundi. The blood and spinal fluid proved to be normal. During the first year in the hospital the patient was considered to be schizophrenic, the acute phase having subsided. He showed no interest, was unemotional and stood about in an inactive, careless manner. Sometimes he would creep under the bed clothes and have to be urged to get up. He never talked unless addressed. He had no desires or wishes. His attention could be held for only a few moments. He was not catatonic. It was difficult to estimate his intelligence. Given commands or problems he might answer one or two questions correctly, then he would refuse to continue, saying "I don't know," "I can't," or "I don't want to." It was difficult at first to be certain if he had agnosia, apraxia or aphasia. On some days he would refuse to answer the simplest questions. Again he might do remarkably well. The differential diagnosis lay between catatonic schizophrenia and a severe organic disturbance of the frontal lobe. By the end of the second year in the hospital he became extremely dull; finally he was confined to bed and only aroused with difficulty. During the last two months, he presented a motor disturbance of striate character. The muscles appeared rigid. When placed on his feet he would maintain a rigid posture with a slight tendency to retropulsion. There were no pyramidal tract signs until just prior to death. He died four years after the onset of the trouble of bronchopneumonia.

The postmortem examination showed marked atrophy of both frontal lobes. The first frontal convolution was most affected. The atrophy extended to the anterocentral gyrus. The tip of the frontal lobe, the tip of the corpus callosum and head of the caudate nucleus were also affected. The rest of the brain appeared entirely normal. From a histologic standpoint, there was no evidence of either an acute or a chronic infection. There was no evidence of syphilis or arteriosclerosis, of multiple sclerosis or any other sclerotic process. There was only a marked atrophy of the nerve elements, with some pigment deposits and increase of fibrous material. It is the author's opinion that the late motor symptoms were due to atrophy extending to the corpus callosum and basal ganglia. The mental picture was due to marked atrophy of the frontal lobes. He states that, in patients he has observed, with atrophy of the occipital and temporal lobes no

such psychiatric disturbances developed. He believes that one might speak of a frontal lobe psychosis in this case, as there was no evidence of an arterial or general senile process. It is his belief that the same symptoms need not be outstanding in a frontal lobe psychosis. Grünthal recently reported a case in which the symptoms were of a restless, euphoric character. Similar cases have been reported by other observers. Some authors have considered these cerebral atrophies as a heredodegenerative process. Kleist maintains the same attitude regarding schizophrenia, and it may be, according to the author, that one is dealing with the same disease process, at different stages. It is his conception that if the patient had died two years earlier, the postmortem examination would have shown the atrophy to be very slight and that one might properly have assumed that one was dealing with schizophrenia.

MOERSCH, Rochester, Minn.

THE SIGNIFICANCE OF OPTIC NEURITIS. NORMAN H. PIKE, Irish J. M. Sc. 6:611 (Oct.) 1927.

Retrobulbar optic neuritis is an interstitial neuritis, and the cicatricial contraction which follows gives rise to a descending atrophy. The entire nerve may be affected, but more frequently only some of the bundles of fibers are involved, the macular bundle in particular. The outstanding characteristics of the disease are a rapid loss of central vision (a central scotoma being present) no fundus changes at first, some pain on pressure over the globe, a pupil which contracts to light but the contraction of which is not maintained and a marked tendency to recover. If the inflammatory focus occurs far forward, affecting the nerve before the central artery and vein leave it, then a swollen disk with blurred edges and even hemorrhages may develop. One of the commonest causes of retrobulbar neuritis is disseminated sclerosis. The protection afforded the optic nerve by its sheath is an effective barrier to direct infection from a nasal sinus.

The term papilledema or choked disk may be used to indicate great swelling of the disk; papillitis when the swelling is slight, and neuroretinitis when there are marked retinal changes in addition to the disk changes. One can divide these into two groups: (1) those due to intra-ocular causes, and (2) those due to retro-ocular causes, i. e., intracranial. To the first belong the large group of cases of neuroretinitis. The commoner conditions giving rise to this trouble are renal disease, arteriosclerosis, syphilis and diabetes. One factor common to these diseases is a high blood pressure in the larger arteries. The ophthalmoscopic changes are of three kinds: edema, exudate and hemorrhages. The edema if slight is not easy to see; it usually affects the papilla and the surrounding retina, being seen in the latter as a grayish reflex. Hemorrhages are most marked in the central regions; the small flame-shaped ones are superficial, the round darker ones deeper. The exudate is seen as white spots. While the blood pressure in the larger arteries is high, there is evidence to show that that in the retinal arteries is lower than normal.

In the choked disk due to intracranial causes the fundus changes are limited to the disk and its immediate vicinity. The edema begins in the upper nasal quadrant and then spreads, the lower temporal quadrant being the last to be obscured. During the course of the swelling, there may be redness and an uneven distention and darkening of the veins with inconspicuous arteries. Finally, the whole disk becomes edematous, the physiologic cup filled in, and one sees a mound-like prominence with fairly defined limits. The veins will become more distended and in parts obscured by the edema; the arteries are hardly visible. Hemorrhages will be scattered around the swelling and on the disk, and soft-edged white patches due to the swelling of the nerve fibers and their products of degeneration will be present. There will be a grayish striation around the prominent mound owing to the edema spreading along the nerve fiber layer of the retina; between the temporal edge of the disk and the fovea, lines of tension may be formed and along these a fan-shaped figure may appear, similar to the star-shaped figure of renal neuro-

retinitis, the front of the fan being toward the macula. Unless relieved, secondary atrophy will take place, the disks shrink, the nerve fibers diminish and the neuroglial fibers and nuclei proliferate with contraction of the retinal arteries and thickening of the perivascular sheaths. Nonintracranial causes of choked disk are rare.

Choked disk is the direct expression of the mechanical agency of increased intracranial pressure. The essential histologic change is an edema separating the nerve fibers of the disk and its vicinity, but as a rule involving the retina but little. The intracranial pressure is circulatory in origin and stands at the same level, and varies with the cerebral venous pressure. The hydrostatic pressure within the enclosed coverings of the eye and the pressure within those of the brain have been found experimentally to rise and fall together under all varying conditions. In tumor of the brain papilledema may arise in either of two ways: the raised pressure in the optic sheath may be due to a comparatively localized rise in intracranial pressure near the tumor itself or the rise may be due to an internal hydrocephalus caused by a tumor remote from the optic nerves. In cerebral abscess, a mild edema of the disk frequently will occur, and the swelling starts and becomes most marked on the side of the abscess. In subarachnoid hemorrhage, soon after the onset, one nearly always finds a bilateral papilledema with retinal hemorrhages near the disk, and, in some cases, vitreous hemorrhages. When vision starts to diminish in cases of choked disk, the progress is usually rapid.

PETERSEN, Montreal.

THE RELATION BETWEEN THE FORM OF THE HAND AND PSYCHOSIS. A. FRIEDEMANN, Arch. f. Psychiat. **82**:439 (Jan.) 1928.

Following the works of Kretschmer on the relation between physique and character, the author took up a more detailed study of the forms and structure of the hands in different psychoses. These studies were concerned mostly with the general description of the form of the hand (relation between breadth and length, shape, contour, consistency, amount of fat tissue, etc.), shape and color of the nails, circulatory conditions, hair and the expression movements of the hand. The investigations were made in fifty-five cases of schizophrenia and forty-five cases of manic-depressive psychosis. The results were afterward verified on a large number of patients both at the Freiburg and at the Zurich clinics.

The results are summed up by the author as follows:

1. The forms of the hands of schizophrenic patients described by Friedemann correspond mostly to the forms described by Kretschmer as leptosome, athletic and dysplastic-infantile types. Few of them are pyknic. Their insertion into the wrist is rather angular. The fingers are long and thin (the length of the phalanx is from two to three times that of the breadth). The movements at the proximal interphalangeal joints of the little finger are markedly restricted. There are thickenings (knots) at the interphalangeal joints. The ends of the fingers are mostly tapering, the nails are long and narrow, two to three times that of the width. The color of the nail varies from a grayish blue to livid. The panniculus adiposus is poorly developed, so that the contour of the bones, muscles, tendons and veins is well seen. The skin is mostly transparent, and tends to be inelastic. The color of the hands is mostly pale or bluish, and the hands are moist, mostly cold, although sometimes they are lukewarm. The hair differs with the different types. In the asthenic (the author designates this type as the aristocratic) person the hair is rather scarce, but in the athletic there is a marked growth. The greatest width is attained at the base of the fingers. The movements of the hand are generally more marked in the fingers than in the whole hand and arm. The hands are generally kept hidden away. On shaking hands, there is generally an initial suspiciousness, and the hand is withdrawn quickly.

2. The hands of persons with manic-depressive psychoses are described as follows: The form corresponds in most cases to that of Kretschmer's pyknic type. The insertion into the wrist is rounded out. The fingers are generally short, and the length of the phalanges is equal to or somewhat greater than the

width. There is no restriction of movement at the interphalangeal joints, and there is no thickening at these joints. The ends of the fingers show no tapering, and are sometimes even slightly thickened. The width of the nail is generally equal to the length of it, or is even slightly larger. The color of the nail is mostly grayish red. The panniculus adiposus is usually well developed, so that the different structures of the hand are not well seen. The skin is elastic, not transparent. The hand is mostly dry and warm, and is grayish red or red. The veins and muscles usually cannot be discerned. The hair is usually well developed, especially in men. The greatest width of the hand is across the middle of the palm, the hand being much broader in comparison with the length, as contrasted with that of the schizophrenic person. There is a poverty of movement of the fingers but a compensatory richness of gesticulation of the hands and arms. In shaking hands, the hands are willingly brought forward, especially in manic patients. The hand is allowed to rest in the position of hand shaking for a long time, and there is no apparent suspiciousness attached to it.

A complete review of the literature is given at the end of the paper.

MALAMUD, Foxborough, Mass.

TUMORS OF THE FRONTAL LOBE. MAX NONNE, Med. Klin. **23**:1 (Jan. 7) 1927.

It is usually easy to make a diagnosis of tumor of the brain if all cardinal signs are present, but, as Nonne says, only too frequently tumors run an unusual course and fail to present the prescribed symptoms. The case which prompted this truism was that of a woman, aged 49, who consulted Nonne because of a marked change in personality, which had been noted for about a year. As her father had died of paralysis it was thought for a time that she might be syphilitic. The patient complained somewhat of headache, and, eleven years previously, had had a left frontal decompression made because she suffered severely from localized left frontal pain. No evidence of tumor was noted at this operation. For nine years following the operation, the patient remained entirely well. Shortly before she was seen by Nonne, a psychiatrist had made a diagnosis of a psychosis and recommended antisyphilitic treatment.

On examination no signs of syphilis were found. There was no evidence of arteriosclerosis; the entire neurologic study gave negative results and there was no evidence of increased intracranial pressure. There were no headaches, dizziness or vomiting at this time. Mentally, the patient was devoid of all sense of judgment; she was silly, unstable and had no appreciation of her condition. The Wassermann reactions of the blood and spinal fluid were negative. During the next month, considerable euphoria and "Witzelsucht" were present, but no mental deterioration was established. Examination at this time failed to show evidence of intracranial pressure. The fundi were normal and there were no physical signs of neoplasm. She rarely had headaches. There was no ataxia or evidence of catatonia.

Because of the mental picture, the possibility of a tumor of the frontal lobe was considered. An x-ray examination of the head showed a shadow extending in from the inner table. An encephalogram was normal. During the following few weeks, the left frontal headache became more marked and there was some local tenderness.

Exploration showed a tumor of the size of a billiard ball pressing down between the frontal lobes to the corpus callosum, but not involving it. The patient did not recover.

At necropsy there was no evidence of syphilis. The tumor was found to be a spindle cell sarcoma, which had involved the dura and also the bone.

Nonne points out that: (1) Large tumors may develop within the cranial cavity without signs of pressure. He has found absence of choked disks in 40 per cent of his cases of tumor of the brain. (2) There may be absence of local headache. (3) The psychic disturbances were of variable type, as is so often noted in lesions of the frontal lobe, but they were not "classical," which is probably

because the tumors did not involve the lobes themselves. (4) Frontal ataxia was absent as the frontal lobes were not affected. (5) Entirely too many of these patients are needlessly treated for syphilis.

It has been Nonne's misfortune to miss several endotheliomas because of the lack of pressure signs. Two of these were diagnosed as cases of idiopathic epilepsy.

MOERSCH, Rochester, Minn.

ANATOMIC OBSERVATIONS IN SYRINGOMYELIA WITH OPTIC ATROPHY. G. HERMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **111**:713 (Dec.) 1927.

There have been no pathologic reports of cases of syringomyelia with optic atrophy, so it is not known whether the optic atrophy is actually caused by the syringomyelia. That the disease process can extend far beyond the spinal cord is well known. It is commonly found in the medulla, where it appears as a slit-like opening. These slits follow the course of the vessels accompanying the glossopharyngeal and vagus roots, and often injure the nuclei of the vagus-accessory group, the tractus solitarius, the fillet and the spinal roots of the acoustic and trigeminal nerves. The slit formation does not extend beyond the region of the facial nucleus. The most extensive syringomyelic cavity yet reported is that described by Spiller. In his case the cavity extended from the sacral region throughout the entire spinal cord, the medulla, the right side of the pons, the right cerebral pedunde and the internal capsule, and ended in the nucleus caudatus, just under the ventricular ependyma. Enders traced the pathologic process through the pons. Optic neuritis and choked disk have been observed in a number of cases. Weisenburg and Thorington assumed the occurrence of hydrocephalus with the syringomyelia as the cause of the ocular symptoms. Hauel believes that the optic atrophy is due to compression by an internal hydrocephalus, and Oppenheim mentions the possibility of the occurrence of tabes with the syringomyelia as the cause of the optic atrophy. Syringomyelia with tabes is rare, but it has been described by Spiller and Songues-Barbe.

Hermann describes a cause of syringomyelia in a child of 14 with bilateral optic atrophy. Necropsy revealed a syringomyelic cavity in the cervical portion of the spinal cord, and in addition to this there was an inflammatory condition at the base of the brain involving the optic chiasm, with perivascular infiltration of round cells and some gitter cells. The process also involved the optic nerves. The optic atrophy is the result, therefore, of the inflammatory changes in the optic nerves and in the chiasm, and Hermann looks on the case as a condition of syringomyelia of the cervical cord with encephalitic changes in the base of the brain and involvement of the optic nerve. The pathogenesis of the case is not clear. The present concept of syringomyelia is that it is a primary gliosis followed by cavity formation due to regressive changes within the gliosis. Because of the occurrence of syringomyelia with tumors or malformations, it has been suggested that syringomyelia is a developmental disturbance. Tanneberg believes it is a cicatrization which runs a chronic course, on the one hand, after a severe trauma and, on the other hand, after noxious stimuli which involve the cord (tumors and unknown noxious agents such as cirrhosis of the liver). Degenerative and proliferative changes in the glia run hand in hand with the other process. Thomas and Hauser, and Nighino have called attention to the relation of the syringomyelic cavity to the blood vessels.

ALPERS, Philadelphia.

THE ETIOLOGY OF MULTIPLE SCLEROSIS (FIRST CONTRIBUTION). O. KAUFFMANN, Arch. f. Psychiat. **82**:576 (Jan.) 1928.

The author introduces the subject by a complete review of the literature on the question of an infectious etiology of multiple sclerosis. The search for a bacteriologic agent was especially stimulated by the works of Steiner and Kuhn, who reported the discovery of a spirochete (*Argentinensis*) in the blood of patients suffering with multiple sclerosis. They were able to cause disease (apparently of

the central nervous system) in animals by injecting this blood into them, and found the same spirochete in the blood of these animals. Since this report, the results of experimental studies have been conflicting. There have been as many who verified wholly or partly the observations of Steiner and Kuhn as those who could not find substantiation of this theory. The author remarks concerning the difficulty in differentiating true from false spirochetes, the unreliability of paralleling diseases in animals with those in human beings, the nonuniformity of the picture of multiple sclerosis in different patients or at different times in the same patient, and numerous other difficulties which help to explain the varying results of different experimenters.

The author made the following experiments: (1) a search for spirochetes in the blood of patients with multiple sclerosis; a search for spirochetes in animals inoculated with blood from such patients and which developed diseases more or less similar to those reported by Steiner and Kuhn; (2) therapeutic attempts on the basis of a spirochetal etiology (arsphenamine) malaria, various metallic salts and Swift-Ellis treatment; (3) inoculation of guinea-pigs with blood from a patient suffering with multiple sclerosis; observation of animals and postmortem examination; (4) observations on guinea-pigs inoculated with poliomyelitis as well as with the so-called spontaneous "guinea-pig paralyses"; (5) inoculation of mice and monkeys with blood from patients with multiple sclerosis.

The author sums up his results as follows: A search for spirochetes in seventy-three cases of multiple sclerosis in human beings resulted in finding pseudospirochetes only; no true spirochetes were found. Guinea-pigs, mice and monkeys were examined, with similar results. The therapeutic attempts so far have not shown definite results. The experiments with inoculation of guinea-pigs resulted in the production of spastic paraparalyses of the hind legs and convulsions in some of the animals. The pathologic picture in the central nervous system was that of an encephalomyelomeningitis. The clinical and histologic pictures were similar to those found in animals inoculated with poliomyelitis and also to those found in the spontaneous paralyses of guinea-pigs. The experiments with mice did not give any results, whereas those with monkeys showed results that were more or less similar to what were obtained in the guinea-pigs. The experiments on the monkeys are not as yet completed. The author is of the opinion that, although all signs point to the infectious nature of multiple sclerosis, there is no definite proof yet that *Spirochaeta argentinensis* is the causative factor.

MALAMUD, Foxborough, Mass.

THE POSTURE OF THE HAND IN CHOREA. W. RUSSELL BRAIN, Lancet **1**:439 (March 3) 1928.

The posture of the hand in chorea is characterized by flexion at the wrist and hyperextension at the metacarpophalangeal joints. The fingers are straight or slightly flexed at the interphalangeal joints and separated. The thumb is hyperextended and abducted. This, according to Wilson, is the "corresponding opposite" of the normal resting posture, and the "physiological shift" he believes can be taken to substantiate the argument that the condition is an abnormal function of the corticospinal system, which need not be structural nor have its ultimate origin on the motor or effector side. The author believes that the position is more an exaggeration of a normal posture and is of simpler explanation.

Synergic extension of the wrist strengthens grip. Extension of the fingers without separation has as synergic movement extension of the wrist. Separation of the fingers and thumb is the foundation of the choreic posture of the hand. In this the prime movers are the dorsal interossei and the extensors of the fingers and the abductors and extensors of the thumb. The synergists are the flexors of the wrist. Abduction of the fingers can be brought about by the extensors of the fingers, but these are also extensors of the wrist and, unless the latter action is counterbalanced, their value as extensors and abductors of the fingers is greatly reduced. Thus synergic flexion of the wrist assists abduction of the fingers. While

this movement, extension and abduction of the fingers with synergic flexion of the wrist is the opposite of the normal resting posture of flexion of the fingers and synergic extension of the wrist, it is just as natural and physiologic a movement as the latter.

Although the choreic posture is normal in its synergic pattern, its exaggeration is pathologic and brings it into relationship with muscular hypotonia. Hypotonia is characteristic of chorea. In hypotonic states, movement meets with abnormally little resistance from antagonists, so exaggeration of posture results. The author believes that the choreic posture of the hand is such an exaggeration of a normal attitude. The same attitude may be observed in other hypotonic conditions and had better be called the "hypotonic posture" of the hand than the "choreic posture." The choreic patient remains capable of assuming the normal resting position described above. The author concludes that he cannot regard this posture as a "physiological shift" and evidence of "abnormal function of the cortico-spinal system" as Wilson maintains.

PETERSEN, Montreal.

COMPARATIVE INVESTIGATION ON THE PINEAL GLAND IN MALE AND FEMALE ANIMALS. EISUKE ISHIKAWA, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **29**:337 (Sept.) 1927.

Considerable attention has been directed recently to the physiology of the pineal body and its function as a gland of internal secretion. Experiments and clinical observations indicate that there must be some difference between the male and the female gland. Ishikawa examined five pairs of dogs, each pair being from a different mother but belonging to the same litter and weighing approximately the same.

He was able to distinguish males from females by the appearance of the subcommissural organ. The difference was that in the male the bud of the subcommissural organ projecting from the aqueduct was much more delicate and slender than in the female. If the two subcommissural organs were compared with respect to their general development it was seen that the male organ is less fully developed than the female. This difference was constant and striking.

The pineal gland, itself, is unusually well developed in the new-born animal. When the gland of the male was compared with that of the female it was seen that the average size of the former was 600 by 900 microns while that of the latter measured less. By absolute measurement the female pineal gland proved to be about 100 microns shorter than the male. Structurally, no difference between the glands of the two sexes could be detected.

Ishikawa concludes from his observations that in the dog, the male pineal gland is quantitatively better developed than the female, but that they are alike qualitatively. On the contrary, in the female the subcommissural organ is better developed, so that one deals here with a vicarious pineal gland. The facts that in the female the gland itself is quantitatively smaller and that the female animal is in general less well developed indicate that the organ is of considerable importance. Most interesting, however, is the vicarious subcommissural organ. It appears that this structure has not only a trophic but also a functional significance.

KAMMAN, St. Paul.

THROMBO-ANGIITIS OBLITERANS: EFFECTIVENESS OF THERAPEUTIC PROCEDURES. SAMUEL SILBERT, J. A. M. A. **89**:964 (Sept. 17) 1927.

Silbert believes that the only satisfactory criterion by which to judge the effectiveness of a method of treatment in cases of thrombo-angiitis obliterans is by its abilities to save the extremities of the patient. Many remedies have been proposed. Many times pain will subside suddenly and for no discoverable reason. Again, relief is thought to be obtained, only to see the patient relapse. Frequently, repeated subcutaneous injections of Ringer's solution and of sodium nitrate have been suggested. Leriche suggested femoral sympathectomy. Insulin is claimed

to have had beneficial effect. Lumbar ramisection has been resorted to as has been deep lumbar x-ray therapy. A recent courageous suggestion has been ligation of the main arterial supply. The author also cites still other methods.

In a previous article, Silbert has reported repeated intravenous injection of hypertonic sodium chloride solution in sixty-six cases observed for a period of three years; he now has eighteen more to add to this series. He uses as a basis for comparison an extensive study of 258 cases of this disease, in all of which the symptoms began before the age of 45.

Silbert is thoroughly convinced that prolonged smoking is the immediate causative factor in the production of this disease. He presents certain arguments to support this belief. In his series of 258 patients who did not receive treatment, 77 per cent or 155 patients lost at least one extremity within five years from the onset of symptoms. Of eighty-four patients treated with hypertonic salt solution, including apparently hopeless cases, 12 per cent have required amputation in four years. He believes cessation of smoking is the most important therapeutic measure.

CHAMBERS, Syracuse, N. Y.

CONTRIBUTIONS TO THE HISTOPATHOLOGY OF MICROGLIA. L. VON MEDUNA, Arch. f. Psychiat. **81**:123 (Nov.) 1927.

Following a review of the literature, the author describes the methods of investigation he has used; these were concerned mostly in describing in a systematic manner the pathologic changes in microglia and also in ascertaining its function. His experiments were carried out on rabbits. Six of these were inoculated with a fixed rabies virus, two with fixed herpetic encephalitis, two were starved, six were subjected to B-avitaminosis and two were subjected to high temperatures (Omorokow). Most of the examinations were made with the Hortega method.

Meduna comes to the following conclusions: (1) There does not exist a pure hypertrophy of the microglia. (2) Elements that until recently have been regarded as hypertrophic usually show signs of marked degeneration. The hyperplastic abilities of microglia are rather restricted. (3) Although microglia does take part in the thickening of the neuroglial plexus, this is not an essential function. (4) One disease is specific for microglia and is found in cases of starvation, B-avitaminosis and over-heating. It is expressed in the form of a degenerative atrophy. (5) The most important function of microglia consists in taking up of pathologic metabolic products of the nerve cells. (6) Following accumulation of metabolism products, there is swelling of the cell and rapid degeneration with liquefaction. (7) The remains of degenerated microglia cells are removed from the tissue by the apolar neuroglia, whereas perivascular elements are probably taken care of by simple osmotic diffusion.

MALAMUD, Foxborough, Mass.

SUBACUTE COMBINED SCLEROSIS OF THE CORD OF SUDDEN ONSET. S. C. H. WORSELDINE, Lancet **1**:323 (Feb. 18) 1928.

Seven days before admission to the hospital, the patient, a native Indian, aged 25, noticed weakness of the legs after a day's work. This condition progressed until finally he was unable to stand. There was complete spastic paralysis of both legs from the hips. The knee jerks were exaggerated and equal on the two sides, with bilateral ankle clonus and Babinski sign. The pupils were normal and active; there was no nystagmus. Sensibility to pain was diminished from 2 inches above the umbilicus downward; hyperesthesia existed from that level to the xiphisternum. Sensations of touch, deep pressure, heat and cold were lost in the legs and in the area below the umbilicus. Diminished sensation was found on rectal examination. The red cells numbered 2,340,000; hemoglogin was 80 per cent, and the color index, 1.7. Poikilocytosis and anisocytosis were present; normoblasts and megaloblasts were found; there were no myelocytes; there was 5 per cent of eosinophils. The patient grew worse in the hospital and was finally invalided home, after which nothing more was heard of him.

PETERSEN, Montreal.

CHORDOMA OF LUSCHKA'S POUCH. ARGAUD and CLERMONT, Ann. d'Anat. path. **5**:145, 1928.

The authors report a sixth case of malignant chordoma arising in the nasopharyngeal wall close to the pharyngeal tonsil. It provoked respiratory difficulty and was removed by the surgeon, who thought it was a nasal polyp. Some months later, the same respiratory difficulty recurred and a sense of deep pressure developed between the eyes. There were no hemorrhages or ocular disorders. The tumor covered the posterior part of the nasal fossae and pressed forward the palate; it was firm, with its base on the posterior pharyngeal wall; it was removed again, being unconnected with bone.

Microscopic examination showed the tumor to be covered by a normal pharyngeal mucosa and a layer of fibrous tissue. The tumor itself consisted of grotesque cells, with branching protoplasm and large vesicular nuclei, the cytoplasm tending to form a syncytium.

The author has collected five other cases of chordomas in this location.

FREEMAN, Washington, D. C.

THE CAUSE OF AN ANXIETY NEUROSIS. R. MCDONALD LADELL, Brit. M. J. **1**:444 (March 17) 1928.

The patient, an unmarried woman, aged 22, was suffering from an anxiety neurosis with the usual train of symptoms. Fear of insanity had become acute since she had read a novel in which the heroine lost her reason. Her favorite literature consisted of children's stories, and she had aspired to write fairy tales. She had an aversion to men who wore glasses or had pimply faces. She was engaged to a rather undemonstrative man, and chided herself for feelings of a passionate nature which she experienced when in his presence. She regarded sex as debasing and animal, although she recognized its necessity, and this attitude probably accounted for her interest in children's stories which are free from the sex theme. Finally, she confided that when she was 5 years of age, her cousin, a pimply and bespectacled youth of 18 years, frequently forced her to submit to intercourse with him. This was later associated with a feeling of guilt which colored her views of all heterosexual relationship. She was horrified at her own desires, and she feared lest her husband should become aware of her early experiences.

PETERSEN, Montreal.

INFANTILE AMYOTONIA AND AMYOTROPHY (DISEASES OF OPPENHEIM, AND WERDNIG-HOFFMANN). M. RUIZ MAYA, Arch. de neurobiol. **7**:218 (Sept.-Oct.) 1927.

The article contains a discussion of the symptoms and course of Oppenheim and Werdnig-Hoffmann diseases based on observations in a case of congenital amyotonia in a child. From a comparison of this case with a case of infantile amyotrophy previously studied, the author concludes that amyotonia and amyotrophy are different syndromes rather than stages of a single disease as is claimed by some authors. Although no Wassermann test was made, the presence of a lesion of syphiloid aspect in the palms of the hands and the fact that there was improvement after mercurial medication are regarded by the author as indications of congenital syphilis; he suspects the existence of a close relation between syphilis and amyotonia in the case described.

NONIDEZ, New York.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 19, 1928

JOHN FAVILL, M.D., *President, in the Chair*

A CASE OF GENERAL PARALYSIS; TYPHOID THERAPY. DR. GEORGE W. HALL.

A man, aged 33, gave a history of an initial lesion at the age of 19. He was first seen in consultation in October, 1927. He was in charge of two nurses in a hospital, but became noisy, violent and talkative, so had to be transferred to a sanitarium. Examination of the spinal fluid showed conditions typical of paresis. Clinically, the patient was euphoric. He wrote many letters and sent checks to friends daily, showing typical delusions of grandeur. He was given fifteen injections of typhoid and paratyphoid, the highest dose being something like two billions. The average temperature reached 103.5 F. He became quieter after the first three or four treatments so that he would cooperate well. I had not seen him for some time until recently, but so far as I can observe he does not have delusions of grandeur, and friends say that he is normal in every way. He has been in this state since the last treatment, about three months before presentation, and expects to return to work within a short time. He has never had an Argyll Robertson pupil nor disturbances of speech. The knee jerks are lively. He answers questions in an entirely normal manner and his employer thinks he is able to return to work.

The use of typhoid vaccine is subject to individual variations; one cannot tell in advance what the dosage must be. I have a patient on this treatment now who started with 25 millions and yesterday had a temperature of 104.5 F., with 40 millions, the seventh treatment. With another patient one might have to go to a billion or a billion and a half before the fifteenth chill. Only by experience can one tell as to the size of each succeeding dose.

DISCUSSION

DR. JAMES C. HASSALL: What would you consider the largest safe dose?

DR. HALL: About twenty-five million as the initial dose, gradually increased with each succeeding dose. The fifteenth dose may require one hundred million or two billion, depending on each reaction.

DR. ROY GRINKER: I recently saw a patient with paresis who was mildly depressed and who apparently had been deteriorating for some time. Malaria inoculation did not take. Typhoid vaccine was given, but no chill was obtained and only a slight fever of from 100 to 101 F. resulted, although nausea was experienced after each injection, in spite of the fact that the dose was rapidly increased, often by one-half billion at a time, until the final dose reached was five billions. The patient gradually became worse and while in the hospital became disoriented and developed hallucinations so that an institution was recommended. However, she was taken home and two months later walked into the office perfectly oriented and much improved mentally and physically. She has maintained this state for six months at the present time. Apparently large doses of the organism cannot do harm and it may not be essential that a high fever accompany the treatment. In a personal communication, Dr. Kunde informed me that he does not believe that fever plays a great rôle in the therapy.

Dr. Hall: I do not know what Dr. Grinker's conclusion is in his case, but those who have had considerable experience with malaria know that one cannot secure a rise of temperature in many instances. The chill is not of importance and if there is no fever I think it inadvisable under any circumstances to continue the treatment. In some cases I have switched from typhoid to malaria and have obtained good results. In other cases I have not had any results from malaria and have had good results from typhoid vaccine. I think it is not advisable to continue treatment if one does not get reactions with comparatively large doses early in the treatment. I might say, however, that Dr. Grinker's initial dose was entirely too high and I believe too large an initial dose lessens the reaction to succeeding injections.

A Specimen of Tumor of the Brain. Dr. James C. Gill.

My object in presenting a history of this case is to show some unusual features. The patient, a man, aged 46, single, a laborer, entered the Presbyterian Hospital on Nov. 14, 1927. He complained of headaches of several months' duration, occasional vomiting and paresis of the left side of about six months' duration, which had been becoming progressively worse, so that at the time of his entrance into the hospital there was almost complete loss of motion; he was able to walk with great difficulty, dragged the left leg, and the left arm was practically useless. In addition, he had occasional epileptiform seizures of jacksonian type involving the left arm. On several occasions he had fallen and apparently lost consciousness.

Examination did not show any particular disturbances besides the nervous manifestations. Roentgen-ray examination of the skull gave negative results. Lumbar puncture did not show any increase in pressure of the spinal fluid. The laboratory report showed a count of one cell, a slightly positive Nonne test and a colloidal gold curve of 1122100000; the Wassermann reaction was negative. Examination of the eyes showed that the pupils were unequal, the right being the larger, but both reacted to light and in accommodation; the extrinsic muscles were normal; there was no nystagmus. Ophthalmoscopic examination showed the disks normal and the media clear. All other cranial nerves were normal. The right knee jerk was probably normal, the left exaggerated; there was no ankle clonus; the right plantar was normal; the left, extensor; Gordon and Oppenheim reactions were present on the left with an occasional positive Gordon sign on the right; the tendon reflexes of the upper extremities were equal and normal; the cremasteric reflex was present and equal on the two sides; the abdominal and epigastric reflexes were present on the right and absent on the left side. The motor power on the right side did not seem disturbed; it was definitely decreased in the upper and lower extremities on the left side. Sensation was apparently normal.

Mentally, the patient was forgetful and childish in many ways, given to outbursts of meaningless laughter. He frequently emptied his bladder in bed without comment. He used profane language in the presence of nurses without being conscious of any impropriety.

A diagnosis was made of a tumor of the frontal lobe on the right side. Dr. Bevan performed an operation, exposing the right frontal lobe, and did not find any evidence of a neoplasm. On the third day, the patient died of bronchopneumonia.

Postmortem examination revealed an extensive cystic glioma, involving almost the entire left frontal lobe, extending as far back as the corpus callosum and involving the internal capsule to a point posterior to the knee. The right hemisphere of the brain seemed normal.

The interesting features of this case were the presence of an extensive tumor in the left frontal lobe with practically no disturbance in the right

side of the body, no evidence of motor aphasia, and the marked disturbance of motion on the left side of the body. It hardly seems probable that pressure on the right motor tracts would offer a satisfactory explanation for the clinical symptoms.

RECURRENT ATTACKS OTHER THAN MIGRAINE AND INFANTILE CONVULSIONS PRECEDING TRUE EPILEPSY. DR. HUGH T. PATRICK and DR. DAVID LEVY.

This article will appear in full in a later issue of the ARCHIVES.

A STUDY OF CEREBRAL TUBERCULOMAS. DR. ROY GRINKER and DR. R. A. LIFVENDALH.

The treatment of tuberculoma of the brain differs radically from other tumors. A study of twenty-one available cases in which necropsy had been performed was undertaken to determine if possible what could be used as diagnostic of them.

These cases were obtained from a material which is not arranged, so that incidence statistics are not possible; however, the incidence of tuberculoma is different today than forty years ago. Starr found in 300 tumors in patients under 19 years of age that 50 per cent were tuberculous, and in a like number over 19 years of age 13 per cent were tuberculous, making a total of 32 per cent for all ages. Similar high percentages from various authors have repeatedly been quoted in the literature until Van Wagenen, in 1927, from Cushing's 1,000 verified tumors found only 1.4 per cent tuberculomas. The difference in incidence has been variously explained by a decrease in tuberculosis in general, by a possible change in the organism, and possibly by the lack of microscopic examinations in the earlier cases.

Almost two thirds of the patients were under 19; the ages ranged from 4 months to 63 years. Two-thirds were colored patients, which corresponds to the usual observation of twice as much tuberculosis in the colored as in the white race. Only four cases were multiple. Most reports show a predilection for cerebellar localization. Van Wagenen found all but three of fourteen tumors in the cerebellum, whereas we found three cerebellar, one pontile and seventeen cerebral.

The pathologic structure of the tubercles themselves differs in no way from tubercle elsewhere. They were usually fibrocaseous and only occasionally in partial calcification. A moderate connective tissue capsule was usually found. A characteristic observation was a zone of softening about the tubercle in turn surrounded by a hyperemic ring. We cannot state whether this is evidence of an allergic phenomenon secondary to a terminal overwhelming tuberculosis elsewhere, analogous to the lighting up of a tubercle in a rabbit's testes on the injection of tuberculin or whether it represents an interference with the blood supply. The effect on distant structures, such as the subarachnoid space, has been most excellently described by Hassin.

The cause of death is of great interest. Seven patients died from miliary tuberculosis, including tuberculous meningitis; ten without tuberculous meningitis, but from tuberculosis elsewhere, and only four of the twenty-one from tuberculous meningitis secondary to the tuberculoma.

We are disappointed in saying that general symptoms of fever, leukopenia, lymphocytosis and the presence of tuberculosis elsewhere are not helpful in the diagnosis. Tuberculomas are a rather benign tumor in that only eight of twenty-one cases presented neurologic symptoms. These eight, in spite of a large tuberculoma, showed mild general intracranial symptoms. Choked disks were not found and only once vomiting with slow pulse; slight headaches were the rule. Jacksonian epilepsy followed by hemiplegia was the most common picture.

As a result of the study of our cases we can state only that focal signs of a large tumor without many general signs, and the location in a child of a lesion not in the posterior fossa should arouse the suspicion of a tuberculoma. Since the majority of the tubercles are symptomless clinically and only four patients died as a result of secondary meningitis, therapy should be directed to the tuberculosis in general. As manipulation of the tubercle, with rare exception, results in fatal meningitis, decompression only should be attempted if operation is necessary. The neurologic surgeon must assume the responsibility of recognizing the tuberculoma grossly in view of the fact that it can be diagnosed for him clinically so infrequently.

Dr. Hassin: Did Dr. Grinker study all of the twenty-one cases histologically or was the diagnosis made only from the macroscopic appearance of the brains? Personally, I have not had clinical experience with tuberculomas, that is to say, I cannot diagnose them. Pathologically, I studied only three cases, in one of which the brain was so badly chopped up that it was of little use. The fact that the meninges are, as a rule, involved in solitary tubercles of the brain or spinal cord would suggest the advisability of utilizing such a complication for diagnosis. I would also suggest to Dr. Grinker that he study the condition of the choroid plexus in tuberculomas of the brain. This probably would be of greater value than statistical reports.

Dr. Theodore T. Stone: I wish to report two cases of solitary, singular tuberculoma in two women.

Case 1.—A woman, aged 44, who had not been sick at any time prior to one year preceding the neurologic examination complained of headache situated in the occipital and upper part of the region of the neck, generalized weakness, and marked loss of weight; she had lost 70 pounds (31.8 Kg.) in a year. In addition, she had altogether four generalized attacks of grand mal epileptic seizures. They were not unilateral at anytime. Neurologic examination revealed the usual signs of unilateral cerebellar tumor. She showed abnormalities of the fifth, sixth, seventh and eighth cranial nerves. She had marked ataxia in the left upper extremity. The left lower extremity showed ataxia, but not as marked as in the left upper. Horizontal nystagmus was evident in fixation to the right. On fixation to the left, nystagmus was vertical and rotary. Spinal puncture did not reveal any abnormal changes. A diagnosis of cerebellar tumor was made. Postmortem examination revealed a large single tuberculoma of the left cerebellar hemisphere.

Case 2.—A woman, aged, 38, complained of headache, vomiting and difficulty in vision, which had been present for the preceding eight months. Examination revealed the usual neurologic symptoms of a cerebellar lesion. Postmortem examination also revealed a tuberculoma of the cerebellar hemisphere.

In neither of the cases had the tuberculoma ruptured outside the cerebellum. Macroscopically, there was no evidence of tuberculous meningitis. The first case showed a left-sided secondary optic atrophy with papilledema of the right eye.

Dr. Grinker: Histologic studies controlled the diagnosis of tuberculoma in all cases. Dr. Hassin apparently missed one of the main points which we have stressed; namely, that meningeal involvement, not as a result of miliary tuberculosis, occurred only four times as an end-result. Signs of tuberculous meningitis do not interest us in the diagnosis of tuberculoma. We shall prefer to diagnose them before the terminal event. The purpose of studying carefully these clinical histories was to elicit some common facts which might help in a correct diagnosis in order that proper therapy or at least not dangerous therapy such as operative removal could be instituted. Although Dr. Hassin stated that he had not seen any clinical cases of tuberculoma, three of the undiagnosed ones presented at this meeting were under his observation.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY AND SECTION OF OBSTETRICS AND GYNECOLOGY

Combined Meeting, Jan. 24, 1928

WALTER M. KRAUS, M.D., *in the Chair*

MERALGIA PARESTHETICA. DR. JAMES H. HUDDLESON.

Meralgia paresthetica, generally considered a syndrome of a certain peripheral nerve alone, may also arise on the basis of a lesion at the level of the cell bodies of the sensory neuron of the second order, as well as more commonly at any level (cell body or process) of the neuron of the first order. Characteristics of the central pain that may arise from destructive plus irritative lesions of cell bodies at and about the level of the second lumbar segment are similar to those of the pain of herpes zoster of the second lumbar root ganglion, sufficiently so to warrant considering them both as possible causes of meralgia. Cases both of zoster and of tabes showing the syndrome of meralgia paresthetica have been reported. Cases of pain with paresthesia, essentially of the same type as that seen in meralgia, and referred peripherally from lesions of syringomyelic type, suggest that the syndrome under consideration may occasionally arise from a localized syringomyelia or hematomyelia.

The extent of the area of the skin affected in meralgia is markedly variable. Sometimes it is only that of the gluteal branch of the lateral cutaneous nerves; sometimes the anterior crural, genitocrural or adjacent nerves are involved in addition to or replacing the lateral cutaneous nerve. The latter may be derived from the first or third as well as from the second lumbar root, and there may also be anastomoses distally. A central disease process could affect a small or large part of the distribution of the peripheral nerve.

Peripheral lesions resulting in meralgia paresthetica are widely various—zoster of the ganglion, tumor, pregnancy, obesity, different types of trauma to the nerve trunk at vulnerable points, abdominal or pelvic inflammatory disease, general infections and intoxications.

If a cause is not found, the following physiotherapy has met with some success as symptomatic treatment: radiant light and heat to the thigh and leg followed by massage of the outer side of the thigh; static brush discharge along the course of the lateral cutaneous nerve. More radical measures suggested are x-ray treatment, injections of alcohol or excision of the nerve.

MERALGIA PARESTHETICA—A NEW CONCEPTION OF ITS ETIOLOGY AND TREATMENT. DR. BYRON STOOKEY.

The etiologic factors in the production of meralgia paresthetica are an abnormal position and angulation of the external cutaneous nerve as it leaves the pelvis. Angulation and traction on the nerve at this point are increased by standing and walking, as are the symptoms of meralgia paresthetica. Abnormal angulation with repeated traumatism due to movements are well known as etiologic factors in the production of later ulnar neuritis secondary to fracture of the humeral condyles and of brachial neuritis due to cervical ribs or fascial prolongation from rudimentary cervical ribs. The mechanism in the production of meralgia paresthetica is comparable to these two well known conditions.

The surgical treatment suggested is section of the external cutaneous nerve without resection, allowing the nerve ends to lie in alinement in order to facilitate regeneration. Defects of from 1 to 2 cm. may be bridged spontaneously when the ends of the nerve lie in smooth fascial planes. Were spontaneous regeneration to take place, the external cutaneous nerve would thus be lengthened and recovery of sensation would follow. In any case, permanent anesthesia in the area of the external cutaneous nerve is to be preferred to the paresthesia and pain found in meralgia paresthetica.

DISCUSSION

DR. FREDERICK C. FREED: I do not feel competent to discuss these two papers. I have seen several patients who had conditions that simulate what Dr. Huddleson and Dr. Stookey have described. Whether it was true meralgia paresthetica I cannot say. I saw one patient who had a large tumor of the pelvis, and because of that tumor suffered much pain in the upper part of the thigh, toward the front. After the tumor was removed, she was completely relieved of all symptoms in the thigh for two or three years. Finally, she became constipated, almost obstipated, and was found to have a number of adhesions in the pelvis that kept the lower intestinal tract from acting as it should. The symptoms of the thigh which she had had previously had not been relieved until she was given colonic irrigations twice a week. She did not complain further of symptoms of meralgia paresthetica.

Not infrequently, one sees a condition in which the patient has a pendulous abdomen, which is probably quite similar to that which Dr. Huddleson has described. This condition draws the center of gravity forward. The patient walks on her toes, strutting forward a bit, after the manner which I think Shakespeare described as "the pride of pregnancy." This in turn produces flat feet and probably stretching of this nerve as it comes out from the deep fascia. Such a patient complains of the symptom spoken of by Dr. Huddleson. A properly fitting corset to support the abdomen and to take pressure off the nerve relieves these symptoms.

On the other hand, one meets patients who complain of a burning sensation or a sensation of distention or constriction in one particular area on the upper part of the thigh. Such trouble is not infrequent in these days of reducing corsets which are rubberized and probably cause constriction of the external cutaneous nerve as it emerges. Removal of the corset relieves the symptoms.

Another patient with a condition similar to this was a writer. She wrote on her knee or on both knees with a board placed across them. That probably produced pressure. When this procedure was stopped the symptom and the pain, which she had thought were due to some pelvic condition, disappeared.

Another condition, which is more like so-called sciatica, occurs when the head of the fetus, less frequently the buttock, exerts pressure in the maternal pelvis and causes not only cramps, but also paresthesia. By having the patient change her position when lying down, one can relieve that condition. Often, having the patient lie on her back, flexing the knees, drawing the knees up toward the chin as far as possible, slowly relaxing again and extending the legs, and repeating that exercise several times is enough to dislodge the fetus and relieve the pressure on the nerve, and thus the symptom.

DR. ISRAEL STRAUSS: One reason why Dr. Stookey has not had many cases of meralgia paresthetica referred to him is that it is an uncommon disease—that is, uncommon to the neurologist, though not uncommon if he takes into consideration every sort of pathologic process from the spinal cord down to the nerve; the neurologist, however, does not consider that as meralgia paresthetica. He does not consider the effects of tumors in the pelvis which cause disturbances in the distribution of this nerve as coming under that category. The first case of this condition I saw was shown to me by Dr. Sachs. He took great delight in giving me the name of the condition. I do not think that changing the name makes a disease more definite. Dr. Stookey knows that once a name is given, it usually sticks. Therefore, if one assumes that meralgia paresthetica is due to neuritis of the external cutaneous nerve, there is no reason why the plan of treatment outlined by Dr. Stookey is probably not the best, because the condition is intractable to treatment.

I consulted Oppenheim's book on this disease and discovered that he spoke of a number of cases in which, with one exception, operative treatment was not performed. His reason for this manner of handling such cases was that the patients had obtained relief after long-continued physical therapeusis. After a

long time, this condition often disappears. The condition in one case, however, was intractable, and, as he states, lasted an exceptionally long time; finally the patient submitted to an operation; the fascia was cut, and the patient was relieved.

I asked Dr. Stookey why one could not obtain the same result in these cases by the injection of alcohol and he answered: One could if one could hit the nerve. But the nerve lies very deep, and its course is not a definite one; therefore, one probably would have a great deal of trouble in making the injection; but there is no harm as far as I can see in cutting the nerve and giving relief to these people. It is true that some of these patients can endure the pain and discomfort, but it is sometimes very difficult for the neurotic person to endure the annoyance.

There is a little clinical symptom in these cases which seems to prove that Dr. Stookey is right. It is additional evidence to that which he has actually seen and found from his study of the cadaver; that is, that these patients, as a rule, do not suffer from the disturbances when lying down. They experience most discomfort when standing, and especially when walking. One can readily see from the position of this nerve that movement of that kind would unquestionably accentuate the condition.

I think that in discussing this condition one should absolutely limit it to disturbances of the peripheral nerve and not take into consideration any cause central to the peripheral nerve.

DR. CHARLES ROSENHECK: I was particularly interested in Dr. Stookey's explanation of the cause of meralgia, and the analogy that it bears to cases that follow fracture of the elbow joint and the secondary results from cervical ribs. While the explanation is ingenious and convincing as far as his case is concerned, I do not believe that it explains the vast majority of cases of meralgia that I have encountered. Association with an orthopedic institution has given me a good opportunity to observe many of these cases. A great number of osteo-arthritic conditions of the spine come under observation in the clinic. I will not quote statistics, but merely state that a great many of the patients complain of pain along the external aspect of the thigh. Invariably, one can demonstrate clinically an osteo-arthritis or spondylitis of the spinal vertebrae. If not found in that way, it is checked by the roentgen ray, which shows the inflammatory process of the articulations of the spinal vertebrae.

In a paper read before the American Medical Association two years ago, I reported twenty-five cases of meralgia paresthetica, carefully checked up by the internist, the laboratory men, the orthopedists and the roentgenologists. Invariably, when clinical evidence of an osteo-arthritic process was not found, x-ray evidence was. I do not wish to go on record as favoring the abolition of the name meralgia paresthetica, because I do not believe that it is an independent entity. It is part and parcel of a radicular syndrome involving the first and second lumbar roots.

Questioning the patient will reveal that he has other symptoms involving the lower lumbar and sacral roots. I believe these particular roots are so often involved because the lumbar vertebrae of that section are physiologically the most active. For that reason, phenomena referable to the external cutaneous nerve, which come off the first and second lumbar root, occur.

Apart from the other explanations given, such as constitutional disturbances, abdominal conditions and injuries directly affecting the nerve, I believe that the vast majority of the cases are due to osteo-arthritis, with secondary radicular involvement. It is easy to understand why the pain disappears when the patient lies down. The pressure is relieved or possibly the vertebrae are alined in a better and more comfortable position, and the irritation ceases for the time being. In a good many cases I get good results by using a brace and physiotherapy; a great many of the patients are cured. Dr. Stookey's explanation that angulation of the nerve is responsible for the disturbance, makes such a disturbance permanent. If his explanation were correct, I am afraid that these patients would

never get well. The truth is, contrary to his view, that many patients are relieved by careful treatment and orthopedic supervision.

DR. E. D. FRIEDMAN: It is characteristic of these cases that no matter how carefully the patients are examined, no changes are found other than the sensory disturbance in the distribution of the external cutaneous nerve of the thigh.

DR. HUDDLESON: There is no objection to considering neuritis of the external cutaneous nerve of the thigh as an entity that can be separately defined as meralgia paresthetica. But it seems that when a central condition can give much the same symptoms it is just as reasonable to classify the central and peripheral conditions together as to separate them; that is, to consider meralgia paresthetica as a symptomatic diagnosis and not a pathologic one. The question of relief by recumbent posture applies even to a case in which the condition is strictly peripheral and due to trauma.

DR. STOOKEY: It seems to me a decidedly backward step to make the diagnosis meralgia paresthetica a catch-all similar to rheumatism. It is well known that a series of conditions — osteo-arthritis of the spine, tumors of the pelvis, pregnancy, trauma of one kind or another — may give rise to a host of nervous symptoms, but it seems to me rather pathetic to destroy the definite clinical picture described by Bernhardt and Roth. Their descriptions applied to the external cutaneous nerve. Most neurologists are agreed that meralgia is limited to distribution of the external cutaneous nerve. It cannot be said, therefore, to be meralgia paresthetica if it is not in this distribution. This is a definite clinical entity which is worth retaining for the sake of clarity, leaving to the waste basket such other conditions as osteo-arthritis of the spine. One knows that this exists, but it is not meralgia paresthetica.

Two years ago, I read Dr. Rosenheck's paper. I asked him what his results were; he said that they were important. A year and a half ago, I asked him if he would be kind enough to send the patients he was unable to cure so that I could examine them, but I have never seen any of them. I do not believe that the cases which Dr. Rosenheck reported could, according to his own definition, be considered as meralgia paresthesia.

THE CONVULSIVE STATE. SAMUEL BROCK, M.D.

Definition.—For a number of years it has been evident that epilepsy is not a disease sui generis but a symptom-complex of many-sided nature. As a consequence, one began to speak of "the epilepsies." Of late, however, the term "convulsive state" has been introduced to replace the time-worn word "epilepsy" with its traditionally restricted connotations. By the convulsive state is meant a paroxysmal disorder of clonic or tonic muscle spasm involving larger or smaller segments of, or even the entire body. The resultant movement is an involuntary, disordered, utterly purposeless one, throwing the part or the entire body out of a normal into an abnormal posture. Whether consciousness is or is not disturbed will depend on considerations to be discussed later.

In the idiopathic type of convulsive state (grand mal) three phases may be recognized in the order of their appearance: a fleeting flaccid stage during which the individual falls, the tonic phase and the clonic phase. Rarely, the attack may be limited to the flaccid stage in which the acute general loss of tone produces sudden "deposturing" or collapse. The tonic stage with unconsciousness is due to suspension of cortical function and the uninhibited activity of centers of the brain stem. The succeeding clonic phase indicates the return of cortical activity, even irritation. The tonic and clonic stages may appear separately in man, and for the sake of clarity will be so considered in the following:

Pathophysiology.—The types of seizures are: (1) tonic and (2) clonic. The tonic type is often seen. It succeeds the transient flaccid stage of the so-called grand mal seizure and is usually generalized. Centers of the brain stem are functionally disconnected from the dominant cerebral cortex, and their uninhibited activity or their isolation results in a decerebrate rigid state. Normally, the

inhibiting impulses are believed to be mediated by the frontopontocerebellar pathways (Weed, Warner, and Olmstead). The stimuli are transmitted from the centers of the brain stem to the final common pathway along so-called extrapyramidal pathways. This tonic state consists of widespread spasm of the extensor muscles: the head is retracted; the back is arched; the extremities are extended and adducted; the hands are pronated; the fingers are flexed; the feet are in an equinus position; and the jaw is tightly closed (Sherrington, S. A. K. Wilson).

In man, the upper extremities are usually flexed and the head and eyes turned to one side. Consciousness is lost. Time will not permit me to go into the well-known accompanying vasomotor, respiratory and pupillary changes nor into the question of auras, etc.

The clonic or jacksonian fit is due to irritation of the motor cortex of the brain; the abnormal stimuli are carried by the intact pyramidal tract to the lower motor neuron, thence by way of its final common pathway to the musculature. If the focus of irritation spreads, then adjacent centers in the rolandic area are affected in a regular manner which is conditioned by their well known anatomic juxtaposition. The movements are interrupted and frequently segmental. When this type of convulsion occurs alone, consciousness is not disturbed until the movement spreads from one half to the other half of the body.

A spinal and bulbar form of convulsion is best seen in cases of strychnine poisoning. Here there is anarchy in the realm of the lower motor neurons, and a

TABLE 1.—*Humoral Factors in the Production of Convulsions*

I. Exogenous:	II. Endogenous:
1. Alcohol, lead (absinth, camphor, monobromate, santonin, picrotoxin, apomorphin, etc.)	1. Uremia
2. Insulin (anoxemia?)	2. Eclampsia
3. Alkalosis (due to hyperventilation)	3. Endocrine dyscrasias:
4. Foreign proteins	(a) parathyroid
	(b) thyroid
	(c) pituitary
	4. Toxins of the infectious diseases in infants
	5. Spasmophilia

tonic extensor spasm which is comparable in many respects to that already described. Consciousness is fully retained.

Factors Involved.—If one analyzes the many factors involved in the production of the convulsive state, it becomes evident that they may be grouped under one of two headings: (*a*) cerebral and (*b*) humoral. The experimental work of W. E. Dandy and R. Elman illustrates this duality best. If a normal cat is given absinth by mouth in large enough amounts, convulsions will result. This is the operation of a pure humoral, exogenous factor. If a lesion is produced in the cerebrum of the animal, either by simple extirpation of the cortex and subcortex or by placing a foreign body beneath the cortex, it will be found from one to five months later that from one third to one seventh of the initial dose of absinth will be convulsogenic. By injuring cerebral tissue, a cerebral factor is introduced.

Certain of these factors deserve especial comment. In rare instances a person may suffer from the convulsive state only when sufficient alcohol is imbibed. Rosett in this country and O. Foerster in Germany have drawn attention to the effects of forced overventilation of the lungs. In normal persons, tetanic features appear. In 55 per cent of epileptic persons, the convulsive state is precipitated. The alkalosis produced by the deep breathing is in some way responsible for the attacks, possibly through disturbance of the calcium ion balance in the blood (F. Georgi). The tetany induced in normal persons points to the parathyroid gland and disturbed calcium metabolism. In this connection, Geyelin, of New York, deserves credit for emphasizing the beneficial effects of starvation on those afflicted with convulsions. Workers in Cobb's laboratory in Boston have proved

that the acidosis accompanying starvation is the decisive factor in the prevention of convulsions.

Strangely at variance with this work is that of the Italian investigator Cuneo, who believes that there is a disturbance in the starch metabolism resulting in the formation of certain acids (acetic, lactic, butyric, tartaric). Normally, the liver and small intestine break these acids up into urea and sodium carbonate; in epilepsy, they are found unoxidized in the urine. Osnato, Killian and their co-workers have found increased lactic acid in the blood and cerebrospinal fluid of epileptic persons in the interparoxysmal period. Acidosis results, in the presence of which the cellular nucleohiston bodies split into nucleinic acid and a convulsogenic proteose. (The salts of the aforenamed acids are also convulsogenic.) Donath (quoted by Muskens) believes that in the convulsive state, alkaloid-ammonium compounds, fragments of normal metabolism, react on a nervous system the threshold of which has been lowered by hereditary, congenital, toxic, infectious or traumatic diseases. These compounds are trimethylamine, choline, creatinine, guanidine, and ammonium carbonate. Donath produced convulsions with all these agents except trimethylamine.

A number of observers have studied the question of the split products of protein metabolism. L. M. Wallace and W. D. Nicol (England) found that about 20 per cent of epileptic persons gave positive reactions of the skin. They removed the offending proteins from the diet in some cases, gave others peptone by mouth and reported good results. Others, including J. S. Collier, were disappointed in the use of protein therapy. In connection with anaphylaxis, V. M. Buscaino's work deserves mention. He examined 396 thyroid glands, and isolated an abnormal protein from the thyroid of 71 per cent of epileptic persons. In Abderhalden tests the serum of epileptic persons reacted positively with the thyroid of epileptic patients much oftener and more intensely than with those of nonepileptic persons. In certain cases, he regards the convulsion as an anaphylactic crisis.

In the group of endogenous humoral factors, endocrine dyscrasia is of especial interest. The rôle of the parathyroids in the convulsive state of tetany is well known. In three cases of severe epilepsy, O. Foerster implanted human parathyroid glands. He reports unmistakably beneficial effects on the number and intensity of the convulsive seizures. In regard to the thyroid gland, Buscaino's observations that have already been mentioned, are of interest.

Elsberg and Stookey showed that thyroidectomized animals are more susceptible to absinth in regard to the production of convulsions. The parathyroid glands may have been injured also in their experiments. The foregoing observations lend weight to the belief that the parathyroid and thyroid glands cooperate in removing toxic convulsogenic elements (foreign protein split products?) from the blood stream (Timme, Zabriskie).

As regards the pituitary gland, two points deserve mention: One is the frequency of signs of dyspituitarism (acromegalic features or Fröhlich's syndrome) and changes of the sella turcica demonstrable by x-ray in epileptic patients. The other is the hypothesis that the pituitary gland is believed to enlarge periodically in a sella too small for it; this results in a suspension of function of the posterior lobe which is said to produce an increase of general cortical irritability. The nearby uncinate gyrus is pressed on and is apt to be the initial explosive focus.

The gonads have been omitted from the table because their precise rôle is difficult to define.

From table 2 it becomes evident that almost all organic cerebral diseases can induce the convulsive state. It is possible to find a single pathologic determinant common to all these states which is the true cerebral factor.

MacRobert in this country and Muskens abroad suggest dysmyelinization as a possible factor. The former stresses "an anatomic defectiveness in which the vital feature is a paucity of functionally active fiber tracts. . . . This specific defect may be but a part of a wide spread neural agenesis or may exist alone, the result of a failure in the final stages of development, namely myelinization of the nerve fibers."

A kind of defective insulation of the nervous stimulus results. In this connection, paroxysmal spasms are rarely encountered in amaurotic familial idiocy, although Hassin stresses the frequent occurrence of decerebrate extensor hypertonus. Dr. B. Sachs does not regard convulsions as an essential part of this disease, in which almost all the ganglion cells of the nervous system degenerate; whereas in encephalitis periaxialis diffusa of Schilder, a disease in which the fiber tracts suffer most in a dysmyelinization process, convulsions are frequent. Yet the dysmyelinization theory hardly seems tenable when one considers the important humoral factors. It has not been proved by any of the finer anatomic studies, and light is not thrown on the convulsive state produced by certain vascular conditions to be described.

The Cerebral Vascular Apparatus.—The observations of O. Foerster seem to show that one will find the basic cerebral factor in the vascular mechanism of the brain. On the operating table he has observed, at least 100 times, a preparoxysmal

TABLE 2.—*Enumeration of Cerebral Factors*

A. Diseases	*B. Irritants*
1. Neoplasms (including bony growths)	1. Mechanical
2. Congenital and heredodegenerative disease	2. Electrical
3. Degenerations and scleroses (multiple sclerosis, tuberous sclerosis, encephalitis periaxialis diffusa, senile cortical atrophy, presenile gliosis, etc.)	3. Thermal
4. Traumatic processes	4. Chemical (strychnine painted on the cortex)
5. Infections and parasitic disease (syphilis, tuberculosis, encephalitis, abscess)	*C. Psychogenic Processes*
6. Vascular disease (vascular spasm, arteriosclerosis, hemorrhage, embolism)	1. Theory of regression (L. Pierce Clark)
	2. Theory of Rosett: the normal epileptoid reaction
	3. Hysteria

TABLE 3.—Vascular States Inciting the Convulsive State

A. Disease of Cerebral Blood Vessels

1. Arteriosclerosis
2. Endarteritis obliterans
3. Angiospastic migraine
4. Raynaud's disease
5. Aneurysms
6. Embolism
7. Congenital smallness of carotids or vessels of the circle of Willis

B. Changes in Cerebral Circulation

1. Heart block
2. Restoration of previously impaired cerebral circulation:
   (a) After drowning
   (b) After strangulation
   (c) After suffocation
3. Pressure on or ligation of carotids and vertebral arteries

vasoconstriction and anemia of the exposed brain with a diminished volume; the tonic convulsion then occurs with a rapid fall of cerebrospinal fluid pressure. The removal of cortical function due to the vasoconstriction permits the unbridled or isolated centers of the brain stem to manifest this tonic decerebrate phase and serves to explain the unconsciousness. Then venous stasis comes on rapidly, accompanied by a great increase in brain volume and cerebrospinal fluid pressure. The stasis now produces cortical irritation and the clonic (jacksonian) phase appears as a consequence. This vasomotor theory (Nothnagel) explains the attacks, sudden onset and cessation and the radiation of a jacksonian cortical attack. The sensory aura and the postparoxysmal weakness may be ascribed to transient loss of function from local anemia. Further weight is lent this vascular basis when one considers the various vascular conditions which are able to provoke the convulsive state.

Recently, more evidence favoring the vasomotor theory is given by the work of O. B. Meyer. Pieces of cortical arteries show rhythmic spontaneous contractions when placed in normal serum. These can be kymographically reproduced.

If the serum of an epileptic person is used, the contractions are absent or diminished; this occurred in fifteen of seventeen cases irrespective of the time (with regard to the paroxysm) of the withdrawal of the serum. In six cases of hyperthyroidism, the contractions were increased.

Some years ago, MacRoberts and Feinier explained the frequency of the convulsive state in neoplasms of the temporal lobe by assuming that the pressure of the tumor interfered with the circulation in the overlying sylvian artery.

Increased cerebrospinal fluid pressure of itself does not cause convulsions (W. M. Kraus), but if other factors are present, then such increase will help precipitate the convulsive state (Elsberg and Pike).

Psychologic Theories.—The convulsive state has also been regarded as essentially of psychogenic origin, especially by L. Pierce Clark. Following the psychoanalytic approach, he regards the fit as a regression, a withdrawal from reality into the blessed nirvana of the intra-uterine fetal states. Objections to this point of view are many. It does not account for the occurrence of convulsions in deep sleep, (which, in itself, is an adequate escape from reality) and the incidence of convulsions in animals of the mammalian phylum, nor does it explain the status type of convulsion with its frequent fatality. This point of view in no way clarifies the convulsive state based on known organic conditions such as general paralysis, tumor, etc.

In a somewhat different category is the ingenious theory of Rosett. He believes that normally "a stimulus requiring sudden movement on the part of the organism or the narrow focusing of attention, and certain functions such as sleep, defecation, sneezing, coughing, parturition, lead to a temporary reduction or extinction of the cerebral functions." This may lead to a "tonic contraction of the entire skeletal musculature resulting in the posture of decerebrate rigidity."

"The biologic purpose of the reaction is the automatic fixation of the relatively central joints preparatory to any possibly needed movement of relatively distal segments of the body and limbs." To its normal incidence he applies the term "normal epileptoid reaction."

Perhaps this conception helps to explain the tendency of the seizures to appear as the patient is going to sleep or awakening ("Vorzugsmomente" of the German writers), and the occasional appearance of convulsions in the beginning of narcosis produced by ether or chloroform (Patch). Yet Rosett is not able to explain the reason for the appearance of that periodic, massive, exaggerated response which constitutes the convulsive state. He has contributed some interesting psychologic sidelights to the problem.

To discuss the hysterical convulsion would require a consideration of hysteria which would take one too far afield. Obviously its mechanism is quite different from the convulsive state herein considered. The reason for the periodicity of the convulsive seizure is unknown. The assumption of any special theory hardly explains it. In fact, I think that when one knows why the attacks are paroxysmal, one will have reached the fundamental understanding of the disorder. Collier believes that the periodicity and other facts argue strongly for a disturbance in metabolism—a "toxipathic" (i e. a humoral) factor as the basic cause.

Heredity.—Many have emphasized the element of heredity in the convulsive state. In his recent analysis, Muskens shows that about one third of his patients had epileptic forbears in the direct and collateral line, and that about one-eighth revealed insanity in the direct and collateral line. In heredity, alcohol played a part in about one-twentieth of the cases, and syphilis in only about one-fiftieth. Striking as these figures are, they do not aid in the study of the fundamental causes of the seizures.

Before speaking of the pathologic process, brief reference may be made to the so-called "reflex epilepsy" which belongs to the field of romance. Diseases in the nasal, aural, dental, genital and other spheres were held responsible for the attacks in some mysterious manner. Muskens, in his analysis of 2,000 cases, found no instance of this type. Today one hears little of this old myth.

Pathologic Process.—Is there a fundamental pathologic process in the convulsive state? Ganglion cell degeneration, subpial marginal gliosis and other more generalized glioses have been described. Gerstmann found atypical and even fetal cells in the molecular cortical layers. Volland found regularly karyolytic and tigrolytic degenerative changes in the anterior horn cells in myoclonic epilepsy. A milky, cloudy pia has been the only observation in cases of focal epilepsy in which biopsies have been obtained (Muskens, and others). Alzheimer at one time (1898) even went so far as to say that "man könnte die epileptischen Anfalle als Folge eines Druckes ansehen, den die herbere geschrumpfte Rindenöberflache auf das tiefer liegende Hirngewebe ausübe." (One could regard the epileptic seizure as the result of a pressure, which the sharply shrunken cortical surface exerts on the deeper lying cerebral parenchyma). Yet with the passing of time, a different attitude of mind has been forced on most observers. This is due to the fact that negative observations have been recorded by careful observers in cases which had neither lasted too long nor had been accompanied by mental deficiency or dementia. The general opinion now held is that the pathologic changes found are the result of the long enduring process, not the cause (Binswanger, Zabriskie, et al). Hence the idiopathic convulsive state does not have an essential pathology. Alzheimer and his pupils believe that the convulsive state is a common attribute of warm-blooded animals and is to be regarded as a reaction produced by a humoral poison on a nervous system in which lessened tolerance, or lowered threshold, has been brought about.

Conclusion.—All facts agree with this concept. It permits the study of neural and extraneural factors — the cerebral and the important humoral ones. It would seem, then, that the convulsive state is either brought about by: (1) a group of poisons operating on the cerebral vascular mechanism and producing vasoconstriction and cerebral anemia, then congestion; (2) by local cerebral disease or disturbed vascular conditions upsetting the vascular equilibrium, or (3) by combinations of the two.

Somewhere in his writings, Francis Bacon says that it is easier to derive knowledge from a state of confusion than from chaos. Knowledge concerning the convulsive state is still in a confused state, but thanks to the work of many investigators all over the world, the grim specter chaos has been put to rout.

THE ECLAMPTIC CONVULSION. DR. WILLIAM E. CALDWELL.

It must be confessed at once that knowledge of the eclamptic convulsion has not yet been rescued out of chaos into the more hopeful realm of confusion. De Lee's dramatic description of the eclamptic convulsion is well known, but I will quote it: "The pupils dilate, the eyes are turned, and the head also, to one side: the patient opens her mouth, then the jaw is pulled laterally, and there may be a cry or a sigh. The whole body becomes rigid; the features are distorted; the arms flexed; hands clinched; the feet inverted; the toes flexed, and the whole person drawn to one side in a tonic spasm. This condition lasts for a few seconds, then the jaws open and close violently, the eyelids also, the twitchings beginning in the face, then usually one arm, then the leg, and now the whole body. This is a violent clonic convulsion, which may throw the patient out of bed against any object. Severe injuries can result — even fractures of the skull or long bones; the tongue is protruded; the teeth may chop it up. Foam, often tinged with blood, comes from the mouth. The respiration is completely stopped, the chest being rigid. The pulse is high and strong; later it grows weaker, but may be hard to feel because of the convulsion. In rare cases the pulse is weak and the arterial tension low from the start, a fact which is explained by degenerative changes in the heart. The blood-shot eyes protrude, the face is swollen, the cyanosis is extreme, the lips are purple — altogether the picture is a horrible one. Gradually the convulsive movements remit, a few twitches or jerks take place, the patient lies quiet, the heart thumping violently against the chest-wall. For a few seconds the woman appears to be dying, but there is a long sigh, and stertorous breathing becomes established, coma supervening. Soon the respirations quiet down. In

the favorable cases the patient wakes up after a short time bewildered, severely sore in all the muscles. After from a few minutes to an hour another fit occurs, or she may have no more. With recurring convulsions the intervals become shorter and the patient lies in deep coma all the time."

The pathologic changes in fatal cases are distinctive in the liver, where areas of necrosis and hemorrhage with thrombi of agglutinated red cells are found in the periportal spaces. Small or large hematomas frequently underlie Glisson's capsule. The kidneys show changes in varying degrees of severity from simple cloudy swelling to the rarer cases of extensive cortical necrosis. Areas of myocardial degeneration are often found in the heart. In the brain and nervous system various observations have been reported: anemia, hyperemia, edema and dehydration. The most constant but by no means invariable observations are multiple hemorrhages of varied size and distribution.

A brief outline of the facts which a satisfactory theory must fit follows:

Eclampsia occurs in the later months of pregnancy with increasing frequency as term approaches. It is more common in primiparas than in women who have experienced multiple pregnancies and in hydramnios. It has a seasonal incidence, being more frequent in the winter and spring months, and is more common in northern latitudes. It is usually though not always heralded by slight or severe degrees of such symptoms as edema, headache, visual disturbances, epigastric pain, rising blood pressure, albuminuria, oliguria and hyperreflexia.

The acuteness of onset of the eclamptic convulsion leads naturally to the idea that it is due to some toxin suddenly released into the blood stream, and research has been directed to the discovery of such a toxin. The tendency of eclampsia to improve following fetal death or expulsion suggests a fetal origin, and unsuccessful attempts have been made to isolate toxins from fetal metabolic products, or from fragments of syncytium and amniotic villi which are continually entering the maternal blood stream. The hypothetic escape of fetal blood of unlike group from that of the mother into the maternal blood stream, with resulting thrombus formation, has not found statistical support. An anaphylactic reaction to fetal products has been suggested, but not proved. Placental decomposition products have been proposed as an explanation of the source of the toxin, but proof is wanting.

A more intensive study of the maternal organism and its toxemias during pregnancy has more recently held the center of attention. Chemical studies of the blood and urine have been made in a large number of cases. Most insistent have been the attempts to find in the retention of some product of protein metabolism the cause for the eclamptic explosion; they have led, for the most part, to negative results. The amount of uric acid in the blood is usually raised, but nonprotein nitrogen is seldom retained, and the nitrogen partition is variable. Recently, the toxic qualities of histamine and guanidine have been studied and have been thought to be important causes of convulsive reactions. The blood sugar is thought by some to be raised in eclampsia; by others, to be low. An increase in the lactic acid of the blood has been described. The study of the inorganic constituents of the blood and their equilibrium are of great interest. Most writers agree that there is a decreased plasma and carbon dioxide combining power. Staeber reports a general tendency to a lowered ratio in the calcium and phosphorus contents of eclamptic blood. Such observations fit in well with the functions which these substances are held to have in the metabolism of muscle irritability. They are not, however, invariably found in eclampsia. Abnormalities of the thyroid and parathyroid glands, ovaries and pituitary glands have been thought to cause eclampsia, and isolated cases appear to support such a conclusion, but such theories leave many facts to be explained. In recent studies, by means of the capillary microscope, spasmodic contractions of the vessels in toxemic and eclamptic patients have been described which suggest the theory of spasmodic constriction of the cerebral arterioles as initiating the mechanism of eclampsia. More evidence along the lines of this attractive theory is required.

There is nothing definitely characteristic about an eclamptic convulsion to differentiate it from the uremic or even the epileptic convulsions. Convulsions occurring in the latter half of pregnancy without albuminuria and without increase in blood pressure may be eclamptic but should certainly demand a thorough neurologic examination to exclude other conditions. The marked reduction in the eclamptic rate which occurred during the war in Germany is significant, since the food supply was greatly curtailed.

Subnormal women, especially when the cardiovascular, renal and nervous systems are affected, should be relieved of every possible strain during pregnancy. Normal women cannot be allowed to put a strain on their alimentary, excretory and nervous systems. The bacterial infections occurring during pregnancy are sometimes enough to upset the delicate balance of the women.

In the vast majority of women with eclampsia, spontaneous labor occurs, and the mortality has been reduced in direct ratio to the discontinuance of operative intervention. Some patients still require operative deliveries, but the proportion is small.

The convulsion, the restlessness and irritability added to an already strained cardiovascular system will cause a disastrous end if not controlled.

During the past thirty years, the work of Tweedy, Loomis, and especially of Strogonoff has gradually worn away the prejudice against the use of opiates, and morphine is used to a great extent in most clinics. For the rapid control of frequently occurring convulsions or mania with the resulting exhaustion, paraldehyde introduced directly into the vein has been effective. Recently, Lazard's suggestion of the use of magnesium sulphate introduced directly into the vein has proved of value in temporarily reducing the blood pressure and quieting the patient. Together with morphine and bleeding, this procedure seems to have reduced the mortality in this condition. Rest and relief from strain are still most valuable means of treatment. A low protein salt-free diet is of value, but milk, in spite of its high protein and mineral salts, seems to be just as efficacious in some cases.

No theory has yet been proposed which satisfactorily explains all the phenomena. To recapitulate, I may quote the points listed by Williams which the required theory must satisfy: (1) the genesis of the hepatic lesions; (2) that the marked edema is usually a favorable sign; (3) the predisposing influence of primiparity, multiple pregnancy, hydramnios; (4) that the disease is more common in northern latitudes than in the tropics; (5) that the incidence increases as pregnancy approaches term; (6) that marked edema is usually a favorable sign, while its absence adds to the gravity of the progress; (7) that true eclampsia rarely occurs, whereas chronic nephritis gives rise to increasingly serious trouble in each succeeding pregnancy; (8) that intra-uterine death of the fetus is usually followed by improvement; (9) that a milk diet which is high in protein and mineral constituents is as efficacious as one low in protein and free of salt.

DISCUSSION

DR. HAROLD BAILEY: Two or three points which have been brought out seem to me might lead to further study. The first part of the papers by Dr. Caldwell and Dr. Brock shows that a possibility exists that a number of conditions are combined which might eventually lead to convulsions. I believe, myself, that in eclampsia there is some circulating metabolite in the nature of a higher amine, and, therefore, I look with favor on the researches of Hofbauer concerning histamine. It is a preliminary study in the right direction. It is known that the particular poison in eclampsia has a tremendous effect on the liver, causing degeneration, and that a hemorrhagic condition exists in other organs, especially in the brain; for instance, it has been pointed out that in eclampsia from 10 to 15 per cent of the cases present hemorrhages of the brain.

I am entirely in agreement with Dr. Caldwell's description of the convulsion itself — that it is a clonic convulsion following a tonic spasm. There is one point about which, I think, something more may be said — namely, that fanciful "field

of romance" Dr. Caldwell mentioned in regard to reflex epilepsy. I know nothing about epilepsy except that I have always described the convulsion of eclampsia as somewhat similar to it. While the patients have no aura, they have a queer condition of pain in the epigastric region that is almost invariably present.

Then there is the condition that is termed reflex eclampsia. A patient who has had a long period of labor accompanied by acidosis suddenly has a convulsion at the time when she is being delivered, either spontaneously or operatively. Urinary symptoms are not present, and the convulsion is not repeated; with or without treatment, the patient recovers.

Dr. Brock, in his chart, also mentioned disturbance of the pituitary glands. In many cases of toxemia of pregnancy there is a condition which somewhat resembles acromegaly; the face grows large although it is not edematous. Possibly this is due to a disturbance of the pituitary glands.

In regard to feeding, cases of eclampsia have occurred following a full protein meal. All obstetricians dread Thanksgiving and Christmas days for fear the patient will overeat of protein.

Dr. Edwin Zabriskie: My one reaction from this meeting is a sympathetic one; it emphasizes to me more than ever the catholic and confused state in which conceptions of this disorder still rest.

Dr. Caldwell mentioned certain things in regard to the placenta in eclampsia which rather disappointed me because, at least on the humoral side of the problem, I was tempted to draw an analogy between the effective power of the placenta to eliminate toxic products from fetal metabolism with that of the cerebral vessels, and to the similar conditions of the cerebral and placental vessels, and to draw an analogy between the proper vasomotor supply of cerebral and placental vessels. But there again, further investigation seems to show that there is at least no positive evidence that the placenta in these states, or in convulsive states, is deficient in its capacity to strain out toxic material in fetal metabolism. I have always been interested in the question of the vasomotor supply of the cerebral blood vessels as a possible factor also in the convulsive state, because I have always been profoundly impressed with the cerebral vascular mechanism for the production of any fit, whether chronic or toxic—I mean to say as the actual mechanism from which the fit starts.

In connection with that, I am reminded that Dr. Brock rather lightly touched on the question of reflex epilepsy. There have been a great many enthusiasts who have decried so-called reflex epilepsy, but at the same time those of us who have lived long enough and who have had sufficient experience have come in contact with competent observers from time to time who have actually had experiences with typical convulsive seizures which have been eliminated by removal of certain sources of irritation. One of my own experiences has been closely associated with the circle of Willis and the sphenoidal sinuses. As far as reflex epilepsy goes, I think that one must conceive that there are certain instances in which the removal of irritating factors, whether they be humoral or irritating in the sense of pressure phenomena, no matter how distal they may be, can operate as a fit-producing factor.

It is my firm belief, however, that in every instance one is dealing with an abnormality, a constitutional factor which, whether it be of the sympathetic nervous system, of the vasomotor system or of the vasomotor centers in the midbrain and the subthalamic region, is invariably present in persons who exhibit convulsive seizures.

Dr. Israel Strauss: The speaker has covered the field of convulsive states in an admirable fashion. His paper is really a critical epitome of present knowledge concerning this subject. Dr. Brock spoke of discarding the term epilepsy; yet he will admit that whenever he touched on the syndrome which the older neurologists have designated as epilepsy, he spoke of a condition called idiopathic. In other words, all that he spoke of as the convulsive state, every condition that was produced by a nontoxic or a definite pathologic process, whether tumor, vessel disease or other condition that was definite, was not the idiopathic form

of the convulsive state which from time immemorial has been known as epilepsy. Therefore, I think Dr. Brock will admit with me that there is really no need of discarding that term. A name in itself is of no service if you do not know its meaning. The term idiopathic characterizes the definite condition, paroxysmal recurring attacks of convulsions occurring in persons as a rule below the age of 35. When a person presents this syndrome after 35, the neurologist always suspects that he is not dealing with the idiopathic condition.

In looking into the cause of this idiopathic condition, so-called true epilepsy, one is faced with the greatest difficulty, because, as Dr. Brock has shown, one does not have any pathologic clue to the condition, as no explanation heretofore offered explains it. Take Foerster's observations of the anemia and subsequent dilatation. I cannot tell why anemia occurs in an epileptic person. The work concerning the disease of vessels by serum has been cited. What is in that serum? Despite all the researches thus far undertaken, it is not known. One does know that certain persons for some reason, which is fundamental, evidently have a condition of the body, whether metabolic or something else, which subjects them to recurrent convulsive states. Therefore, I see no reason for failing to use the term epilepsy if it is understood in its proper sense.

In the condition of eclampsia, the obstetrician has an admitted problem much more limited than that of the neurologist in true epilepsy, because eclampsia does not occur in men and it does not occur in a woman unless she is pregnant. Therefore, obstetricians have a definite cause underlying the development of the eclamptic state. I believe that it is also true, to a certain extent at least, that if pregnancy is interrupted, the eclamptic state is interrupted in most instances. Why, therefore, has it been impossible for the obstetrician in a problem so limited as this to find the cause? All the changes found in the liver and other organs are regarded by pathologists as secondary to something which has relation to the fetus. What that is has as yet not been learned. The obstetrician is in a far better position to study eclampsia than neurologists are to study idiopathic epilepsy.

Dr. Michael Osnato: One of the reasons why so little is known about the convulsive state or epilepsy, if you like, is that neurologists for some reason have, until now, taken exclusive charge of the investigations. It has not been until the physiologist, those neurologists and neurosurgeons who work in physiologic laboratories and the biochemists became interested in this problem that anything has been learned about it.

About six years ago, the study of the biochemistry of epilepsy was begun at the Post-Graduate Hospital and the Manhattan State Hospital. Cases were first selected very carefully, those with any organic features being eliminated. There were 130 patients ranging in age from 3 to 68. An effort was made to eliminate all patients with so-called symptomatic seizures from this group. Studies were made of the p_H of all of them and nothing was found to confirm Geyelin's conception that there was an alkalosis in these cases. The calcium did not show any departure from the normal; the cholesterol, phenols and other substances that have been at one time or another regarded as related to the pathogenesis of epilepsy were also studied. Two important and definite things were found: one has been referred to by Dr. Brock. Quite regularly an increase was found in the content of lactic acid in the blood and spinal fluid, not in any time relation to the convulsive seizure. Secondly, and of more importance, was the presence in the spinal fluid of these patients of a protein which was not globulin or albumin and which was not coagulable. Without exception, the cases studied showed either a high normal amount or a marked increase in the protein content in the spinal fluid. These results were carefully checked up.

We were loath to say anything more when we published this work after reading our results in London last summer. A possible explanation, however, is offered by Dr. Cuneo's theories. It is known that a reaction of the blood toward the acid side will immediately cause a break down of the nucleoprotein in the cellular content of the blood; the leukocytes are chiefly affected. Nucleic acid and a proteose with convulsant properties is liberated. We made the observation

years ago and confirmed it many times, that there is a leukopenia before and coincident with the epileptic seizure, which is confirmatory of this point of view. Also it is likely that the protein discovered by us is a proteose. Concerning this, however, we are not ready to speak definitely, but it is quite likely that our two observations are related. Too many unrelated things have been put into this classification of epilepsy.

I agree strongly with Dr. Strauss that the term epilepsy should be preserved and applied with care to the cases always known as idiopathic epilepsy — those cases that are entirely free from organic features.

Dr. Brock: I think that Dr. Bailey and the neurologists do not use the term "reflex" in exactly the same way in this connection. A real toxic or humoral factor is not the type of reflex which I have sought to discredit, and that applies to Dr. Zabriskie's comments as well. Cleaning out a nasal sinus or regulating digestion rarely eliminates the humoral factor; I do not believe these are causes of "reflex epilepsy." In the latter connection, one is referred to nasal polyps, aural cerumen, adhesions to the clitoris and other conditions. These so-called "reflex" initiators of the attack, I believe, have been much overemphasized in the past.

If the hysterical seizure is eliminated and the endocrine element properly evaluated, the residuum that is called "reflex epilepsy" does not exist.

I think Dr. Strauss' point is a critical and excellent point. There are unquestionably two points of view, but it seems that in studying epilepsy in human beings one must study other convulsogenic factors as well. I quite agree that the peculiar state spoken of as "epilepsy," with its periodicity and its tendency to recurrence is unique, and that animal experimentation does not produce a comparable disease state; at the same time, one must study epilepsy from all points of view. As was said in my paper, when the cause of the recurrence of the seizures is known, the fundamental cause of human epilepsy will have been reached.

I am in hearty sympathy with Dr. Osnato's comment. His substantiations of Cuneo's work with the illuminating light it throws on the humoral factors, and the isolation of a convulsogenic proteose is important.

Neurologic Aspects of Injuries at Birth. Leon Hastings Cornwall.

I shall attempt merely to delineate certain recorded facts and opinions. Among the various intracranial lesions ascribed as causes of infantile palsies are: porencephaly, microcephaly, atrophy, cysts, localized areas of encephalitis with softening, leptomeningeal hemorrhage, intracerebral hemorrhage, subdural hemorrhage, sinus thrombosis and syphilis. It seems to me that one is warranted in excluding from discussion under this title known developmental defects such as true porencephaly, microcephaly, defects due to aplasia and agenesia, amaurotic family idiocy, tuberous sclerosis and various other conditions, including état marbré, status marmoratus and status dysmyelinatus of Vogt. It is well recognized that these are based on defects of the germ plasma that must have had their inception in the prenatal period. In passing, I will mention the importance of intra-uterine infections, such as encephalitis, as important factors in the production of abnormalities of the nervous system of infants. That this may occur, I can testify from my own experience. I have seen pathologic evidence of encephalitis in the brain of an infant who died a few hours after birth. Collier holds that all cases of diplegia are due to primary degeneration of the cerebral neurons, but Dr. Sachs takes issue sharply with this view, maintaining that diplegia as well as monoplegia, hemiplegia and paraplegia may be the result of natal and postnatal factors as well as prenatal influences. I cannot discuss the controversial aspects of this question, but when one recognizes the fact that intracranial hemorrhages have been proved to occur during parturition, it is difficult to escape the conclusion that such occurrences, when bilateral, may result in diplegia. Spasticity, as one would expect, is a common characteristic of such injuries and this is accompanied by hyperreflexia, contractures, and frequently convulsions and mental defects. Dyskinetic phenomena, such as choreic, athetotic or choreo-athetotic move-

ments or other evidence of impairment of the control of associated movement may be encountered if and when the basal ganglia, cerebellum, nucleus ruber, substantia nigra or their connections are implicated. An atonic astasic type has been described by Foerster; a flaccid atonic type, known as cerebrocerebellar diplegia, by Clark; a pure cerebellar type by Batten and von Wyss; and a form designated as infantile cerebral diataxia by Hunt.

The following is a classification of the birth injuries that come within the domain of the neurologist:

I. Cranial Bones: *A*, indentations; *B*, fissures; *C*, fractures.

II. Intracranial Structures *A*, compression; *B*, hemorrhage: (1) epidural; (2) subdural; (3) subarachnoidal; (4) intraventricular, and (5) intramedullary (massive or petechial); *C*, necrosis due to ischemia with or without secondary hemorrhage.

III. Vertebrae: (*a*) separation, (*b*) torsion, (*c*) subluxation and (*d*) fracture.

IV. Spinal Cord: (*a*) compression; (*b*) edema; (*c*) hemorrhage; (*d*) avulsion of roots; (*e*) rupture.

V. Nerve Roots, Plexuses and Peripheral Nerves: (*a*) edema, (*b*) hemorrhage, (*c*) small tears and (*d*) complete rupture.

The difficulty of determining the exact site of intracranial hemorrhage has been recognized for a long time. The best method for this dissection is that of Beneke, which consists of opening the skull along the sagittal suture, pulling the parietal bones down and then ablating both hemispheres, thereby allowing inspection of the tentorium.

Omitting consideration of cephalhematomas, external and internal, and injuries of the cranial bones, subdural hemorrhages are perhaps the most important of all, especially when they originate in the vicinity of the tentorium cerebelli, the anatomic disposition of which makes it vulnerable when the anteroposterior diameter of the fetal head is increased by lateral compression. The first and most severe kind of tear is through the free edge, when both blades are frequently torn. The second type of injury is through the upper blade only and is milder than the first. The third, and least serious, consists of hemorrhage between the blades or at the edge of the falx.

Subarachnoidal hemorrhage is frequently associated with the subdural variety, from which it cannot be differentiated symptomatically. An absence of blood in the spinal fluid negates the diagnosis of subarachnoidal hemorrhage, but its presence does not rule out subdural extravasation. This subject has been especially emphasized by Sharpe and Maclaire, who found blood in the spinal fluid in 13 per cent of 100 consecutive lumbar punctures made within forty-eight hours after birth. They advise this procedure in every case evincing the mildest signs of cerebral irritation or of increased intracranial pressure, a state of severe shock being the exception. Many authorities hold the opinion that small amounts of blood in the subarachnoid space will be satisfactorily taken care of by natural means. While this is true to a certain extent, it is also a fact that blood in the subarachnoid space acts as an irritant. Bagley has shown, in experimental work on dogs, that blood introduced into the cerebral subarachnoid space enhances the susceptibility to convulsing agents, and that this effect can be counteracted by opening the subarachnoid space and allowing communication to the air.

I want to voice my hearty accord with Sharpe and Maclaire in their objection against lumbar puncture performed on patients who are in a state of severe shock until the acute stage has subsided. A state of deep shock is strongly suggestive of grave hemorrhage, with possibly a free communication between the subarachnoid space and the venous sinuses. The physiologic experiments of Wegefarth have shown that cerebral arterial pressure is greater than subarachnoid pressure, and that the latter is, in turn, greater than the venous pressure. He was able to establish a direct communication between the subarachnoid space and one of the large venous sinuses without noting any blood in the subarachnoid space. Directly on reduction of the subarachnoid pressure by the removal of spinal fluid, there

was a free flow of blood from the sinus into the spinal fluid. The conclusion would follow that the higher pressure in the spinal fluid acts as a natural barrier. Reduction of this would favor an increase in the hemorrhage. In the case of smaller extravasations of capillary origin, I doubt if this effect obtains, and I favor drainage. Mere mention can be made of hemorrhages into the ventricles and substance of the brain. The former is accompanied by deep coma, and, if unilateral, there may be deviation of head and eyes to the side of the lesion. Spasticity, opisthotonos and alternate, slow, rhythmical adduction and abduction of of the arms and legs are observed.

Large extravasations into the brain substance are limited, for the most part, to the soft brains of premature infants. Disseminated petechial hemorrhages are common. A detailed discussion of symptoms cannot be indulged in, as they depend on the size and location of the lesions.

Lack of time prevents consideration of the injuries to the spinal cord, brachial and lumbosacral plexuses and peripheral nerves, and I shall leave these features to be covered by Dr. Pierson and those who participate in the discussion.

DISCUSSION

DR. RICHARD N. PIERSON: What is the problem of obstetricians in regard to the central nervous system of the new-born? How many of the injuries that one sees, such as feeblemindedness, hydrocephalus and epilepsy are due to obstetric injuries? Having gone over the literature with the help of Dr. Cornwall and having discussed it with him, it seems to me fair to say that our responsibility for that large group of dissimilar disorders of the nervous system is rather small. On the other hand, one must admit a great responsibility for another type of injury, for an injury of the central nervous system which neurologists never see. Holland and others who examine large numbers of the new-born at autopsy have discovered that at least 50 per cent of their material shows an injury of the central nervous system, enough to cause death.

Obstetricians must admit that they are responsible for a large amount of injury to the central nervous systems. On the other hand, as I have just said, both Ford in Johns Hopkins and Crothers in Boston have reviewed the literature with a great deal of care and have come to the conclusion that cases of hydrocephalus are never due to injury at birth. One must admit that a small percentage of cases of epilepsy are due to such injury. This is also true of meningeal tears.

As an obstetrician, I will present the result of my study on the problem of hereditary defects of the central nervous system. Clearly, there is a marked division of opinion among experimental biologists and neurologists as to whether most of these are true defects of germ plasm or characteristics which are definitely inherited according to mendelian rules, or whether they are due to embryos which are adversely affected during intra-uterine life.

A large amount of biologic experimental evidence shows that a most extraordinary condition of the central nervous system as well as other structures can be had by changing the environment of the embryo. It is established, in my opinion, that most of these important developmental defects of the central nervous system are not injuries caused at delivery but are either defects of the germ plasm or the effect of the environment on the growing embryo in the uterus.

When considering the injuries admitted and the type of clinical conditions that causes them, one thinks at once of forced deliveries. Dr. Cornwall has told you of the type of lesions commonly encountered. It is true that these lesions occur, and my experience is exactly as he has represented, that subdural hemorrhages and arachnoid hemorrhages are the common ones; premature labor is one of the most important predisposing factors to such injuries. Therefore, one must take particular pains to try to prevent the accident of premature labor.

Prevention consists in preventing the difficult type of forceps deliveries. That means a direct understanding of the mother's pelvis, estimation of the relation

of the child to the mother's pelvis and examination of the patient under an anesthetic early in labor. If incision is needed, it must be carried out early enough for both the mother and the child? Cesarean section, even, is performed early in doubtful cases. The danger has been reduced to a marked degree; the operation of craniotomy has practically been abolished.

Another type of delivery which is most dangerous to the baby is the version and breech delivery. Crothers, before any one else in this country and more insistently than any one else, has demonstrated that traction is unphysiologic and a most dangerous thing from the standpoint of the central nervous system of the infant during birth.

In vertex delivery, there is slow molding of the head, with the child's existence and the perfect circulation guaranteed by its cord; whereas, in the other method, the infant's cord is compromised so that asphyxia occurs many times. There is traction on the spine by violent molding of the head through the mother's passages, with many injuries to both the brain and the spinal cord. In work many men have done, there has been found a high percentage of injuries to the brain, tears of the dura and tentorium, and also injury to the spinal cord, even including fracture.

Traction, even in the most skilled hands, is a dangerous procedure; therefore, version and breech delivery is not an operation of election. It is always reserved for cases in which one cannot perform cesarean, section because of danger to the mother; it is admittedly a dangerous operation for the infant because many experiences have shown that these infants are seriously injured both in mind and body. Breech deliveries for the same reason are very hard on the baby. Few clinics can show a better percentage of mortality than from 10 to 12.

Crothers, in his follow-up of injured children in Boston, has found that a considerable number of injuries to the spinal cord are definitely due to breech deliveries. The prevention is care which recognizes the breech presentation and changes it to a vertex in the early stages of labor.

Dr. Ford, in his excellent monograph commenting on these things, makes the statement that obstetricians are well agreed about the problem involved in these injuries. I wish that were true, but it is not. Dr. Potter in Buffalo performs a version for a breech presentation electively on every patient he can get to in time; on some, when he is in doubt, he performs a cesarean section.

Some obstetricians advocate strongly certain kinds of anesthesia for every patient; others do not. There is marked disagreement among excellent obstetricians as to the wisest policy to pursue in regard to the mother and the child. My position would be that if one advocates a certain type of anesthesia, one may make the infant stand the risk in the interest of the mother; such would be the position of those who advocate version and breech extraction. With many that seems an unsound position and it cannot possibly be adhered to without danger to the infant.

So much for the point of view in regard to prevention. Again I want to repeat that it is my opinion that most of the inefficient work causes death to the patient, in other words, the central nervous system of these infants is shocked so that they die.

The brachial injuries in most cases are obviously due to two or three types of technical difficulties. The first is impacted shoulders, when the shoulders are impacted behind the symphysis and the physician pushes down and flexes the head violently causing traction on the brachial plexuses. This is common in breech deliveries and in version and breech delivery. The prevention of those things is the proper conduct of the cases along the lines already defined.

One other thing that must be mentioned is the violent method of resuscitation in vogue some years ago, which practically no obstetrician uses now. The violent Schultze method of swinging the baby by suspension at the axillas can easily cause brachial injuries.

It seems to me that the problem of whether the prevention of this great group of miscellaneous disorders of the central nervous system, which may be hereditary

or environmental in the uterus, depends on future experimentation. Having proved that some are hereditary, one thinks of eugenics, birth control and therapeutic abortion. It is a broad sociologic problem and not merely an obstetric one.

One group I forgot to mention is the congenital group of diseases. Syphilis is the classical example. That is the one condition which is known to be congenital, a disease acquired during intra-uterine life, so that the infant is born with the infection. This can be recognized and prevented by diagnosis of the disease in the parent beforehand and treatment of the mother when infected.

DR. BERNARD SACHS: For many years I have been hoping that the neurologist and the obstetrician would meet each other face to face on some of the questions brought up this evening, particularly this question of what the responsibility of the obstetrician is in regard to injuries sustained at birth and how much or how little he is expected to do in order to obviate these conditions. I think that obstetricians have been rather fortunate because of the recent publications of Ford and Crothers and Putnam. It seems to me that has given them a great deal of comfort — I believe much more comfort than I personally can get from those two monographs. Dr. Crothers' contribution, revealing the extreme injuries to the spinal cord, is important, and reveals conditions which neurologists had not suspected.

A few years ago, one of the physicians connected with Columbia University showed a pathologic specimen from Sloane Maternity Hospital. I was astounded to see the amount of injury that could be done to the spinal cord after obstetric manipulations, not necessarily because of them. That is new to me, and proves that breech presentation is not as easy to handle as it is supposed to be.

I am not at all in agreement with Ford's conclusions concerning injuries to the brain. He has simply taken a huge number of cases, which he has arbitrarily labeled "congenital diplegia," and if his statistics are correct, he is not using the customary clinical nomenclature. He has given his statistics in such a way as to show, if I remember correctly, that of 280 odd cases in a pediatric department, something like 235 were cases of true "congenital plegias." That is a proportion that no one with neurologic experience of many years has ever seen in any clinic. It is entirely contrary to my own experience. So I believe that while we have been at some trouble to differentiate between incomplete diaplegia, double hemiplegia and what we considered true congenital diplegia, Ford has mixed up things very much, and his statistics, to my mind, are not pertinent. Moreover, it is a great mistake, the same mistake that Collier has made. I have taken occasion to criticize Collier and his associates for that in a previous publication. They have found certain cases of congenital diplegia which it was known were not due to birth injuries. They have made the generalization and now claim that all cases of diplegia are of prenatal origin — of the hereditary type rather than due to any disturbance occurring during labor. That is true of some cases, and I admit that in former days the injury due to manipulation during labor was overrated, and perhaps the number of cases of diplegia that were to be explained in some other way was underrated. I want to assure the obstetricians that however any one may try to juggle with statistics, plenty of damage is done as the result of manipulations during labor. There is a large number of cases of hemiplegia, and above all of monoplegia and of incomplete diplegia, a considerable number of cases of defective mental development in later years and of epilepsy and idiocy that are to be ascribed to the disturbing labor.

One thing is brought out distinctly in all our studies, and I have been interested in this subject for over forty years, and that is that the most unfortunate class of all are the first born children. The most serious question for obstetricians to handle is, how is one going to shorten the period of labor in primiparas? That is really the one important question.

I understand that through the work of Arthur Stein, Watson and others, it has been shown that by the judicious use of pituitary the period of labor, particularly in primiparas, can be shortened. That one thing will diminish to a great extent the number of cases of hemiplegia, of idiocy, of imbecility and of epilepsy.

Whether the method of using pituitary will be successful or not or whether there are other suggestions, remains for the obstetricians to say. Shorten the period of labor in primiparas, and thus avoid prolonged compression of the child's skull.

Dr. J. R. Losee: I will present four slides which have been taken from Eardley-Holland's well known monograph "On the Causation of Fetal Death." The first slide demonstrates the normal tentorium cerebelli and falx cerebri. The others present the various lacerations of these membranes secondary to difficult delivery. I have studied the autopsy statistics at the Lying-In Hospital for the past three years. There were approximately 15,000 deliveries, of which 1,089 were stillbirths or cases in which the new-born died. Six hundred and twenty-three autopsies were performed, of which number thirteen (2 per cent) presented fracture of the skull. These lacerations varied from laceration of the pericranium between the bones to definite linear fractures. No epidural hemorrhage was observed, but in nearly all cases there was subdural hemorrhage secondary to laceration of the membranes. Fracture of the skull in itself is seldom the cause of death; the associated injuries, such as laceration of the membranes, with hemorrhage, are the most serious. Subdural hemorrhage was observed 134 times, or in about 21 per cent of the cases. Of these hemorrhages, sixty-six, or 50 per cent, were associated with laceration of the tentorium cerebelli and eight presented a laceration of the falx cerebri. Blood was observed both above and below the tentorium, but there was neither intraventricular nor intracerebral hemorrhage. Subdural hemorrhage in premature infants is occasionally associated with blood in the ventricles. Breech deliveries, with or without version, are frequently associated with laceration of the membranes. This is well known.

There were twenty-one cases of complete separation of the vertebrae in this series, ten of which took place between the fifth and sixth cervical. In one, the cord was completely separated. All were associated with hemorrhage in the subdural space and in the soft tissues about the vertebrae. All of these occurred in breech deliveries and, from the study of the lesion, it seems to have been produced by a manipulation in which the head was fixed in the pelvis as the fulcrum and, with the body as a lever, extension was applied over the mother's pubis. In this series, rupture of the liver was observed once, but in referring to the history I believe this accident was due to efforts at resuscitation. Rupture of the abdominal viscera is extremely uncommon.

Dr. Alfred Taylor: As Dr. Sachs said, I have been hoping for a long time to have an opportunity to discuss the question of brachial plexus injuries with obstetricians. The fact that these injuries have occurred in infants that have been delivered spontaneously without the assistance of either a midwife or an obstetrician means that the lesion is not necessarily the fault of the obstetrician. On the other hand, when the mechanism of these injuries is considered, it seems obvious that the obstetrician may or may not be the essential cause of the injury. If in a given case the injury is inevitable, the manipulations of the obstetrician may or may not seriously aggravate the degree of injury. My wish is to emphasize one particular feature in the etiology, the essential point in which is difficulty in labor. I am positive that the one thing which causes damage to the brachial plexus is stretching of the nerves. The stretching is caused by separation of the head and neck from the shoulder on the side of the injury. When this subject was first investigated with Clack and Prout, I took occasion to secure about twenty stillborn infants, or infants that had died within a day or two of birth, and to attempt to reproduce the lesion by the various mechanisms which at that time were said to be the etiologic factor. The one thing which was stressed in the subject of etiology was the question of pressure, pressure by fingers. Another thing that was favored theoretically was pressure by the clavicle. It was found in these twenty experimental infants that the only form of manipulation that would reproduce the injury was holding of the head on one side and exerting traction on the shoulder. When this was done to a sufficient degree, lesions of

the brachial plexus would be produced that were identical with those found in exploration of fresh lesions in living children, lesions which would ultimately produce exactly the conditions found at operation a long time after birth, after cicatrization had occurred.

If one will visualize the fact that traction mechanism is the sole cause of injuries to the brachial plexus, then it seems to me that obstetricians have a cleancut fact on which to base their manipulations during the process of birth.

If, as one of the speakers this evening said, it is frequently the fact that when a shoulder sticks under the symphisis and then the head is manipulated in the process of delivery in order to get the shoulder down, the traction mechanism for damage to the plexus is started. If, in addition, one makes a crutch of the hand and pries on the head as a lever, a perfect mechanism for producing a brachial plexus lesion is established and one is lucky if the child does not have a lesion if that manipulation is used. In the breech presentation the head is stuck in the pelvis, and the process of delivery is by traction on the shoulders. Traction pulls both shoulders down from the head, and the plexus that happens to be strained a little more or is a little weaker is damaged. I have seen between six and a dozen — I have not the actual figures — bilateral injuries of the brachial plexus. It is interesting that all the injuries occurred in breech presentations. I have never seen a bilateral rupture when the presentation was vertex, and one can readily see why.

Another interesting thing about the bilateral lesions is that usually they are both relatively minor injuries, which is perfectly logical when one considers the mechanism, because the two plexuses have shared the strain and neither one has been pulled so far as to give a complete rupture.

If in the process of delivery there is much lateral deviation either during the manipulation of the body in a breech delivery or during the manipulation of the head in a vertex delivery, the risk of causing a brachial plexus injury will vary with the degree of flexion.

In the experimental group of twenty cases it happened that there were six in which some of the roots, either one or more, were torn from the cord. I think that percentage, nearly 30, is pretty well carried out also in the brachial plexus lesions that one sees. It is not uncommon to find one or two roots avulsed from the cord. In two operative cases in which the lesion was excised and in which it looked like an ordinary cicatricial mass of nerve damage, I was much surprised to have the pathologist report that a posterior root ganglion was included in the specimen, which was entirely extraspinal. This shows that evulsion of the root from the cord is by no means an uncommon event.

The frequency of these lesions varies in different cities. For instance, in this town it is now relatively uncommon for a birth palsy of serious degree to occur when obstetricians were employed. I happened to see a number of cases within a few days of birth. In all of those in which an obstetric specialist had taken care of the delivery the lesion was relatively slight, and most of the patients recovered spontaneously.

In Boston where, I understand, the theory of delivery is to use a great deal more speed, a tremendous number of birth palsies of this type occur. I think that Sever, who has written a great deal on the subject, had at one time a list of 1,500 children who were coming to his orthopedic clinic for lesions of this type of greater or lesser severity. A Boston friend tells me that the obstetric department teaches that in cases of breech delivery, the procedure must be rapid in order to save the child's life. If one attempts to perform a rapid delivery, the chances of causing this lesion are enormously increased. Therefore my plea to the obstetrician would be, "in manipulation avoid as far as possible separation of head and neck from shoulder either in breech or in vertex delivery."

I think the obstetrician should also receive a suggestion with regard to the treatment in these cases. It is my common experience in seeing children of this type, and I presume that I have seen 300 or 400 of them up to the present time, that in many (I will say not delivered by obstetric specialists but in the ordinary

course of events in the more populous but less well cared for sections of the city) the lesion frequently is not noticed for three or four days. It seems impossible that an arm could be totally paralyzed and the condition not noticed by either the family or the physician, but this may happen. Again, many times the physician, feeling his responsibility, says, "Oh well, that will take care of itself as the child grows older." That, to my mind is a serious defect in the care of the child, because if proper treatment is not given for the first five or six months, even if regeneration of the nerves occurs pretty well spontaneously, the child is handicapped by the secondary contractures that follow this lesion. Some muscles of the arm may not be paralyzed, some may be totally paralyzed and some may be partially paralyzed. If the arm is left in the usual position, the muscles which have not been paralyzed undergo contracture. That contracture gives certain mechanical deformities to the extremity which makes it perhaps only 25 per cent as valuable to the person as it would be if he were given proper treatment from the start and secured all of the spontaneous recovery which he could get.

In the average birth palsy from injury to the brachial plexus the shoulder muscles, the flexors of the elbow, the supinators of the forearm and the extensors of the wrist are paralyzed. The pectoralis major is partly paralyzed and partly not. If the child is allowed to remain in the characteristic position or if the arm is merely bandaged to the body, the muscles which are likely to undergo change are left in a contracted position and the muscles which have been paralyzed are overstretched by this position; therefore, the worst possible thing for the child is being done.

It is therefore important, to my mind, in birth palsy lesions of this type, to insist that the arm be kept in proper position so that the maximum amount of recovery will occur spontaneously, and so that nothing will be lost while one is waiting to see if surgical repair of the nerves is indicated.

The typical position for the best result for the child, if he is going to get any degree of spontaneous recovery, is the upright position; abduction of the shoulder to 90 degrees which relaxes the muscles there; relaxation of the external rotators if they are paralyzed; relaxation of the elbow flexors which are paralyzed; relaxation of the supinators which are paralyzed, and relaxation of the extensors of the wrist which are paralyzed.

If the extremity is kept in that position by brace or pinning the arm to the pillow during the early part of the child's life, one can afford to wait a sufficient length of time to see whether the child is going to make a spontaneous recovery or if something is to be done. If one waits a year and the arm is kept in that position and physical therapy is properly used, and it is obvious that something ought to be done to the plexus to give the best results, there are none of the malformations which are secondary to the nerve damage to prevent recovery of a useful arm. Any child who has not made a satisfactory spontaneous recovery in six months after having been kept in proper position (after the first three weeks during which the traumatic neuritis subsides) and who is being treated with physical therapy, would be best served by a proper surgical repair of the brachial plexus. When these plexuses are repaired, one can by no means be certain that the arm will be perfect. In a series of eighty or ninety operative cases, only three or four have been practically normal. The patients have made a recovery that is so good that it would take a careful neurologic examination to find any defect. The result in a great majority of the cases will be an arm which is defective more or less, and nobody can tell until the final result is obtained just how great that defect is going to be. I am sure, from having followed cases in which the treatment has been nonoperative for two or three years without satisfactory results and in which operation has then been employed, that one can immensely improve the functional value of the arm by performing surgical repair of the brachial plexus in properly selected patients.

DR. BENJAMIN P. WATSON: I think that the obstetricians were feeling rather complacent about this whole situation until Dr. Sachs spoke. From the work of

Dr. Eardly Holland and others who had shown the frequency of these intracranial lesions in stillborn children, I think most obstetricians and obstetric teachers have realized and have taught the frequency of those injuries and have instructed students to avoid them as far as possible as they themselves have done.

The work of Dr. Caldwell, for instance, and Dr. Pierson in showing the frequency of the injuries of the spinal cord in breech deliveries brought forth clearly the mistakes that were being made in the ordinary breech delivery. But I am afraid Dr. Sachs has brought an even stronger accusation against obstetricians. May I make a suggestion that neurologists make more use of autopsy material in these new-born babies and try to get more definite information as to just what type of lesion may be produced by a birth injury? Personally, I have never seen a massive hemorrhage in the substance of the brain. All our mistakes, as Dr. Pierson said, are buried. Hemorrhages at the base of the skull are so massive as to cause death to the child.

It is difficult to be certain of just which type of intracranial lesions will produce the conditions of which Dr. Sachs has spoken. Personally, I have known of only one case of hemorrhage from a ruptured middle meningeal artery. That was a definite case; the child was operated on at once and recovered. Strangely enough, three days afterward the child developed symptoms on the other side, and an operative procedure was carried out on the opposite side of the skull with success. That is the only case I have known of an injury of that sort.

I think there we are between the devil and the deep blue sea when it comes to preventing those injuries by shortening the period of labor. If one shortens the labor by any means known at present one will inflict further injury to the child, and the problem is not so easy as might appear from the statement that if one shortens labor one will diminish the number of cases of injury at birth. I think the opposite might be true.

DR. LOUIS C. SCHROEDER: To the pediatrician the problem of injury at birth is not a question of placing the blame on poor obstetrics or on any particular procedure. So many premature children, many full term infants delivered normally and not a few infants delivered by cesarean section show evidence of cerebral hemorrhage that I feel the problem far transcends the consideration of obstetrical technic alone. That unwarranted manipulation and the application of unphysiologic force may result in disaster is well known. What is not known is why certain infants give evidence of bleeding when, so far as can be judged, no undue force has been used.

When the causes are known it is only a question of time and education before they are removed. No one at all conversant with the problem can deny that the teachers of obstetrics are attacking it in a serious way and that their efforts will result in the reduction of these accidents to a minimum. The problem in its entirety, however, requires a wide program which needs the help of many. The first requisite is the securing of every possible autopsy and, corollary to that, the training of competent pathologists. The value of autopsies is getting tardy recognition when hospitals are being graded in part on the percentage secured. But the securing of autopsies is secondary to the type of men who perform them. In the not far distant past some autopsies were performed by men whose chief claim to distinction was their ability to take off the calvarium in thirty seconds. It fell to my lot as an intern to hold a stop-watch in such an instance. Many men can perform an excellent autopsy on an adult, yet have difficulty in properly demonstrating a tentorial tear in an infant. It takes time to reveal the entire spinal cord in an adult, but the problem is not nearly so formidable in an infant. The percentage of autopsies in which the entire length of the spinal canal and its contents can be fully described is probably very small.

With the securing of a sufficient number of autopsies and the competent reporting of the conditions found, we have a foundation on which we may build. The superstructure will require primarily the aid of obstetricians and neurologists, and for that reason it is particularly pleasing to see a combined meeting of these sections of the Academy.

It is not within the province of the pediatrician to tell what must be done, but that both the pediatrician and the neurologist can contribute in many ways to the solution of this perplexing problem is readily admitted. It has always seemed reasonable to me that if it were possible for a competent neurologist to see the cases of true or possible birth injuries at an early stage, they could add immeasurably to the data needed in making correct diagnoses. Among other things, an infinitely greater amount of information about the spinal fluid in the new-born is needed, about the relative value of spinal and cistern taps, about the blood of the new-born and the permeability of the vessel walls. Only by the cooperation of all branches of medicine can these things be found out.

It is reported that from 40 to 50 per cent of deaths in the early days of infancy are caused by cerebral hemorrhages. Surely the subject is worth earnest study.

Book Reviews

PYGMALION, OR THE DOCTOR OF THE FUTURE. By R. M. WILSON, M.B., CH.B. Price, $1. New York: E. P. Dutton & Company, 1926.

In this volume the author, by contemplating the attributes and vision of the physician of the future, warns against the materialistic attitude of the present-day physicians. He reminds him that the science of medicine is not the science of disease, but the science of life. He challenges the assertion that a symptom is the evidence of disease and points out that it is more accurate to think of such as a reaction to life. He would have the physician see the remote, as well as the immediate, cause of distress. For example, pain in the stomach may or may not be the direct consequence of disease. In that the patient is the sum total of all his emotions, the physician of the future will be equally interested in this emotional field. He will not have the narrow view of the physicist, who thinks of water in terms of H_2O, but one who sees water in terms of babbling, gurgling brooks, broad rivers, mighty oceans, and the romance of the sea. The physician will thus speak to his patients in terms of life and not of disease. When a serious organic condition presents itself he will not fill the patient's soul with gloom, but with every honest agency "desensitize" it. He will provide the "esprit de corps." Such a physician will be "a humanist, a man with the widest possible knowledge of human motives, one who is cultured, ripe in intelligence, and not lacking in emotional sympathy." Such a physician will not only understand organic disease, but will be the priest who brings comfort when others fail, and the parent who thinks in terms of life and love. So the author remarks: "I will look forward to the time when the practice of medicine will include within its scope every influence of known potency over human spirit, and when the practitioner, like Pygmalion, will look forward on his work and see, not disease and death, but the glowing lineaments of life."

MEINE MYELOGENETISCHE HIRNLEHRE. By PAUL FLECHSIG. Price, 6.90 R. M. Pp. 122. Berlin: Julius Springer, 1927.

This recent small monograph by Flechsig is divided into two parts. The first part deals with an account of Flechsig's life, written by himself, while the second portion is concerned with the theory of myelogenesis. The autobiographic portion is probably of more than limited interest since it contains an account of Flechsig's struggles against stern opposition in his fight for the theory of myelogenesis. It is interesting reading, and, for those interested in scientific neurology, an inspiring record of a battle against prejudices. The second portion of the monograph, dealing with the theory of myelogenesis, will be of much wider interest than the first. Flechsig does not bring any new facts to light in this discussion. It is a full summary of his stand on the question of myelogenesis, and for those who wish a concise account of Flechsig's work as contained in his "Anatomie des menschlichen Gehirns und Rückenmarks auf myelogenetischer Grundlage," this monograph is of great value. Indeed, he constantly refers to his former work in this summary, particularly to the illustrations contained therein. Flechsig discusses the principles of myelogenesis, and then the myelogenesis of the various regions of the brain. The myelogenesis of the medulla and the cerebrum is fully discussed, and considerable time is devoted to the association centers of Flechsig. Of particular interest is the evidence which Flechsig brings to bear in attempting to prove on a myelogenetic basis that the seat of the psyche is in the prefrontal lobes.

The monograph is well written, and for those who wish a concise and summarizing account of the theory of myelogenesis, a valuable work.

THE EFFECT OF THE RELATIONSHIP BETWEEN THE FATHER AND THE CHILD ON THE DESTINY OF THE LATTER. By C. G. JUNG. Price, 7.20 M. Pp. 18. Leipzig: Franz Deuticke, 1927.

In this short monograph Jung discusses the influence which the affective relationship between the father and the child exerts on the future life of the latter. He considers that the father has as great, if not greater, influence than the mother, and points out that association tests indicate that two members of a family — e. g., mother and daughter — who are unconscious rivals for the father's affection will show a similar reaction type of word association. He cites four cases which are typical of some of the results of the father's influence. When the daughter is attached strongly to her father, she will seek a mate who bears as close a resemblance to the father as possible. If her desire is frustrated either by the death of the husband or her inability to reproduce in her own love life a situation similar to that of her childhood, except that she plays the rôle of wife to the father substitute, she may develop a psychoneurosis even to the degree of finding her lost father in delusions. The son of a dominant father may be unable to compete with him for the mother, and in seeking a love object will be attracted to elderly married women and invariably incur the husband's displeasure and punishment. If a boy develops a strong attachment to his father, he may become a rival with his mother for the father's affection, and, consequently, develop homosexual trends.

The author points out that certain races — such as the Jews — have a strong father attachment, which they idealize as the father God. The father God becomes the personification of the repression of their infantile sexuality, and because of this repression they are prone to develop psychoneurotic symptoms.

This contribution is one of real value to those interested in the study of development of personality and is especially important to those studying the problems of children.

PLÖTZLICHE UND AKUTE ERKRANKUNGEN DES NERVENSYSTEMS. IHRE ERKENNEN UND IHRE BEHANDLUNG. By S. FLEISCHMANN. Price, 12 M. Pp. 291. Berlin, S. Karger, 1927.

This monograph by Fleischmann deals with the diseases of the nervous system having sudden and acute onset. It is made up of sixteen lectures discussing cerebral hemorrhage and softening, traumatic cerebral lesions, comatose states, inflammations of the brain and its membranes, acute diseases of the spinal cord and of the peripheral nervous systems, poisonings of the nervous system, hyperkinetic attacks and attacks of pain, and attacks of functional and endocrine origin. Fleischmann attempts to bring together the histories, methods of investigation, diagnosis, and treatment of these diseases and discusses also their physiologic and pathologic processes. This is necessary because in diseases with sudden and acute onset there is not the leisure nor the advantage of repeated observations such as is afforded in chronic diseases. While the book contains little that is new, it brings together in a practical and satisfactory way facts that are not available in the usual textbooks. The discussion of the diagnosis of these various conditions is particularly good.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. Abt. V. Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus. Teil 5 B. Price, 3.90 R. M. Pp. 188. Berlin: Urban & Schwarzenberg, 1926.

This little pamphlet contains two articles: "Methoden zur Untersuchung des überlebenden Zentralnervensystems," by Hans Winterstein of Rostock and "Die Methoden zur Funktionsprüfung von Muskeln und Nerven beim Menschen mittels des galvanischen und faradischen Stromes." Both articles are rather ingenious physiologic methods for investigation of some of the obscure functions of the nervous system. The first article makes use of the methods of

keeping the nervous system of animals "alive" by keeping up the circulation with known isotonic solutions. The literature is quoted rather extensively as in most German articles.

THE EXAMINATION OF THE CENTRAL NERVOUS SYSTEM. By DONALD CORE, M.D., MANC., F.R.C.P., LOND. Price, $3.50. Pp. 239. New York: William Wood & Company, 1928.

In this little book of 239 pages, the author gives a comprehensive description of the methods of examination of the nervous system. It is divided into nineteen chapters and there are fourteen illustrations. The book is obviously designed for the student and general practitioner and gives adequate instruction in the methods of examination and interpretation of symptoms elicited. One great fault of the book is that there are not enough illustrations.

METHODIK DER UNTERSUCHUNGEN VON NERVENELEMENTEN DES MAKRO-UND MAKRO-MICROSKOPISCHEN. GEBIETES. By W. WOROBIEW and OSCAR ROTHACLER. Price, 18 R. M. Pp. 130. Berlin, 1926.

This is a manual for the macroscopic and microscopic study of the body. It consists of a special vital technic which has been used for many years by Worobiew and his students and is now published for the first time. The book contains a detailed discussion of technic for vital examination and staining and is fully illustrated.

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