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DEVELOPMENT OF THE MENINGES

FURTHER EXPERIMENTS

SAMUEL C. HARVEY, M.D.

HAROLD S. BURR, PH.D.

AND

ERNEST VANCAMPENHOUT, M.D., PH.D.

NEW HAVEN, CONN.

In 1926, we (Harvey and Burr [1]) presented experimental evidence supporting a hypothesis of the senior author that the pia-arachnoid membrane is a structure which developmentally is an analog of the sheath of Schwann of the peripheral nerve and is a derivative of the neural crest. Harvey Cushing [2] has called attention to the fact that Oberling,[3] in 1922, advanced a similar hypothesis based on histopathologic studies. The experiments reported by us (Harvey and Burr) consisted in transplantations of the nervous system of Amblystoma, carried out with and without neural crest. The results of those experiments indicated clearly that when the nervous system was transplanted without neural crest no cellular investment could be found interposed between the brain and the surrounding mesenchyme. Portions of the neural tube which were transplanted with neural crest gave clear evidence of the presence of a definitive cell layer, immediately surrounding the nervous system, of characteristically different form from the outer lying mesenchyme. At that time the following conclusion was drawn. "Certain ectodermal elements derived in large part from the neural crest are contributed to the mesenchyme and take part in the formation of the leptomeninx." Attention must be called to two important points: First, this conclusion does not state that the leptomeninx is derived exclusively from neural crest. The experimental evidence indicates

From the Departments of Surgery and Anatomy, Yale University School of Medicine.

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1. Harvey, S. C., and Burr, H. S.: The Development of the Meninges, Arch. Neurol. & Psychiat. **15**:545 (May) 1926.

2. Cushing, H.: Studies in Intracranial Physiology and Surgery, New York, Oxford University Press, 1926.

3. Oberling, C.: Les tumeurs des méninges, Bull. Assoc. franç. p. l'étude du cancer **11**:365, 1922.

that the primordium is of neural crest origin. To it is added, during development, mesodermal elements, in all probability carried in with the developing blood vessels. Second, the conclusion includes no statement regarding the mechanics of lamination of the meninges. It may well be that the escape of cerebrospinal fluid from the central nervous system is the exciting cause of such lamination. Another explanation is, however, possible. Lamination may well be a pressure phenomenon, the result of the expansion of the nervous system against the investing supporting structures of the head and body. An experimental investigation of this problem should be undertaken, since the experiments already reported have shown no such clear relationship between meningeal lamination and the escape of cerebrospinal fluid. Transplantation of portions of the nervous system to the flank of a salamander does not reproduce the physical environment of a normal neural tube. One might expect, then, to find a difference in the molding of the supporting structures. That the growth of the central nervous system does contribute a molding factor has already been demonstrated (Burr [4]).

In a recent publication from Weed's laboratory, Flexner [5] has presented the results of a group of experiments parallel to those reported by us (Harvey and Burr). Their findings are at complete variance with our observations. The difference, however, may well be one of interpretation of the microscopic material. The very nature of the transplantations precludes differentiation of the nervous system and its environing structures in a completely typical fashion. It is, therefore, necessary to interpret the observations in terms of a working hypothesis. The findings are never proof, but rather are clues pointing the direction of further investigation. Hence, it was deemed wise to extend the original experimental work in as many directions as possible. The results of some of these possible extensions are here reported.

EXPERIMENTAL STUDIES

The original experimental studies of the development of the meninges reported (Harvey and Burr [1]) have been extended in three directions: First, using the method of chorio-allantoic grafts, portions of the nervous system of the chick, with and without neural crest, were implanted on the allantoic membrane of nine and ten day chick embryos, close to the point of bifurcation of a blood vessel. The second method involved selective staining of the neural crest by Nile blue sulphate, with subsequent study of the distribution of the Nile blue-containing cells in Amblystoma. The third procedure involved heteroplastic trans-

4. Burr, H. S.: The Effects of the Removal of the Nasal Pits in Amblystoma Embryos, J. Exper. Zool. **20**:27, 1916.

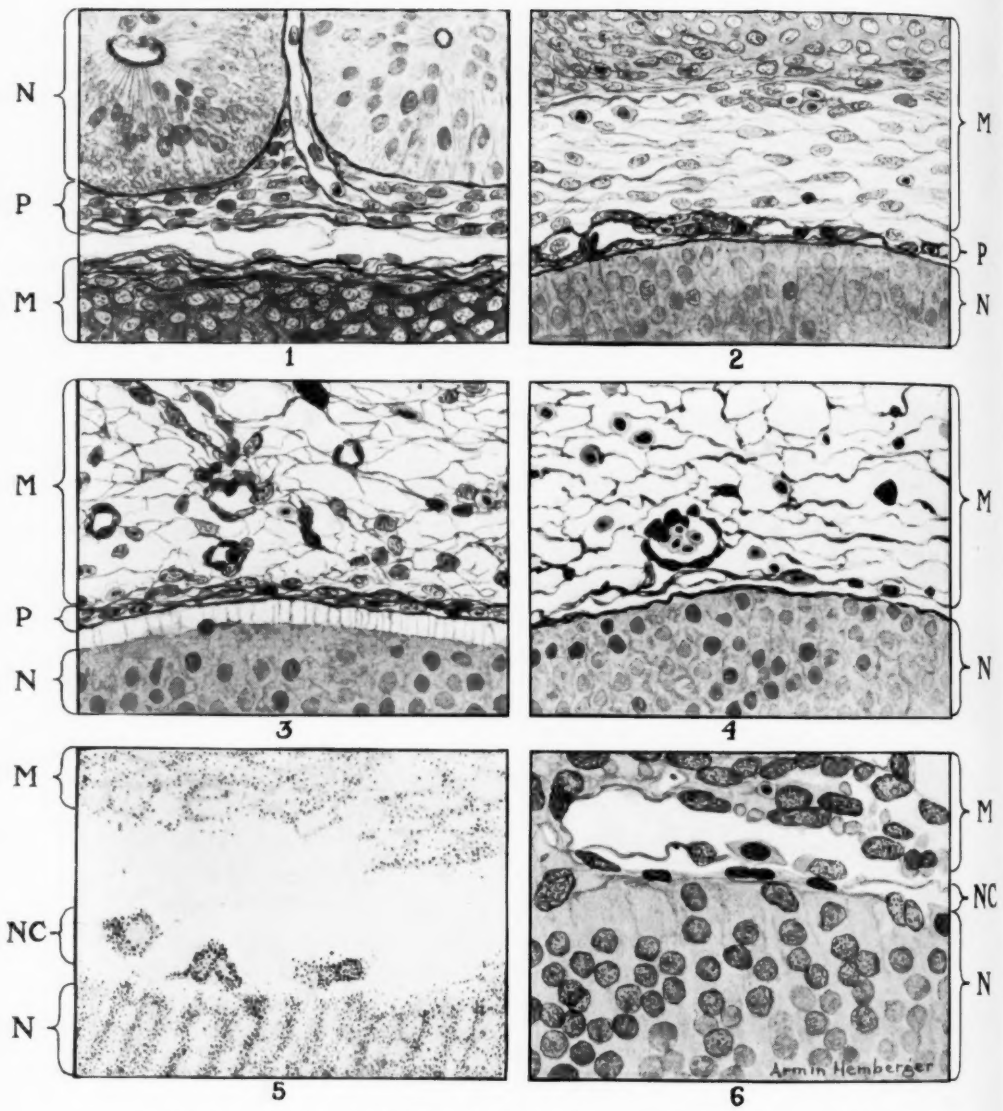
5. Flexner, L. B.: The Development of the Meninges in Amblystoma, Contrib. Embryol. **20**:31, 1929.

plantation of the neural tube with neural crest of a closing neural fold stage of Rana on the flank of a stage 25 (Harrison) Amblystoma larva. The size of the cells in Amblystoma was considerably greater than that of the cells in Rana; hence, it should be possible to determine in a transplantation the origin of the cellular investment of the transplanted portion of the nervous system.

The chorio-allantoic grafts were performed by one of us (Van Campenhout). Two series of implantations were performed. In the first, the prosencephalons of fifty hour chicks were implanted on the allantois of a one hundred and ninety-two hour host. After about two hundred hours, the implant was fixed and prepared for microscopic study. A parallel series of experiments was made which involved the implantation of the entire abdominal or thoracic sections, including the nervous system, myotomes and viscera. Under the conditions of the experiment, the first series consisted of grafts of the nervous system without neural crest; in the second, grafts of the nervous system with neural crest. The results obtained confirmed in every respect the findings previously reported for Amblystoma. The method employed resulted in a high percentage of successful implantations. The nervous system proliferated and differentiated in a reasonably typical fashion. The surrounding tissues are related to the nervous system in an understandable manner, though minor variations exist, owing, in all probability, to differences in the immediate physical environment.

It is possible, nevertheless, in the majority of the cases studied, to recognize typical arrangements which provide valuable evidence of the true relationships. In *1* and *2* of the accompanying figure, the conditions found in an implant of spinal cord with neural crest are shown. The nervous system indicated at *N* is in both instances covered by a thin layer of closely packed cells, *P*, ectal to which lies the mesenchyme, *M*. In *1*, a blood vessel can be seen entering the nerve tissue from the origin of the primitive pia-arachnoid, *P*. The mesenchyme in *1* is condensed and flattened to form a definitive sheet on the deep surface of the cartilage. A definitive space can be seen between *M* and *P*. In *2*, the pia-arachnoid can be seen containing blood vessels, but the mesenchyme is applied in a loose network to its outer surface, with no intervening space. Part *3* is a drawing from a section of a normal chick of corresponding age, showing an almost parallel condition to that seen in *2*. Some shrinkage of the nervous system has left a fiber-bridged space between the neural elements and the external limiting membrane of the nervous system, outside of which can be seen the closely packed cells of the pia-arachnoid. The mesenchyme is a loose reticulum not yet condensed into a definitive membrane.

The results from the converse of the foregoing experiments are shown in *4*. Here the prosencephalon was implanted as free from



1, Section through chorio-allantoic graft of nervous system with neural crest. *N*, nervous system; *P*, primordium of pia-arachnoid; *M*, mesenchyme. *2*, Similar section. *3*, Section from normal chick embryo of corresponding age. *4*, Section through graft without neural crest. Note absence of cell layer on surface of nervous system. *5*, Section through Amblystoma embryo, the neural crest of which was stained with Nile blue sulphate. Note dye in neural crest cells but not in nervous system or mesenchyme. *6*, Section through heteroplastic transplant of Rana on Amblystoma. Note four small neural crest cells, *NC*, on surface of Rana nervous system, *N*. Ectal lies a blood vessel and the surrounding mesenchyme, *M*, of the large cells of Amblystoma.

neural crest as possible. In all probability, at the time of operation no neural crest cells can be found in the chick embryo cephalic to the trigeminal ganglion. Hence, transplantation of the prosencephalon presumably produces an implant that is virtually free from neural crest. The result is strikingly different. The nervous system at *N* presents a clearly defined limiting membrane, ectal to which can be found no traces of closely packed cells or a primitive pia-arachnoid. The loose reticulum of the mesenchyme is closely applied to the surface of the nervous system without an intervening sheet of cells. These findings seem to point clearly to a definite difference in the cellular envelop of the nervous system in the two series of operations. In the first series, in which the nervous system with neural crest was transplanted, a characteristic cellular sheath lies interposed between the nervous system and the mesenchyme. In the second series, in which the nervous system was transplanted without neural crest, no such definitive sheath can be seen. It may be concluded, therefore, that in the chick, as in Amblystoma, the fundamental cellular primordium of the pia-arachnoid is derived from neural crest.

The second method of investigation employed was that of selective staining of the neural crest with Nile blue sulphate. This selective staining was accomplished in two ways. In one, small agar strips impregnated with Nile blue sulphate were applied to the crests of the neural folds during the time of closure. The underlying neural crest absorbs the dye from the agar, and the subsequently stained neural crest cells can then be followed for a considerable interval of time. A parallel method was used in which the entire embryo was placed in Nile blue sulphate at the stage of closure of the neural folds and was permitted to remain there a varying number of hours so as to stain selectively only ectodermal structures. Too long an immersion results in the dye penetrating the subjacent mesoderm. Here, again, after a varying length of time, the animals were fixed and prepared for microscopic study. In both of the foregoing instances no stain other than Nile blue was used. In 5 are shown the conditions to be found fifteen days after treatment. The nervous system can be seen with its cells packed full of a brownish pigment, always to be found in the nervous system of larval salamanders. Lying on the surface there can be seen three cells containing many dark blue granules at *NC*. Outside of these blue-stained neural crest cells lies a considerable space bounded on its outer surface by the loose reticulum of the mesenchyme, *M*. By discarding those embryos in which there was a trace of nile blue in mesodermal structures, one may safely conclude that the blue-stained cells on the surface of the neural tube are of ectodermal origin. Furthermore, since the only wandering ectodermal cells are the neural crest cells, it may be con-

cluded that this is evidence of a distribution of neural crest cells about the surface of the neural tube. Since these animals were fixed at stage 38 (Harrison), the blue-stained cells cannot be the wandering cells of the sympathetic nervous system or of the chromaffin system. The latter have already wandered to more distant portions of the embryo. Again, there is evidence that the nervous system is surrounded during development by a sheet of neural crest cells which form the basis of the pia-arachnoid.

Finally, heteroplastic transplantations of the nervous system and neural crest of the frog, Rana sphenocephala, were made on the flank of Amblystoma punctatum hosts. Under the conditions of the experiment, the small cell tissue of the donor lies embedded in the large cell mesenchyme of the host. As the inner investing membrane of the nervous system is derived from neural crest, the nervous system of the frog should be surrounded by a small cell membrane of donor origin. Furthermore, since every precaution was taken to avoid a transplantation of frog mesenchyme, no donor mesenchyme should be found surrounding the nervous system in a transplant. Surrounding the transplant, however, one might reasonably expect to find the large cell mesenchyme of the Amblystoma host.

The conditions found as a result of the experiment are shown in *6*. After a period of about fifteen days, the animals operated on were fixed and prepared for microscopic study. In only a small percentage of the cases was there adequate differentiation of the transplant. In the majority of instances, the Rana material either failed to differentiate or was resorbed. On the other hand, when differentiation was adequate, a characteristic picture could be recognized. The nervous system of the frog, *N*, bore on its ectal surface scattered small cells which could be derived only from the neural crest of the frog, since this was the only non-nerve tissue transferred. Four such cells can be seen at *NC*. Outside of these cells lies a blood space invested by the mesenchyme of the Amblystoma host. The nuclei of the cells of the latter can be seen to be much larger than the nuclei of the four neural crest cells derived from the frog. Here again is another kind of evidence to indicate that the immediate investment of the nervous system is a derivative of the neural crest.

COMMENT

On page 47 of Flexner's article appeared this sentence: "Certainly the opinion is warranted that both ectodermal and entodermal elements enter into the formation of the dura, arachnoid and pia, and that the presence of the first two membranes is dependent not only on the cellular elements indispensable to their formation, but on other factors as well."

Attention is called to the fact that this is almost an exact parallel of a statement we (Harvey and Burr) made and corroborated in the findings reported. These clues point definitely to the following conclusion. During early development of the nervous system it is surrounded by a thin enveloping neural crest, outside of which lies the loose reticulum of the mesenchyme. The latter is, in most regions, derived from the mesoderm, but the experimental work of Stone [6] has definitely demonstrated the presence of ectodermal elements in the mesenchyme of the head region. It may well be, therefore, that in the head region the pachymeninx, as well as the leptomeninx, possesses ectodermal constituents, but further experimentation is necessary to demonstrate that fact.

In later development, the original primordium of the leptomeninx is in all probability added to by derivatives of the mesoderm. It, therefore, becomes a compound membrane the reactions of which to trauma and pathologic changes are determined by the particular cellular component involved. These reactions may sometimes be typically ectodermal and sometimes mesodermal, and, in all probability, they are sometimes a combination of both.

The exact mechanisms that bring about the organization of the primordia of the meninges is another matter entirely, concerning which our experiments give little evidence. The escape of spinal fluid from the central nervous system may well be a determining agent. It is possible, on the other hand, that pressure phenomena developed by differential growth rates between the central nervous system and the supporting structures are also important. Further experimental work is necessary before the relative merits of the foregoing suggestions can be determined.

SUMMARY

1. Chorio-allantoic grafts of the nervous system of the chick, with and without neural crest, have shown that (*a*) the neural tube with neural crest possesses a characteristic cellular membrane on its outer surface, and (*b*) transplants without neural crest show a complete absence of that cellular layer.

2. Selective staining of the neural crest with Nile blue sulphate results in the finding of Nile blue-stained cells surrounding the unstained nervous system, with the similarly unstained mesenchyme surrounding the whole.

6. Stone, L. S.: Experiments Showing the Rôle of Migrating Neural Crest (Mesectoderm) in the Formation of Head Skeleton and Loose Connective Tissue in Rana Palustris, Arch. f. Entwcklngsmechn. d. Organ. **118**:40, 1929.

3. Heteroplastic transplantations of Rana sphenocephala on Amblystoma hosts have shown that the Rana nervous system possesses an envelop of small cells of neural crest origin surrounded by the large cell mesenchyme of the host. These results add further confirmation to the original thesis that in the development of the meninges the primordium of the leptomeninx is derived from the neural crest and that of the pachymeninx from the mesenchyme.

THE SUBDURAL SPACE AND ITS LININGS

TIMOTHY LEARY, M.D.
AND
EDWARD A. EDWARDS, M.D.
BOSTON

Since the monumental work of Key and Retzius[1] it has been generally accepted that the subdural space is lined by endothelium (mesothelium), as are the serous spaces. Mallory,[2] in 1920, asserted that the subdural space is not lined by endothelium, but by fibroblasts, the cells lining the dura being highly differentiated fibroblasts and those covering the arachnoid, less highly differentiated fibroblasts. His findings, however, have not influenced histologists or neuropathologists, even though Harvey and his associates[3] have called attention to the differences in origin and reaction of the dura and the pia-arachnoid. Lear and Harvey[3c] concluded from experimental evidence that the dura is lined by mesothelium derived from the mesenchyme, while the lining (covering) of the arachnoid is made up of cells more highly differentiated than those of the dura, and therefore more stable in character.

In a study of subdural hemorrhages the great differences between the functions and reactions of the arachnoid and the dura led us to a comparative investigation of the linings of the serous cavities and the subdural space.

Functionally, the pia-arachnoid is an important membrane. It provides for the carriage of the large vessels (which the brain demands) over the surface of the organ in such a manner that only relatively small vessels actually penetrate the tissues of the brain; with its connections it serves to produce and distribute the cerebrospinal fluid, which equalizes pressure in the brain and cord, in the subarachnoid space and in the ventricles; it is the substitute for a lymphatic system for the brain and forms a water bed for that organ. Among the membranous structures of the body it is *sui generis*. On the other hand, the dura

1. Key, A., and Retzius, G.: Studien in der Anatomie des Nervensystems und des Bindegewebes, Stockholm, Samson and Wallin, 1875, vol. 1, p. 162.

2. Mallory, F. B.: The Type Cell of the So-Called Dural Endothelioma, J. M. Research **41**:349, 1920.

3. (*a*) Harvey, S. C., and Burr, H. S.: The Development of the Meninges, Arch. Neurol. & Psychiat. **15**:545 (May) 1926. (*b*) Sayad, W. Y., and Harvey, S. C.: The Regeneration of the Meninges: the Dura Mater, Ann. Surg. **77**:129, 1923. (*c*) Lear, M., and Harvey, S. C.: The Regeneration of the Meninges: The Pia Arachnoid, ibid. **80**:536, 1924.

is simply the lining of a bony cavity, a mechanical support for the brain and for the large sinuses needed to remove the venous blood.

The covering of the pia-arachnoid is a relatively impermeable membrane. The subarachnoid space of both the brain and the cord can be filled by injection without escape of the injection material into the subdural space. Blood introduced into the subdural space, without injury to the arachnoid, is trapped within that space and does not escape into the subarachnoid space, though macrophages may carry pigment into the arachnoid.

Within the pia-arachnoid impermeability is also marked. Among abnormal materials alcohol is the only substance to which permeability is almost complete. To methenamine, chloroform and ethyl carbonate (urethane) permeability is partial; to toxins and antitoxins it is slight or absent.[4] Zylberlast-Zand[5] has shown that this impermeability, the barrier action that protects the central nervous system, is a function of the pia-arachnoid and not of the choroid plexuses. The barrier action of the pia-arachnoid between the blood and the central nervous system has been the subject of many papers. Essick[6] believed that the cells lining the subarachnoid spaces were macrophages. Kubie and Schultz[7] demonstrated that the chief cells, the arachnoid lining cells, were distinct from the macrophages.

The arachnoid can limit the extension of infection from the subarachnoid to the subdural space, can retain fluid in edema and can prevent invasion of meningiomas; it does not organize and remove blood from the subdural space in subdural hemorrhages; though capillaries have been seen in the membrane, it has no capillary bed.

The dura does not prevent extension of infection of its tissues to the subdural space, is invaded by meningiomas, organizes and removes blood from the subdural space and has a standard capillary circulation.

Extensive injury to the dura, but without injury to the arachnoid, is not followed by adhesions.[3b] Regeneration of the dura occurs rapidly even when relatively large pieces (up to 30 sq. cm.)[8] are removed.

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4. Levinson, A.: Cerebrospinal Fluid in Health and Disease, St. Louis, C. V. Mosby Company, 1929.

5. Zylberlast-Zand, N.: Rôle protecteur de la pie-mère et des plexus choroides, Rev. neurol. **40**:235, 1924.

6. Essick, G. R.: Formation of Macrophages by the Cells Lining the Arachnoid Cavity in Response to the Stimulus of Particulate Matter, Contrib. Embryol., 1920, no. 42, p. 377.

7. Kubie, L. S., and Schultz, G. M.: Vital and Supravital Studies of the Cells of the Cerebrospinal Meninges in Cats, Bull. Johns Hopkins Hosp. **37**:91, 1925.

8. Cushing, H.: The Third Circulation and Its Channels, The Cameron Prize Lectures, New York, Oxford University Press, 1926, p. 36.

Injury to the arachnoid is followed by the formation of adhesions between the dura and arachnoid, even though the dura has not been injured.[3c] Moreover, the protective barrier action is lost if the pia-arachnoid is damaged.[5]

In studies of the response to injury of the membranes lining the subdural space one gets the impression that the dura is held in check from establishing adhesions to the arachnoid, in the normal body, only by the integrity and resistance of the cells covering the arachnoid. If these cells are damaged, adhesion promptly follows.

EMBRYOLOGY OF THE MENINGES

"The view that the meninges all come from the mesenchyme, and that the cerebrospinal fluid is an exciting agent in their differentiation has been generally accepted" (Flexner[9]). Weed,[10] to whose work we owe our knowledge of the method of production of the subarachnoid spaces, recognized that there was a difference between the cells lining the dura, which could be outlined by silver precipitation, and those covering the arachnoid, which did not lend themselves to the silver process. Harvey and Burr[3a] transplanted (*a*) cerebral hemispheres of embryos of Amblystoma punctatum (stages 28 to 30, Harrison) *without* neural crest cells and (*b*) portions of the midbrain *with* neural crest cells into other embryos of the same stages. As a result of these experiments and others on pig and chicken embryos, they concluded that the accepted view, that the pachymeninx and the leptomeninx have a common origin in the primitive mesenchyme, was incorrect, and that certain ectodermal elements, derived in large part from the neural crest, are contributed to the mesenchyme and take part in the formation of the leptomeninx. Flexner,[9] after repeating these experiments, could not agree with Harvey and Burr that the pia-arachnoid owes its origin to neural crest cells, but he found that: "Entodermal and ectodermal mesenchyme enter alike in the formation of pachymeninx and leptomeninges." Harvey, Burr and Van Campenhout[11] continued their study by chorio-allantoic grafts in chickens, and found that in the absence of neural crest the pia-arachnoid fails to develop; that mesenchymal elements are not excluded from the formation of the pia-arachnoid, and that the neural crest and the mesenchyme, aided by the presence of the cerebrospinal fluid, form the investing membranes of the central nervous system.

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9. Flexner, L. B.: The Development of the Meninges in Amphibia: A Study of Normal and Experimental Animals, Contrib. Embryol., 1917, no. 110, p. 33.

10. Weed, L. H.: The Development of the Cerebrospinal Spaces in Pig and in Man, Contrib. Embryol., 1917, no. 14, p. 86.

11. Harvey, S. C.; Burr, H. S., and Van Campenhout, E.: Development of the Meninges in the Chick, Proc. Soc. Exper. Biol. & Med. **28**:974, 1931.

Kappers [12] called attention to the fact that the external layer of the so-called dura in the spine is derived from the endosteal or endochondral connective tissue, and follows all of the sinuosities of the bones, while the internal dural membrane develops from the mesenchymatous blastoma immediately adjacent to the meninx primitiva. He believes that the outer layer in the spine should not be spoken of as a part of the dura, but as the endochondrium or endosteum of the vertebral column.

In the skull, however, there is early fusion of the membranes, which become one. After fusion the membrane serves as the internal perios-

Fig. 1.—Cell sheet from the pericardium; × 50. Compare with figure 6.

teum or endosteum of the skull, having no functions other than those of a support to the brain and to the venous sinuses, as indicated. If the dura contains ectodermal elements, as Flexner claims, they do not manifest themselves in any way that has been recognized. The dura has the character and functions of a fibroblastic membrane.

TECHNIC

In the investigation of the lining of the cavities studied, the technic employed as simple and apparently dependable. It was found possible,

12. Kappers, C. U. A.: The Meninges in Lower Vertebrates Compared with Those in Mammals, Arch. Neurol. & Psychiat. **15**:281 (March) 1926.

by scraping the surfaces of the serous cavities where they were backed up by firm connective tissue membranes, to remove the lining layer of cells in the form of sheets that could be smoothed out as continuous membranes. The end of a clean slide served as scraper, the fingers of the left hand furnishing a support in the case of the pericardium and the pleura overlying the pericardium. In the peritoneum the surface scraped was over the lining of the rectus abdominis muscle and its fascia.

The accompanying illustrations show the continuous sheet of cells which is obtained in a satisfactory preparation. The pericardium furnishes the most perfect sheets, the lining layer peeling readily from the underlying connective tissue. No suggestion of fibroblastic cells is found adhering to the cell sheet.[13]

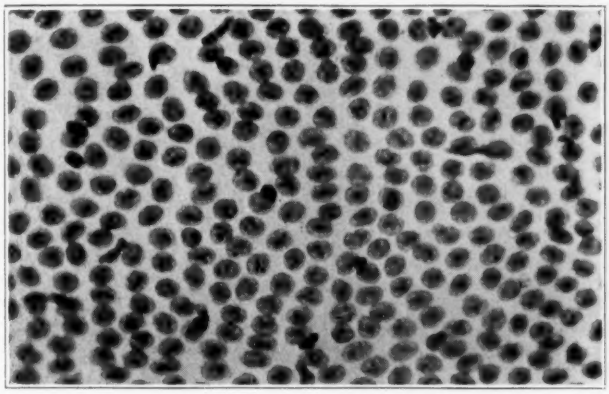

Fig. 2.—Detail of the pericardial mesothelium; × 370.

13. It is evident that in these serous cavities the lining cells do not represent flattened fibroblasts, but constitute as definite and cleancut a layer of cells as the epithelial surfaces of the body and its organs. According to Lewis: "It seems probable that endothelium is a real differentiation from the primitive mesoderm, while mesothelium is more in the nature of a transformation in the form of the cells, due to environment" (J. Exper. Med. **38**:257, 1923). He found experimentally that in cultures fibroblastic cells growing against the surface of a cover glass became flattened and withdrew their processes, and the cell bodies accommodated their edges to those of contiguous cells. In our preparations, the separation of the lining of the serous spaces from the underlying connective tissue, as a well defined layer, bespeaks a differentiation that is greater than that of form alone. Attempts to separate the endothelium-lining blood vessels as a cleancut detacheable layer, by the method described, were not successful, the subendothelial tissues of the intima tending to cling to the endothelial surface cells. The differentiation tends to be sharper, in this respect, in the case of the serous lining cells.

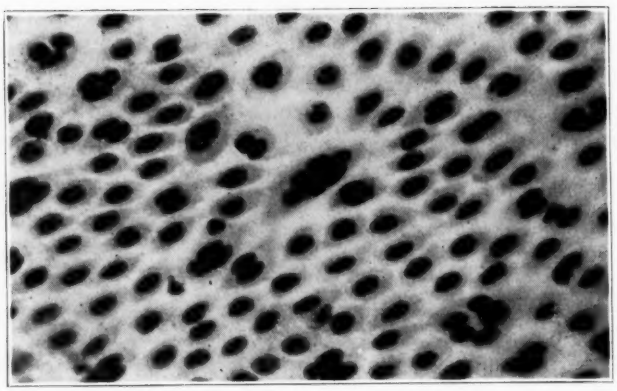

Fig. 3.—Giant cells in the pericardial mesothelium; × 370.

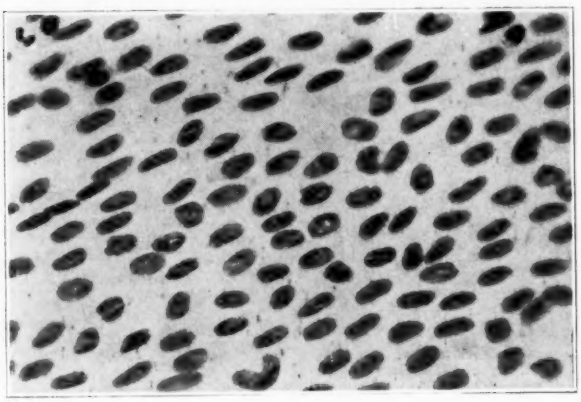

Fig. 4.—Pleural mesothelium; × 370.

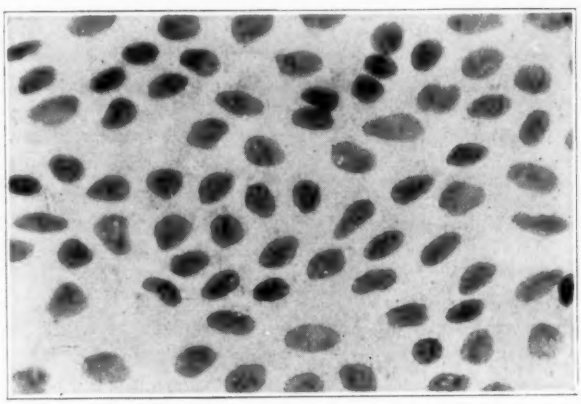

Fig. 5.—Peritoneal mesothelium; × 370.

The picture in the dura, on the other hand, is totally unlike that described in the serous spaces. The product obtained by scraping is minimal, and microscopic examination discloses largely elongated cells having the appearance of fibroblasts and showing varying degrees of fibril formation. Spreads under low power suggest preparations of young fibroblasts cultured in vitro. A small number of flattened cells with oval nuclei, which exhibit no tendency to fibril formation, are also found.

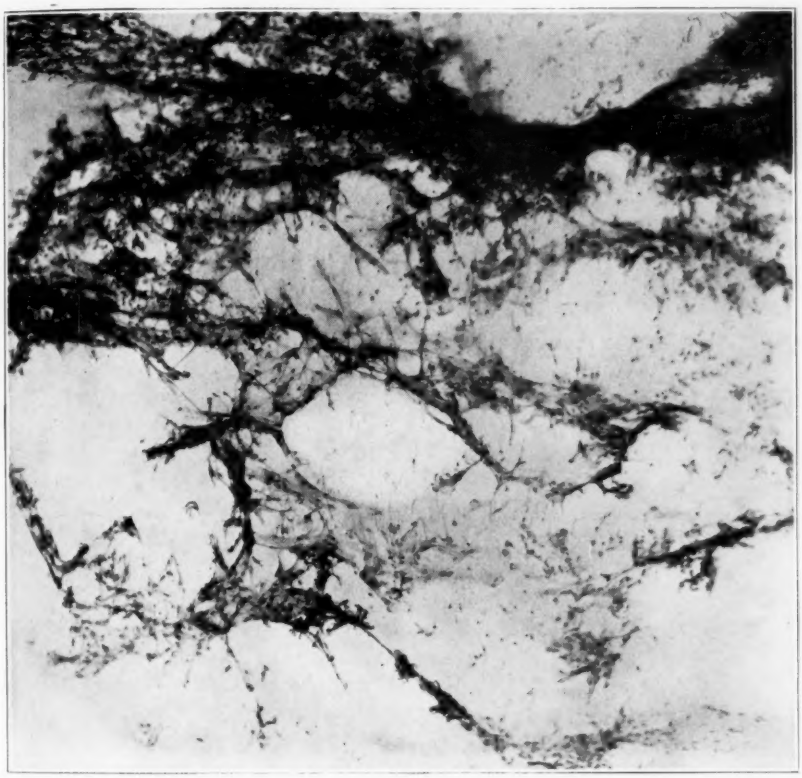

Fig. 6.—Spread of scraping from the dura; × 50.

By peeling the inner layer of the dura from the deep layers it is possible to obtain a membrane that is not too thick to stain and examine microscopically. Such peelings disclose that the dural lining is in considerable part made up of naked fibroblastic cells. Particularly along the vessels, and scattered here and there, are found collections of cells, many of which are flattened, with oval nuclei, but their presence appears to be of accidental origin. Though silver preparations may show a continuous sheet of cells, as illustrated in the embryo (Weed) and in

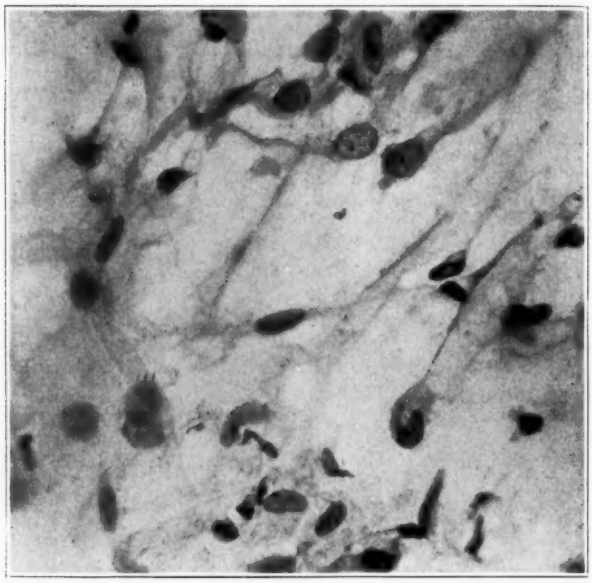

Fig. 7.—Detail of the cells found in scrapings from the dura; × 500.

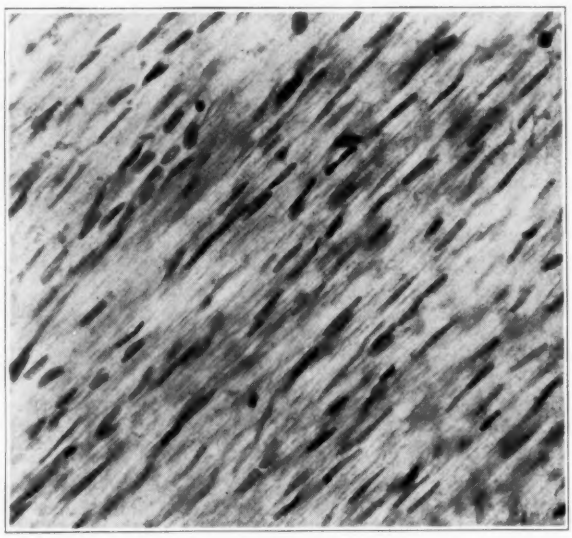

Fig. 8.—Inner surface of the dura from a peeling. The central portion of the field is occupied by fibroblasts with their elongated nuclei. On the borders and rarely in the center are the oval vesicular nuclei of flattened cells; × 235.

the adult (Key and Retzius), our preparations show only a discontinuous layer of flattened cells. The vessels on the inner surface of the dura protrude slightly into the subdural space, and it is suggested that the flattened cells that occur along and about them have their origin in explants from the arachnoid, or may arise from the flattening of fibroblasts, which Lewis [14] has found to occur experimentally. The cell whorls that are found on the dural surface arise probably from explants from the arachnoid.

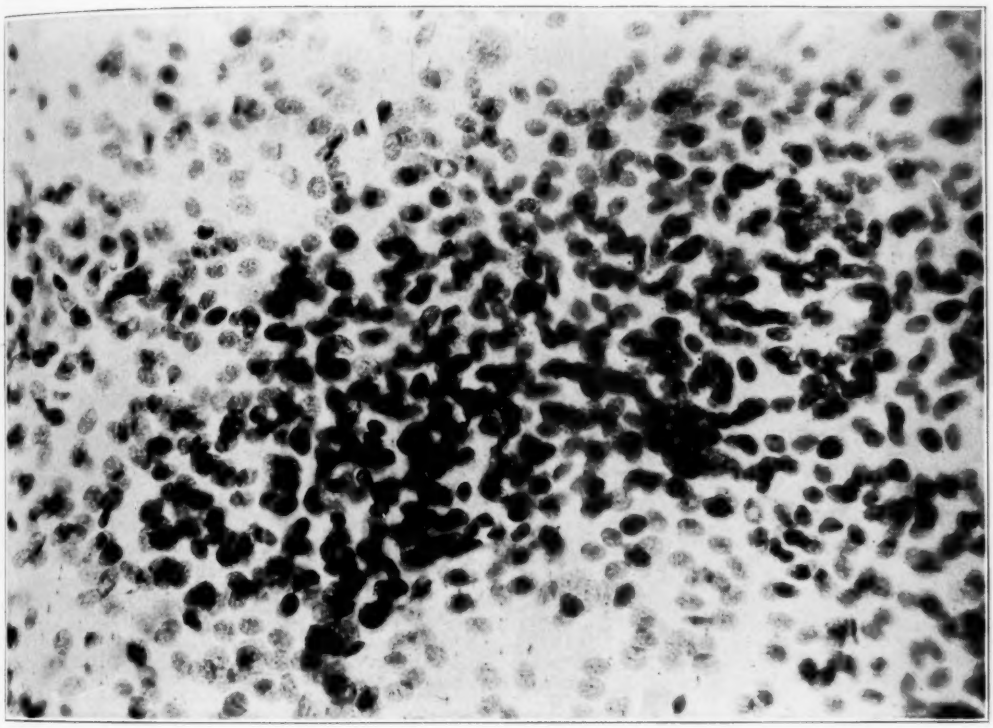

Fig. 9.—The surface of the arachnoid from a peeling. In the center of the field is a cell cluster; × 370.

Per contra, the pia-arachnoid is covered by a continuous layer of flattened cells with oval vesicular nuclei. They do not appear to be always alined in a single layer, but give one the impression of irregular arrangement. The orderly grouping shown in the serous linings does not occur here. The most perfect thin preparations of this membrane can be obtained from the cauda equina. The cell whorls, made up of cells which Cushing has named "meningocytes," are deposited with a

14. Lewis, W. H.: Mesenchyme and Mesothelium, J. Exper. Med. **38**:257, 1923.

regularity that is striking. One can occasionally demonstrate a flattened lining cell covering the surface of such a cell whorl, but in general it is not possible to follow the lining layer of cells over the tops of the cell clusters.

COMMENT

The sharp distinction between the lining of the dura and the covering of the pia-arachnoid is manifest. From this point of view it is evident that the subdural space does not correspond to the other serous cavities. The origin of the membranes that line the space perhaps explains the differences in the character of the two surfaces. The work

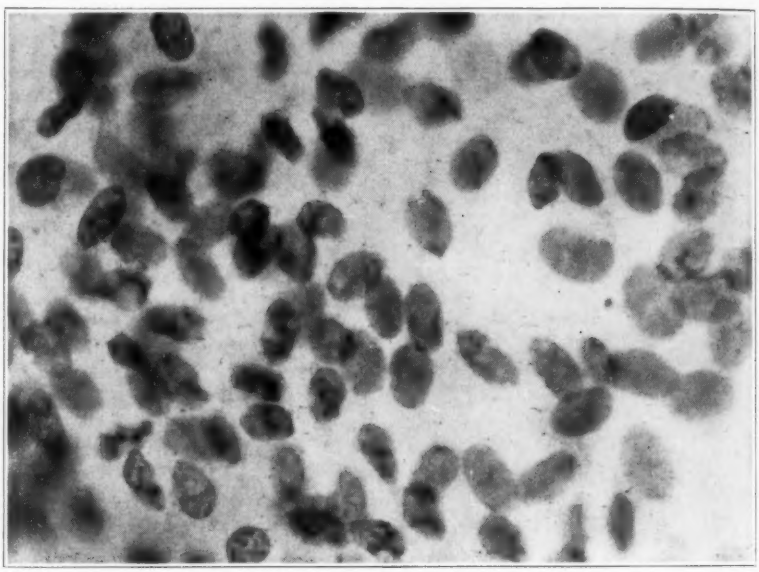

Fig. 10.—Detail of the cells of the arachnoid surface; × 560.

of Harvey and Burr indicates that the pia-arachnoid fails to develop in the absence of neural crest (ectodermic) cells. These cells apparently control the formation of the pia-arachnoid as the tissues of the mesenchyme invade and vascularize it. The relative impermeability of the membrane is explainable on the basis that its chief cells are of ectodermic origin and unlike the mesothelium covering organs in serous spaces. The formation of the subdural space embryologically is perhaps due to the separation of the surface covered by these cells from a layer of mesenchyme which becomes the inner layer of the dura.

One can account for the relative simplicity of the dura by the concept that the skull with its lining dura forms an articulation, as do other bones. In this case, however, the articulation is not with bone, but with

soft tissues, i. e., the brain and its covering pia-arachnoid. The lining on the dural side is made up of fibroblastic tissue, which Maximow [15] has demonstrated to be the lining of the other bony articulations.

The readiness of the dura to produce adhesions if the arachnoid barrier is injured is thus accounted for. The dura with its naked fibroblastic cells is analogous to any exposed connective tissue surface, prepared to form granulations and adhesions unless restrained. On this basis, not only the formation, but the persistence, of the subdural space makes it necessary to postulate an opposing surface covered by cells capable of preventing closure of the space by growth from the dura.

That mesothelium would satisfy all of the requirements indicated for the arachnoid covering and lining is improbable.

SUMMARY

Evidence is presented to prove:

1. That the subdural space does not correspond to the serous spaces.

2. That the dura is not lined by mesothelium but by fibroblastic tissue.

3. That the arachnoid is covered by cells which do not appear to be mesothelial, which are probably of ectodermal origin and to which the arachnoid apparently owes its impermeability.

It is suggested that the cranial subdural space develops as the result of the contiguity of two structures of different evolution: (*a*) the brain and the pia-arachnoid, in which ectodermal elements predominate, with reference to function; (*b*) the skull and its fused lining, the dura, with mesodermal (mesenchymal) elements predominating. These structures show continuity only at limited points.

15. Maximow, A. A.: A Text-Book of Histology, Philadelphia, W. B. Saunders Company, 1930, p. 192.

MYELITIC AND MYELOPATHIC LESIONS

III. ARTERIOSCLEROTIC AND ARTERITIC MYELOPATHY

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

Pathologic changes in the cord due to sclerosis of the spinal vessels (nonsyphilitic) are much less frequent than those in the brain due to disease of the cerebral vessels. In a series of about two hundred cases of cerebral arteriosclerosis which came to necropsy within the last six years, we could find only two which also showed sclerosis of the spinal vessels with myelopathic changes.

Myelopathic lesions from partial or complete occlusion of the vessels due to arteritis are more frequent than those due to arteriosclerosis. The changes in the vessels are the result of the direct effect of an infectious or a toxic process on the vessel walls (arteritis). These cases differ from those described under "myelitis" by the fact that in the latter the infectious agents (bacteria or their toxins) produce inflammatory changes in the cord proper. The two most common causes of vascular occlusion are atherosclerosis and syphilis; of these, syphilis is by far the most common (syphilitic thrombosis of the spinal arteries).

REPORT OF CASES OF ARTERIOSCLEROSIS

CASE 1.—L. W., a man, aged 56, was admitted to the hospital on Oct. 8, 1926, with the history that four months before admission pain in both knees, difficulty in walking and urinary and fecal incontinence had developed.

Neurologic Examination.—There were: weakness of the upper extremities; flaccid paralysis of the lower extremities; absence of all deep and superficial reflexes; a positive Babinski sign on the left; hypalgesia from the third cervical to the fifth dorsal segment; analgesia and anesthesia from the fifth dorsal to the fifth sacral segment, and loss of vibratory and joint sensibility from the toes to the fifth dorsal segment. There were also some trophic disturbances over the sacrum and hip.

Course.—The patient died on Oct. 14, 1926.

Clinical Diagnosis.—The diagnosis was infectious transverse myelitis.

Gross Examination.—The brain showed no abnormalities.

The dura appeared normal. The spinal cord was distorted, had a nodular appearance and was swollen at the fourth, sixth and ninth dorsal segments. The

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From the Neuropathological Laboratory, Montefiore Hospital.

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

anterior spinal artery was thin and empty. The veins on the posterior surface of the cord were varicose. On sectioning, the cord appeared translucent at the second, fourth and seventh dorsal segments; the anterior horns were unaffected.

Microscopic Examination.—The adventitial walls of the cerebral vessels were thickened. There were also some necrobiotic areas.

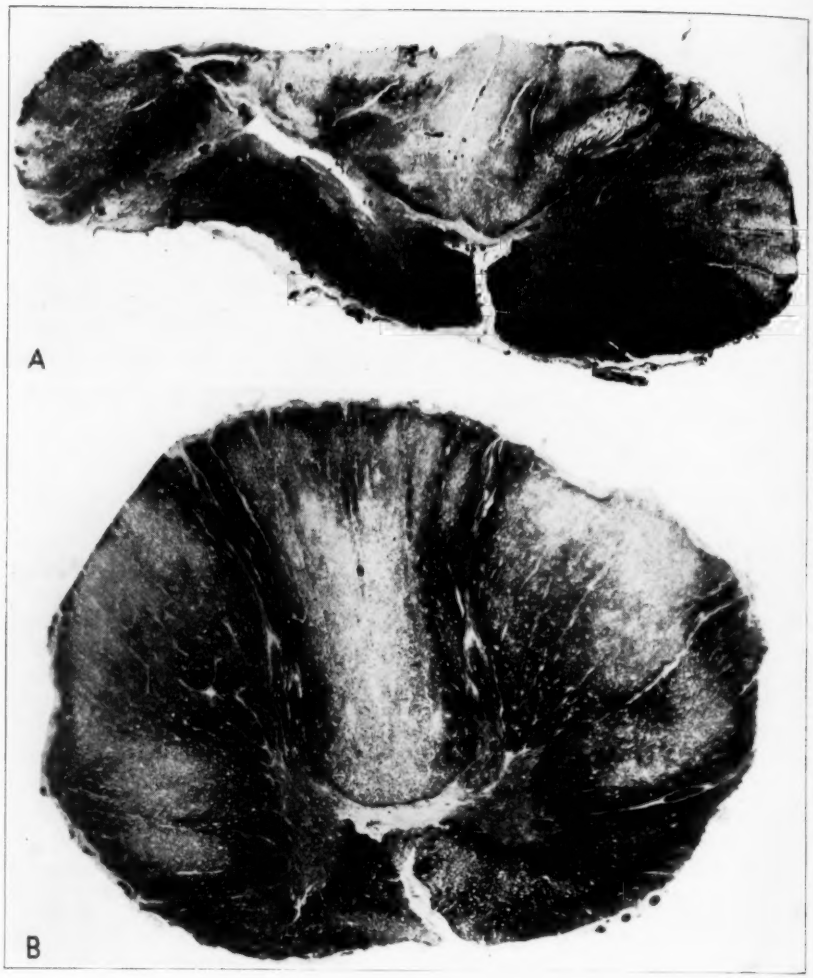
The myelin sheath stain showed demyelinization of the posterior and lateral columns at the second cervical segment (fig. 1 *A*); it was almost complete between the first and tenth dorsal segments (fig. 1 *B*), and from this tenth dorsal level down the process was a descending one. With the sudan IV stain, the demyelinated areas showed clusters of compound granular corpuscles in the adventitial spaces of the vessels. The intraspinal vessels showed extensive thickening of the adventitia and intima, with marked narrowing and complete obliteration of the lumens (fig. 1 *C*). Occasionally, so-called round cell infiltrations were seen; these, however, when stained with selective stains, were found to consist of varieties of compound granular corpuscles. The meninges were not thickened. The cresyl violet stain showed the anterior horn cells throughout the degenerated areas in various stages of disintegration; in the cervical region there was a large accumulation of pigment. Longitudinal sections stained with the myelin sheath method showed destruction of the myelin sheaths. With the Bielschowsky stain, a number of axis cylinders were seen to have undergone destruction, the few remaining ones being fragmented, swollen and of corkscrew appearance. With the Mallory and Victoria blue stains, the cord showed a tendency to gliosis, an attempt at tissue repair. The glia fibers had a parallel arrangement.

Microscopic Diagnosis.—The diagnosis was myelopathy—arteriosclerotic.

Comment.—Although clinically the level of the lesion appeared to be at the third cervical dermatome, the predominating pathologic process was between the first and tenth thoracic segments. It is noteworthy that in certain respects the histopathologic process resembled that of subacute combined degeneration in pernicious anemia. It differed, however, in its tendency toward a patchy progressive gliosis, a process rarely observed in cases of untreated pernicious anemia.[1] The gliosis was not as dense as in multiple sclerosis or in tabes dorsalis, although it was more dense than the gliosis in ascending or descending degeneration. The vessels of the cord, especially the branches of the posterior spinal arteries, showed marked atherosclerotic changes with obliteration of the lumens.

Case 2.—E. G., a woman, single, aged 43, was admitted to the hospital on June 25, 1918, with the history that in October, 1917, she began to have paroxysmal attacks of pain in the right foot. The paroxysms lasted for from fifteen to twenty minutes and were associated with stiffness in the right lower extremity and spontaneous flexion movements at the hip and knee joints. During the first four months of the illness she had also a slow and spastic gait. The pain gradually became more severe, and extended to the knee, thigh, hip and lumbar region. Later, a sensation of tightness developed in the involved extremity. In April, 1918, she was admitted to Mount Sinai Hospital and subjected to an exploratory laminec-

1. Davison, Charles: Subacute Combined Degeneration of the Cord: Changes Following Liver Therapy, Arch. Neurol. & Psychiat. **26**:1195 (Dec.) 1931.



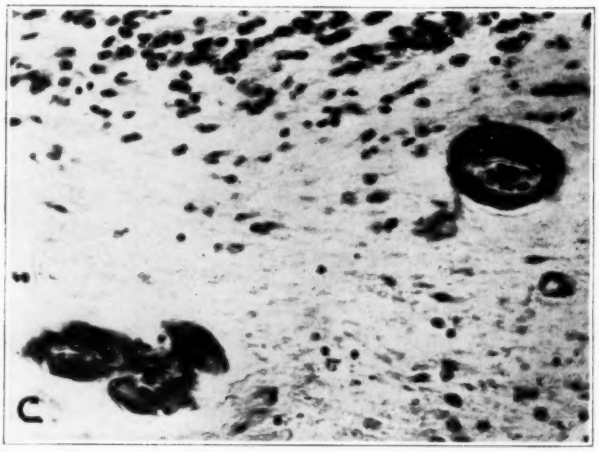


Fig. 1.—*A*, transverse section of the cervical cord, showing distortion and demyelinization of the posterolateral tracts. Myelin sheath stain (Weil modification). *B*, transverse section of the thoracic cord, showing complete demyelinization of practically all the fiber tracts. Myelin sheath stain (Weil modification). *C*, thickening of the intraspinal blood vessels and narrowing and occlusion of the lumens; Van Gieson stain; × 100.

tomy. The laminae of the first five dorsal vertebrae were removed. Following incision of the dura, a large amount of cerebrospinal fluid escaped under pressure. The cord appeared somewhat atrophic and congested. Probing of the subarachnoid space upward and downward revealed no tumor. The condition remained practically unchanged.

Examination.—General examination revealed a systolic murmur at the apex, with an accentuated second aortic sound; the blood pressure was 160 systolic and 90 diastolic.

Neurologic examination revealed evidences of bilateral involvement of the pyramidal tract in all extremities, with spasticity and contractures. There was an indefinite sensory level at about the midthoracic region, below which there was diminution in sense of pain, touch and temperature, less marked in the lower extremities, and some disturbances in posterior column sensibility in the right lower extremities. There was urinary and fecal retention, with slight trophic disturbances in the lower extremities.

Laboratory Studies.—These gave negative results.

Course.—The patient remained in Montefiore Hospital for twelve years, during which there was a gradual increase of the neurologic signs and symptoms, the sensory level ascending to the uppermost cervical region. As time went on the intrinsic muscles of the hands and lower extremities became atrophied. The blood pressure varied from 160 systolic and 90 diastolic to 186 systolic and 96 diastolic. The patient became bedridden, and spinal automatism, marked trophic (arthritic) changes and sphincteric incontinence developed. She died from bronchopneumonia thirteen years after the onset of the illness.

The various clinical diagnoses offered were: intramedullary disease of the cord, spinal gliosis, spinal pachymeningitis with secondary softenings of the cord and intramedullary neoplasm.

Gross Examination.—A small endothelioma was present in the region of the left temporal lobe. Section of the brain revealed scattered areas of discoloration. The left middle cerebral and internal carotid arteries showed definite atheromatous plaques.

The upper portion of the spinal cord appeared atrophic.

Microscopic Examination.—Sections of the brain from the scattered areas of discoloration showed hyaline degeneration of the smaller vessels. Sections of the internal carotid artery stained with resorcin-fuchsin revealed thickening of the intima and media. The changes in the medulla oblongata were similar to those in the brain.

Sections from the sixth thoracic segment, stained according to the myelin sheath methods, showed distortion and demyelinization of the posterior and lateral columns (fig. 2*A*). With the hematoxylin-eosin and Mallory phosphotungstic stains, the destroyed areas appeared homogeneous and contained numerous vessels with marked atherosclerotic and hyaline changes (fig. 2*B*). Atherosclerotic changes were also observed in the vessels of the meninges and of the posterior nerve roots, and in the gray matter. In contrast to the marked sclerotic changes in the posterior spinal arteries, those in the anterior arteries were minimal. The meninges were slightly thickened. No compound granular corpuscles were seen; the destroyed areas were replaced by glia cells and fibers. The anterior horn cells showed swelling, with eccentrically placed nuclei; some cells appeared pyknotic and showed a lack of Nissl substance. In longitudinal sections stained for myelin sheaths, these were found destroyed. With the Bielschowsky stain, the axis cylinders of the posterior and lateral columns were seen to be destroyed. The

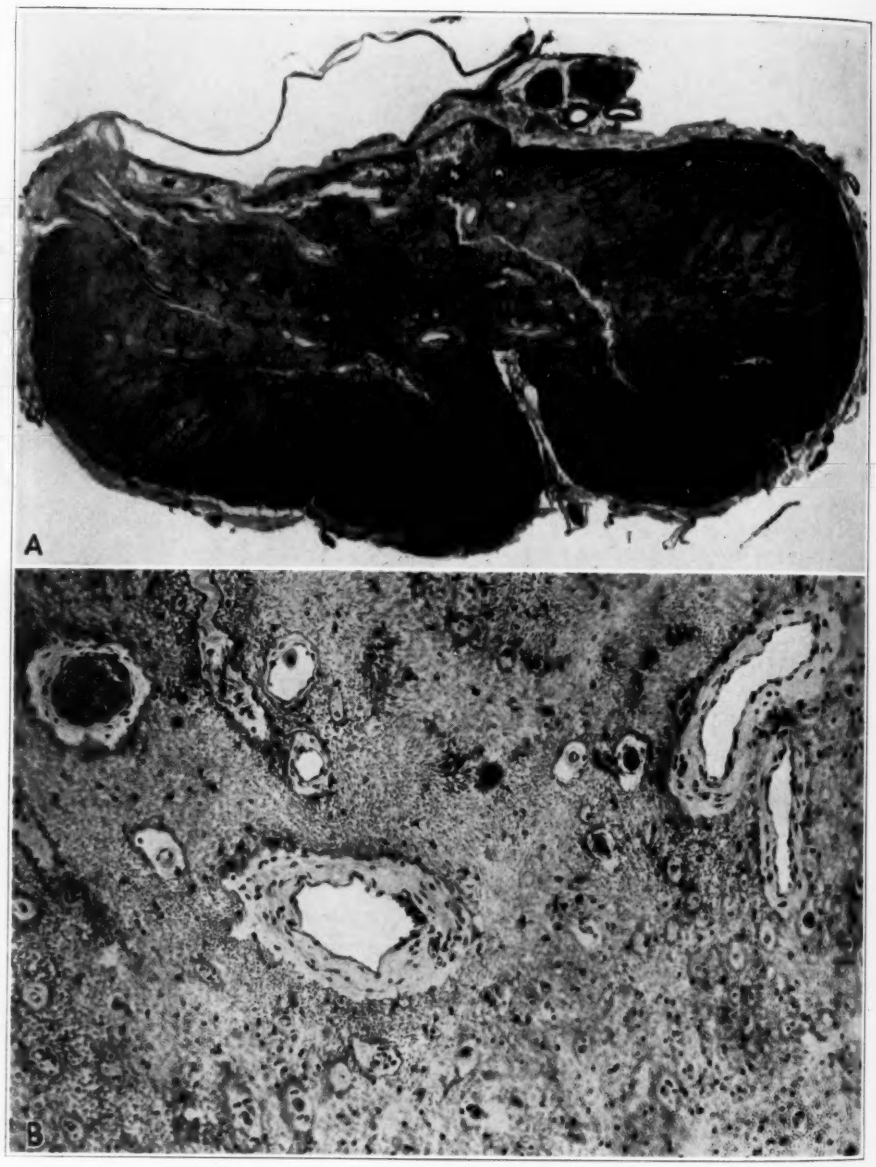


Fig. 2.—*A*, transverse section of the sixth thoracic segment, showing distortion and demyelinization of the posterolateral tracts. Myelin sheath stain (Weil modification). *B*, hyaline changes in the blood vessels from the posterolateral tracts. Hematoxylin-eosin stain; × 150.

Victoria blue stain showed the destroyed areas replaced by dense glia fibers running in a parallel direction. Sections from the ninth and eleventh dorsal and the lumbar segments showed patches of gliosis and changes in the vessels similar to those described.

Microscopic Diagnosis.—The diagnosis was myelopathy—arteriosclerotic.

Comment.—This case is undoubtedly one of cerebral and spinal arteriosclerosis, with secondary areas of softening replaced by glia tissue. The changes in the vessels were typical of atherosclerosis. It is noteworthy that at the onset of the disease the clinical picture was that of an extramedullary neoplasm. Exploratory laminectomy revealed no neoplasm, but an atrophic and congested cord with a large accumulation of cerebrospinal fluid (arachnoiditis), which probably gave rise to the symptoms of compression of the cord. The great variability and indefiniteness of signs and symptoms led to various diagnoses. This is not surprising if one attempts to correlate the pathologic findings with the clinical picture. In this connection we wish to point out that on superficial examination the appearance of the brain, brain stem and cord was not unlike that of disseminated sclerosis. Only detailed histologic examination revealed the true nature of the process, which was one of multiple softenings due to circulatory interference from arteriosclerosis. The small endothelioma found in the left temporal lobe was an accidental postmortem finding and played no rôle in the clinical features of this case.

GENERAL COMMENT

Discussion.—Henneberg [2] described arteriosclerotic processes with changes in the cord, which he designated "chronic myelitis." He included in this group the senile cord changes found in paralysis agitans, perivascular sclerosis, ischemic sclerosis and rarefactions in the form of necrotic foci. Demange,[3] Leyden,[4] Eisenlohr,[5] Oppenheim,[6] Siemerling,[7] Sanders [7] and others reported cases of senile paraplegia and senile paralysis which were attributed to a process allied to arterio-

2. Henneberg, R.: Die Myelitis und die myelitischen Strangerkrankungen, in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1918, vol. 2, p. 695.

3. Demange, E.: Contribution à l'étude des scleroses médullaires d'origine vasculaire, Rev. de méd. **4**:753, 1884; Contributions à l'étude des lesions sclereuses des vaisseaux spinaux, ibid. **5**:1, 1885.

4. Leyden, E.: Ueber chronische Myelitis und die Systemerkrankungen im Rückenmark, Ztschr. f. klin. Med. **21**:1, 1892.

5. Eisenlohr, C.: Akute Myelitis dorsalis, Virchows Arch. f. path. Anat. **73**:82, 1878.

6. Oppenheim, H.: (*a*) Textbook of Nervous Diseases, translated by Alex Bruce, New York, G. E. Stechert & Company, 1911, vol. 1, p. 331; (*b*) p. 304.

7. Cited by Oppenheim.[6a]

sclerosis and to sclerotic changes, especially in the white matter near the vessels. We have also observed similar cases, but owing to the slight and rather indefinite pathologic process which they presented, they are not included in this paper.

Although no cavitations of the cord were found in our cases, it is well to bear in mind that occasionally cavitations may occur in large areas of softenings after absorption of the degenerated products. Sometimes such cavities traverse several segments of the cord and produce a picture of syringomyelia.

REPORT OF CASES OF ARTERITIS

CASE 3.—S. L., a girl, aged 14, was admitted to the hospital on Aug. 31, 1926, with the history that four weeks before admission motor and sensory paralysis of both lower limbs and a vaginal discharge had suddenly developed. Immediately after the onset of the illness she had urinary retention and obstinate constipation, for which she was admitted to another hospital, where she was subjected to antisyphilitic treatment without benefit.

Examination.—On admission to Montefiore Hospital, medical examination gave negative results, except for the presence of a seropurulent vaginal discharge.

Neurologic examination revealed flaccid paraplegia, with absent patellar, achilles and abdominal reflexes; no pathologic reflexes, and complete loss of all forms of sensation from the fifth sacral to the fifth lumbar segments, above which there was diminution up to the eighth thoracic dermatome. There was also urinary and fecal incontinence.

Laboratory Data.—The spinal fluid contained 30 cells per cubic millimeter, but no excess of albumin or globulin. There was no evidence of subarachnoid block. The Wassermann reaction was 3 plus with the blood and negative with the spinal fluid. The blood showed a severe secondary anemia. The urine contained albumin and pus cells. A vaginal smear showed no gonococci. Roentgen examination of the vertebral column gave negative results.

Course.—The neurologic condition remained unchanged until one month after admission, when the sensory disturbances ascended to the second thoracic segment. At this time there developed pyelonephritis, and one month later bronchopneumonia, to which the patient succumbed on Oct. 10, 1926. During her stay in the hospital, the temperature was between 103 and 105 F.

Gross Examination.—Except for marked pallor, the brain showed no gross abnormalities.

On removing the spinal cord, extradural granulation tissue was found in the lower lumbar region. In the region of the cauda equina the meninges appeared thickened and the dura infiltrated with blood. The cord was thin at the eleventh and twelfth dorsal segments and on section showed grayish discoloration at the tenth dorsal segment. From the third lumbar segment to the lower sacral region, the cord appeared distorted and mushy.

Microscopic Examination.—Sections of the spinal cord, stained with the myelin sheath stain, showed almost complete demyelinization of all fiber tracts from the twelfth dorsal segment to the sacral region (fig. 3*A*). Sections from the cervical to the twelfth dorsal segments showed ascending degeneration of the posterior columns and cerebellar tracts. With the hematoxylin-eosin and sudan IV stains,

the demyelinated areas were seen to consist of conglomerations of compound granular corpuscles. The meninges were slightly thickened, and almost all branches of the anterior spinal artery showed intimal and adventitial thickening, with infiltration by inflammatory cells. In some areas the meninges were also infiltrated with compound granular corpuscles. The vessels at the fifth lumbar and first sacral segments were markedly narrowed, with almost complete obliteration of their

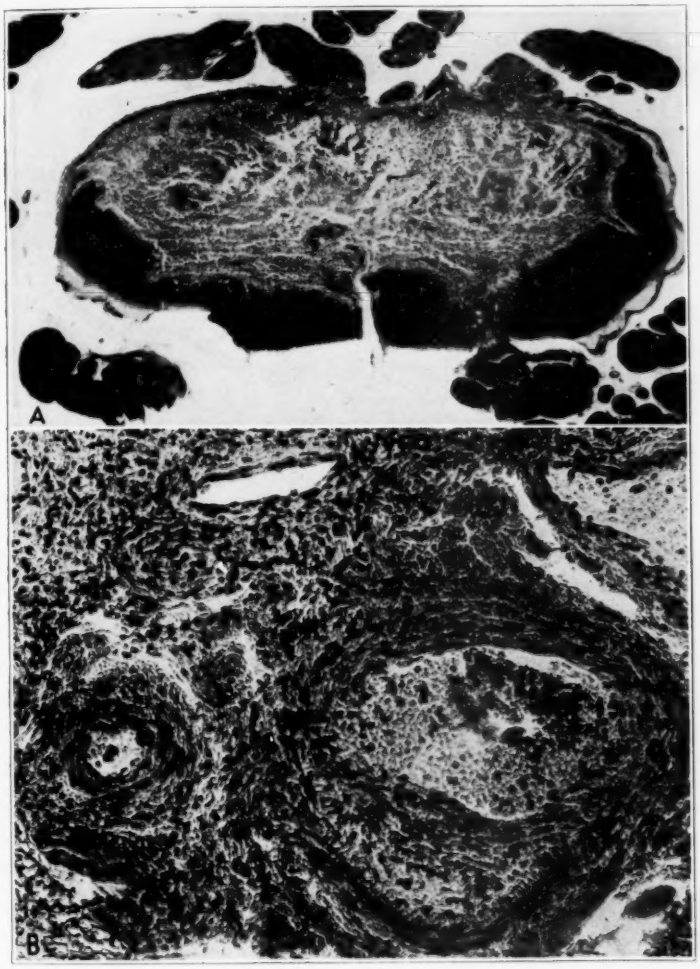


Fig. 3.—*A*, transverse section of the lumbar cord, showing demyelinization of practically all fiber tracts. Myelin sheath stain (Weil modification). *B*, thickening and infiltration of the walls of the spinal arteries. Van Gieson stain; × 150.

lumens (fig. 3 *B*). The remaining vessels of the cord showed a proliferative endarteritis. With the cresyl violet and Nissl stains, the anterior horn cells from the twelfth dorsal to the first sacral segment were seen to be completely destroyed. In longitudinal sections most of the myelin sheaths appeared completely destroyed.

With the Cajal and Bielschowsky stains, the affected areas between the twelfth dorsal and first sacral segments showed marked destruction of the axis cylinders; here and there a few axis cylinders appeared fragmented; some were swollen, and others had a corkscrew appearance. With the Mallory phosphotungstic and Victoria blue stains, there was little or no evidence of gliosis. The regressive glial changes were much further advanced than in pernicious anemia. We were unable to demonstrate, by Jahnel's method, spirochetes in the cord.

Microscopic Diagnosis.—The diagnosis was myelopathy; arteritis; syphilis (?).

Comment.—The sudden onset, the appearance of the vessels between the twelfth dorsal and fifth lumbar segments and the histopathologic picture pointed to thrombosis or occlusion of the anterior spinal artery, with secondary softening of the cord in that area. Although the blood showed a 3 plus Wassermann reaction on one occasion, it is questionable whether syphilis was the cause of the pathologic process in the cord. It is also difficult to state whether or not gonorrhea was a factor. No evidences of invasion of the cord substance by inflammatory cells were found. What appeared to be inflammatory cells were really varieties of compound granular corpuscles. The affected vessels (fig. 3*B*) resembled those observed in syphilis, although it is well known that other infections may produce similar changes. The histopathologic process within the cord would have been the same regardless of the nature of the infective organism affecting the vessel walls. In view of these facts, we are unable to determine the precise etiologic factors at play.

Case 4.—L. R., a man, aged 48, was admitted to the hospital on Oct. 26, 1926, with a history of anterior poliomyelitis at the age of 6 months, and inability to walk until the age of 7.

Eight months before admission he was ejected from a street car, landing on the street in a sitting posture. Following this, he was able to walk some distance and boarded another car, but on reaching his destination was unable to rise from the seat. He was taken to Bellevue Hospital complaining of coldness and numbness in the legs, and difficult and burning urination. He stayed there for five days, after which he was discharged. After this he was confined to bed at home for nineteen weeks, during which he had shooting pains and paresthesias in both lower extremities and gradually increasing constipation. On Dec. 25, 1925, he was taken to Mount Sinai Hospital, where he remained for six weeks. In July, 1926, he attempted to walk, but was able to do so only with the aid of a crutch.

Neurologic Examination.—On admission to Montefiore Hospital, the pupils were slightly irregular, but reacted well to light and in accommodation. The left upper extremity was weaker than the right and showed coarse fibrillations. The motor power of the lower extremities was poor (possibly a residuum of poliomyelitis). The right lower extremity was flaccid, and there was slight atrophy of the muscles of both lower extremities, which was greater on the left. The patellar, achilles, abdominal and cremasteric reflexes were absent. Sensory examination showed total loss of all forms of sensation below the third lumbar segment, impairment between the third lumbar and twelfth dorsal segments and a zone of hyperalgesia between the ninth and twelfth dorsal segments. There was loss of the sense of position in the right big toe.

Laboratory Data.—Roentgen examination disclosed advanced spondylitis in the lower dorsal and upper lumbar regions. The spinal fluid was clear and contained 3 cells per cubic millimeter. There was no subarachnoid block. The Wassermann reactions of the blood and spinal fluid were negative. The urine contained albumin and a few white and red blood cells.

Course.—The condition was stationary until July 30, 1928, when the patient became disoriented and psychotic; cystitis and bronchopneumonia developed, from which he died on August 16.

Clinical Diagnosis.—The diagnosis was degenerative lesion of the lower lumbar cord and conus following trauma. The possibilities of an arachnoiditis or of an intramedullary neoplasm of the cord were also considered.

Gross Examination.—Only part of the lower dorsal, lumbar and sacral portions of the spinal cord were available for study. On cutting the dura, the vessels of the cord were found to be prominent and tortuous. On sectioning the cord, the lumbar region appeared translucent.

Microscopic Examination.—With the myelin sheath stain, the lower dorsal segments showed demyelinization of the posterior columns and of the crossed pyramidal tracts. The direct pyramidal tracts were fairly well preserved. The lumbar segments showed demyelinization of all columns (fig. 4 *A*). Under a higher magnification, the myelin was seen to be completely disintegrated, and in some areas the cord had a hyaline appearance. With the van Gieson stain, the meninges appeared thickened. The anterior and posterior spinal arteries showed marked proliferation of the intima and adventitia and partial occlusion of the lumens, changes typical of Heubner's endarteritis syphilitica (fig. 4 *B*). In several areas of the cord there was a proliferating endarteritis, and some of the vessels showed perivascular round cell infiltration. A few of the vessels in the posterior columns were thrombosed, and some contained organized thrombi. The cord was edematous and showed signs of liquefaction necrosis. The Bielschowsky stain showed that the axis cylinders had undergone complete destruction; in the area of liquefaction necrosis, they had a slightly granular appearance. There was poor glial proliferation, as shown with the Mallory phosphotungstic and Victoria blue stains. Sections of the lumbar region (from the second lumbar to the first sacral segments), stained with sudan IV, showed an accumulation of compound granular corpuscles. The anterior horn cells, especially of the lumbar region, were in various stages of degeneration, varying from swelling, pigment atrophy and vacuolization to complete destruction. Considering the extensive involvement of the fiber tracts, the anterior horn cells were less affected.

Microscopic Diagnosis.—The diagnosis was myelopathy; arteritis; syphilis (?).

Comment.—The appearance of the vessels was that observed only in syphilis. In addition to this, there was some slight perivascular infiltration within the cord. The predominating process, however, was one of vascular occlusion of the spinal vessels followed by softening and an unsuccessful attempt at repair. It is difficult to say what rôle the poliomyelitis during infancy and the trauma three years before death played in the causation of the pathologic process. One cannot deny the possibility that the basis of the pathologic process may have been a combination of all three factors (syphilis, trauma and poliomyelitis). The changes in the vessels were chiefly those of syphilis.

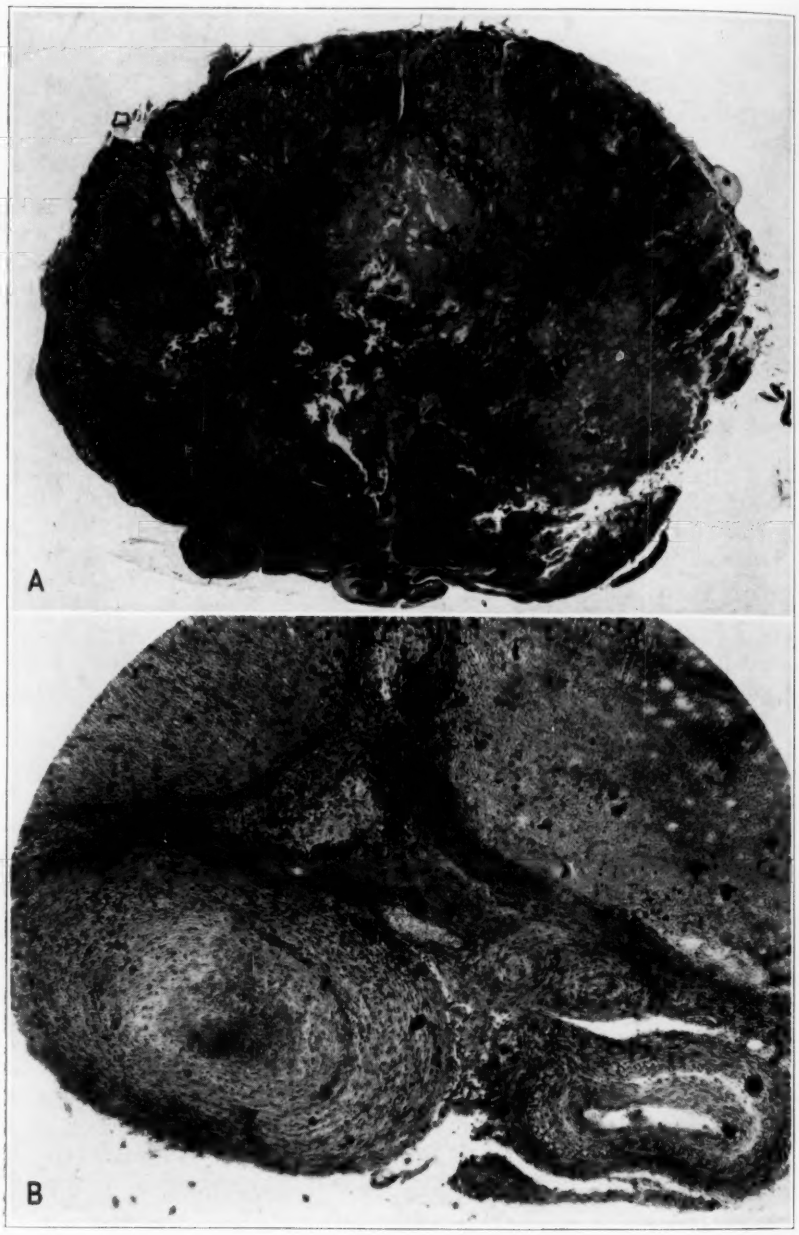


Fig. 4.—*A*, transverse section of the lumbar region, showing demyelinization of all fiber tracts. Myelin sheath stain (Weil modification). *B*, Heubner's endarteritis of the anterior spinal vessels. Van Gieson stain; × 60.

CASE 5.—G. M., a man, aged 68, was admitted to the hospital on Dec. 13, 1929, with a history of substernal pain and dyspnea on exertion for ten years. In 1924, he experienced shooting pains in the legs, and involuntary spasmodic extension movements of the left foot and toes developed. He was treated for syphilis and coronary sclerosis. In June, 1930, paraplegia and sphincteric incontinence suddenly developed.

Examination.—Medical examination revealed generalized arteriosclerosis, coronary sclerosis, chronic bronchitis and emphysema.

In June, 1930, neurologic examination revealed bilateral ptosis, a sluggish reaction of the pupils to light and in accommodation, flaccid paralysis of both lower extremities, a diminished left knee jerk, an absent left ankle jerk, a bilateral Babinski sign and absent abdominal reflexes. There was a loss of all forms of sensation from the toes to the sixth dorsal segment; the perianal region was relatively spared. There was urinary and fecal incontinence.

Laboratory Data.—The blood pressure was 88 systolic and 55 diastolic. The Wassermann reaction was negative with the blood, and 4 plus with the spinal fluid on three occasions. The gum mastic curve was 4444200000. The total protein measured 54. There were 7 lymphocytes per cubic millimeter. There was no evidence of subarachnoid block.

Course.—The patient became progressively worse, bronchopneumonia developed, and he died on April 9, 1931.

Clinical Diagnosis.—The diagnosis was thrombosis of the spinal arteries; cerebrospinal syphilis.

Gross Examination.—The brain was not removed.

The spinal cord showed a constriction at the sixth dorsal segment and thickening of the dura. The gray matter was hemorrhagic in the right cervical region.

Microscopic Examination.—Sections from the cervical region of the spinal cord, stained with the myelin sheath stain, showed partial demyelinization of the posterior columns, pyramidal tracts and cerebellar pathways (fig. 5). The cord between the third and sixth dorsal segments had a pseudoheterotopic appearance; the dura was thickened, and the outline of the fiber tracts was barely visible. The anterior half of the cord was destroyed between the sixth and eighth thoracic segments. In the lumbar and sacral segments there was descending demyelinization. With the hematoxylin-eosin and cresyl violet stains, sections from the cervical and upper dorsal regions showed thickening of the meninges and of the posterior spinal vessels, and proliferation of the intima and adventitia of the other vessels of the meninges and roots (fig. 6*A*). The substance of the cord consisted of numerous proliferated and dilated vessels (fig. 6*B*), a few of which were infiltrated by lymphocytes and plasma cells. Hemorrhages were seen in the gray matter on the right side. The ganglion cells of the dorsolateral and anterolateral columns were completely destroyed; the few remaining nerve cells in the other regions were shrunken and pyknotic, and some showed chromatolysis and neuronophagia. Similar changes were found between the fourth and eighth dorsal segments, except that about half of the cord substance was destroyed. Below the third lumbar segment there were no hemorrhages, but the intraspinal vessels showed changes resembling those described in the previous sections. In the sudan IV sections the destroyed area was filled with compound granular corpuscles. With the Bielschowsky stain, the axis cylinders in the demyelinated area were seen to have undergone marked destruction, fragmentation, swelling and granular disintegration. In sections stained with Victoria blue there was a slight gliosis, except in the hemorrhagic areas, where the glial response was poor.

Microscopic Diagnosis.—The diagnosis was myelopathy; arteritis and endarteritis; syphilis.

Comment.—The clinical history, the repeatedly positive serologic tests and the histopathologic findings of the spinal vessels pointed to myelopathy due to arteritis. The myelopathy was also secondary to the hemorrhages in the gray matter. The hemorrhages, most likely agonal processes, are analogous to the cerebral hemorrhages observed in cerebral syphilis. The inflammatory cells in the walls and perivascular spaces of the vessels of the cord substance were partly in the nature of a true

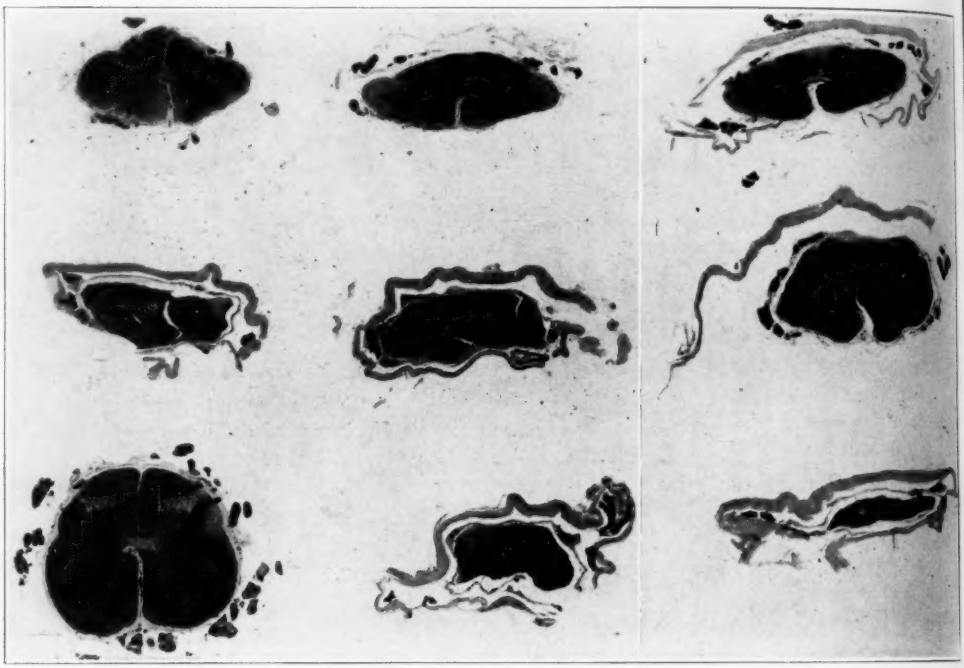


Fig. 5.—Transverse sections of the spinal cord from the cervical to the lumbar regions. Note the demyelinization of the posterior columns and crossed pyramidal tracts in the cervical and upper dorsal regions. The middorsal regions are markedly distorted, with the anterior half of the cord destroyed. The dura is thickened. Myelin sheath stain (Weil modification).

arteritis of the type seen in syphilis, and partly a secondary reactive phenomenon, or what Spielmeyer designated a "symptomatic inflammation." The essential pathologic process in this case was a myelopathy due to complete and partial vascular occlusion.

Case 6.—A. B., a woman, aged 51, was admitted to the hospital on Dec. 8, 1930. In July, 1930, difficulty in speaking and chewing, weakness in the right arm and leg and a right facial palsy gradually developed. Two months later, the difficulty in speech and chewing, as well as the facial paralysis, cleared up, but the weakness

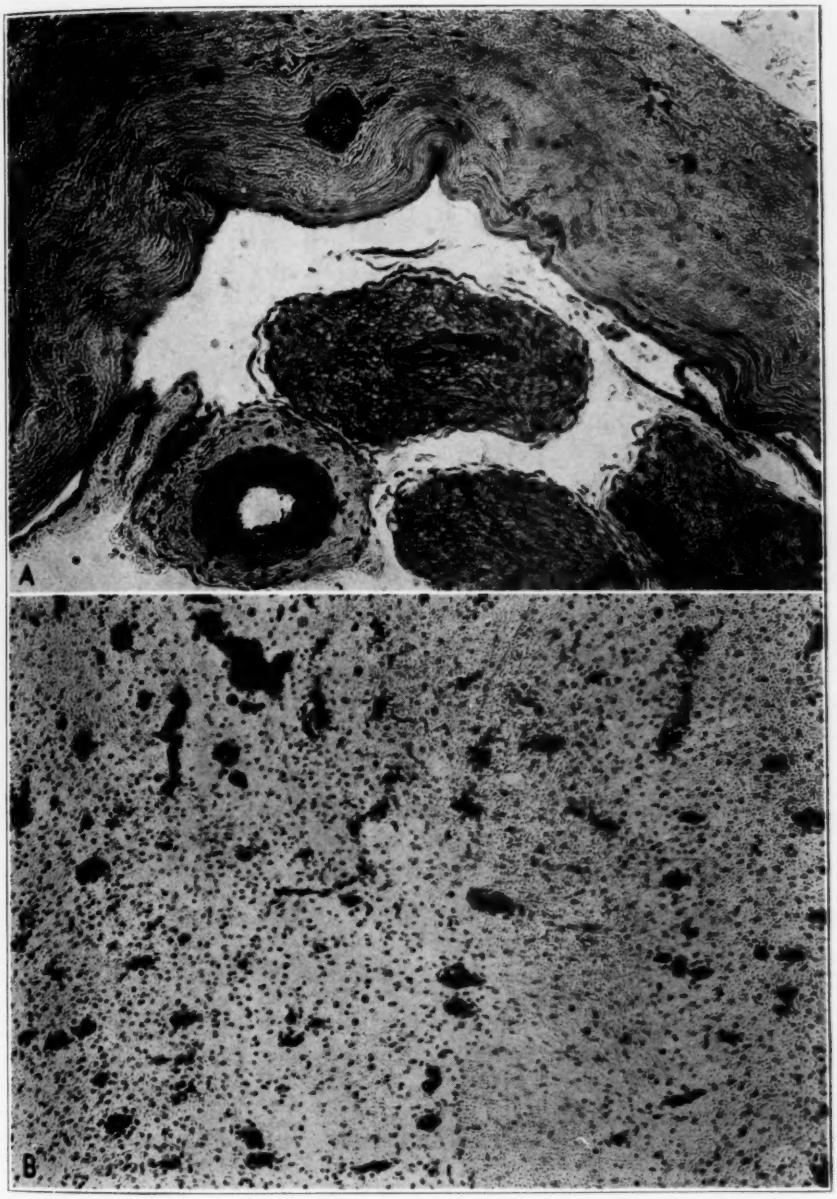


Fig. 6.—*A*, thickened dura and proliferation of the intima and adventitia of the posterior spinal vessels. Cresyl violet stain; × 100. *B*, proliferation, endarteritis and dilatation of the smaller vessels of the cord substance. Cresyl violet stain; × 100.

of the right arm and leg increased. In November, 1930, there was a recurrence of the speech disturbance. From the onset of the illness she had constant headaches and frequent dizzy spells, but never lost consciousness. One week before admission she began to vomit.

Examination.—There was an enlarged heart, with a soft systolic murmur which was loudest at the apex and transmitted over the precordium.

Neurologic examination showed a coarse tremor of the right hand and jaw. There were slight left internal strabismus, questionable weakness of the right superior rectus and coarse nystagmus in all directions. Extreme lateral gaze to the left could not be maintained for more than a few seconds. The pupils were equal and reacted normally to all stimuli. There were hypalgesia and hypothermesthesia in the distribution of the left trigeminus. There was no corneal hypesthesia. There was no atrophy of the muscles supplied by the motor branch of the trigeminus. There was a slight right peripheral facial weakness. The palate moved poorly but equally on both sides. The right shoulder could not be raised as well as the left. There was no atrophy or weakness of the sternocleidomastoid and trapezii muscles. The tongue deviated to the right. There were slight hypotonia of the right upper extremity, clumsiness of the right hand, weakness of the right upper and lower extremities and pyramidal tract signs in the right upper and lower extremities. There were hypesthesia and hypothermesthesia over the entire left side of the body and face. All other forms of sensation were normal. The speech was dysarthric and nasal.

Laboratory Data.—The blood pressure was 160 systolic and 80 diastolic. The Wassermann reaction of the blood was 4 plus on two occasions. Manometric studies showed evidences of complete subarachnoid block. The spinal fluid showed a Froin syndrome; the total protein was from 114 to 154 mg.; the Wassermann reaction was negative; there were 90 lymphocytes per cubic millimeter; the gum mastic curve was 0024100000. Iodized poppy seed oil 40 per cent, which was injected on Dec. 30, 1930, was arrested at the fifth dorsal vertebra.

Course.—The patient received intensive antisyphilitic treatment without benefit. She died of bronchopneumonia on Jan. 16, 1931.

Clinical and Anatomic Diagnosis.—The diagnosis was pachymeningitis, with myelopathy due to vascular obstruction (syphilis); cerebral thrombosis; gumma of the pons and medulla oblongata; bronchopneumonia.

Gross Examination.—There were an area of softening of the left neostriatum of the brain and a gumma of the pons and medulla oblongata. The histologic findings in these structures are omitted.

The dura in the midthoracic region was markedly thickened, and the cord appeared completely destroyed.

Microscopic Examination.—A section from the eighth thoracic segment of the spinal cord showed extensive thickening of the meninges, which were adherent to the cord. The latter was completely destroyed and showed cavitation (fig. 7). The meninges and cord were the seat of one mass of inflammation consisting of lymphocytes and of plasma and endothelial cells. Most of the vessels showed extensive thickening of the walls. The latter were infiltrated by inflammatory cells of the type usually seen in panarteritis. There were also observed evidences of periarteritis. Some of the vessels were typical of Heubner's endarteritis syphilitica. The nerve cells, as well as the myelin sheaths, axis cylinders and glia, were completely destroyed. There was an ascending and descending degeneration of the segments above and below this level.

Microscopic Diagnosis.—This diagnosis was myelopathy; arteritis; syphilis.

Comment.—Different pathologic processes were found in the central nervous system in this case. There were an area of softening in the neostriatum and internal capsule, a gumma in the pons and medulla oblongata and an arteritis and pachymeningitic process in the midthoracic region of the cord. Owing to the presence of neostriatal and pontile symptoms, the level of the lesion of the cord could not be determined clinically until an injection of iodized oil was performed. The cord was mushy in the midthoracic region, and on removal purulent material exuded from it. It is difficult to state definitely whether the pathologic process was due solely to vascular obstruction or to a combination of vascular obstruction and meningeal inflammation. The changes in the

Fig. 7.—Transverse section of the right dorsal segment, showing thickening of the meninges, which adhered to the spinal cord. Cavitation of the greatest part of the spinal cord. Myelin sheath stain (Weil modification).

vessel walls with secondary circulatory interference were sufficient to account for the main pathologic process in the cord, which was one of myelopathy.

CASE 7.—H. L., a man, aged 57, was admitted to the hospital on Jan. 12, 1931, with the history that in 1927 paralysis of the left upper and lower extremities, some disturbance in speech and difficult urination suddenly developed. The hemiplegia gradually cleared up. In August, 1930, he again began to have difficulty in walking.

Neurologic Examination.—On admission, the left pupil was irregular and miotic and reacted poorly to light. There were: weakness of the left lower extremity;

an ataxic gait; ataxia in the finger-to-nose test; a positive Romberg sign, and clumsiness in performing skilled acts. The triceps reflexes could not be elicited. The left abdominal reflexes were absent. The left knee and ankle jerks were more active than the right. There was no Babinski sign. There were bilateral Mendel-Bechterew and left Rossolimo signs. Sense of pin prick was diminished over the right lower extremity and up to the tenth dorsal segment. In this extremity he called hot, cold, and cold, hot. Sense of touch was unimpaired. Vibration sense was lost from the toes to the sacrum. There was impaired position sense in the toes. Urinary incontinence was present.

Laboratory Data.—The Wassermann reaction of the blood and spinal fluid and the gum mastic test were negative. The blood pressure was 180 systolic and 105 diastolic. The urine was normal. At another hospital, the patient had had a 4 plus Wassermann reaction of the blood.

Course.—The patient was subjected to antisyphilitic therapy without much benefit. On July 2, 1931, an intractable hiccup developed, and he died on July 24.

Clinical Diagnosis.—The diagnosis was myelopathy; syphilis.

Gross Examination.—The brain showed no abnormalities.

There was translucency of the posterior columns and crossed pyramidal tracts of the spinal cord.

Microscopic Examination.—The outstanding picture of the brain was sclerosis of the cortical vessels. The right vertebral artery showed a markedly thickened intima and splitting of the lamina elastica. There were calcareous deposits between the media and the intima. In one area there was a slight inflammatory focus between the adventitia and the media.

Sections of the spinal cord, stained with the myelin sheath stain, showed extensive thickening of the meninges in the lower cervical and upper thoracic regions. The pia-arachnoid was more thickened than the dura. The lower cervical region showed demyelinization of the posterior columns (fig. 8), the cerebellar pathways and part of the crossed pyramidal tracts; in sections below the latter, the columns of Burdach were more demyelinated than those of Goll. There was also demyelinization of the pyramidal tracts and of the cerebellar pathways in the upper dorsal segments. In the lower dorsal region the demyelinization in the posterior columns was less extensive. In the cresyl violet sections of the cervical region, the meninges were markedly thickened. The pia-arachnoid consisted of proliferated arachnoidal cells; inflammatory cells were absent. Throughout the pia-arachnoid the spinal arteries were extensively thickened, especially the intima; this was best observed in the lateral spinal artery. There was partial demyelinization of the posterior roots, and their vessels were hyalinized. The small vessels of the cord substance showed slight thickening. Throughout the cord there were small necrobiotic areas, especially in the ventrocerebellar pathways. The anterior horn cells, except for occasional pyknosis and corkscrew processes, showed nothing of note. Despite the extensive thickening of most of the spinal vessels, their lumens were not completely obliterated. In longitudinal sections the disintegration of the myelin was found in the posterior and lateral columns of the lower cervical and upper dorsal segments. The axis cylinders showed various stages of destruction; some were broken down, others were swollen, and still others had a corkscrew appearance. In the Victoria blue preparations, the glia showed slight regressive changes in the areas of destruction.

Microscopic Diagnosis.—The diagnosis was myelopathy; endarteritis; syphilis.

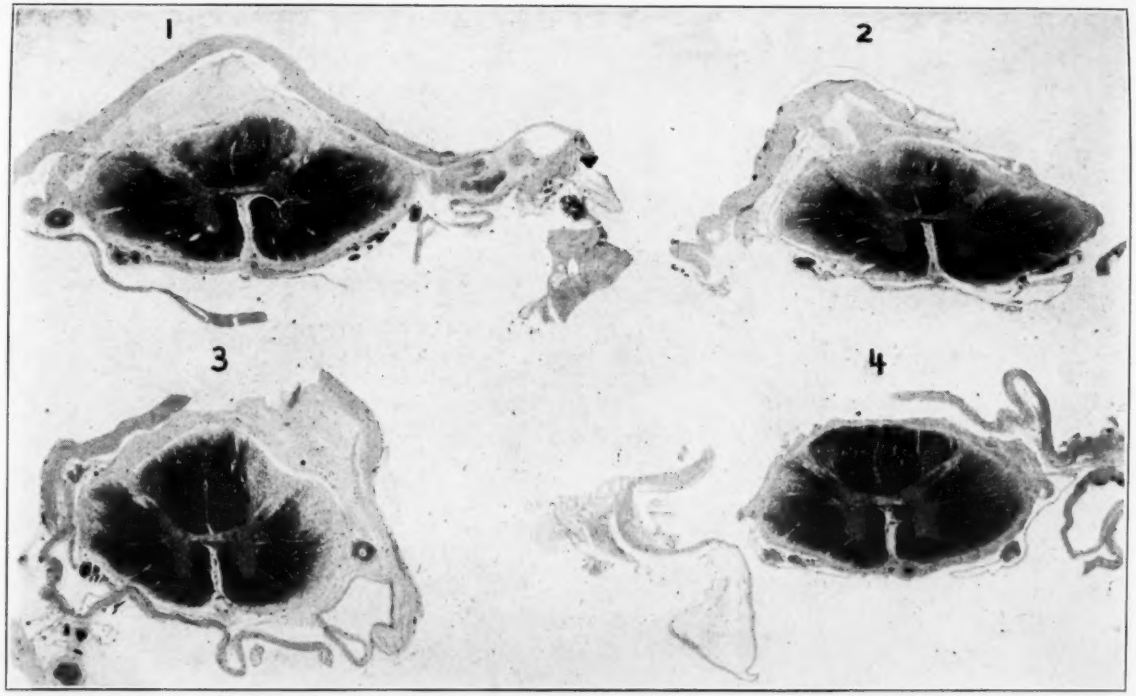


Fig. 8.—Transverse sections from the lower and upper thoracic regions (*1, 2* and *3*), showing thickening of the pia-arachnoid, demyelinization of the dorsocerebellar pathways, crossed pyramidal tracts and partial demyelinization of the posterior columns. Section from the lower dorsal region (*4*), showing demyelinization of the crossed pyramidal tracts.

Comment.—The vessels of the spinal cord, especially the posterolateral ones, showed marked endarteritic changes. This accounted for the limitation of the pathologic process to the posterolateral surface of the cord. Owing to the incomplete obliteration of the vessels, the demyelinization was not as extensive as in the myelopathies due to complete vascular occlusion. Part of the demyelinization in the posterior columns may also be accounted for by the thickening of the pia-arachnoid, which was most severe over the lower cervical and upper dorsal regions. In the lower dorsal region, where the pia-arachnoid over the dorsal columns was not thickened, there was only slight demyelinization of the columns of Burdach; this, however, may have been secondary to the demyelinization of the posterior roots. The posterior roots were demyelinated on account of the extensive hyalinization of the vessels.

CASE 8.—Y. K., a woman, aged 30, was admitted to the hospital on Feb. 4, 1929, with a history of tuberculosis since 1912. In March, 1929, lancinating pains in the right thigh and weakness in the right lower extremity developed.

Examination.—Medical examination revealed extensive bilateral pulmonary tuberculosis and a right tuberculous hip.

Neurologic examination showed weakness of the left upper and right lower extremities, which was most marked in the extensors of the foot. There was slight hypertonicity of the right lower extremity, as well as atrophy in the muscles above the right knee. The deep reflexes were hyperactive, more so in the right lower extremity. There was a right Babinski sign. Sensory examination revealed hypesthesia, hypalgesia and hypothermesthesia below the fourth dorsal dermatome, except in the perianal region, in which sensation was normal. There was diminished vibratory sensibility in both lower extremities, with disturbances in the postural sense of the right big toe.

Laboratory Data.—The sputum was positive for tubercle bacilli. The urine contained albumin, hyaline and granular casts and white and red blood cells. Lumbar puncture revealed partial subarachnoid block. The spinal fluid contained 7 cells per cubic millimeter and a total protein of 41.5. Roentgen examination showed arthritic changes in both sacro-iliac synchondroses.

Course.—The patient remained in status quo until four months before death on April 7, 1930, when there appeared also a slight Horner's syndrome on the left side.

Clinical Diagnosis.—The diagnosis was abscess of the spinal cord.

Gross Examination.—On removing the spinal cord, about 5 cc. of thick, purulent material exuded at the level of the second dorsal segment. A smear for tubercle bacilli from this material gave negative results. The cord showed several constrictions and felt soft between the first and sixth thoracic segments. On cutting the cord, the fiber tracts in the cervical and upper dorsal regions could not be made out.

Microscopic Examination.—With the myelin sheath stain, a section of the cord at the upper level of the constriction was seen to be completely distorted; only some remnants of white fiber tracts and gray matter could be seen (fig. 9*A*). Under a higher power lens, most of the myelin sheaths were seen to have undergone marked destruction, those remaining being swollen and disintegrated. With the hema-

toxylin-eosin stain, the pia-arachnoid was seen to be markedly thickened, and between it and the cord there were numerous accumulations of lymphocytes, plasma cells and endothelial cells (fig. 9 *B*). The blood vessels of the meninges were thickened, and the adventitial coats were infiltrated by inflammatory cells. Occa-

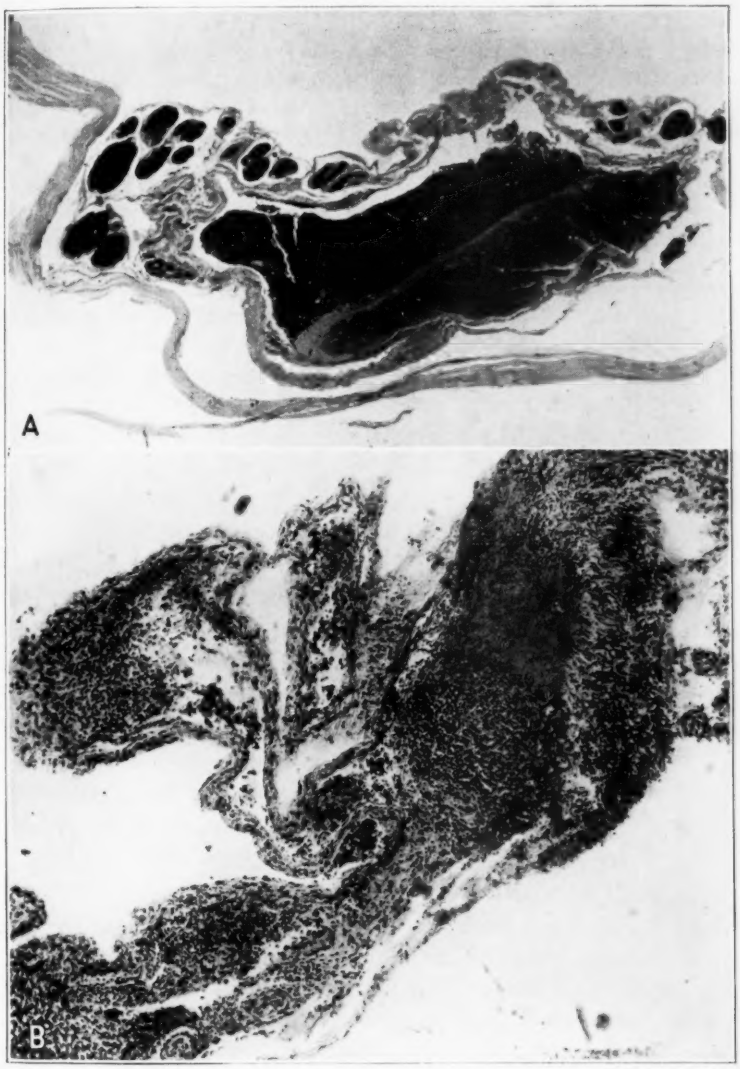


Fig. 9.—*A*, transverse section of the spinal cord in the upper dorsal region, showing distortion of the spinal cord. Myelin sheath stain (Weil modification). *B*, section showing the inflammatory process found in the subarachnoid space. Note the small thickened vessels; × 90.

sionally, giant cells were observed. The lymphocytes, although limited to the space between the meninges and the spinal cord, invaded some of the roots and in

one segment penetrated into the cord substance. In sections stained with sudan IV, the remaining fiber tracts were filled with compound granular corpuscles, which clustered around the blood vessels. In sections stained with Mallory's phosphotungstic acid stain, the destroyed cord appeared honeycombed. There were proliferation of the blood vessels and a poor glial response. Sections in the areas of constriction, stained with cresyl violet, showed that only a few anterior horn cells were left, and these had also undergone various changes: swelling, loss of Nissl substance, eccentricity of the nuclei, ischemia, shrinkage and complete neuronophagia. Longitudinal sections, stained with the myelin sheath stain, showed a marked destruction of myelin. With the Bielschowsky stain, most axis cylinders were seen to be completely destroyed, those remaining being broken down and swollen, with a corkscrew appearance. In sections stained with Victoria blue, there was a poor glial reaction. Sections below the third dorsal segment showed marked compression and distortion of the cord. The anterior and posterior spinal arteries were infiltrated with round cells and had narrow lumens. The sections of the cord where these vessels were obstructed showed numerous accumulations of compound granular corpuscles. The changes between the eighth and twelfth dorsal segments were not pronounced. Except for a descending demyelinization of one of the crossed pyramidal tracts, no noteworthy changes were observed in the lumbar and sacral regions.

Microscopic Diagnosis.—The diagnosis was myelopathy; periarteritis (tuberculosis); infectious myelitis, slight.

Comment.—At necropsy, thick purulent material exuded from the cord at about the second thoracic segment. Histopathologic study of sections taken from this level showed that the space between the leptomeninges and the spinal cord was filled with round, plasma, endothelial and occasional giant cells. These changes were part of a tuberculous abscess within the subarachnoid space. As a result of this inflammatory mass, the spinal cord was subjected to two types of changes: (1) perivascular infiltrations, thickened adventitial coats and compression of the vessels and cord by the abscess, leading to vascular obstruction; (2) a direct invasion of the spinal cord at its margins by the inflammatory process. The latter process was less extensive than the former.

GENERAL COMMENT

Six cases are included in the arteritic group. In case 3, the positive Wassermann reaction of the blood and the changes in the vessels of the cord suggested syphilis as the etiologic factor. In case 4, the symptoms of involvement of the cord came on suddenly after a fall; the vessels resembled those observed in syphilis, although the absence of a history of syphilis and positive serologic tests seem a priori to exclude this disease as a cause. Trauma of the cord could not produce this type of vascular change, although it might have precipitated vascular occlusion. There were no evidences of infection or intoxication to which the endarteritis of the spinal vessels could be attributed. As far as we know, the type of vessel change found in this case has never been

described in poliomyelitis, a disease which the patient is said to have had early in childhood. In case 5, the clinical history and serologic and histopathologic evidences were definitely syphilitic. In addition to intimal and adventitial thickening of the meningeal vessels, there were proliferating endarteritis and dilatation and hemorrhages of the vessels of the cord substance. The inflammatory cells found in some of the walls and perivascular spaces of the vessels were partly due to syphilis and partly to a secondary reaction—"symptomatic inflammation" (Spielmeyer). The essential histopathologic picture in the cord was a myelopathy due to circulatory interference. In case 6, the clinical picture was obscured by signs of involvement of the neostriatum, pons and medulla. The process in the midthoracic region of the cord was definitely myelopathic and due to syphilitic endarteritis. In case 7, the myelopathy was due to the endarteritic changes of the lateral spinal arteries and slightly to the thickened pia-arachnoid. The involvement of the posterior roots was due to the hyalinization of its vessels. In case 8, the abscess between the meninges and the cord led to a twofold process: (1) compression of the vessels followed by vascular interference, and (2) arteritis and periarteritis, with ensuing myelopathy, also due to vascular interference. The slight inflammation found at the periphery of the cord was insufficient to account for the entire symptomatology in the case.

In all cases the changes in the myelin sheaths and the axis cylinders were essentially similar. The glial response was poor in all. There was a slight gliosis in case 5.

The changes in the cord in these cases were not due to infection but to circulatory interference from vascular occlusion. Some evidences of slight inflammation were found only in three cases (cases 4, 5 and 8); this, however, was not sufficient to account for the predominating pathologic process. In syphilis and tuberculous meningitis, slight inflammatory changes may be found at the periphery of the cord in the form of wedge-shaped cones and bands projecting into the white matter, whereas other parts of the cord may show softening as a result of vascular obstruction. As is well known, the pial vessels are rarely spared in syphilis and tuberculosis and are usually the starting point of the pathologic process. Cavity formation may occur in cases of softening when the glia fails to proliferate. Exceptionally only may an isolated gumma be found in the cord.

In vascular syphilis of the cord, a complete transverse lesion, without involvement of other parts of the neuraxis, is unusually rare. In our series only one case (case 3) showed a transverse myelopathic process with no other involvement of the nervous system.

Some older writers, such as Leyden,[4] Gowers [8] and others, included cases of syphilitic meningomyelitis under the head of "chronic myelitis." Bastian [9] long ago recognized that "true inflammatory softenings very rarely occur as pathologic states," and that most of the cases are due to thrombosis of the vessels. Similar views were held by Oppenheim,[6b] Bruns,[10] Schmauss,[11] Singer,[12] Rosin [13] and others.

Spiller [14] also emphasized that "A rapidly developing paralysis of the lower limbs or of all four limbs is suggestive of thrombosis of the vessels of the spinal cord, and the resulting lesion is one of myelomalacia. It is not an infrequent development in spinal syphilis, and when it occurs in such cases it is still the result of thrombosis of the vessels of the cord sclerotic from syphilis." Mon-Fah Chung [15] and others stressed the importance of syphilis in thrombosis of the spinal arteries. In some of Chung's cases there was very little meningitis associated with the thrombosis. Our cases would seem to confirm the views held by these observers. In this connection it is noteworthy that Henneberg mentioned cases of myelomalacia following syphilis in which neither endarteritis nor gummatous processes could be demonstrated.

SUMMARY

Myelopathic lesions secondary to circulatory interference within the cord from partial or complete occlusion of the spinal or meningeal vessels, or of both, may be due to arteritis or to arteriosclerosis. Of these, the latter, in contrast to the frequency of cerebral lesions due to atherosclerosis, is unusually rare, arteritis being much more common. In our eight cases of myelopathy due to vascular disease, there were two cases of atherosclerosis and six cases of arteritis. In the latter, syphilis was a factor in five cases and tuberculosis in one. Except for the changes in the vessels, the histopathologic picture of the arteritic group does not differ essentially from that of toxic myelopathy. Clini-

8. Gowers, W. R.: Diseases of the Nervous System, Philadelphia, P. Blakiston's Son & Co., 1903, vol. 1.

9. Bastian, H. C.: Thrombotic Softening of the Spinal Cord as a Cause of So-Called Acute Myelitis, Lancet **2**:1531, 1910.

10. Bruns: Ueber Myelitis, Neurol. Zentralbl. **15**:518, 1896.

11. Schmauss, H.: Die Anwendung des Entzündungsbegriffes auf die Myelitis, Deutsche Ztschr. f. Nervenh. **26**:390, 1904.

12. Singer, H. D.: The Pathology of So-Called Acute Myelitis, Brain **25**:332, 1906.

13. Rosin, H.: Akute Myelitis und Syphilis, Ztschr. f. klin. Med. **30**:129, 1896.

14. Spiller, W. G.: Rapidly Developing Paraplegia Associated with Carcinoma, Arch. Neurol. & Psychiat. **13**:471 (April) 1925.

15. Chung, Mon-Fah: Thrombosis of the Spinal Vessels in Sudden Syphilitic Paraplegia, Arch. Neurol. & Psychiat. **16**:761 (Dec.) 1926.

cally, cases of myelopathy due to arteritis present unusual difficulties in diagnosis. They may begin suddenly or gradually; they may begin with signs and symptoms of a level lesion of the cord; some of them may show evidences of diffuse involvement of the neuraxis at the onset; others may present a clinical picture of infectious myelitis, posterolateral sclerosis or multiple sclerosis, and still others may present a picture of an intramedullary or an extramedullary neoplasm. Of diagnostic aid may be the fact that soon after the onset there appear symptoms indicative of involvement of other components of the neuraxis, resembling in this respect the cases of toxic myelopathy. Another helpful diagnostic aid is the finding of clinical, serologic or cytologic evidences of syphilis.

Histopathologically, the atherosclerotic group showed marked destruction of the nerve cells, myelin sheaths and axis cylinders, accompanied by dense gliosis. In the arteritic group the changes were similar, except that the glial response was poor.

RHYTHMIC MYOCLONUS OF THE MUSCLES OF THE PALATE, PHARYNX, LARYNX AND OTHER REGIONS

A CLINICAL REPORT OF THREE CASES

HENRY ALSOP RILEY, M.D.
AND
SAMUEL BROCK, M.D.
NEW YORK

Of all the interesting manifestations that disordered function of the central nervous system may occasion, abnormal involuntary movements are perhaps the subject of the most intensive investigation and the greatest discussion. When these movements appear in the superficial musculature they naturally attract the attention of the clinician and the patient, but when they occur in less conspicuous muscles they often remain undiscovered, or are ignored and receive less attention than their inherent interest would seem to warrant. To this second group belong the abnormal involuntary movements of muscles, such as those of the palate, pharynx, larynx, diaphragm and other structures.

The syndrome to be described consists of constantly recurrent rhythmic contractions of certain muscles, chief among which are the muscles of the oropharynx. In the patients who manifest the fully developed picture of the disorder there are, in addition to the abnormal involuntary movements, other evidences of disturbed function due to interference with the normal action of the structures in the cerebellomesencephalometencephalic regions of the brain.

These rhythmic movements of the larynx, pharynx, etc., have received a number of different designations; the one which was originally used and which appeared in the majority of the published reports was "nystagmus." The term would seem rather unfortunate because nystagmus, by definition, means only a nodding. By long usage the term nystagmus has been associated throughout all medical literature with the movement of the eyes due to a disturbance of the oculomotor mechanism induced by disease or experiment. This restriction of the term nystagmus is so well recognized and the derivation of the word implies a movement so foreign to the subject in question that it would seem unwise to extend the use of the term to the abnormal involuntary movements under discussion. The other unqualified term, "myoclonus," applied to this clinical condition by many writers also seems to be incom-

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plete and inadequate. The term myoclonus connotes a rapid twitchlike contraction of a single muscle. It does not convey any conception of constancy, rhythm or regularity in amplitude. These movements, whenever observed, have presented a rhythmic character, a constancy and a regularity in extent which are paralleled only by the abnormal involuntary movements characterized as tremor. However, tremor is due to alternating contractions in antagonistic muscle groups. Such reciprocal innervation is not necessarily present in the muscles involved in this abnormal involuntary movement. On the other hand, one seems to be dealing with simple muscle twitches followed by relaxation. It would therefore seem more correct to designate this condition as "rhythmic myoclonus."

This movement is frequently an isolated one, appearing only in the muscles of the soft palate, but it may manifest itself in the muscles of the pharynx, larynx, face, lips and eyes, and may even involve the muscles of the extremities. Since the muscles of the palate, pharynx and larynx are implicated almost regularly in this syndrome, it is not surprising to find that the first reports of these movements were supplied by otolaryngologists, the first case having been recorded, according to Gallet, by Politzer in 1862. In many instances, the muscles about the orifices of the eustachian tubes are involved, the contractions of these muscles producing a sudden opening of the eustachian tube with a resultant click which is audible to the patient and may be heard even by observers at some distance from the patient. This rhythmic clicking noise has frequently been the only subjective feature of the syndrome. In all probability, many "silent" myoclonias of the palate and pharynx and similar contractions of other muscles may exist without attracting the attention of the patient or clinician.

Following the discovery of these movements by otolaryngologists, a considerable number of reports have appeared in neurologic literature not only describing these localized myoclonic contractions, but also extending materially the muscular territory which may be affected. The titles of the various articles describing these movements have been assembled in the list of references appended to the thesis by Gallet [1] on this subject, which appeared in 1927. To this list Gullain and Mollaret have added further references which either escaped the attention of Gallet or appeared subsequent to his contribution. Gallet gathered thirty-seven cases; about one-half were reported in detail, while in the remainder only the character of the movements and their location were mentioned, without any indication of any associated

1. Gallet: Le nystagmus du voile: Le syndrome myoclonique de la calotte protubérantielle, Thèse de Paris, 1927.

involvement of other structures. The reports of a number of postmortem examinations were included in his thesis.

During the latter part of 1931, two reviews of the condition appeared, one by Leshin and Stone [2] in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, the other by Guillain and Mollaret [3] in the *Revue neurologique*. According to Leshin and Stone, the number of reported cases presenting isolated rhythmic movements of the palate exceeds one hundred. According to Guillain and Mollaret, the number of instances in which the movement appears synchronously in other muscle groups amounts to about fifty. Guillain and Mollaret in the *Revue neurologique* described two cases, and Leshin and Stone reported one additional case in which the more widespread distribution of the contraction was observed.

Analysis of the cases showing these abnormal involuntary movements demonstrates that the patients may be grouped according to the distribution of the contractions. The first great distinction is whether the involvement is limited or widespread. In the first group of about one hundred cases, the disturbance is limited strictly to the palate. These cases may be further separated into two subdivisions according to whether the movements are unilateral or bilateral. This differentiation into separate categories according to unilaterality or bilaterality seems unessential, since the second case reported by Guillain and Mollaret presented a transformation from a strictly unilateral to a later bilateral involvement. In the second group the movements, although synchronous, implicate muscles which may be situated at considerable distances from one another, although the great majority of the muscles concerned are innervated by the cerebral nerves. The clinical picture presented by these patients is of great interest, for the distribution of the twitching may be extensive and the combinations of involved muscles quite varied. In the first case of our series the movement implicated structures as far apart as the left eye and the left upper extremity, with participation of many of the intermediate muscles. Freystadtl reported the appearance of the disturbance as far caudad as the intercostal and abdominal muscles, while von Bogaert examined one patient in whom the muscles of one of the lower extremities was involved in addition to some of the muscles supplied by the cerebral nerves.

The following analysis was based on forty-three cases: twenty-seven cited by Leshin and Stone, eleven collected by Gallet, two

2. Leshin, N., and Stone, Theodore T.: Continuous Rhythmic Movements of the Palate, Pharynx and Larynx, Arch. Neurol. & Psychiat. **26**:1236 (Dec.) 1931.

3. Guillain, G., and Mollaret, P.: Deux cas de myoclonies synchrones et rythmées vélo-pharyngo-laryngo-oculo-diaphragmatiques, Rev. neurol. **2**:545 (Nov.) 1931.

described by Guillain and Mollaret and three the records of which are embodied in this report. In thirty-nine instances in which the sex was given, twenty-one were males and eighteen were females. The age incidence at the time of observation in decades computed for thirty-six cases was of interest; there were no cases in the first, four in the second, three in the third, four in the fourth, four in the fifth, eleven in the sixth, nine in the seventh and one in the eighth decade. About 70 per cent of the cases occurred between the ages of 41 and 70 years. The age does not indicate in all cases the time of appearance of the movement, since in only a few instances was this fact specifically noted.

In the history, headache was not uncommon. Dizziness and various cerebellar symptoms were complained of in about two fifths of the cases. Difficulties in speech and swallowing were present in about one fourth of the cases. Signs of oculomotor involvement were comparatively frequent, consisting of isolated external rectus palsy, dissociation of conjugate deviation, limitation of lateral gaze, loss of convergence, etc., occurring either singly or in all sorts of combinations. In only five instances was the twitching unilateral; in the second case of Guillain and Mollaret, the involvement was at first unilateral but later became bilateral. The rate of the contraction varied from 50 to 240, the majority presenting a rate of from 140 to 180 contractions per minute. All the cases presented the movement of the palate. Not infrequently the patient heard a clicklike sound, due to the sudden opening of the orifice of the eustachian tube by the contraction of the adjacent muscles. This sound is best described as similar to that produced by snapping one thumbnail with the other. The uvula moved upward or to one side. The posterior pharyngeal wall usually moved in a portière-like manner, the superior constrictors of the pharynx participating equally, or in some cases the muscles of one side contracted more extensively than those of the opposite side. Although the vocal cords are often involved in the combined form, they may be spared; the entire larynx may be raised in a rapid upward movement. In the three cases included in this report the movement of the entire larynx was upward. It was impossible to determine the specific muscles responsible for the elevation of the larynx.

The rhythmic contraction of other muscles, which accompanied the movement of the palate, larynx or pharynx—the essential feature of this syndrome—appeared in diverse locations. Synchronous movements of the eyes were observed. The displacement was occasionally quite different in the two eyes, being upward in one and lateral in the other. A true nystagmus was present as a vestibular manifestation due to the essential underlying disease, its tempo being different from that shown by the characteristic movement. In certain cases the oculomotor dis-

turbance combined an independent vestibular component (true nystagmus) with the myoclonic contraction, as in the case of Guillain and Mollaret and in our case 1. In these instances special care was needed to unravel the two types of ocular movement. In the face, the muscles about the angle of the mouth and the chin muscles participated in about one quarter of the cases. This involvement of the lips and chin was usually unilateral and resembled the twitching seen in epilepsia partialis continua. The latter movement, however, shows much more irregularity in its amplitude and tempo than the myoclonic contractions. The diaphragm was also involved occasionally, viz., in seven of forty-three cases. Possibly, its implication was missed at times. Involvement of the muscles of the neck produced in some instances displacement of the larynx or nodding movements of the head. The muscles of the floor of the mouth, the intercostal muscles and even the muscles of the abdominal wall have been reported as presenting synchronous contractions. The possible combinations of muscular involvement are numerous. In van Bogaert's case the muscles of the right side of the mouth, chin, platysma and orbicularis palpebrarum, corrugator supercilii, both halves of the diaphragm and muscles of the right upper and lower extremities twitched, in addition to the muscles of the soft palate, posterior pharyngeal wall and vocal cords. In rare instances, the musculature of the extremities on one side participated, as in the case cited, in another described by Oppenheim and in the upper extremity in case 1 reported here.

While the movements were remarkably constant, they yielded readily to the dominance of reflex and cortical control, being suspended or diminished during swallowing, vocalization, etc. Moreover, once having begun, the movements, according to the published reports, never disappeared. They were much more apt to spread and involve progressively other muscles. In one further respect these movements were unique; i. e., they continued during sleep.

The occurrence of various types of involuntary movement in the muscles of the face, trunk and extremities is frequent, but similar dyskinesias affecting the oculomotor apparatus are rare. Isolated infrequent twitchlike movements of one eye have been seen in various types of involvement of the central nervous system, particularly in the degenerative diseases, such as multiple sclerosis. Individual or conjugate deviation of the eyes, oculogyric crises and slowness of movement in gaze are frequently seen in epidemic encephalitis, and athetoid and choreiform movements are seen rarely in disease of the basal ganglia. Constant movements of the eyes are recorded in only a few isolated conditions. They are seen in hereditary, familial or congenital nystagmus. Orzechowski has described a dysmetric ataxia due to cerebellar

disease in which there is present a variable chaotic agitation of the eyeballs with movements of variable amplitude which cease on extreme lateral deviation of the eyes. The same author has also described what he calls an "opsoclonie" in which there is a continual state of agitation, the movements being rapid, unequal and usually in the horizontal plane. These movements are usually associated with polyclonias, myokimias, tremor of the fingers, chin, lips, eyelids, etc. No other disorder known to us produces the peculiar movement of the eyes here described, with its rhythm, unvarying amplitude, constancy and peculiar distribution, for example, affecting one eye alone and the two eyes differently in the cases to be described.

Rhythmic movements of the nose, lips, chin, tongue and jaw have been seen repeatedly in paralysis agitans of either the arteriosclerotic or the chronic encephalitic type, but the occurrence of the contractions in the palate, pharynx, larynx and floor of the mouth in this syndrome is unique. Gabrielle Lévy attributed one of her cases of palatal and pharyngeal involvement to a chronic encephalitis, the movements being associated with other widespread hyperkinetic phenomena of the parkinsonian type. Foix also mentioned the resemblance to, and association of this type of contraction with, a true parkinsonian involvement. The history of the first patient in this series definitely suggested an encephalitic basis, and examination disclosed certain parkinsonian features—a relative immobility of the face, loss of associated swinging of the left upper extremity and slowness in speech and other skilled acts. These features were not convincing, however, and the mode of onset and the definite improvement made an encephalitic causation doubtful.

While signs of disturbed function in other systems were common, this peculiar movement occurred frequently as the sole manifestation of disease in the central nervous system. Hemiplegia or evidences of involvement of the pyramidal tract appeared in about two thirds of the cases. Sensory disturbances with a hemisomatic distribution were found in about one seventh of the cases. The pseudobulbar syndrome and indications of cerebellar involvement often coexisted. The diagnoses made for thirty-five patients observed clinically and in eight cases coming to autopsy gave an idea of the usual etiologic factors. In fifteen, no diagnoses were ventured; in nineteen, lesions due to hypertensive vascular disease were regarded as responsible for the production of the syndrome; in two cases, syphilis; in three other instances, tumor, and in one patient, multiple sclerosis. In another example, sequelae of epidemic cerebrospinal meningitis were believed to be the cause of the clinical picture. In a case reported by Gabrielle Lévy, chronic epidemic encephalitis was the etiologic factor. In the case of Oppenheim and

Siemerling an aneurysm of the vertebral artery was found. In one of our cases the possibility of the traumatic rupture of a metencephalic telangiectasia was suggested by the history and the presence of a facial nevus.

A number of these cases have been examined post mortem. Of five cases (three reported by Klein, one by Graeffner and another by Kelly), in four multiple vascular lesions and in the other multiple degenerative lesions (presumably due to vascular disease) were found in the brain stem. The more recent cases reported by Foix and Hillemand, Gallet, von Bogaert and Bertrand are of greater value than the earlier reports, owing to the more careful and more detailed examination of the central nervous system. As stated by Guillain and Mollaret, earlier reports cannot be depended on because the specimens were not examined in serial sections.

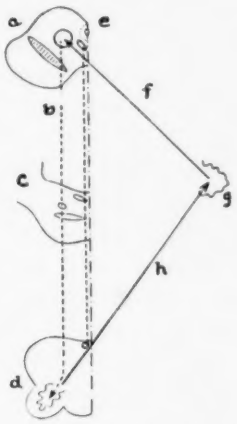
PATHOLOGIC CHANGES PRODUCTIVE OF RHYTHMIC CLONUS

The description of the various pathologic processes presented a striking uniformity in the principal features disclosed post mortem. As a result of the histologic examination in four cases, Foix and his pupils came to the conclusion that the movements, the essential feature of this syndrome, resulted from lesions situated in the tegmentum of the pons varolii. The central tegmental tract, the olivary nuclei and the reticular substance of the metencephalic tegmentum were involved in all of the specimens, while the other fiber bundles traversing the tegmentum did not regularly show any participation in the disease process. The posterior longitudinal fasciculus was inconstantly involved, but in cases in which it was implicated the interruption of its fibers could be held responsible for the disturbances in ocular control, particularly the nystagmus. They did not believe that involvement of this bundle caused the contractions; neither did they establish any involvement of the bulbar nuclei.

The first study of van Bogaert and Bertrand confirmed the view that an involvement of the central tegmental tract and the adjacent reticular formation produced the symptoms. They also described a degeneration of the posterior longitudinal fasciculus. In their second study, they did not find secondary degeneration or involvement of the central tegmental tract, but they established the presence of a "total hypertrophic atrophy" of the left inferior olivary nucleus and the accessory olivary nuclei, with degeneration of the fiber layers in relation with the right dentate nucleus and a degeneration of the right superior cerebellar peduncle, its decussation and the left red nucleus.

The involvement of the dentate nucleus was also found by Klein, Foix, Chavany and Hillemand. Van Bogaert and Bertrand called atten-

tion to the frequent involvement of the olivary and the dentate nuclei in myoclonus-epilepsy. They regarded the contractions as due to an anatomic or functional release of infranuclear motor centers from the control exerted by more cephalically situated motor mechanisms. They called attention to the fact that a tremor may develop as a result of a lesion of the superior cerebellar peduncle, using this as an example of the effects produced by an interference with the chain of neurons in the cerebellar system of motor control. They believed that the movements characteristic of this syndrome resulted from lesions of the tegmentum at various levels which may affect any one of the following: the superior cerebellar peduncle, the reticular tegmental substance, the central tegmental tract, the inferior and accessory olivary nuclei and the dentate



Lesions situated within the triangle and affecting the structures indicated in the diagram are held responsible by Guillain and Mollaret for the production of the rhythmic myoclonus characteristic of this syndrome: *a*, red nucleus; *b*, posterior longitudinal fasciculus; *c*, central tegmental tract; *d*, inferior olive; *e*, aqueduct of Sylvius; *f*, superior cerebellar peduncle; *g*, dentate nucleus, and *h*, olivodentate fibers. (From Guillain and Mollaret: Rev. neurol. **2**:545 [Nov.] 1931.)

nucleus, one link of the chain of neurons being involved in one instance and a different link in other instances. It would appear that either the inferior olivary or the dentate nucleus must be affected to produce the contractions.

No detailed descriptions of the pathologic changes in the cells or fibers were given by Gallet, Guillain and Mollaret or Leshin and Stone. A descending degeneration of the central tegmental tract was described by Gallet and quoted by him and by Guillain and Mollaret from other observers. In discussing the lesions discovered in the region of the olivary nuclei, a "total hypertrophic atrophy" was men-

tioned. It was also described as a pseudohypertrophy. In the illustrations, the affected olivary nucleus appears swollen; its outline is less distinct and the normal convolutions are obscured. A degeneration of the cells of these nuclei was mentioned but not described. Gallet mentioned that this cellular change indicated a peculiar type of "transsynaptic" degeneration, the process extending across the synapse and causing a change in the next link in the chain of neurons. This definitely suggests the similarity of the degenerative process to the systemic diseases which affect the pontile nuclei, the dentate nucleus, the olivary nuclei and the tracts connecting these structures, such as olivopontocerebellar atrophy. A descending degeneration in the olivospinal tract was also described which could be followed into the upper cervical segments. (This may add confirmation to the supposition that this tract is a descending one.) Guillain and Mollaret concluded that the anatomic problem still contains a considerable amount of uncertainty and that discordant elements are still present. No one factor seems constant. Lesions of the various structures thought to be responsible for this clinical picture have been demonstrated in other patients who have not exhibited the contractions characteristic of this syndrome. The essential feature may be a "short circuit in the central coordinators." To illustrate their views Guillain and Mollaret outlined an area including the inferior olivary and accessory nuclei, the dentate nucleus and the red nucleus. Disturbances in equilibrium in the forces acting between these nuclei and over the pathways connecting them, in their opinion, produced the characteristic movement.

Three cases with extensive involvement are included in this report.

REPORT OF CASES

CASE 1.—*History.*—J. G., a man, aged 38, Irish, an engineer, was admitted to the New York Neurological Institute on Dec. 22, 1930, with the following complaints: weakness and tremor of the left arm and leg, coldness and numbness of the right half of the body, slight impairment of vision and slowing down of movement and skilled acts.

The patient had been in fairly good health until early in May, 1930, when he fell down a flight of stairs while intoxicated. He was apparently unconscious for twelve or fourteen hours. On regaining consciousness, he noted a moderate loss of power in the left arm and leg. He also noticed the presence of blood in the right external auditory canal. About one week after the injury, double vision appeared and persisted, irrespective of the direction of gaze, for a period of about three months. He believes that vision is still somewhat impaired and that his eyes are sensitive to light.

Immediately following the acute onset, he was conscious of a clicking noise vaguely localized in the top of his head. This was rhythmic, constantly recurring and so loud that it could be heard at some distance. About a week following the injury, the patient began to notice involuntary, jerky movements of the left hand,

forearm and leg. These movements were usually exaggerated by any attempt to control them. At about the same time he felt a numbness and coldness which extended throughout the entire right side of the body and face. The involuntary movements of the upper extremity and the subjective sensory disturbances have diminished somewhat recently.

Ever since the injury, the patient had noticed a general slowing down of his movements. There had been a moderate impairment of memory for past events. His hearing had become less acute. A week or two after the injury, an intermittent noise in the right ear, like that of escaping steam, was present for a few days.

In 1925, he had fallen, while intoxicated, struck his head on the sidewalk and had been unconscious almost three days. There were no sequelae. He had had no operations. He had had measles at the age of 12 and a mild attack of influenza in 1918. During the latter he was in bed for about a week with a slight fever and chills and felt exhausted. He was rather drowsy for a month or two afterward, but he slept poorly. During the past few years these disturbances in sleep have returned for short periods. A history of venereal disease was denied. He has suffered from occasional headache in the left side of the vertex. He was in good health for a considerable period immediately before the accident in May, 1930. He has used whisky and gin steadily since he was 18, with periodic excesses since the age of 28. Marked nervousness and, at times, hallucinations followed these bouts.

The family history disclosed alcoholism in several members.

Neurologic Examination.—The patient was well developed, seemed somewhat slow in his reactions and movements, presented a suggestion of a masked facies and suffered from a moderate confusion. There was a slight forward flexion of the body, with a suggestion of parkinsonian progression, some unsteadiness, and slight dragging and excessive swinging of the left foot. He was unsteady in walking on the toes or heels, and very unsteady in walking on a line and backward. Associated movements of the trunk, arm and head were decreased on the left side. Equilibratory coordination was normally performed with the eyes open. With the eyes closed, there was a slight tendency to sway toward the left, which was present also when the patient was standing on the left foot alone. Nonequilibratory coordination in the right upper and lower extremities was normal. Movements of the left upper extremity showed a marked intention tremor. There was some ataxia in the left lower extremity. Succession movements were impaired; the check element was disturbed, and abnormal rebound phenomena were present in the left upper extremity. The skilled acts of the left upper extremity were interfered with by the intention tremor. Speech was slow.

Abnormal Involuntary Movements: These motor disturbances fell into two groups. The rhythmic myoclonus was a constant movement affecting various muscles. Wherever seen, it consisted of two components: the first, a rapid twitch-like movement of moderate amplitude; the second, relaxation and return of the structures to the position of rest, the return being slower and less sudden than the muscular twitch. The rate of this recurrent contraction was the same in all the affected muscles—about 184 to the minute. The movement was rhythmic and constant. It was present at the left corner of the mouth, presenting a movement of closure of the lips, which was more marked in the lower lip. Occasionally and less markedly, similar movements were seen at the right corner of the mouth. The contractions were present: in the chin, producing an elevation of the left side; in the base of the tongue; in the soft palate, resulting in an elevation of the uvula and a movement of both faucial pillars toward the midline, and in the muscles of the pharyngeal wall. Both sides of the pharynx seemed to be affected, but the greater involvement of the muscles on the left side produced a general movement

of the pharyngeal wall to the left and downward. The twitchings were not greatly inhibited by phonation. The arytenoid cartilages presented the same type of movement with the same rhythm as that seen in the pharynx. The movements of the arytenoid cartilages appeared to be bilateral. The muscles elevating the left wing of the nose and upper lip were involved to a minor extent. The contractions could be seen also in both anterior triangles of the neck, but it was difficult to determine the muscles involved. The entire larynx moved upward in rhythmic excursions. Movements of the diaphragm could not be demonstrated by fluoroscopic examination. A synchronous nodding movement of the head was also present. At rest, the left upper extremity presented no constant twitching but, occasionally, the extensor muscles of the left forearm developed a movement of the same character and rhythm as that seen in the muscles involved in the constant myoclonus. When the left arm was stretched forward, contractions of the flexors and extensors of the hand and fingers gradually developed and continued with the same familiar rhythm. The second type of abnormal involuntary movement was an intention tremor. When acts were carried out by the left upper and lower extremities, a definite tremor of the intention type, distinctly cerebellar in its characteristics, made its appearance.

Reflexes: All the deep reflexes were overactive, more so in the left extremities. The left knee jerk was pendular, a Hoffmann sign was present and Babinski and Chaddock signs were elicited on the left. There was moderate weakness in the left upper and lower extremities, with slight atrophy of the interosseous muscles in the left hand. The trunk-thigh sign of Babinski was slightly positive in the left lower extremity.

Sensation: There was a moderate reduction in tactile sensibility associated with a definite, disagreeable paresthesia and a slight diminution in the perception of pain affecting the right side, including the face. Reduction in the sensibility of the right half of the face was not so intense as in the right half of the body. The hypalgesia was accompanied by the disagreeable quality already noted. The disturbance in temperature sensibility presented the same type and distribution as that found for pain. The appreciation of vibration was diminished in the right leg and was accompanied by a disagreeable sensation. Muscle tendon sensibility was normal.

Cerebral Nerves: The function of the olfactory nerves was normal. An examination of the optic and oculomotor nerves was made by Dr. Thomas H. Johnson. Visual acuity and fields were normal. The upper margin of the right disk appeared hazy. The palpebral fissure measured: right, 10 mm.; left, 8 mm. Ocular movements were unrestricted. There were rhythmic and regular nystagmoid jerks on lateral gaze. A rhythmic vertical movement of the left eye was seen particularly well when the left disk was viewed through the ophthalmoscope. The right pupil measured 5 mm.; the left, 4 mm.; they were slightly irregular, reacted promptly to light, both directly and consensually, with a doubtful reaction on accommodation and convergence. The right corneal reflex was sluggish. The changes in sensibility of the right side of the face and head have been mentioned. A slight right lower facial paresis was present. The auditory conduction formulas were normal. The drums were normal. Examination of the ears (Dr. Page Northington) showed a 14.4 per cent loss of hearing in the right ear and 20.8 per cent in the left ear. Examination of the vestibular function showed normal responses from the right ear. From the left ear the reactions were active, but instead of a horizontal nystagmus with head retracted there was an oblique nystagmus. Both sets of semicircular canals presented normal irritability. Spontaneous nystagmus was present in the left eye, which readily gave way to the induced type of nystagmus.

It was thought that there was no destructive lesion involving the vestibulo-ocular pathways; on the other hand, an irritative lesion was believed to exist in the right pontile region. Examination showed that the pharynx was normally sensitive to gross stimulation. The larynx was normal in conformation, color and function. There was no difficulty in swallowing (Dr. Edmonde D. Neer). The spinal accessory and hypoglossal nerves were normal in function.

Systemic Examination.—There was an irregular telangiectasia on the forehead, just to the left of the midline. The heart and lungs were normal; the liver was palpable at the costal margin; it was not sensitive. The blood pressure was 130 systolic and 75 diastolic. The temperature was normal; the pulse rate varied between 60 and 102 per minute; the respiratory rate was from 18 to 22 per minute.

The blood count was normal. The Wassermann reaction of the blood was negative. Urinalysis gave negative results. Examination of the spinal fluid showed: 2 cells per cubic millimeter; globulin, 1 plus; protein, 48; colloidal gold curve, 0000000000; Wassermann reaction, negative. Roentgen examination of the skull gave negative results. Fluoroscopic examination showed the chest, diaphragm and heart to be normal.

Mental Condition.—The intelligence quotient was 0.71. During this test the patient was greatly confused and spent most of the time in asking questions.

Course.—The patient was reexamined at the New York Neurological Institute on March 9, 1932. At this time he presented essentially the same condition. Coarse myoclonic movements were especially marked in the left forearm and hand; fibrillary contractions of the muscles of the tongue and a slight facial tremor were noted. Sensory examination showed that the disturbances in touch, pain and vibration had diminished greatly. He still complained that the right side of the body and face was slightly numb. The signs of pyramidal tract involvement had disappeared.

Case 2.—*History.*—R. G., aged 50, Jewish, a housewife, who was seen through the courtesy of Dr. S. Philip Goodhart, director of the neurologic service of the Montefiore Hospital, was admitted to the Montefiore Hospital on March 22, 1932, with the complaint of weakness and numbness in the left half of the body. The onset had been fairly sudden, on Feb. 21, 1932, when, on awakening, she noticed weakness in the left upper and lower extremities. She carried on her household duties, but in the course of a few hours the weakness, accompanied by numbness, increased and became so severe that she was unable to stand. She also noticed diplopia, which lasted for about a week. During the next two weeks the weakness and numbness improved to a considerable extent, but at the time of admission to the hospital on March 22 she was still unable to walk. The history of past illnesses presented a series of disturbances of apparently vascular origin. In 1928, she suffered a laceration of the left hand. The patient became unconscious and a generalized convulsion developed, which lasted for about five minutes. It was later noticed that the left extremities and side of the face were paralyzed. She recovered completely from these symptoms in about six weeks. In the early part of December, 1929, she experienced an attack of dizziness and fell, striking the back of her head. There were no immediate results from this fall, but later in December occipital headache and nausea developed, and the patient became stuporous, remaining in this condition for about six hours. On returning to consciousness she was irrational and showed definite impairment of memory and judgment. On Dec. 17, 1929, the following physical signs were observed: cerebellar ataxia; asynergia in the left extremities, with the appearance of abnormal involuntary movements presenting an athetotic character; left hyperreflexia, without abnormal plantar

responses; left external strabismus; marked diminution of all of the associated movements of the eyes, except downward gaze; rotatory nystagmus in both eyes, and vertical nystagmus in the right eye. She was incontinent. The blood pressure ranged from 188 systolic and 110 diastolic to 212 systolic and 142 diastolic. A diagnosis of "multiple cerebral hemorrhages and a possible thrombosis of the basilar artery" was made.

The patient had had typhoid fever at 14. She was married at the age of 24 and had four children. She had no miscarriages or abortions and passed through the menopause at the age of 48. She had complained of nocturia since 1928.

Her mother had died at 48 years of age from a "heart attack."

Neurologic Examination.—The patient was confined to bed or a chair; she was right-handed. It was impossible to test the patient's gait or equilibratory coordination because of the motor difficulties. She presented a gross unsteadiness in performing the finger-to-nose and the heel-to-knee and along-shin tests in the left extremities. Skilled acts were performed normally with the right upper extremity, but with marked difficulty with the left upper extremity on account of a flaccid hemiparesis of moderate degree.

Abnormal Involuntary Movements: The patient presented a combination of abnormal involuntary movements, similar to those in case 1, but complicated further by the presence of a definite left hemiparesis. There was an intention tremor, which affected the left upper and lower extremities, with distinct evidences of asynergia of the cerebellar type. In addition, there were rhythmic movements of certain muscle groups. These movements were constant, rhythmic and persistent during sleep, and presented a rate of 120 to the minute. The contractions were present in the muscles of the left eye, producing a combined upward and lateral deviation. It was not exactly constant in rate or amplitude, the twitchlike movements being exaggerated at times and the rhythm disturbed by some other motofacient element. The movement of the right eye was synchronous with the excursions of the left eye, but was directed upward. No true nystagmus was observed, but movement of the eyes to the left seemed to alter the aforementioned excursions, a change perhaps due to the addition of a vestibular or a cerebellar element. The muscles of the left angle of the mouth showed a movement of the same rate and rhythm as that noted in connection with the eyes, resembling a sucking movement. The contractions were almost but not entirely inhibited by raising the lips and by speaking. Similar twitches were seen in the floor of the mouth, resulting in an elevation of the base of the tongue. The contractions also appeared in the anterior triangles of the neck, producing rhythmic retraction in these areas. The soft palate and uvula moved upward in response to the myoclonic contraction, followed by a slower return to a position of rest. The muscles in the posterior pharyngeal wall showed bilateral contractions, synchronous on the two sides, producing a portière-like adduction movement of the pharynx, together with a less extensive downward movement. The entire larynx was elevated, the movement being synchronous with the contractions already described. No involvement of the diaphragm was demonstrated by fluoroscopic examination.

Reflexes: The reflexes of the left extremities were somewhat increased, with positive Hoffmann, Babinski and confirmatory responses in the left lower extremity. The abdominal reflexes were not elicited, except for a weak contraction of the muscles of the left lower abdominal segment.

Speech: This was somewhat nasal and thick, and presented definite scanning qualities.

Sensory Examination: This was unsatisfactory.

Cerebral Nerves: The visual acuity and fields were normal. The left fundus showed a hyperemia; the fundus of the right eye presented a small retinal hemorrhage and some edema of the retina, but with little or no sclerosis of the vessels. The pupils were unequal, the left being larger than the right. Conjugate movements of the eyeballs showed weakness in left lateral gaze, marked weakness of the right external rectus, limitation of upward gaze and the presence of the abnormal movements already described. There was some dissociation of the optic axes on conjugate movement. Convergence was poor. The position of the eyes at rest presented a right internal strabismus. There was a left facial flattening, which was more marked in the upper part of the face. The lower two thirds of the left side of the face was somewhat flat, but this disappeared on volitional movements.

Systemic Examination.—The urine contained a faint trace of albumin. The chemical composition of the blood was normal and the Wassermann reaction was negative. The spinal fluid was normal and its Wassermann reaction was negative. Tracings of the labial and ocular movements, projected on the same film with the electrocardiogram, showed that the movements were not synchronous with the heart beat.

Diagnosis.—Multiple vascular lesions of the brain stem on a hypertensive basis were diagnosed.

CASE 3.—*History.*—C. B., a girl, aged 12½, Jewish, who was seen through the courtesy of Dr. Emanuel D. Friedman, director of the neurologic service of the Beth Israel Hospital, was brought to the Beth Israel Hospital on March 29, 1932, with the following complaints: staggering gait, headache and vomiting. The illness had begun in 1929. In the past three years the gait became progressively more unsteady and she suffered from a considerable degree of dizziness, so extreme that at times she fell. In walking, she veered to one or the other side. This disturbance in gait gradually became worse. She had severe headache of a generalized nature, occurring principally in the morning and lasting for several hours. Recently, the headache had become worse and more constant. The vomiting was apparently related to the quality and quantity of food, being preceded by nausea and retching and never projectile in character. It had increased.

The father had acquired syphilis several years before marriage, but had been treated and was regarded as cured. The Wassermann reaction of the mother's blood had been negative several years before; she had had no spontaneous miscarriages.

The patient had had measles, diphtheria and chickenpox. The tonsils and adenoids had been removed.

Neurologic Examination.—The patient was pale and thin, and presented a rather precocious mental development. She appeared chronically ill. The gait showed ataxic unsteadiness, with a tendency to veer irregularly to one or the other side. She showed a tendency to fall to the right, with the eyes either open or closed. There were ataxia, asynergia and adiadokokinesis in the extremities, more marked in those of the left side. Cerebellar speech was present.

Abnormal Involuntary Movements: The patient presented a combination of an intention tremor, more marked in the left upper and lower extremities, and a rhythmic myoclonus similar to that described in cases 1 and 2. The movements were present in the muscles of both angles of the mouth, and were more marked on the right side. The muscles of the right side of the chin were affected, producing an elevation. There was a retraction of the right ala of the nose, producing a widening of the nostril. The soft palate presented elevation and left lateral deviation of the uvula; adduction movements of the anterior and posterior pillars of the

fauces were present. The muscles of the pharyngeal wall were similarly and synchronously involved, producing the familiar portière-like movement of adduction. The larynx as a whole was elevated rhythmically and constantly. The internal laryngeal musculature was not involved. The movement was not completely inhibited by volition. The contractions were constant, persisted during sleep and were not inhibited, although they were somewhat obscured, by volitional movements. The contractions were synchronous in all the muscle groups involved, occurring about 204 times per minute. They were not synchronous with a nystagmus present on lateral gaze. When the patient walked there was a tendency to a general tremor of the body and head. No involvement of the diaphragm was demonstrated by fluoroscopic examination.

Reflexes: The reflexes of the upper and lower extremities were active and equal. The lower abdominal reflexes were present. There were no abnormal reflexes in the lower extremities. There was no motor weakness.

Sensation: This was normal.

Cerebral Nerves: The visual acuity, fields and fundi were normal. The pupils were equal and regular in outline, and they reacted to light and in accommodation. The right palpebral fissure was wider than the left. The movement of the eyeballs was not limited in any direction and the power of convergence was well maintained. There was a marked nystagmus, present particularly in upward and extreme lateral gaze. It was more marked in the eye toward which the gaze was directed. There was also a vertical nystagmus in each eye, the movement being upward and to the left with a slight clockwise rotatory deviation. The nystagmus was not synchronous with the rhythmic myoclonus. The corneal reflexes were present. The facial innervation was normal and taste was undisturbed. Caloric tests showed that a normal nystagmus developed and continued for forty seconds after the irrigation of each ear, not accompanied by past pointing or vertigo, but by a tendency to fall to the right. The patient was intellectually alert and cooperative.

Systemic Examination.—The urine contained considerable quantities of acetone but no sugar. A blood count showed a secondary anemia. The pulse and respiratory rates were normal. The blood pressure was 104 systolic and 54 diastolic. The patient weighed 54 pounds (24.4 Kg.).

Diagnosis.—At the time of discharge a diagnosis of a "midline cerebellar neoplasm" was made.

Course.—The patient was readmitted to the hospital on April 6, 1932. At this time, roentgen examination of the skull showed depressions along the inner table of the skull due to increased intracranial pressure. The spinal fluid was slightly cloudy; it contained 2 cells; total protein was 125 mg.; globulin, 1 plus, and albumin, 2 plus. The pressure was 80 mm., with normal responses to compression of the jugular veins and on straining. The Wassermann reaction of the blood was negative in the patient and both parents. At a somewhat later date, bilateral papilledema developed.

On June 11, the patient was operated on by Dr. Walter E. Dandy, in Baltimore, on account of increasing symptoms. At operation, a midline cerebellar medulloblastoma was found and, in great part, removed. The cerebellar symptoms and the rhythmic myoclonus were still present after the removal of the neoplasm.

Comment.—The preceding clinical studies show the results of lesions situated in the area delimited by Guillain and Mollaret. The first patient presented definite evidence of cerebellar involvement in speech, disturbances of equilibrium, intention tremor and loss of synergy

in succession and other movements. The involvement of the spinothalamic tract and the coincident evidence of disturbance in the posterior longitudinal fasciculus, as shown by the nystagmus, implicate the tegmentum of the mesencephalometencephalic segments. The second patient had many vascular accidents. The presence of ataxia in the left upper and lower extremities, the disturbance of conjugate gaze, the weakness of the right external rectus and the nystagmus provide ample evidence of the existence of localized lesions in the same vicinity. Case 3 showed a cerebellar symptomatology, with a disturbance in gait and position, Romberg sign, ataxia, which was present in all but more marked in the left upper and lower extremities, cerebellar speech and nystagmus. In this case, the clinical diagnosis of a cerebellar neoplasm was confirmed at operation. Since the patients are all alive no further information concerning the anatomic conditions in the brain stem is available.

GENERAL COMMENT AND SUMMARY

The recording of these three cases adds no new features to the already well recognized facts. That the three cases should be encountered in the course of a year indicates, perhaps, a more widespread prevalence of the disorder than might be supposed from the relatively small number of recorded cases. Every case showing evidences of involvement of the pontile region and cerebellum should be carefully investigated for the presence of these movements. The evidence concerning the probable clinical localization of the lesions would corroborate the conclusions advanced by Guillain and Mollaret from the study of their clinical material and the examination of postmortem specimens, since all of our cases indicate that the metencephalic region of the brain stem, including the cerebellum, is the undoubted site of pathologic involvement. Final identification of the particular diseased structures which produce this syndrome must await the histologic investigation of cases in which the clinical manifestations appear in a pure form. Only in such instances can one be justified in predicating a causal relation between the pathologic data and the clinical disturbance.

PALATAL MYOCLONUS

REPORT OF TWO CASES WITH NECROPSY

WALTER FREEMAN, M.D.

WASHINGTON, D. C.

Continuous rhythmic myoclonic movements of the palate and pharynx have evoked considerable interest recently in France under the stimulus of Foix,[1] and his pupils have continued the work so lamentably cut short, as witnessed by the thesis of Gallet [2] and the careful anatomic investigations of van Bogaert. Leshin and Stone's [3] recent report covers particularly the German and the English literature, but contains only six cases in which necropsy was performed. Foix believed that he had found the specific lesion underlying the condition, namely, destruction of the central tegmental fasciculus in the pons, but the studies of Klien [4] and more recently of van Bogaert and Bertrand [5] have thrown some doubt on the constancy of this lesion. These authors and others have incriminated the dentate nucleus of the cerebellum. In both conditions, however, there is an accompanying hypertrophic degeneration of the inferior olive, a lesion that has been found in all cases of palatal nystagmus coming to necropsy.

CLINICAL FEATURES

The characteristic movements consist of quick contraction of the muscles affected, followed by a somewhat longer period of relaxation. They are repeated constantly at the rate that is characteristic for the individual patient which varies in different cases from 50 to 180 per minute. They are often not perceived by the patient, but he may complain of twitching of the corner of the mouth, or, if the orifice of the

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From St. Elizabeth's Hospital.

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

1. Foix, C.: Contribution à l'étude des ramolissements protubérantiels, Rev. de méd., Paris **1**:287, 1926.

2. Gallet, J.: Le nystagmus du voile, Thèse de Paris, Portiers, Société française d'imprimérie, 1927, p. 139.

3. Leshin, N., and Stone, T. T.: Continuous Rhythmic Movements of the Palate, Pharynx and Larynx, Arch. Neurol. & Psychiat. **26**:1236 (Dec.) 1931.

4. Klien, H.: Ueber die pontinvierlichen rhythmischen Krämpfe des Gaumensegels und der Schlingmuskulatur, Monatschr. f. Psychiat. u. Neurol. **43**:79, 1918.

5. van Bogaert, L., and Bertrand, I.: Sur les myoclonies associées synchrones et rhythmiques par lésions en foyer du tronc cérébrale, Rev. neurol. **1**:203 (Feb.) 1928.

eustachian tube is involved, he may be conscious of a peculiar clicking sound. The extent of involvement varies greatly from isolated movements of the palate to involvement of the pharynx, fauces, larynx, tubal orifice, tongue, corner and floor of the mouth and diaphragm. In patients who have been followed over a period of months there may be extension to more and more groups of muscles, even in some cases to the intercostal muscles and to those of the fingers. The movements are always synchronous, but are usually interrupted, at least in the earlier stages, by voluntary activity. They do not interfere with normal activity in talking or swallowing, nor are they associated necessarily with either sensory disturbances or reflex changes. The respiratory rhythm is unimpaired. They continue indefinitely, remaining uninfluenced by drugs, and they are decreased but not abolished during sleep. Local anesthetization of the parts does not abolish the movements.

In association with these movements, there are usually other indications of cerebral disease, and according to Leshin and Stone these movements were considered hysterical only in from 10 to 12 per cent of the cases. The nature of the underlying disease process varies from case to case, including disseminated sclerosis, arteriosclerotic softening and tumor. The rhythmic movements seen in certain cases of chronic encephalitis may be allied phenomena, but they show greater variability and a different distribution. Signs of cerebellar and particularly of pontile involvement are usually present. More or less spastic paralysis, sensory dissociation, cerebellar asynergia and paralysis of associated lateral movements of the eyes may be observed in different cases, and in certain ones the symptomatology is overshadowed by the syndrome of intracranial hypertension.

The two cases to be reported occurred in arteriosclerotic persons with definite indications of focal damage to the nervous system. Pathologic examination revealed a wealth of lesions, but the most consistent finding was infarction of the central tegmental fasciculus in the pons.

REPORT OF CASES

CASE 1.—*History.*—A white man, aged 58, who was admitted to the hospital on March 19, 1928, died on Sept. 17, 1928. The diagnosis was psychosis with organic disease of the brain, hypertension, congestive cardiac failure and myoclonus of the palate.

The patient was admitted in a confused, irritable, disoriented state, and was very feeble, with a marked defect in speech. He had worked as a laborer until three years before admission, when symptoms of congestive failure developed. He was alcoholic, and his four children had died in infancy. An episode of blindness had occurred with later improvement, and more recently urinary retention had required catheterization on two occasions. A year previous to admission he had become forgetful and confused, and had placed lighted cigarets in his pocket.

Physical Examination.—There were enlargement of the heart to the left with accentuation of the second aortic sound, markedly sclerotic vessels and moist râles

at the bases. The blood pressure was 244 systolic and 124 diastolic. The urine contained some albumin and granular casts, but the renal excretion was practically normal. The blood and spinal fluid were normal.

Neurologic Examination.—There were equal regular pupils of extremely small size which did not respond to light. The eyes moved fairly well toward the right, but in looking toward the left the right eye did not travel beyond the midline, and the left showed marked nystagmus. Upward and downward movements were preserved, but in convergence the right eye did not pass beyond the midline. The face was somewhat flattened on the left side, and there was regular myoclonic twitching at the left lower corner of the mouth. Facial mimicry was reduced on the left side, although voluntary mobility seemed normal. The masseter muscles contracted well; the patient said that he felt pin pricks equally on the two sides, but the corneal reflex was weak on both sides and there was not much reaction to deep pricking of the face.

The pharynx was the seat of rhythmic twitching on the left side, associated with synchronous movements of the soft palate. These movements were regular and of similar amplitude, occurring at the rate of 110 per minute. They were interrupted momentarily by phonation, during which the palate was elevated in the midline. The gag reflex was active on both sides and was more evident on stroking the pharynx than the palate. The voice was harsh and weak; articulation was indistinct. The tongue protruded to the left and was agitated by irregular tremors, particularly on the left side. These were different from the rhythmic twitches of the pharynx and mouth. The mouth was full of dry saliva, and the patient made rather frequent swallowing movements. The head was held turned toward the left, inclined slightly forward and to the right.

Muscular power was weak in the left hand, but movements were rapid and coordination was good, practically no tremor being seen in the finger-to-nose test on either side. Muscular tonus was increased, and the reflexes were lively. Sensibility to pain seemed unimpaired, but other forms of sensation could not be tested on account of the patient's confusion. The abdominal reflexes were present bilaterally. The lower limbs were hypertonic, with exaggerated reflexes, which were about equal on the two sides, without clonus or a Babinski sign. The patient stood well with the eyes either open or closed. His posture was stooped, and the hands were held close to the side. In walking, however, he tended strongly to deviate to the right and to fall forward. This was also observed when he stood with the arms extended forward. He walked with short steps, there being no particular difference on the two sides. A diagnosis was made of cerebral arteriosclerosis with infarction in the tegmentum of the pons.

Course.—Progress was downward, and the patient died of pulmonary gangrene, probably due to aspiration of buccal contents.

Necropsy.—There was slight atrophy of the brain, with meningeal thickening and pronounced sclerosis of the arteries at the base. The pons appeared slightly rounded but not softened. Section revealed marked atrophy of the right caudate nucleus and putamen, with some reduction in the globus pallidus. There was a small softening of the white matter beneath the central convolutions on this side, and two small infarcts were found in the lateral nucleus of the left thalamus. The brain stem was cut in serial sections. The alterations of chief significance were as follows:

1. Atrophy of the right pyramidal tract due to the subcortical lesion previously mentioned and also to a focus in the base of the pons.

2. Atrophy of the left median fillet due to a sharply defined focus of softening involving the outer two thirds of this structure just above the motor fifth nucleus.

3. Atrophy of the right central tegmental fasciculus, with corresponding hypertrophic degeneration of the homolateral olive, due to an infarct cutting through this bundle at the lower end of the posterior colliculi.

4. Partial destruction of the right brachium conjunctivum with hypertrophic degeneration of the left red nucleus, caused by the same infarct.

5. Atrophy of the right median longitudinal fasciculus, due to infarction of this structure at a slightly lower level.

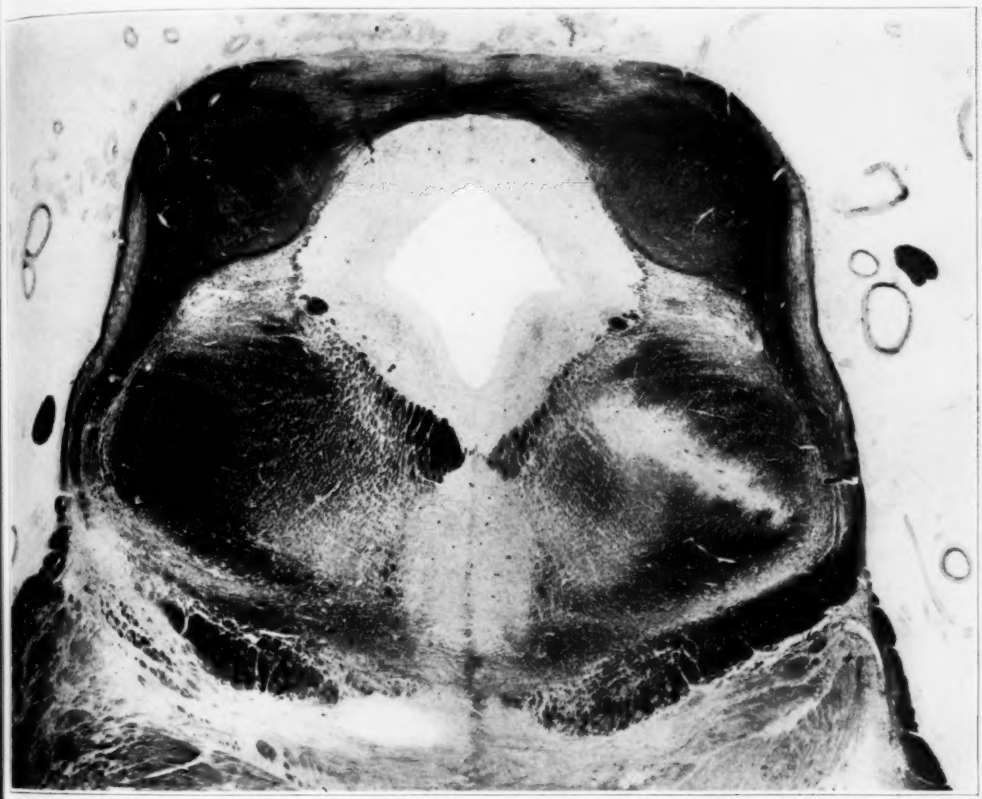

Fig. 1 (case 1).—Cystic infarct destroying most of the central tegmental fasciculus on the right side caudally. This infarct also damages the brachium conjunctivum, and a nearby one catches the median longitudinal fasciculus. Note also the degeneration of the outer part of the median lemniscus from an infarct on the left.

The infarct of the tegmentum (fig. 1) extended from close to the periventricular gray matter ventrolaterally to the brachium conjunctivum, involving this structure to a rather notable degree and destroying some of the reticular formation and particularly the central tegmental fasciculus. It was in the form of a fissure about four times as long as it was wide, and was apparently due to occlusion of the long circumferential artery at this level. Occlusion of another branch of this artery was probably responsible for the infarction of the median longitudinal fasciculus at a somewhat lower level.

The degeneration resulting from the tegmental infarct could be followed caudad as far as the olivary body (fig. 2). This showed marked enlargement, with reduction in cells and rarefaction not only of the periolivary stratum of fibers but also of the hilus. This was most marked in the ventrolateral portion in the middle and upper levels of the olive, and did not involve the accessory organs. The olivospinal fasciculus of Helweg seemed degenerated on the right. When the central tegmental fasciculus was traced upward, it was lost in the decussation of the brachium conjunctivum. The left red nucleus showed definite pallor throughout and defi-

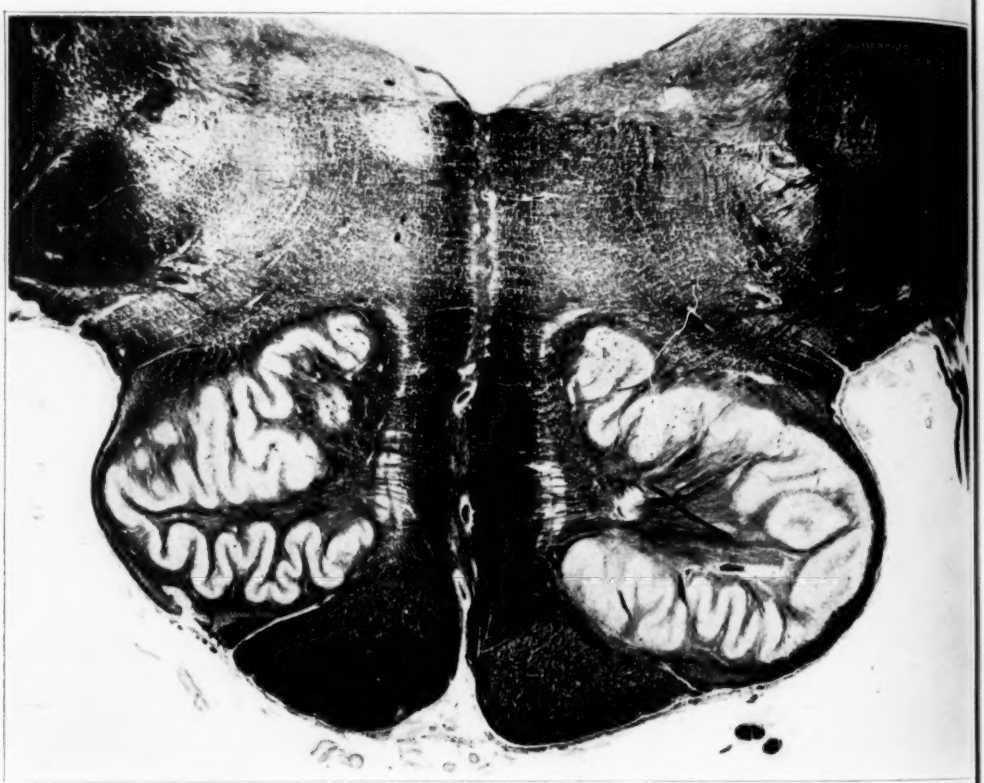

Fig. 2 (case 1).—Hypertrophic degeneration of the olivary body on the right side and absence of the central tegmental tract dorsolaterally. The capsular and hilar olivary fibers are diminished. Note also the homolateral degeneration of the pyramidal tract and the contralateral degeneration of the lemniscus. A minute infarct lies close to the floor of the fourth ventricle.

ciency in the capsular fibers on the mesial and ventral aspects. The dorsal decussation was much smaller on the left side, and the ventral one on the right. Just how much of this was due to involvement of the superior cerebellar peduncle and how much to that of the central tegmental fasciculus could not be determined.

The degeneration of the median longitudinal bundle was almost complete at the level of the infarct noted, but became less and less noticeable in more distant sections. The degeneration was more marked in the ascending fibers and could

be traced as far as the oculomotor nucleus, while the descending degeneration faded out at the level of the abducens nucleus. The more mesial fibers were affected.

The damage to the left median fillet remained relatively constant in its ascending course out into the thalamus. Below the infarct, definite degeneration could be noted, with some reduction in the contralateral dorsal nuclei.

The facial nuclei on both sides appeared normal. There was a small infarct on the left side in the concavity of the arch laterally, but the root did not seem to be affected in any marked degree.

Comment.—Owing to the confusion manifested by this patient, no satisfactory examination could be carried out, especially as regards sensibility. The tendency to fall to the right may have been due to involvement of the contralateral medial fillet, but rather more to that of the brachium conjunctivum on the same side even though there was no marked asynergia in the hands. The flattening of the face, especially in emotional movements, with preservation of voluntary movements, is also referable to this region, and the integrity of the voluntary movements shows that the infarct in the region of the facial knee was not significant. The failure of the right eye to move beyond the midline in lateral conjugate deviation was evidently due to the lesion of the median longitudinal fasciculus, although at the time this was not recognized on account of the absence of inward movement of the eye in convergence. The oculomotor nuclei were not involved, although a minute focus of softening occupied the left median longitudinal fasciculus close to the nucleus. The root fibers were slightly diminished on the left side. The palatal myoclonus is to be ascribed to the destruction of the central tegemental fasciculus since, although palatal myoclonus may occur following destruction of the dentate nucleus, the olivary degeneration is crossed and the myoclonus is homolateral. The brachium conjunctivum is probably not concerned with the phenomenon.

In terms of arterial occlusion, many branches of the basilar artery were affected. Lesions in the base of the pons were minute but numerous, probably depending on the paramedian branches. Occlusion of the short circumferential arteries was probably the cause of the rather large lesion at the upper end of the basis pontis on the right side and of the degeneration of the lemniscus on the opposite side, while occlusion of the long circumferential branches leading into the tegmentum affected the central tegmental fasciculus and brachium conjunctivum and the median longitudinal fasciculus.

CASE 2.—*History.*—A white man, aged 71, who was admitted to the hospital on April 8, 1931, died on June 27, 1931. The diagnosis was: psychosis with cerebral arteriosclerosis, fracture of the humerus, hypostatic pneumonia and myoclonus of the palate.

The patient had an enviable record of local public service as a lawyer, but in December, 1929, he suffered from a stroke, with paralysis of the right side and a defect of speech. After several weeks he was able to return to work, but in Decem-

ber, 1930, he became forgetful, confused and irritable, and was treated for hypertension. In the early part of 1931 he became disoriented and expressed delusional ideas, lost control of the sphincters and displayed lack of emotional control.

Physical Examination.—The patient was feeble and emaciated, with sclerotic arteries and hypertension (the blood pressure was 200 systolic and 120 diastolic). The heart was somewhat enlarged, with a systolic murmur at the aortic area. The urine contained a trace of albumin and some hyaline and granular casts. The blood serum was normal.

Neurologic Examination.—There was an aphasic defect of semantic type with some nominal features. When given a matchbox, the patient said: "Safety matches. I ought to know what to do with that, but it requires considerable calculation to make the proper division into units." Again, on picking up a pencil, he said: "There is something of a disability about this dime." In addition, there was apraxia. He was unable to strike a match, but took up a pocket knife and struck this on the box. During the examination he carried on a flowing conversation, but it was endowed with little propositional value. The words were well enunciated, the vocabulary was large, and the rhythm and flow of speech were normal. He tended to repeat words over and over, in a more or less inappropriate fashion. The pupils reacted to light and in accommodation, the ocular movements were slightly defective to the left, and there was no nystagmus. The fundus could not be seen on the left on account of lenticular opacity, but on the right there was a sharply defined disk with markedly sclerosed arteries. The visual fields were full to coarse testing. The muscular control of the face was poor and there was little facial movement in smiling, but no spasmodic laughing or crying was observed. The tongue was protruded in the midline with rather marked fine tremors.

The palate and pharynx were agitated mostly on the left side by a constant rhythmic twitching at the rate of about two per second, lifting the uvula to that side and elevating the vault of the palate. This did not interfere with the patient's speech, and was interrupted during phonation. Articulation was somewhat impaired by loss of the teeth.

The upper limbs showed some rigidity but no spasticity, and the reflexes were reduced. No grasping or thumb signs were observed. There was fairly good coordination in slow movements, but rapid pronation and supination brought out rather marked irregularity of movement. There was no dysmetria or past pointing. The lower limbs were more spastic, with ankle clonus on the right and a positive Babinski sign on both sides. The patient could not cooperate in the sensory examination beyond recognizing the vibration of a tuning fork in the fingers but not in the lower limbs. He reacted normally to painful stimuli, however. He stood alone with difficulty, and took short steps, dragging the right foot and balancing slightly with his arms.

The patient was treated on several occasions for congestive myocardial failure. He sustained a fall resulting in fracture of the humerus. Soon after this he showed dysphagia with attacks of coughing, and pneumonia developed from which he died with a high temperature (107 F.).

Necropsy.—There were cardiac hypertrophy with mitral stenosis, hypostatic pneumonia and generalized arteriosclerosis. The brain was rather markedly atrophic, with considerable clear fluid in the arachnoid meshes and some opacity of the membranes. The vessels at the base presented patchy atheroma, but no superficial focal lesions were evident. On section, several small foci of softening were found in the subcortical white matter and in the gray nuclei at the base. Section through the pons slightly above the nuclei of the fifth nerve disclosed minute lesions in the basis pontis on both sides. At the level of the main trigem-

inal nuclei on the right side was a small fissure in the tegmentum occupying the location of the central tegmental fasciculus and extending down through the median fillet slightly into the basis pontis (fig. 3). Section through the medulla showed marked hypertrophy and pallor of the right olivary body, with some reduction in the left pyramidal tract. The cerebellum showed an infarct in the white matter on the left side, but no involvement of the dentate nucleus.

Microscopic examination of the olivary body showed enlargement on the right side, mostly in the lateral portion (fig. 4). There was little involvement of the accessory bodies. There was broadening of the gray lamina, with disappearance of many of the ganglion cells, those remaining showing no increase in the amount

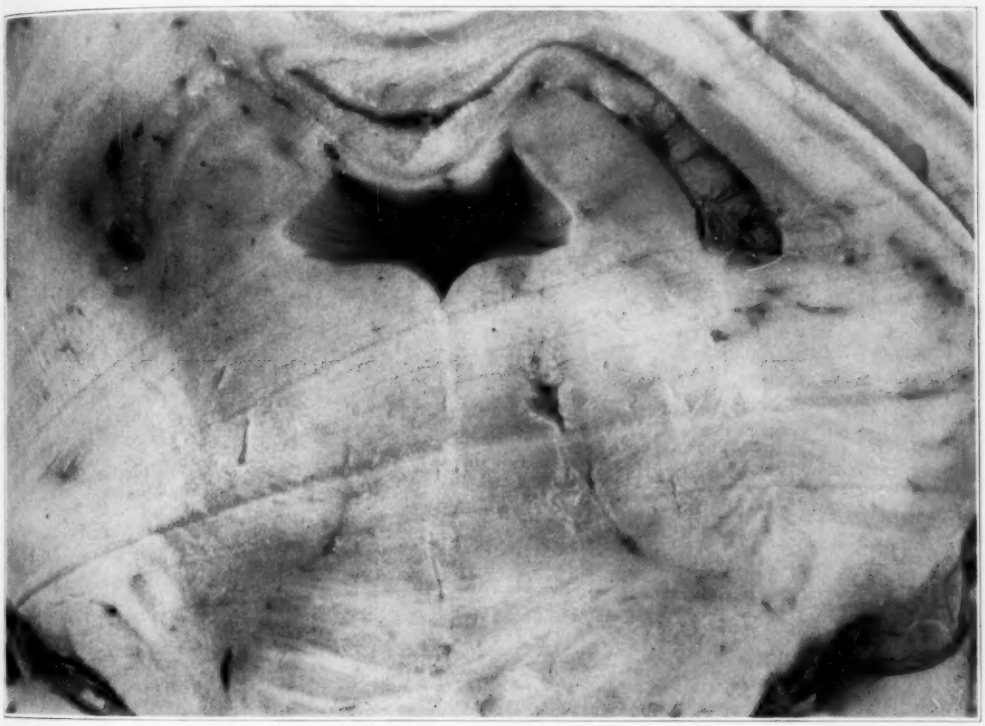

Fig. 3 (case 2).—Cross-section of the pons showing a cystic infarct of the tegmentum on the right side involving the area of the central tegmental fasciculus.

of pigment present. The periolivary system of fibers was greatly reduced, and the hilus was very pale. There was some reaction on the part of the glia, and fairly numerous rod cells were visible, a few of them being loaded with fat. The local arteries were sclerotic and had a few small round cells in their sheaths. The gliosis was both cellular and fibrillar, many large bloated forms being visible, occasionally forming a *Gliarase*. Milder changes were found on the left side. The dentate nuclei showed similar changes of mild degree and enlarged perivascular spaces, which were more marked on the left side, with a good deal of pigment present. At the level of the roof nuclei, on the left side, there was a rather large infarct in the cerebellar white matter, lateral to the dentate nucleus and apparently

involving some of the fibers going to the vermis. Section through the pons revealed integrity of the brachium conjunctivum, median fillet and median longitudinal fasciculus, but marked reduction of the central tegmental fasciculus, although the section did not pass through the infarct itself. Infarcts were present in the base of the pons. The cerebellorubral connections seemed normal on both sides. The pyramidal tracts in the peduncle appeared practically normal.

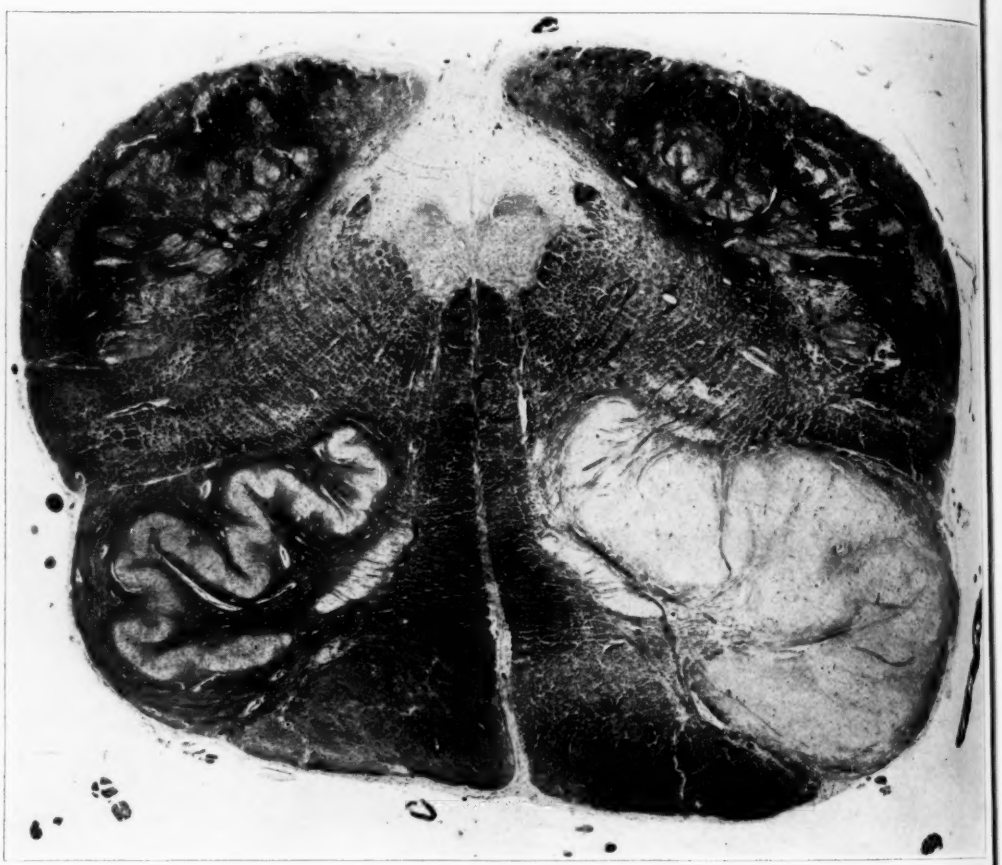

Fig. 4 (case 2).—Hypertrophic degeneration of the right olivary body with loss of capsular and intra-olivary fibers and degeneration of the central tegmental fasciculus.

Comment.—The spasticity was apparently due to the bilateral pontile infarcts, since no significant lesions were found at higher levels and the base of the peduncle was normal, while below the pons the pyramidal tracts were slightly degenerated. No explanation was forthcoming in regard to the aphasic and apraxic symptoms observed, and they were thought to be due to functional circulatory changes. The myoclonus

of the palate seems best explained by the infarct occupying the tegmentum and destroying the central tegmental fasciculus, thereby leading to hypertrophic degeneration of the homolateral olivary body.

ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS

The central tegmental fasciculus is most prominent in the pons below the decussation of the brachium conjunctivum. There is some disagreement concerning its origin, constitution and course. Ranson [6] spoke of it as the thalamo-olivary fasciculus, but Anton and Zingerle [7] found it well developed in a case of olivopontocerebellar agenesis, and I can substantiate this on the basis of another case. These authors stated that von Bechterew located its origin in the region of the third ventricle, in contrast to Edinger, Obersteiner and Villiger, who preceded Ranson. Kappers [8] favored its origin in the pretectal area caudal to the thalamus, while Morrison [9] believed that it arises in the globus pallidus and receives components from the red nucleus. It appears to be a predominantly descending fasciculus. That it has connections with the olivary body can scarcely be doubted from its position in the dorsolateral capsule of the olive, and from the fact that the olive shows marked alterations after its degeneration. In olivary aplasia, however, this tract is still observed below the olive as a recognizable bundle and joins the ventral column of the spinal cord below the pyramidal decussation. Anton and Zingerle were unable to follow its upper course on account of a break in the sections, but I have observed its apparent gathering into a number of small compact fasciculi running cephalad dorsally from the red nucleus to be lost apparently in the substantia innominata of Reichert in the vicinity of the fasciculus lenticularis. In case 1, in which an uninterrupted series of sections was examined, the upper reaches of this tract did not appear as markedly affected as those below the infarction, but there was some difference on the two sides, the right tract being somewhat smaller. Whether there is a component joining the tract from the tectum opticum is not altogether certain, but the fibers lie close to those of the posterior commissure, and since the tract increases in importance below this level some addition is likely. I was not able to examine the substantia innominata with cell stains in order to determine whether there was any retrograde degeneration of the large multipolar cells.

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6. Ranson, S. W.: Anatomy of the Nervous System, Philadelphia, W. B. Saunders Company, 1920, p. 219.

7. Anton, G., and Zingerle, H.: Genaue Beschreibung eines Falles von beiderseitigem Kleinhirnmangel, Arch. f. Psychiat. **54**:8, 1914.

8. Kappers, C. U. A.: Vergleichende Anatomie des Nervensystems, Haarlem, de Erven F. Bohn, 1920, vol. 2, pt. 2, p. 913.

9. Morrison, L. R.: Anatomical Studies of the Central Nervous Systems of Dogs Without Forebrain or Cerebellum, Haarlem, de Erven F. Bohn, 1929.

The degeneration of this tract is apparently the cause of degeneration of the olivary body of the same side; yet the olive may show the same type of degeneration without involvement of the central tegmental fasciculus, but following a lesion of the opposite dentate nucleus. It has long been known that the olive degenerates when the cerebellum is damaged, although the schematic localization of Holmes and Stewart [10] is not accepted by all authors. The greatest degeneration takes place when the hilus of the dentate nucleus is destroyed. Yet this lesion is not associated with degeneration of the central tegmental fasciculus. On the other hand, the destruction of the brachium conjunctivum in its course within the pons does not seem to bring about olivary degeneration. It is possible, therefore, that the olivocerebellar fibers are gathered into a fasciculus that is vulnerable in toto in the vicinity of the dentate nucleus. This is indicated by the work of Ley.[11] The nature of the homolateral degeneration of the olive in cases in which the central tegmental fasciculus has been damaged is somewhat more obscure, since the tract is predominantly if not entirely a descending one, and transneuronal degeneration is not supposed to occur in the mature nervous system. To invoke some fiber components ascending in the central tegmental bundle and others running to the opposite dentate nucleus is orthodox but ineffective in the elucidation of the complete olivary degeneration that takes place when either of these structures is damaged.

I have examined the sections from a case of Shugrue, the report of which is not yet published, in which a tumor of the roof of the fourth ventricle impinged on both dentate nuclei. The left olivary body was degenerated; the myoclonus was almost limited to the right side. The flattening of the pons was so great that the tegmentum was reduced to a thin ribbon of tissue, and lateral conjugate movements of the eyes were almost suppressed. Moreover, there was invasion by the tumor of the left tegmentum, and tumor implants occurred elsewhere in the ventricular system. The frequency of tumors involving the dentate nucleus and the corresponding rarity of palatal myoclonus throw serious doubt on the suggestion that damage of the dentate nucleus provokes this symptom.

Hypertrophic degeneration of the olive may take place without palatal myoclonus having been observed. This is especially true in the cases of Ley, in which cerebellar symptoms were present. Nevertheless, it has been observed in cases of palatal myoclonus in which the central tegmental fasciculus was reported to be intact and in which the lesion was

10. Holmes, G., and Stewart, T. G.: On the Connections of the Inferior Olives with the Cerebellum in Man, Brain **31**:125, 1908.

11. Ley, R. A.: Contribution à l'étude des localisations cérébelleuses et du syndrome cérébelleux, Arch. internat. de méd. expér. **2**:5, 1925.

apparently purely cerebellar. Such was the conclusion of van Bogaert and Bertrand, but after careful study of their report I cannot help believing that an additional lesion was overlooked because of the concurrent disturbance of associated lateral movements of the eyes, a phenomenon generally conceded to depend on a lesion of the median longitudinal fasciculus.

The peculiar movements and their peculiar distribution have not been adequately explained. From their tempo, rhythm and constancy, they might be allied to the constant tremors of mesencephalic origin. They present little of the character of parkinsonian tremors, and they are apt to be interrupted by volitional activity. From their rate and constancy in the individual patient, they might be thought of as oscillations dependent on the action currents of the corticobulbar neurons that have escaped normal damping on account of destruction of the extrapyramidal pathways. If such were the case, however, drugs would have more marked effects on them. Moreover, the movements are, if anything, increased in cases presenting pyramidal lesions. The distribution of the movements makes it necessary to invoke the faciorespiratory mechanism so interestingly treated by Wilson.[12] The involvement of the larynx and diaphragm as well as the corner of the mouth in some cases is enough to warrant the premise that this is a complex reaction system, and the synchronism of the movements indicates that the system is a unit.

In searching for normal homologs of these movements, breathing, swallowing, laughing, crying, panting, coughing and other acts were considered, but it seemed that the closest approximation was the act of yawning. The myoclonic movements of all these parts are believed to be miniature yawning movements. The first and least repressible part of a yawn is the elevation of the palate. Moreover, whereas in normal inspiration the vocal cords are in abduction, in yawning there is a tendency to adduction, and this is true in the syndrome under discussion. The mechanism of yawning is not well understood, but the pathways of respiratory control have been elaborately charted by Lumsden and by Graham Brown,[13] and the course of the respiratory "arresting" pathway which arises on the under surface of the frontal lobe would seem to agree fairly closely with the central tegmental fasciculus. Incidentally, yawning is a fairly common symptom in disease at the base of the frontal lobe. The occurrence of yawning has not been mentioned in the cases of palatal myoclonus, nor was it studied in the cases reported here. I suggest that degeneration of the central tegmental fasciculus allows the appearance of constantly recurring abortive yawning movements.

12. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood & Company, 1929, p. 260.

13. Brown, Graham, quoted by Wilson.[12]

Whether there is an associated mimic paralysis is not certain. It was observed on the left side in case 1, but only a general reduction in facial expression occurred in case 2. None of the reports is very clear in this regard. Moreover, in cases of mimic paralysis no accompanying myoclonic twitching of the palate has been recorded. It would appear that palatal myoclonus is not closely related to the mimic mechanism, although both of them play on the same organs and form parts of the faciorespiratory synkinesis.

SUMMARY

Two cases are reported in which myoclonic movements of the palate and pharynx were observed during life, associated with infarction of the central tegmental fasciculus and hypertrophic degeneration of the olivary body. Both of these cases were complicated by the occurrence of numerous lacunae in the brain stem and elsewhere.

The central tegmental fasciculus is believed to constitute a part of the automatic faciorespiratory synkinetic system. It would appear to arise in the substantia innominata of Reichert, mostly contralateral but with some homolateral fibers decussating through the posterior commissure, and to fuse with the ventral ground bundle of the spinal cord. Its relationship to the inferior olive is evidently close on account of the degeneration of this latter structure after damage of the tract.

The myoclonic movements of the palate and pharynx are part of a more complex movement, which in its full development comprises synchronous rhythmic movements of all the faucial musculature and of the larynx, face and diaphragm and sometimes the intercostal muscles and fingers. It is suggested that this movement is part of the faciorespiratory synkinesis related not to mimic but to yawning.

ABSTRACTS OF DISCUSSION OF PAPERS BY DRS. RILEY AND BROCK AND BY DR. FREEMAN

Dr. L. J. Pollock, Chicago: The more recent communications on this clinical subject will, no doubt, allow one to observe more and more of these cases. I recently saw a woman, aged 39, who had complained of vertigo, a choking feeling and slight difficulty in walking for four months. On examination, the significant things that were noted were as follows: There was a combined synchronous myoclonic contraction of the palate in a vertical direction, of the left pillars and of the posteriorpharyngeal walls at a rate of about 130 to 150 per minute with a similarly synchronous contraction in the vocal cords. Occasionally, on phonation there seemed to be a slight paresis of the right vocal cord. There were similar movements in the tongue, lips and upper extremities. Lastly, she had a spontaneous rotary nystagmus to the right, and on looking to the left both phases became equally rapid.

The significance of these movements is difficult to evaluate. One may speculate considerably as to their resemblances to otherwise normal repetitive movements, such as gagging, rather than that of yawning. The fact that the movement has a

rapid and slow component is of some significance; in that respect it greatly resembles such diphasic reflexes as are seen, for example, in a scratch reflex.

DR. M. NEUSTAEDTER, New York: A woman, aged 50, whom I have had under observation for a year following trauma of the head with momentary loss of consciousness, developed a similar clonus which disappears only on swallowing and chewing. She has a left hemihypesthesia and a loss of scleral and pharyngeal reflexes. As a coincidence, when I discussed this case with my interns, one said to me, "I can do that; I have been doing that for twenty years." He demonstrated this phenomenon, which was impossible on speaking or swallowing.

DR. J. RAMSAY HUNT, New York: I observed two cases, during the epidemic of encephalitis, in which there was a rhythmic tremor of the soft palate. This was a constant tremor. In one case there was a synchronous clonic movement of the lower jaw. In both cases, the history and associated symptoms made the diagnosis of encephalitis a positive one.

My explanation of the palatal tremor was based on a theory of central inhibition which I presented before this association in June, 1923. According to this conception, central inhibition is dependent on a specific inhibitory cell, of the Golgi type variety, and is based on the development of chorea when the small cells of the neostriatum are involved. These cells are found throughout the central nervous system, in the spinal cord and in all aggregations of gray matter, including the cerebral cortex, where the granular layers belong to this cellular type. Any specific involvement of this group of cells would therefore paralyze inhibition and release the excitatory function of the cells. Encephalitis is a disorder which curiously effects a release of motility at a number of levels, for example, myoclonus at the spinal level and chorea at the striatal level. The changes of character in encephalitis of children are also characterized by a loss of inhibition in the psychic sphere.

A localized involvement of these small inhibitory cells in relation to the glossopharyngeal mechanism would cause a release of function and the development of rhythmic tremor. Of course, a group of cases such as Dr. Riley has described must embody a great many different conditions and mechanisms, and this is only one thought in connection with a peculiar symptom, of which the pathologic physiology is difficult to explain.

DR. FREEMAN: Within the past two weeks I have observed a patient suffering from illuminating gas poisoning. Every time he opens his mouth there are myoclonic twitchings of the uvula, succeeded by a definite yawn.

CEREBRAL CIRCULATION

XXI. ACTION OF HYDROGEN SULPHIDE

HENRY S. FORBES, M.D.
AND
CATHERINE C. KRUMBHAAR, A.B.
BOSTON

In the earlier papers of this series evidence has been presented to show that the caliber of arteries supplying the mammalian cortex is regulated by at least three mechanisms: first, by sudden and extreme alterations in systemic arterial pressure;[1] second, by vasomotor nerve impulses transmitted to arteries and arterioles of the pia;[1a] third, and much the most frequently active mechanism, as well as the strongest, by chemical influences acting directly on the blood vessel walls (either on the muscle fibers themselves or through some local reflex).

During investigation of the last of these mechanisms it was found that various chemical substances, histamine,[2] acetylcholine,[3] amyl nitrite[3] and lactic and hydrochloric acids,[4] and increased tension of carbon dioxide[5] caused dilatation of blood vessels in the pia. The present paper adds to this list another acid—hydrogen sulphide. This gas diffuses rapidly through living membranes, notably the walls of the intestines.[6] Various channels of absorption have been investigated and the effects compared.

This study was aided by a grant from the Josiah Macy, Jr., Foundation.

From the Neurological Unit, Boston City Hospital, and the Department of Neuropathology, Harvard Medical School.

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

1a. Forbes and Wolff.[1] This mechanism appears to be much less strong than the vasomotor control of vessels in the skin and other extracranial organs.

2. Forbes, H. S.; Wolff, H. G., and Cobb, S.: The Cerebral Circulation: X. The Action of Histamine, Am. J. Physiol. **89**:266, 1929.

3. Wolff, H. G.: The Cerebral Circulation: XI. a. The Action of Acetylcholine; b. The Action of the Extract of the Posterior Lobe of the Pituitary Gland; c. The Action of Amyl Nitrite, Arch. Neurol. & Psychiat. **22**:686 (Oct.) 1929.

4. Unpublished data from this laboratory.

5. Wolff, H. G., and Lennox, W. G.: The Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097 (June) 1930.

6. McIver, M. A.; Redfield, A. C., and Benedict, E. B.: Gaseous Exchange Between Blood and Lumen of Stomach and Intestine, Am. J. Physiol. **76**:92, 1926.

METHOD

Pial arteries of cats under sodium barbiturate anesthesia were observed through a cranial window. The technic previously described [7] was modified only by two slight changes: First, in order to reduce venous bleeding the animal's head was raised during the operation; second, to prevent leakage of cerebrospinal fluid hot yellow wax was applied to the skull outside the metal rim of the window.

The animals were given hydrogen sulphide in four different ways:

1. Local application: Hydrogen sulphide dissolved in Ringer's solution or in distilled water was irrigated beneath the cranial window, replacing an equal amount of cerebrospinal fluid, which was allowed to escape. For control the same solutions were used minus the hydrogen sulphide.

2. Lungs: Hydrogen sulphide diluted with air was inhaled from a rubber bag through a tracheal tube with inspiratory and expiratory valves.

3. Peritoneal cavity: Undiluted hydrogen sulphide was injected by syringe.

4. Rectum: Undiluted gas was injected either by syringe or by rubber bag at a pressure not over 400 mm. of water.

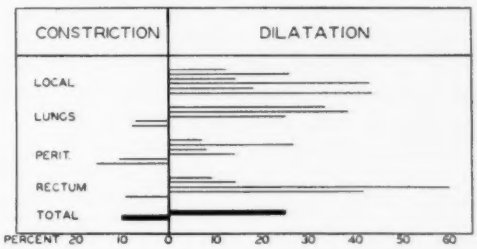

Chart 1.—Effect of hydrogen sulphide on the degree of change in the diameter of the pial artery. Each fine line represents the percentage change—dilatation or constriction—during a single experiment. The broad lines represent the average changes of all groups.

FINDINGS

Reaction of Pial Artery to Hydrogen Sulphide

Reaction of Pial Artery	Local (Surface of Brain)	Lungs	Peritoneal Cavity	Rectum	Total
Number of trials	6	5	7	6	24
Dilatation	6	3	4	4	17
Constriction	0	2	2	1	5
No change	0	0	1	1	2

Not only was the total number of dilatations greater than the number of constrictions (seventeen to five), but the degree of dilatation also was much greater than the degree of constriction, as shown in chart 1.

When applied locally to the surface of the brain, hydrogen sulphide in Ringer's solution caused dilatation in every instance, as shown in

7. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

the table. The degree of dilatation was approximately the same as with a solution of carbon dioxide in Ringer's solution (chart 2). Normal Ringer's solution caused no change in arterial caliber. Distilled water alone (p_H slightly less than 7) caused a slight dilatation; hydrogen sulphide in distilled water caused a marked dilatation (chart 3).

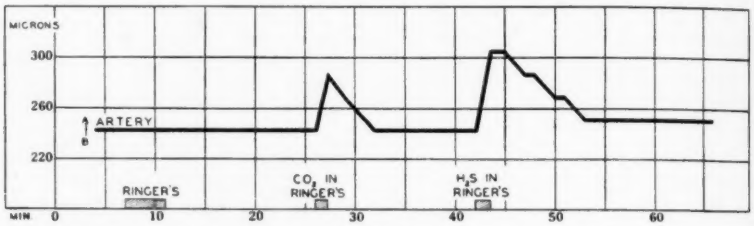

Chart 2.—Effect of the local application of hydrogen sulphide. Irrigation with Ringer's solution (control) beneath the cranial window had no visible effect on the pial artery. Carbon dioxide in Ringer's solution caused an 18 per cent dilatation of this vessel. Hydrogen sulphide in Ringer's solution caused a 26 per cent dilatation of this vessel. In this and the following charts (except chart 8) the ordinates represent femoral arterial pressure in millimeters of mercury, diameter of pial arteries in microns, and cerebrospinal fluid pressure in millimeters of Ringer's solution; the abscsissas, time in minutes. The broad line indicates the diameter of a pial artery, and is so plotted that its upper edge records the correct measurements and time relations. The short line *AB* represents an extent of change in arterial diameter that could be accurately measured. A change of half this extent is of doubtful validity.

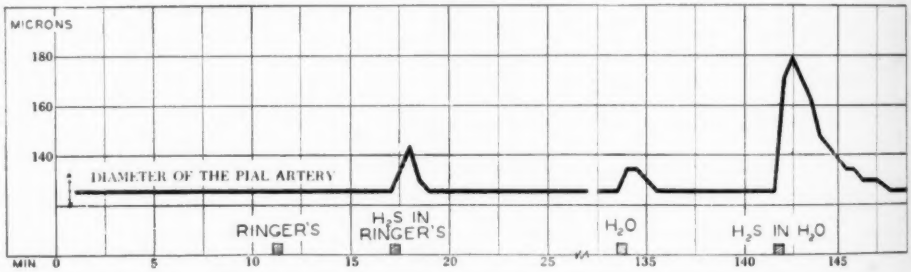

Chart 3.—Effect of local application of hydrogen sulphide. Ringer's solution (control) caused no change in the pial artery. Hydrogen sulphide in Ringer's solution caused a 14 per cent dilatation of this vessel. Distilled water (p_H 6.6 $\pm$ 0.2) caused a 7 per cent dilatation. Hydrogen sulphide in distilled water caused a 43 per cent dilatation.

Inhalation caused dilatation three times with relatively strong gas mixtures [8] and constriction twice with more dilute gas. The effect of

8. A measured volume of gas from the hydrogen sulphide generator was mixed with a volume of air in a rubber bag. Thus it was possible roughly to compare doses, but since no analyses were made, only the general terms "strong" and "weak" have been used.

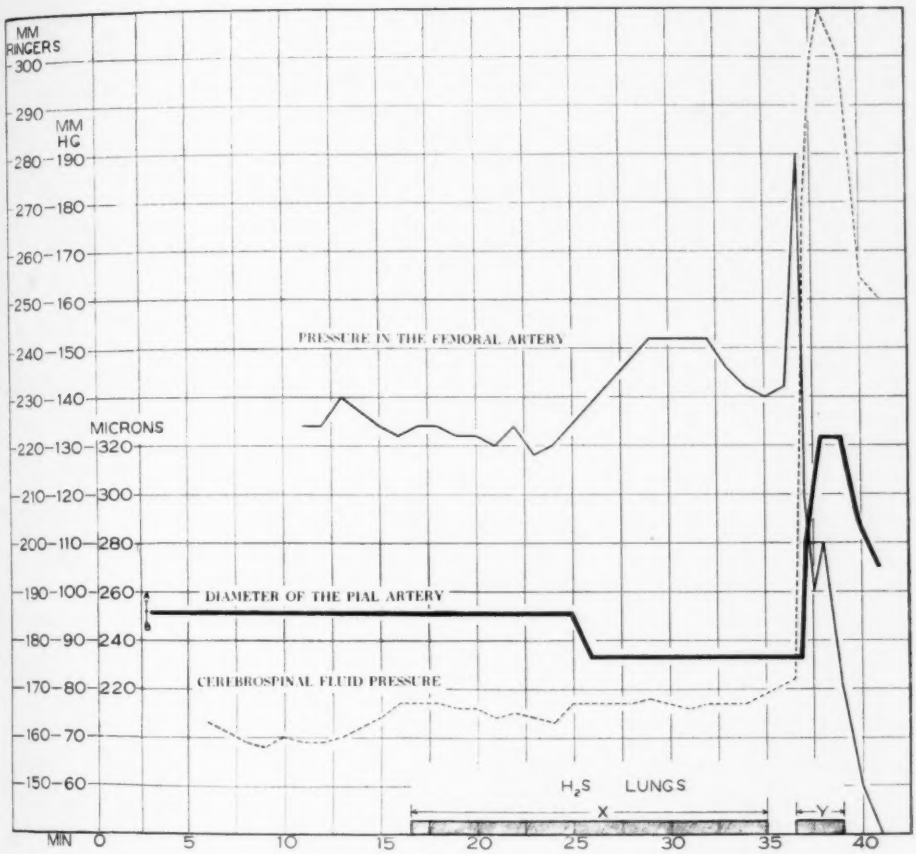

Chart 4.—Result of inhalation of hydrogen sulphide: effect of weak versus strong mixtures of gas. *X* indicates the period of inhalation of weak gas; *Y*, the period of inhalation of strong gas. After a two minute inhalation of weak gas, hyperpnea was noted and seven minutes later the constriction of the pial artery (7 per cent), in spite of a rising arterial pressure. Less than half a minute after inhalation of the stronger gas started the arterial and cerebrospinal fluid pressures rose sharply and the pial artery began to dilate. The arterial pressure now rapidly fell from 190 to 100 mm. of mercury; the pial artery continued to dilate (total, 39 per cent) and the cerebrospinal fluid pressure rose to 310 mm. of Ringer's solution. Then both pressures fell, respiration stopped, the circulation began to fail (progressive slowing of blood flow was clearly seen in all pial vessels) and the the pial artery became narrower.

dosage on pial artery diameter is shown in chart 8. Not only the amount of gas absorbed, but the rate of absorption determines its physiologic effect, and the extent of this effect may be measured roughly by changes in respiration and blood pressure. These changes, in addition to the volume of gas injected or inhaled, have been used to help classify experiments according to strength of dose. With the strong gas the intracranial pressure usually rose (in one case from 171 to 310 mm. of Ringer's solution, as shown in chart 4) and the systemic arterial pressure first rose and then fell abruptly while the pial arteries were still dilating.

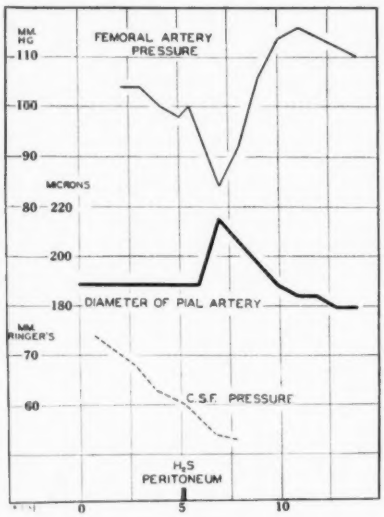

Chart 5.—Result of the peritoneal injection of hydrogen sulphide: variable effect of a small dose (10 cc.) (see chart 6). During this experiment the cerebrospinal fluid pressure was falling owing to the previous injection of a hypertonic solution (25 cc. of 50 per cent urea, intraperitoneally, two and a quarter hours before). The purpose of this injection was, by dehydration, to be certain that the cortex was not pressing against the cranial window, thus avoiding possible artefacts due to local interference with the pial circulation. The pial artery dilated 14 per cent within two minutes of the injection of hydrogen sulphide into the peritoneal cavity. The behavior of the arterial pressure suggests that dilatation of splanchnic and other vessels occurred simultaneously with dilatation of the cerebral vessels.

Intraperitoneal injection caused dilatation if a strong dose was given. A smaller amount of gas sometimes gave a dilatation (chart 5) and sometimes a constriction (chart 6). Respirations became deeper and more rapid, and with the larger doses an odor of hydrogen sulphide was noticed in the expired air, and a solution of lead acetate through which the expired air was passed gave a positive test for lead sulphide.

Rectal administration of hydrogen sulphide gave similar results. Pial arteries dilated with a large dose and showed no change, or were constricted slightly with a small one (chart 7). In order to make sure that some of the observed changes might not be due, reflexly or otherwise, to mechanical pressure of the gas in the rectum, air was injected at similar pressures. No change in the diameter of the pial vessels was observed, though a transient small rise in intracranial pressure usually occurred. This, however, never exceeded 9 mm. and usually was half that figure. Mere insertion of the rectal tube sometimes was accompanied by a similar rise of a few millimeters (chart 7 *C*). (In one case the rise was 20 mm. for two minutes.)

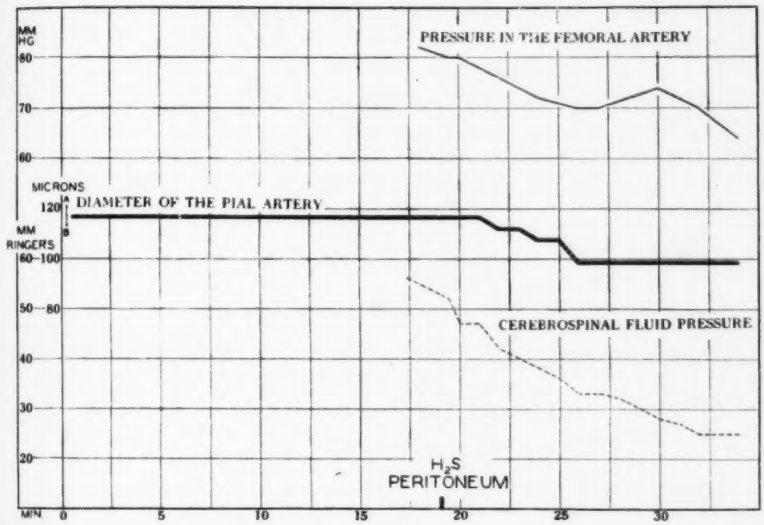

Chart 6.—Result of peritoneal injection of hydrogen sulphide: variable effect of a small dose (see chart 5). The fall in cerebrospinal fluid pressure was due to previous injection of hypertonic urea (the same dose as that described for chart 5) four hours previously. The pial artery constricted 15 per cent, but did not return to its former size.

The rate of absorption from the rectum and from the peritoneal cavity was approximately the same, the shortest time interval between the injection of gas and the appearance of an odor of hydrogen sulphide in the breath (or a precipitate in the solution of lead acetate) was less than three minutes. Shortly before this test became positive, the pial arteries began to dilate and to throb more strongly, the pulse pressure increased, and the pulsations in the cerebrospinal fluid manometer became greater.

When the animal was saturated with hydrogen sulphide, the blood was bright red in the pial veins as well as in the arteries. The color

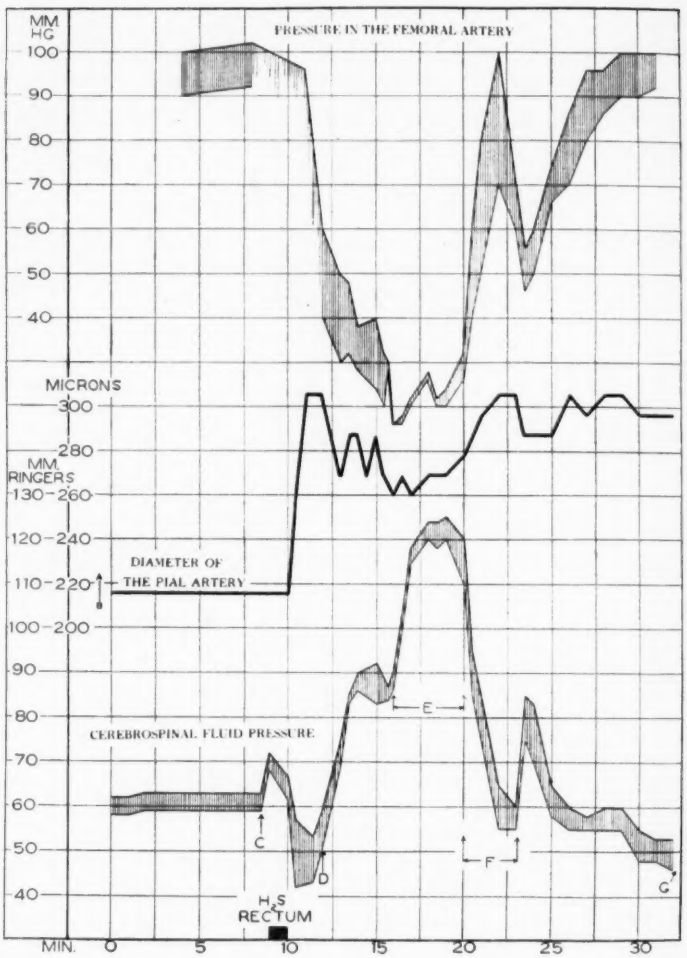

Chart 7.—Effect of rectal injection of a strong dose of hydrogen sulphide. *C* indicates the time at which the rectal tube was inserted; *D*, the time the odor of hydrogen sulphide was noticed in expired air; *E*, the period of apnea; *F*, the period of beginning spontaneous respirations, at first slow and shallow, then rapid and "panting"; *G*, animal "light"; odor of hydrogen sulphide gone from expired air. Pulse pressure is indicated by fine vertical lines in the arterial curve, and cerebrospinal fluid pulsations by similar lines in the cerebrospinal fluid curve. The pial artery dilated 42 per cent within three minutes of the beginning of the rectal injection of 30 cc. of hydrogen sulphide.

was similar to that seen in carbon monoxide asphyxia, presenting a striking contrast to the color of pial vessels in normal animals. (In these the arteries appear almost scarlet and the veins purplish. During circulatory failure, or asphyxia from lack of oxygen, the arteries become purple like the veins, and both sets of vessels appear lilac before the flow of blood stops.) With hydrogen sulphide the bright red color persisted for ten or fifteen minutes after the flow had completely stopped; then, first in the veins, the color changed slowly to purple.

One rather surprising finding was the rapidly lethal reaction to hydrogen sulphide when the gas was absorbed in sufficient amounts from the rectum. Though this action has long been known [9] it seems remarkable considering that the gas is normally present in the large intestine.[10]

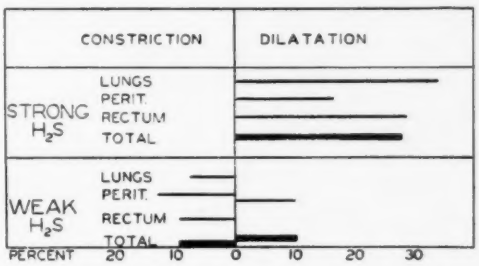

Chart 8.—Effect of dosage of hydrogen sulphide on pial arteries. The narrow lines represent the average degree of dilatation or constriction for all experiments within each group (as designated); the broad lines, the average dilatation or constriction for all groups. The terms "strong" and "weak" are used in accordance with the definitions given in footnote 8.

The following protocol gives an idea of this action.

A healthy adult cat, weighing 3.35 Kg., was tested. No anesthetic was given. The following observations were made:

12:34: Hydrogen sulphide, 30 cc., by syringe into rectum.

12:34½: Rapid respirations.

12:36: Strong odor of hydrogen sulphide in breath.

12:37: Apnea; pupils widely dilated; unconscious.

12:38: Rapid respirations.

12:39: Slowly regaining consciousness; lying flat; muscles relaxed.

12:45: Still panting very fast; conscious. Pupils normal size; rectal injection of 15 cc. and then of 30 cc. more of the gas was followed by very rapid respirations, clonic muscular contractions, tonic extensor spasm, dilatation of pupils, complete muscular relaxation, coma for three quarters of an hour and death.

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9. Chaussier, 1803, quoted by Mitchell, C. W., and Davenport, S. J.: Hydrogen Sulphide Literature, Pub. Health Rep. **39**:1, 1924.

10. Wells, H. Gideon: Chemical Pathology, Philadelphia, W. B. Saunders Company, 1920, p. 590.

COMMENT

The slight degrees of constriction observed during the earlier stages of absorption of hydrogen sulphide may have been due to a blowing off of carbon dioxide during the period of increased respiration. Similar constrictions have been noticed in the earlier stages of anoxemia due to carbon monoxide inhalation [4] or to simple lack of oxygen.[5] When dilatation occurred during the later stages of absorption of hydrogen sulphide, vigorous hyperpnea had already developed. That dilatation did occur in spite of this is good evidence of the strong vasodilator action of the gas, since hyperpnea by itself causes constriction.[5]

The change in color of the venous blood from purplish to bright red was very striking, and at no time during life was the color of reduced hemoglobin apparent. This observation would seem to throw doubt on the statement of Haggard [11] that, in the living animal, hydrogen sulphide merely converts oxyhemoglobin to reduced hemoglobin, but forms no new compound with the latter.

The possibility has been considered that constipation headache might be caused, at least in part, by absorption of hydrogen sulphide from the intestine and its consequent influence on intracranial circulation. In our experiments, however, it was not until relatively large amounts of this gas were given per rectum that measurable effects on pial vessels or intracranial pressure were observed. Under clinical conditions, therefore, it seems improbable that the traces of hydrogen sulphide normally found in the human intestine are responsible for the symptoms occurring during ordinary constipation.

SUMMARY

Hydrogen sulphide in relatively strong dosage acts on the cerebral circulation in a manner similar to other acids, causing dilatation of arteries in the pia. This dilatation occurs regardless of the channel through which absorption takes place, but only after the animal is severely asphyxiated. The dilatation and rise in intracranial pressure are observed during strong hyperpnea and rapidly falling blood pressure, indicating that the chemical control of the caliber of cerebral arteries is more powerful than the hydrostatic.

In smaller doses the gas often causes a slight constriction of pial arteries is more powerful than the hydrostatic.

Thus, another chemical agent, hydrogen sulphide, is added to those already known to have a strong influence on the flow of blood within the cranium.

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11. Haggard, H. W.: Toxicology of Hydrogen Sulphide, J. Indust. Hyg. **7:** 113, 1925.

CEREBRAL CIRCULATION

XXII. VENOUS PRESSURE; EFFECT ON CALIBER OF PIAL ARTERIES

KNOX H. FINLEY, M.D.
Fellow of the National Research Council
AND
HENRY S. FORBES, M.D.
BOSTON

In this series of investigations on cerebral circulation many of the data have been obtained by using a special method of measuring arteries in the pia through a cranial window. In order to interpret these findings correctly, it is necessary to recognize a number of factors which may affect the results. Aside from the one experimental factor—purposely introduced into each experiment—a number of secondary factors arise, owing to physiologic adjustments taking place within the experimental animal. Some of these, for example, systemic arterial pressure and cerebrospinal fluid pressure, have been measured as a routine procedure; others have been studied only occasionally. Venous pressure is of the latter group. It is possible, as suggested by Naffziger,[1] that fluctuations in systemic venous pressure may cause appreciable changes in the caliber of the cerebral arteries during various experimental procedures. The present experiments were undertaken in order to throw light on this point.

METHOD

Cats were used, anesthetized with sodium barbiturate; the routine cranial window technic of this laboratory[2] was followed, and intracranial pressure and femoral arterial pressure were recorded as usual. Systemic venous pressure was taken from the unligated external jugular vein (by a cannula passed through the subclavian vein into the lumen of the jugular) ten times, and from the leg vein (brachial) four times. The venous pressure was raised by injections of warm Ringer's solution, from a reservoir 400 mm. above the level of the animal's heart, into the femoral vein. The temperature of the solution was kept at 37 (± 2) C. Heparin (75 mg. per kilogram) dissolved in from 8 to 10 cc. of Ringer's solution was given intravenously to prevent clotting in the cannulas. (This injection of heparin by itself caused no change in the diameter of the pial vessels, during an observation period of half an hour.)

From the Department of Neuropathology, Harvard Medical School, and the Neurological Unit, Boston City Hospital.

1. Naffziger, H. D., in discussion on Wolff, H. G., and Forbes, H. S.: The Cerebral Circulation: IV. The Action of Hypertonic Solutions, Arch. Neurol. & Psychiat. **20**:73 (July) 1928.

2. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

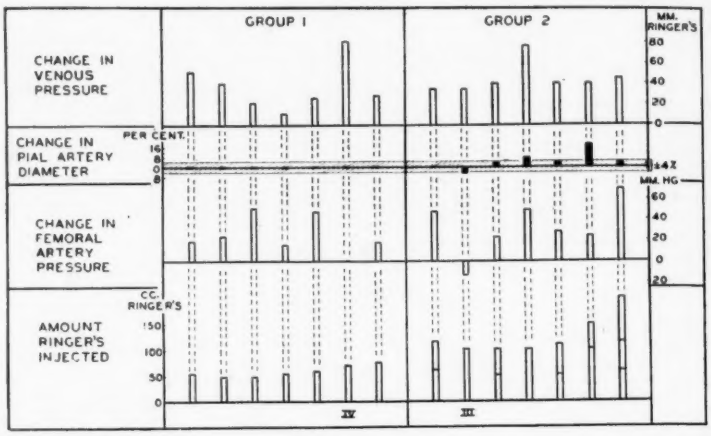

Chart 1.—Effect of intravenous injections of fluid on venous and arterial pressures and on caliber of pial arteries during the injection. Each column on the abscissa line represents the total volume of Ringer's solution injected. The subdivisions in certain columns each represent a separate injection, the top subdivision representing the last injection, and with this the other factors—arterial pressure, etc.—are correlated. The vertical dotted lines are merely guide lines to aid the eye in comparing the various factors. The earlier injections, in the cases of multiple injection, were all made within an hour of the final injection and, owing to the increased blood volume, affected the response to the final injection. Changes in diameter of the pial artery are recorded in terms of percentage of its diameter during a control period. The cross-hatched area, which indicates a change of 4 per cent in the diameter of this artery, represents an extent of change so small as to be of doubtful validity. Only changes greater than this are considered significant and are mentioned as definite changes. Numerals *III* and *IV* refer to two experiments, the details of which are given in charts 3 and 4, respectively.

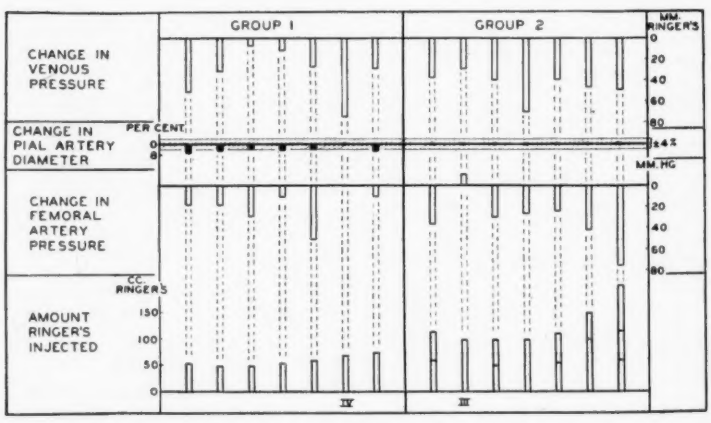

Chart 2.—Effect of intravenous injections of fluid on venous and arterial pressures and on caliber of pial arteries following the injection. The description given for chart 1 suffices for this chart as well.

RESULTS

Intravenous injections of Ringer's solution were carried out fourteen times in nine animals. The amount of fluid injected was found to influence the results; therefore, the injections have been divided into two groups of seven each:

Group 1: injections of less than 100 cc. (from 50 to 75 cc.).

Group 2: injections of 100 cc. and over (from 100 to 200 cc.).

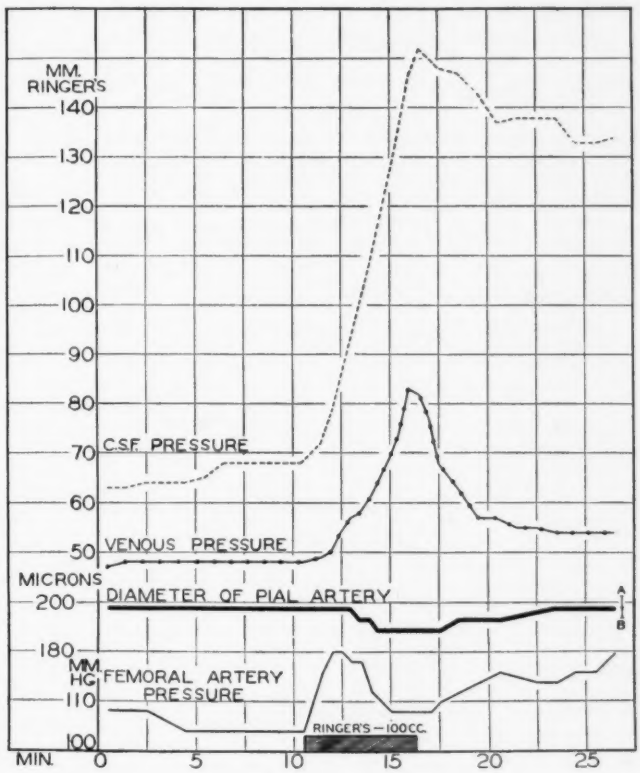

Chart 3.—Relation of changes in size of pial artery to alterations in systemic arterial pressure. During the first part of the intravenous injection of fluid (100 cc. of Ringer's solution) the artery showed no change in spite of a rise in all three recorded pressures. Two minutes later, while venous and cerebrospinal fluid pressures continued to rise, the arterial pressure fell, and at the same time the pial artery constricted slightly. Following the injection both venous and cerebrospinal fluid pressures fell, arterial pressure rose slowly, and the pial artery dilated slowly, regaining its original size.

In charts 3 and 4, records of arterial, venous and cerebrospinal fluid pressures were made at intervals of one minute or less. The cross-hatched area at the bottom of the chart represents the period of the intravenous injection. The line *A-B* indicates the extent of change in the diameter of the pial artery which could be accurately measured. Changes of one-half this amount are not considered significant.

The effect of the injections on venous and arterial pressures and on the size of the pial arteries is shown, in summarized form, in charts 1 and 2. The purpose of these charts is to show, graphically, the relative changes in these various factors during each period of injection (chart 1) and following it (chart 2) until a base line was again established. During the injection there was always a sharp rise in venous pressure, the height of which varied from 11 to 81 mm. of Ringer's solution (average, 40 mm.). In group 1, during the injection, the pial artery remained unchanged in every case. In group 2, it remained unchanged four times,[3] dilated twice and constricted once (chart 1). Of

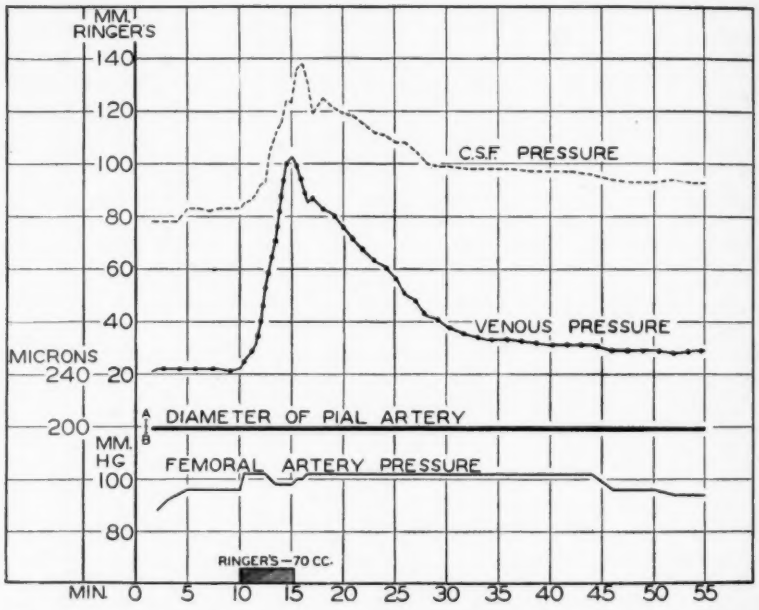

Chart 4.—Effect of a sudden rise in venous pressure on diameter of pial artery. Intravenous injection of Ringer's solution (70 cc.) was made slowly to avoid any marked rise in arterial pressure. The venous pressure rose 81 mm. in five minutes, yet the pial artery remained unchanged.

fourteen trials, therefore (both groups), the artery maintained its original caliber unchanged during the injection eleven times and showed a measurable change in caliber three times. On each of these three occasions the change was paralleled by a change in systemic arterial pressure; i. e., dilatation occurred with a rise in pressure, constriction with a fall.

3. "Unchanged" is here used to mean no change of more than 4 per cent. Changes of 4 per cent or less do not exceed errors in observation and are not considered significant.

In chart 1, the arterial pressure during injection *III* is charted merely as a fall, since the previous brief rise in pressure caused no change in the pial vessel, and the constriction occurred during the fall of pressure. It is rather striking that this constriction occurred during (and in spite of) a sharp rise in venous pressure.

In both groups the systemic arterial pressure changed during the injection in every case but one. In this case the injection was made slowly on purpose to avoid such a change, and here the pial artery showed no change in caliber either during or after an injection of 70 cc. of fluid, although the venous pressure rose abruptly 81 mm. (chart 4 and chart 1, injection *IV*).

After the injection (in both groups), while the arterial pressure was falling toward its previous level, the pial artery was constricted four times out of fourteen trials (chart 2).[4] On the whole, it may be said that the pial arteries proved to be unresponsive to changes in venous pressure alone. In every case when a constriction occurred the arterial pressure was falling at the time. If the blood volume was greatly increased by one or more large intravenous injections of Ringer's solution, the pial artery dilated sometimes during the rise in arterial pressure, and constricted during the subsequent fall. Even under these rather extreme conditions, the degree of change in arterial caliber was far less than that observed in response to such chemical agents as histamine, carbon dioxide and carbon monoxide, and also definitely less than the usual response to sympathetic and vagus stimulation.

COMMENT

Weed[5] has shown that when Ringer's solution was injected intravenously the intracranial venous pressure varied directly with the systemic venous pressure. It is evident, then, that in our similar experiments the intracranial venous pressure exerted no more effect on the pial arteries than did the systemic venous pressure.

SUMMARY AND CONCLUSION

An abrupt rise in venous pressure, followed by a fall, caused no measurable change in the diameter of the arteries in the pia, provided the systemic arterial pressure remained constant. If, however, a sudden change in arterial pressure occurred with the alteration in venous pres-

4. "Constricted" means a change to a diameter less than that measured in the control period; it does not refer to a return to normal after a period of dilatation.

5. Weed, L. W., and Hughson, W.: Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol. **58**:101, 1921.

sure, a small change in the size of the pial arteries sometimes took place. Without exception, these changes in the caliber of the vessels paralleled the changes in arterial pressure—dilatation with a rise in pressure, constriction with a fall.

Changes in systemic venous pressure, within the limits recorded in these experiments, have no effect on the caliber of the arteries in the pia.

PAIN AND TOUCH FIBERS IN PERIPHERAL NERVES

PETER HEINBECKER, M.D.
GEORGE H. BISHOP, PH.D.
AND
JAMES O'LEARY, M.D.
ST. LOUIS

The primary object of this investigation has been to detect by physiologic means the fibers in peripheral nerves which conduct the impulses that give rise to painful sensation. Both man and animals have been employed as experimental material. The results have been interpreted in the light of previous investigations of the properties of the different groups of nerve fibers occurring in various nerves, their action potentials being recorded, both in excised preparations and in situ, by means of the cathode-ray oscillograph. Secondarily, we have been interested in the differences in quality between the sensation resulting from stimuli applied to cutaneous nerve organs and that from stimuli applied to nerve trunks directly. We also believe our data support the hypothesis that nerve fibers occur in groups, not only according to size and conduction rate, but also according to their terminal connections, such that a group of fibers which have similar properties in a nerve as detected by their action potentials also include the fibers that serve similar functional mechanisms in the body.

The analysis of nerves by means of their action potentials as recorded on the cathode-ray oscillograph has afforded considerable support for the theory of specificity of nerve pathways. While fully confirming the all-or-none law and the idea of the nonspecificity of the nerve impulse as such, it has been shown that a mixed nerve can be separated on the basis of threshold and rate of conduction of its potentials into groups of fibers (Erlanger and Gasser [1]), certain axon properties of which can be correlated with the diameter of the fiber (Gasser and Erlanger [2]), that these groups can be further differentiated as consisting of fibers of two distinct physiologic types (Bishop and Heinbecker [3]) which differ in duration of potential, chronaxia and

From the Departments of Surgery, Ophthalmology and Anatomy of the Washington University School of Medicine.

1. Erlanger, J., and Gasser, H. S.: Am. J. Physiol. **70**:624, 1924.
2. Gasser, H. S., and Erlanger, J.: Am. J. Physiol. **80**:522, 1927.
3. Bishop, G. H., and Heinbecker, Peter: Am. J. Physiol. **94**:170, 1930.

refractory period, and that, further, the physiologic properties by which these types are distinguished can be correlated in general with the histologic character of the fibers (Bishop and Heinbecker [3]). In many cases it can be shown that a group of fibers falling in one narrow range, the potentials of which give a discrete and recognizable elevation in the record, include all of those elements the activity of which contributes to a given physiologic result. Fibers, therefore, seem to be grouped together in their physiologic properties on a functional basis; that is, similar groups in different nerves and in different animals may serve the same specific function. This applies to both afferent and efferent elements so far as studied.

For instance, Erlanger [4] found that, in the two branches of the femoral nerve innervating skin and muscle respectively, the cutaneous nerve lacked the first element of the potential record and lacked the group of fibers corresponding to this. Since this element is present in both dorsal and ventral roots, it was concluded that both muscle motor and sensory components were included in the corresponding group of fibers. On the basis of Ranson's inference that pain is mediated by small fibers, Erlanger assigned this function to a fourth group of fibers then recognizable, but since he has more recently expressed serious doubts as to the existence of this group (Erlanger, 1930), his inferences as to pain are, perhaps, inadequate to support a theory of specificity. Heinbecker (1929) found that the two effects on the heart induced by stimulation of the vagus nerve were mediated respectively by two groups of fibers the potentials of which were observably different. Hinsey and Gasser [5] correlated a specific potential elevation in the dorsal root with vasodilation and the Sherrington contracture in mammalian muscle after degeneration of its motor nerves. Bishop and Heinbecker,[6] analyzing the functional responses to stimulation of the cervical sympathetic nerve, found that vasoconstriction, dilation of the pupil and retraction of the nictitating membrane were represented by discrete fiber groups in the nerve, recognizable by their potential elevations. Much of the previous work on nerve stimulation, in which responses are classified in terms of threshold, while lacking the evidence now obtainable from records of the nerve potential, can be readily interpreted on independent analysis of the same nerves in terms of threshold and potential picture, as showing specific groupings of fibers for specific physiologic activities, both in afferent and in efferent components, and in both somatic and autonomic systems. Thus, from both neurologic and physiologic evidence, the peripheral nervous system

4. Erlanger, J.: Am. J. Physiol. **82**:644, 1927.

5. Hinsey, J. C., and Gasser, H. S.: Am. J. Physiol. **92**:679, 1930.

6. Bishop, G. H., and Heinbecker, Peter: Am. J. Physiol. **100**:532, 1932.

appears to be constructed out of specific groups of fibers, the boundaries of which do not overlap sufficiently to obscure the scheme. The further evidence from neurologic study of lesions in the cord and brain stem indicates that the central nervous system is constructed on a similar plan, differing mainly by a rearrangement of these same or corresponding nerve fiber components into tracts. The natural inference, supported also by considerable evidence, is that this physiologic specificity extends to some extent into the higher centers.

Ranson and Billingsley [7] have contributed a study indicating that painful stimuli and those causing reflexes associated with pain are mediated by a group of fine fibers passing via the dorsal root to Lissauer's tract. For instance, they separate out from the larger fibers of the root in the seventh lumbar nerve of the cat to form a lateral division, after cutting of which such reflexes are not obtained on stimulation of the root. Ranson and Billingsby concluded that, of this bundle of fine fibers, most of them are unmyelinated, and they tentatively assigned to this unmyelinated component the mediation of pain, etc. In the spinal tract of the trigeminal nerve a similar group of fine fibers mediates similar reflex stimuli, but in this nerve the fibers are mostly myelinated (Ranson [8]). In the bifurcation of the dorsal root fibers at the T leading from the ganglion cells, the branch passing centrally to the root is smaller than that passing peripherally to the tissues, and in cross-sections of the root and nerve this difference in size of the fine fibers is still observable. Ranson has repeatedly recognized that the lateral division of the dorsal root contains myelinated, as well as unmyelinated, axons, and the inference that the latter mediate pain rather than the former seems to be based on the relative numbers of the two types found, and no final proof has been claimed for the hypothesis. In fact, Ranson seems to be of the opinion that the two types are not fundamentally different, and that the position of the tract and the size of the fibers is of more significance than the degree of myelination. Thus, in the spinal tract of the fifth nerve, myelinated axons are considered the homologs of the unmyelinated axons of the dorsal root (Ranson [9]).

Analysis of many nerves of different fiber composition by means of the cathode-ray oscillograph has indicated (Bishop and Heinbecker [3]) that a correlation can be made between the rates of conduction and other functional properties of the fiber groups of a mixed nerve and the anatomic types of fibers of which such groups consist (fig. 1). In

7. Ranson, S. W., and Billingsley, P. R.: Am. J. Physiol. **40**:571, 1916.
8. Ranson, S. W.: J. Comp. Neurol. **23**:259, 1913.
9. Ranson, S. W.: Cutaneous Sensory Fibers and Sensory Conduction, Arch. Neurol. & Psychiat. **26**:1122 (Dec.) 1931.

particular, in sympathetic nerves it can be shown rather conclusively that a late potential propagating at the rate of about 1 meter per second or less is always assignable to unmyelinated fibers; that another potential traveling at from 5 to 10 meters per second (in mammalian nerve) is assignable to myelinated efferent fiber, and that one propagating still faster, at from 15 to 30 meters per second, is afferent. Erlanger and Gasser [10] have shown that the dorsal root has a fiber component, the action potential of which propagates at 2 meters per second or less, but they have refrained from committing themselves

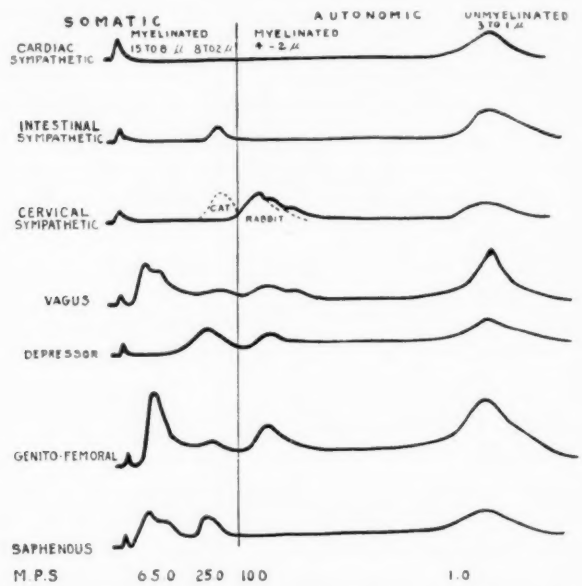

Fig. 1.—Diagram of nerve action potentials after conduction, where the different potential components separate out due to differences of conduction rate. In nerves with only one type of fiber the potential resulting from stimulation can obviously be assigned to this type. Then, in other nerves showing two or more potential elements with a corresponding fiber constitution, further correlations are possible between the physiologic response and anatomic structure. The vertical line drawn across the figure separates the potentials from two general types of fibers, the later groups myelinated or unmyelinated, having time functions about four times longer than the earlier. (Refractory period, chronaxia and duration of potential.) Finally, by leading from the nerve still attached to the animal, into the oscillograph, the functional response of the animal can be correlated with the fibers stimulated. We have not detected any afferent unmyelinated fibers in the nerves so far studied.

as to whether these fibers were identical with the unmyelinated ones observed by Ranson.

10. Erlanger, J., and Gasser, H. S.: Am. J. Physiol. **92**:43, 1930.

Two questions emerge from this situation. First, are the fibers which mediate painful impulses assignable to a specific group in a mixed nerve, or do fibers from various groups contribute to painful sensations? Second, are all painful impulses confined to the fibers collected into the lateral division of the spinal roots, or into analogous tracts? These questions are obviously interrelated and are arbitrarily differentiated only for easier analysis from the experimental side. The first aspect of the problem is dealt with in this communication.

It will be shown first that in the saphenous and other peripheral nerves of the dog and man, painful stimuli and those causing reflexes associated with pain are carried over fibers that are of the myelinated type, the impulses of which are propagated at velocities of from 15 to 30 meters per second, and the potentials of which in the record of the total action potential after conduction along the nerve separate out into a well defined and specific elevation. They are a completely different type of fibers physiologically from the unmyelinated fibers of the sympathetic system, even from the myelinated fibers of the sympathetic, and in fact different from the unmyelinated fibers of the vagus or depressor nerves.

I. DIRECT STIMULI TO EXPOSED HUMAN NERVE

An opportunity was offered in connection with the amputation of a leg, occasioned by diabetic gangrene of the foot, to stimulate directly the saphenous nerve of man without an anesthetic. The patient's acquaintance with painful sensations was intimate and recent, the pain in his foot having kept him awake at night. After local anesthesia to the foot, he immediately went to sleep, waking promptly, however, when the nerve in the leg was adequately stimulated. Stimuli were applied by means of a Harvard inductorium through platinum wire electrodes, with the nerve lifted free from the underlying tissue. A pendulum interrupter timed stimuli at adjustable intervals, a convenient frequency proving to be 2 per second. This nerve was then excised and transferred to iced Tyrode's solution; a second nerve as near the same size as could be found was dissected out of the leg after amputation, and the two nerves were examined by means of the cathode-ray oscillograph about one-half hour later, at 37 C.

It was found that at no strength of stimulus available with the apparatus did the patient report pain from one stimulus only. It was shown later that the stimulating apparatus was capable of stimulating all the fibers of the nerve. At a frequency of 12 every five seconds, and at a strength of stimulus that was found to give definitely painful sensation very promptly at a much higher frequency, reflex twitches of the muscles of the leg appeared following the seventh stimulus; the patient's face showed definite contortions at the tenth, and he

groaned at the twelfth, whereon stimulation was stopped. It was observed repeatedly that the facial aspect, especially curling of the lips, just preceded a verbal report of painful sensations and was a reliable index of threshold responses. (However, for actual threshold of pain sensation, see section III.) Owing to the exigencies of the situation, experimentation was stopped previously to what would have been considered a satisfactory culmination of the procedure from the purely scientific point of view. The nerve stimulated failed during the experiment, whereon a slight further dissection to fresh nerve allowed a repetition of the results.

The stimulating apparatus, after the procedure described, was transferred without alteration or resetting to the laboratory, and there employed to stimulate the nerves. The nerve on which the experiments had been performed gave a low action potential, but one not adequate for analysis. The other nerve was in excellent condition as compared with many other human nerves that have been studied (unpublished), and it was analyzed thoroughly. At the strength of stimulus which gave pain on the tenth repetition, the companion nerve showed a potential, after 41 mm. of conduction, as diagrammed in figure *2 B*. When stronger stimuli were applied, the further complete potentials of this nerve appeared as in figure *2 A*, which is the normal record for such a nerve in man and other animals. The noteworthy fact is that the threshold of the last potential of figure *2 B* and of the still later potential of figure *2 A* proved to be as 1 : 5. This is a uniform finding for such nerves in the dog and man (limits 1 : 4 and 1 : 6).[10a] Since, in the experiments before excision of the nerve, the temperature was doubtless somewhat lower than in the laboratory thermostat, less of this potential would have been elicited in the pain experiment rather than more. By no possibility could this stimulus have been strong enough to call forth the potential elevation traveling at 1.5 mm. per second. Pain must have been mediated, therefore, by fibers, the threshold of which was lower and the conduction rate higher than were these functions for the final group. Since slightly weaker stimuli than those producing pain failed to cause pain at much higher frequency, the correlation of these two procedures indicates that pain was mediated by the specific group of fibers, the potential of which caused this second elevation. No pain was caused by fibers conducting more rapidly than this, and of lower threshold. We obtained no adequate evidence

10a. Warm-blooded nerves on removal from the body may alter considerably as regards the threshold ratios of their potential maxima. After equilibration the values approach those given here for normal nerves.

concerning the final group in this experiment,[11] except that it was not necessary to stimulate it to arouse painful sensations.

II. CORRELATION OF RESPONSE TO STIMULATION OF EXPOSED NERVES WITH THE SIMULTANEOUS ACTION POTENTIAL RECORD IN DOGS

The preceding experiment raises the question whether the difference in the conditions under which stimulation and potential recording were carried out might vitiate the obvious interpretations of the results. It was shown in experiments on dogs that the experiment on man was valid and reproducible.

Under ether anesthesia the dogs were prepared for recording the blood pressure from the femoral artery on one side, and for recording nerve response from the saphenous nerve on the other side. The nerve was exposed and freed for 50 mm. and drawn through a glass tube and across electrodes fixed within it (fig. 3). This apparatus was strapped firmly to the leg with tape so as to move with the leg, the

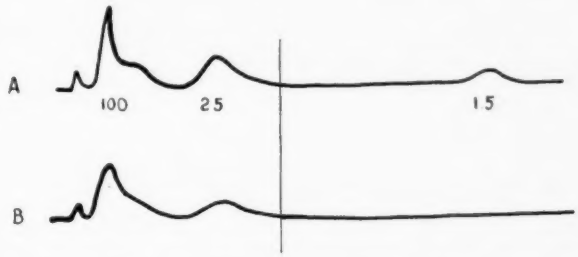

Fig. 2.—Diagram indicating measurements obtained from cutaneous nerve of man: *A*, potential response recorded at strength of stimulus sufficient to stimulate all the fibers in the nerve; *B*, potential response recorded at strength of stimulus employed in human experiment which caused painful sensations.

leg being strapped to the dog board. A tampon of wet gauze was placed over the nerve where it entered the tube, and the whole limb was wrapped in dry bandage. With a wet filter paper lining the tube, such a preparation is active for over two hours, and an experiment lasted less than an hour. Several of the nerves were also recorded at the end of the experiments in the incubator after excision (table), and all the potentials corresponded to the diagram of figure 2. The experiments were carried out only after full recovery from the anesthetic.

11. The patient had difficulty in describing this pain, but when asked whether it felt in any way like the previous pain in the toe he assured us that it did not, and finally stated that it felt as if we were "whipping" him. At a rate of only 2 stimuli per second this difference has at least one obvious basis. For the quality of sensation resulting from electrical stimulation of nerves, see section III. As to the fact that the stimuli when adequate were truly painful, there could be no question. Stimuli below threshold for pain gave rise to no report of sensation, but the condition of this patient may account for this, concerning which also refer to section III.

Response to Stimulation.—Frequency was variable from single stimuli to 12 per second, and strength, from threshold for first nerve potential response to well over the maximum for all fibers of the nerve. Condenser changes were used as stimuli (Bishop and Heinbecker [3]) delivered through a rotating circuit maker which synchronized the stimulus with the deflections of the oscillograph electron beam. Four hundred millimeters per millivolt sensitivity were available; the shock artefact was balanced out in the record by the wheatstone-bridge technic (Bishop [12]). The dog was insulated, the nerve grounded between stimulating and lead electrodes, and an arrangement achieved which eliminated disturbance of the nerve record due to the animal's movements (fig. 3). The wires passing from the electrodes to the apparatus were thoroughly shielded with web tubing to avoid antennal effects. Electrodes consisted of loops, bent at the ends, of the iron wires employed as

Threshold Ratios in Man and the Dog of Fibers of Lowest Threshold (Tactile) and Those to Which Pain Can Be Assigned

Experiment	Man	Dog
1	1:6.0	1:6.1
2	1:5.5	1:5.0
3	1:5.0	1:5.0
4	1:5.5	1:6.2
5	1:7.0	1:4.7
6	.....	1:5.2
7	.....	1:6.0

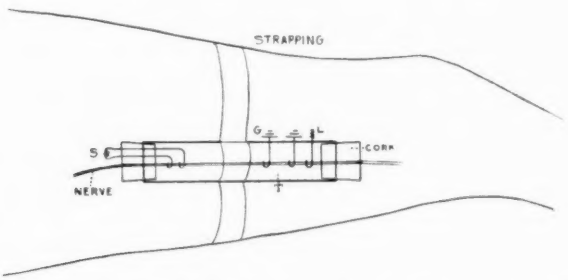

Fig. 3.—Arrangement of saphenous nerve for simultaneous recording of nerve action potentials and reaction of the animal to stimulation: *S*, stimulating electrodes; *G*, ground lead; *L*, recording leads; *T*, glass tube housing nerve and electrodes at nearly body temperature.

leads to the apparatus, the aforementioned ground electrode lying along the nerve a short distance for low-resistance contact.

The results from all experiments (five dogs) agreed in the following respects: No signs of pain were observed at any strength or frequency with less than three stimuli, usually at least five being required. The thresholds for struggling movements and for vocal protest (taken as signs of painful sensation) were the same. There was with one exception a sharp rise of blood pressure at the same

12. Bishop, G. H.: Am. J. Physiol. **82**:462, 1927.

approximate threshold as for pain, although with weaker stimuli lesser rises were sometimes observed, usually followed by a fall at the end of stimulation. The exception gave a fall or no change followed by a rise at the end of stimulation in certain trials, a rise in others with painful stimuli, and with weaker stimuli a fall in all cases, usually only at the end of the stimulation. The threshold for pain (by the foregoing criteria) was sharply defined in all cases for stimulation of 2 per second or over if the stimulus was repeated ten or more times. Just below this strength no signs of pain appeared at rates up to 12 per second, for any number of stimuli. In all cases the thresholds for pain and for specific potential elevation in the nerve record were the same within 10 per cent. This potential was the same component as that correlated with pain in the human case.

In general, threshold effects alone were sought for painful stimuli, stimulation being continued at a given strength and frequency only until a definite response was obtained. The stronger the stimuli the fewer were required for threshold effects, down to the lower limit of from three to seven stimuli for different preparations. This lower limit was obtained only when the potential record showed that the second potential elevation had nearly reached its maximum, indicating that the fibers responsible for the effects were distributed throughout most of the range for this group. No sensory effects of any kind were recognizable before the threshold for pain was reached. This, and the necessity for repeated stimuli, both in dogs and in the human subject, led us to believe that no sensation could be induced by direct stimulation of exposed nerves below the threshold for pain, but this, as will be seen later, proved to be an error.

In a few cases stimulation was pushed further to find whether pain was confined exclusively to the fibers giving rise to the second potential elevation, or whether the still slower final group would contribute. The number of stimuli required for the threshold was the same in either case, but it seemed possible that the slower fibers might require more stimuli to reach the threshold effect than the faster ones. The reactions to the greater strength of stimulation, however, proved to be so violent when the threshold number was significantly exceeded that our failure to detect a greater degree of response by the criteria available was thought not to be very decisive. No appreciably greater changes in the blood pressure were observed with the stronger stimuli in the few experiments so performed.

Reflex muscular responses from the limbs proved to be the most variable of any responses except lowering of blood pressure. They were estimated and not recorded, by feeling for muscle responses with the fingers. There is some question whether any such responses occurred before the threshold for pain. They were always elicited somewhere in the range of the potential record associated with pain, but not always at its threshold, and usually not with one stimulus, unless this was a very strong one.

III. STIMULATION OF HUMAN NERVES IN VIVO

The experiments on dogs thus corroborate in all essential details the experiment on man, both as to painful stimuli and as to correlation with potential records, except that in the experiments on animals, while the correlation of presumably painful responses with action potentials was immediate and direct, we had no verbal corroboration of our inference as to whether the stimuli were actually causing sensation of pain. We therefore attempted a third correlation in human beings, taking the threshold for contortion of the mimetic muscles and struggling movements in normal healthy unanesthetized human subjects as corresponding to the threshold for the same signs in dogs; and then, inferring that the action potentials also corresponded, we could obtain intelligent reports of the sensations experienced when fibers both above and below the pain-threshold level responded.

Stimuli were applied through electrodes, one indifferent, consisting of a wet pad with a wire woven through it for a lead, the other a medium-fine steel sewing needle coated with soft de Khotinsky cement, and the end ground off to a slanting point on a fine emery wheel. The needles were tested for leaks through the insulation by applying 45 volts across a pair of them in a beaker of Ringer's solution. If bubbles rose from anywhere except the end when a needle was cathode, the coating was repeated. The other electrode, in shape like a horseshoe, encircled the needle. If this was placed farther away, spread of current through muscles led to direct responses which were very disconcerting; when placed locally, direct twitches were usually recorded only at strengths of stimuli that were far above the threshold for painful sensation.

One other datum was needed, and this was obtained from a dog. The femoral nerve was prepared for recording action potentials, and besides this, an insulated needle was thrust through the skin alongside the same nerve higher up in the leg. It was not to be expected that the same strength of stimulus would be equally effective on the nerve in situ and in air, but the relative threshold strengths required for any two potential waves might also be different with the different stimulating circuits. It has regularly been found that if the threshold values for two potential components are taken with charges from a small condenser and then taken again with a large one, the ratio between the two threshold values will be

smaller when the larger condenser is used. This we presume to be due to the difference in times of discharge of the condensers. Since the resistance of the arm is less than the resistance of the nerve alone, the charging time for a given condenser will be less, and the ratio of thresholds for the different potentials should be larger in the body than in excised nerve.

It was found that, with a 0.01 microfarad condenser to stimulate, the ratio of voltages for thresholds of the first potential group of the saphenous nerve of the dog and of the pain group was $\frac{1.3}{7.5} = \frac{1}{5.8}$ on the bare nerve, electrodes being 7 mm. apart, and $\frac{60}{95} = \frac{1}{4.75}$ in the body, with the needle stimulus and an indifferent electrode. (The first ratios are in voltages found.) This is the opposite change from what would have been expected on the foregoing reasoning; evidently other factors affecting distribution of current in the dog's body are more significant than the resistance effect alone. In the human body our results show a ratio near 1:5 to 1:6 between the threshold for tactile and for sharp pricking sensation (table). Since the human cutaneous nerve in the thermostat also gave this same ratio for the thresholds of the first and second main potential groups, and since the threshold of the second potential is approximately the same as the threshold for pain, we infer that the threshold for tactile sensation is the threshold of the most irritable fibers in the nerve.

Types of Sensation.—It seems to be generally reported that the only sensation called forth by direct electrical stimuli to nerves is pain. Without exception, our subjects reported that this was not true. Several of them, to be sure, stated at first as the stimulus strength was increased from threshold (and this was the regular initial procedure) that the mild and difficultly analyzable tactile sensation became slightly painful quite gradually, but in no case was there failure to recognize a new and distinctly disagreeable stimulus at a specific threshold above this.[13] In every case in which initial pain was reported, the record was altered by the subject himself after the stronger stimuli had been received to the effect that the first sensation was not really definitely painful, but felt as if it were about to become so, or was only "uncomfortable." We can corroborate this from the same experience, and assign the first impression in part to nervous apprehension after having the needle thrust into one's arm and in part to the strangeness of the sensation, to confusion from its absence of localization and to an undue expectation of pain, because of foreknowledge of the main purpose of

13. This circumstance was so noticeable that it led to the designation of the chair in which the experiments were performed as "the anxious seat."

the research.[14] Weaker stimuli at higher frequency after stronger had been applied were interpreted as tactile, such as rubbing or stroking. No sensations of temperature have been reported.

Procedure: It was not intended that the subject should be acquainted with the procedure before the trial, but unfortunately in some cases extravagant rumors involving an ordeal by torture traveled faster than did invitations to our prospects, and some explanation was necessary. The subject was seated, blindfolded, with arm relaxed on a pillow out of view of the stimulating keys, which could be operated either quietly or with an audible click. The subject signaled any sensory impression from the arm by a tap with the other hand at the beginning and end, following by an unprompted description of the sensation, in turn followed by answers to noncommittal questions, all stimuli being repeated several times and with variation of order, intensity, frequency or duration as the test demanded. Particular attention was directed to the following considerations: whether the threshold for a given type of sensation varied with frequency of stimulation; whether the quality varied with frequency for a constant strength of stimulation at various levels above the threshold; whether sensations graded smoothly from one to another as strength of stimulus was increased, or were specifically recognizable as discrete components, and at what frequency of stimulation the separate stimuli could be appreciated as "flickering," or were fused into a continuous sensation. The two types of sensation will be referred to hereafter as "tactile" and "painful," with the distinct reservation that the first sensation was not recognizable as any specific type of tactile sensation ever experienced by the subject from stimuli to the skin, and that the second sensation was not painful at threshold and was again not a normal painful sensation at any strength. The quality of sensation reported will be dis-

14. One subject reported no definite line between tactile and pricking sensation, stating that the one graded smoothly into the other. Four threshold determinations at different times, however, agreed to within 3 per cent both as to absolute values of potential and as to the ratio between the thresholds for touch and for prick. When several medium-strength stimuli were delivered unexpectedly at 10 per second during the course of a conversation, the subject said "Ouch!" and gave a start quite reminiscent of the dogs under similar conditions, and compared the sensation to one that a dentist would be informed of while a tooth was being filled. The same stimulus was reported as not painful when it was expected, and called forth no facial or body movements. We quote this instance particularly as illustrating the conditioning effect of the psychologic state of the subject and as indicating the ambiguity involved in calling the stimuli "painful." The stronger stimulus causes a pricking sensation referred to the skin; the pricking may be painful; in fact, it always becomes distinctly painful with strong stimuli, while below this no stimulus of any frequency gives pain, and the higher the frequency the less unpleasant.

cussed later. Tests were applied to seven persons: two of the authors, two physiologists, two chemists and one pharmacologist.

Thresholds: Only two types of sensation were reported, of which we could obtain all gradations of intensity up to a maximum, giving only minor changes of quality for different frequencies. It was first necessary to correlate these two sensations with the events of the experiments on dogs by means of relative threshold values, and this could be done with some exactitude. The first sensation was obviously tactile; the second as obviously painful, when strong enough, but the dog gave no sign of tactile sensation. The human subjects usually showed curling of the lip and general facial contortions only at somewhat above the threshold for verbal reports of the second sensation. The threshold for pain was, therefore, inferred to correspond to the potential picture from the dog's nerve that accompanied "painful" responses; that is, just above threshold for the second potential. The ratio of thresholds for the two sensations (the second being not painful at threshold) in all human subjects fell between 1:4.9 and 1:6.2 (table), while that for the dog's first and second potentials stimulated in the same manner was 1:4.75, and for the dog's nerve in air the ratios varied from 1:5 to 1:7. Since the threshold for signs of pain in the dog is uniformly not far above the threshold for the second potential (at from 5 to 10 per second frequency), the threshold for the first tactile sensation in human subjects must lie close to the threshold for the first potential of the nerve. This is further confirmed by the ratio for these two potentials in excised human cutaneous nerves, which is about the same (1:5) as for the excised saphenous nerve of the dog.

Distribution of Sensation in Fiber Groups.—The first potential of the cutaneous nerve is the beta wave (Erlanger[4]; an alpha wave occurs only in the muscle branch of the femoral). We find that the first tactile sensation increases in intensity throughout the range of increasing stimulus strength until the threshold for a different sensation is reached, beyond which discrimination of tactile intensity is masked. This means that the tactile sensation (for direct stimulation of the nerve at least) increases with increasing strength of stimulus at a constant frequency, throughout the range of the first two parts of the first potential elevation, or throughout the beta and gamma waves, with no detectable change of quality. The inference that temperature sense is mediated by the gamma group of fibers (Gasser and Erlanger, 1929) is not borne out by these experiments, although our failure to elicit any temperature sensation precludes a final judgment. If present in the pain group, it is masked by the more intense sensation of pain. Neither have we succeeded in finding any pattern of frequency and

intensity that would remotely suggest temperature except insofar as the pain itself might be said to have something of the quality, not of warm and cool, but of hot and cold, particularly hot.

As in dogs, so in the experiments on human subjects, an increase in either rate or intensity of stimulation above threshold for pain caused an increase of the same sensation. The intensity of sensation continued to increase up to at least twice the threshold for pain, which would include most, if not all, of the fibers contributing to the second potential elevation concerned. In one case, in order to test the severity of the experimental procedure employed on dogs, as well as the enthusiasm of one of the subjects, the stimulus at a frequency of 20 per second was increased progressively up to a value that should stimulate even the last group of fibers, and each series maintained long enough to satisfy the subject that he was receiving a fair sample of that particular brand of experience. Above twice the threshold for pain he was unable to distinguish differences of strength of stimulus, but direct and reflex stimulation of muscle probably complicated the subjective picture. We therefore feel that we have not been able to test adequately by this technic whether stimulation of the slowest fibers of the nerve (presumably the unmyelinated ones) can cause pain; our experiments afford no evidence that they do. The subject tested thinks that if stimulation of the last group of fibers were as effective in causing painful sensation as was stimulation of the previous group he would certainly have been able to detect the difference in effect. Failure to obtain further increases of blood pressure above those associated with the earlier potential in dogs might be cited as equally inconclusive, but pointing in the same direction.

Qualitative Differences in Sensation from Stimuli of Different Frequency.—It has been said that increasing the strength of stimulus within the range of one type of sensation did not result in perceptibly different qualities of sensation. This does not apply so strictly to changes of frequency. Threshold was first found for a frequency of 30 per second, and then 60 per second and single stimuli of that strength were tested. For touch, single stimuli could be detected if attention was fixed on them, usually at the same threshold as at 30 per second, or sometimes at slightly higher values, while at 60 per second the sensation was "smoother" and more definite. At slightly above threshold the repetitive character of the stimulus could be recognized at 30 but not always at 60 per second, and this persisted throughout the range of intensity above threshold. At two or three times threshold value the sensation was reported as "uncomfortable" or "painful" up to 30 per second, but usually as "not so unpleasant" at 60 per second, even up to the threshold for pain. Such "painful" reports were uni-

formly revised to "uncomfortable" after more severe stimulations giving rise to a second type of sensation had been experienced. Near threshold values for tactile sensation, low frequency stimulations sometimes gave a report of a sensation as of insects crawling; higher frequency (60 per second), one of gentle rubbing or of stroking with cotton wool. No sensations of pressure were reported other than light touch.

Threshold for pain was tested in the same manner at a frequency of 30 per second. The first report was usually a "sharp pricking," of which the repetitive character could be detected at slightly above threshold. Here again, and contrary to our expectation from the previous experiments on dogs and man, single stimuli could be detected regularly even when of threshold value, although a series of two or three were reported as "one" or "several" variably. Two in quick succession were usually reported merely as stronger than one alone, and a higher frequency as stronger than a lower unless attention was called to the matter of frequency. At 30 per second it could still be recognized that the stimulus was repetitive or "rough," but at 60 per second the stimulus was usually recognized as smooth or continuous. This applied to all intensities of pain. Two subjects stated that 60 stimuli per second, while distinctly more tolerable than 30 per second, could still be recognized as repetitive.

It has been stated that in the amputation experiment one stimulus of any strength failed to call forth a report of pain, and in dogs gave no evidence of response. The later subjects who reported a pricking sensation from one stimulus were asked to describe the difference between one and several stimuli at 2 per second well above threshold for pain. No curling of the lips or contortions of the shoulders were noticeable with less than three or four stimuli, and three were said to hurt more than one. At this rate the analogy to "whipping" was obvious, each stimulus being a separate sharp prick; and while each of three was reported as being equally severe as a sensation, a series became increasingly "unpleasant" or "uncomfortable" as well as painful. One stimulus, even though strong, usually caused no protest, while after several, expressions of remonstrance often bordered on the abusive. There is apparently a summation of effectiveness here that is not to be evaluated in terms of intensity of sensation alone, and seems to be not entirely a matter of rational evaluation, but rather to have a distinctly emotional content.[14]

When the higher frequency was employed (60 per second), adaptation was reported; the sensations rose rapidly to a maximum in this case, and then definitely decreased again. This is not a frequency that would evolve depressed impulses in nerve fibers. The adaptation might be a central effect. At the same strength, 60 per second was always reported as distinctly less unpleasant than 30 per second, the latter

being a stabbing pain, the former smooth or steady; the subject could "stand the pain longer" at the higher frequency. This may be compared with the same difference in tactile sensation; 60 per second was "smooth" or "pleasant," and 30 per second was "uncomfortable," even to the point of being designated initially as painful. Adaptation did not occur at 30 per second. The difference here is possibly a matter of adaptative decrease of central effect, and possibly a matter of unpleasant emotional reaction to a stimulus that is perceptibly repetitive, and which, in a sense, is anticipated as well as perceived.

COMMENT

The obvious shortcoming of this work is that we have failed so far, not only to find any sensory effect from stimulation of the slowest group of fibers in the dorsal roots (the unmyelinated fibers), but even to discover whether they are in fact sensory or motor. To be sure, they have a potentially "motor" function, as shown by Hinsey and Gasser,[5] that of causing vasodilation and contracture of denervated muscle, but until these are demonstrated not to be axon reflex phenomena from sensory fibers this might not be considered conclusive. There is, of course, the possibility, so far unproved, that impulses over these fibers might cause other types of "pain"; we have not accounted for such sensations as aches or deep pressure pain or, for that matter, for temperature sensations. These are being investigated. The type of painful sensation that we can correlate with the smallest and slowest myelinated axons of sensory nerves is such as one would obtain from a prick, cut or superficial abrasion.

However, we cannot agree with the inference which Ranson appears to make, that the small myelinated and unmyelinated fibers of the dorsal roots are to be classed together functionally, or that the two types merge, the one with the other, as if myelinated axons were only unmyelinated ones that had acquired a myelin sheath. We would infer, rather, that the paucity of unmyelinated axons, for instance, in the spinal tract of the trigeminal nerve, as compared with the dorsal roots (Ranson)[9] indicated that some function mediated by the unmyelinated fibers of the dorsal root was not subserved by the trigeminal. These two types of fibers in question have distinct physiologic properties, and we find from a study of their action potentials no transitional forms. The unmyelinated fibers of the dorsal roots have the properties of unmyelinated fibers elsewhere; for instance, the rate of conduction and threshold of the unmyelinated fibers of the dorsal root are the same as are those functions of sympathetic unmyelinated fibers in the same nerve (unpublished work on the saphenous nerve), and the refractory period is the same as that of unmyelinated axons that are demonstrably motor;

and these properties, as compared with the same values for the small myelinated fibers carrying pain impulses are as about 4:1 with a clean interval between them.

Our results are consistent with certain of those of Adrian, Cattell and Hoagland [15] that repetitive stimuli to fibers of fast conduction rate (in our experiments demonstrably giving tactile sensations when stimulated) do not cause painful sensations. Adrian's rates of stimulation were, moreover, faster than ours and still faster relatively since they applied to a cold-blooded animal. These authors further report that in the frog, fibers, the action potentials of which would indicate them to be unmyelinated ones by our criteria, seem capable of conveying impulses giving rise to pain. In the records they publish these slow action potentials have amplitudes of a quarter or more of those of fibers the responses of which caused no sign of pain. If such slowly conducted potentials are, indeed, those of unmyelinated axons, a greater difference would be expected in the single fibers with which they are dealing. The smallest myelinated axons of the B group to which they assign their fast fibers would be at least 6 microns, the largest unmyelinated not over 2 microns, the ratios of cross-sectional area, therefore, 9:1, and the potential amplitudes of unmyelinated axons as compared with myelinated almost certainly deviate from the area ratio promulgated by Gasser and Erlanger [2] for myelinated fibers, in the sense that the potentials of unmyelinated axons are very materially lower than their diameters would indicate. The foregoing correlations involved are not, however, particularly precise.

In another communication (Adrian [16]), fibers with a conduction rate faster than would be properly assigned to unmyelinated axons are reported to convey impulses arousing painful sensations in the frog. Adrian pointed out that the conduction rates observed in these fibers do not place them in any one of the groups of axons found by Erlanger and Gasser [10] unless it be the so-called B group, to which the latter authors specifically assign a sympathetic motor function. The apparent discrepancy here is due to a confusion in terminology based on an error in interpretation. There can be shown to be two groups of B fibers, quite readily distinguishable (Bishop and Heinbecker [3]), to which Erlanger and Gasser have assigned one function. In the cat, dog, rabbit and man, both groups are present in certain sympathetic nerves, but only one in the saphenous nerves studied by Erlanger and Gasser, and this is a sensory group; in fact, it is the group of fibers the responses of which cause pain. The other group studied by Erlanger and Gasser in the sciatic nerve of the frog and present in many sympathetic nerves

15. Adrian, E. D.; Cattell, McK., and Hoagland, H.: J. Physiol. **72**:377, 1931.
16. Adrian, E. D.: J. Physiol. **74**:17, 1932.

of both warm-blooded and cold-blooded animals is assignable to myelinated sympathetic motor axons. Its absence from the saphenous and sciatic nerves of the dog and cat corresponds to the absence in these nerves of postganglionic myelinated fibers, the unmyelinated sympathetic fibers present contributing to a much slower potential. Some of the conduction rates reported by Adrian for fibers responsible for pain in the frog are faster than would correspond to the sympathetic efferents, but they do fall into the range of the afferent group, inconspicuous, but demonstrably present in the frog (Heinbecker and Bishop [17]) which corresponds to the group responsible for pain in warm-blooded animals. Our results in part, therefore, confirm those of Adrian, that relatively rapidly conducting fibers are involved in painful responses.

With reference to those fibers the conduction rates of which are slower than would seem to correspond with sensory groups of fibers, and in general, to Adrian's statement that there is present a continuous range of fibers rather than a specific grouping, it has been pointed out previously (Bishop and Heinbecker [3]) that analysis of the nerve shows a series of potential maxima in a continuous distribution rather than a discontinuous picture, especially where conduction rate is the criterion; further, that threshold measurements give better differentiation, and that particularly in the two parts of the B elevation (sensory and motor components) does such overlapping of conduction rates occur. Knowledge of properties other than conduction rate (refractory period, duration of potential, etc.) will be necessary to complete the analysis of conditions in this range of fibers.

SUMMARY

A group of myelinated fibers in the peripheral nerves of man and the dog have been identified as those which conduct impulses resulting in painful sensation.

These fibers give rise to a recognizable potential component with a conduction rate of from 30 to 15 meters per second. Their short chronaxia and absolutely refractory period measurements identify them as belonging to the somatic type.

Tactile sensations are conveyed by the largest and most irritable myelinated fibers in a sensory nerve trunk.

Direct stimulation of exposed peripheral human nerves results in only two sensations, touch and pain.

17. Heinbecker, P., and Bishop, G. H.: Am. J. Physiol. **96**:613, 1931.

Differences in the quality of sensations experienced on direct stimulation of exposed nerves and those resulting from stimulation of sensory skin endings are discussed.

The findings lend considerable support to the theory of the specificity of nerve pathways. Nerve fibers seem to occur in groups, not only according to size and conduction rate, but also according to their terminal connections.

EFFECTS OF ALCOHOL ON THE CHRONAXIA OF THE MOTOR SYSTEM

WILLIAM MALAMUD, M.D.

E. LINDEMANN, M.D., PH.D.

AND

H. H. JASPER, PH.D.

IOWA CITY

The appreciation of the fact that in the reactions of muscle or nerve tissue to electrical stimulation the duration of the current is just as important as, if not more than, its intensity has opened up a new field in the investigation of this branch of physiology. Ever since the introduction of this concept by Lapicque, in 1909, there has been a steadily growing interest in the subject and an ever increasing accumulation of experimental data in its theoretical and practical aspects. At present the literature has reached such dimensions that it would be altogether outside the scope of the present communication to attempt even a brief review of it, especially since it has been done in such a thorough fashion by Lapicque,[1] Bourguignon,[2] Fredericq,[3] Stein,[4] von Weizsäcker[5] and others. In introducing the special phase of the subject that we shall discuss, we shall restrict ourselves to a brief statement of the features that are particularly related to it.

With the electrical stimulation of muscle or nerve tissue a reaction can be obtained only if the current used is above a certain minimum intensity. This, the theshold intensity, has been designated by Lapicque as the rheobase. Different tissues, or the same tissue under different conditions, may have different intensity thresholds. These facts have long been known, and until recent years have served as the central feature in most investigations in the field. It was found, however, that in the reaction to a continually flowing current of an intensity above that of the rheobase, only a small fraction of the total duration is actually

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From the Iowa State Psychopathic Hospital.

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

1. Lapicque, L.: L'excitabilité en fonction du temps, Paris, Presses Universitaires de France, 1926.

2. Bourguignon, G.: La chronaxie chez l'homme, Thèse de Paris, 1924.

3. Fredericq, H.: Chronaxie, Physiol. Rev. **8**:501, 1928.

4. Stein, J., and Quincke, H.: Ergebnisse der Chronaximetrie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **60**:513, 1931.

5. von Weizsäcker, V.: Elektrische Untersuchung des Tonus, Deutsche Ztschr. f. Nervenh. **124**:117, 1932.

utilized. Lapicque was able to show that by using currents of an intensity well above that of the rheobase (he uses an intensity twice that of the threshold) the duration can actually be measured. This time factor, then, for which he used the term chronaxia, is the minimum duration of flow of a current of an intensity twice that of the rheobase that is necessary to produce a reaction in the tissue. In studies of the chronaxias of different tissues under various conditions, Lapicque and his followers have brought forward a number of phenomena that at present form the central feature of his theory.

The Lapicque group stated that: (1) Normally, muscles with different functions have different chronaxias, whereas muscles belonging to the same synergic group have equal or nearly equal values. They found that the directly antagonistic extensors and flexors of a given anatomic group (such as the extensors and flexors of the forearm) have consistently different chronaxias. In the forearm, for instance, the chronaxia of the extensors is about twice that of the flexors. (2) In a given extremity, the chronaxia of the distal muscles is higher than that of the proximal ones. (3) The different parts of a physiologic unit associated in the transition of a given impulse have equal or nearly equal chronaxias. Thus, for instance, in the process of the transition of a motor impulse, the different parts, i. e., the center, neural pathways and muscles, all have equal chronaxias. This phenomenon is termed isochronism. The theory has been advanced that normal coordination can take place only when the different parts of these units are isochronic.

These phenomena have subsequently been investigated by other observers. Some of them could not be substantiated by a number of workers, the point most seriously involved being the phenomenon of isochronism. Thus, Rushton,[6] Grundfest[7] and others were able to demonstrate that nerve-muscle units could function under conditions of heterochronism, which would "make it hard to believe that identity of chronaxia is a necessary condition for conduction between two tissues." Other phenomena, however, have been corroborated and shown to be of great significance in the study of animal and human physiology. In addition to this, consistently occurring deviations from these rules were demonstrated in tissues functioning under abnormal conditions. The importance of such a method of approach need hardly be stressed. To the experimental neurophysiologist it opened up a new approach for the investigation and understanding of the integration and coordination

6. Rushton, W. A. H.: Lack of Isochronism Between Muscle and Nerve, Am. J. Physiol. **97**:557, 1931.

7. Grundfest, H.: Heterochronism in the Single Fiber Nerve-Muscle Complex of the Retrolingual Membrane, Proc. Soc. Exper. Biol. & Med. **29**:441 (Jan.) 1932.

phenomena in the neuromuscular activities. To the clinical neuropsychiatrist it offers an opportunity of attacking the problem of coordination disturbances in the field of nervous and mental diseases. The approach to the latter was particularly facilitated by the perfection of apparatus for the measurement of chronaxia by Bourguignon, Stein and others, which makes it available for use at the bedside. Within the last few years a great deal of work has been done in this direction, and the results are highly promising. Bourguignon,[7] Stein [8] and Marinesco,[9] working independently, have demonstrated consistent deviation in the chronaxias of muscle and nerve tissue in cases of neuromuscular diseases, it being highly probable that these changes in chronaxia were definitely related to the disturbances in motor performances and coordination.

It was with this in mind that we have undertaken an investigation of the effect of alcohol on chronaxia. Clinically, it is well known that alcohol affects to a pronounced extent the motor coordination as well as the psychic control of behavior, and our purpose was to determine whether changes in chronaxia could also be demonstrated under such conditions.

APPARATUS AND PROCEDURE

The choice of apparatus was made primarily with the idea of making it available for bedside use. For this purpose a portable modification of the Bourguignon apparatus was constructed by one of us, its reliability and practicability having been demonstrated in a previous investigation.[10] The principle on which it is based is the fact, demonstrated by the experiments of Hoorweg, that the time duration of the discharge of a condensor is, within certain limits, proportional to its capacity. Since, in measuring the chronaxia one must determine first the minimum intensity and then the minimum duration of a given current, the apparatus must permit the measuring of the intensity of the incoming current, and then provide for the loading with this current of a series of graduated condensors the capacities of which can be measured. This is obtained in the following set-up:

The regular alternating current is rectified and stepped up to 180 volts by means of a national B-eliminator, type 3580. This is then led through an induction-free potentiometer with fine and coarse adjustments which permit the gradation in intensity, determining it in terms of volts. The current thus brought up or down to the desired intensity is then carried through a double pole and double

8. Stein, H.: Untersuchungen über die Chronaxie des Muskels, Deutsche Ztschr. f. Nervenh. **100**:203, 1927.

9. Marinesco, G.; Sager, O., and Kreindler, A.: Ueber eine neue Methode der Funktionsforschung des Zentralnervensystems: Die Subordinationschronaxie in der Pathologie, Arch. f. Psychiat. **90**:517, 1930.

10. Jasper, H. H.: A Laboratory Study of Diagnostic Indices of Bilateral Neuromuscular Organization in Stutterers and Normal Speakers, Psychol. Monog., to be published.

rocker switch, which leads to and from a bank of condensors arranged in such a way that any capacity from 0.001 to 12 microfarads can be obtained by the manipulation of dials. A milliammeter and voltmeter are mounted in the charging circuit so that both potential and intensity of the current can be determined. The rocker switch is arranged in such a way that when it is thrown to the one side it connects the charging circuit coming from the eliminator with the bank of condensors, loading them up to the desired capacity. When it is thrown over to the other side it disconnects the condensors from the charging circuit and connects them with the electrodes leading to the subject. Thus, the loaded condensors can be made to discharge a current of known capacity into the subject. Before it actually reaches these electrodes, however, the discharging current is carried through a resistance of 15 ohms so as to take care of the slight changes in resistance occurring in the body of the subject. The current is then led into two silver electrodes which can be applied to the desired points in the body of the subject. The indifferent or anodal electrode, 8 by 18 cm. in size, is placed on the chest, whereas the effective electrode, 16 mm. in diameter, made nonpolarizable by plating it with silver chloride and soaking its flannel covering with isotonic solution of sodium chloride, is placed on the desired point of stimulation.[11] The determination of the rheobase, which must precede that of the chronaxia, could be obtained by measuring the intensity of the current coming directly from the eliminator. It has been found recently, however, that a continuous current sent directly through the skin suffers a great deal of deformation, and, therefore, we have followed the example of Stein and determined the rheobase on the basis of a current loaded into a large condensor of 10 microfarads.

The procedure of determination was as follows: The subject was seated comfortably in a chair, with the arm to be used immobilized on the arm of the chair next to the apparatus. The indifferent electrode was soaked with a solution of sodium chloride and fastened on the chest by a band passing around the thorax. The effective electrode was then used to ascertain the motor point of the muscle to be tested. In determining this point, care was taken not to confound the point that has a chronaxia characteristic for this particular muscle with the other point, which, as shown by Lapicque, has a chronaxia similar to that of the antagonist. First, the circuit leading through the 10 microfarad condensor was connected with the electrodes and the potentiometer arranged to allow a charge of an intensity well above the usual threshold. The effective electrode was then moved about the expected motor point. By successively throwing the rocker switch from one side to the other, the condensor was loaded and discharged into the subject. When a good response was obtained each time for several successive discharges, the point was marked with ink, and then the intensity was reduced until the slightest perceptible response was received at the point of stimulation. After several trials this intensity was taken as the rheobase.

The intensity was then doubled and the current led through the subdivided condensors in order to determine the capacity. One usually starts with a capacity of zero, and gradually increases it by manipulation of the dials until the slightest but still perceptible contraction is observed. When this has been observed distinctly for several consecutive discharges, the threshold capacity has been obtained. This capacity multiplied by four represents the chronaxia in terms of sigma (one one-thousandth of a second). To make sure of this determination, it is necessary

11. A more detailed description of this apparatus was given in the report of a previous investigation.[10]

to redetermine the rheobase at the point where the capacity was obtained and to consider the determination of the chronaxia as valid only if the rheobase remains constant.

Material.—Nine subjects, all male (graduate students and members of the hospital staff), were used in the experiments. The chronaxia values of antagonistic muscle groups of both upper extremities were determined shortly before, during and at the end of the intake of an amount of alcohol sufficient to produce definite intoxication with mental changes or signs of motor incoordination. The experiments were carried out in the evening. The subjects were advised to take only a light meal at 6 o'clock. About an hour after the meal, the first chronaxia values were determined. Alcohol was then given in 25 per cent solution of 95 per cent alcohol in ginger-ale or beer. The subjects took about 200 cc. of the solution at intervals of from thirty to forty-five minutes. The chronaxia was then determined as soon as definite signs of intoxication, such as exhilaration and talkativeness, were noted, or when the subjects themselves reported feelings of changes in the control of the motor functions. At the end of the experiment, that is, when it was thought that the subject had taken all the alcohol it was advisable to give him, the last determinations of the chronaxia were made. This general plan of taking a record of the triceps, biceps and extensors and flexors of the forearm on both sides for three separate readings worked out successfully in only some of the cases. In the others certain factors that could not be avoided did not allow the carrying of this plan to completion. In the first place, we thought it advisable to consider as valid only readings that were taken while the subject was cooperative and did not, because of the effects of the alcohol, tend to interfere with the determination. Although, whenever such interference was encountered it was always in a good natured way and could be partially controlled, a number of the determinations had to be left out as not altogether valid. Then, again, in some cases the bad effects, such as nausea, came on so suddenly that the determinations had to be interrupted before they were actually completed. Finally, in some instances the administration of the drug had to be discontinued so soon after the second determination that it was useless to attempt a third one.

Throughout the experiment, observations were made of the behavior, verbal production and motor coordination of the subjects, along with the record of the rheobase and chronaxia determinations.

PROTOCOL AND RESULTS

CASE 1.—D. C., aged 20, weighed 145 pounds (65.8 Kg.); he was of pyknic habitus and unaccustomed to alcohol. He was given 200 cc. of 95 per cent alcohol. He drank slowly, showing little change in his mental condition, but from the very beginning a steadily increasing motor incoordination. In this subject, the determinations of only the right triceps and biceps muscles before and at the end of the administration of the alcohol are available. They are:

	Right Biceps		Right Triceps	
	Rheobase	Chronaxia	Rheobase	Chronaxia
Before experiment	40	0.08	68	0.24
At end of experiment	49	0.16	66	0.08

In this subject there was definite incoordination, with no changes mentally. There was little change in the rheobase, but a reversal in the biceps-triceps relationship (from a ratio of 1:3 to one of 2:1).

CASE 2.—M. S., aged 26, weighed 160 pounds (72.6 Kg.); he was of pyknic habitus and unaccustomed to alcohol. He was given altogether 160 cc. of 95 per cent alcohol. After the second dose he began to show thickness of speech, and complained of inability to coordinate his arms and legs when attempting to move about. Later, he began to talk about feeling that things around him were changing. There was no excitement, although there was increased "push" of speech. The determinations were:

	Right*							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	35	0.12	30	0.176	35	0.184	40	0.396
After 160 cc	45	0.12	45	0.120	45	0.224	40	0.140

	Left							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	40	0.13	45	0.37	40	0.22	40	0.41
After 160 cc	45	0.12	45	0.10	50	0.24	45	0.208

* In this and the subsequent tabulations, R stands for rheobase and Ch for chronaxia.

In this subject there was definite incoordination with some mental change. The rheobase showed either no change at all or a slight increase, in the extensors as well as in the flexors. The chronaxia values showed a definite change; those of the extensors actually approached those of the flexors, and in two instances there was a reversal of the normal ratio.

CASE 3.—W. W., aged 30, weighed 155 pounds (70.3 Kg.); he was of pyknic, athletic habitus. He was an occasional drinker. Two hundred cubic centimeters of 95 per cent alcohol was administered. After the third dose he began to show marked incoordination, especially in the left arm, in which there also developed tremor. The incoordination continued to increase, and toward the end of the experiment the subject began to show steadily increasing excitement and combativeness. Three determinations were made:

	Right				Left			
	Biceps		Triceps		Biceps		Triceps	
	R	Ch	R	Ch	R	Ch	R	Ch
Beginning of experiment	20	0.14	90	0.35	22	0.05	76	0.09
After 125 cc	22	0.16	74	0.38	37	0.08	76	0.13
After 200 cc	40	0.10	96	0.40	20	0.09	65	0.05

In this case there was definite incoordination, especially on the left side, and later excitement and combativeness. The rheobase showed definite but inconsistent fluctuations, but the chronaxias showed the following: a reversal of ratio on the left side (from about 1:2 to about 2:1) and an exaggeration on the right (from 1:2.5 to 1:4).

CASE 4.—D. L-s., aged 35, weighed 150 pounds (68 Kg.); he was of athletic, asthenic habitus, and was an occasional drinker. He was given 180 cc. of 95 per cent alcohol. He began to report uncertainty in motor coordination after the third dose. This continued to increase with subsequent doses. Mentally, he just showed

somewhat increased talkativeness, but otherwise no change in behavior. The determinations were:

	Right							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	28	0.152	35	0.336	35	0.216	45	0.444
After 120 cc.	35	0.216	30	0.228	30	0.424	40	0.384
After 180 cc.	35	0.112	40	0.156	30	0.348	40	0.400

	Left							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	25	0.148	40	0.272	40	0.196	40	0.452
After 120 cc.	30	0.120	40	0.144	35	0.472	45	0.500
After 180 cc.	25	0.112	30	0.120	40	0.396	40	0.400

In this subject, there was definite subjective and objective incoordination, with little mental change. The rheobase showed slight fluctuation, but the chronaxia values were all changed, with a definite tendency toward equalization of the flexor-extensor values, and in some instances, even a reversal of the ratio.

CASE 5.—R. B., aged 28, weighed 148 pounds (67.1 Kg.); he was of asthenic habitus. He was given 160 cc. of alcohol. After the second dose he expressed subjective feelings of incoordination, and toward the end of the experiment was quite unsteady and dizzy. Mentally, he showed practically no change except for some increased "push" in speech. After the fourth dose nausea developed, and the experiment had to be discontinued.

The determinations were:

	Right							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	35	0.140	25	0.312	35	0.228	45	0.420
After 160 cc.	40	0.144	45	0.156	40	0.228	40	0.240

	Left							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	25	0.148	40	0.328	35	0.256	45	0.488
After 160 cc.	25	0.160	45	0.248	35	0.508	40	0.604

In this subject, there were signs of moderate incoordination and dizziness, but no mental changes. The rheobase showed slight and inconsistent changes, but the chronaxia values of all the extensors and one of the flexors changed, causing an equalization and leading to a 1:1 ratio in three of the four flexor-extensor groups.

CASE 6.—H. K., aged 26, weighed 180 pounds (81.6 Kg.); he was of athletic habitus and a habitual drinker. He was given 200 cc. of 95 per cent alcohol. After the third dose, he began to show signs of incoordination, which increased with the subsequent doses. Mentally, he showed little change. There was some nausea after the fourth dose. The determinations were:

	Right Biceps		Right Triceps	
	R	Ch	R	Ch
Before experiment	36	0.11	72	0.28
After 160 cc.	42	0.12	74	0.19
After 200 cc.	24	0.10	60	0.15

There was definite, even if moderate, incoordination with little mental change. The rheobase was decreased in both biceps and triceps. The chronaxia value of the biceps showed little change, but there was a decrease in that of the triceps, changing the ratio of 1 : 2.5 to 1 : 1.5.

CASE 7.—D. L-k., aged 24, weighed 155 pounds (70.3 Kg.); he was of dysplastic, asthenic habitus and was unaccustomed to alcohol. One hundred and fifty cubic centimeters of alcohol was given. Soon after the first dose he began to show an increased "push of speech," excitement and combativeness. These symptoms continued to increase rapidly until, at the end of the experiment, it was difficult to control him. There was no definite indication of any motor incoordination. The determinations were:

	Right							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	25	0.148	50	0.260	35	0.168	50	0.396
After 150 cc.	35	0.080	45	0.312	30	0.184	45	0.540

	Left							
	Biceps		Triceps		Flexors		Extensors	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	25	0.160	35	0.232	30	0.132	40	0.396
After 150 cc.	25	0.132	35	0.252	40	0.120	40	0.460

In this case there were marked mental changes with practically no motor incoordination. The rheobase showed some inconsistent changes. The chronaxia values changed definitely, most of the flexor chronaxias showing a decrease, while all the extensor values increased, so that the original ratios were more pronounced.

CASE 8.—G. L., aged 22, weighed 130 pounds (59 Kg.); he was of asthenic habitus and drank very little. Only 120 cc. of alcohol was taken, following which the subject became nauseated and ill, when the experiment had to be discontinued. There were definite mental changes in the form of increased talkativeness, some confusion and excitement, but no signs of motor incoordination. The determinations were:

	Right				Left			
	Biceps		Triceps		Biceps		Triceps	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	31	0.08	92	0.35	20	0.16	105	0.35
After 120 cc.	30	0.09	100	0.44	32	0.12	110	0.44

In this case there were definite mental changes and nausea, but no signs of incoordination. The rheobase showed an appreciable increase only in the left biceps. The chronaxia values, however, showed the same changes as in the previous case, that is, a tendency for an exaggeration of the normal extensor-flexor ratio.

CASE 9.—M. W., aged 25, weighed 175 pounds (79.4 Kg.); he was of athletic habitus and a habitual drinker. He was given 200 cc. of 95 per cent alcohol. Following the third dose, he showed increased talkativeness and some excitement,

but no signs of incoordination at any time during the experiments. The determinations were:

	Right				Left			
	Biceps		Triceps		Biceps		Triceps	
	R	Ch	R	Ch	R	Ch	R	Ch
Before experiment	32	0.09	105	0.35	43	0.13	106	0.40
After 120 cc.	32	0.09	96	0.44	44	0.13	140	1.32
After 200 cc.	28	0.09	130	0.80	45	0.09	140	2.16

In this subject, then, there were mental changes without any involvement of coordination. The rheobase showed some slight changes, especially in the triceps. The chronaxia values, however, showed much more marked changes, here as in the previous two cases tending toward an exaggeration of the normal biceps-triceps ratio.

ANALYSIS OF RESULTS

The first feature that becomes apparent on analysis of the results cited is the fact that the rheobase values either were not influenced by alcohol at all or, when they were, the changes produced were so slight or inconsistent that they could not be looked on as reliable indicators of the effects of alcoholic intoxication. Contrary to this, however, the chronaxia values were affected in all cases, even if not in the same way in all. In order to bring together in a systematic fashion all of the changes and ascertain whether they bear any relationship to the other effects of the intoxication, we present them in graphic form in the accompanying charts. We have arranged in four pairs of charts the chronaxia values in the four flexor-extensor groups, before and after the administration of alcohol. The figures on the left hand vertical margin represent chronaxia values in terms of sigma. The figures along the horizontal line refer to the cases cited. Each case is represented by a dot, these being connected by lines (continuous for flexors and interrupted for extensors).

The first pair of charts (chart 1) represent the chronaxia of the left biceps and triceps. It will be seen here that before the administration of alcohol the chronaxia of the triceps are all higher than those of the biceps. In most cases the ratios are about 1 : 2, although in some the difference between biceps and triceps is even higher. Following the intake of alcohol, there are changes in the biceps-triceps relationships in all cases. The nature of the changes is different in different cases, and from this point of view can be divided into three groups: (1) cases 2 and 3, in which the ratios have been reversed; (2) cases 4 and 5, in which there has been a diminution of the original difference, with a tendency toward equalization of the flexor-extensor values; (3) cases 7, 8 and 9, in which there has been an increase of the normal difference.

It can be seen also that the biceps values have in general shown much less tendency to change than those of the triceps.

In the next pair (chart 2), representing the right biceps-triceps values, there is a more or less similar situation, with the cases falling

into three groups and the triceps changes being by far the most pronounced. One rather prominent deviation is seen in case 3, which in this instance shows an increase of the normal ratio instead of the reversal observed on the left side.

The third pair of charts (chart 3) shows the chronaxias of the flexor-extensor group of the left forearm. Here, too, one sees the three

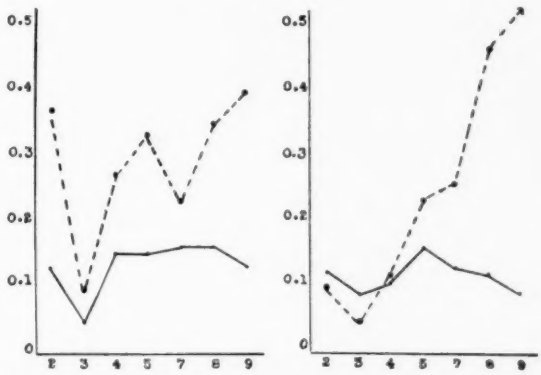

Chart 1.—Chronaxia values of left biceps (continuous line) and triceps (interrupted line) before (left) and after (right) the intake of alcohol.

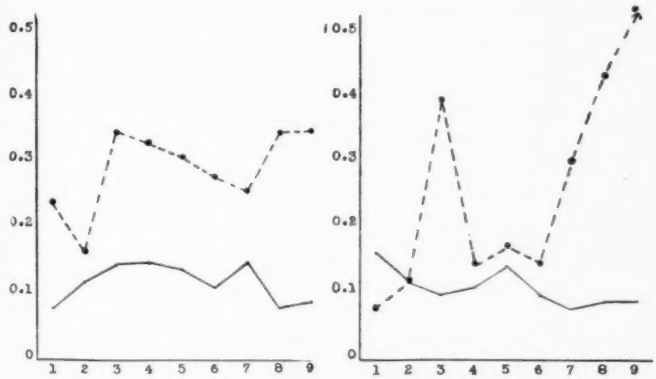

Chart 2.—Chronaxia values of right biceps (continuous line) and triceps (interrupted line) before (left) and after (right) the intake of alcohol.

groups, but the flexors and extensors participate equally in producing the change.

A similar situation is found in the fourth pair of charts (chart 4), that is, the same three groups and the same behavior of the flexor-extensor muscles.

Observations of the behavior and coordination of the subjects show that the changes were predominantly in the field of coordination in cases

1, 2, 4, 5 and 6, and mostly mental in the cases 7, 8 and 9, whereas case 3 showed marked changes in both fields. Comparing the two analyses, it will be noted that subjects in whom we found a predominance of coordination disturbances, showed either a tendency to equalization of the chronaxias or a reversal of the normal ratio. Contrary to this, the subjects with a predominant mental change showed an increase of the

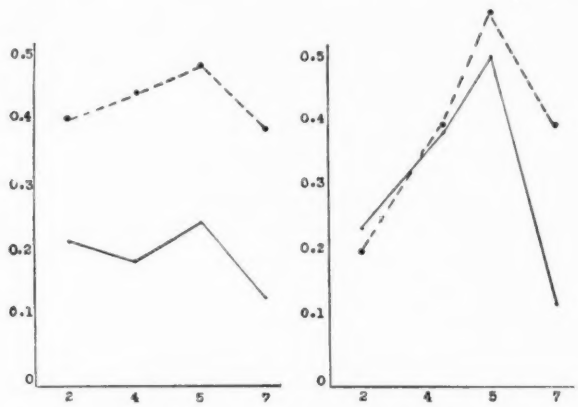

Chart 3.—Chronaxia values of left flexors (continuous line) and extensors (interrupted line) of forearm before (left) and after (right) the intake of alcohol.

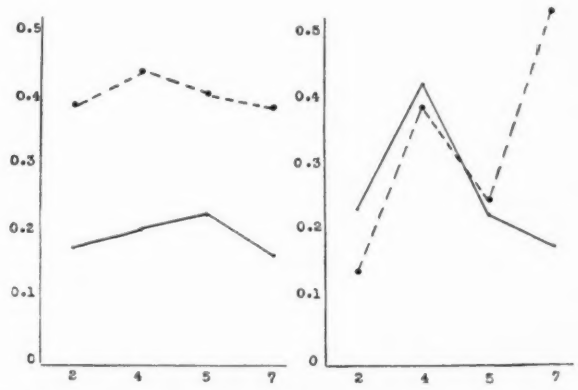

Chart 4.—Chronaxia values of right flexors (continuous line) and extensors (interrupted line) of forearm before (left) and after (right) the intake of alcohol.

normal difference between flexors and extensors. The only deviation from this correlation was in case 3. Here there were both incoordination and mental changes of a pronounced degree, whereas the chronaxias showed a reversed ratio on the left and an increased normal ratio on the right. It should be emphasized that the incoordination was most marked on the left and was accompanied by tremor on that side.

COMMENT

In discussing our findings, especially in their relation to reports on more or less similar investigations by other observers, we wish to stress particularly two phases of our results: (1) alcohol causes certain changes in the chronaxia relationships of antagonistic muscles; (2) these changes are associated with certain effects on the behavior and motor coordination of the subjects.

As regards phase 1, investigations have been reported by Kajiwara,[12] in collaboration with Lapicque [13] and with A. and B. Chauchard.[14] They studied the effect of alcohol on the motor chronaxia in the frog, rabbit, dog and man. They found primarily that, under normal conditions, the lower animals did not show as consistent a relationship between the flexors and extensors as is usually found in man. This made the evaluation of the results somewhat complicated. There were, however, definite changes caused by the alcohol, and these showed a general tendency toward an equalization of previously unequal chronaxias of the flexor-extensor antagonists. In man (four subjects were used) the general effect was a decrease of the chronaxia values of the extensors with little or no change in the flexors, which, therefore, tended to produce an equalization. In a small number of the determinations and when the doses were strong, there was a tendency to an increase in the extensor chronaxia. In general, then, these studies show the same results that we found in two thirds of our cases, namely, that alcohol causes an equalization, even up to a reversal, of the flexor-extensor chronaxia relationships.

Closely related to these studies are investigations that have been reported by M. and L. Lapicque [15] on chronaxia values of muscles following decapitation, section of the spinal cord and section of the nerves in frogs and dogs. The normal flexor-extensor chronaxia ratios were either reversed or equalized (i. e., resulting in a ratio of 1 : 1) following these separations of the muscle from the central nervous system. Lapicque designated the chronaxia of this type as "chronaxie de consti-

12. Kajiwara, S.: Recherches sur le mechanisme des troubles de la coordination nerveuse sous l'influence de l'alcool, Thèse de Paris, 1931, no. 216.

13. Lapicque, L., and Lapicque, M.: La chronaxie de subordination: Sa regulation réflexe, Compt. rend. Soc. de biol. **99**:1947, 1928. Lapicque, L., and Kajiwara, S.: Changements dans les chronaxies périphériques sous l'influence de l'alcool, ibid. **105**:632, 1930.

14. Chauchard, A.; Chauchard, B., and Kajiwara, S.: Action de l'alcool sur l'excitabilité des neurons moteurs de l'écorce cérébrale, Compt. rend. Soc. de biol. **105**:778, 1930.

15. Lapicque, M.: Action des centres encéphaliques sur la chronaxie des nerfs moteurs, Compt. rend. Soc. de biol. **88**:46, 1923. Lapicque, L., and Lapicque, M.: Modification des chronaxies motrices périphériques par les centres nerveux supérieurs, ibid. **99**:1390, 1928; footnote 13.

tution," as contrasted with the chronaxia of muscles working in relation with the central nervous system, which he termed "chronaxie de subordination."

One link between these experiments and those of Kajiwara and ours is furnished by some investigations by Lapicque of the effects of ether and chloroform anesthesia on the chronaxias of animals, in which he found similar tendencies toward equalization and reversal. In other words, the anesthetic changed the subordination chronaxia to one of constitution. Another link in this chain is suggested by the reports of Travis and Dorsey [16] on the effects of alcohol on the reflex time. These authors found that under the effect of alcohol the latency period of the patellar reflex was definitely shortened. Furthermore, a similar shortening of the reflex time was found, on the one hand, following decerebration and section of the spinal cord in animals, and, on the other hand, in patients with lesions of the upper motor neurons.

All these investigations serve as links in a chain of evidence pointing to the conclusion that the administration of alcohol in certain doses acts in the same manner as the isolation of the peripheral neuromuscular apparatus from central mechanisms. This would justify the conclusion that, in at least our first six cases, the alcohol acted in a way similar to the experimental change of the chronaxia of "subordination" into that of "constitution." We leave open for future discussion how much light this throws on the understanding of the question of "inhibition" in general.

Discussion of phase 2 of our problem may be introduced by the findings of Travis and Dorsey that in the case of reflex time the change produced by alcohol is similar to that produced in lesions of the pyramidal tract or other upper motor neuron disturbances. More specifically related to our own work are the reports on chronaxia determinations in patients with neurologic disturbances. Bourguignon [2] found approximation or equalization of the chronaxia values of antagonistic muscles in lesions of the motor cortex. Stein [8] found equalization of chronaxias of all the muscles of the upper extremities in cases of parkinsonism, in a case of tumor of the central gyrus and in one of infantile spastic paralysis. He stressed that these changes in chronaxia relationships are particularly pronounced in cases of fresh lesions and manifest themselves most sharply in the cases of parkinsonism following an effort toward the motorization of the affected limb. Apparently the attempt at carrying out coordinated motor activity, when coordination has been

16. Travis, L. E., and Dorsey, J. M.: Effect of Alcohol on the Patellar Tendon Reflex Time, Arch. Neurol. & Psychiat. **21**:613 (March) 1929; Effect of Alcohol on the Patellar Tendon Reflex Time in Dogs, ibid. **24**:48 (July) 1930; Patellar Tendon Reflex Time in Psychiatric and in Neurologic Cases, ibid. **22**:99 (July) 1929.

rendered difficult by the lesion, is particularly closely associated with equalization of the chronaxias of antagonistic muscles. Stein furthermore found a reversal of the chronaxias of the flexor-extensor groups of the toe in cases of positive Babinski signs. Marinesco,[9] too, found a tendency toward equalization of the flexor-extensor chronaxias in cases of parkinsonism, tetany and decerebrate rigidity. Finally, findings of a similar nature are reported by S. Weiss.[17]

These results, too, then point to the conclusion that in cases in which the normal relationship between the central mechanisms and the periphery are disturbed (i. e., when we are dealing with a chronaxia of "constitution" rather than of "subordination"), an equalization or reversal of chronaxias takes place. In the clinical material, however, a new factor is added to the picture, namely, the concomitant disturbances in normal coordinated motorization. In our experiments the results with the first six cases are in keeping with this trend of thought. In other words, alcohol, which is known to have an effect similar to that of isolating the peripheral neuromuscular apparatus from the central one, has caused a reversal or tendency toward equalization of the chronaxia values in cases in which it has also produced a pronounced degree of incoordination. The results in the last three cases would speak for the same state of affairs in a negative way; i. e., when there was no disturbance of coordination the chronaxias did not change in that direction. At present we do not feel justified in undertaking an interpretation of the relationship of the mental changes to the increase of the normal difference of the flexor-extensor chronaxia values. We can just register it as an important, even if as yet unexplained, phenomenon.

It is interesting to speculate on the meaning of this relationship of motor coordination and chronaxia. The theory has been advanced that the specificity of chronaxia of different muscle groups serves to put them in tune with specific impulses coming from the central mechanisms or even the sensory periphery. Furthermore, when the usual chronaxia values are changed a lack of ability results on the part of the peripheral neuromuscular units to, so to speak, "choose" the proper impulse. For this theory we would have to assume that in the normal person there exists in this connection an arrangement not unlike the so-called "resonance" principle recently advanced by Weiss.[18] His experiments on the relationship between this principle and chronaxia have failed to show direct connections; nevertheless, the possibility of a more or less similar situation is not definitely excluded.

17. Weiss, S.: Beiträge zur Chronaxie des neuromuskulären Apparates, Deutsche Ztschr. f. Nervenh. **121**:1, 1931.

18. Weiss, P.: Das Resonanzprinzip der Nerventätigkeit, Wien. klin. Wchnschr. **44**:1211, 1931.

SUMMARY

1. Alcohol given in certain doses causes changes in the motor chronaxia, in coordination and in the mental state of the subject.

2. In two thirds of the cases the normal flexor-extensor chronaxia relationship changed, with a tendency toward equalization or even reversal. In these cases there were pronounced coordination disturbances with no or minor mental changes.

3. In a third of the cases the normal chronaxia differences between flexors and extensors became exaggerated. In these the mental changes predominated, the coordination not being affected to any appreciable extent.

DISCUSSION

Dr. Israel S. Wechsler, New York: I find it difficult to discuss this paper for the reason that a few uninterpreted facts have been presented. Previous attempts have been made to study the effect of alcohol and the relationship of chronaxia to other clinical conditions, and Dr. Malamud's paper is interesting from that point of view, as well as the application of physiology to clinical medicine. However, the number of cases presented is not sufficiently large to prove anything definite, and there are a great many possibilities of error in the technic of testing chronaxia. Many of Dr. Malamud's figures may well fall within normal limits. To have pathologic significance, chronaxia should vary twenty, fifty, one hundred and two hundred times the normal. From a purely technical point of view, there is little difference, in testing chronaxia, whether one uses the motor point or the muscle, for there is an isochronism in the motor point and the muscle.

Chronaxia may be employed in gaging neuromuscular degeneration. It is a better index, provided sufficient records are kept, and it gives a much better chance of prognosticating results and testing the actual degree of recovery than by means of the reaction of degeneration.

Dr. G. F. Fulton, New Haven, Conn.: I have read the manuscript of Dr. Malamud's paper with great interest, and to a certain extent I share Dr. Wechsler's reticence in offering an opinion as to the significance of the results. I do not, however, quite share his view that one must have a difference in chronaxia of 100 per cent in order to be sure that one is dealing with a pathologic condition. The fact that in many of Dr. Malamud's cases the ratios between flexors and extensors were reversed is undoubtedly significant, particularly as they were associated with corresponding disturbance of locomotion.

I think that it is probably also significant that there were wide variations between individual experiments, because it is a common fact that alcohol affects different people in a different manner, depending on tolerance, individual idiosyncrasies and the like. But the interpretation of the results is not entirely clear. Dr. Malamud suggested that the results are essentially due to a release of the lower spinal segments from higher control. I think that he is probably correct in this inference, but there is no proof that the alcohol has not acted directly on the anterior horn cells of the spinal cord.

It is interesting in this connection that Flourens, in his early experiments on the cerebellum in 1824, pointed out that on slicing the cerebellum more and more deeply the symptoms of incoordination came to simulate the corresponding symptoms of incoordination produced by alcohol. He suggested that the primary seat

of the action of alcohol is on the cerebellar centers, and so far as I know there has never been any experimental evidence to disprove this contention.

In regard to the chronaxia as a measure of excitability of nerves, it has been the fashion recently—perhaps to a greater extent than Dr. Malamud realizes—to discredit the conception altogether. A group of "young Turks" in physiology has recently pointed out that isochronism does not hold between nerve and muscle; i. e., individual nerve-muscle preparations, when measured with fine bore electrodes, are not in fact isochronous one with another, and on account of this the theory has been discredited. Personally, I am not prepared to dismiss the whole idea of isochronism, for it is undoubtedly significant that slow tissues are as a rule innervated by nerves the rate of conduction of which is slow and the threshold of stimulation of which is high. In the cases of degeneration to which Dr. Wechsler referred, it is certainly true that as degeneration proceeds the chronaxia and the threshold of stimulation rise; i. e., it becomes necessary to apply a stimulus of a greater intensity and duration to evoke contraction than in the normal state.

I shall refer briefly to a number of recent observations on the higher primates, which I think have a bearing on this particular fact. If in the monkey one removes the foot area, no degeneration or atrophy occurs in the smaller muscles of the affected extremity, but on cutting the spinal cord, degeneration occurs; in primates, e. g., the gibbon and the chimpanzee, we found evidence of degeneration of the nerve fibers to the smaller muscles of the foot from cortical lesions alone, which was shown by a marked rise of excitability of motor nerves and early Marchi degeneration.

I am not aware that in clinical literature these smaller nerves have been studied. I think it would be worth while if Dr. Malamud, for example, could study the chronaxia of the small muscles of a hemiplegic extremity immediately after the hemiplegia had occurred and at successive intervals thereafter. I am sure that in that way he would secure significant information concerning the progress of the degeneration which results in peripheral motor neurons as a result of isolation from cortical control.

This brings me to the final point: Cutting off the cells of the "final common path" from cortical control leads to changes in the anterior horn cells, which may result in their actual degeneration. The changes in the excitable properties of the neurons are the earliest manifestation of the change which ultimately leads to degeneration of the anterior horn cells, and the importance of following the course of the alterations which ultimately cause degeneration is obvious.

Dr. Malamud's approach is an important one, and I feel strongly that it has a wider application than has as yet been given.

DR. ADOLF MEYER, Baltimore: I wish to draw attention to the fact that we are dealing here with the utilization of the time factor, as opposed to the factor of mere quantity of energy, in a way that may possibly bring us closer to correlation between the physiologic mechanisms and the psychobiologic functions. Evidently the psychobiologic functions can have a representation of their differential character in the physiologic mechanisms. I am thinking of the facts demonstrated by Dr. Richter with regard to decerebrate rigidity in the sloth. The sloth lives in a pendant position and thus depends largely on the flexors, in contrast to animals that stand on their legs. In the sloth there is an extensor rigidity which is altered to a flexor rigidity by decerebration. Evidently there is deeply rooted in the physiologic mechanisms a peculiarity that we understand in its full meaning only when we view the biologic entity, the life habits of the animals. It is possible that while in the tests of quantity we have not been able to make any correlation between the psychobiologic reactions of an organism under different modifications,

and specifically the correlation between the detailed physiology and the actual full-fledged psychobiologic reaction, we may, through the utilization of the time factor, i. e., the chronaxia, come closer to correlations. That has nothing to do with the actual material of the paper presented by Dr. Malamud. That is for those to discuss who are familiar with the technic and the technical principles involved. From the point of view of general principles, there is something there that intrigues and appeals to me, and it is the fact that the chronaxia of certain muscles seems to be dependent on what a certain muscle does in that biologic unit and type; it therefore may give an interesting means of coming closer to correlation of function and organismal properties, wherein so far we have failed.

Dr. H. G. Wolff, New York: The following experiments may have a bearing on Dr. Malamud's observations. Recently, Dr. Altenburger and I, working in Professor Foerster's clinic in Breslau, made some determinations of the vestibular influence on skeletal muscle.[19] It was observed that when the ear was irrigated with cold water, the usual flexor-extensor chronaxia difference disappeared. Equalization occurred instead, such as was mentioned by Dr. Malamud as occurring during certain phases of the effects of alcohol on his patients.

In order to determine, if possible, the pathways involved in this effect, we examined a group of patients on whom chordotomy had been performed. In such subjects we were unable to produce equalization after irrigation of the ear with cold water. We assumed then that the pathway involved in the chronaxia alteration of the skeletal muscle was among those destroyed by the operative procedure. It seemed likely, judging from the site of the operation, that the vestibulospinal tracts were implicated.

It is doubtful whether vestibular influences are the only ones that produce such equalization, but, as already suggested, there may be some relationship between our observations and those of Dr. Malamud.

Dr. William Malamud, Iowa City: In reply to Dr. Wechsler, I may point out that our conclusions did not depend on variations in the quantity of change of chronaxia; as with other observers, we felt that the most important factor was the change in ratio of antagonistic muscles. It is a matter of relationship of the chronaxias of the flexors and extensors, and if in alcohol intoxication there is a change in this ratio just as there is in a number of other conditions that I mention in the paper, this may explain the disturbances in motor coordination that are observed clinically.

I disagree with Dr. Wechsler that it does not matter where you place the electrode, because Lapicque found in the extensors, for instance, certain points away from the motor point where a chronaxia equal to that of the flexors can be obtained, and one must be careful to ascertain the motor point and to mark it with ink or with skin pencils as well as to redetermine it after the chronaxia has been taken. As to interpretation, we felt that the facts did not warrant any further interpretation than we offered.

In reply to Dr. Fulton, I do not wish to discuss the question whether we deal here with a release from upper motor neuron control. Lapicque, in the experiments with alcohol in animals, found results similar to ours and was of the opinion that the alcohol releases what he calls the chronaxia of "constitution" as contrasted with that of "subordination;" whether that is really so or whether there is some other explanation I do not know. In his opinion it is a release of the muscle from the upper motor neuron control.

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19. Altenburger, H., and Wolff, H. G.: Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:657, 1932.

Discrediting the concept of chronaxia by showing that the muscle, nerve and center may sometimes not be exactly isochronic is open to discussion. As a fact, Lapicque, did not say that they have to be exactly the same, but only that they are so within certain limits. But even if that were not so, I do not think that one could discredit the whole concept on that basis.

Dr. Fulton's suggestion that one should study the chronaxias in fresh lesions of the pyramidal tract is important. Stein carried out studies of this type, and he found that the most marked changes were present only in recent cases, gradually wearing off, sometimes even to a normal subordination chronaxia. This seems to support the idea of release from upper neuron control.

I am grateful to Dr. Meyer for his discussion, because that was just the point of which we were thinking. I think that there is an important factor there; we find it especially so when we consider the changes that we found in other cases, for example, in cases of catatonic schizophrenia with no signs of an organic lesion but with changes in chronaxia which could be reversed to normal by the administration of sodium amytal.

I am obliged to Dr. Wolff for his statement. I did not know of the work to which he referred. I do know that Lapicque has produced the same changes by complete section of the cord, finding that in this way he could change the chronaxia of subordination to one of constitution.

TEN YEARS' EXPERIENCE IN THE TREATMENT OF EPILEPSY WITH KETOGENIC DIET

HENRY F. HELMHOLZ, M.D.
AND
HADDOW M. KEITH, M.B. (TOR.)
ROCHESTER, MINN.

It is now ten years since the treatment of epilepsy by means of the ketogenic diet was started at the Mayo Clinic. During this period, 369 children up to the age of 14 years have been treated and kept under as close observation as possible by means of written reports from the parents and in many cases by return visits of the patients to the clinic. A report of the progress in these cases was published in 1925,[1] 1927[2] and 1930.[3] In these reports it was noted that 30 per cent of the patients with idiopathic epilepsy were "cured;" that is, they were free from attacks for one year or more, although they had returned to a normal diet. Approximately 23 per cent were reported improved. As was pointed out in the report of 1930, in the ultimate analysis these cases must be considered failures, but the improvement has been such that the parents feel that more has been accomplished by the diet than by any other means, and they are willing to continue with it.

In compiling the present report we have again separated the so-called idiopathic cases and the symptomatic, and it is the former group that we shall consider mainly. There were 51 cases in the symptomatic group, but these are not considered in the results of treatment by diet, although the patients were put on a diet. It was explained to the parents that only slight success could be expected, yet they were willing to undertake the supervision of the child's diet for a trial period.

Of the total number of 369 patients we have eliminated 189 as unsuitable for the consideration of results. The condition of 51 of these patients was symptomatic: 22 had been observed for less than six months; 89 did not cooperate sufficiently to give the diet a fair trial; the condition of 4 patients was not classified; in 9 patients who are well

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From the Section on Pediatrics, the Mayo Clinic.

1. Peterman, M. G.: The Ketogenic Diet in Epilepsy, J. A. M. A. **84**:1979 (June 27) 1925.

2. Helmholz, H. F.: The Treatment of Epilepsy in Childhood: Five Years' Experience with the Ketogenic Diet, J. A. M. A. **88**: 2028 (June 25) 1927.

3. Helmholz, H. F., and Keith, H. M.: Eight Years' Experience with the Ketogenic Diet in the Treatment of Epilepsy, J. A. M. A. **95**:707 (Sept. 6) 1930.

the diet was probably not responsible, and we can obtain no information with regard to the remaining 14.

Twenty patients were treated for a period of from six months to one year. Four of these have been free from attacks for from six to twelve months and are still on the diet. The condition of 9 has improved, and the remaining 7 have failed to show improvement.

There are, then, 160 patients whom we have traced for periods up to ten years, and about whom we have sufficient information to consider the results of the treatment by diet. Of these patients, 58 are well, and we believe that the improvement is due to the ketogenic diet. This is 36 per cent of the group under consideration. Thirty-four patients are improved (21 per cent), and the treatment of 68 (43 per cent) was definitely a failure so far as the diet is concerned. All of the 58 patients who are well have reported to us by letter within the past few months, as have those who showed improvement. A number of those whose condition was considered a failure have not been heard from recently, but our information leaves no doubt as to the failure of the diet to benefit them.

We have considered as cured only patients who have been free from attacks for at least a year, have gradually resumed a normal diet and have remained free from attacks up to the present. In the improved group we have placed those who have remained on the diet for long periods because they are much better under this regimen, and also patients who have resumed normal diet but still have an occasional attack. One of the latter has had an attack in four years. Another has slight attacks about once a year. A third has occasionally what may be attacks of petit mal, although he was having attacks of grand mal when he started the diet. One patient who had been free from attacks for six years and on a normal diet for four years had three attacks in the summer of 1930 and was again placed on the ketogenic diet. He has had no further attacks of any kind and is still on a ketogenic diet.

Eighty-nine patients did not cooperate sufficiently to permit us to judge the effect of the diet. These patients stayed on the diet less than two months, or they did not adhere strictly to the diet and were never in satisfactory ketosis. A few patients in this group were well on the diet, but they became tired of it, and attacks recurred when the diet was stopped.

In 1927, 18 patients had been free from attacks for more than a year; only 12 are still in the cured group. Two were reported as improved in 1930, and 3 others have had occasional attacks. One patient has had a recurrence of attacks but has not returned to the diet as advised. At the same time, 8 patients were reported as free from attacks for a year or less. Of these 8, 6 are still in the cured group, and 2 were improved when last heard from. Twenty patients were

reported as improved. One of these has since joined the cured group; 3 remain improved, 7 have derived no benefit, and 9 have not cooperated for several years (table 1).

These figures emphasize the fact that the observation of epileptic patients must continue over a period of many years, and that patients are not necessarily "cured" at any time. A good example of this is a patient who began the ketogenic diet in 1925. He was free from attacks for five years, when they recurred; they are still present, as his mother did not cooperate in the resumption of the proper diet. As there have recently been other methods proposed for treating epileptic patients, such as dehydration (Fay,[4] Bauer[5] and McQuarrie[6]), it has been difficult to compare the results with those in the present study, as there has been no report of freedom from attacks in such cases over periods longer than from ten to twelve months.

TABLE 1.—*Results of Treatment (from 1927 to 1932).*

		Status in 1932			
	Patients	Cured	Improved	No Benefit	No Cooperation
Status in 1927					
Free for more than 1 year	18	12	5	..	1
Free for 1 year or less	8	6	2*	..	..
Attacks on resuming normal diet	3	1	1	..	1
Improved	20	1	3	7	9
Status in 1930					
Free more than 1 year	42	35	5	..	2
Free less than 1 year	11	7	3	..	1
Improved	41	6	15	3	16

* 1930; no information was obtained for 1932.

The results for the 51 patients with symptomatic epilepsy are of course much less encouraging. Only 5 patients are free from attacks, and 1 of these is taking large doses of phenobarbital. The other 4 have been free for periods of fourteen months, three and a half years, five years and six years, respectively. Eleven patients are improved, according to the statement of parents. Three patients have died, 1 by drowning, 1 during influenza and status epilepticus and 1 apparently

4. Fay, Temple: The Convulsive State and the Results Obtained by Limitation of Fluids, read before the New York Academy of Medicine, Dec. 11, 1928; Some Factors in the "Mechanical Theory of Epilepsy," with Especial Reference to the Influence of Fluid, and Its Control, in the Treatment of Certain Cases, Am. J. Psychiat. **8**: 783 (March) 1929; The Therapeutic Effect of Dehydration on Epileptic Patients, Arch. Neurol. & Psychiat. **23**:920 (May) 1930; Epilepsy: Clinical Observations on the Control of Convulsive Seizures by Means of Dehydration, J. Nerv. & Ment. Dis. **71**:481 (May) 1930.

5. Bauer, E. L.: The Management of Epilepsy, with Special Reference to Diet, Pennsylvania M. J. **32**:690 (July) 1929.

6. McQuarrie, Irvine: Epilepsy in Children: The Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**: 451 (Sept.) 1929.

in status epilepticus alone. The condition of the remaining 32 patients has not changed appreciably, or is worse.

There has been considerable discussion as to the reason for the action of the ketogenic diet in controlling the attacks. Wilder's [7] original hypothesis was that the anesthetic action of the aceto-acetic acid was responsible for the anticonvulsive effect. One of us (Keith [8]) has made a study of the effect of acetone bodies on experimental convulsions in rabbits. The convulsions are produced by the injection of small amounts of thujone, the active principle of oil of wormwood, into the marginal ear vein. It has been shown that acetone, ethyl aceto-acetate, diacetone alcohol and aceto-acetic acid all have anticonvulsive properties, but that the aceto-acetic acid and its sodium salt have by far the most

TABLE 2.—*Summary of Results*

		Patients	Per Cent
Patients on ketogenic diet		369	
Patients with symptomatic epilepsy		51	
Patients with idiopathic epilepsy		318	
Patients who failed to cooperate	89		
Patients treated less than 6 months	22		
Patients treated for 1 year	20		
Free from attacks	4		
Improved	9		
Not benefited	7		
Patients treated more than 1 year		160	
Free from attacks	58		36
Improved	34		21
Not benefited	68		43
Unclassified	4		
Well, not due to diet	9		
No information	14		

marked effect. The effect is less marked than with a similar quantity of phenobarbital, but the latter has a more marked soporific effect.

McQuarrie has suggested that the dehydrating effect of the diet is a factor in preventing the convulsions, and Fay has used limitation of fluid intake as a method of treating epilepsy. In rabbits, extreme dehydration with sucrose solution had some anticonvulsive effect,[8a] but this was not so marked as the effect of the diacetone alcohol, which was itself less effective than aceto-acetic acid or its sodium salt.[8c] As

7. Wilder, R. M.: The Effect of Ketonemia on the Course of Epilepsy, Bull. Mayo Clinic **2**: 307 (July 27) 1921.

8. Keith, H. M.: (*a*) Influence of Various Factors on Experimental Convulsions, Proc. Staff Meet., Mayo Clin. **5**:204 (July 23) 1930; Effect of Various Factors on Experimentally Produced Convulsions, Am. J. Dis. Child. **41**:532 (March) 1931; (*b*) Further Studies on the Influence of Various Factors on Experimental Convulsions, Proc. Staff Meet., Mayo Clin. **6**: 410 (July 8) 1931; Further Studies of the Control of Experimentally Produced Convulsions, J. Pharmacol. & Exper. Therap. **44**: 449 (April) 1932; (*c*) Factors Influencing Experimentally Produced Convulsions, Arch. Neurol. & Psychiat. **29**:148 (Jan.) 1933.

stated in 1930, it has been generally accepted that dehydration has little if any effect on the seizures of petit mal. In our experience patients whose convulsions were not controlled by the ketogenic diet were not rendered free from attacks by the restriction of water. Bridge and Iob [9] have noted that elimination of sodium chloride during fasting has been coexistent with improvement of patients who have epilepsy, and they think that the combination of acetone bodies, acidosis and elimination of sodium and extracellular fluid from patients on a ketogenic diet is responsible for its favorable effect.

SUMMARY

The result in the treatment of 369 patients with epilepsy by means of the ketogenic diet is summarized in table 2. Fifty-one of these patients had symptomatic epilepsy, 42 were treated for one year or less, and 89 did not cooperate sufficiently for us to judge the effect of the diet. Twenty-seven patients could not be included in the group in which treatment was satisfactory for the reasons indicated. This leaves a group of 160 on which to judge our results. Of these, 36 per cent are well, 21 per cent are improved and 43 per cent were not benefited. These figures are similar to those in previous reports (1927 [2] and 1930 [3]).

The reason for the therapeutic anticonvulsive action of the ketogenic diet is considered. It is pointed out that aceto-acetic acid and its sodium salt are able to prevent experimentally produced convulsions in rabbits, that their action is not quite so pronounced as the action of phenobarbital, but is greater than that of the other acetone bodies tested and is more marked than even that of extreme dehydration.

9. Bridge, E. M., and Iob, L. V.: The Mechanism of the Ketogenic Diet in Epilepsy, Am. J. Psychiat. **10**:667 (Jan.) 1931; Bull. Johns Hopkins Hosp. **48**: 373 (June) 1931.

ETIOLOGY OF POLYNEURITIS

I. S. WECHSLER, M.D.
NEW YORK

In a paper written two years ago,[1] I made a preliminary report on a number of cases of polyneuritis of obscure etiology and ventured the opinion that they were the result of unrecognized avitaminosis. I also discussed the relation of gastric and hepatic disturbances to the etiology of alcoholic polyneuritis; the rôle played by pernicious vomiting in the production of polyneuritis of pregnancy and of other types of polyneuritis; the effect of starvation in cachectic polyneuritis; the influence of gastro-intestinal and hepatic impairment in polyneuritis from arsenic and phosphorus poisoning; the part played in the occasional occurrence of diabetic "polyneuritis" by the exclusion of foodstuffs rich in vitamins, and the rare forms of neuritis in children suffering from severe gastro-intestinal disturbances. The conclusion was also reached that in polyneuritis, which has hitherto been regarded as due solely to specific causes, food deficiency or avitaminosis plays a definite, possibly ultimately decisive, rôle.

Since the publication of the paper, I have had occasion to observe a number of other cases which bore out the views originally expressed, and subsequent reference to the literature confirmed in some measure the theoretical conclusions reached at the time. Limited experimental work was also undertaken, but the results were not different from those of the more extensive investigations along the same lines by others, so that they will not be included in this paper. In any case, the desire is to call attention to the clinical phase of the problem, the pathologic or experimental evidence incidentally alluded to merely serving as confirmatory evidence of clinical observation. Much experimental work will be needed, however, before positive opinions will be fully justified. Although a fairly large number of cases of polyneuritis in which the question of food deficiency seems to have played some part were observed, I shall report only five in which neither the diagnosis nor the rather decisive etiologic factor was in doubt. I shall also include a brief résumé of four of the eight cases included in the preliminary report.

From the Neurological Department of the Montefiore Hospital and the New York Neurological Institute.

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

1. Wechsler, I. S.: Unrecognized Cases of Deficiency Polyneuritis (Avitaminosis?), M. J. & Rec. **131**:441 (May 7) 1930.

REPORT OF CASES

CASE 1.—G. B., a woman, aged 53, was admitted to the Neurological Institute on March 15, 1930, her chief complaint being inability to walk for the preceding three months. The patient had enjoyed good health up to two months before the onset of the present illness, when she began to suffer from persistent diarrhea and severe loss of appetite. In October, 1930, her memory showed signs of failing. The patient had chronic alcoholism.

Examination showed a poorly nourished, emaciated woman, looking older than her years and very ill. Her memory was poor for past and recent events; she was confused and disoriented and filled in gaps in her memory (confabulated); she probably hallucinated. The speech was dysarthric. She could not walk without support, and when she did there was a steppage gait. The Romberg sign was positive, and there was a finger-to-nose ataxia on the left. There was coarse tremor of the fingers, hands and feet. There were generalized muscular weakness, particularly of the extensors of both wrists, and also generalized hypotonia and moderate atrophy of the musculature of the extremities. Both ankle jerks were absent; the other deep reflexes were markedly diminished and just elicitable. Because of the marked hyperalgesia of the soles, the plantar reflexes could not be tested. The abdominal reflexes were not elicited. Owing to the mental condition of the patient, a sensory examination could not be carried out. The cerebral nerves were normal; the fundi showed arteriosclerotic vessels.

The red and white cell counts were practically normal; the color index was 0.9; there were slight microcytosis, macrocytosis and poikilocytosis. Chemical examination of the blood gave normal results. Urinalysis showed a faint trace of albumin and a few casts. Serologic examination of the blood gave negative results. The spinal fluid was normal, and there was no block. The diagnosis concurred in was Korsakoff's syndrome and polyneuritis, on an alcoholic basis, precipitated by deprivation of food (anorexia) and diarrhea.

The patient was given fruit and tomato juices, viosterol and later a full diet rich in vitamins. Improvement was rapid and fairly remarkable. Her speech became clear; mentality improved; she regained muscular power, so that she could walk unassisted. With recovery, pin and needle sensations developed in the extremities, which later cleared up. She was discharged less than two months after admission, practically recovered physically and remarkably improved mentally.

CASE 2.—H. N., a man, aged 39, was admitted to the Neurological Institute in October, 1931. He complained of weakness in the legs, arms and hands, pain and tingling in the legs, toes and fingertips, hypersensitiveness of the palms and soles, and loss of appetite, weight and potency. The patient had been drinking whisky excessively for the past year, and his appetite had been so bad that he ate practically nothing. In April, 1931, the symptoms described came on gradually. There was a history of possible visual hallucinations.

On admission he was rather emaciated, mentally somewhat dull and emotionally depressed but well oriented and cooperative. The gait was unsteady; he could not walk on his heels; the Romberg sign was positive; he showed slight finger-to-nose ataxia; skilled acts were poorly performed; there was tremor of the fingers; the ankle jerks were absent; all other deep reflexes were present and somewhat overactive; the abdominal reflexes were present; the cremasteric reflex was absent; there was no Babinski sign; muscular volume was poor throughout, and atrophy was marked in the small muscles of the hands and the calf muscles; muscle power was weak throughout; there were hypalgesia, hypesthesia and hypothermesthesia,

of glove and stocking distribution, and there was tenderness of the nerve trunks. The cerebral nerves were normal. There was a seborrheic dermatitis of the face and dryness of the skin of the hands and legs, but, according to a dermatologist, the lesions were definitely not pellagrous. The blood count was normal; serologic tests, both of the blood and of the spinal fluid, were negative, though the protein in the latter was increased; gastric analysis showed absent free hydrochloric acid and a total acidity of 3, with lactic acid present. Series of gastro-intestinal roentgenograms were normal.

The clinical diagnosis concurred in was polyneuritis due to food deficiency and chronic alcoholism. Because of the malnutrition the patient was given a diet rich in vitamins. Marked improvement immediately followed. Appetite returned; power was regained; the tremor and the nerve tenderness disappeared; the sensory changes receded, and the mentality cleared up. The patient was discharged practically cured one month after admission.

CASE 3.—M. B., a woman, aged 46, was admitted to the Neurological Institute in April, 1932, with the complaint of severe pains in both lower extremities, the whole left arm and the right hand and weakness of all the limbs. For years she had vomited after meals, owing to what she called indigestion, and had restricted her diet to spinach, chicken and chicken broth. In November, 1931, she noticed weakness of the legs. In December, the vomiting became more severe, and this condition lasted for two months. A diagnosis of gallstones was finally made; she was operated on in March, 1932, and after recovery from the cholecystectomy was brought to the Institute. The pains had begun in December, 1931, and by January, 1932, she was totally unable to walk. Except for the loss of 55 pounds (24.9 Kg.) in weight, the history was irrelevant. She was not alcoholic.

The patient was unable to walk on account of weakness and pain; there was some ataxia in the left upper extremity; the legs could not be tested for incoordination. The radial and ulnar reflexes were absent in the left upper limb and biceps and triceps jerks were barely elicited, while those of the right arm were normal. Both patellar reflexes were absent; the ankle jerks were barely elicited. The abdomen was too flabby to show reflexes; there was no Babinski sign. There was great weakness of the upper extremities, which was most marked in the wrists and fingers, especially so in the left hand. There was bilateral footdrop; the left lower limb was practically completely paralyzed; the right was very weak. There was marked hypotonia of all limbs. Atrophy was present in the left forearm, in the intrinsic muscles of the hands and in both feet, although edema of the legs obscured the atrophy. There was marked tenderness of the muscles and nerves. There was typical "glove and stocking" impairment of sensation. Touch, pain and temperature sensations were diminished in the lower limbs and in the left hand. The tongue was smooth and reddish. Serologic examination gave normal results. Other laboratory tests gave no significant results, with the exception of showing an absence of free hydrochloric acid in the gastric contents.

There was no question as to the diagnosis of polyneuritis. Owing to the history of vomiting for a period of years and the restriction in diet, the patient was given a mixed diet, rich in vitamins, with bemax and brewers' yeast, and also orange and lemon juice. To date, the tenderness has disappeared and power has begun to return, especially in the lower extremity, so that she is apparently on the road to recovery.

CASE 4.—A. M., a woman, aged 56, was admitted to the Neurological Institute in September, 1931. The chief complaints were: difficulty in walking, numbness of the lower extremities, weakness of the hands and tingling sensations in the hands and feet. The onset is said to have been gradual, over a period of years,

but the main symptoms actually dated back six months, that is, to March, 1931. At that time she received a number of injections of neoarsphenamine, which were followed by marked loss of appetite, intolerance for fruits and vegetables and vomiting. She lost weight rapidly and became progressively weak, and burning of the tongue, tingling of the fingers and atrophy of the hands developed. The menopause had set in at 50. The past and family histories were without significance. She had been a consistent beer drinker.

Neurologic examination revealed: a steppage gait, a positive Romberg sign, fine tremor of the extended hands, absence of all deep reflexes, sluggish abdominal reflexes, no Babinski sign, bilateral footdrop, weakness of the flexors and extensors of the hands and wrists, atrophy of the interossei, partial reaction of degeneration in the muscles of the hands and feet, and glove and stocking loss of all forms of sensation; the cerebral nerves were practically normal. There was slight edema of the legs. The blood pressure was 140 systolic and 90 diastolic. The tongue was smooth and shiny.

The cell count showed from 3,120,000 to 4,370,000 red cells and from 6,200 to 9,200 white cells; the hemoglobin was 64 per cent, and the color index was 1 or less. There was some microcytosis and macrocytosis; reticulocytes ranged from 1.2 to 3 per cent. Chemical examination of the blood, urinalysis and Wassermann tests of the blood and spinal fluid gave normal results. Gastric analysis showed consistent absence of free hydrochloric acid and the presence of lactic acid; the total acidity ranged from 3.6 to 16.6.

The patient was given liver therapy and a full diet, with one cake of yeast daily. She was discharged markedly improved eight weeks after admission.

Comment.—In this case the question arose whether there was spinal degeneration on the basis of pernicious anemia, even though the syndrome was not one of posterolateral sclerosis. The clinical picture was definitely that of polyneuritis, and a polyneuritic syndrome due to anemia was postulated, though the anemia was never severe. The rapid onset following vomiting and other gastro-intestinal symptoms pointed to the development of polyneuritis in a patient with mild pernicious anemia, who was also alcoholic. The additional factor to be taken into consideration was the arsenical poisoning following medication with neoarsphenamine, which precipitated the gastro-intestinal disturbances.

Case 5.—S. N., a woman, aged 36, was admitted to the Montefiore Hospital in December, 1931. The illness dated back at least one year and had been characterized in the beginning by vomiting and loss of weight. In August, 1931, she was operated on at Mount Sinai Hospital for carcinoma of the stomach. The liver was found uninvolved, and a subtotal gastrectomy was done. She vomited for some time after the operation, but later improved sufficiently to be discharged to her home. She was readmitted to the hospital three weeks later, because of recurrence of vomiting and increasing weakness of the legs to the extent that she lost the power of walking. At the same time she began to have shooting pains in the legs. These were soon followed by pains in the hands and weakness of the arms. At that time she showed objective sensory disturbances in all the extremities, absence of knee and ankle jerks and diminished deep reflexes in the arms, absent abdominal reflexes, normal plantar reflexes, marked loss of power in the limbs and generalized atrophy. The laboratory findings were not significant. The condition was regarded as polyneuritis due to food deficiency, and the patient was given a diet rich in vitamins, whereon she began to improve.

On admission to the Montefiore Hospital, she showed practically the same neurologic signs. The deep reflexes were absent; the sensory loss for all modalities was of the glove and stocking variety; the paresis and atrophy of the extremi-

ties were still considerable, with corresponding hypotonia. Gastric analysis showed absence of free hydrochloric acid; the red cell count was normal; the hemoglobin was 80 per cent, and the benzidine test was positive.

The patient was given a high caloric, vitamin-rich diet and hydrochloric acid. She began to show definite improvement in that the sensory loss receded and power in the limbs returned. Unfortunately, metastases made their appearance, and despite the definite recession of the polyneuritis she died several months after admission.

CASE 6.—M. W. E., a boy, aged 17, was admitted to the Montefiore Hospital with the complaints of weakness, anorexia, nausea, occasional vomiting, dyspnea, pain in the calves and clumsy gait. Nine months previously he had suffered for a short time from dyspnea and pains in the calves and swelling of the ankles, and the same complaints reappeared one month before admission. It is worthy of special note that for years the boy lived on bread, potatoes, cereals and pastry, but ate no fresh vegetables, drank no milk and did not touch meat.

General examination, including all laboratory tests, gave negative results except for low blood pressure (95 systolic and 60 diastolic), and the absence of free hydrochloric acid in the gastric contents. Neurologically, he showed: ataxic gait, positive Romberg sign, diminished deep upper reflexes and absence of ankle and knee jerks, present but unequal abdominal reflexes, the right being greater than the left, and weakness of the lower extremities, especially of the extensor muscles. All forms of sensation were impaired in the distal parts of the four extremities, giving a typical glove and stocking distribution.

There was no doubt of the diagnosis of polyneuritis, probably caused by a deficiency in food. He was given a full diet, rich in vitamins, and dilute hydrochloric acid. He improved sufficiently within ten days to be discharged, and soon recovered completely.

CASE 7.—N. Z., a housewife, aged 36, was admitted to the Montefiore Hospital complaining of the loss of 50 pounds (22.7 Kg.), pains in all extremities and inability to walk and feed herself. She had begun to vomit in the latter months of her fifth pregnancy, then had the grip, and finally could not retain any food. Following delivery she began to have pains, and later weakness of the limbs.

General examination, including search for metals, gave altogether negative results. Neurologically, there were flaccid paralysis of the extremities, atrophy of the muscles of the forearms, hands, legs and feet, bilateral footdrop and wristdrop, absence of deep reflexes, loss of all forms of sensation in the typical glove and stocking distribution and nerve tenderness.

A diagnosis of polyneuritis following vomiting of pregnancy and food deficiency was made. The patient was given a full diet, rich in vitamins, and showed remarkably rapid improvement.

CASE 8.—G. L., a housewife, aged 35, was admitted to the Montefiore Hospital complaining of pains and dysesthesias in the extremities and swelling of the ankles. She had been treated for asthma with pollen desensitization and epinephrine for a number of years, during which she had restricted her diet to chicken broth, bread, potatoes and oatmeal, omitting fresh vegetables and eggs. Ten weeks before admission she began to suffer from severe diarrhea; then swelling of the ankles and, finally, pain and numbness in the extremities appeared.

General medical examination showed chronic fibroid phthisis and a palpable liver; all other examinations, including laboratory tests, gave negative results. Neurologically, there was a syndrome typical of polyneuritis, including loss of power in the distal parts of all extremities, with left footdrop, atrophy of the muscles of the forearms, hands, legs and feet and loss of all forms of sensation in

the distribution of the peripheral nerves of the hands, legs and feet. The neuritis was attributed to the vomiting and food deficiency. She began to show improvement as soon as she was given a diet rich in vitamins.

CASE 9.—W. S., a woman, aged 42, was admitted to the Montefiore Hospital with the complaints of pain, numbness and weakness in the limbs. She had been vomiting for the past two years, and the symptoms had set in three months before admission. When the patient was brought to the hospital she could neither stand nor walk.

General examination showed moderate secondary anemia; the liver was considerably enlarged and the spleen palpable. There was no fever and no history or evidence of an infection; the blood was normal, and the serologic tests and roentgen examination of the bones showed no pathologic process. Neurologically, there were bilateral footdrop, weakness of all the extremities, absence of knee and ankle jerks, analgesia in the glove and stocking distribution, anesthesia and impaired position and vibratory sensations in the hands and feet and tenderness of the nerve trunks.

The cause of the enlargement of the liver and spleen was not determined, and the case was at first regarded as one of "toxic-infectious" polyneuritis. When emphasis was put on the history of persistent vomiting, food deficiency was taken into consideration, and the patient was given a diet rich in vitamins. She recovered sufficiently to be discharged to her home.

STUDY OF THE LITERATURE

Since Eijkman [2] first reported the experimental production and cure of polyneuritis gallinarum by means of diet, a vast literature has grown up on the subject of food deficiencies, which are now known as avitaminoses. Sherman and Smith [3] have recently brought the whole subject up to date. Owing to the obscurity of many of the problems of the vitamins, there is as yet no unanimity as to specific etiologic or pathologic factors and no certainty as to clinical manifestations. Although it is agreed that absence of vitamin B is a definite factor in the production of beriberi, the disease is still regarded in some way as toxic-infectious in nature. Recently, Bernard [4] also expressed such an opinion and added that one must include another etiologic factor, namely, an excess of carbohydrates; he also stated that the polyneuritis is a sequel to beriberi and need not be a part of the clinical picture. Randoin and Lecoq [5] have produced chronic polyneuritis in pigeons by feeding diets lacking only the antineuritic vitamin B and containing the other vitamins, that is, B_2 or G. Sandles [6] reproduced nutritional polyneu-

2. Eijkman, C.: Virchows Arch. f. path. Anat. **149**:187, 1897.

3. Sherman, H. C., and Smith, S. L.: The Vitamins, American Chemical Society, Monograph Series, ed. 2, New York, Chemical Catalog Company, 1931.

4. Bernard, N.: Beriberi, Ann. Inst. Pasteur **47**:508, 1931.

5. Randoin, L., and Lecoq, R.: Production de polynévrite chronique typique, Compt. rend. Soc. de biol. **101**:11, 1929.

6. Sandles, M. R.: Experimental Nutritional Polyneuritis in Rats, J. Nutrition **2**:409, 1930.

ritis in rats, and von Hofmeister [7] showed that chronic polyneuritis can develop in rats on diets merely deficient in, but not entirely lacking, the antineuritic vitamin. Sandles showed further that there is a "definite gradation of symptoms correlated with the extent of the deficiency of the vitamin in the food supplied." Both of these facts probably have clinical significance and bear on the problem of polyneuritis discussed in this paper. Attention has been called to the fact that most cases of beriberi are preceded by indigestion and many by diarrhea, and Burnett and Howe [8] have pointed out that malabsorption or deficiency of vitamins may manifest itself clinically merely in impaired digestion, diarrhea, colitis and asthenia, before the occurrence of nervous signs. They pointed out that one is dealing here, as it were, with a reversible process; namely, the absence of vitamin causes lack of appetite, malabsorption and poor assimilation, and these in turn bring about deficiency of vitamins. In this connection, allusion might also be made to the rare occurrence of polyneuritis in children following severe and prolonged gastro-intestinal disturbances. Another interesting fact, recently pointed out by Sheldon, Doyle and Osterberg,[9] was the occurrence of protracted nausea and vomiting in five of forty patients treated with arsenic in whom polyneuritis developed. It is of great interest that they found no correlation between the quantity of lead and arsenic in the body or excreted in the urine and the occurrence of polyneuritis. Incidentally, it might be pointed out that polyneuritis develops in very few patients of the tens of thousands treated with large quantities of arsenic for syphilis. The arsenic generally given intravenously does not damage the gastro-intestinal mucosa, and, far from causing anorexia and malabsorption, often leads to a gain in weight.

As bearing on clinical manifestations, the report of Bender [10] has some significance. He reported the cases of three patients suffering from malnutrition and the mental symptoms of pellagra, without neuritis; one of them had an ulcer and two carcinoma of the stomach. In a very suggestive article, although he gave no detailed reports of cases, Shattuck [11] called attention to the occurrence of beriberi in persons with chronic alcoholism, tuberculosis, cancer, diabetes, syphilis, marasmus

7. von Hofmeister, F.: The Beriberi of Rats, Biochem. Ztschr. **128**:540, 1922.

8. Burnett, F. L., and Howe, P. R.: Malabsorption in Deficiency Diseases, J. A. M. A. **58**:1705 (May 28) 1927.

9. Sheldon, W. D.; Doyle, J. B., and Osterberg, A. E.: Neuritis from Arsenic and Lead, Arch. Neurol. & Psychiat. **27**:332 (Feb.) 1932.

10. Bender, W. L.: Pellagra Secondary to Lesions of the Stomach Interfering with Nutrition, J. A. M. A. **84**:1250 (April 25) 1925.

11. Shattuck, G. C.: The Relation of Beriberi to Polyneuritis, Am. J. Trop. Med. **8**:539 (Nov.) 1928.

of children and pregnancy, all on the basis of an avitaminosis. But it is not alone vitamin B which has been shown to bring about degeneration of the nerves. Hughes, Lienhardt and Aubel [12] fed pigs a diet deficient in vitamin A, and the animals showed incoordination, spasms and impaired vision. Histologic examination showed degeneration of the optic, femoral and sciatic nerves, in addition to involvement of the spinal cord. Wills and Mehta [13] showed, by feeding experiments on rats, that pernicious anemia of pregnancy occurring in women of Bombay is due to a deficiency of vitamins A and C and possibly other vitamins. Although the topic is somewhat foreign to the discussion of polyneuritis, one might bring up the question of Addison's anemia as a possible avitaminosis.[14] Acrodynia has been regarded by Bayfield [15] and Patterson and Greenfield [16] as a deficiency polyneuritis. Orton and Bender,[17] however, suggested that in acrodynia and pellagra there is a secondary avitaminosis due to lack of absorption of food; that there is a specific selectivity of toxins or infections or food deficiency which leads to disturbances of the vegetative nervous system, and that there is a falling out of cells in the lateral horns of the spinal cord which belong to the sympathetic nerves.

Mellanby,[18] working with vitamin A, produced degeneration in the spinal cord and made a number of valuable observations. From his experiments showing that foods rich in vitamins could prevent degeneration of the cord by the ergot toxin, and that their absence increases the degenerative effect of the toxin, there arises the significant fact pertinent to this discussion, namely, that it is not alone the endotoxin or exotoxin which brings about involvement of the nerves, but that an additional factor, namely, avitaminosis, comes into play. He pointed out that there is widespread insufficiency of vitamin A in the general diet of highly organized communities, and that "it is important that it should be recog-

12. Hughes, J. S.; Lienhardt, H. F., and Aubel, C. E.: J. Nutrition **2**:183, 1929.

13. Wills, L., and Mehta, M. H.: Production of Pernicious Anemia in Rats by Deficiency Feeding, Brit. M. J. **1**:1167, 1930.

14. West, R.: Pernicious Anemia as a Deficiency Disease, Ann. Int. Med. **3**:132, 1929.

15. Bayfield, A. N.: A Polyneuritic Syndrome Resembling Pellagra-Acrodynia (?) Seen in Very Young Children, Am. J. Dis. Child. **20**:347 (Nov.) 1920.

16. Patterson, D., and Greenfield, J. S.: Erythredema Polyneuritis, Quart. J. Med. **17**:6, 1923.

17. Orton, S. T., and Bender, L.: Lesions in the Lateral Horns of the Spinal Cord in Acrodynia, Pellagra and Pernicious Anemia, Bull. Neurol. Inst., New York **1**:507 (Nov.) 1931.

18. Mellanby, Edward: The Experimental Production of Degeneration in the Spinal Cord, Brain **54**:247 (Sept.) 1931.

nized that the pathologic changes can often be produced by natural foodstuffs." Castle, quoted by Mellanby,[18] found degeneration in the cord and brain and of peripheral nerves in nine of fourteen cases in which animals were deprived of antineuritic vitamin B_1 and B_2. Mellanby further called attention to the fact that vitamin A is stored in the liver, but in varying amounts in different subjects.

It is of interest that the first case of polyneuritis and psychosis reported by Korsakoff[19] developed after pregnancy, and that similar cases have been described in puerperal septicemia, typhus, icterus and diabetes. That the syndrome occurs in chronic alcoholism is, of course, well known, but it is astonishing how many cases have been reported following pregnancy, and it is of extreme importance in connection with the views put forward in this paper that practically all instances of polyneuritis gravidarum were preceded by intractable vomiting and hence "starvation." Von Hösslin,[20] in an extensive article, reported hyperemesis gravidarum in cases of polyneuritis. Ely[21] cited the occurrence of memory defects of the Korsakoff type, together with polyneuritis, following toxemia of pregnancy. The patient vomited incessantly for six weeks, and neuritis developed two weeks after the uterus was emptied. Weill-Hallé and Layain[22] described a case which developed in a woman, aged 37, during the third month of pregnancy, following persistent vomiting. The patient recovered after delivery. Ledoux[23] reported the occurrence of polyneuritis during the third month of pregnancy in a woman, aged 20, who suffered from incessant vomiting. He stated that "mononeuritis is more common than polyneuritis" and mentioned involvement of the optic, sciatic, trigeminal and intercostal nerves. He cited Albeck,[24] who reported on eleven cases from the literature and an equal number of cases personally observed by him. Dupouy and Courtois,[25] who reported the occurrence of polyneuritis with mental symptoms in a pregnant woman, aged 39, following uncontrollable vomiting, pointed to hepatic insufficiency as a cause. They stated that Korsakoff's syndrome on the basis of pregnancy occurs more

19. Korsakoff, S.: Ztschr. f. Psychiat. **46**:475, 1890.

20. von Hösslin, Rudolph: Die Schwangerschaftlähmungen der Mütter, Arch. f. Psychiat. **40**:445, 1905.

21. Ely, Frank A.: J. Nerv. & Ment. Dis. **56**:115, 1922.

22. Weill-Hallé, B., and Layain, F.: Polynévrite et syndrome de Korsakoff aur cours de la gestation, Bull. et mém. Soc. méd. d. hôp. de Paris **51**:145 (Feb.) 1927.

23. Ledoux, E.: Polynévrite gravidique, Presse méd. **37**:516 (April 20) 1929.

24. Albeck, V.: Ueber Polyneuritis gravidarum, Arch. f. Gynäk. **117**:41, 1922.

25. Dupouy, R., and Courtois, A.: Des psychoses gravidiques et en particulier de la psychopolynévrite, Encéphale **25**:301 (April) 1930.

commonly in primiparas (so does toxemia of pregnancy), mainly between the ages of 20 and 30, and that the condition may set in either at the beginning or at the end of pregnancy.

Carmichael and Stern [26] stated that the "imbibition of alcohol lowers resistance and permits degeneration of the nervous system through the action of toxins or through lack of essential nutritive factors." As to the question of inflammation versus degeneration in alcoholism, they pointed to the occurrence of simple chromatolysis and parenchymatous changes, to the absence of neuronophagia and to the essential degenerative process in the peripheral nerves. Most patients also showed degeneration of the posterior columns. In view of the fact that lipochrome deposits are found in chronic alcoholism and pellagra, they suggested food deficiency as a common factor which permits the toxins to act on nerve cells. Winkelmann [27] stated that lipochrome deposit occurs only in pellagra. It is well known that pellagra is more likely to occur in alcoholic persons. Hassin [28] further stressed the degeneration of ectodermal tissue in lead neuritis, in which also the brain and cord take part, as against the proliferative and exudative changes in inflammation of the nerves. Sir Frederick Mott,[29] in describing the pathology of Korsakoff's disease, pointed out the wasting of the tangential fibers of the cortex, the presence of chromatolysis and the absence of Nissl granules and of infiltration of lymph and plasma cells. In fact, he stated that these changes are the same as those occurring in poisoning due to lead and arsenic. He made the interesting observation, which argues rather against the view set forth in this paper, that cirrhosis and ascites occur infrequently in both alcoholic psychosis and alcoholic polyneuritis. He expressed what seems to be a partially contradictory opinion that, because of the absence of cirrhosis, alcohol is a coefficient and not a direct cause of insanity; that the effects of alcohol depend on organic constitution, and that Korsakoff's syndrome may be the result of a metabolic disorder. Mott also pointed out the degenerative changes in the peripheral nerves, posterior roots, sensory ganglia and columns of the spinal cord, as against the absence of inflammatory reactions. Finally, Ohkuma [30] stressed the chronic progressive degenerative changes of the nervous system in alcoholism.

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26. Carmichael, E. A., and Stern, R. O.: Korsakoff's Syndrome, Brain **54**:189 (June) 1931.

27. Winkelmann: Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:38, 1926.

28. Hassin, G. B.: Lesions Produced by Lead vs. Encephalitis, Arch. Neurol. & Psychiat. **6**:268 (Sept.) 1921.

29. Mott, Frederick W.: The Nervous System in Chronic Alcoholism, Brit. M. J. **2**:1403 (Nov. 5) 1910.

30. Ohkuma, T.: Pathologic Anatomy of Chronic Alcoholism, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:94, 1930.

COMMENT

The more one ponders the problem of the etiology of polyneuritis, the more unsatisfactory appears the answer as to ultimate causes. So, too, the invocation of "toxic" or "infectious" factors in obscure cases in which no cause can be ascertained seems to be dubious if not entirely without foundation. Even in cases in which a specific poison is definitely incriminated, the question justly arises: Why does polyneuritis develop in some exposed persons and not in others? To say that it is a matter of constitution, of lack of resistance, of idiosyncrasy or an overwhelming toxin is ultimately to beg the question. The fact is that millions of people drink, a very large number of them consistently and to excess, and yet polyneuritis develops in only a comparatively small number. Thousands suffer from diabetes, untold numbers of patients receive medications containing arsenic and mercury and many persons are exposed to lead and other poisons, and only a small proportion of them have neuritis. It would seem, therefore, that the answer commonly given is not the ultimate or even the whole one, at least not in all cases, and that further investigation is necessary before the question of etiology can be finally settled. Without claiming to be able to solve the problem, an attempt will be made to correlate a few additional facts which may throw light on the etiology of polyneuritis.

The question of pathology, too, is not satisfactorily answered. It is not the object of this paper to raise anew the quarrel with the word neuritis as falsely descriptive of the pathologic process which it purports to describe. Attention has long ago been called to the fact that ectodermal tissue does not react by means of inflammation as does mesodermal tissue. Nor is the substitution of the word neuronitis any more satisfactory, certainly not for degenerative processes. Without cavilling at words, however, it is necessary to reemphasize that, with few exceptions, the substances which are presumed to cause neuritis actually do not cause inflammation. Alcohol, for instance, does not cause true inflammation of the nervous system, while lead gives rise to degenerative changes in the brain (encephalopathy) and spinal cord. It is legitimate, therefore, to ask: Why will a substance which leads to degeneration of the central nervous system bring about inflammation of the peripheral nerves if by chance it affects them? Diabetes, too, may give rise to degenerative changes in the spinal cord, in fact more commonly than involvement of the peripheral nerves. The diphtheria toxin certainly causes no inflammation, and the same may be said of mercury and arsenic. Therefore, the conclusion is justified that in nearly all cases one is dealing with a degenerative process. This may be of some significance in the correlation of degenerative changes resulting from

food deficiency with those occurring on the basis of other specific factors.

Bearing in mind both pellagra and beriberi, the question naturally arises whether those cases of polyneuritis in which no etiologic factor can be found actually belong to the one or the other disease. Aside from the fact that both conditions are rare in the city of New York, the cases under discussion do not bear a clinical resemblance to either beriberi or pellagra, and yet in most of those cases there was a history of vomiting, diarrhea, loss of appetite, emaciation or some hepatic disturbance. They may therefore be regarded as cases of food deficiencies or avitaminoses, even though they cannot be truly labeled as cases of beriberi. The important point, however, seems to be that the avitaminosis is due not so much to lack of ingestion of food, although that too is a factor, as to inability to digest, assimilate or metabolize because of disease which originally had nothing to do with avitaminosis. The case of polyneuritis which followed, first, excessive vomiting, and then gastrectomy for carcinoma, illustrates the point, and the other cases which were consequent on diarrhea and vomiting from other causes are equally significant. Cachexia polyneuritis probably belongs in this group, and acrodynia polyneuritis, too, may be mentioned in this connection. It is well known, of course, that avitaminosis causes loss of appetite, which in turn prevents ingestion of vitamins, thus establishing a vicious circle.

However, if gastro-intestinal and hepatic disturbances interfere with digestion and assimilation of food, and consequently also of foodstuffs containing vitamins, the absence of which bring about degeneration of the nerves, then the presence of such disturbances in cases of polyneuritis due to specific causes may be the ultimate factor in the production of degeneration of the nerves. This view is fortified by a number of observations. It is known that phosphorus, for instance, attacks the liver, and in severe poisoning will cause yellow atrophy. Arsenic corrodes the gastro-intestinal mucosa, and brings about anorexia, vomiting and diarrhea. That these changes do not occur in all cases does not invalidate the argument; the important point is that they can and do take place. Alcohol does even more. It attacks the gastric mucosa and the liver. Loss of appetite is extremely common, and vomiting is not rare. Many alcoholic persons do not eat, or if they do eat, do not digest, or if they digest, they do not assimilate. They are food starved and therefore are vitamin starved. So that one is dealing not only with a specific poison but with an additional avitaminosis. The cases herein reported illustrate this, and the view as to the genesis of the polyneuritis is fortified by the fact that the patients responded promptly when foods rich in vitamins were furnished, and they were made to eat.

It is of great significance that the patient with pregnancy polyneuritis observed by me and practically all of the patients whose cases have been recorded in the literature suffered with severe vomiting for weeks or months. It would seem that because of actual starvation these patients suffered from avitaminosis and consequent neuritis. It is also of interest that Korsakoff's syndrome occurs in pregnancy; in fact, the first syndrome so described was in a pregnant woman. In diabetes, too, one is dealing with a degenerative rather than an inflammatory process, and it is a question whether the peripheral nerves are involved. But what is perhaps more important is that diabetic persons are deprived for dietetic purposes of many of the foodstuffs which contain in large measure the vitamins necessary for the nervous system. So that here, too, the question of a food deficiency assumes considerable importance. Finally, it is of more than passing significance that in practically all cases, no matter from what cause, in which the gastric contents were examined free hydrochloric acid was either entirely absent or reduced almost to zero. Whether this fact can be correlated with the absence of free hydrochloric acid in pernicious anemia is difficult to say for want of more evidence. It is of importance, however, that various observers have recently expressed the opinion that food deficiency or avitaminosis may be one of the factors in pernicious anemia and one of the causes of the degenerative changes in the spinal cord.

From the meager evidence at hand it is impossible to express any definite opinion as to the nature of the food deficiencies in the cases herein reported and certainly none as to the specific vitamin involved. The evidence from the therapeutic tests merely confirms the view that the patients suffered from avitaminosis; that is, they began to show recovery when foods rich in many vitamins were given. From the extensive clinical and experimental researches recorded in the literature, the probability is that privation of vitamin B or B_2 (G) is the underlying cause of neuritis. However, recent experimental work, particularly that of Mellanby, has shown that absence of vitamin A may lead to degenerative changes in the spinal cord and also of the spinal roots and nerves. Therefore, until more clinical and experimental work can be carried out, one may have to be satisfied with the more general statement of vitamin deficiency in the cases of polyneuritis described in this paper, and in the treatment of such patients foods rich in all vitamins will have to be supplied until more specific knowledge has been gained.

CONCLUSIONS

While the facts presented in this paper do not justify any positive statements, they warrant a few tentative conclusions. 1. Many cases of polyneuritis of obscure origin are probably neither toxic nor infectious

in nature, at least not in the sense in which those two words are generally used, but more likely are deficiency syndromes. Even if, from their clinical appearances, they cannot be regarded as cases of beriberi or pellagra, they might still be grouped with the avitaminoses. This view is fortified in a given case if one can elicit a history of prolonged loss of appetite, diarrhea or vomiting, absence of free hydrochloric acid or other outright evidence of gastric, intestinal or hepatic disease. Sometimes the therapeutic test of giving foodstuffs rich in all vitamins or, if possible, administering special vitamins will serve to prove the point. It might be well to bear in mind that people sometimes deprive themselves of a foodstuff because of fads or fear of disease or on medical advice, and unknowingly suffer from avitaminosis, and that even regular diets, unless properly balanced, may be deficient qualitatively or quantitatively in antineuritic vitamins. Pregnancy polyneuritis, which is almost invariably preceded by severe vomiting and hence starvation, certainly belongs in this group.

2. In many cases of polyneuritis which have hitherto been regarded as due solely to a specific cause, such as alcohol, lead, arsenic or phosphorus, one finds an additional, possibly determining, factor in avitaminosis. This may be due to involvement of the gastro-intestinal tract or the liver, of which there is not infrequently clinical evidence. Such a view may serve to explain why polyneuritis develops in only certain patients, although all are exposed to the same poison. In any case, one is justified in giving foodstuffs rich in vitamins even if a specific cause can be found, and it need not interfere with the measures directed toward the elimination of the special cause.

3. The fact that the general pathologic changes are degenerative rather than inflammatory and are similar to the degenerative changes seen in avitaminoses furnishes pathologic evidence of some value. Furthermore, the fact that in lead and diabetic neuritis, for instance, the central nervous system degeneration is as important as peripheral degeneration, if not more so, adds another significant point, as does the argument that the poisons which are presumed to cause inflammation of the peripheral nerves actually cause degenerative changes if they affect the central nervous system.

4. While in beriberi and pellagra the antineuritic vitamins B_1 and B_2, or G, are involved, in some obscure cases and in some others in which the avitaminosis seems to play the decisive rôle, it may be that other or additional vitamins are concerned. No evidence has been presented to show which vitamin is involved in these cases, so that clinical and laboratory experimentation is necessary to furnish positive clues to the special deficiency factors. However, there is some experimental

evidence which proves that absence of vitamin A and, possibly also C and D, can lead to degenerative changes in the spinal cord, the roots and nerves, and that their presence will prevent degeneration by poisons which sometimes affect the nervous system. Conversely, it is possible, and this has been claimed by many observers, that in every case in which there is a deficiency of antineuritic vitamins there must be an additional toxin or poison to bring about degenerative changes. This leads to the assumption of a reversible process which may indeed serve as an explanation for the cases of neuritis of obscure etiology and for some of the others in which a specific poison is at fault.

MEASUREMENT OF ELECTRICAL SKIN RESISTANCE

MAURICE LEVINE, M.D.
CINCINNATI

One of the vital concepts of psychiatry is the emphasis on the functions of the personality as a whole. Such an emphasis involves a consideration of an integrated person—integrated from less complex functional units at lower levels—physicochemical, anatomic and physiologic. Such a concept makes imperative a study of the integrating forces, especially at the psychobiologic level and at the next lower level, the physiologic. In the integration of physiologic and psychobiologic functions, the activity of the central nervous system, of the vegetative nervous system and of the endocrine system is of major importance. The behavior and mentation of the individual as a whole make use of the functioning of these systems. It follows that a study of the activity of these systems is a necessary part of the understanding of the individual psychiatric patient, and consequently that adequate methods of examination of these systems are necessary.

Many a physiologic technic and measurement have been applied in the field of psychiatry with but indifferent success. Most of them—blood pressure, pulse rate, temperature, metabolic rate and chemical composition of the blood—are usually not easily influenced by psychobiologic changes, and certainly not so easily as is the quantity studied in the present work—the electrical skin resistance. The reason for this influence is not altogether clear, but apparently the wide range of variation in skin resistance and its close relationship to the vegetative nervous system make it a sensitive method of approach in psychobiologic studies. It may be that the skin resistance is an indicator of wide fluctuations which are not readily counterbalanced by compensatory physiologic mechanisms. Body temperature and pulse rate, for example, are the stable result of a large number of more primary fluctuations and compensations; apparently the skin resistance, on the other hand, is a measure of more primary fluctuations.

Recent work has shown that the measurement of the electrical skin resistance is one of the most sensitive methods of examination of the vegetative nervous system. The immediate change in skin resistance in states of emotion and the changes in sleep and in stupor are out-

From the Psychobiological Laboratory of the Phipps Psychiatric Clinic, Johns Hopkins Hospital, and the Department of Psychiatry, University of Cincinnati.

standing examples. In part, also, it may throw light on the state of affairs in the central nervous system and in the endocrine system, e. g., in narcolepsy and in hyperthyroidism.

It is futile to adopt a perfectionistic attitude toward such a sensitive method. So many factors are involved that a perfect technic and interpretation of results are obviously matters for the future. But the possibilities of help from such a sensitive measurement make necessary an attempt to standardize the procedure as much as possible, to make it clinically applicable under fairly controlled conditions and to remove the major sources of error. The work reported in the present paper is such an attempt.

In the mass of material on the electrical reactions of the skin, two facts stand out: first, that the theoretical physics of the reactions is not known with any degree of exactness, and second, that a study of the electrical reactions of the skin offers clinical methods and facts of definite, if as yet uncertain, significance. For the experimenter with a clinical bias, the practical approach is to use the method for what light it can give on clinical phenomena without expecting a perfect explanation of the exact physics and physiology involved. On the other hand, the clinical phenomena studied may throw light on the physics and physiology of the reactions. It is obvious that the clinical study must be such that errors are eliminated as far as possible, and the method must be brought to a degree of uniformity to insure the comparability of records taken under different conditions.

The term "electrical skin resistance" is applied to the apparent resistance offered by the body to the passage of an electrical current. The term "electrical skin resistance" is used in preference to "electrical body resistance" because it has been shown that the resistance is localized almost entirely in the skin itself; puncture of the skin beneath the electrodes reduces the resistance almost to zero (Richter[1]). It may be that polarization and counterelectromotive force phenomena play a rôle in the production of the phenomenon that is called skin resistance. With that problem I am not concerned here. No matter what the fundamental electrophysical explanation may be, there is a standard technic for measuring a quantity which, it would seem, remains the same, uninfluenced by a standard process of measurement, but varying with the psychobiologic and physiologic condition of the subject examined. Even if one is not perfectly certain of the kind of thing being measured (whether it is actual resistance, polarization or counter electromotive force), one is relatively certain that one is making quantitative measurements which can be correlated with certain psycho-

1. Richter, C. P.: Proc. Nat. Acad. Sc. **12**:214 (March) 1926.

biologic and physiologic facts, and which can be used as a method of attack in the study of such facts.

Attention should be called to the fact that the present studies are essentially concerned with the electrical skin resistance, rather than with the galvanic skin reflex ("psychogalvanic"). Electrical skin resistance is the term applied to the apparent quantity of resistance offered to the passage of a direct electrical current applied to the skin. The apparent skin resistance usually remains grossly constant from minute to minute. Small fluctuations are called "spontaneous galvanic waves"; when the fluctuations occur immediately after an external stimulus (from one to four seconds), they are called "galvanic skin responses," "psychogalvanic reflexes" or Fère phenomena. (Even without the passage of an external current, apparently corresponding changes in the potential of skin areas take place in response to stimuli. These are the so-called Tarchanoff phenomena, and to them also the term psychogalvanic reflex is sometimes applied). A great deal of work has been done on the psychogalvanic reflex, and apparently the net result for psychiatry is that occasionally a study of galvanic responses to word stimuli will reveal areas of excessive sensitivity in the personality make-up. Further, the amount and type of responsiveness in general may have some correlation with the patient's general condition. It is unfortunately true, however, that for clinical psychiatry these facts have had only a limited significance. It has seemed advisable, therefore, to attack the problem of the grossly constant skin resistance level, rather than that of its minor fluctuations (the psychogalvanic reflex), for several reasons: (1) The facts established about the skin resistance level seem more definite and more constant; (2) the psychogalvanic reflexes seem to be dependent in part on, and to be modified by, the level of the skin resistance on which the psychogalvanic is superimposed. (For example, the galvanic skin reflexes in the cat are diminished or absent when the skin resistance is high—Levine and Wolff.[2])

A NEW PORTABLE DERMOHMETER

Up to the present time, investigation of the skin resistance has been limited by the fact that no adequate method was available for studying the skin resistance under basal conditions. The promising fact appears, however, that even under partly uncontrollable conditions some important results have been obtained. The limitations involved in such studies were in part based on the fact that the apparatus was not portable, so that the patient was brought to the laboratory for examination, with the possibility ever present of having the results

2. Levine, Maurice, and Wolff, H. G.: Cerebral Circulation: Afferent Impulses from the Blood Vessels of the Pia, Arch. Neurol. & Psychiat. **28**:140 (July) 1932.

vitiated by changes in skin resistance which result from variable responses to variable conditions of activity, new surroundings and previous activities. In short, a portable apparatus offers the possibility of eliminating at least some of the uncontrollable variables. Portability of apparatus makes possible also the study of patients who are physically too weak or too sick to come to the laboratory and of those whose condition makes it unwise or unsafe for them or for others to have them leave the ward.

Several portable arrangements have been devised for the study of the galvanic skin reflex, but so far as the literature reveals, no satisfactory portable apparatus has been devised for the study of skin resistance. In the types of apparatus planned primarily for psychogalvanic reflex studies the arrangement fails to meet the desired conditions for measurement of the skin resistance level: (1) by using alternating instead of direct current (as in the Hathaway apparatus), thereby getting results which show little difference from person to person, differences which apparently are evident only when direct current is used; (2) by using the finger tips for the skin areas studied, thereby ignoring the tremendous difference in skin resistance between areas rich in sweat glands (palms and soles) and other areas (e. g., the dorsal surface of the hands and feet), and (3) by using the Wheatstone bridge arrangement, which complicates the apparatus unnecessarily and does not provide a wide enough range of measurement.

The principle of the present apparatus is simple. A direct current of known amperage (2 micro-amperes) is passed through the body, and the voltage necessary to produce the passage of such an amperage is measured. By Ohm's law, the voltage measurement is translated into terms of ohms. Since the same amperage is used on all subjects, the voltage necessary to send through this amperage depends entirely on the resistance offered by the body of the subject (and the electrical connections). The quantity of 2 micro-amperes was chosen because that quantity does not have a direct effect on the skin itself and does not change the skin resistance (see later).

The present apparatus consists of two galvanometers (pattern L, Unipivot, Cambridge Instrument Company), a potentiometer controlled by coarse and fine adjusting knobs, a storage battery of 9 volts and a selector switch by which connections are made to the four areas of skin studied. One galvanometer is used as an ammeter, and is calibrated in micro-amperes; when the resistance reading is taken, the potentiometer knobs are rotated until the ammeter indicates the passage of 2 micro-amperes. The other galvanometer is used as a voltmeter; when the ammeter needle indicates the passage of 2 micro-amperes, the voltmeter needle indicates the voltage necessary to send through this amperage. From the indicated amperage and the indicated voltage the resistance in ohms can be calculated directly. Since all measurements are taken with the same amperage, this calculation can be done beforehand for all voltages; hence the voltmeter indicator in the present apparatus is calibrated in ohms, rather than in volts, and the resistance

is read directly. A special range switch is attached to the voltmeter to make more exact readings possible in the lower ranges. At the lowest range, readings are made from 0 to 50,000 ohms, at the second range from 0 to 500,000 ohms and at the third range from 0 to 5,000,000 ohms. Resistances higher than 5,000,000 ohms can be made by using an amperage of 1 micro-ampere instead of 2 micro-amperes and multiplying the resistance reading by 2.

The electrical resistance of the apparatus proper is less than 800 ohms. The resistance of the apparatus plus the electrodes and connections has never been found to be more than 1,000 ohms. Such a resistance is small enough to be a negligible quantity in comparison with the range of readings from 10,000 to 5,000,000 ohms. The resistance of the circuit remains constant, and any defect in the wire or electrodes which might change the resistance is easily discovered

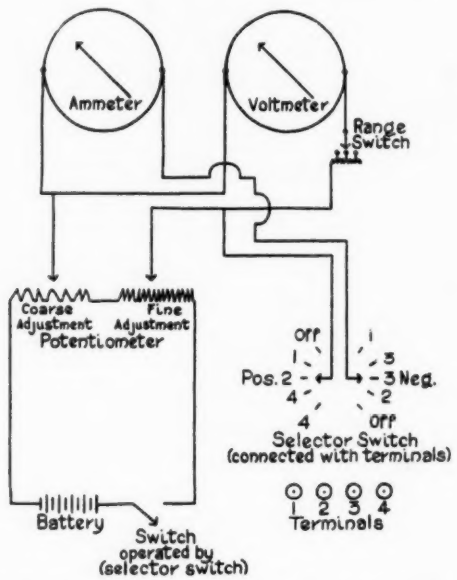

Fig. 1.—Wiring diagram of the dermohmeter, the apparatus used in the measurement of the electrical skin resistance.

by checking the apparatus against a resistance box of known standard values (to be described).

In the apparatus the wires leading from the galvanometer—potentiometer—battery set-up are connected with a selector switch. This switch contains four positive and four negative terminals, so that measurements may be taken in sequence from four connections: (1) from the back of the right hand to the palm of the right hand, (2) from the back to the palm of the left hand, (3) from the back of the right hand to the back of the left hand and (4) from the palm of the right hand to the palm of the left hand. The wires from the selector switch are connected with four terminals to which the electrodes are connected.

The term dermohmeter is used to describe the present apparatus, which consists of a voltmeter and range switch, ammeter, potentiometer, battery, selector switch and terminals, mounted in a carrying case. The size and weight of the dermohmeter are approximately those of a portable typewriter. (The apparatus was assembled by the Cambridge Instrument Company, Ossining, N. Y.)

The procedure followed in the use of the apparatus involves the following steps:

1. The dermohmeter, mounted on a table supplied with rubber-tired wheels, is brought to the patient's bedside with a minimum of noise and disturbance, and is placed, so far as possible, out of range of the patient's line of vision.

2. The palmar and dorsal surfaces of the hands are washed lightly with alcohol.

3. The electrode stands are placed on the bed, one on each side of the patient; his hands are placed on the stands, and the movable rubber-covered clamps are adjusted against the wrists and finger tips to keep the hands in comfortably supported positions.

4. The surfaces of the zinc electrodes are wiped off and rubbed with a cloth until the zinc-mercury amalgam surface glistens.

5. The surface of the zinc electrodes is covered with a paste of kaolin mixed with saturated zinc sulphate.

6. The handles of the electrodes are placed in the electrode posts on the electrode stands in such a position that the electrode paste makes a smooth, moderately firm contact with the areas of skin to be studied.

7. The four wires leading from the electrode stands are attached to the terminals on the dermohmeter.

8. The clamping devices on the galvanometers are unlocked, permitting the indicators to come to equilibrium at or near the zero points. (The selector switch is "off," so that the patient is not in series with the dermohmeter.) If the galvanometers at this point are not at the zero points, the galvanometer screws are rotated to bring the indicators to zero.

9. The selector switch is then turned to the desired connection (e.g., right palm to left palm). Usually at this point there is a small deflection of the ammeter indicator, owing probably to a difference in potential of the areas of skin studied. (This small deflection is independent of the electrodes used.) If there is a large deflection, the connections are checked, or a new set of electrodes is attached.

10. The knobs controlling the potentiometer adjustment are now rotated from their previous zero position (thus sending an increasing current through the apparatus and the patient) until the ammeter indicator has moved two large scale divisions to the right, indicating the passage of a current of 2 microamperes. The voltmeter indicator has moved to the right also, during this step, and if it goes off the scale the range switch is adjusted to provide for a shorter deflection to correspond with the voltage used.

11. The reading of the voltmeter (calibrated in ohms) is multiplied by the factor (1, 10 or 100) of the range switch used, to give the skin resistance of the patient in ohms.

Steps 9, 10 and 11 are then repeated for each of the other three connections desired, i. e., right back to left back, right palm to right back and left palm to left back. After the measurements have been taken, the galvanometers are clamped, the hands are removed from the electrode stands, and the paste is cleaned off with water.

PORTABLE ELECTRODE STANDS

A modification of the electrode stands devised by Richter [3] was used. Figure 3 indicates their construction and use. They differ from his stands in

3. Richter, C. P.: Brain **50**:216 (June) 1927.

their portability. Each consists of a wood base 10 inches (25.4 cm.) by 6 inches (15.2 cm.), on which are fastened four adjustable upright bars (covered by soft rubber pads), which serve to hold the hands in position. In addition, on the wood base are fastened brass connecting posts into which the handles of the electrodes are fitted when measurements are made. These connecting posts are attached to binding posts for the wires leading to the dermohmeter.

The electrode stands are sufficiently light in weight so that they may be placed on the bed, beside the patient, when records are taken on recumbent patients, or they may be placed on a table in front of the patient (or even held in his lap) when records are taken with the patient in the sitting position. They are

Fig. 2.—The dermohmeter, portable skin temperature apparatus, electrodes, electrode stands, paste and wet and dry bulb thermometers mounted on the carriage at the bedside.

sufficiently comfortable so that the patients may relax completely, with the hands in position in the electrode stands.

Similar electrode stands were constructed for the measurement of the skin resistance of the feet (especially in the study of the effects of lumbar sympathectomy). With these stands, records may be taken with the patient lying comfortably in bed. The areas of skin studied corresponded to the areas of the hand studied, the dorsal surface halfway between the ankle and toes, and the sole halfway between the heel and toes.

Emphasis should be placed on the fact that these electrode stands afford opportunity for the study of independent variations in the dorsal and palmar skin resistance. It is imperative that these surfaces be

studied independently. The methods which ignore this fact—(1) the frequently used method of studying the resistance of the finger tips, (2) the method of studying the combined resistance of palmar and dorsal surfaces and (3) the method of studying the combined resistance of the palmar and arm surface (Peterson and Levinson [4])—are subject to a serious source of error and must fail to discover important differences. My results have made it clear beyond question that the resistances of these areas vary independently, and that there may be, e. g., in narcolepsy, an increase in the palmar skin resistance with a decrease in the dorsal skin resistance. If these areas were not measured independently the increase of the palmar skin resistance might equal the decrease of the dorsal skin resistance, and the sum of the palmar and

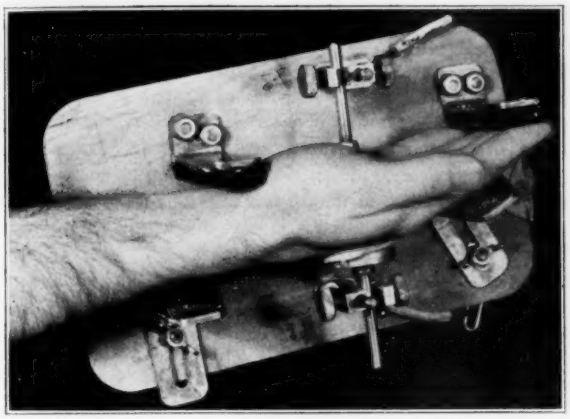

Fig. 3.—The electrode stand, with the electrodes in place against the hand, which is held in place by rubber-covered supporting posts.

dorsal resistances might be the same at the end of the period as at the beginning. In this way, the important fact of the increase of palmar skin resistance during relaxation in narcolepsy might never have been discovered.

A further example of the great importance of measuring palmar and dorsal surfaces independently is this: If one is studying the skin resistance of patients showing a stupor reaction, one might find little difference in the skin resistance of a patient in a depressive stupor from that of a patient in a catatonic stupor. But if one studies the palmar and dorsal surfaces independently, one finds definite differences. A

4. Peterson, W. F., and Levinson, S. A.: The Skin Reactions, Blood Chemistry and Physical Status of "Normal" Men and of Clinical Patients, Arch. Path. 9:151 (Jan.) 1930.

patient in a depressive stupor and one in a catatonic stupor may both show a skin resistance of 500,000 ohms for each hand (i. e., 1,000,000 ohms resistance for the four surfaces of the two hands), and yet may be fundamentally different in skin resistance. In the case of depressive stupor, the palmar resistance may be 600,000 ohms and the dorsal resistance 400,000 ohms, a total of 1,000,000 ohms for the four surfaces; in a catatonic stupor the palmar resistance may be 20,000 ohms and the dorsal resistance 980,000 ohms (again a total of 1,000,000 ohms for the four surfaces). This method permits the important generalization about stupor, that in depressive stupor the palmar resistance is usually high, and in catatonic stupor the dorsal resistance is usually high and the palmar resistance low.

RELATIVELY NONPOLARIZABLE ELECTRODES

The literature is full of descriptions of electrodes and their limitations. It was found in the present work that errors resulting from these difficulties were of two kinds: (*a*) gross errors which could be recognized quickly and overcome easily and (*b*) small errors which provided only negligible sources of error. The electrodes used were circular zinc disks 1¼ inches (3.1 cm.) in diameter and ¼ inch (0.64 cm.) in thickness, attached to brass rods. The contact with the skin was made by means of a paste of kaolin mixed with saturated zinc sulphate. The gross errors appeared when the brass rod was not connected tightly enough with the zinc disk, or when the surface of the zinc was tarnished. Such errors were apparent as soon as the electrodes were applied to the skin, because they produced an immediate large deflection of the ammeter indicator, owing to a battery effect. This provided an immediate warning of a defect in the apparatus, before measurements were taken. The possibility of a variable and uncontrollable error arising from battery effects set up through impurities on the surface of the zinc was avoided in all electrodes (1) by using pure zinc, (2) by scraping the surface clean and (3) by covering the surface of the zinc with a zinc-mercury amalgam, formed by dipping the zinc disk in mercuric chloride and then rubbing it on pure mercury until the surface was covered by a mirror-like glistening surface of the zinc-mercury amalgam. This process was repeated at intervals of about a week. When the electrodes were treated in this way, large resting currents due to battery effects from the electrodes rarely occurred, and when they did, the electrode was discarded temporarily until its surface could be scraped off and a new coating of amalgam applied. The minor errors which were still present were found to be negligible, i. e., to produce an apparent increase or decrease in resistance of only from a few to a few hundred ohms. Repeated experiments were performed on this point, and it was found that the skin resistance measurement was approximately unchanged when the electrodes were removed and a different pair used. It was found repeatedly, for example, that if one set of four electrodes gave a palmar resistance reading of 50,000 ohms and a dorsal resistance reading of 400,000 ohms, the electrodes attached to the backs of the hands could be substituted for the electrodes attached to the palms of the hands, and the resistance would still be approximately 50,000 ohms palmar, and 400,000 ohms dorsal (with perhaps a change of 1,000 or 2,000 ohms, which is within the range of skin resistance changes that occur spontaneously in a few minutes without changing the electrodes). Repeated experiments demonstrated also that the entire set of four electrodes could

be removed and four new ones used without more than a negligible change in the resistance readings.

It was found, further, that it was practically impossible to polarize the electrodes with the amount of current used. In order to test the polarizability of the electrodes, the apparatus was set up exactly as if the skin resistance of a patient was to be measured. Instead of placing the paste on the electrodes against the skin of the patient, however, the electrodes were moved together, so that the paste on their surfaces was continuous. When this contact was made, the ammeter indicator showed a very small deflection, apparently due to a battery effect from zinc and its inevitable slight impurities. The resistance of the apparatus and the electrodes was then measured, and usually approximated from 500 to 1,000 ohms. The current sent through the circuit was then increased until not only 2 micro-amperes but 10 micro-amperes (with the corresponding increase in voltage) were sent through. Repeated experiments were performed in which such currents were sent through the circuit for from two minutes to sixty minutes. At the end of that period the current was reduced to zero. It was found that the battery effect had not changed in any case more than one small division of the scale. The resistance of the circuit was again measured, and in no case was it found to have changed more than 100 ohms. In short, it was found that currents far greater than those involved in the usual measurements of the subject's skin resistance failed to produce any but negligible changes in polarization or resistance of the apparatus or electrodes.

A CONSTANT RESISTANCE BOX FOR THE CALIBRATION OF THE DERMOHMETER

Until the present, no adequate method has been used for the calibration of the apparatus used in the measurement of the electrical skin resistance. Obviously such a method is essential, since it is imperative to know whether changes found from day to day or from week to week in the skin resistance are due to actual changes in the skin or to changes in the apparatus used for the measurement.

The required calibration of the apparatus was made possible by the use of a resistance box containing known resistance coils varying from 1,000 ohms to 10,000,000 ohms. Such a resistance box provides a nonfluctuating, almost absolutely constant known resistance. The procedure of calibration is to connect the dermohmeter to the resistance box instead of to the patient. The resistance box is set to provide a certain known resistance for the circuit; 2 micro-amperes of current are sent through this resistance (as in measuring the unknown resistance of a patient) and the resistance indicated by the dermohmeter is recorded. If the dermohmeter is accurate, the known resistance of the resistance box plus the approximately known resistance of the dermohmeter parts (about 800 ohms) should equal the resistance reading obtained from the dermohmeter.

THE EFFECT OF CLEANING THE SKIN WITH ALCOHOL

In order to remove any grease or oil on the areas of skin studied, the skin is lightly washed with alcohol as a routine procedure. Heavy rubbing is avoided, since occasionally such rubbing lowers the skin resistance, especially of the backs of the hands. A number of experiments were performed to determine whether the application of the alcohol itself might change the skin resistance, on the supposition

that such application might directly affect the temperature of the skin, the circulation in cutaneous vessels or the permeability of the epithelial cells.

The first series of experiments to determine the effect of washing the skin with alcohol was performed on eleven patients. Each patient was examined on two days, while lying comfortably relaxed in bed. On the first day, both hands were washed with alcohol, and two or three minutes later the skin resistance was measured; on the second day, only the right hand was washed with alcohol and the left was not washed, and again after two or three minutes the skin resistance was measured. The comparison of the ratio of skin resistance of the two hands on the first day with the ratio of the skin resistance of the two hands on the second day would indicate the presence or absence of a change due to washing with alcohol. In the present experiments, the conditions on the second day were in some cases slightly different from the conditions on the first day; the body temperature, room temperature and time of day were not exactly the same on the two days, but none of these factors supposedly affects one hand more than the other. The only difference between the conditions of the two days that might affect one hand without affecting the other was that on the first day both hands were washed with alcohol and on the second day only one hand was washed with alcohol. Hence any difference in the ratio between the right and left hands might be considered to be due to the effect of washing with alcohol, if the effect is constantly in one direction, or to internal, as yet unexplained, variables, if the changes are not in the same direction.

It was found that the ratio of the skin resistance of one hand to the skin resistance of the other hand changed from the first day to the second day (as it almost always does from day to day even when all conditions are apparently unchanged). There was no evidence, however, that this change was in one direction. In five cases, the ratio of the right hand to the left hand was increased; in six cases, it was decreased. In the five cases in which the ratio increased, the average increase was 1.01, with a variation from 0.07 to 2.49. In the six cases in which the ratio decreased the average decrease was 0.89, with a variation from 0.03 to 2.23. From these results, the conclusion is justified that washing the skin with alcohol produces no effect on the electrical skin resistance. The procedure is worth retaining, however, as a means of obviating sources of error that might result from an accumulation on the skin of a large amount of oil, grease or dirt.

The problem of the effect of washing with alcohol on the skin resistance was approached in another way. Both hands were washed with alcohol and the skin resistance taken several times. Then one hand was removed from contact with the electrodes and again washed with alcohol, the other hand remaining in contact with the electrode. Measurements of the skin resistance of the two hands were then made, to determine whether the second washing with alcohol had changed the skin resistance. Twenty-one experiments were performed in this way, and in none did the washing with alcohol produce any change of importance. Occasionally, there was a slight change of the resistance of the rewashed skin, and occasionally a slight change of the resistance of the other hand. In no case did the change make any material difference in the ratio of the resistance of the two hands or in the height of the resistance level. Charts of two of these experiments are reproduced in figures 4 and 5.

THE EFFECT OF THE PASSAGE OF THE CURRENT

It is well known that the passage through the skin of an electrical current of large magnitude lowers the electrical skin resistance

(Richter [5] and Wechsler [6]). This fact affords the possibility of a large source of error, since the technic of the measurement of the electrical skin resistance is based on the passage of an electrical current through the skin. It is therefore of prime importance to use an electrical current small enough to avoid this major source of error. We have found that the current used with the present apparatus is never of sufficient magnitude to change the skin resistance. In some patients

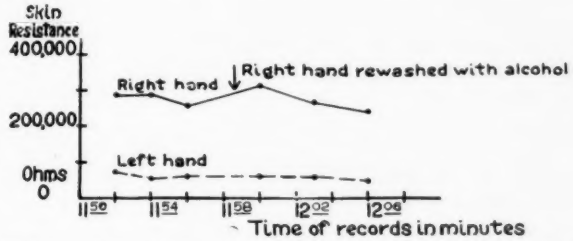

Fig. 4.—Effect of washing with alcohol. In this figure and figure 5, the ordinates indicate the skin resistance of each hand, in ohms. The abscissae indicate the time of the record in minutes. One hand was rewashed with alcohol at the time indicated by the arrow.

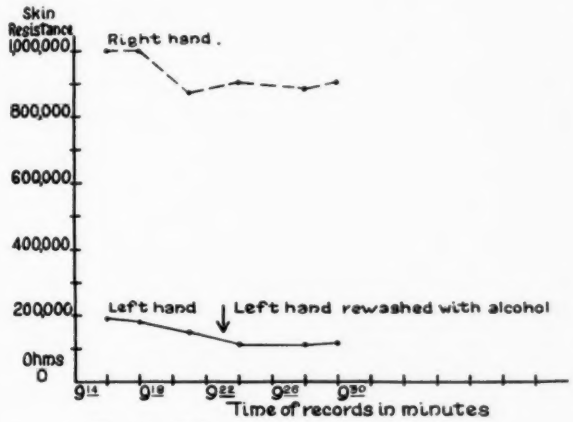

Fig. 5.—Effect of washing with alcohol.

on whom continuous records were taken over a long period of time, involving the repeated passage of the current, the resistance at the end of the period was approximately the same as at the beginning of the period. In other patients, the resistance was lower at the end of the period than at the beginning. In still other patients, the resistance was higher at the end of the period than at the beginning. It is obvious from this that the constant factor of the passage of the current does not affect the skin resistance.

5. Richter, C. P.: Am. J. Physiol. **88**:596 (May) 1929.
6. Wechsler: Arch. Psychol. **76**:48, 1925.

To make more certain of this point, however, a series of experiments was performed in which the apparatus current was passed through one hand repeatedly, the other hand being used as a control.

Two of the accompanying charts (figs. 6 and 7) demonstrate the results of such experiments. The skin resistance of both hands was measured, then repeated measurements of one hand were made (indicated by the large dots), during which the usual current was passed through that hand. Then the resistance of both hands was measured again. The charts show definitely that the passage of the

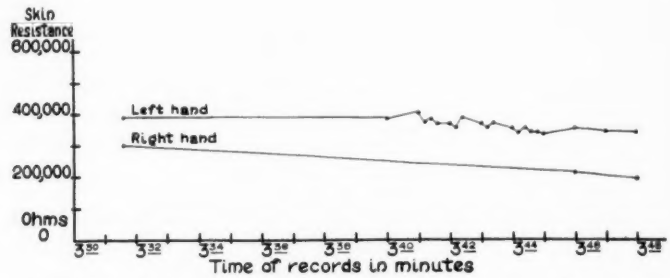

Fig. 6.—Effect of the passage of the apparatus current. In this figure and figure 7, the ordinates indicate the skin resistance of each hand, in ohms. The abscissae indicate the time of the record in minutes. The dots indicate the passage of a current of 2 micro-amperes.

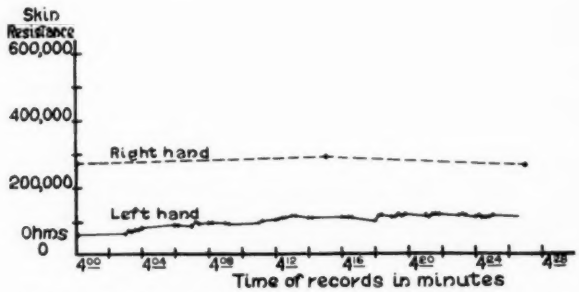

Fig. 7.—Effect of the passage of the apparatus current.

electrical current of the magnitude used in the present work does not change the electrical skin resistance.

THE EFFECT OF CONTACT WITH THE PASTE

A further source of error might be expected in the direct effect of the paste (of kaolin and zinc sulphate) on the skin. One might expect that the paste, soaking the skin, might lower its resistance, or that the paste might provide stimuli which could produce changes. But again the fact that after long periods of contact with the paste, the resistance may, in different patients, remain the same, may increase or may decrease, offers strong evidence against the idea that the paste itself can change the skin resistance.

Just as with the problem of the passage of the current, this issue was settled by a series of experiments in which the resistance of the two hands was measured,

then one hand was kept in contact with the paste and the other hand, as a control, was removed from contact with the paste. After a varying period of time, the resistance of the two hands was measured again. It was found repeatedly that the contact with the paste produced almost no change in the skin resistance.

THE EFFECT OF THE CONSISTENCY OF THE PASTE

Another source of error might be expected to lie in the consistency of the paste. Landis,[7] in his criticism of the work of Richter [1] on the skin resistance during sleep, implied that the drying of the paste during sleep may explain the changes found during sleep. Such an objection is not justified, since the changes take place in the reverse direction when the patient awakes, with the same paste still in use. Undoubtedly, in the mixing of the paste fairly large variations in consistency occur. The standard of consistency used is that the mixture be sufficiently coherent so that it does not flow and that it be sufficiently soft to be stirred with a spoon.

The problem was attacked experimentally by using paste of different consistencies in the measurement of the skin resistance of the same subject. The skin resistance was measured, using paste of the same consistency for both hands; then the electrodes were removed from one hand and the paste replaced by paste of a different consistency (in some experiments of thicker, and in some of thinner, consistency). Results similar to those shown in the charts on the effect of washing with alcohol, were obtained. In no case did the change in the consistency of the paste produce an alteration greater than the minor fluctuations in skin resistance observed without changing the consistency of the paste.

THE EFFECT OF THE TEMPERATURE OF THE ELECTRODE PASTE

In the use of the present apparatus and its connections, it has been evident that the temperature of the paste had little or no effect on the electrical skin resistance, in contradistinction to the findings of Westburgh,[8] who found that changes in the temperature of his electrodes modified the resistance. It is to be noted, however, that in his work the contact between electrode and skin is made by a solution, not by a paste as in these experiments, and further that in his experiments the skin of the tips of the fingers was used, rather than the skin of the palms and backs of the hands. These differences may account for his observation of a source of difficulty which was not found in the present arrangement.

My observation is that the temperature of the paste does not alter the electrical skin resistance except when the paste is very cold or very warm, perhaps enough to produce a systemic effect, with a change in the temperature-regulating mechanism.

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7. Landis, E. M.: Am. J. Physiol. **81**:124 (June) 1927.

8. Westburgh, E. M.: Psychogalvanic Studies of Normal and of Abnormal Subjects: For the Purpose of Determining the Reliability of the Galvanometer in Investigating the Emotions, Arch. Neurol. & Psychiat. **22**:453 (Sept.) 1929.

Certainly when the temperature of the paste is between the limits of 18 and 34 C., the temperature of the paste does not influence the electrical skin resistance. When the temperature of the paste is beyond those limits, an occasional slight effect is observable. Furthermore, even when the temperature of the paste is as low as 1 or 2 C., little effect is to be found. High temperatures of the paste (above 40 C.) change the skin resistance occasionally.

SUMMARY

1. A new apparatus, the dermohmeter, for the measurement of the electrical skin resistance is described.

2. The apparatus is portable; its use eliminates previously uncontrolled factors and permits the examination of a wider range of patients.

3. Portable stands for the support of the hands and feet and of the electrodes applied to the skin are described.

4. The necessity of independent determinations of the resistance of the skin of palmar and dorsal surfaces is emphasized.

5. Electrodes made of zinc disks coated with zinc-mercury amalgam and covered with a paste of kaolin and saturated zinc sulphate solution are relatively nonpolarizable and provide only negligible sources of error.

6. A constant resistance box is used for the calibration of the dermohmeter.

7. The electrical resistance of the skin is not materially altered by the procedure used in its determination: (*a*) the application of alcohol to the skin; (*b*) the passage of the current; (*c*) contact with the electrode paste, and (*d*) the consistency and temperature of the electrode paste.

SYNDROME OF THE FIBRILLARY ASTROCYTOMAS OF THE TEMPORAL LOBE

BENNO SCHLESINGER, M.D.
VIENNA, AUSTRIA

Among the gliomas of the temporal lobe a particular type of tumor has been encountered at operation. The tumors have usually been described as deep-seated, grayish and of firm consistency. Histologically they have proved to be fibrillary astrocytomas. These tumors have no definite demarcation from the adjacent nerve tissue and, in this respect, differ markedly from the cerebellar astrocytomas, which are fairly well demarcated and separable from the nerve tissue of their vicinity. At Dr. Cushing's suggestion a tabulation and investigation of these cases were made in order to determine whether their clinical symptomatology was not sufficiently characteristic to justify a preoperative histopathologic diagnosis.

The incidence of these tumors was comparatively small among a large series of gliomas of the temporal lobe. Only eleven cases were classified as fibrillary astrocytomas. The description of the growths is based on Dr. Cushing's operative notes and drawings. Although the majority of the patients died—the average survival period being approximately one year—no autopsy could be obtained. At operation, the sylvian fissure was found to be pushed upward, and the gyri of the temporal lobe were widened and flattened. No trace of tumor could be seen on the surface, and the growth, in most instances, was not disclosed until the electrosurgical incision was carried down to a considerable depth. During the further operative procedure, the temporal lobe was uncapped, the tumor, as a rule, was removed as radically as possible, and a cavity as big as a hen's egg was cleaned out. The inferior horn of the lateral ventricle was usually opened, and the edge of the tentorium and the region of the gasserian ganglion were frequently exposed. In some instances the impression was gained that the growth extended below the inferior furrow of the insula reili into the brain stem, but there was, as a rule, no suggestion of any appreciable degree of invasion of the adjacent parts of the hemispheres, and especially no indication of an extension into the frontal lobe. These operative findings were consistent with the ventriculograms, which showed the inferior horn obliterated and the third ventricle pushed well over the midline.

Presented before the Society of Neurological Surgeons, Boston, June 2, 1932.

CLINICAL FEATURES

The syndrome to be described was produced by solid fibrillary astrocytomas, which occupied the deeper part of the temporal lobe.

A few of these symptoms deserve special consideration.

Hemisyndrome and Lower Facial Weakness.—This was represented by a hemiparesis or monoparesis, hemihypesthesia or monohypesthesia, exaggeration of the deep or loss of the superficial reflexes and the presence of pathologic reflexes, several or all of these findings being present on the side opposite the tumor. One case showed, in addition to disturbances of cutaneous sensibility, impairment of deep sensibility and hypostereognosis. There was a bilateral exaggeration of the deep reflexes in six cases, but weakness and hypesthesia were always

Symptoms in the Eleven Cases

Symptoms	No. of Cases in Which Found	
Hemisyndrome	11	
Lower facial weakness	11	
Mental deterioration	11	
Epileptic attacks	10	
Choked disk	10	
Aphasia	6	(of 7)
Headaches	9	
Failing vision	7	
Anisocoria	7	
Homonymous field defects	7	(of 8 examined)
Cerebellar signs	4	
Hallucinations of taste and smell	4	
Diplopia	3	
Auditory symptoms	2	
Sixth nerve palsy	1	
Stiffness of neck	1	
Dysphagia	1	
Apraxia	1	
Limitation of ocular movements upward	1	

restricted to the side opposite the lesion. The most striking feature of the hemisyndrome was the weakness of the lower part of the face, evidence of which was frequently detected only or especially by involuntary movements.

Mental Deterioration.—Mental disturbances were observed in every instance, though at the time of admission to the hospital some of the patients showed only slight mental impairment, even though the neurologic features of the case were fully developed. The mental symptoms began, as a rule, with an impairment of memory for recent events, difficulty in concentration and easy fatigability. When the changes were more advanced, the patients showed a complete lack of interest and a considerable degree of mental dulness. A few of them still had some insight into their own mental condition; others, however, showed want of judgment or were more or less euphoric. A third group of patients was semistuporous, confused and disoriented as to time, place and person. This general deterioration of intellect, no matter how far

advanced, was in some cases preceded, accompanied or followed by emotional disturbances and by changes in personality.

Epileptic Attacks.—Nearly all kinds of epileptic and epileptiform attacks have been recorded. The patient in case 1 had grand and petit mal attacks; the one in case 2, grand mal attacks of focal type; the one in case 3, petit mal attacks; the one in case 4, sensory jacksonian seizures; the one in case 5, uncinate attacks; the one in case 6, grand mal attacks of focal type; the patients in cases 7 and 8, grand mal attacks pointing to the right side; the patient in case 9, grand and petit mal attacks, and the one in case 10, sensory jacksonian attacks and grand and petit mal seizures. The petit mal and jacksonian seizures occurred in many cases with a striking frequency, many attacks a day being not unusual. They were, as a rule, not immediately followed by transitory or permanent motor disturbances.

Choked Disk.—In one instance there was no choked disk at the time of the first admission of the patient; in another case, the fundi were reported to be probably within normal limits; in a third case, there was only a slight, hardly appreciable elevation on both sides, but it was distinctly more outspoken on the side opposite the lesion. In the remaining cases, there was an elevation between 1 and 4 diopters, in three of which it was more marked on the side of the lesion.

All cases in which pupillary disturbances were observed showed anisocoria, the pupil being enlarged on the side of the lesion in one case, and on the opposite side in six cases. In two of these cases both pupils were enlarged, the one on the opposite side being more dilated. The light and convergence reactions were very poor in these cases, apparently due to the comparatively high degree of choking in most instances and the reduced visual acuity. The frequent enlargement of the pupil on the side opposite the lesion—homonymous to the field defect—is of interest in connection with the well known observation of Behr [1] that lesions of the optic tract are associated with a dilatation of the pupil on the opposite side. It is likewise of interest to recall that Trendelenburg,[2] by experimental section of the optic tract on one side, produced a contralateral enlargement of the pupil. In my cases the widened pupil on the opposite side was probably due to the pressure involvement of the optic tract, which must have been affected by the deep-seated tumor.[3] In the case in which the pupil on the homolateral side was enlarged, the oculo-

1. Behr: Die Bedeutung von Pupillenstörungen für die Herddiagnose der homonymen Hemianopsie, Deutsche Ztschr. f. Nervenh. **46**:93, 1916; Zur topischen Diagnose der Hemianopsie, Arch. f. Ophth. **70**:340, 1909.

2. Trendelenburg, quoted by Behr.[1]

3. It must be kept in mind, however, that an enlargement of the pupil on the opposite side not infrequently occurs also in parietal and especially in occipital lobe tumors, probably due to the involvement of Gratiolet's radiation.

motor nerve might for some reason have been more exposed to the pressure than the tract.

Field Defects.—In eight of the eleven cases reliable field examinations could be obtained, the remaining patients being too uncooperative on account of their general physical or mental condition. Seven of the eight cases showed homonymous field defects. In two there was a homonymous lower quadrantanopia and in five a homonymous hemianopia, the macula having been spared in six of the seven cases. The sparing of the macula, therefore, does not speak against the localization of a lesion in the temporal lobe.

Aphasia.—This was present in six of the seven patients with lesions on the left side. There were all transitions from a slight nominal aphasia to the severe degrees of sensory aphasia, as evidenced by verbal and literal paraphasias, difficulties in understanding and difficulties in writing.

Cerebellar and Quadrigeminal Symptoms.—Ataxia, hypotonicity, deviation while walking, a tendency to fall to one side and nystagmus were noted in four cases. There was no constant relation between the side of the lesion and the directions in which the falling and the deviation occurred. Nystagmus to both sides and upward was present in one of the two cases in which there were other cerebellar signs; a choked disk of 4 diopters, and widely dilated and unequal pupils, with poor reaction both to light and in convergence. In another patient with impaired pupillary reactions, who likewise had cerebellar symptoms, the upward movements of the eyes were limited. The symptoms in both cases probably indicated a marked pressure effect on the quadrigeminal or midbrain region. In one of the three patients with tremor, the second and third fingers on the side opposite the lesion were chiefly involved.

Auditory Symptoms.—The infrequency of these symptoms is noteworthy. One patient lost his hearing on the side opposite the lesion a short time before admission to the hospital; another patient complained of an occasional ringing in his ears.

Age of Patients.—At the time of admission one patient was in the second decade of life, two were in the third, three in the fourth, four in the fifth and one in the seventh decade, the average age being 47 years.

Duration of Illness.—Nine of the eleven patients had a history of illness of more than one year's duration, and six of them a history of more than two years' duration. The shortest history covered a period of two months; the longest, one of eleven years, the average duration of the illness, i. e., the time between the appearance of the first symptoms and the verification of the lesion, being three years. (The figures are:

two and eight months, one, one, one and one-half, three, three, three and three-fourths, four, four and one-half, five and eleven years.)

Chronology of Symptoms.—Several symptoms showed an unmistakable tendency toward a chronological order. In the ten cases in which they were reported, the epileptic attacks were always the first recorded symptom and preceded, in most instances, the succeeding symptoms for a long period. In a few cases, the presence of other symptoms, such as defects in memory or disturbances of speech, were, retrospectively, found to have been present at the same time at which the epileptic attacks had occurred, but they were slight and inconspicuous. Mental deterioration and headaches appeared mostly in the early stages; impairment of vision and, if present, diplopia occurred, as a rule, in the later stages of the disease. Between these symptoms, which showed a tendency toward a certain order, various other symptoms, such as aphasia and olfactory, sensory and motor disturbances, were interposed in no definite succession.

The Clinical Syndrome.—The essential points, therefore, include a long-standing history of antecedent epileptic attacks which, in the same patient, may have different manifestations and which long precede the other symptoms, such as progressive mental deterioration, sensory or motor disturbances, and so on. The examination reveals, in the average case, a middle-aged patient with memory defects and some mental dulness, a bilateral choked disk and homonymous field defects, with an enlarged pupil on the side that corresponds to the affected part of the visual fields. A definite lower facial weakness is present on the contralateral side, where other motor, as well as sensory, disturbances with exaggeration of the deep reflexes may be found. Pathologic reflexes may be present on the side opposite the lesion, or there may be a bilateral general increase of tendon reflexes. It may be mentioned that the histologic type of two gliomas of the temporal lobe could be predicted after the symptomatology, based on the study of the remaining cases, had been worked out.

The general clinical features of these tumors may be illustrated by the report of one case, which approaches the average type fairly closely, a comment, therefore, not being necessary.

REPORT OF A CASE

CASE 4.—*A middle-aged man with attacks of numbness and weakness of the left side, of three years' duration, difficulty in concentration, blurred vision, headaches and diplopia. Choked disks, left facial weakness of the central type, quadrantanopia and hemihypesthesia. Subtotal removal of large solid fibrillary astrocytoma of the right temporal lobe. Uneventful postoperative recovery. Relief of symptoms.*

History.—Mr. Lester N. M., aged 33, a hoisting engineer, who was referred by Dr. Ernest E. Daland of Boston, was admitted to the hospital on Oct. 30, 1930. The family history was unimportant apart from the fact that both the

patient and his mother were left-handed. His previous health had always been excellent, and he was able to continue work until one week before admission.

Attacks of Left-Sided Numbness and Weakness: The first of these attacks occurred three years prior to admission, the second one, eight months later. Since then the attacks had gradually increased in frequency until the patient had as many as a dozen each day. They never lasted more than from five to ten seconds. They were sometimes preceded by a slight, brief feeling of nausea. The patient likened the attacks to a wave or an "electric shock," which began at the head, rapidly spread down over the left half of the body and then disappeared. During these brief spells, which were associated with slight dizziness, he lost control of the left side of the body; the left knee gave way, and he fell unless he was holding on to something with his right hand. All of the spells started in the head and progressed downward. He had noted that if he tried to speak he had some difficulty in articulating the words. He never lost consciousness during these attacks. He had had them near his engine and had burned his left hand on the steam pipes. At the time of the spells, sensation on the left was absent. After the attacks were over, the patient rapidly regained control of the left side, and within a minute or two he was able to carry on his work without the slightest trace of muscular weakness, but there had occasionally been a slight unsteadiness and shaking of his left hand for a short while.

Mental Deterioration: During the last two months, the patient had noticed a definite difficulty in concentration and said that his head felt "as if it is not clear."

Impairment of Vision: Three or four weeks before admission the patient noticed that his vision became blurred. In reading small newspaper print, the words tended to run together, and at the time of admission he had considerable difficulty in reading small print.

Subjective Hemianopia: For the same time, the patient had felt as though there were a curtain on his left side.

Headaches: The patient had never had any headaches until three weeks prior to admission, since when he had been having increasingly severe fronto-occipital headaches, which were more marked on the right side of his head. They were most severe in the morning, gradually wore off as the day progressed and were aggravated by stooping down, straining at stool, etc. The headaches became so severe a week prior to admission that the patient was forced to cease work and consulted his physician, which led to the present admission.

Unsteadiness in Walking: This had been present for the past three weeks.

Diplopia: The patient had noticed transient diplopia on several occasions since admission.

Previous Treatment: During the past year the patient had been on a regimen of phenobarbital; during this time, he thought that the attacks had been rather less frequent.

Examination.—There was some inability in concentration. The second cranial nerve showed acute bilateral choking, 3 diopters on the right and 2 diopters on the left. There was a left lower quadrantic homonymous defect (fig. 1). The visual acuity in the left eye was 20/30; that in the right eye, 20/30 + 3. Examination of the third, fourth and sixth cranial nerves revealed anisocoria; the left pupil was the larger. There were a few nystagmoid jerks on looking to the left, but no true nystagmus. Examination of the fifth cranial nerve showed a definite diminution in thermal sensation on the left side of the face. There was also a slight but unmistakable deviation of the jaw and of the tongue to the left. Examination of the seventh cranial nerve showed a slight but definite left facial weakness of the central type. The other cranial nerves were not involved.

When the power of the left hand was tested, the hand fell off the instrument, with tremor. The tonus was normal. There was a definite diminution in thermal sensation, and the patient was less readily able to recognize the difference between hot and cold on the left side of the entire body. There were also a relative left astereognosis and a loss of muscle sense of the left fingers and toes. The tendon reflexes were normally active on both sides; the abdominal reflexes were absent on the left side; there were no pathologic reflexes. The usual tests of coordination were performed, with a slight terminal ataxia on both sides. Gait and station were objectively normal. Roentgen studies showed no localized changes or signs of pressure.

Diagnosis.—A diagnosis of a right temporal rather than an occipital tumor was made, but ventriculographic confirmation was indicated.

Preoperative Course.—From November 2 to 8, there was no change. On November 12, it was learned that the patient had been having considerable headaches during the past two or three days. That morning he had a sudden collapse for a minute while being turned over in bed. Agonizing headache occurred after-

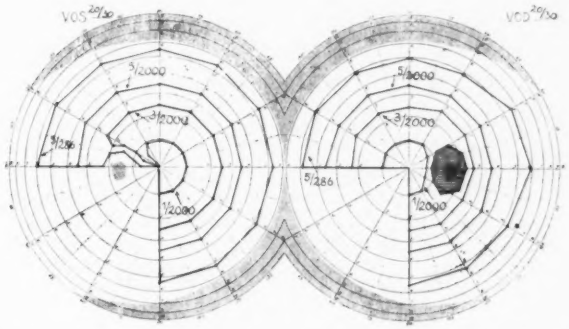

Fig. 1 (case 4).—Left homonymous quadrantanopia with split macula. Preoperative fields.

ward and was followed by a second, more severe, collapse, with cyanotic color and sighing respiration. A ventricular tap was done immediately afterward. The dura was under extreme tension. The needle struck the left ventricle at a depth of 4.5 cm. from the dura. There followed a shooting out of clear colorless fluid at "terrific tension." The needle was withdrawn after 70 cc. had escaped. Just before the tap was made, the patient was very cyanotic, his pulse rate was rising, and the respirations were reduced to 4 per minute and had almost ceased. After the escape of fluid, the respirations returned again, and within five minutes the patient's color was good and he was breathing normally, though he would not respond. It was thought that air should not be introduced, and a right osteoplastic operation was performed immediately.

Operation.—A right median flap was turned down without difficulty. Generous subtemporal decompression was provided. The dura was reasonably tense, and was deflected upward. The temporal convolutions were greatly widened; the temporal lobe was exceedingly soft; the sylvian vessels were pushed upward. No needle was introduced. An incision was made with the electric needle close to the sylvian vessels. An unmistakable soft, grayish, suckable tumor, which proved to be an enormous one, was disclosed immediately under the surface. Uncapping

of the temporal lobe was performed. The growth was outlined with the sucker. The chief mass of the growth was tilted out after fully from two to three hours of manipulation. The cavity (fig. 2) was cleaned out as radically as possible by combined scalloping and suction, posteriorly running back into the occipital lobe and running far up under the sylvian fissure. Several minor branches of the middle cerebral artery were strung out by the sucker and secured by clips. The ventricle was almost certainly opened, but no fluid was obtained owing to the removal of 70 cc. Troublesome bleeding from a small periosteal artery was checked finally by electrocoagulation. A single protective drain was left in the huge cavity and led out through the scalp. The bone flap was replaced. The tumor was a typical fibrillary astrocytoma (fig. 3).

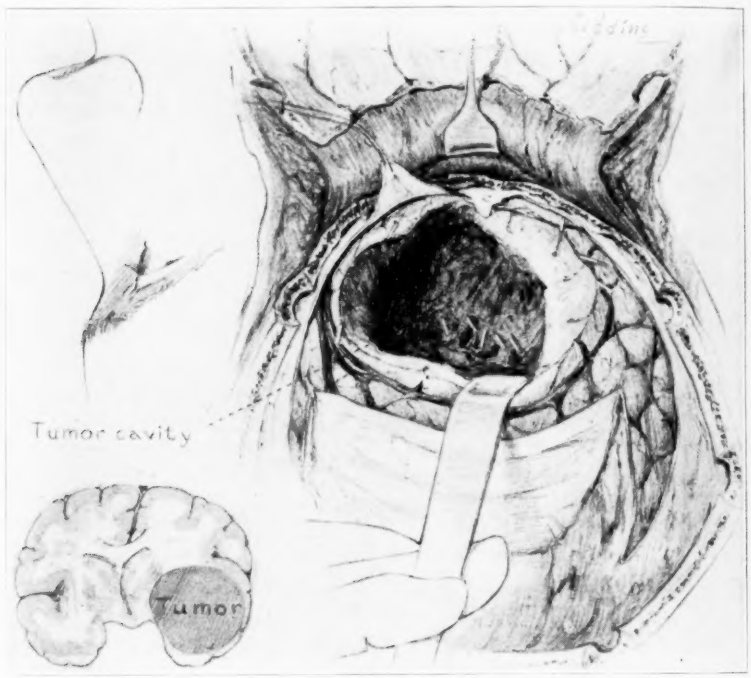

Fig. 2.—Drawing made from operative sketch to indicate field before replacement of bone flap; also, in subsketch, approximate site and size of tumor mass.

Postoperative Course.—Some attacks of numbness and twitching occurred in the left arm. The choking increased to 3 diopters on the right and 2 diopters on the left, after having receded to about 1.5 diopters on both sides. Two lumbar punctures were done. On November 29, it was learned that there had been no headaches since the operation, and no attacks during the preceding few days. The patient had noticed definite improvement in vision. The wound was well healed. At the time of writing this report the patient had been walking around for a week. Left homonymous hemianopia was complete. Choking still measured from 1.5 to 2 diopters bilaterally. The pupils were equal; there was no deviation of the jaw or facial weakness. There was no demonstrable hypesthesia to hot

and cold, loss of deep muscle sense or astereognosis. Cerebellar tests were performed normally. There was no motor weakness and no aphasia.

On November 30, the patient was discharged home. The decompression had filled up a little, but was quite soft.

Postoperative Reports.—On Jan. 7, 1931, the patient was much improved. He said that at times he could see things in the left visual field. There was less blurring of central vision. The fundi were flat. The decompression was flat and soft. There was no aphasia. The hand grips were equal. There was complete left homonymous hemianopia to rough test. On March 12, it was learned that he had been back at work since January 15. He still had a left homonymous

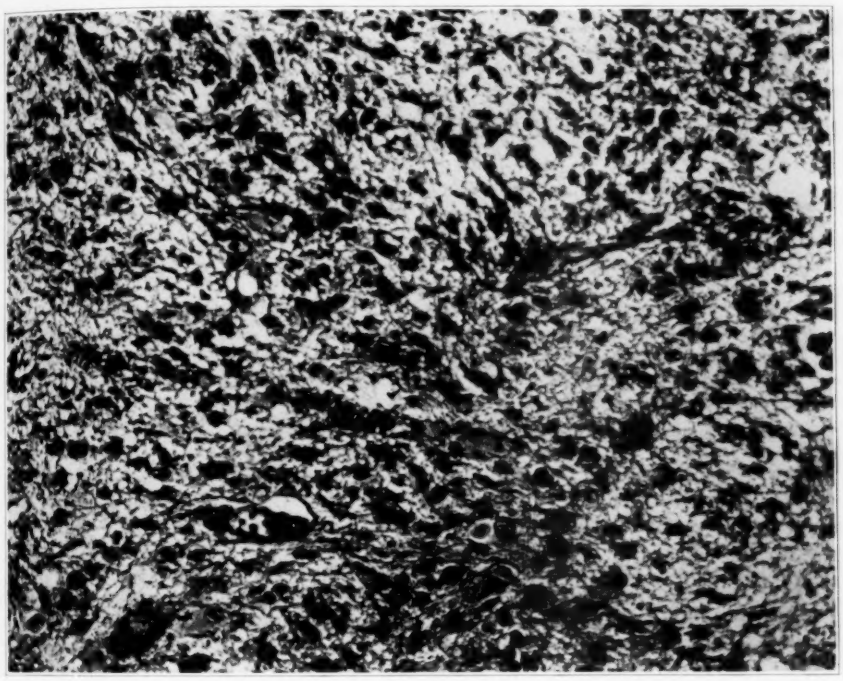

Fig. 3 (case 4).—Typical fibrillary astrocytoma.

hemianopia. The decompression area was flat and soft. On May 15, he showed a continued satisfactory condition. He had been working regularly, although he had a different, less responsible job than previously. The left homonymous hemianopia persisted. He had had no headaches. There was an occasional feeling of numbness and twitching in the left hand, but none in the left leg, and these were present only when he was especially nervous and fatigued, which was not often. The decompression was sagging. There was no aphasia or astereognosis. The fundi were flat.

The description of the clinical syndrome already given and exemplified by the report of one case needs to be completed in a certain direction. The presence of sensory jacksonian attacks, as encountered in

two of my cases, may obviously be misleading in drawing attention to the postcentroparietal region, even in the presence of hemianopic field defects and aphasic troubles which are compatible with the diagnosis of a large parietal tumor. It may be recalled, moreover, that in many cases the fields could not be tested satisfactorily. Motor jacksonian attacks or grand mal attacks of focal type may, likewise, suggest the presence of a suprasylvian tumor. It is, therefore, necessary in every case in which any kind of attack of the so-called focal type is present, to exclude the presence of a glioma of the temporal lobe and carefully to search for symptoms in the temporal lobe, such as anisocoria, deafness, tinnitus, uncinate attacks and dreamy states, unilateral exophthalmos, fulness and tenderness of the temporal region, calcification in the middle fossa, ipsolateral involvement of the fifth nerve and homolateral or contralateral ptosis. Apart from the clear roentgenologic signs or the externally visible manifestations of a tumor of the temporal lobe, which are, however, infrequent, no one of these symptoms alone is characteristic, but a combination of two or more of the signs is unquestionably of diagnostic value.

There was no possibility of working out sufficiently the symptomatology of the protoplasmic astrocytomas, the series of astrocytomas which are classified as purely protoplasmic being too small in relation to the fibrillary ones. Many of the protoplasmic astrocytomas, moreover, were mixed lesions or showed signs of rapid growth, thus approaching the glioblastomas.

It is important that there were differences between the clinical features as produced by the solid astrocytomas and those produced by the astrocytomatous cysts. The latter occurred more frequently in children, and the average age of the patient was accordingly lower, most of the patients being between 20 and 30 years of age, as contrasted with the patients with solid lesions, the average age of whom was 47 years. Only 60 per cent of the patients with cysts showed mental disturbances. An illustrative case report is presented.

A school boy, aged 10, was admitted to the hospital with the history of frequent attacks of semiconsciousness, suggesting dreamy states, for the preceding four months. The attacks were followed by headaches. For the same period vision had been blurred, and for from three to four weeks diplopia and dizziness were present.

On examination, there were: bilateral acute choking of 5 diopters; incomplete right hemianopia; apparently intact reading vision, and weakness of the right external rectus. Examination of the extremities and the body revealed nothing abnormal except bilateral diminished tendon reflexes.

Right anteroposterior and postero-anterior stereograms of the skull showed a thin vault with fairly marked signs of intracranial pressure, but no localized changes. On trying to perform a ventriculogram, a cyst was struck which contained xanthochromic fluid. Forty cubic centimeters was evacuated and replaced

by 25 cc. of air. The cystogram showed a huge cyst in the left temporal lobe. At operation the cyst was emptied and a mural nodule, situated in its outer wall, was tilted out and removed together with the overlying cortex. The patient was in perfect health three and one-half years after the operation, and made a remarkable record at school.

There were definite differences between the symptomatology of the fibrillary astrocytomas and the glioblastomas of the temporal lobe. A study of the latter showed that their history was characterized by a rapid development of the disease, the symptoms covering a period of a few months or weeks. Epileptic attacks were uncommon, and there was no tendency to a chronological order of the symptoms. A greater degree of motor and sensory disturbances than in the benign type of gliomas seems to play an important part in the symptomatology of the glioblastomas. An illustrative case report is as follows:

A man, aged 27, was admitted to the hospital five weeks after the onset of easy fatigability and two weeks later of right-sided frontal headaches. At the same time numbness of the entire left side of the body and face developed. One week later weakness of the left side appeared and advanced to an almost complete hemiplegia.

On examination, the patient was found to be restless and uncooperative, complaining of severe headaches. The left-sided sensory and motor disturbances were evidenced by analgesia of the face and leg with a diminution of the corneal reflex, a complete lack of position sense in the upper and lower extremity, paresis of the seventh and twelfth nerves, paresis of the upper extremity and complete paralysis of the lower extremity. The left upper extremity was semiflexed and flaccid, the deep reflexes being absent; the left leg was outwardly rotated, the foot being in equinovarus position. The deep reflexes were increased, and there were a suggestive ankle clonus and a positive Babinski sign. Station and gait could not be tested. Examination of the fundi revealed a bilateral acute choked disk with hemorrhages on both sides, the elevation measuring 1.5 diopters on the right and 1 diopter on the left. The mental condition of the patient cleared up transitorily, and an examination of the fields could be performed. This showed a left lower quadrantanopia, with sparing of the macula. The pupil on the left side was definitely enlarged. At operation a large glioblastoma of the right temporal lobe was found and partially removed. The patient was markedly improved when he left the hospital.

SUMMARY AND CONCLUSIONS

The deep parts of the temporal lobe are a favored seat of the fibrillary astrocytomas. To these lesions corresponds a clinical picture that seems to be sufficiently cleancut to justify a preoperative histologic diagnosis. The chief symptoms show a fairly outspoken tendency to appear in a certain chronological succession. The history, covering, on the average, a period of three years, is almost invariably initiated by one or more of the various kinds of epileptic attacks. Mental disturbances, beginning as failing memory for recent events and general mental insufficiency, are constant, appear in the early stages of the disease and

may proceed to an almost complete loss of memory and a marked intellectual deterioration. Choked disk, which was present in ten of eleven cases, failing vision and diplopia occur later. There are always either sensory or motor or both sensory and motor disturbances on the side opposite the lesion, particularly a definite weakness of the lower part of the face. There are, likewise, in almost every case in which reliable perimeter and screen tests can be obtained, homonymous field defects. Aphasia was present in the vast majority of patients with lesions on the left side. Anisocoria was an outstanding feature, the pupil on the side opposite the lesion usually being enlarged.

I wish to express my gratitude to Dr. Harvey Cushing for his kind permission to publish this paper from his clinic.

Clinical Notes

PARAPLEGIA IN FLEXION AND THE SYMPTOM OF LHERMITTE

Subacute Combined Degeneration of the Cord

GEORGE B. HASSIN, M.D., CHICAGO
Professor of Neurology, University of Illinois, College of Medicine, and Attending Neurologist, Cook County Hospital

Subacute combined degeneration of the cord is such a well defined clinical and pathologic entity that diagnosis, as a rule, is not difficult. However, cases occur in which a diagnosis is rendered uncertain because of accidental features foreign to this morbid entity. Of these I shall take up paraplegia in flexion and the so-called symptom of Lhermitte. While the former has been described in subacute combined degeneration of the cord, the symptom of Lhermitte has not.

REPORT OF A CASE

History.—A white man, an American, aged 45, with a good personal and family history, was admitted to the neurologic service (Dr. Gerty) of the Cook County Hospital on Feb. 6, 1932, because of loss of weight, general weakness and difficulty in walking. The illness had begun two years previously with sphincter disturbances (occasional incontinence of the bladder and rectum). These disturbances soon disappeared, but for the last four months he had been unable to urinate, except by overflow. One year after the onset, he began to experience pain in the back of the neck, which radiated down the spine to the legs and toes. The pain was severe and was characterized by the patient as "electric shocks" which would occur with each movement of the head. This kept up for several months, when the patient began to suffer from "cramps" in the big toes and difficulties in walking. The cramps were associated with tingling in the feet and legs, while in walking the patient reeled to the left. For the last two months he was hardly able to walk. Aside from the "electric shocks," cramps, tingling and reeling gait, he also complained of a dead feeling "up to the waist line."

Examination.—The patient was poorly nourished. The temperature was 98.7 F.; the pulse rate was 88, and the respiratory rate was 24. The blood pressure was 140 systolic and 96 diastolic. The musculature, especially that of the lower extremities, was flabby and atrophied; the bladder was distended up to the umbilicus. Speech was normal. The gait was spastic. In walking the patient reeled to the left and had to be supported. Muscle power was diminished in both the upper and

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From the neurologic service of Cook County Hospital and the Neuropathology Laboratory of the University of Illinois College of Medicine.

the lower extremities. Passive movements were spastic, especially in the lower extremities; active movements were weak, also more in the lower extremities.

Reflexes: The left achilles tendon reflex was absent; the rest of the reflexes, as well as the periosteal, including the mandibular, were exaggerated, especially on the right, with positive Babinski, Rossolimo, Chaddock, Gordon, Schaeffer and Mendel-Bechterew signs. Patellar and ankle clonus was absent. The abdominal and cremasteric reflexes were also absent. "Irritation of the soles of the feet" caused withdrawal of the corresponding extremities. The corneal, conjunctival and pharyngeal reflexes were present. The cranial nerves were normal; there was no nystagmus; the pupils and fundi showed no abnormalities; however, a subsequent note by an ophthalmologist read: "The changes suggested syphilis or multiple sclerosis."

Sensibility: Touch, pain and temperature were felt throughout; the sense of position was lost in the lower extremities where the vibration sense was impaired "below the knees." On a subsequent examination (Feb. 24, 1932) the sense of touch was absent and that of pain was diminished below the iliac spine.

Laboratory Data: The red blood cells numbered 4,700,000; on two other occasions the counts were 3,400,000 and 3,620,000 red cells; the white cells numbered 8,150, 7,700, and 7,400; hemoglobin was 80, 65 and 76 per cent; the color index was 1.2. A differential white blood cell count showed: polymorphonuclears, 55 per cent; lymphocytes, 45 per cent, and no abnormal forms.

Analysis of the stomach contents (Feb. 12, 1932) showed an alkaline reaction, the presence of blood and the absence of free hydrochloric acid.

Spinal puncture revealed absence of a block and a normal spinal fluid which gave a negative Wassermann reaction. This reaction was also negative with the blood.

Course.—The condition progressed. The right leg became definitely atrophic; the anesthesia, below the spine, became more evident, and complete incontinence of the bladder set in. On Feb. 27, 1932, three weeks after the patient's entrance to the hospital, marked flexion of both legs suddenly developed. The legs were flexed at the knees, and the thighs were flexed on the abdomen; it was not possible to extend them, actively or passively; any attempt to do so was accompanied by pain. The upper extremities were not paralyzed, but were weak. No note has been found as to the condition of the defense reflexes, except a mention of the withdrawal of the leg on irritation of the soles. Extensive bed sores developed, and the patient exhibited marked mental confusion. The temperature became elevated on March 1, 1932, and signs of bronchopneumonia appeared, to which the patient succumbed on March 4, 1932.

Summary.—The onset occurred with electric-like, shooting pains down the spine, followed by paresthesia, weakness and spasticity in the lower extremities, exaggerated tendon reflexes with pathologic plantar reflexes, loss of the achilles tendon reflex on the left, paraplegia in flexion, achlorhydria and absence of a blood picture characteristic of pernicious anemia.

Anatomic Observations.—Examination of the spinal cord revealed degeneration of the posterior, lateral and anterior columns of the cervical, dorsal and lumbar

regions. The posterior columns were more affected than the lateral, in which the pyramidal and the direct spinocerebellar tracts were involved. The extent of the degeneration can be seen from the photographs shown in figure 1.

Microscopically, the affected areas containing the products of nerve degeneration were rarefied and fenestrated and showed the so-called status spongiosus usu-

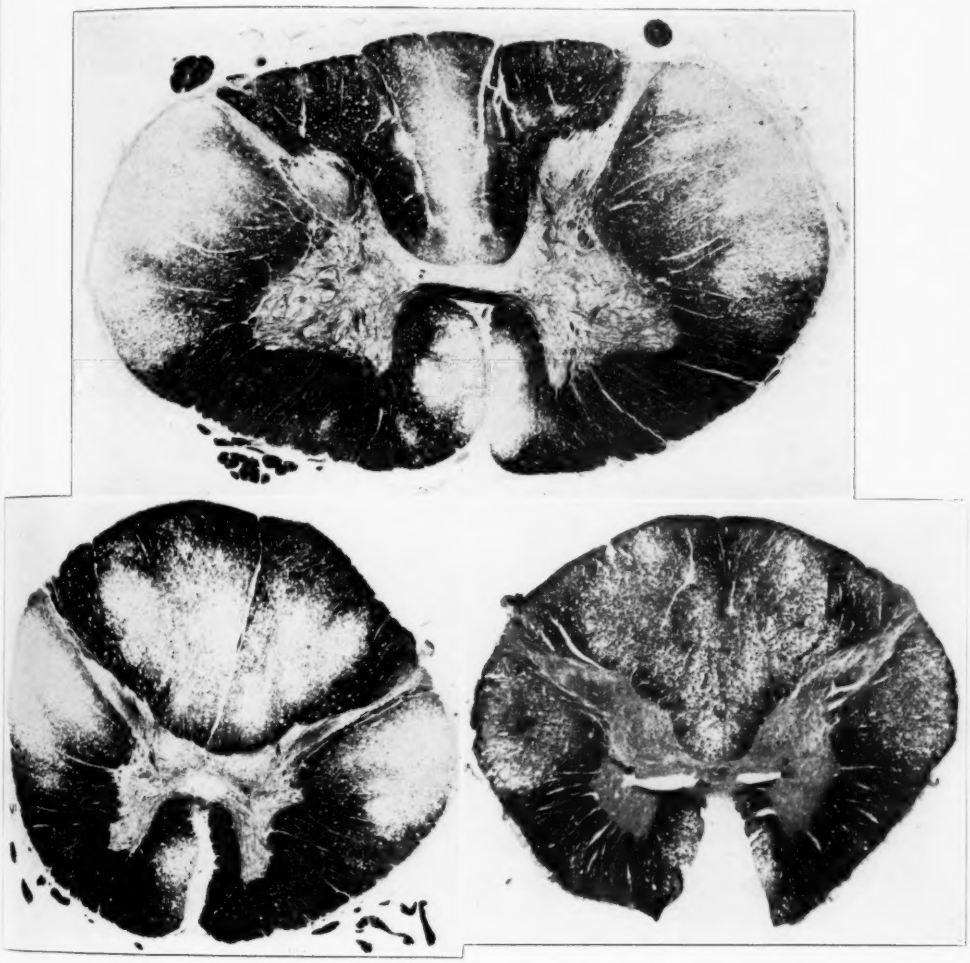

Fig. 1.—The various levels (cervical, thoracic and lumbar) of the spinal cord showing the areas of degeneration in the posterolateral and anterior columns. Weigert-Pal stain.

ally seen in subacute degeneration of the cord. Scarlet red stain revealed among them numerous fat granule bodies (gitter cells) in various stages of formation. Longitudinal sections of the spinal cord exhibited the several phases of degeneration of the cord, from a practically normal state to that of secondary degeneration

with the formation of glial scar tissue (fig. 2). The gray substance was preserved; like the white matter, it exhibited no signs of inflammation or patches of sclerosis. The blood vessels often showed dilated adventitial spaces filled with gitter cells. In the brain the changes were as extensive and noteworthy as in the spinal cord

Fig. 2.—Longitudinal section of the posterior columns of the spinal cord. The area at *1* contains practically normal nerve fibers; the area at *2* is much degenerated, appearing as a glia scar. At *3*, the status spongiosus can be discerned; it contains large accumulations of destroyed nerve tissue, not yet removed to the blood vessels. Bielschowsky stain; counterstain by Alzheimer-Mann method.

and possessed the same macroscopic and microscopic features. The histologic diagnosis was subacute combined degeneration of the cord.

COMMENT

The outstanding features in this case were the history of shooting pains, in the form of electric shocks, down the dorsum of the spine, and the paraplegia in flexion. The former was described by Lhermitte and his associates [1] as an early symptom of multiple sclerosis; its occurrence in this condition has been confirmed by Wechsler,[2] Patrick,[3] Read [4] and others. It has also been observed in concussion, tumors of the cord and Pott's disease. Lhermitte attempted to explain this phenomenon, which he considered of diagnostic value in multiple sclerosis, by irritation of nerve fibers deprived of myelin, that is, by demyelinization. It would probably be proper to see in this painful phenomenon a manifestation of swelling of the spinal nerve fibers, similar to what occurs in peripheral neuritis. Demyelinization is a late phenomenon; it follows the stage of the electric shocks which, as pointed out, occur very early. Notwithstanding the fact that multiple sclerosis and subacute degeneration of the cord are common diseases, the symptom of Lhermitte is rare. Additional factors are probably at play—either special sets of sensory nerve fibers are affected, or the destructive process is exceptionally severe. Neither of these hypothetical factors can be demonstrated pathologically. They show only that the symptom of Lhermitte may also occur in subacute combined degeneration of the cord, and that it is not specific.

Of much greater interest is the other unusual feature in this case—the paraplegia in flexion. Babinski,[5] who renewed the interest in this phenomenon, considered it significant of an irritation of the pyramidal tract of the spinal cord, or of its compression. Further observations, clinical as well as pathologic, showed that paraplegia in flexion occurs also in cortical, capsular, pontile and many other organic cerebrospinal lesions without the cord being compressed. Marchand [6] mentioned a dozen of these lesions, and Alajouanine [7] recognized a spinal and a cerebral type of paraplegia in flexion. Some have considered it to be a special type of paraplegia which possesses clinical and pathologic features different from the well known type of Charcot-Erb's paraplegia. It was claimed that in the latter the paraplegia is in extension, the tendon reflexes are exaggerated, the Babinski sign and clonus are present, the cutaneous reflex of defense is absent and the pyramidal tract is degenerated. In contrast, in Babinski's paraplegia, the paralysis of the lower extremities is in flexion, the tendon reflexes are diminished,

1. Lhermitte, Levy and Nicolas: Presse méd. **35**:610, 1927. Lhermitte, J.: The Sensation of an Electrical Discharge as an Early Symptom, Arch. Neurol. & Psychiat. **22**:5 (July) 1929.

2. Wechsler, I.: A Case of Multiple Sclerosis with an Unusual Symptom, Arch. Neurol. & Psychiat. **19**:364 (Feb.) 1928.

3. Patrick, Hugh T.: The Symptom of Lhermitte in Multiple Sclerosis, Arch. Neurol. & Psychiat. **23**:1075 (May) 1930.

4. Read, Charles F.: Multiple Sclerosis with Lhermitte Sign, Arch. Neurol. & Psychiat. **27**:226 (Jan.) 1932.

5. Babinski, J. B.: Sur une forme de paraplégie spasmodique consécutive à une lésion organique et sans dégénération du système pyramidal, Bull. et mém. Soc. méd. d. hôp. de Paris **16**:342, 1899; Paraplégie spasmodique avec contracture en flexion et contractions musculaires involuntaires, Rev. neurol. **19**:132, 1911.

6. Marchand, L.: Considérations sur la paraplégie en flexion à propos d'un cas, Encéphale **19**:191, 1924.

7. Alajouanine, T.: Sur un type de paraplégie en flexion d'origine cérébrale avec exagération de l'automatisme médullaire, Paris, Octave Doin, 1923.

the Babinski sign is absent, the defense reflex is marked and the pyramidal tract is not degenerated. The one is a cutaneous reflex; the other, a tendon reflex. According to followers of Babinski, the phenomena observed in this type of paraplegia signify "liberation" of the spinal centers, which become automatic, that is, independent of the brain, and result in exaggeration of the defense reflex or, what is the same, in increased spinal automatism. An additional factor is seen by some (Alajouanine,[7] Gordon,[8] Schaller[9]) in the involvement of the extrapyramidal fibers. By extension from the pyramidal to the extrapyramidal system, the morbid process is transformed from paraplegia in extension into paraplegia in flexion (Gordon[8]).

It is obvious, interesting as the foregoing physiologic interpretations may be, that they must be substantiated by pathologic studies. The fact that paraplegia in flexion occurs in a great variety of extremely complicated conditions denotes that it does not signify a lesion of any definite system, whether pyramidal, extrapyramidal or combined. Of special interest in this connection is the occurrence of paraplegia in flexion in such a variety of degenerative states as multiple sclerosis (Souques,[10] Babinski[5]), amyotrophic lateral sclerosis (Anglada[11]) and subacute combined degeneration of the cord (de Jong,[12] Hall and Hirsch[13]) and the condition described in the case reported here. In all these morbid states the pyramidal tract is extensively involved in the absence of any element of compression; the Babinski sign is usually present, and the tendon reflexes are exaggerated.

Yet, with all these signs, paraplegia in flexion occurs in defiance, as it were, of the rules generally laid down for its differential diagnosis. In other words, the phenomena of paraplegia in flexion seen in some cases of amyotrophic lateral sclerosis, multiple sclerosis and subacute combined degeneration of the cord do not support the claims of Babinski and his followers. It is obvious that the classification of the paraplegias as already outlined is artificial, and that their clinical teaching and that of spinal automatism are based on speculation and are in need of revision.

DISCUSSION

DR. GEORGE W. HALL: I think that the more cases of multiple sclerosis and the more cases of combined degeneration of the cord one sees, the more uncertain one becomes as to the differential diagnosis. I have now a record of two cases, in one of which the patient has been under care for a year or so. I made a tentative clinical diagnosis of combined degeneration of the cord before the contents of the stomach were examined. In that case I was mistaken. Free acid was present, and there were no signs of anemia. The patient experienced remissions and exacerbations, but I think that, on the whole, she has improved considerably as compared with her condition a year ago.

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8. Gordon, A.: Flexion Paralysis of Spinal or Cerebral Origin, J. Nerv. & Ment. Dis. **62**:354, 1925.

9. Schaller, W. F., and Gilman, Philip K.: Spastic Paraplegia in Flexion, Arch. Neurol. & Psychiat. **10**:512 (Oct.) 1923.

10. Souques: Rev. neurol. **21**:376, 1911.

11. Anglada, Jean: Sclérose latéral amyotrophique ascendante avec manifestations douloureuses et paraplégie en flexion intense, Montpellier méd. **32**:73, 1911.

12. de Jong, H.: Un cas de sclérose combinée dans l'anémie pernicieuse avec polynévrite, présentant les symptomes d'une "paraplégie des vieillards," Acta psychiat. et neurol. **2**:105, 1927.

13. Hall, George W., and Hirsch, E. F.: Paraplegia in Flexion with Subacute Combined Degeneration of the Cord, Arch. Neurol. & Psychiat. **23**:257 (Feb.) 1930.

Yesterday, Dr. Fentress and I saw a patient at the hospital in whom the clinical picture was exactly that of subacute combined degeneration of the cord. Because of the symptoms present, I was so sure of the diagnosis that I ordered a test meal to be given this morning. More than a normal amount of free hydrochloric acid was found in the contents of the stomach. The hemoglobin is of a minus index, and there is no anemia. A spinal puncture has not yet been made, but it looks as though a diagnosis of multiple sclerosis will have to be made. There are no changes in the eyegrounds and no disturbance in speech, but the patient complains of numbness in the hands and feet and has a bilateral Babinski sign, complete loss of vibratory sense and considerable diminution of sense of position.

Dr. Walter Schaller reported a case in the "Year Book of Neurology," 1927, in which, if I remember correctly, an autopsy was made. The patient had not had anemia, and yet the histologic picture was that of subacute combined degeneration.

DR. PERCIVAL BAILEY: I think that Dr. Hassin is correct in saying that the pathologic condition in these cases is not well known. I understood him to say that Babinski considered that paraplegia in flexion indicated compression of the spinal cord. I think that was perhaps true in the beginning, but I am sure that it is not Babinski's belief at the present time, since Alajouanine has described several cases of cerebral origin in which the pathologic process presumably did not occur primarily in the spinal cord.

DR. LEWIS J. POLLOCK: I wonder whether in the various cases that have been reported there has been any attempt to correlate the degeneration with the destruction of any particular tracts, such as the rubrospinal and vestibulospinal pathways?

DR. A. B. YUDELSON: I believe that at the last annual meeting held at Elgin a case of multiple sclerosis, not with complete paraplegia but with Lhermitte's sign, was presented. I do not know whether the report of that case has been published since then, but all of the signs pointed to multiple sclerosis, with exaggerated patellar reflexes and Lhermitte's sign. I wish to know whether this case should be classified with the cases reported by Drs. Hassin and Bailey.

DR. G. B. HASSIN: Schaller's case, to which Dr. Hall referred, was, I think, that of a tumor of the spinal cord which, according to Schaller, involved the tectospinal and vestibulospinal tracts. He thus tried to explain the paraplegia in flexion by the involvement of the extrapyramidal system, a view also advocated by Gordon. In my pictures they were not affected. The pictures of Gordon were not convincing, probably for technical reasons.

Dr. Bailey is right in stating that Babinski's original views as to the paraplegia in flexion signifying pressure on the cord were somewhat modified. I have mentioned Alajouanine's classification of these cases into two types, the cerebral and the spinal. Babinski's views were mentioned by me for historical reasons only. The teaching of paraplegia in flexion is rather a hopeless problem; it is of no special clinical or pathologic value, for it is misleading at the bedside, and, if it were ignored many mistakes in diagnosis would be avoided.

DR. GEORGE W. HALL: Dr. Hassin is not speaking of the case that I mentioned. Dr. Walter Schaller did report a case of paraplegia in flexion as Dr. Hassin states.

SPECIAL ARTICLE

TRAINING OF THE NEUROLOGIST: NEUROLOGIA IRREDENTA

HENRY ALSOP RILEY, M.D.
NEW YORK

It is perhaps timely to consider briefly a topic that should be of real interest to neurology as a specialty. For the purpose of dramatizing it to some extent this subject may be designated as neurologia irredenta. The term irredenta supplied much of the propulsive power to the forces culminating in the Great War, and the aspirations contained within it played a preponderant rôle in the remaking of the maps of Europe. The redemption of territories which were the spoils of previous wars was one of the most powerful influences swaying peoples and parliaments.

Neurology, too, has her irredenta, spheres of activity and of influence which should be hers, but which have for one reason or another fallen under the control of related branches of medicine. It is not, however, of necessity, that an irredenta should become such a realty through conquest. In many instances, other factors may be operative in the process of alienation. In all fairness, neurology itself has been largely to blame for these lost spheres of influence and activity. The very existence of this irredenta contains implications which bode ill for the future of our specialty. An inquiry into the underlying causes may lead not only to the redemption of the neurologic irredenta but to the correction of the fundamental reasons for its existence. The principal losses which neurology has suffered during the past may be enumerated as follows: (1) epidemic cerebrospinal meningitis, (2) anterior poliomyelitis and (3) cerebrospinal syphilis. The losses which seem imminent are: (1) dorsolateral sclerosis with pernicious anemia, (2) the convulsive states and (3) perhaps the psychoneuroses. The fate of the second group will depend on an appreciation of the growing probability that neurologists may be deprived of the care of these disorders of the nervous system and on the steps taken by neurologists to meet this impending situation.

A Presidential Address before the New York Neurological Society, New York, Oct. 4, 1932.

Epidemic Cerebrospinal Meningitis.—Today, this is a disease of considerable rarity in the neurologic wards and special neurologic hospitals of New York. The patients suffering from this disease are to be found principally in the medical wards of the general hospitals. Epidemic cerebrospinal meningitis is considered by the internist as an acute infectious disease of the body as a whole, with manifestations in all systems, to be studied and diagnosed bacteriologically and to be treated by immunologic procedures. Can one not logically question such conclusions and propose that the conduct of such cases can best be confided to the neurologist? The neurologist is justified in seeking a directing influence not only in the diagnosis but also in the therapy of this disease, for the predominating symptoms result from the action of the disease agent on the central nervous system, the cardinal diagnostic features are of a neurologic character, the outstanding pathologic inroads are on the nerve tissues and the therapeutic approach consists of procedures which are the acquired technic of the neurologist—intravenous, intraspinal and occasionally intracisternal or intraventricular puncture. The diagnosis is in large part bacteriologic, but one for which any well organized laboratory is competent to assume responsibility.

The recovery of the treatment of epidemic meningitis cannot be accomplished by idle vaporings or "windy suspirations of forced breath." To regain control over this and other infectious diseases of the nervous system it is essential to bring about an improvement in the present treatment of these diseases, an elaboration of new lines of therapy and a satisfactory demonstration that better and more efficient management can be provided in special neurologic wards and neurologic hospitals.

The avenues of approach which seem to hold the greatest promise are the production of new or more powerful and refined serums, with the elimination of the hazardous reactions sometimes resultant on their use, and the scientific development of mechanical methods for the more thorough and efficient application of the curative serums to the nooks and crannies of the subarachnoid space. The first item in this program calls for the services of trained bacteriologists and immunologists, but these scientists can usually be found in any well staffed hospital or medical school and it should not be difficult to enlist their aid, provided that the clinical neurologist will evince an interest sufficient to evoke and maintain the necessary laboratory cooperation. The bacteriology of the central nervous system is almost a virgin field for systematic exploration; the rôle of the viruses in the production of disease of the nervous system is an almost unopened book; the real

advances in the bacteriology of the central nervous system still await the inspired touch. The second item is the more thorough and resourceful application of various mechanical procedures to the treatment of these infections. There will be presented at this meeting the theory and practical application of a most promising form of treatment, not only for the meningitides but also for many other types of infection of the central nervous system as originated by Kubie and applied practically by Retan. Last year, Cornwall reported a spectacular recovery in an apparently hopeless case of meningitis owing to the more effective dissemination of the curative serum by means of air introduced into the subarachnoid space. These are examples of new and imaginative methods by which startling and impressive improvement can be established in the care and treatment of the infectious diseases of the nervous system. The demonstration of the fact that progress has been made in the orthodox management of these conditions by those most familiar with the battle ground may well reestablish the leadership of the neurologist in the care of these disorders. Neurology must develop a broad and an imaginative bacteriologic contact and a resourceful and persistent therapeutic program.

Anterior Poliomyelitis.—In its acute stages this condition is now treated by the pediatrician and internist and is considered by them as an acute infectious disease of the entire organism. In its later states it has been appropriated by the orthopedist and the physical therapist. It is but natural that the pediatrician should be in contact with these cases at the beginning of the illness, since the disease appears predominantly within the age range which is his special domain, but in regard to its most comprehending management much that has been said concerning the meningitides could be repeated here; the major localization of the disease process, the symptoms, the diagnostic and therapeutic requirements, all involve the special training and the application of measures which should be the obligation and the opportunity of the neurologist. The most inviting avenues of approach are again those involving bacteriologic and immunologic research, but great possibilities of infinitely improved treatment and the prevention of the tragic crippling of many victims may be brought about by the more efficient control of the disease in its early stages. The chronic phase should no longer be left entirely in the hands of orthopedists and physical therapists; a combination of these agencies under the guiding hand of the neurologist should result in more efficient and successful treatment of the patient.

Neurosyphilis.—Under this term are included the many forms of this infection, tabes, dementia paralytica, the tabetic form of dementia paralytica and cerebrospinal and meningovascular syphilis. During the past two decades the incidence of these disorders has been gradually

but steadily declining in the private and clinic practice of the neurologist. Two contributing factors immediately present themselves as explanatory of this state of affairs. The first is the natural decrease in the prevalence of these late manifestations of syphilis because of the routine use of the Wassermann test, leading to prompt recognition of the disease in its early and often symptomless stages, and because of the much enhanced efficiency of early treatment by means of the various arsenical compounds. The second factor is the assumption of the treatment of these diseased nervous systems by syphilologists. This condition of affairs is based on the premise that the treatment of syphilis, no matter in what organ it appears, is the natural right of the syphilologist. Considering the usual unfamiliarity with the functions of the nervous system manifested by the majority of general practitioners and other specialists, the assumption of responsibility for the treatment of neurosyphilis by those unacquainted with evidences of disorder activity of the nervous system is accompanied by definite dangers. The treatment of syphilis of the nervous system should be entrusted to those who are familiar with the signs and symptoms of neurologic disease, who can evaluate properly the many intricate evidences of clinical implication of the neural tissues and who can differentiate between the processes of the disease and the all too frequent evidences of toxic action of the potentially dangerous therapeutic materials which are employed. Every neurologic clinic should have a treatment division whose special duty it is to conduct and to improve the therapy of these essentially neurologic conditions. Members of our specialty should treat these patients themselves or refer their cases to neurologists who are devoting themselves to the development of the technic of administration of these specific remedies and to the scientific investigation of the most efficient medicaments. To turn these cases over to the care of physicians unskilled in the recognition of signs of neural involvement is not conducive to the best interests of the patient. A reasonable increase in aggressiveness on the part of the neurologist in both the diagnostic and the therapeutic spheres of activity would redound to the benefit of the specialty and of the patient.

Combined Sclerosis.—During the past five years definite evidence has arisen that dorsolateral sclerosis, associated as it almost always is with pernicious anemia, is in danger of being absorbed by the internist and the hematologist. In a considerable number of cases the presence of pernicious anemia is never dreamed of by the patient or the internist until attention is called to this possibility by the proper evaluation of the tingling, numbness and minor evidences of pyramidal tract involvement which are so often the first definite signs of the hemic or central nervous disorder. The proper estimation of these symptoms and signs and the discovery of the underlying disorder often await the neurologist.

In many instances the incapacitation of the patient through advanced involvement of the nervous system far overshadows the systemic evidences of the blood dyscrasia. Will the neurologist complacently watch the management of this disorder of the nervous system pass into the hands of the internist or the hematologist? If history repeats itself, he probably will—but is it inevitable or is it to the best interests of the patient? This question may be answered in the negative, for the internist or the hematologist is not equipped to recognize the evidences of central nervous involvement or to assume the proper treatment of neurologic complications. Rather let the neurologist take a page from the book of the other specialists and perfect himself in the treatment of this disease, which still remains, in the absence of more intimate knowledge, one of the blood and blood-forming organs. Equipped with the knowledge and experience necessary for the proper management of the nervous manifestations and applying the latest advances in the treatment of the blood itself, he can offer the patient the best and most efficient care.

Convulsive States.—Epilepsy, or better, the convulsive state with its many forms, is still, in the absence of more exact knowledge, considered to be a disease of the central nervous system. Until a few years ago, this disorder was gladly allowed to rest on the doorstep of neurology and in many instances there it remained, receiving scant courtesy and grudging recognition from the neurologist. No branch of medicine has evinced any overwhelming desire to assume the care of these unfortunate patients, who constitute an appreciable proportion of the population. The neurologist himself showed little inclination to study the problem energetically until the metabolist began to manifest an active and growing interest in the investigation and management of this large group of patients. The neurologist has awakened belatedly to his vast responsibility and opportunity and then only under the spur of the establishment of "epilepsy clinics" in other departments of the outpatient service and the active competition of the metabolist in private practice. Whether or not this tardy awakening has been too late is difficult to determine at present, but the danger of loss of control over this extensive clinical material and of the opportunity hidden within the mystery of the disease is imminent. Only a realization of what the loss of this opportunity will mean to the neurologist can prevent this eventuality from taking place, The situation requires early and energetic steps. The essential constitution and the management of this disorder must be investigated along new lines, and the application of all the acumen that we possess must be brought to bear on the problem. Will the metabolist, the endocrinologist or the physiologist be the one to solve this enigma or will neurology contribute the directing force of its experience to the elucidation of this problem?

Psychoneuroses.—Perhaps the greatest danger that threatens neurology today is the possibility of the passage of the care of the psychoneuroses into the hands of psychoanalytic psychologists and psychiatrists. If this tendency continues to develop and remains unopposed by members of our specialty, it will not be long before the great mass of patients suffering from these psychogenic disorders will be lost to the neurologist and neuropsychiatrist. The passage of control over this group of patients would be a grievous blow to neurology, would deprive us of a field of activity of absorbing interest and would perhaps do the cause of neuropsychiatry as well as the best interests of the patient an inestimable injury. The day should never arrive when neurology admits that this term no longer includes the psychoneuroses and allows its field of activity to be circumscribed and limited to disturbances produced by demonstrably diseased structures of the nervous system, abandoning the field of the psychogenic disorders to the psychiatrist or the psychologist.

The psychoneuroses constitute a middle ground between the activities of the neurologist and the psychiatrist, and much may be said to justify the rivalry between the two groups to obtain the controlling interest. No justification whatsoever can be found for the unwarranted assumption of the care of these patients by nonmedical groups. There should be no need for argument to unite the entire medical family against this intrusion on the field of the care of the sick.

The most constructive contribution of modern times to the understanding of the psychoneuroses has been made by Freud, whose early training was in the field of organic neurology. Whatever one may think of psychoanalysis in its therapeutic applications, it cannot be denied that it has discovered and applied a thoroughly new method of study to the psychoneuroses. From the standpoint of the student this new technic has thrown a flood of light on these conditions. It would be an act of ignorance to exclude the freudian contribution to the study of the psychoneuroses, and it would be as egregious an error to believe that all patients suffering from psychogenic disorders should be treated by psychoanalytic methods.

From the standpoint of contribution to the investigation and treatment of the psychoneuroses, psychiatry has no more valid claim to these fields than has neurology. There is no accepted basis for the assumption that the nonpsychoanalytically trained psychiatrist is better equipped to understand and treat psychoneurotic patients than the similarly limited neurologist. The psychoneurotic patient needs and requires the services of the organic neurologist for the differential diagnosis and the psychoanalytically trained neurologist or neuropsychiatrist for his study and treatment.

The impelling and irrefutable argument for at least the preliminary management of the psychoneuroses by the neurologist is the absolute necessity for the elimination of the possibility that organic disease is the basis for the symptoms of which the patient complains. This applies unquestionably to the anxiety states, depressions, hysterical psychoneuroses, neurasthenic conditions and tics and spasms of the compulsive states. The obsessions, manias and phobias present less of the possibility of diagnostic error in the failure to recognize an organic foundation for the psychic disorder than the preceding group. It is the common experience of neurologists to be confronted with symptoms apparently of a purely psychogenic order in the early stages of tumor of the brain, encephalitis, multiple sclerosis and many other structural disorders of the nervous system. During the course of many of the infectious, degenerative and circulatory disturbances of the nervous system, psychic symptoms predominate. The neurologist is the only one who can properly elicit and evaluate the signs of organic involvement. The first step in the proper management of any nervous disorder is differential diagnosis. A failure to determine properly the character of the process affecting the patient is often fraught with disaster to his best interests. The most promising time for treatment to be applied is before the destructive processes have progressed to an irremediable degree. These points are sufficient to establish the indispensability of the neurologist in the management of the psychoneuroses.

The combination of training along organic neurologic lines with the insight gained by a thorough grounding in psychoanalytic investigation and therapeusis will provide the optimum equipment for the management of this group of patients. The most efficient care of the patient, the intellectual interest of the neurologist and his demonstrated capacity to manage these conditions successfully demand that the neurologist maintain his position in relation to this class of patients, and that he improve and by the addition of the psychoanalytic technic amplify his methods and intensify his efforts, rather than surrender this field of scientific and humanitarian interest. This field of neurologic activity is not as yet an irredenta, but the possibility of it becoming so in the near future is threatening unless the neurologist bestirs himself.

COMMENT

The question of recapture of the lost activities and of defense against threatened disappearance of others is not a commercial or a financial one; it is not one of selfish possession but one of service—not a quest for aggrandizement of the neurologist but one of advantage to the suffering patient, the unknowing subject of the contest. The neurologist is entitled to believe that his more exact knowledge of the

structure of the nervous system, his greater appreciation of its functions and his more intimate contact with the disordered conditions of the nervous system render him more competent to manage these disturbances than those whose principal activity has been elsewhere.

Why have these fields of endeavor been lost to the neurologist? There are undoubtedly a number of reasons. There are natural ones, such as the production of serums by immunologists in the treatment of infectious disease and the discovery by internists of the effect of extracts of the liver and gastric mucous membrane on pernicious anemia, with incidental improvement of the associated central nervous manifestations. But what excuse is there for the neurologist to sit idly by and watch the exploitation of the treatment of syphilis of the central nervous system by syphilologists and dermatologists? Why should the discovery of the partial control of convulsions by dietary supervision deprive the neurologist of the opportunity of treating these conditions when he has been in contact with the manifestations of the convulsive state from time immemorial? It is difficult to recall any new or startling innovations in the treatment of neurologic ailments that have been developed by the neurologist himself. Is it that the intricacies of diagnosis have so engrossed neurologic thought and effort that the desire to alleviate suffering and restore disordered function has become atrophied? Is therapeutic initiative deadened by the usual result of neurologic disease, the irreplaceable destruction of nervous tissue and the consequent impossibility of a *restitutio ad integrum?* Is it a lack of imagination in evolving new methods or a lack of industry in applying old ones? Why did it remain for the pediatrician to develop the therapy of chorea by hyperthermia, which was originated by a neurologist for the treatment of dementia paralytica? Why does the physical therapist constantly instruct us in the treatment of our patients? Why are the current advances in our knowledge of such toxemias as those produced by lead, with its notable effect on the nervous system, both central and peripheral, left to others to develop? It is difficult to find the proper reply to these questions; in all probability no one answer would be sufficient. Many factors have led to the present situation, but now the economic stimulus is being added; possibly it may stir into activity what scientific interest has failed to awaken; perhaps the ever-constricting boundaries of our influence will energize us to efforts which in the future will reflect more credit on us than our past accomplishments. What must be done to regain this irredenta? Many lines of activity are patently open to the neurologist. A real bacteriology of the diseases of the nervous system must be developed. This implies the enlisting of resourceful, able and imaginative bacteriologists and immunologists in the problems of infection of the nervous system—

scientists of the highest caliber working in collaboration with neurologists of vision and insight. Association in a similar bond should be established with metabolists. The metabolism of the central nervous tissues, the rôle of the neural structures in physiologic processes and the possible field of therapeutic endeavor in this sphere are almost unploughed fields of investigation. Great opportunity for advance also lies in the application of the energy which has until now been expended on the investigation of morbid processes and the refinements of clinical diagnosis to the much more practical field of therapy. The same acumen, interest, industry and resourcefulness must be expended on the prevention and cure of disease or on the minimizing of its effects as have been so abundantly spent on the more theoretical aspects of our art and science.

The failure of the neurologist to protect himself and his specialty against the active or passive pressure of other branches of medicine has made itself felt also in the standing of neurology in relation to other departments in some schools of medicine. In many centers for medical instruction neurology has never been able to establish its independent identity, and in other quarters neurology has suffered a definite decrement in importance.

The vitality of neurology may be self-evident, but its reputation as a living and active branch of medicine is combated and belittled by many other branches of medicine. It would seem that it is time, not only because of the encroachments of other specialties, but also by reason of the definite loss of prestige in some quarters, that neurology bestir herself and make evident the real importance of the specialty to the rest of medicine. The future of neurology lies in our hands; the return of the irredenta and the safeguarding of our intellectual and practical spheres of influence depend on vigilance, effort, imagination and purpose.

Abstracts from Current Literature

SECTION OF THE SPINAL ANTEROLATERAL COLUMNS IN MAN. O. FOERSTER and O. GAGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:1 (Jan.) 1932.

Literature.—Section of the anterolateral columns of the cord for relief of pain was first suggested and carried out by Spiller and Martin in 1911. Foerster and Gagel state that, independently and almost at the same time, the procedure was carried out by Tietze and Foerster. More careful scrutiny of this statement shows that the operation by Tietze and Foerster was carried out in December, 1912, reported before a society on June 6, 1913, and published in the *Berliner klinische Wochenschrift,* Aug. 11, 1913, p. 1499, in the report of the meeting of the society. On the other hand, the operation in the case of Spiller and Martin was performed on Jan. 19, 1911, and was published in *The Journal of the American Medical Association,* May 18, 1912, p. 1489. The operation was performed twenty-three months before Tietze and Foerster's and a report of it was published seven months before Tietze and Foerster performed their operation, and nearly fifteen months before any report of their operation was published. The operation by Tietze and Foerster was for gastric crises; that by Spiller and Martin was for pain in the lower limbs.

To Frazier belongs the credit of advocating warmly the use of the operation in various conditions and for outlining clearly its indications. Foerster has performed chordotomy in twenty-six cases, to which are added three more in which the operations were performed in his clinic. Of these twenty-nine cases autopsy was performed in nine, the interval between operation and death being eight days (in two cases), one month (in one case), three and one-half months (in two cases), eight months (in one case), two and one-quarter years (in one case) and from five to six years (in two cases).

Anatomy of the Anterolateral Column: There has been some question about the origin of the crossed anterolateral columns. The prevailing concept was that these tracts originated from the cells of the substantia gelatinosa rolandi. That this is not so is shown by the fact that after section of the anterolateral columns in four cases retrograde degeneration was found in the large cells of the posterior horn. These large cells differ from, and have no relation to, the substantia gelatinosa. The cells of the latter in the four cases studied showed no changes. Incidentally, also, no changes were found in the cells of Clarke's column. Foerster and Gagel state that the anterolateral columns have nothing to do with the cells of the substantia gelatinosa, and that the fibers in these columns arise only from the large cells of the posterior horn. Another problem with regard to the fibers in the anterolateral columns is whether the fibers cross immediately or gradually. The prevailing concept is that the decussation takes place over several segments of the spinal cord, about five or six. Foerster has denied this concept in previous works, and Foerster and Gagel now assert again that the decussation of these fibers takes place rapidly, so that the fibers from one posterior horn are all crossed at the upper limit of the next highest segment. The proof of this lies in clinical observations. Foerster and Gagel cite several cases to show that the decussation of fibers of the anterolateral columns coming from a single segment is complete within the next higher segment. This holds true for cervical and dorsal segments. Foerster and Gagel cannot say whether or not it is true of the lumbar segment, because they have never performed lumbar chordotomies. This is a matter of some practical importance, because the general practice in chordotomies is to cut the cord about five or six segments above the upper level of the pain. This is not necessary, as shown by the cases of Foerster and Gagel.

It has been generally assumed that the fibers which reach the anterolateral columns, once they get there, remain there, and ascend vertically in the cord. This is not so. A part of the fibers during their ascending course get out of the anterolateral area into the posterolateral region, corresponding in position to the dorsal spinocerebellar tract of Flechsig. These fibers take the same course

as those arising from Clarke's column; viz., they penetrate into the corpus restiforme and the cerebellum. The dorsolateral tract, therefore, contains two categories of fibers; first, Flechsig's bundle arising from Clarke's column and, second, a tract arising from the posterior horn cells, running in the anterolateral column and then getting into the dorsolateral area. It is not possible to say whether all the anterolateral fibers which pass up in the dorsolateral tract reach the corpus restiforme, or whether a part of them take the same course in the medulla as the other fibers which have remained in the anterolateral area, namely, to the formatio reticularis and the thalamus. The chief mass of the fibers ascending in the anterolateral columns reach their destination in the region of the formatio reticularis of the medulla and pons. Foerster and Gagel were able to follow a number of fibers to the colliculi and thalamus. The tractus spinothalamicus without a doubt ends in the basal portions of the lateral nucleus of the thalamus. That a part of the fibers of the anterolateral columns bend backward from the formatio reticularis to the brachium conjunctivum and cerebellum has long been known.

It has also long been known that the anterolateral columns, too, contain descending fibers, the tractus tectospinalis, tractus deiterospinalis, tractus reticulospinalis, tractus Darkschewitchi and tractus rubrospinalis. In all their cases Foerster and Gagel were able to follow descending degeneration after anterolateral section. In these cases there was degeneration in the anterior columns as well, so that it is assumed that the descending fibers in the anterolateral columns pass down in part in the anterior columns. They were able to find degeneration only in the cells of Deiters' nucleus after anterolateral section. There was no retrograde degeneration in the red nucleus, the colliculi or the nuclei Darkschewitchi.

Pathophysiology of the Anterolateral Column: There is no doubt that the anterolateral columns carry pain and temperature sensations to the brain. Stimulation of these columns with the faradic current causes severe pain, chiefly in the leg when the thoracic cord is stimulated and in the arm and leg when the cervical cord is irritated. Mechanical stimuli are also capable of causing pain. Foerster says also that on section of the anterolateral column, which is always carried out under local anesthesia, severe pain is elicited in either the leg or the arm of the opposite side, depending on the level of the section. Extramedullary and intramedullary processes cause pain, particularly trauma, tumors and multiple sclerosis. This pain is designated as anterolateral column pain.

After section of the anterolateral column, there is complete analgesia in all the body segments the apparent paths of which enter the nervous system below the level of section, with the exception of the dermatomere at the upper limit of the infralesional segment. The analgesia involves the skin, tendons, bones, muscles and fascia and, in bilateral chordotomy, the viscera. Spontaneous pains of peripheral origin disappear. Only the contralateral half of the body is affected and analgesic. The analgesia is at first complete, even the severest pains disappearing. Only in the anogenital region have Foerster and Gagel failed to secure a complete cessation of sensation of pain after chordotomy.

Temperature sense is affected like pain sense in all cases of bilateral chordotomy. In many cases of unilateral chordotomy it was by no means completely eradicated, and in many cases it was found to be only slightly affected. In one case sensation of heat was almost completely retained, while cold was appreciated as warmth.

After unilateral chordotomy, pain sensation is altered to a certain degree on the homolateral side. This is not discernible by ordinary clinical methods. The intensity of stimulation, however, is increased, and the chronaxia is prolonged on the homolateral side, indicating that not all the fibers from the posterior horns cross, some of them remaining homolateral. In severe cases of pain, therefore, it is wisest to do a bilateral, rather than a unilateral chordotomy. The same holds true for temperature sense. The tracts for this are not completely crossed, as had already been indicated. It is only after bilateral chordotomy that a complete thermanesthesia is obtained.

Still other forms of sensation are affected by anterolateral chordotomy, particularly tickling sensation and all pleasurable or painful sensations. The unpleasant feeling which usually accompanies vibratory sensation is lost after chordotomy,

and only the vibration itself is appreciated. Likewise, the unpleasant sensation which is felt on applying the electric current to the skin is lost.

The generally accepted dictum is that the senses of touch and pressure are conducted in the homolateral dorsal column and the crossed anterolateral column, and that injury of one or the other leaves these sensations intact. Foerster and Gagel state, however, that by the use of finer testing methods it is possible to demonstrate that touch sensation is also decreased after anterolateral chordotomy. This change is present on both sides of the body, but is more marked on the contralateral side. Foerster and Gagel interpret this to mean that both anterolateral columns have to do with tactile impulses to a definite body area, but that the crossed tract is more important than the uncrossed, just as in pain sensation.

Position sense and passive motion were in no way affected by anterolateral chordotomy.

The problem of the restitution of sensation after chordotomy is important. Immediately after operation there are complete analgesia and thermanesthesia. After a variable time — weeks, months or a year or more — pain sensation returns to a certain degree, and with it the spontaneous pains for which the operation was performed, without, however, their regaining the former intensity. This recurrence comes earlier in unilateral than in bilateral chordotomy. This involves first the deeper tissues, the bone and other parts, while stimulation of the skin does not cause pain. Sooner or later, pain sense returns, earliest in the anogenital area and then in other zones. Normal pain sense is never regained. Temperature sense returns earlier than pain as a rule, and, furthermore, one may state dogmatically that sensation of heat will return first, and cold will be appreciated as warmth. This paradoxical temperature reaction is characteristic of a certain degree of restitution of sensation. Later, cold sensation returns. Temperature sense never returns to normal, and fine shades of difference are not appreciated.

How is it that pain sensation returns after complete analgesia following chordotomy? There are several reasons, but one of the most important is that the homolateral fibers still function and can conduct pain impulses. This is shown by the fact that pain returns sooner after a unilateral than after a bilateral chordotomy. Foerster and Gagel again emphasize the necessity of performing bilateral chordotomy in cases of severe pain. What is true of pain is even more true of temperature sensation. How is it, however, that pain returns after bilateral chordotomy? Foerster and Gagel explain this on the basis that some of the fibers in the anterolateral column leave this column orally and pass up with the corpus restiforme by the tract of Gowers. It is possible that some of these aberrant fibers pass directly into the formatio reticularis in the medulla and reach the thalamus. If this is so, it would explain the return of pain impulses. Foerster and Gagel believe also that the dorsal columns conduct pain despite contrary teachings. They base their arguments on the fact that touching the exposed column of Goll causes severe pain in the leg, touching the column of Burdach causes severe pain in the arm and touching the obex produces severe pain in the sacrum and anogenital zone. Furthermore, after section of the posterior columns, Kroll found a decrease in the number of pain spots and an increase in chronaxia. Finally, the sympathetic fibers are important in the restitution of pain sensation.

Pain sensation is carried by the crossed anterolateral columns, the homolateral columns, the peripheral zone of the dorsolateral columns, the long ascending tracts of the posterior columns and the sympathetic system. The crossed anterolateral tract is the chief tract, the others being accessory tracts the eradication of which does not produce analgesia, but rather a mild deficit which is detectable by finer methods. When the crossed tract is thrown out, there is complete analgesia, because the whole system is upset, despite the integrity of the other tracts. Sooner or later pain returns through the intact tracts.

Are the pain and temperature senses carried in different columns? Clinical observations have long shown, especially in traumatic cases, that temperature sense may be reduced or absent, and pain sense intact. Foerster and Gagel state that they are separate, thermal sensations lying dorsally in the anterolateral columns,

i. e., just under the dorsolateral columns, and pain sensations lying in the tract just under the temperature area.

The question arises whether there is a segmental arrangement of the fibers in the anterolateral columns. Foerster and Gagel state definitely that there is. The fibers are arranged so that the most caudal fibers (sacral) lie peripherally, while the most oral fibers (cervical) lie deep. The fibers are arranged in semicircles around the anterior horn. Head pointed out this arrangement of fibers some time ago.

In none of the cases was there paralysis of any sort which could be attributed to the anterolateral section. In only one case was one leg paretic for several weeks, and at autopsy it was found that the lateral column was injured. Foerster and Gagel emphasize this point because cases of paralysis after anterolateral chordotomy have been reported in the literature. This can be due only to a simultaneous injury of the pyramidal tract. Furthermore, in no case of cervical or high thoracic chordotomy has there been any paralysis of respiratory muscles. Also, there have been no ataxia and no disturbance in bony equilibrium after chordotomy.

Foerster and Gagel assert that the anterolateral columns definitely carry vegetative tracts. In one case, secretion of sweat was decreased over one half of the body after chordotomy, and it is postulated that these fibers run in the dorsal part of the anterolateral tract. Furthermore, the efferent arm of the vasoconstricting reflex runs in the anterolateral tract. All cases of anterolateral chordotomy in the cervical cord showed a Horner's syndrome. It has been known for a long time that there is a pupil-dilating tract from the corpus subthalamicus to the cervical cord, but it has not been known in what part of the cord the tract runs. Foerster and Gagel state, on the basis of their chordotomies, that it runs in the anterolateral columns. After bilateral chordotomy, bladder symptoms occur in the form of retention. Erection and ejaculation are not influenced by chordotomy.

None of the twenty-nine patients died immediately after the operation; two died eight days later. Of the twenty-nine cases, eleven were tabes with severe gastric crises. In two of these cases chordotomy relieved the crises, which recurred later. In seven cases the relief was prompt and lasting, and was accompanied by a gain in weight often of from 30 to 35 pounds (14 to 16 Kg.). These cases have been followed for from five months to five and one-quarter years. In one case in which the relief was only temporary, a chordotomy was performed on the other side; this resulted in great, but not complete, relief. It was found at necropsy that the chordotomy was not complete. Foerster and Gagel believe that bilateral chordotomy in the uppermost thoracic cord in cases of gastric crises is extremely beneficial.

The second group of four cases comprised pain from neuromas due to amputation, in all of which the operation was performed with good results. The third group was composed of five cases of carcinomatosis of the vertebrae. In these, too, the pain was relieved. The operation was performed in three cases of radiculitis and in two cases with marked flexion contraction of the lower extremities.

ALPERS, Philadelphia.

PHYSIOLOGY AND PHYSIOPATHOLOGY OF THE CORPUS STRIATUM AND SUBTHALAMIC REGION. JEAN LHERMITTE and J. O. TRELLES, Encéphale **27**:235 (March) 1932.

Chapter 1 of this article is an extensive review of the anatomy of the corpus striatum. The review shows the close gross and histologic relationship between the putamen and caudate nucleus. Then follow: (1) the corpus luysii, in which myelinization and comparative anatomic studies indicate a close relationship to the striatum; (2) the locus niger, with abundant melanin-bearing cells, probably an outgrowth of the globus pallidum. The histology is described in minutia. The Vogts admit some degree of somatotopic disposition in the striatum; i. e., that certain cellular groups exercise control over certain body segments. Thus, the

anterior groups correspond to the cephalic region, the midgroups to the superior members and the posterior groups to the pelvic and abdominal sections. The main tract connections are: On the motor side, striothalamic; striorubric; strioluysian; strionigric; striomesencephalic (to nuclei of Darkschewitch and posterior commissure) and strio-infundibular (to vegetative centers); on the sensory side (1) those from the cortex; most investigators deny any direct cortical contacts with the striatum; corticoluysian fibers are disputed, but corticonigric connections have been demonstrated by Dejerine and von Monakow (frontonigric) and Winkler (temporonigric); (2) thalamic, joining the thalamus with caudate, putamen and pallidum; (3) commissural. In general, the conclusion is that the thalamus bears much the same relation to the corpus striatum that the ascending parietal cells do to the pyramidal.

Physiology: In animals of different levels the degree of influence by suprathalamic and subthalamic sectioning varies on account of the relative development of the cortex and thalamostriatum. Experimentation with monkeys in deep narcosis, stimulated by bipolar electrodes, indicates that neither the lenticular nucleus nor the pallidum is excitable through the internal capsule or by direct stimulation. Kinnier Wilson, however, demonstrated occasional bilateral twitchings of the eyelids and contractions of the contralateral side of the face with the needle in the center of the striatum. Wilson used a highly controlled technic designed to obviate irradiation to adjacent fibers, and his finding of less reaction than Bechterew (reactions in contralateral extremities) may be accounted for by this fact. Hess, in Zurich, passed an interrupted current through limited zones of the caudate nucleus in the cat, and obtained certain movements. Wilson passed a current of from 3 to 5 milliamperes for from five to ten minutes and thereby obtained exactly limited lesions in the monkey. No motor disturbances were obtained when the lesions were limited to the lenticular nucleus, but there was a slight awkwardness or maladdress in the contralateral limbs. No paralyses, trembling, or impaired sensory findings were in evidence, although there was a very slight increase of the tendon reflexes.

The conclusion of these endeavors is, then, that the corpus striatum in monkey (and probably in man) is unaffected by the faradic current, and that limited areas of destruction seem to occasion only insignificant disturbances of motility. These facts point to the possibility of still more reduced activity of the corpus striatum in man in the future. But it must be remembered that in none of these experiments was the entire corpus striatum destroyed in a way analogous to that in Westphal-Strümpell's disease or progressive lenticular degeneration.

More gross destructions resulted in certain interesting facts. F. H. Lewy performed unilateral destruction and confirmed in general the observations of Wilson, i. e., awkwardness of the opposite side. With bilateral destruction there resulted paucity of movements, slight rigidity of the trunk, weakened reactions of equilibration, and attempts by the animal to draw food toward itself with awkward, hesitant movements. There was, however, no true paresis. The picture, thus, is similar to that resulting from classic pathologic changes of hypokinetic hypertonicity in encephalitis in human beings. Pachon and Marsalet and Edwards and Boggs have performed experiments on the dog, and L. Morgan on the cat. Morgan found that pallidal lesions provoked the appearance of spontaneous contractures that simulated athetosis.

Studies have been made of chemical poisoning, with somewhat contradictory results because of the difficulty of preventing widespread diffusion of the chemical agent. It is well known that carbon monoxide exerts its maximum effect on the striatum, but there is evidence that it also affects other areas, even the cortex. Mella showed by intraperitoneal injections of manganese that chorea and athetotic movements slowly developed.

The Corpus Striatum as a Vegetative Center: Bechterew found that either excitation or destruction of the corpus striatum modified both respiration and motions of the digestive tract. Prüss, by stimulation of the midzone of the caudate, observed increased arterial tension, with lowering of the pulse and respiratory rates. Aschner believed that the caudate plays a rôle in glycogenesis; Aranson and Sachs

thought that it exercises control through thermal and vasomotor centers. Marinesco, Negro and others regarded the pallidonigral system as belonging to the parasympathetic system, i. e., for vasomotor, salivary and lacrimal activities, whereas Salomon viewed it as sympathetic. Thus, it is clear that the corpus striatum has vegetative functions, but the details are not clear.

The Corpus Striatum as a Factor in Articulation: Undoubtedly this structure plays an important rôle in articulate language, as evidenced by the articulatory difficulties in Wilson's disease, Huntington's chorea and pseudosclerosis. Severe damage to the lenticular nucleus produces disturbance in speech even to the point of anarthria.

The Corpus Striatum in the Expression of Emotion: It is known that the striatum is important in emotional expression. At times, in diseased conditions, it may be only the outward expression that is altered; in other instances the inner experience of emotion is altered. The accepted opinion is that while the voluntary expression of emotion is centered in the cortex, automatic control is in the general region of the striatum.

Pathologic Physiology of the Corpus Striatum: Because the blood supply is not limited to any given arterial branches for a definite region of the corpus striatum, and because edema of surrounding areas always tends to mask or confuse the focal nature of the main lesion, it is almost impossible to find strictly limited lesions in human pathologic material. In hemiplegia on a strictly lenticular nucleus basis the initial voluntary paralysis appears to be replaced by rigidity, and, if on the left side, to produce marked articulatory disturbance. But there are no sharp differentiations between lenticular and ordinary capsular hemiplegia. A few cases of hemichorea with a strictly localized pathologic process have been reported by Liepmann-Vogt and Jakob. In these instances cysts or softenings were present in the caudate nucleus. On the other hand, such limited findings as are reported for the pallidum indicate the rôle of this structure in muscular tonus.

Neurologists have jumped to unjustified conclusions as to physiologic functions on the basis of necropsy findings checked against previously known symptoms and signs. This is, of course, well known in the concepts of "negative and positive symptoms," wherein conditions resulting from damage at one level permit the appearance of new symptoms from another level. However, the best accumulations of evidence point to the strictly motor functions of the corpus striatum, namely, rigidity, hypertonicity, akinesis and diminution of spontaneous movements and of reactive adaptive movements. The clinical pictures are those of bilateral athetosis, chronic chorea, akinesia, dysarthria and anarthria, emotional amimia, torsion spasm, and perhaps static trembling. The corpus striatum is not strictly a motor center but, rather, a coordinating mechanism with a certain amount of functional automatism. From the high incidence of its involvement in encephalitis, it appears that the locus niger, probably has functions associated with the corpus striatum. There is no certainty that it has any primary motor function. The corpus luysii is believed to be related to the clinical condition known as hemiballism. In this condition, in which there is extreme torsion and jerking of one side of the body, the lesion usually focalizes in the body of Luys.

The review closes with an exhaustive bibliography.

ANDERSON, Los Angeles.

SIZE AND SHAPE OF OCULAR IMAGES: III. VISUAL SENSITIVITY OF DIFFERENCES IN THE RELATIVE SIZE OF THE OCULAR IMAGES OF THE TWO EYES. A. AMES, JR., and KENNETH N. OGLE, Arch. Ophth. **7**:904 (June) 1932.

This is the third of a series of articles relative to the size and shape of ocular images and the factors connected with differences in the sizes and shapes of the ocular images (Ames, A., Jr.; Gliddon, G. H., and Ogle, K. N.: Size and Shape of Ocular Images: I. Methods of Determination and Physiologic Significance, ARCH. OPHTH. **7**:576 [April] 1932. Carleton, E. H., and Madigan, L. F.: II. Clinical Significance, ibid. **7**:720 [May] 1932). The second of the two articles

considered the clinical significance of the size and shape of the images, and this, the third, considers the visual sensitivity and differences in the relative size of the ocular images of the two eyes. The purpose of the study is, first, to determine the threshold of the ocular images of the two eyes, i. e., to determine the least perceptible difference in the size of the two ocular images that can be recognized, and, second, to determine the angular size of fusional areas on the peripheral retina and their relation to a difference in the size of the ocular images.

It has been generally assumed that a difference of less than 5 per cent in the relative size of the ocular image was too small to have any physiologic importance, and hence could be neglected. It would appear that there are two grounds for this assumption: (1) The ocular resolving power decreases so rapidly in peripheral vision that small differences in the size of the ocular images are below the threshold of discrimination; (2) the discrepancies in the position of the boundaries of ocular images which differ by only a small percentage are very small compared with the size of fusional areas, and as a result are easily fused and nullified, so to speak. The authors cite this, but do not state it as a proved fact.

The visual capacity to detect a difference in the size of the ocular images in the horizontal meridian has the same basis as the binocular capacity for differentiating images in space, i. e., perception of depth. Further, this binocular capacity for perception of depth is in turn dependent on the capacity of the single eye to differentiate position, i. e., the monocular resolving power. Because, as the author states, "this capacity to discriminate differences in the size of the ocular images in the two eyes is based on binocular depth perception and monocular resolving power, its threshold and limiting values should be obtainable from the existing voluminous and authoritative data on monocular resolving power and binocular depth perception."

The capacity to resolve a difference of position of 40 seconds at an angle of 5 degrees from the fovea means that at 5 degrees one should be able to detect a difference in the size of the ocular images of 0.22 per cent. The capacity to resolve a difference in position of 65 seconds at an angle of 10 degrees from the fovea means that at an angle of 10 degrees one should be able to distinguish a difference in the size of ocular images of 0.18 per cent. A difference of position of 90 degrees at an angle of 20 degrees from the fovea means that at an angle of 20 degrees one should be able to distinguish a difference in size of ocular images of 0.12 per cent. In general, this would indicate that the threshold value for distinguishing a difference in the size of the ocular images in the two eyes is between 0.12 and 0.25 per cent. Further, it would indicate that the sensitivity to difference in the size of ocular images on the periphery should be greater than that at or near the fovea.

In Dr. Ames' laboratory, it was found repeatedly, in the determination of the relative size of the ocular images, that a change of less than 0.25 per cent in the size of the image of one eye relative to that of the other was noticeable. It is probable that the mean deviation lies well below 0.2 per cent of the difference in the size of the ocular images. These observations dealt with the sensitivity to size differences for near vision. The evidence was that the sensitivity is even greater than this for distance vision; it may be less than 0.1 per cent.

If, then, the maximum of 0.25 per cent difference in size is granted by the peripheral resolving power, the investigators wished to learn the extent to which differences in the relative size of the ocular images were nullified, so to speak, by the corresponding fusional areas. In the literature, the angular extent of these areas at the fovea had been given as ranging from 5 to 26 minutes of an arc in the horizontal meridian, and from 3 to 4 minutes of an arc in the vertical.

The author's quotation from Hoffmann follows: "The capacity to separate double images from each other is better developed in some persons than in others, and, as already remarked, it increases with practice. For this reason, even with sharply defined small objects, we can give no generally valid limits for the cognition of separate double images. The limits are widest and the individual differences are greatest due to the contributory factor of binocular depth perception when only cross-disparity is in question. They are narrower, as Panum already showed,

when longitudinal disparity is used alone, since in that case no depth perception appears. In Volkmann's experiments, in which he studied in the stereoscope the perception of double images of fine black lines, the limits for the cognition of double images of vertical lines—that is, cross-disparate double images—when he made use of Helmholtz's corrections varied in the different experimental subjects between 26 and 5 minutes (the latter after considerable practice); for the perception of high-distant (longitudinal disparate) double images, however, only between 3 and 4 minutes. If it is a case of less clearly defined objects, then the limits are so wide that the objects—which are reproduced in the vicinity of the fovea and to which our attention is predominantly directed—are still seen single even with a somewhat larger degree of disparity; and the double images which are always present in normal vision of very indirectly seen object are only occasionally observed. If, namely, one directs one's attention to one of the latter, a movement of regard is immediately elicited which brings its image on the fovea and therefore abolishes the double images."

In other experimental work, it seemed as if in the vertical peripheral meridians the angular area was smaller than in the horizontal meridians. Also, the differences in the angular extent on the fovea are large relative to small percentage differences in size. This is no longer true at the periphery. If 7 seconds is taken as the size of the angular extent at the peripheral angle of 0.5 degree, it is seen that the area is very large relative to the difference in size of the ocular images; i. e., it is about equal to the angular difference in size of ocular images that differ by 20 per cent. Near 7 degrees, however, while the angular area has increased slightly, the angular difference in the size of the ocular images has increased much more rapidly.

The last question which the authors consider is whether the capacity to see singly ocular images that differ by less than a certain per cent prevents such difference from having a physiologic effect on perception. If the disparity in size is in the horizontal meridian, it makes itself known through a change in depth localization, even though images are fused. If the difference in size is in the vertical meridian, it cannot make itself known by a change in depth localization, as a difference in the vertical meridian is not associated with depth localization. The changes which occur in the horizontal meridian result from the binocular capacity to differentiate position in the horizontal meridian.

The capacity for discrimination of the relative sizes of the ocular images varies. In conclusion, the last paragraph is quoted verbatim: "In general, physiologic stimulations, irrespective of their nature, pass unnoticed if their magnitudes are below the sensibility threshold. When their magnitudes are above the threshold, there follows a readaptation, or an effort at readaptation, on the part of the organism. The physiologic importance of the adaptation depends on many factors. It would seem reasonable to assume that those factors determining the adaptation to size differences between the eyes are very similar to those which determine the adaptation to refraction differences. The threshold values for the least perceptible differences in the refractive condition or for the monocular capacity to differentiate distance are near 0.12 diopter. Two or three times that amount is generally considered sufficient to cause ocular trouble. By analogy, two or three times the threshold value for size discrimination, that is 0.50 per cent, should have the same effect."

SPAETH, Philadelphia.

INFECTION OF THE CENTRAL NERVOUS SYSTEM WITH TORULA. WALTER FREEMAN, J. f. Psychol. u. Neurol. **43**:236, 1931.

This scholarly contribution is based on forty-three cases of infection with Torula collected from the literature, including one case reported by the author in collaboration with Weidman. In nineteen of the cases Freeman had the opportunity to study sections of the brain. His general summary and conclusions are as follows: Torular infection of the nervous system is a chronic disease with a rather indefinite clinical picture but clearcut and characteristic pathology. It is sometimes only part of a general infection with the organism, but in many

cases the specific lesions are found only in the meninges. The fungus is usually readily cultivated and will reproduce lesions in experimental animals resembling those in man.

The disease usually begins insidiously, with headache and rigidity of the neck becoming increasingly more severe, and later associated with vomiting; visual disturbances, varying from dimness to actual blindness, hemipareses or hemiplegias, aphasia and occasionally convulsions are added; the disease usually terminates in progressive stupor, coma and respiratory failure. In some cases there are no symptoms referable to the nervous system; in others the first symptoms are memory defects and personality changes. Disturbances of sleep are fairly common. The course is usually progressive, although short remissions are occasionally observed. Some cases terminate fatally without the usual symptoms and signs of bacterial infection; others may show a moderate rise in temperature, with marked leukocytosis. There is no anemia except in the prolonged cases with malnutrition.

The clinical picture resembles that of tuberculous meningitis, except for the absence of fever and the rather prolonged course. In many instances the presence of tuberculosis elsewhere in the body has led to the erroneous diagnosis of tuberculous meningitis, in spite of the negative spinal fluid findings. In other cases, with evidences of an expanding intracranial lesion in the absence of signs of infection, the diagnosis of intracranial tumor was made, followed by decompression or exploration. Occasionally, abscess has been suspected.

The diagnosis is made by finding the torula in the spinal fluid. Errors have been made in a number of cases through inadequate examination of the spinal fluid sediment, the pathologist reporting the presence of large numbers of erythrocytes or lymphocytes when later examination revealed the presence of the organism. There are, however, cases in which the fungus does not appear in the spinal fluid and in which it resists cultivation. Antemortem diagnosis has been made from frozen sections of the cerebellar meninges removed at operation. The fungus usually is easily cultivated.

Evidences of involvement in other parts of the body are rare. Occasionally a lesion may be found in one lung, and more rarely a general infection is indicated by obtaining the torula in pure culture from the blood and urine. The neural symptoms dominate the clinical picture, except in cases of extensive and advanced tuberculosis, in which torulosis may be merely an intercurrent terminal infection.

Treatment of the cerebral invasion has thus far proved futile. Torular infection in other parts of the body is a much less serious condition, and a number of recoveries have been recorded.

Necropsy reveals granulomatous meningitis, usually basal. In a few instances the dura, skull and semilunar ganglia may be invaded. The cerebral subarachnoid as well as the ventricular fluid is often turbid or gelatinous. In more than half the cases there is also a most peculiar involvement of the cerebral cortex that looks in advanced cases like soapsuds, and in other instances like blisters or pits whose contents may be clear or turbid and do not flow out when cut across. Sometimes pearly dots are found widely distributed in the cortex. Similar alterations may be found in the basal ganglia resembling acellular myxomas that project into the ventricle, with a thin ependymal lining. If not cystic, the basal ganglia appear mottled. Discrete granulomas are occasionally found; these are spherical in shape and compress the adjacent structures. The cerebellar meninges are often invaded, but the parenchyma less so, although the white substance may appear mottled, or even fissured. Histologic examination reveals three types of lesions: meningeal, perivascular and embolic. The intracerebral lesions may be either cystic or granulomatous, and are associated with varying degrees of inflammatory reaction. The meninges show diffuse or circumscribed granulomas with endothelial hyperplasia, fibrosis, moderate round cell infiltration and giant cells. Organisms are usually numerous. Although the endothelial hyperplasia may be marked, an inflammatory reaction in the cerebral substance is rare. The cysts are due to enormous accumulations of fungi with

their surrounding mucoid capsules, often associated with very little mesodermal reaction. The granulomas are produced by large collections of endothelial cells, many of which have phagocytosed the invading organism. The mottling observed in fresh sections is due to extensive destruction of the parenchymatous elements. The larger granulomas have a delicate fibrillar reticulum but consist mostly of large collections of organisms. Granulomas and cysts form by internal expansion of the collections of fungi and not by any chemical action on the nerve tissue. Distorted but well stained ganglion cells may be observed near the encapsulated organisms. There is usually little, if any, neuroglial reaction, although in the cases of diffuse necrobiosis there is apt to be a moderate increase in the fiber-forming elements and in the microglia, with a tendency to rod-cell formation. Fat derived from the degenerated parenchyma is practically absent. The fungus penetrates from the meninges along the perivascular sheaths of the blood vessels, forming flask-shaped cysts in the uppermost layers of the cortex. In some cases the cyst formation is extensive, as in the "soapsuds" cases, and subsidiary cysts of various sizes are encountered. In other instances the cysts may remain more or less solitary. Deeper in the cortex there are other cysts and granulomas that appear to have arisen through embolism. Similar lesions found in the basal ganglia would seem to support this view as to their origin, and capillary emboli are occasionally observed consisting of torulae. The gray matter is especially affected, and small foci are found surrounding the sylvian aqueduct and fourth ventricle.

Of the other organs in the body the lungs are most frequently involved, both acute and chronic lesions having been described. In the few instances of generalized invasion reported the kidneys, spleen, lymph nodes, bone marrow, liver, suprarenals, thyroid and skin have been affected. There is apt to be more pronounced inflammatory reaction in these organs than in the brain; this is probably due to the normally greater amount of mesodermal tissue in them.

Although Torula is found rather extensively distributed in nature, only a few of the species are pathogenic. Torula is distinguished from similar organisms by the absence of mycelia, by the formation of spores, by the presence of a capsule and by little tendency to ferment sugars. Certain species seem to resist artificial cultivation. On the basis of this study Freeman makes a tentative subdivision into two species, although he admits that the criteria for this subdivision are incomplete. In one type the organism is characterized by its large size, its occasional umbrella shape, its narrow capsule and its feeble invasive power for the brain, although it has relatively greater reaction in the mesodermal elements. The other type of organism shows an active tendency to formation of cerebral cysts, little reaction, small size, large capsule and easy cultivability. An intermediate third variety of organism may exist. According to the author, the term "histolytica," introduced by Stoddard and Cutler to designate this organism, is a misnomer, because it has no digestive action. The organism isolated from most cases is pathogenic for animals, rats and mice being most susceptible, although guinea-pigs show the most characteristic lesions in the brain and testes. A long time is often necessary for the development of the lesions, six months or more having been required in several instances. The lesions are striking in their lack of reaction.

The portal of entry is never the skin but probably the respiratory tract, either the lungs, the tonsils or the sinuses being suggested in a number of cases. The pharyngeal exudates occasionally found are probably terminal. The lymph nodes apparently furnish the most evident barrier to general invasion.

KESCHNER, New York.

TECHNIC OF VESTIBULAR EXAMINATIONS IN NEUROLOGY. J. RAMADIER and R. CAUSSÉ, Rev. d'oto-neuro-opht. **10**:305 (May) 1932.

Examination of the cochlear apparatus is not included in this discussion for the reason that rarely, except in lesions of the cerebropontile region, does an intra-

cranial disease cause auditory troubles. In diseases of the internal ear a caloric test to determine whether the labyrinth is excitable, hypo-excitable or inexcitable is sufficient, but in intracranial disturbances of the central vestibular pathways the examination must be complete. In the former the symptomatology is always essentially the same; in the latter the vestibular manifestations exhibit a great many modifications. It is true that the symptomatology of otolabyrinthine conditions presents variations, but they are quantitative; the phenomena, their order and even their evolution are of a constant type. Almost always it embraces the three fundamental phenomena, vertigo, nystagmus and spontaneous deviations of the trunk and limbs. The spontaneous nystagmus is always horizontal-rotatory, and the spontaneous deviations are bilateral and involve the various segments of the body. In the same way, alterations of reflectivity concern all the fundamental reactions—vertigo, nystagmus and deviations. These alterations are found with all three classic vestibular tests. In addition, this syndrome is usually accompanied by auditory disturbances. The deviations of both the trunk and the extremities are made toward the same side, and the nystagmus is toward the side opposite the deviations. When there is total areflectivity to the tests, the spontaneous signs of irritation are not long in disappearing.

On the other hand, the symptomatology in intracranial conditions of the vestibular pathways is characterized by extreme variations and numerous modifications of the composition of the syndrome, its arrangement and its evolution. Frequently it is incomplete, often being represented by only one sign—spontaneous nystagmus or deviation of the arms, and even this sign may be manifested only in part; the nystagmus may be horizontal, rotatory, vertical or oblique; the deviation, unilateral or limited to one member or a segment of one member. This incomplete character is found also in the provoked reactions. One reaction may be absent while the others are present, such as nystagmus without vertigo or the reverse, deviation without nystagmus; or rotatory nystagmus may not occur while horizontal nystagmus is normal, or the deviation may be limited to one limb. Again, the reaction to one test may be exaggerated and to another diminished; the spontaneous inclination of the body in the Romberg test may be in an inverse direction to the deviation of the arm; spontaneous nystagmus and spontaneous deviation may be toward the same side, or the spontaneous nystagmus may be bilateral. Finally, the evolution of the phenomena is not subject to rule: A violent nystagmus may persist indefinitely, while tests indicate a total areflectivity of the labyrinth. Any departure from the typical vestibular syndrome suggests the probability of an endocranial lesion.

The details of the examination are discussed under the following heads: inspection of the tympanic membrane; spontaneous reactions—vertigo, nystagmus, segmental deviations, falling (the Romberg test) and walking with blinded eyes—provoked reactions, and the caloric galvanic and rotation tests.

The presence of impacted cerumen or a perforated drum membrane will influence the results of the tests. Spontaneous vestibular reactions are subjective (vertigo) and objective (modifications of muscular tonus, shown in the eyes, limbs and body musculature). True labyrinthine vertigo is accompanied by a sensation of displacement of the body and the erroneous sensation of rotatory displacement of surrounding objects. The patient must differentiate it from headache, giddiness and the tendency to lipothymia, which may simulate it. A true rotary vertigo is rare in patients with neurologic conditions. Except in acute exacerbations of disseminated sclerosis, syringobulbia, Friedreich's disease and, perhaps, certain tumors of the fourth ventricle, vertigo in neurologic disease is of little intensity and is out of proportion to the other spontaneous signs. The absence of vertigo in the presence of an intense spontaneous nystagmus is presumptive evidence of a central disturbance. Spontaneous nystagmus is searched for in the four directions of gaze and in the act of accommodation, with and without the use of Bartel's spectacles; the influence of the different positions of the head on the nystagmus is observed; its intensity, form and direction are noted. Precise observations are necessary.

To determine segmental deviations, the test of the extended arms is preferred. (Static tests give more constant and trustworthy results than kinetic.) The deviation of the arms occurs only after a short interval and rarely attains a large amplitude. It is one of the most sensitive and precise tests of all. Segmental deviations almost always consist of movements of abduction and adduction. The Romberg test is best made with the use of a plumb line, and it should be noted whether changes in the position of the head influence the inclination. The pelvic girdle test is, in effect, the pulsion test of Marie and Bouttier. In executing the test of walking blindly, the observer follows the patient, retaining the same position in relation to him when giving the commands.

Instrumental tests are antiphysiologic because of their intensity and their nature, and are disagreeable for the patient. In executing the caloric test two methods are used, one weak and one strong. In the former, the ear is filled with water at 25 C. After thirty seconds the head is placed upright, Bartel's spectacles are put on the patient, and the eyes are examined for nystagmus: The head is put backward 60 degrees, in which position a horizontal nystagmus should appear; then the head is inclined 45 degrees toward the shoulder opposite the ear that is being tested, in order to bring out rotatory nystagmus. It should be noted that the rotatory nystagmus does not always appear even in normal persons. To investigate rotatory nystagmus properly, all three tests, douching, rotation and galvanic, are required. The head is now placed upright, the test for deviation of the extended arms is made, and the patient is questioned in regard to vertigo. If the weak test is inconclusive, resort is had to the strong test, which consists in irrigating the ear with water at 25 C., using 100 cc. or more. The caloric test gives information as to the degree of excitability of each labyrinth and as to the presence of each form of nystagmus, horizontal and rotatory. In a normal person, nystagmus lasting about one minute, deviation of the arms and vertigo should appear after the weak test.

The galvanic test reveals the threshold of excitability to the current for nystagmus and falling, and the form of nystagmus, which is normally horizontal-rotatory. The test is applied with the patient standing; the current is gradually applied until swaying begins (at from 2 to 3 ma.) and nystagmus appears (3 to 4 ma.). If by douching or rotation, rotatory nystagmus has not been elicited, the galvanic nystagmus will be horizontal. Bourguignon's studies of chronaxia should be extended.

The usual technic of ten turns in twenty seconds is employed in the rotation test. The past pointing reaction is not utilized because of its unreliability. The optimum position for eliciting rotatory nystagmus is with the patient on a turning table with the head 90 degrees backward from the vertical. To elicit vertical nystagmus the head of the patient is turned to the right and the table rotated. The reaction of vertical nystagmus is remarkably stable in contrast to rotatory nystagmus. Horizontal nystagmus is elicited by turning the patient with the head upright and well supported.

Rotation furnishes important information. Postrotatory nystagmus is the result of two excitations, peripheral and central; the former is due to movement of the endolymph, the latter to a brusk interruption of the reflex caused by the rotation (per-rotatory). The physiologic response to rotation is the per-rotatory nystagmus. Even turning of the head through an arc of 90 degrees is sufficient to produce nystagmus, but it is ordinarily masked by fixation of the eyes. It may be perceived by palpation through the closed lids. DENNIS, Colorado Springs, Colo.

THE MONOCULAR MOVEMENTS. ALEXANDER DUANE, Arch. Ophth. **8**:530 (Oct.) 1932.

This article is another of the posthumous publications of Alexander Duane's writings, published through the courtesy and permission of Mrs. Duane. These various chapters represent the work of an authority who devoted his professional life to scientific research in a field to which he so ably contributed.

The article deals with the monocular movements of the eyeball, and is subdivided into a certain number of subgroups. The first deals with a nomenclature of the monocular movements. One must remember that the movements the eye executes from the primary position comprise rotations about all three axes, vertical, transverse and fore-and-aft. From a clinical standpoint it is better to classify all possible movements, first, as to the direction in which the eye is pointing, and second, whether the eye as it turns in any given direction also rolls about its fore-and-aft axis. His table on nomenclatures follows:

Ductions (Direction Movements)

1. Rotations about vertical axis:
   Adduction, or rotation of eye toward nose
   Abduction, or rotation of eye toward temple
2. Rotations about transverse axis:
   Elevation (superduction), or rotation of eye upward
   Depression (subduction), or rotation of eye downward
3. Direction movements produced by a combination of 1 and 2:
   Oblique movements
   Torsions (cycloductions)
4. Rotations about fore-and-aft axis (visual line):
   Intorsion, or tilting of the vertical meridian of the eye toward the nose
   Extorsion, or tilting of the vertical meridian of the eye toward the temple

A discussion of Listing's law and Sherrington's law then follows. The former is as follows: When the line of sight passes from the primary position to any other position, the wheel rotation (torsion) of the eyeball in the second position is the same as if the eyeball had been rotated about a fixed axis perpendicular to both the first and the second directions of the line of sight. Continuing the explanation of this law, Dr. Duane then gave some space to a discussion of the center of rotation of the eyeball, and as to how the eyeball rotates.

The same arrangement of text applies to the discussion of Sherrington's law, and the law as he gives it is that every ocular movement is effected by a combination of two actions: first, a contraction of the muscles that act to carry the eye in the direction that the movement is designed to effect; second, a simultaneous relaxation of the muscles that carry the eye in the opposite direction. Thus, it is plain that several muscles always cooperate in effecting a single movement. If the inferior rectus is paralyzed and the attempt is made to carry the eye straight outward, it is evident that according to the theory presented the eye, ordinarily held level by the mutually counteracting and increasingly strong pull of the superior and inferior recti, should now, owing to the unopposed pull of the superior rectus, deviate upward, and that this upward deviation should increase as the eye is abducted. This is what actually occurs in paralysis of the inferior rectus.

In the next subsection, Dr. Duane considers the muscles concerned in the performance of the different direction movements and the way in which they cooperate, i. e., movement straight out, movements straight in, movement straight up and straight down, movement up and out, and up and in, movement down and out and down and in.

This discussion of reciprocal action is clear and detailed. It is especially interesting to notice how Sherrington's law works out when one considers any single one of these movements, for instance, the action of movements straight down. The superior rectus and inferior oblique are relaxed, and the eye is carried down by the inferior rectus and superior oblique. The abducting and adducting actions of the latter muscles counteract each other, as do the abducting and adducting action of the external and internal recti so that the eye is kept from swerving to right or left as it goes down. Moreover, as the torsional actions of the inferior rectus and superior oblique nullify each other, the vertical meridian is kept vertical.

The muscles are then classified according to their action; i. e., there are three abductors, three adductors, two elevators, two depressors, two intortors and two extortors. In looking straight to the front, up and down, in or out, there is no

torsion. However, in looking up and in and down and out, there is intorsion, while in up and out and down and in, there is extorsion. Listing's law and experiments with after-images demonstrate this well.

The next subject is fundamentally diagnostic in that it describes the diagnostic directions of the gaze. According to another standard textbook on the extraocular muscles, these diagnostic directions of the gaze are the same as if one was considering them to be left hand or right hand elevators or depressors.

The field of monocular fixation is then considered. It represents that portion of space that can be seen by central fixation without moving the head. One must distinguish between the field of fixation and the field of excursion, in that the field of fixation is often cut off in places by the nose or the overhanging brow. However, the eye can still follow the object beyond the boundaries of vision provided the other eye still fixates and follows it. A large table is included in this section showing the measurements of the field of fixation.

Dr. Duane then discusses in great detail the part each muscle takes in performing duction and torsion movements. This may be considered as the field of action of the individual muscles. By means of a drawing, this is graphically shown. It is rather interesting that, here also, Sherrington's law plays a great part in keeping the eye in a certain position by the simultaneous direction of various individual muscles. The amount of work done by each muscle can be covered approximately from the measurements of the excursions in different directions. Also, the part taken by the head in supplementing the various ductions is considered.

Duane quotes Fischer, who found, from the examination of six hundred cases, that under conditions of natural vision most persons could move the eyes only 12 degrees before calling in supplementary movements of the head. In many the range was less than this; in one only was it more.

The article closes with a consideration of the fields of ordinary and of forced excursion. In this former field the limits are usually between 40 and 50 degrees if fixed by the tension of the opposing muscles, and in the latter, i. e., in the field of extraordinary examinations, the excursion may be as much as from 70 to 80 degrees in, as much as 70 degrees downward and 50 degrees upward. Apparently, the extent of this is limited only by the check ligaments. The entire chapter is a most valuable one because of its lucid discussion of monocular movements, a subject that has, usually, many poorly chosen and loosely used qualifying and descriptive adjectives.

SPAETH, Philadelphia.

POSTURE OF THE HEAD IN TUMORS OF THE POSTERIOR FOSSA. B. S. BEILIN, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:664 (Feb.) 1932.

A characteristic posture of the head in lesions of the posterior fossa has been known since the time of Batten (1903). He reported a case of cerebellar tumor in which the head was bent toward the shoulders and the face was turned to the side of the tumor. This he found was directly opposite to the posture assumed after removal of the cerebellum. Stewart and Holmes found that the posture of the head is often characteristic in intracerebellar and extracerebellar lesions. The head is bent toward the side of the focus so that the chin points in the opposite direction. This posture is neither constant nor pathognomonic, for they found it in tumors of the pons, mesencephalon and frontal lobe. Other authors do not consider the posture of the head of much value in diagnosis, since it is turned now one way, now another. They have offered various explanations: Cushing looked on it as a defense against pain; Wilson, as a symptom of partial decerebration, and Horsley, as a vestibular sign. Brain found a rotated cerebellar position of the head in lesions of the internal ear, the eighth nerve, the pons, the midbrain, the cerebellum and the forebrain. He concluded that this posture is a consequence of disturbance of a tonic reflex from the labyrinth under the influence of which the extensor muscles of the neck maintain equilibrium and overcome the weight of the head. Experimental destruction of one labyrinth or auditory nerve produces a rotation of the head to the injured side. Foci in the pons, midbrain or forebrain can produce a rotation, either to the side of the focus or to the opposite

side. Foci limited to the cerebellum produce no rotation. There is rotation toward the diseased side in diseases of the middle ear and in tumors of the acoustic nerve. In five cases in which the pons and midbrain were involved there was rotation to the normal side. Cerebellar tumors may cause rotation either to the normal or to the diseased side.

Beilin studied the posture of the head in tumors of the cerebellopontile angle, tumors of the cerebellar hemispheres (extracerebellar and intracerebellar), tumors of the midline (vermis and fourth ventricle) and intrapontile tumors. There were twelve tumors of the cerebellopontile angle, all but one of which were tumors of the acoustic nerve. In all twelve cases there was a characteristic posture of the head: The chin was turned toward the side of the tumor; the ear was turned to the opposite side. In explanation of this, the following possibilities are suggested: 1. The spinal accessory nerve was irritated by the tumor and by overaction caused rotation of the head. 2. The posture of the head was compensatory for diplopia. 3. It arose as a disturbance in the tonus coming from the labyrinth and cerebellum.

The rôle of the spinal accessory nerve may be dismissed. While the head is rotated chiefly by the muscles innervated through the spinal accessory nerve, other muscles too are concerned, innervated through the cervical nerves. Hence, stimulation of the spinal accessory nerve alone is not enough to produce posture of the head in question. Furthermore, in Beilin's cases of tumor of the cerebellopontile angle, the chin was directed toward the side of the tumor. This indicates a loss of function of the eleventh nerve, rather than an overstimulation. Further, the eleventh nerve is rarely involved in tumors of the cerebellopontile angle. The suggestion that the posture of the head is a compensation for diplopia is not logical. According to this theory, the patient assumes a certain position of the head in order to shut out the false images. If the muscles rotating the eyes to the left are paralyzed, the head is turned to the left; if there is paralysis of upward and downward movement, the head is pushed forward. The difficulty with this theory lies in the fact that postures of the head of the type described in this paper were observed in patients without diplopia, that closing of the eyes does not change the position of the head, and that such postures are seen in blind patients.

The labyrinth, therefore, plays an important rôle in postures of the head. The otolith apparatus has a direct influence on the postures of the head (Ewald), and any pathologic change in this apparatus is followed by a corresponding change in posture. Beilin attributes the posture of the head in the cases of tumor of the cerebellopontile angle to an irritation of the vestibular nerve. Bartels found a deviation of the head in rabbits after section of the eighth nerve, similar to the posture in the cases of tumor of the angle. After section of the right acoustic nerve the snout was turned to the left and vice versa. Similar results were observed by Leidler and van Gehuchten. After section of the vestibular nerve and the fibers from the vestibular nerve to the posterior longitudinal bundle, they found a deviation of the head toward the side of the focus; if the latter fibers were cut at the level of the genu of the facial nerve there was, in addition to the rotation of the head, a rotation of the body on its long axis.

Beilin was unable to find any constant posture of the head in his cases of cerebellar tumor. In extracerebellar tumors the posture of the head was similar to that in the tumors of the cerebellopontile angle. In cases of intracerebellar tumor, the posture of the head is exactly the opposite from that in tumors of the angle; that is, the chin is turned to the healthy side and the back of the head is toward the tumor.

In midline tumors of the posterior fossa the posture of the head is characteristic. Beilin's findings agree with those of Heuvers, that in cases of block between the third and fourth ventricles the head is flexed backward, but in cases of block between the fourth ventricle and the cisterna magna the head is bent forward in order to relieve the compression of the medulla.

In intrapontile tumors, the head may be turned either to the healthy or to the diseased side.

ALPERS, Philadelphia.

PERSONALITY AND GROUP FACTORS IN THE MAKING OF ATHEISTS. G. B. VETTER and MARTIN GREEN, J. Abnorm. & Social Psychol. **27**:179 (July-Sept.) 1932.

In this attempt at a study and analysis of an atypical opinion group, 600 questionnaires were sent by mail to a random sample of the members of the American Association for the Advancement of Atheism. Three hundred and fifty replies were received. The results when tabulated were as follows:

Age Distribution: The ages were grouped in five year classes and compared for distribution with similar groupings for the male sex in the census data for the United States of 1920. In general, the atheists include less than a chance quota of the age groups below 50 years. Between 50 and 60 the ratios are about even. About 60, the atheist age groups are larger. The only exception is that the age group of 30 to 34, inclusive, has about 4 per cent more than its chance quota.

Place of Birth: For purposes of regional comparison the states were grouped into five divisions, Northeast, Middle West, South, Great Lakes and Far West. The percentages of atheist distribution were then compared with the total populations of these groups in the United States census of 1900. All these groups of states, with the exception of the Southern group, contributed more than their proportional quota to the atheist sample, particularly the Northeast and Far West. The South alone ran far behind.

Sex: Of the 350 questionnaires returned, 325 were from men. This is about the ratio of the sexes in the total membership roll of the organization.

Parental National Origins: The parents of 24 per cent of the atheists were born in different countries. For the population as a whole this percentage is about 8. Only 42 per cent of the atheists' parents were native American born.

Religion of Parents: Protestant parents contribute more than their quota when compared to the number of them in the United States, Catholics much less. The single exception is in the case of Baptist parentage. Jews and Methodists seem to make the largest proportional contribution to the ranks of the atheists.

Changes in Parental Religious Beliefs: In only 30 cases was a change reported.

Intensity of Religious Activity and Observance: Atheists rated their parents as of more than ordinary piety.

Preference for a Parent: Twenty-seven per cent reported being more congenial with the father, 73 per cent with the mother.

Mortality of Parents: One half of the atheists had lost one or both parents before they were 20 years of age. This is at least twice the normal mortality rate for that age group. The atheists comprise twice as many of oldest children as of youngest children.

Education: About 14 per cent of the atheists had a parochial school background. Thirteen per cent had some contact with private schools. From the best estimates that could be obtained of parochial school enrolment it would seem that the group contained about twice the chance number of parochial school products. The percentage of atheists with three years of high school exceeds by 24 per cent the average for the population as a whole; high school graduates exceed the population average by 29 per cent and 39 per cent have at least four years of college or professional school training.

Ages of Leaving Church and of Becoming Atheist: In the group from 15 to 19 years, 46 per cent had left the church and 35 per cent had become atheists. The next largest numbers (21 per cent) were converted to atheism between the ages of 20 to 24.

Personal Data: Almost a third of the group reported that they believed that they had had both an unhappy childhood and an unhappy adolescence.

Other interesting findings were: Over three fourths of the group reported living in urban districts (one half of the general population was rural at the time the median atheist of this group lost his faith). At the time when they dropped their religion, twice as many were living in places where their own faith was a minority group as were living where their own faith was the dominant one. A typical case is that of the Catholic who became an atheist while living in Salt Lake City. At the time when they broke with their religious faith only 21 per cent were married. Of the unmarried, 79 per cent, about one-half reported having

had sexual intercourse. The marriages of the atheists exhibited a tendency already noticeable in the marriages of their parents, that of marrying persons with faiths other than their own, 43 per cent to persons of different religious stock. The results showed a high percentage of change in political opinions toward the radical end of the spectrum. Before becoming atheists, only 26 per cent were socialists or communists; now, 54 per cent are socialists or communists. All but 18 per cent openly avowed their antireligious opinions and beliefs. Fifty-eight per cent claimed that their atheism interfered with either their social or their business life or both. Forty-two per cent found their opinions no bar or handicap whatever.

WISE, Howard, R. I.

LIBIDINAL TYPES. SIGMUND FREUD, Psychoanalyt. Quart. **1**:3 (April) 1932.

On the basis of the predominance of libido investment in the mental apparatus, Freud describes certain psychologic types of human beings. He states that a classification should be more than a mere corollary from our knowledge or assumptions about the libido. It should also be recognizable in everyday experience, and should serve as a tool for clarifying observations. In the psychic field these libidinal types need not be the only ones, and one might establish a great number of other psychologic types by taking other characteristics as a starting point. But in any case, these types should not coincide with clinical pictures. On the contrary, they should include all the variations which, practically speaking, fall within the limits of the normal. Their extreme forms, however, might approximate clinical pictures, and in this way help to fill in the supposed gap between the normal and the pathologic.

Freud describes the three main types as follows: The erotic type is seen in persons whose chief interest — the relatively largest amount of libido — is bestowed on the love life. To love and, more particularly, to be loved are all-important for them. They are mastered by the fear of losing love, and are therefore especially dependent on others who have love to deny them. Even in its pure form this type is frequent.

The compulsive type is distinguished by the predominance of the super-ego, which is differentiated from the ego under high tension. This type is mastered by the fear of conscience instead of by the fear of losing love; he is, so to speak, inwardly rather than outwardly dependent; he displays a high degree of self-reliance, and becomes the actual, for the most part, conservative pillar of civilization.

The narcissistic type is essentially negatively characterized. There is no tension between the ego and the super-ego. There is no predominance of erotic needs. The chief interest is directed toward self-maintenance. The individuals are independent and seldom intimidated. A large amount of aggression which, moreover, is expressed in readiness for activity, is available to the ego. Loving is preferred to being loved. People of this type impress others as "personalities" and are peculiarly fitted to serve as support for others, to assume the rôle of leadership, to add new stimulus to cultural development or to attack the existing order.

The mixed types — erotic-compulsive, erotic-narcissistic, and narcissistic-compulsive — occur much more frequently, and seem actually to permit of a satisfactory grouping of the individual psychic structures as they have come to be known through analysis. In the erotic-compulsive type the power of the instinctual life seems restrained by the influence of the super-ego. The simultaneous dependence on present day human objects and on the survivals of parents, teachers and persons who serve as models reaches an extreme degree in this type. The erotic-narcissistic type has the greatest frequency. It combines antitheses that may be mutually reduced by the combination; one may learn from this type, in comparison with the other two erotic types, that aggression and activity are in direct proportion to the predominance of narcissism. The narcissistic-compulsive type proves to be the most valuable variation for civilization, for it combines vigorous activity with outward independence and respect for the dictates of conscience, and reenforces the ego as opposed to the super-ego.

Another mixed type, theoretically possible, namely, erotic-compulsive-narcissistic would be no type at all, but the absolute norm, the ideal harmony. One thus becomes aware of the origin of the phenomenon of the type: One or two of the three chief investments of the libido have been favored to the advantage of the other.

The question of the relation of these libidinal types to pathology can be answered by saying that the definition of these types throws no new light on the genesis of the neuroses. All of the types may exist without neurosis. The pure types with a definite preponderance of one of the mental faculties (*Instanzen*) would seem to have the better chance of appearing as pure character forms, while one might expect the mixed types to offer a more favorable soil for neurotic conditions. No final decision should be made about these relationships without specially directed, careful investigations.

The erotic types correspond with hysteria in case of illness and the compulsive types with obsessional neurosis, but this supposition shares in the uncertainty just mentioned. The narcissistic types, since they are exposed to rebuffs from the outer world by virtue of their general independence, have a special disposition to psychosis, and for the same reason are peculiarly susceptible to criminality.

PEARSON, Philadelphia.

POLIOMYELO-ENCEPHALITIS: TREATMENT BY HUMAN IMMUNE SERUM. JEAN MACNAMARA and F. G. MORGAN, Lancet **1**:469 (Feb. 27); 592 (March 5) 1932.

Between November, 1924, and August, 1931, 873 known cases of poliomyeloencephalitis occurred in Victoria, Australia. One hundred and thirty-three patients were treated with human immune serum. No patient was benefited after paralysis had set in; so serum therapy in cases advanced to this degree was discontinued.

The authors describe the usual method of treatment with the serum as it has been carried out in many centers in this country. They believe that lumbar puncture is not essential for the making of an accurate diagnosis in all cases. When it is performed, the fluid is immediately examined, the needle remaining in place for the introduction of serum if a diagnosis of poliomyelitis is made. In estimation of the dose of serum required, the following factors were taken into consideration: the age and size of the patient; the degree of toxemia; the stage of the epidemic; the duration of the illness, particularly the signs of meningeal involvement, and the cerebrospinal fluid findings. A number of patients were seen in whom a history of an undiagnosed illness, lasting for from a few to as many as eight days, was obtained. This was followed by an interval of apparent recovery lasting for from two to three days. A second phase of the illness, however, soon occurred, with pain in the neck and back, fever and a "spine sign" described by the authors. Such a patient is in grave danger unless serum is administered quickly. The development of tremor and of hyperesthesia suggests that some involvement of the motor cells and sensory ganglia has occurred. such symptoms call for a larger dose than should be given to a patient under suspicion in whom the "spine sign" has developed after a few days' observation. The type of cell found in the spinal fluid may be of assistance in estimating the dose required. When most of the cells are lymphocytes paralysis is not far off, and therefore the dose should be very large.

The initial dose of serum used has rarely been less than 50 cc. After the cerebrospinal fluid has been allowed to escape, a slightly smaller quantity of serum is administered intrathecally, and the remainder of the dose is given intravenously even though venesection may be necessary. The patient should be carefully reexamined twelve, eighteen and twenty-four hours later. Even though the dose has been adequate, spinal rigidity may persist, but the temperature falls and the general condition definitely improves. These patients are usually constipated, dehydrated and slightly acidotic, as the pain in the neck prevents the

ingestion of sufficient fluid. Therefore, after administration of serum, a brisk aperient should be administered and carbohydrate and fluid be given freely. If improvement was not marked within eighteen hours, it was considered that an insufficient dose had been given, and a further dose of from 30 to 40 cc. was injected intravenously. The failures in the series have taught the authors the importance of examination twelve, eighteen and twenty-four hours after the first injection of serum, with subsequent injections if no improvement is manifest. Furthermore, such frequent examinations have demonstrated that the use of an antiseptic substance in the convalescent serum is injurious. It is emphasized that the virucidal property of the serum available for use should be repeatedly tested by inoculation of monkeys against specimens of serum obtained in the different epidemics. The writers suggest careful after-care of all potential donors in the intervals between epidemics for the provision of serum stock in an emergency.

Only seven failures were recorded in the complete series treated. Four of these cases shared one feature in their course in common, namely, delay between withdrawal of a large quantity of cerebrospinal fluid and the administration of serum. With one exception they are the only cases in which this delay occurred. In the others, examination of the fluid had been made forthwith and serum administered within one hour after lumbar puncture. It is therefore probable that the failure in these cases may have been due to one or both of two factors: (1) delay, the elapse of hours, allowing death of the anterior horn cells to occur before passive immunity was induced, and (*2*) the fact that the actual withdrawal of large quantities of cerebrospinal fluid during the preparalytic stage may have actually determined an involvement of the cord.

It is of interest to note that in 84 of the specimens of spinal fluid examined in which determinations of chloride were made, the content ranged from 700 to 760 mg. per hundred cubic centimeters. This normal chloride content in the presence of pleocytosis is strikingly important as a diagnostic aid.

BECK, Buffalo.

SLEEP AND THE BRAIN CORTEX. J. A. M. A. **98**:2291 (June 25) 1932.

In an exhaustive review of sleep, a subject that concerns the physician as well as the layman in many ways, Kleitman (Sleep, *Physiol. Rev.* **9**:624 [Oct.] 1929) of the University of Chicago remarked that the problem has yet to be solved. There is no authority but that of facts, and until isolated observations have been repeatedly confirmed they cannot be classed as established facts. We are so commonly accustomed to think of sleep as part of the physiology of the brain that we may fail to consider to what extent other parts of the body or their functions may be responsible for, or involved in, the more or less complete unconsciousness under discussion. Is the cerebral cortex an essential factor in sleep? In attempting to answer this important query, physiologists have been reminded of the published records indicating that decorticated animals can sleep. This was true, for example, in the classic observations of Goltz in 1892. He reported that dogs deprived of their cerebral cortex exhibited phenomena of sleep.

In this connection the distinctions that have been stressed by Szymanski (*Arch. f. d. ges. Physiol.* **171**:324, **172**:424, 430, 1918; *Ztschr. f. allg. Physiol.* **18**:105, 1920) in interpreting the phenomena of unconsciousness may be recalled. He demonstrated conclusively that some animals have one long period of rest in twenty-four hours and that others have several such periods. He termed them monophasic and polyphasic animals. The polyphasic are the "lower" animals, which make little use of their distance receptors for obtaining information about what is going on around them. Szymanski points out, however, that even among the monophasic animals, including man, the young are polyphasic. In the case of adult man, interest centers in the monophasic manifestation often referred to as diurnal sleep, represented by the characteristic prolonged periods of unconsciousness and comparative inactivity. Dogs exhibit the same phenomena.

In a reinvestigation of the possible existence and localization of a sleep center, Kleitman and Camille (Studies on the Physiology of Sleep: VI. The Behavior of Decorticated Dogs, *Am. J. Physiol.* **100**:474 [May] 1932) of the University of Chicago Department of Physiology have observed that decorticated dogs have several periods of sleep alternating with periods of activity each twenty-four hours. Their activity consists of almost incessant walking in circles. The most constantly occurring period of sleep follows shortly on feeding. The conclusion is made that diurnal sleep in dogs depends on the presence of the cerebral cortex for its establishment and persistence. In other words, normal dogs can stay up all day and then sleep through the night, whereas decorticated dogs have half a dozen periods of sleep in twenty-four hours.

The Chicago physiologists accordingly believe that there is no conflict between the subcortical and the cortical theories of sleep. The first account for sleep in general, the second for the special diurnal type of sleep seen only in higher animals and in man. As Kleitman and Camille point out, diurnal sleep, developed around the twenty-four hour cycle of day and night, is thus a definitely cortical phenomenon, has its center or is localized in the cerebral cortex, and disappears when the cortex is removed. That explains, they add, why all those who study the sleep of higher animals and man cannot help seeing the tremendous influence of cortical processes, habits and conditioned reflexes on the onset of sleep. In man the habit of going to bed at certain hours and of waking up at a definite time each morning is not inborn but acquired by experience. That the subcortical sleep tendencies are ever ready to exert their action is demonstrated by the fact that most people can fall asleep not only at their habitual bedtime but at almost any time, if a condition is brought about wherein the number of afferent impulses reaching the cerebral cortex is greatly reduced. After a meal the primordial tendency to sleep is especially powerful and asserts itself with great ease, if permitted to do so. As Kleitman has elsewhere pointed out, practically we are born into a social organization in which diurnal sleep is the universally accepted mode of sleeping. The new-born baby is a truly polyphasic creature, to use Szymanski's classification. The first habit the mother tries to develop in a baby is that of an unbroken night's sleep. As he gets older, other functions develop a periodicity that coincides with the enforced sleep periodicity. For instance, a temperature curve develops, with a minimum at night, and produces a disinclination to activity at night. Even the modest tear apparatus stops its function at bedtime, producing dry eyes and favoring their closure. Attempts to influence or induce sleep may well be based on some of the fundamental facts now on record.

EDITORIAL.

SYMMETRICAL AND ANALOGOUS ASSOCIATED MOVEMENTS IN ONE EXTREMITY DURING PASSIVE MOTION AND ELECTRICAL STIMULATION OF THE OTHER HOMONYMOUS EXTREMITY. LEO ALEXANDER, J. f. Psychol. u. Neurol. **44**: 177, 1932.

Two cases are described in which, following active motion, with, as well as without, reenforcement of one upper extremity, there appeared analogous symmetrical associated movements in the contralateral upper extremity. The associated movements also appeared following passive motion and during electric stimulation. The associated movements were limited to the distal segments of the extremity, especially the fingers. In one patient with cerebral infantile paralysis, associated movements in the paralyzed arm could be elicited only by passive motion and by electric stimulation of the nonaffected arm, whereas in the other patient, who had postencephalitic parkinsonism and who also had suffered from epileptiform seizures until puberty, associated movements could be elicited in either upper extremity by electric stimulation and by passive motion of the other upper extremity. Occasionally, under certain conditions, such as feeble electric stimulation, associated movements could be elicited which, though not analogous, were markedly symmetrical in the homonymous segment of the opposite limb. These were the only

2 of a total of 53 cases of cerebral infantile paralysis, postencephalitic parkinsonism, arteriosclerotic and syphilitic hemiplegia, Huntington's chorea, chorea minor and various forms of epilepsy, in which contralateral associated movements could be elicited during passive motion and electric stimulation. There were 38 cases of postencephalitic rigidity, with disturbances in the normal associated movements of the upper extremities during walking in 34 cases; these disturbances were bilateral in 18 and unilateral in 8; in 2 cases they were absent on one side and pathologically increased on the other; in 4 cases they were absent on one side and diminished on the other, and in 2 they were diminished on one side and normal on the other. Only 4 patients with postencephalitic rigidity showed no disturbances of the normal associated movements in the arms while walking. In 20 of the 38 cases no contralateral associated movements were observed. In 17 cases, contralateral associated movements were elicited only on intensive reenforcement, and in only 1 case could symmetrical analogous associated movements be elicited in one hand during active motion of the other, even without reenforcement. In none of the 38 cases of postencephalitic rigidity could contralateral associated movements be elicited during passive motion or electric stimulation. This, according to Alexander, would seem to indicate that the loss of normal associated movements during walking bears no relationship to pathologic contralateral associated movements. These two conditions are apparently dependent on different localizations of the pathologic process.

Contralateral associated movements are by no means uniform manifestations. First, there can be distinguished among them those induced by active motion with reenforcement and those which may also appear without reenforcement. Of an entirely different character are the contralateral analogous associated movements induced by passive motion and electric stimulation. Most frequent are the associated movements observed during reenforcement, less frequent those without reenforcement and least frequent those occurring during passive motion and electric stimulation. In the cases in which contralateral associated movements appeared during passive motion and during electric stimulation, the former also appeared during active motion with and without reenforcement. The reverse, however, of this was not true.

The paper is concluded with a lengthy discussion of the pathophysiology of associated movements. The discussion, however, is based on a review of the literature on the subject and on pathologic observations in cases, reported by other observers, which the author believes were similar to those studied by him clinically for this contribution.

KESCHNER, New York.

METASTATIC CARCINOMA OF THE OPTIC DISK. WILLIAM THORNWALL DAVIS, Arch. Ophth. **8**:226 (Aug.) 1932.

Metastatic conditions connected with the central nervous system are not especially frequent. Of tumors which metastasize, only 4.77 per cent involve the central nervous system. Davis considers first, briefly, the rarity of metastases to the intra-ocular portion of the optic nerve. He was able to find only 3 instances in the literature, while one observer alone reported 118 cases of metastatic carcinoma of the choroid. Of the 3 cases of metastases into the papilla, one was a glioma reported by Grinker (Tumors of the Optic Nerve, *Arch. Ophth.* **4**:497 [Oct.] 1930); the second, a scirrhus cancer, reported by von Graefe, and the third, also a scirrhus cancer, reported by Knapp (Knapp, H.: A Case of Carcinoma of the Outer Sheath of the Optic Nerve Removed with Preservation of the Eyeball, *Arch. Ophth. & Otol.* **4**:323, 1874).

Davis' case was one of scirrhus cancer of the right breast; an operation had been performed six months prior to the presentation of the ocular symptoms. At that time recurrences were also present in the original field of operation. An examination of the fundus of the left eye revealed the nasal half to be elevated about 6 diopters. This portion of the disk was separated from the normal temporal half sharply, so that there was a perpendicular wall dividing the halves, producing a most unusual appearance. The elevation extended into the retina above for 3

disk diameters, below for 4, and nasally for 8 disk diameters, gradually sloping off to the normal retinal level. The surface of the elevation was grayish white. There was no movement or undulation over it. It was indistinctly lobulated. The vessels were normal as they lay on it. It was thought, at the time of the examination, that this elevation of the disk and retina was due to an intracranial metastatic carcinoma that extended along the sheath of the optic nerve without involving the nerve itself to any extent, as indicated by the visual fields.

Three months later, there was further definite increase in the pathologic condition. The highest point of the elevation was now opposite the temporal edge of the disk. The outlines of the elevation were as first described, involving the inferior temporal artery and vein, the inferior nasal artery and vein, the superior nasal artery at its beginning and the nasal branch of the superior nasal artery and vein. The patient died one month later, apparently from a cerebral growth. No autopsy was obtained.

This paper was presented at a medical meeting and was discussed rather extensively. The discussion brought out that perhaps the principal reason for the rarity of carcinomatous metastases to the orbit is that the ophthalmic artery leaves the internal carotid at a right angle, and that metastases into the disk from the choroid are not so uncommon. Suker cited the case of an infiltrating tumor mass in the left middle fossa; at autopsy it was found that it involved the medial half of the middle fossa, the left half of the temporal lobe, the posterior half of the left frontal lobe, the left side of the pons and the left optic tract and chiasm. The tumor extended into the left optic foramen, and filled the posterior third of the orbit with soft tumor tissue. Goldstein and Wexler reported metastasis to the optic nerve and its sheath.

Some of the conclusions in the discussion are: Metastatic carcinomas within the eyeball and into the optic nerve up to the chiasm are not so unusual as the statistics of Clapp, Suker and Grosvenor would indicate, for the following reasons: The intra-ocular metastasis is often very small and in such sections of the fundus as not to cause more visual disturbance, because the patient is frequently in a state of carcinomatous cachexia; the metastasis in the choroid is frequently of slower growth than metastasis in the brain or elsewhere, and the patient succumbs before attention is attracted to the eye.

Only too infrequently is the eyeball included in a routine postmortem examination. Many globes taken from patients who have died of carcinoma have shown choroidal carcinoma.

SPAETH, Philadelphia.

COLLECTED PAPERS, RESEARCH INSTITUTE OF EXPERIMENTAL THERAPY, MOSCOW, STATE MEDICAL PUBLISHING COMPANY, 1932, p. 139.

This interesting volume is devoted to the studies of a special research institute which was established by its director, J. G. Liwschitz (since deceased), who was responsible for organizing this institute for experimental therapy and under whose direction the various research problems were studied during the first year of its work. The director was especially interested in chronic conditions, such as dementia paralytica and schizophrenia, in which pharmacologic therapy has only a limited application, and in which he believes that a more specific biologic therapy would be of more use. Special attention was devoted to the preparation of the extracts of the various organs on the basis of the theory that some substances have a special inhibitory or stimulating effect on the respective organs from which they are derived.

Liwschitz found that lipoids are of a special significance in neurosyphilis by virtue of the fact that lipoids are known to bind the excessive antigens in the organism, thus making the defensive reactions available more quickly and efficiently in the fight against the spirochetes. He has isolated a special substance from the brain, which was largely used in these experiments. In a group of 73 cases of various forms of syphilis of the central nervous system, 36 patients were able to return to work, 23 improved a great deal, slight improvement was noted in 4 cases, there was no change in 7 cases, and in 3 cases the treatment did not alter

the progress of the disease. Lipocerebrin was given every day intramuscularly or subcutaneously in doses of 2 cc.

D. V. Kissin and A. M. Simskaja report the chemical analysis of lipocerebrin. It is an alcoholic extract of the brain in the form of an emulsion. The total nitrogen was 1.12 per cent, cholesterol 37 per cent and phosphorus 1.37 per cent, which means that the phosphates made up about 30 per cent of the preparation and that 13 per cent was cerebrosides. There are probably other substances which are not known. A study of the metabolism of the patients before and after treatment with lipocerebrin was made by Dodogorskaja. There was no significant difference in the residual nitrogen, uric acid, potassium and calcium in the blood. The cholesterol content was studied in 52 patients, showing definite diminution in the blood after treatment. In the patients who improved, the lecithin phosphorus was definitely increased, due to the introduction of the outside phosphorus in the lipocerebrin. In spite of the fact that lipocerebrin contains a great deal of fat, its injection intravenously into animals did not result in embolism. It was also found by Birjukow that lipoids were definitely increased and slowly returned to normal after intravenous injections. The brains of animals which were studied after treatment showed increase in the lipoid content of parenchymatous cells and pointed to an increased functional activity of the cells.

In addition to the work on neurosyphilis, Zetlin reports his results with a testicular extract, which in castrated roosters caused the reappearance of secondary sex characteristics, resulting especially in a growth of the comb. The results are similar to those obtained by Moore, Gallagher and Koch (*Endocrinology* **13**:367, 1929). Birjukow and Liwschitz found that simultaneous injections of dextrose and trypan blue increased the permeability of the cerebrospinal fluid barrier. The experiments were done on rabbits, and autopsy was performed five days after the original injection; even when dextrose was given a few hours before, the same phenomenon took place.

The whole volume shows striking, fresh and original ideas, with a marked tendency to theorize, and speculation combined with a certain lack of critical judgment, which bespeak the enthusiasm of the authors. The book is characteristic of the work done in Russia, where one encounters a good deal of originality, enthusiasm and faith.

KASANIN, Howard, R. I.

MULTIPLE AND SYMMETRICAL PARALYSES OF THE CRANIAL NERVES, OF SUCCESSIVE EVOLUTION, ASSOCIATED WITH A GENERALIZED PARETIC CONDITION: INFECTION OR INTOXICATION. ANDRÉ-THOMAS AND H. SCHAEFER, Rev. d'oto-neuro-opht. **10**:253 (April) 1932.

The tendency is more and more to attribute to infection a certain number of syndromes of the nervous system that attract attention by their rapid appearance and by the diffusion of their symptoms. A man, aged 30, was seen on Oct. 1, 1931, complaining of diplopia, nasal voice, dizziness, vague pains in the arms and lassitude. The troubles had existed for about eighteen days. He felt queer when he walked, was agitated and had diplopia. Two days later the nasal voice appeared, and liquids were regurgitated through the nose. There had been no sore throat, fever, vomiting or any previous infectious disease. Ten years previously some visual difficulty and dizziness had existed. Two years before, he had been seized suddenly with malaise and vomiting, and had a sensation of emptiness of the head. Examination revealed: limited excursion outward of the eyes, homonymous diplopia, which was increased on looking to the right and left, normal visual acuity and fields and perfect accommodation and eyegrounds; the palate was immobile; the pharyngeal reflex was present, and the larynx normal. Sensibility and the reflexes were normal, except on the internal borders of the forearms and hands. The patient had noticed, some days previously, some involuntary movements of flexion of the fingers and, in typing, he did not feel the keys so well. Lumbar puncture revealed a normal fluid, except for a slight increase in albumin, with no lymphocytosis. The Bordet-Wassermann reaction was negative in the fluid and in the blood. Following the puncture there was

slight transitory stiffness of the neck and slow micturition. On the following day the bilateral paralysis of abduction was complete, and movements of elevation were not complete. Flexion of the fingers was weak, as were also the pronation reflexes and the styloid and olecranon reflexes on the left. They were abolished on the right side. Movements of the feet and toes were feeble. In swinging the arms, the excursions in the right were a little more ample. The patient grew worse; paralysis of the superior recti became complete. Action of the levator palpebrae was feeble, and he was much depressed and fatigued. The neck was stiff; respiration and pulse rate were slow, and the tendinous and osteoperiosteal reflexes in the arms were abolished.

Under the intravenous use of sodium salicylate, with camphorated oil and epinephrine subcutaneously, the patient began at once to improve. The nasal voice and difficulty in swallowing disappeared, but a bilateral facial paralysis occurred, which was more marked on the left side, and Kernig's sign was faintly positive. At the end of four weeks all the paralyses had disappeared.

The clinical picture suggested an infection or intoxication that affected the neuraxis throughout its whole extent, but with a predilection for the pedunculobulbopontile region. The paralyses of the cranial nerves were characterized by their short duration, perfect symmetry and by their successive evolution during active treatment. They resembled postdiphtheritic paralysis in their rapid course and in their departure from the palate when the limbs became involved. If this case had occurred during an epidemic of encephalitis, it would doubtless have been classed as such. Perhaps some infections act like encephalitis by their diffuse localizations, and others act especially by intoxication. Both hypotheses can be defended. The prognosis must be guarded, as relapses may occur.

DENNIS, Colorado Springs, Colo.

SIZE AND SHAPE OF OCULAR IMAGES. METHODS OF DETERMINATION AND PHYSIOLOGIC SIGNIFICANCE. A. AMES, JR., GORDON H. GLIDDON and KENNETH N. OGLE, Arch. Ophth. **7**:576 (April) 1932.

Leaving aside pathologic conditions, one usually considers only two factors in determining whether the eyes of a person are functioning properly: first, the refraction, and second, the muscle balance. If there are emmetropia and orthophoria for both distance and near vision, it is assumed that there is nothing the matter with the function of the eyes. There is a third factor, however, which appears to be of importance. This is the relative size and shape of the ocular images of the two eyes. The importance of this factor becomes evident when one considers the use of the eyes in binocular vision and the physiologic part played by the brain when the ocular images of the two eyes are combined.

The authors first discuss stereoscopic vision from the standpoint of the eyes acting as a stereoscopic camera. In the superposition of the two images, one on the other, regardless of where this superposition occurs, three conditions are necessary: (1) The two cameras must be pointed toward the same object field; (2) the images must be in sharp focus, and (3) they must be of the same size and shape. Further, they discuss the distribution of the nerve elements in the two eyes, in that, by reason of an unequal distribution of these elements, unequal sizes of the images could occur.

The methods of determining differences in the size and shape of the ocular images and the apparatus are described in detail. Various probabilities are then presented relative to the physiologic effect and nature of the size and shape of ocular images, as to (1) the rôle they may play in vision, (2) the locus of manifestation of size differences, (3) threshold sensibility to a difference in the size and shape of the ocular images, (4) size and amplitude, (5) the correlation of a change in the size and shape of the ocular imagines with other ocular functions and (6) difference in the size and shape of ocular images as a disturbing factor in vision.

From the standpoint of the ophthalmologist, the work that these investigators have done is most important. They have shown under these various headings that a difference in size causes not only a false interpretation of binocular depth, but one that varies with different distances of fixation. They seem to think that the locus of the beginning of an excitation arising from differences in the two ocular images is not in the eyes but in the brain, where the images from each eye are combined. They discovered that differences in the size of the ocular images exist with other ocular functions, especially in fusion and the phorias. As to the difference in the size and shape of the ocular images as a disturbing factor in vision, they suggest on the basis of their work various possible reasons. The author's concluding paragraph follows:

"In general, it can be said that associated with an abnormal difference in the size and shape of the ocular images there is a derangement of the space world as known from binocular vision. Moreover all abnormal differences in the ocular images constantly make themselves known through disturbances in visual perceptions. There would naturally be an attempt to correct such differences through alterations of the size and shape of ocular images. As size and shape of ocular images are apparently correlated with other functions of the eyes, there is a possibility that they play a major rôle in the functioning of the eyes and may be responsible for at least some of the ocular conditions and abnormalities of functioning that are not now thoroughly understood."

SPAETH, Philadelphia.

THE IMPACT OF CULTURAL FORMS UPON CHILDREN'S BEHAVIOR. JOHN LEVY, Ment. Hyg. **16**:208 (April) 1932.

Not all of the burden of a child's development is to be placed on his emotional or physical adequacy; rather must some of this duty be assigned to society. Children of similar psychic and physical constitution will develop different types of behavior under different social influences. Indeed, one fruitful source of conflict is social instruction—that is, discipline. For example, in children from superior social strata personality problems result from the dual attitude of love and fear toward the parents, while children from inferior economic classes come into conflict with social authority rather than with their own parents. In either case the problems of the child in a civilized community contrast with the cheerful, untroubled maturation of the barbarian in Samoa whose cultural simplicity permits little conflict. The Samoan household consists of thirty or forty persons loosely connected by blood; all of the women assume a maternal rôle toward all of the children; authority is thus so widely dispersed that rebellion is impossible and emotional attachment is innocuous.

The Oedipus complex is an example of the influence of social force rather than an instance of instinctive human response. Thus, in Trobriand Island, society is matrilineal, the family being supported by the mother's brother. Paternity is not understood, and the uncle receives the emotions—love or jealousy—attaching to the father in our culture. In this community, brother and sister are separated and must not show any intimacy; incest between these siblings is the gravest of crimes. Dreams described by the Trobriand Islanders show an interest in precisely this forbidden relationship. There is no taboo on sexual play or overt heterosexual advance with members of another family, and in these islands perversions and frigidity are practically unknown. This may be compared with the sex inhibitions imposed by modern Western culture, resulting (Levy believes) in masturbation, perversion and sexual delinquency. It is probably true that romantic love cannot exist in another type of family and sexual organization, so that it would appear that the emotional and ideal aspects of the relationship blossom as the physical directness of it is hampered.

Not only are the cultural characteristics and the adjustment problems much the result of social forces, but basic temperamental qualities may be viewed as resulting from such conditions. The contemplativeness of the Hindu, the musical

inclination of the Negro, the stoicism of the Indian, the passionateness of the Spaniard, the practicalness of the American—are all explicable as responses to simple social forces. Thus, in India, no premium is placed on speed; competition is an inconsequential force. Persistence and patience thus become the desirable Hindu traits.

Even sanity may be considered, to an extent at least, as a cultural concept. Thus in Dobu, every one outside of one's immediate family is considered a witch bent on one's destruction. The generous or tolerant nature is abnormal there, and would be considered insane. On the other hand, a fiercely paranoid attitude is accepted as the proper and right-thinking point of view.

It is well, therefore, to seek for social forces rather than for inherent personal inadequacies as explanation of conflict.

DAVIDSON, Newark, N. J.

THE PATHOGENESIS OF THE CONNECTIVE TISSUE AND GLIAL ENCAPSULATION OF BRAIN ABSCESSES. E. KNAPP, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:44, 1932.

The human body attempts to wall off abscesses in the brain, just as elsewhere in the body, in order to protect itself against bacteria and their toxins. This capsule consists of younger or older connective tissue, depending on the age of the lesion. There are three zones in the connective tissue encapsulation of brain abscesses: (1) an inner granulation zone consisting of round cells, capillaries and nerve elements; (2) a demarcation zone with many vessels, glia, plasma and round and spindle cells, the latter being derivations of the vascular adventitia and giving rise to an intercellular, fibrous substance; (3) an irritative zone, the appearance of which depends on the strength of the capsular formation. In fresh abscesses without capsule, there are dilated vessels in this zone with leukocytes, lymphocytes, plasma cells and histiocytes. In a well formed capsule, on the other hand, there are few exudative elements.

It was unknown for some time that the demarcation zone of an abscess could be formed of neuroglia instead of connective tissue. Investigators in the early twentieth century asserted that neuroglial elements took no part in the capsular formation of abscesses. Recent studies, such as those of Diamond and Bassoe, make similar assertions. Balado and Franke found that many abscesses of the brain are surrounded not by one, but by several, capsules, all of which are fibrous and not neuroglial. There are some authors who assert that the neuroglia does take part in the formation of abscess capsules. Nauwerck described an abscess capsule composed entirely of neuroglia. His case was that of a man, aged 63, in whom, following a revolver shot in the head thirty-eight years before presentation, an abscess in the left frontal lobe developed. There was some pus in the abscess, but the wall was composed of pure glial elements.

Knapp investigated nineteen cases of brain abscess, regardless of their age or etiology. In one case, the cause of his report, there was an abscess, four and one-half years old, which followed a shot in the head. The capsule in this case consisted almost entirely of neuroglial elements, with some fibrous tissue structures. Homen asserted that in the formation of brain abscess both connective tissue and glial elements take part, the former predominating. Lowendowsky believed that the neuroglia takes part in the process only in scar formation after operation. Nauwerck maintained that the glial capsule follows on a connective tissue capsule, but how this metamorphosis takes place is left unexplained.

In none of the other eighteen cases was there evidence of participation of the neuroglia in the capsule formation. Knapp found that the formation of a capsule does not depend entirely on the age element. He found a capsule in an abscess which was only two or three weeks old and failed to find them in abscesses which were a year old.

ALPERS, Philadelphia.

INDUCED MOVEMENTS. F. M. LISSIZA, Sovjetsk. Psychoneurol., 1931, nos. 2-3.

Lissiza presents the first case in the literature of induced changes of tone (*induzierte Tonusveränderungen*), described by K. Goldstein, that has been studied histologically. The changes were excited in the contralateral upper limbs under the following conditions: When one forearm was drawn aside and a little upward, the other arm slowly repeated these movements, remaining in the terminal attitude as long as the passively abducted arm was kept in this attitude. (Superficial irritations did not excite such movements.) Furthermore, in the right arm, in which the induced movements were in general more intense, the same movements were brought about also by extension of the homolateral knee joint. From time to time the induced movements were followed by dyspnea and facial movements.

On histologic study, a glioma affecting the white and part of the gray substance of the lower part of the left parieto-occipital lobe was discovered. This glioma originated in the dorsal part of the right temporal region and insula, but did not reach the nucleus lenticularis; then it grew into the corpora quadrigemina, and finally affected other regions (brachia conjunctiva), growing in patches. Lissiza assumes that the patchlike manifestations were the latest. Important changes in the cells were observed in: (1) the nuclei rubres; (2) nucleus oculomotorius, bilaterally; (3) the upper part of the medulla oblongata and tegmentum pontis (including the substantia reticularis of this region); (4) the caudatum and putamen (chiefly the large cells). The cells of the left nucleus dentatus, the olives and the anterior horns of the cervical enlargement were affected in considerably smaller number. The nuclei of Deiters, the nuclei acustici, the middle part of the medulla oblongata (substantia reticularis), the cortex of the cerebellum, the right nucleus dentatus and the anterior horns of the thoracic part of the spinal cord were practically unchanged (except some individual cells). Degeneration was present in the paths of conduction (the left fasciculus pyramidalis, the fasciculus longitudinalis utriusque, and part of the left lemniscus medialis), and some degeneration was present in the right fasciculus pyramidalis and the column of Burdach.

In considering the clinical picture and the histopathologic changes the author emphasizes particularly that the induced movements were present only in the terminal period of the illness, when there probably had appeared the later patches of the tumor which had destroyed the brachia conjunctiva, Lissiza comes to the conclusion that the induced movements depended chiefly on disease involvement of the cerebellar system. He thinks that the slow destruction of the cell elements of the red nuclei and the superjacent parts of the substantia reticularis did not exclude the appearance of induced movements. In addition, he observed a peculiar reflex of the fifth toes in response to skin irritations.

PENZIK, Charkow, U. S. S. R.

A PHILOSOPHER LOOKS AT MENTAL HYGIENE. JOHN MALCOLM MACEACHRAN, Ment. Hyg. **16**:101 (Jan.) 1932.

Beginning with the pythagorean definition of a philosopher as a spectator of life, devoid of personal, selfish interest in it, MacEachran reviews the development of the meaning of the term "catharsis." He points out that it had originally a religious significance, and was employed by the devotees of Dionysos who put themselves at peace with themselves by becoming worked up into an ecstatic delirium. This frenzy was spoken of as *katharsis* or purification of the soul. It was soon recognized that music had a cathartic effect, and could be used for soothing hysterical patients either directly or by rousing them to a pitch of excitement which terminated in a restful sleep. Pythagoras further discovered that musical harmony was based on certain mathematical relationships. He extended this idea to include personal harmony, too, and taught that health and happiness required a harmonious attunement of body and soul; that qualities

and experiences must be in a specified quantitative relationship, avoiding all extremes of intemperance. This concept of the need for personal harmony was expanded by Plato into a complete philosophy of life, and his suggestions as to happy living represent sound and modern principles of mental hygiene today. He taught that the physician who treated the body without treating the soul (mind) was attacking but a minor part of the person. He suggested a plan of life in the "Republic" and in the "Laws" which accords well with current concepts of intelligent social planning. He recommended first that offspring be begotten along eugenic principles, that the pregnant woman be carefully safeguarded and that the new-born child be removed from its parents to guard it from the effects of overprotection. He planned an education both cultural and physical for the child. Only stories which the child could understand and which contributed affirmatively to the development of his character, could be told in the schools. Physical training was stressed without being overemphasized, and extremes in this as in other things were avoided. Education was to be devoid of compulsion, forcing or punishment. Nothing should be done to leave the child with a feeling of resentment or disgrace. This careful technic to avoid the inflicting of an inferiority complex sounds modern, indeed; yet it was proposed by Plato twenty-three hundred years ago. Play was to be spontaneous, and children were to be encouraged to devise their own amusements. They should be so trained that when they did right they would experience pleasure and when they did wrong they would feel pain. This seems to be a method of conditioning reflexes two millennia before Watson. These simple rules, Plato believed, would lead to human happiness: a safeguarded birth; infancy protected from oversolicitous parents; graded education always purposive, never distasteful; stimuli designed to instil feelings of confidence, never of fear; temperate physical training; spontaneous play, and an establishment of the right things with the pleasant ones. The program has yet to be improved on.

DAVIDSON, Newark, N. J.

SURGICAL NEUROPATHOLOGY OF TUMORS OF THE CENTRAL NERVOUS SYSTEM. Z. J. HEYMANOVITCH, Rev. d'oto-neuro-opht. **10**:110 (Feb.) 1932.

This article is a statistical study of the material in the neurosurgical clinic of the Ukranian Psychoneurologic Clinic during its first eight months of existence. Of 430 cases of organic lesions there were 81 cases of tumor, in 56 of which operation was performed, 43 extirpations and 13 decompressions.

	Location, per Cent	Diagnosis Correct, per Cent
Base of the brain	45	75
Temporal lobe	18.5	33
Frontal lobe	18.5	50
Temporoparietal	3	100
Frontoparietal	6	50
Quadrigeminate body	6	100
Fourth ventricle	3	?
Spinal tumors, 16 cases	..	...

The operative mortality for the spinal tumors was 12.5 per cent; for the cerebral tumors, 7.5 per cent. The diagnosis was correct in the cases of spinal tumor, but several times the lesion was two or three vertebrae lower than was thought, because the localized meningitis above the tumor led to error. Among the cases in which the results were successful there were a case of tumor in the quadrigeminate region, one of a tumor in the floor of the fourth ventricle and seven successive cases of tumor of the cerebellopontile angle.

The problem of the relation between the character of the tissues in the cerebral tumors on which operation was performed and their clinical aspect (Bailey and Cushing) was systematically studied. In addition to the influence of various forms

of tumor on the prognosis, other questions were studied, namely: the influence of the evolving tumor on the topography (the rôle of reactive gliosis, especially marginal glioblastosis of gliomas); the influence of localized meningitis around a tumor; the resistance of nerve tissues in certain cases of cerebral tumors; the differential diagnosis between diffuse gliosis and glioma; the diagnosis of neuroectodermal tumors accompanying tuberous sclerosis, and experimental tumors. A study of the cerebrospinal fluid was made in a specially equipped laboratory.

In addition to increasing the knowledge of the surgeon, histopathologic studies habituate him to make a functional and purely histologic diagnosis and aid him to arrive at a correct prognosis, thus indicating the limits of his operative efforts.

DENNIS, Colorado Springs.

CONTRIBUTION TO THE STUDY OF INTERMITTENT HEADACHE. A. P. THOMSON, Lancet **2**:229 (July 30) 1932.

Twenty-five patients with intermittent headache associated with the menstrual period were examined. Seventeen had well marked abnormalities in the roentgenographic appearance of the sella turcica. The presenting symptom of all patients was severe intermittent headache which had occurred with particular intensity at the time of menstruation. In the vast majority the headache occurred before the period; in a few it occurred at varying intervals after its onset, and in the least number it began simultaneously with menstruation. In all of the women who had borne children there was improvement in the hemicrania during pregnancy and lactation, varying from complete relief in most patients to only a slight amelioration.

Of the seventeen patients with roentgenologic abnormalities in the region of the sella turcica, nine showed complete ossification of the interclinoid ligaments, and in three the sella was smaller than usual; three patients had such prominent overhanging posterior clinoid processes that they nearly made contact with the anterior, although in each a small gap definitely intervened; three showed marked absorption of bone in the dorsum sellae. The author suggests that the usual anatomic description of the diaphragma sellae as a fold that almost completely roofs in the sella turcica is incorrect. Normally the diaphragma sellae is so incomplete that moderate swelling of the pituitary can occur without inducing intrasellar tension. When interclinoid ossification exists, however, the diaphragma sellae may be unusually well developed, and so predispose a person to intrasellar tension.

All the patients were treated with ovarian follicular hormone. Theelin was found to be generally most satisfactory. Sixteen of the patients were markedly improved, but four showed no apparent effect.

Some of the evidence which the author gives in support of the view that this series of paroxysmal headache was due to the development of local tension in the sella, particularly at the time of menstruation, is: (1) the recent experimental work in monkeys, which shows that menstrual bleeding depends on the activity of the anterior part of the pituitary body; (2) the occurrence of menstrual headaches for many years in two women who subsequently had tumors of the pituitary body; (3) two instances of direct inheritance of interclinoid ossification and a tendency to menstrual headache; (4) the failure to demonstrate similar roentgenologic abnormalities in persons who do not complain of headaches; (5) the improvement in the headaches in a fair proportion of the cases following the administration of the ovarian follicular hormone, which in animals has been shown to reduce the size of the pituitary body.

BECK, Buffalo.

HEREDITARY ATAXIA. S. DAWIDENKOW and N. ZOLOTOWA, J. f. Psychol. u. Neurol. **44**:377, 1932.

The authors report an atypical case of hereditary ataxia in a woman, aged 44; the illness began at 24, and there was an exacerbation at 33; both of these events followed pregnancy. The disease was characterized by slight remissions. Exami-

nation revealed: ptosis, Argyll Robertson pupils, pale optic nerve heads, very slight nystagmus, paresis of the facial and hypoglossal nerves, scanning speech, dysphagia, adiadokokinesis, slight tremor of the hands, cerebellar ataxia in the extremities, cerebellar gait, depressed ankle jerks and progressive intellectual deterioration. The first symptom noted by the patient was ptosis. The patient's three children, though they show slight but definite symptoms of the disease, are not considered abnormal by their relatives. The eldest son, aged 18, has the habit of continuously "raising the eyebrows"; a daughter, aged 17, shows an early but definite dysarthria, sluggish pupils and slight nystagmus; another daughter, aged 8, shows a sluggish pupillary light reflex. The patient's mother, aged 63, has been ill since 30, following an attack of typhus. Her illness is also characterized by frequent remissions. Her pupils are sluggish to light but react normally in accommodation; she has slight horizontal nystagmus, poor convergence, dysphagia, scanning speech, ataxic gait, dysmetria, slight hypotonia of the extremities and absent patellar and ankle jerks. The patient's maternal grandfather probably also had a mild form of the disease, for he is said to have had dysarthria and dysphagia during the last years of his life. In addition to the direct heredity of the disease through four generations, the patient's maternal aunt had a rudimentary symptom complex of the same disease. This woman's allegedly normal mother, a sister of the patient's maternal grandfather, showed sluggish pupillary light reflexes.

It is noteworthy that, in addition to hereditary ataxia, the family was also burdened with several other hereditary anomalies, such as suicide, depression, oligophrenia (four females and three males), migraine, "nervousness," "irritability," hallux valgus (three generations) and isolated cases of left-handedness and of deaf-mutism.

The authors comment on the variations and mutations of the clinical picture of hereditary ataxia in the various generations in this family, although every case was characterized by the presence of ocular symptoms which may be regarded as basic for this family. These symptoms are disturbances in the pupillary light reflexes, slight nystagmus, poor convergence and ptosis. To a lesser extent, dysphagia was also a basic symptom. It is also interesting that with each successive generation the symptom complex had a tendency to diminish in severity, and one generation escaped the disease.

KESCHNER, New York.

STUDIES OF THE ETIOLOGICAL RELATIONSHIP BETWEEN THE SOMATIC AND PSYCHOTIC DISTURBANCES IN PERNICIOUS ANEMIA. A. W. HOCHFIELD, J. Nerv. & Ment. Dis. **75**:3 (July) 1932.

A review of the literature reveals that most reports dealing with psychoses in pernicious anemia date back to the era prior to the advent of the Minot-Murphy liver diet, the case terminating fatally, and there is nothing to prove that had the patients survived they might not have recovered from the psychoses. The authors disagree in their conclusion. Close analysis of the case records shows that in most of the cases in which psychoses were present no definite etiologic relationship to the psychosis was proved, many of the patients presenting a history of previous psychotic attacks or other predisposing factors. In this respect the same may be said of the reports covering cases in which the liver diet was used; when improvement did result, it may be attributed to the general systemic improvement.

A study of seven patients treated with liver diet, five of whom showed a good remission of the anemia revealed: (*a*) In most, the psychosis developed after some environmental trauma, frequently after the patient had received specific treatment for a long time. (*b*) Despite the treatment, the neurologic symptoms progressed in several cases, but in none was any improvement noted. (*c*) Autopsy in one case with death as the result of an intercurrent infection revealed no changes characteristic of pernicious anemia in either the brain or the cord. (*d*) In four of the five successful remissions of the anemia, the patient recovered completely from the psychosis, but no parallelism between the improvement in the blood picture and

that of the psychosis could be demonstrated. (*e*) All seven cases presented psychoses of the affective type, of which six were profound depression. (*f*) Special laboratory investigations in three cases revealed two patients with a low basal metabolic rate, which was successfully counteracted with thyroid extract, and one patient with an abnormal sugar tolerance curve, which approached normal standards as the depression resolved. (*g*) A history of suicidal tendencies or actual attempt on the part of the patient was often obtained.

A specific toxin as the *agent provocateur* of the psychosis must be excluded on the basis that so few patients with pernicious anemia have mental disorders and, furthermore, were it the same noxious agent that produces the cord changes the patient should not recover from the psychoses, since the neurologic symptoms are not affected by the liver therapy. The author regards the psychosis as a separate entity which runs its natural course, the pernicious anemia in some instances acting as the precipitating or aggravating factor.

HART, Greenwich, Conn.

SULLA DETERMINAZIONE E SUL DIFFERENZIAMENTO DEL CRISTALLINO IN RANA CATESBIANA (SHAW). P. PASQUINI, J. Exper. Zool. **61**:45 (Jan. 5) 1932.

In embryos of Rana catesbiana, with medullary folds just closed and an incipient tail bud, the primary formative cells of the lens do not develop in the complete absence of the eye; i. e., the development of the lens is not independent. The rudiment of the lens, at least until the stage of the incipient tail fin, is therefore not determined, and lacks the power of self-differentiation. In slightly more advanced stages, the eye transplanted heterotopically induces a lens to form in foreign epidermis, provided it establishes contact with the epidermis by means of its distal wall; it is independent of the area of contact. Lens ectoderm from which the influence of the eye is removed may form abortive lenses, thus demonstrating a tendency of the placode to autodifferentiation, at the time when the specific potencies of the region are segregated. The lens reaches its full normal differentiation only in association with fragments of the retina, either in the place where it normally develops or in other regions. Ectoderm of the trunk, as well as branchial ectoderm and that of the head, can give the lens-forming reaction when brought into contact with the eye rudiment, the inducing faculty of which lasts until the later tail-bud stages. The lens rudiment is incapable of autodifferentiation in these stages. The close relation between the optic vesicle and the lens-forming ectoderm and the dependence of the latter on the continued presence of the former are demonstrated by the fact that induction may be incited independently of the morphologic integrity of the eye rudiment, provided part of its elements are histologically differentiated. The induction of the lens corresponds to the stage in which the distal wall of the optic vesicle presses against the inner ectodermal layer by the greater part of its surface and not earlier, but the independent development of the lens removed from the stimulus of the eye is of a minimal degree and is limited to tail-bud and later stages.

The facts gathered indicate that the nature of the stimuli which first determine the lens and bring about its subsequent hyalin differentiation is physical rather than purely chemical. This dynamic stimulus does not seem to be able to exert its action across the mesenchyme, which, in cases in which the optic vesicle is partially removed, may separate the remaining eye rudiment from the ectoderm. From the conditions encountered in Rana catesbiana it may be inferred that this species forms an extreme case in regard to the independent origin of the crystalline lens.

WYMAN, Boston.

REFLEXES AND OTHER MOTOR ACTIVITIES IN NEW BORN INFANTS. L. BEVERLY CHANEY and MYRTLE B. MCGRAW, Bull. Neurol. Inst., New York **2**:1 (March) 1932.

The authors studied the reflex reaction in 125 apparently normal infants as a portion of research on normal child development. Twenty-five of these infants

were examined at the time of birth in the delivery room. The remaining 100 included 10 for each day of age during the first ten days of life. They designate the infants just born as partunate and term as neonate those examined on various days in the maternity nursery.

A review of the literature having special bearing on this subject exposes the main points of agreement and controversy among previous investigators. The extent of the study, the technic of examination and the method of evaluation are outlined in detail. The reflex activities investigated include the biceps, triceps, patellar, achilles, periosteal, abdominal, plantar, Oppenheim, foot, leg, thigh, cutaneous, oral, sucking, blinking, pupillary, convergence, grasping and Moro reflexes. Sitting postural, standing postural and crawling reactions and reactions to auditory stimuli were also studied. The results, which are recorded in detail, indicate that the tendon reflexes are more easily elicited from partunates than from neonates, but that neonates are far more responsive to cutaneous stimulation. Results of plantar stimulation varied greatly but dorsiflexion of the toes was the most characteristic response, and the author has found nothing to substantiate the contention that certain reflex patterns, such as the Babinski sign, are in infants a normal reflex reaction caused by an immature nervous system. The grasping reflex was obtained in greater strength and frequency from the neonates than from partunates. The Moro reflex was one of the most consistent of all reflex patterns. Cutaneous stimulation indicated a greater degree of perception and response in the distal than in the proximal segments.

Perhaps the most significant result of the authors' work is the persistence of variation of response on the part of the subject to identical stimuli. This variation in behavior to situations at a time when environmental influences are minimal is indicative of variation in structure and potentiality of reaction, and must have a significant relationship to variation of behavior in later life.

KUBITSCHEK, St. Louis.

INVESTIGATIONS ON THE DEVELOPMENT OF THE HORTEGA MICROGLIA. K. VON SANTHA, Arch. f. Psychiat. **96**:37 (Jan.) 1932.

Since the discovery and description of the microglia by Hortega there has been a dispute concerning the origin of this cellular element. Hortega considered that these cells are of mesodermal origin. According to him, they develop from certain embryonic cells in the adventitia of the blood vessels, which give rise to the endothelial cells and the microglial elements. In the process of development the microglia cells go through the same stages as they do in certain diseases of the brain, only in a reverse order. The first stage is that of gitter cells, the second that of ameboid cells, the third, that of cells with pseudopodia, and the final stage, that of microglia. Because of this Hortega considered the gitter cells that are found in early infancy not significant of any disease process, but physiologic in nature.

The author studied sections of the central nervous system of embryos, as well as early postnatal specimens of rabbits, rats, cats, dogs, pigs and calves and human embryos. On the basis of his observations he comes to the following conclusions: 1. In the embryos of rabbits and rats, at about the midperiod of pregnancy, there are no gitter cells, which are so characteristic of the same animals at birth. At the same time one finds in the parenchyma full grown microglia cells. At this time the microglia are diffuse and show definite relationships to the blood vessels. At this time, too, one finds peculiar adventitial cells along the course of the capillaries, which seem to give rise to microglial elements through a succession of stages, but at this stage no gitter cells could be found. 2. The large foci of gitter cells at the time of birth seem to be definitely related to the development of the microglia cells, and seem to find their way into the nerve tissue by a process of migration. At the same time, however, the microglia cells also develop by the usual mitotic processes. 3. In the human embryos and in those of the pig one finds only mature microglia cells during the second

half of the intra-uterine life. 4. All the findings point to the mesodermal origin of the microglia; no evidence has been found that would speak for an ectodermal or ependymal origin. The microglia cells are closely related embryologically to the reticulo-endothelial system.

MALAMUD, Iowa City.

IRRADIATION AND CONCENTRATION OF THE PROCESS OF STIMULATION IN THE CENTRAL NERVOUS SYSTEM: A CONTRIBUTION TO THE STUDY OF CONDITIONED DEFENSIVE REFLEXES. E. B. BABSKY, J. f. Psychol. u. Neurol. **44**:429, 1932.

Pavlov's method of studying conditioned reflexes has made it possible to investigate the principal functions and most important physiologic processes of cerebral activity. Investigations by this method have shown that the most complex and remarkably delicate activity of the cerebral cortex is based on six fundamental physiologic processes: (1) excitation, (2) inhibition, (3) irradiation and concentration of both these processes, (4) analysis, (5) association and synthesis and (6) induction. As soon as excitation or inhibition occurs in the cerebral cortex the process radiates to a more or less extensive region of the cerebral hemispheres. After a while the process becomes limited to a definite point in the brain; that is, it becomes concentrated at that point. During a given period of time there occur in the cerebral cortex a number of points in which the excitation or inhibition process is concentrated. In this way, one may look on the cerebral cortex as a mobile "mosaic" which, owing to external stimuli and an internal struggle of the nerve processes, constantly changes its appearance.

By studying the conditioned salivary reflexes, the phenomena of irradiation of the inhibition processes in the cerebral analysators have been well established. There is still little definite information at hand as to the phenomena of irradiation and concentration of the excitation process. In view of this, Babsky studied conditioned motor defense reflexes and established the following rules, which characterize the variable relations between irradiation and concentration of the excitation process in the central nervous system: 1. Every concentrated excitation point limits and diminishes the irradiation of this process. 2. The concentration of the excitation process depends on the variable relations between the intensity of the excitation irradiation and the degree of excitation in the concentrated area. 3. The intensity of irradiation of the excitation is in inverse proportion to the degree of concentration of the inhibition process.

KESCHNER, New York.

A DESCRIPTION OF THE CENTRAL NERVOUS SYSTEM OF THE PORPOISE (TURSIOPS TRUNCATUS). ORTHELLO R. LANGWORTHY, J. Comp. Neurol. **54**:473 (April) 1932.

Material for this study consisted of ten young adult male porpoises. The gross structure of the brain is described by the aid of drawings. The whole brain is foreshortened in its anteroposterior extent and widened laterally as a result of the telescoping of the frontal and parietal bones as well as the modification of the anterior portion of the skull associated with the production of the blowhole mechanism. The cerebral hemispheres are large, and the convolutional pattern is extremely complex, surpassing that found in the cerebral hemispheres of man. The cerebellum is also large and consists of a vermis and two large hemispheres. The olfactory nerve and bulb are lacking, and the olfactory cortex is poorly developed. The optic nerve is well developed. The fifth nerve is large, although only a vestige of the ophthalmic branch remains. The cochlear nerve and its connections with the brain are strongly developed. The head of the caudate nucleus lies on the surface of the brain just anterior to the optic chiasm. The calcarine fissure is well marked. The corpus callosum is fairly well developed and in its general form and proportions shows a marked resemblance to that of man. The thalamus is well developed.

The cerebral cortex as stained by thionine shows a very primitive architecture, with few cells and poor differentiation of the cell layers. A large motor area is developed at the extreme frontal pole of the cortex. The motor cortex and the projection areas appear to be surrounded by large areas of undifferentiated cortex, similar in all areas. For further microscopic study sections were stained by the Weigert-Pal method. The cochlear apparatus appears extremely well developed. The superior olive, acoustic lemnisci with their nuclei, acoustic colliculi and acoustic geniculates are all large. Large numbers of fibers reach the acoustic cortex. The temporal lobe is enlarged, carrying with it the lateral ventricle. A large association area has developed around the acoustic projection area. Throughout, the ventricular system has kept pace with the growth of the cerebral cortex. No posterior horn of the lateral ventricle is demonstrated.

FRASER, Philadelphia.

CORTICAL CENTRES OF THE LABYRINTH. E. A. SPIEGEL, J. Nerv. & Ment. Dis. **75**:504 (May) 1932.

Cortical centers for the labyrinthine impulses have not as yet been thoroughly established, although excitation of the labyrinth leads to distinct sensations of dizziness. Experiments of Magnus and Rademaker support the idea of the frontal lobe as the terminal station of vestibular impulses, while Mills and Monakow supposed it to reside in an area behind Wernicke's center. The author, making use of the works of Baglioni, Amantea, Alimenti and others on the increased reflex excitability induced by strychnine, based his study on twenty-eight dogs and cats in which to different circumscribed cortical areas were applied blotting paper soaked with a strychnine solution stained with toluidine blue in order to recognize undesirable spreading of the strychnine. In order to stimulate the labyrinth, the animals were rotated in a Bárány chair. In these experiments the author found that parts of the arcuate gyrus behind the sylvian fissure, corresponding to the parts of the temporal lobe in man which adjoin the occipital and parietal lobes, if soaked with strychnine for from half an hour to eight hours would be hypersensitized to such an extent that rotation of the animal produced not only typical labyrinthine reflexes but also convulsions. Spasms of the face and other parts of the body developed thereafter in some cases. While loud noises could produce similar attacks, painful stimuli and violent concussion, such as striking the board with a hammer, did not produce such attacks. However, the author succeeded in producing these reflex convulsions in only fourteen of his twenty-three experiments, and considered that in the others the cortical excitability had not been sufficiently increased. He found that dogs responded more satisfactorily to the experiment than cats, of which only half responded with epileptiform convulsions after rotation. Passive movement of the eyes in a horizontal plane and irritation of the central trunk of the vagus nerve by a faradic current did not produce convulsions. In spite of the total extirpation of the cerebellum, it was still possible to produce convulsions by labyrinthine stimulation. From these experiments the author thinks that cortical representation of the labyrinth has at least been established in a part of the temporal lobe, although the more exact limits will require further study for their determination.

HART, Greenwich, Conn.

EYE AND EAR IN "SEASICKNESS." MAYNARD M. METCALF, Arch. Ophth. **8**:269 (Aug.) 1932.

The mechanics of seasickness have always been of interest. In 1930, Lebensohn, in discussing carsickness, made the following statement: "From these experiments, one can definitely conclude that carsickness is due to labyrinthine stimulation rather than to optic nystagmus. Optic nystagmus is easily tolerated and is not accompanied by depressive gastric phenomena. The impulses from the labyrinth, however, are depressive. Though carsickness is based on labyrinthine irritation, it is nevertheless true, I believe, that errors of refraction and of muscle balance predispose a person to this malady." Metcalf believes that Lebensohn's statements are not adequate—that carsickness is more complex than he indicated.

Metcalf himself was his best subject because of his unusual susceptibility to seasickness.

By means of fixation tests and deliberate stimulation with nicotine, he carried out various experiments, which allowed him to draw the following conclusions: 1. Stimulation of the eye, apparently, and stimulation of the retina with changing images and without much, if any, motion of the eyeball can produce nausea, dizziness and, if persisted in, vomiting. This seems in disagreement with Lebensohn's conclusion, though he emphasized motions of the eye rather than retinal images. 2. Tobacco seems to render the same semicircular canals hypersensitive. 3. Overstimulation of normal balancing organs probably is an efficient cause of dizziness, nausea and vomiting, if exceedingly slight stimulation of balancing organs hypersensitized by tobacco can produce the same effects. 4. Symptoms of the ear (dizziness) usually precede symptoms of the stomach (nausea) in the onset of seasickness. 5. Excessive motion, as on shipboard or on a railway train, can produce seasickness during sleep or in the dark, indicating that retinal stimulation is not necessary to produce it. 6. While either stimulation of the eye or stimulation of the semicircular canals can produce seasickness, it is probable that both types of stimulation are generally involved. 7. The matter is still more complex, for there seems to be sufficient indication that previous disturbance in the stomach, due to indigestible food or too much food, may increase liability to seasickness under proper stimulation.

SPAETH, Philadelphia.

LIPODYSTROPHY: A REPORT OF SIX CASES IN CHILDREN. A. H. PARMELEE, J. A. M. A. **98**:548 (Feb. 13) 1932.

Parmelee states that lipodystrophy is defined by Coates as a "disease especially liable to affect children 5 to 8 years of age, in which characteristically there is a loss of subcutaneous fat of the face, neck, thorax, arms and abdomen, without assignable cause or gross symptoms of ill health. In association with this, there is in addition, in females, an increase of subcutaneous fat below the iliac crests." The outstanding features are the thin, almost cadaverous looking face and upper part of the trunk, while the lower part of the trunk and the legs look either normally or better than normally well nourished. Also, there is no loss of muscular power or disturbance of sensation over the parts affected, and the patient is active and strong and well in every other respect. Although the face often appears pale, no anemia can be demonstrated. The onset is usually in early childhood. Absolutely no clue to the etiology of this strange disease is as yet at hand, though many writers have indulged in interesting speculations. The author goes into detail concerning the speculation as to etiology, because in six cases reported by him the onset seemed definitely to have followed some trauma to, or infection of, the nasopharynx, and of the reported cases there are thirteen in which the onset dated from such conditions as measles, pertussis, influenza, pneumonia, tonsillitis, tonsillectomy and otitis media. In his cases, two followed tonsillectomy, one tonsillitis, one measles, one measles and pertussis and one diphtheria, measles, pertussis and tonsillectomy. The close relationship of infections of the upper respiratory tract to encephalitis with its favorite localization in the midbrain brings strongly to mind the possibility, at least, that there may be some etiologic connection in this disease. None of the patients showed any laboratory or clinical evidence of disturbance of the endocrine glands. Emphasis is laid on the possibility that toxic or infectious derangement of central trophic centers in the thalamic and subthalamic areas of the midbrain may be the main etiologic factor.

EDITOR'S ABSTRACT.

SUPRASELLAR TUMOR BEGINNING AS AN ATYPICAL RETROBULBAR NEURITIS. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **10**:104 (Feb.) 1932.

The patient, a strong healthy woman, aged 41, began to suffer with violent headache in February, 1930. Failing vision in the left eye followed, and this

condition progressed in spite of intranasal and external operations on the left frontal, ethmoidal and sphenoidal sinuses. Vision was reduced to counting fingers at 1 meter, and repeated examinations with the perimeter and Bjerrum's screen revealed a pronounced contraction for white in the temporal half and central scotoma for colors. Neurologic and roentgenologic examinations revealed no anomalies. A provisional diagnosis of suprasellar tumor was made and roentgenotherapy was instituted, with some relief from the headaches for a short time. The field in the right eye now began to show a temporal contraction for red, and vision began to fail. During the course of trephining for an intracranial exploration, the left frontal sinus was entered and was found to be filled with pus and granulations. Later, the operation was completed and a soft encapsulated tumor (gliosarcoma), embracing the chiasm and optic nerves and attached to the anterior part of the third ventricle, was removed with curets. Recovery was prompt. Vision in the right eye returned to 6/8 and the field to 55 degrees, and in the left eye a small fragment of vision returned in the superonasal quadrant.

The occurrence of headache several months before the failure of vision and the gradual failure of vision exclude typical retrobulbar neuritis and indicate the atypical form. The results of repeated examinations with the perimeter and screen, in spite of the absence of roentgenologic signs, warranted the diagnosis of suprasellar neoplasm. The slow evolution confirmed the diagnosis and demonstrated that the modifications of the visual fields alone are sufficient to justify early radical operation. To be of value, examinations of the fields must be repeated often with the Bjerrum screen. The color tests permit the discovery of notches in the fields before the tests with white reveal them, contrary to the opinion of Cushing, Gaudissart and others.

DENNIS, Colorado Springs.

PATHOGENESIS OF THE AURICULOTEMPORAL SYNDROME AND OF INNERVATION CONTROLLING SWEATING OF THE FACE. E. K. EVZEROVA and E. YA. BARANOVSKY, Ukrain. Psychoneurol. Inst. **20**:48, 1932.

Evzerova and Baranovsky describe a case of the auriculotemporal syndrome in a girl 16 years old. When she chewed hard food, reddening of the cheek developed and was followed by sweating. There was a zone of hyperesthesia in the area of the auricularis magnus and the auriculotemporal nerves. There was a scar behind the ear in which presumably the great auricular nerve was involved. The nerve was dissected out centrally to the scar, and not far from its emergence from the cervical plexus. One month later the syndrome could no longer be elicited. In the second case, there was likewise a scar involving the great auricular nerve. At operation two branches of the great auricular nerve were dissected free from the scar, not far from the nerve's emergence from the cervical plexus. Histologic studies of the removed fibers revealed the existence of a chronic interstitial neuritis. Examination made two weeks later revealed no sensory disturbance of that side of the face. The reddening-sweating syndrome could be elicited, but it was not as intense as before. Apparently the syndrome was conditioned by more than one nerve. The auriculotemporal nerve was likewise involved. From the experience in both cases, the authors state that the resection of the great auricular nerve causes complete cessation of sweating in the lower portion of the face and a rather insignificant disturbance of sensation. Apparently sympathetic sweat fibers pass in the great auricular nerve, while sensory nerves are rather few. Fibers accompanying blood vessels likewise play a rôle in the sweating. Irritating impulses pass by way of the ninth and fifth cranial nerves and by way of the great auricular and auriculotemporal nerves. The preganglionic portion of the reflex arc is located in the thalamus-hypothalamus, while the postganglionic path passes through the auriculotemporal and the great auricular nerves.

EDITOR'S ABSTRACT.

COMPARATIVE STUDIES ON THE NUCLEUS PREOPTICUS PARS MAGNOCELLULARIS AND THE NUCLEUS LATERALIS TUBERIS IN FISHES. H. H. CHARLTON, J. Comp. Neurol. **54**:237 (Feb.) 1932.

The nucleus preopticus pars magnocellularis and the nucleus lateralis tuberis have been investigated in a large series of fishes. The material consisted of stained and serially mounted sections of the brains of one cyclostome, three selachians, six Ganoidei, one hundred and thirteen different species of teleosts and one of the Dipnoi. A reconstruction chart of each brain was made to show the relative length and position of these nuclei. The nucleus preopticus pars magnocellularis is present in every brain examined, with the exception of two or three elasmobranch representatives. The length of this nucleus does not affect its midpoint position, nor is it related to body size. An aggregation of cells situated at varying distances caudal to the nucleus pars magnocellularis and termed by Holmgren simply "large cells" has been studied in a lesser number of forms. Evidence is presented for considering them a part of the nucleus preopticus pars magnocellularis which, owing to some neurobiotactic influence, has become separated from the main nucleus. The nucleus lateralis tuberis is a group of cells lying on either side of the infundibulum, extending anteriorly almost to the level of the commissura horizontalis and lying close to the ventral surface of the hypothalamus. This nucleus was not found in nine teleosts and in only two forms, Amia calva and Lepidosteus, below the teleosts. The position of the nucleus lateralis tuberis is extremely variable. In some forms it seems to show a division into medial and lateral parts. A new tuber nucleus, probably homologous with the nucleus lateralis tuberis, is described and provisionally termed the nucleus ventralis tuberis, pars posterior. The author suggests that a great amount of work is necessary before the true significance of the nuclear variations and migrations described here are completely understood.

ADDISON, Philadelphia.

THE PROBLEM OF THE "BLOOD-BRAIN BARRIER." H. SCHMIDT, Arch. f. Psychiat. **95**:303 (Oct.) 1931.

The author discusses the question of the existence of a blood-brain barrier in addition to the blood-cerebrospinal fluid barrier. The existence of the latter the author considers as being beyond any question of doubt. Clinically, as well as anatomically, enough evidence has been advanced to show that there is a barrier between the blood and the cerebrospinal fluid. The question remains: Can certain substances enter directly from the blood into the tissues of the brain without passing through the cerebrospinal fluid, and, if so, is there any structure between these two that could be considered as a blood-brain barrier?

The experiments have been undertaken in rabbits through the aid of toxic and nontoxic vital stains. The spinal fluid was examined following that, and after the death of the animal the tissues were studied histologically for the penetration of the substances. On the basis of these investigations the author comes to the conclusion that such a barrier does exist, and that it has the function of regulating the passage of substances directly from the blood into the brain tissues. Whether this barrier can be considered as a special structure placed between the blood and the brain tissue, or whether it should be looked on only as a characteristic of either the blood or the brain tissues themselves remains a question. In the future, however, when one considers the problem of exchange of substances between the central nervous system and the blood, one will have to take into consideration not only the blood-cerebrospinal fluid barrier but also a similar barrier between the blood and the central nervous system tissue itself.

MALAMUD, Iowa City.

QUANTITATIVE MANAGEMENT OF CONTRACTION IN LOWEST LEVEL CO-ORDINATION. C. S. SHERRINGTON, Brain **54**:1 (April) 1931.

In his Hughlings Jackson lecture, Sherrington speaks of the well known jacksonian levels and confines himself to the lowest. Sampled by afferent stimula-

tion, the motor center soon reveals that every reflex fractionates its muscle into packets. Different grades of excitement exist in the motor center from zero, subliminal, maximal to supramaximal; which may be more broadly considered as subliminal, subtetanic and maximal. When the stimulus of the afferent nerve is reduced, fewer of its fibers are excited. A gradual degradation occurs in the contraction-tension. Adrian and his co-workers have shown that one and the same motor unit climbs through successive grades of excitement in the opening phase of reflex response. The subliminal fringe contributes to the adjustment of the reflex contraction on the basis of its extensity; the subtetanic gives the power to grade contraction, and the maximal group limits more and more the further increase of the reflex muscular response. The motor center is a "summation mechanism," grading the excitation of the individual motor units, causing its faster or its slower firing. The "upstanding" reflex may be considered as a single functional entity, since the postural contraction or tonus is not essentially different from other forms. Even in the spinal scratch reflex, posture not merely alternates with the movement but accompanies it and dovetails in with it. From this succinct and penetrating lecture, the author concludes that "there are in the nervous system heights of excitation and depths of inhibition higher and deeper and with grades of adjustment ampler than muscle with all its subtleties can commensurately express."

MICHAELS, Boston.

PSYCHALGIAS: STUDY OF THEIR FREQUENCY AND CHARACTERISTICS BY MEANS OF PROCAINE SKIN TEST AND BY EFFECT OF SUGGESTION. J. H. PRATT, L. A. GOLDEN and JOSEPH ROSENTHAL, J. A. M. A. **98**:441 (Feb. 6) 1932.

A study of a hundred and ten cases of psychalgia is presented. Only two of these showed definite organic disease, one being a case of pleurisy and pneumonia, and the other, intercostal neuralgia due to herpes zoster. In ninety-five of the cases, the pain was completely removed. The success with a hypodermic needle alone was equal to that with injection of procaine. In eight cases there was partial relief from pain; in seven the procedure failed, in a few instances even increasing the pain. Injection into a small area often caused the pain from a large area to disappear. In forty-five cases freedom from pain lasted from one day to eighteen months, while in visceral diseases, studied by Weiss and Davis and by Rudolf and Smith, pain always returned within twenty-four hours and usually within from two to six hours. In twenty-two cases there was no pain for five days or more following the test. The pains were located in all parts of the body. The most common location was the back, and next in order of frequency the abdomen. The part of the abdomen most usually affected was the right lower quadrant. No less than 11 per cent of the total number of cases might have been mistaken for chronic appendicitis. The authors' results show the frequency of psychalgias. They confirm Sydenham's statement in regard to hysteria, that "this disease, if I calculate right, most frequently occurs of all chronical diseases."

EDITOR'S ABSTRACT.

DISTRIBUTION OF AFFERENT FIBERS VIA THE SYMPATHETIC TRUNKS AND GRAY COMMUNICATING RAMI TO THE BRACHIAL AND LUMBOSACRAL PLEXUSES. A. KUNZ and D. I. FARNSWORTH, J. Comp. Neurol. **53**:389 (Dec.) 1931.

This article presents a study of the myelinated fibers of relatively large and medium caliber which occur in the gray rami communicantes. The authors have extended to the cat experiments already made in a preliminary way on the dog. The cat proved more advantageous for this study because the ratio of myelinated to unmyelinated fibers in the gray rami is materially greater in the cat than in the dog. One of the experiments was to cut both roots of the thoracic spinal nerves, from the first to the eighth inclusive, on one side of the body, just distal to the spinal ganglia, leaving the communicating rami intact. After allowing from two to five weeks for degeneration, the gray communicating rami from the sixth to eighth cervical and first thoracic nerves of both sides were

fixed in osmic acid and examined for myelinated fibers. In all cases there was a much reduced number of myelinated fibers on the side on which the operation was performed, and this reduction involved the fibers of relatively large and medium caliber to a far greater extent than those of small caliber. It is deduced that the degenerated fibers are components of the dorsal roots of thoracic nerves, which after reaching the sympathetic trunk run upward in it and leave it through the gray rami of the brachial plexus nerves, in order to join the somatic rami of the spinal nerves for peripheral distribution. Similar experiments were done in the lumbar region for a study of the gray rami to the lumbosacral plexus.

ADDISON, Philadelphia.

SPINA BIFIDA AND CRANIUM BIFIDUM: RESULTS OF PLASTIC REPAIR OF MENINGOCELE AND MYELOMENINGOCELE BY A NEW METHOD. WILDER PENFIELD AND WILLIAM CONE, J. A. M. A. **98**:454 (Feb. 6) 1932.

Thirty-three cases of spina bifida, cranium bifidum and rachischisis reported by these authors represent all such cases seen by them during a given period of time and should therefore comprise an average collection of such cases. Of the patients, nineteen who presented either a posterior cranium bifidum or spina bifida were operated on, with no deaths. The sac of a myelomeningocele or meningocele is a mechanism for the transmission of cerebrospinal fluid into the blood stream. This the authors have shown histologically and experimentally. Amputation of such a sac is likely to precipitate acute hydrocephalus and should never be carried out unless there is no connection between the sac and the cerebrospinal fluid spaces. An operation is described which provides for the preservation of the sac beneath a protective tent of fascia. This sac continues to absorb cerebrospinal fluid. The operation therefore does not increase the likelihood of the development of hydrocephalus in such cases. If paralyses are already present, it is impossible, of course, to promise restoration of function, although in chronic cases there is sometimes improvement in such paralyses because tension on nerve elements included in the sac is relieved. Plastic repair of the meningocele and the myelomeningocele should be carried out at the end of the third or fourth week of life or earlier. In the absence of paralysis the procedure yields highly satisfactory results.

EDITOR'S ABSTRACT.

COMPLETE BUT TRANSITORY PARALYSIS OF THE SIXTH NERVES IN AN OVERWORKED PERSON. JEAN-SÉDAN and J. BERTHIER, Rev. d'oto-neuro-opht. **10**: 261 (April) 1932.

An industrial engineer, aged 42, was suddenly stricken with supposed blindness and was in an extreme state of anxiety. Vision was 10/10 in each eye, and there was intense convergent strabismus, due to paralysis of both external recti. The diplopia persisted at all distances of fixation. The patient stated that the symptoms appeared suddenly after a day of hard work and that for a long period he had undertaken an unusual amount of mental effort. He did not smoke or drink, and his general health was excellent. There were no pathologic signs in the cardiorenal or nervous systems, except of the sixth pair. He was sent to a hotel and put at complete rest, with the result that improvement was so prompt that he refused any further examination. He has remained well. The probable diagnosis is a symmetrical vascular spasm affecting the sixth nuclei or the fibers at their emergence from the sixth nuclei. Payan has shown that the central arteries from the vertebral and basilar trunks course from in front backward along the raphe, and terminate at the motor nuclei at the level of the fourth ventricle. The vertebral arteries, in particular, give off radicular branches to the external motor oculi. Aubaret has reported several cases of temporary symmetrical paralysis of the external recti and Jean-Sédan has reported a case of temporary and relapsing paralysis of the external recti in the course of acute glaucoma. Lapersonne mentioned double transitory paralysis of the external recti as an early symptom in tabes and dementia paralytica.

DENNIS, Colorado Springs, Colo.

CLINICAL FEATURES OF ACUTE PRIMARY INFECTIOUS POLYNEURITIS. M. S. MARGULIS, Arch. f. Psychiat. **95**:392 (Oct.) 1931.

The problem is discussed on the basis of fifty-five cases of this disease observed over a period of three years. The chief features of the clinical picture are objective and subjective sensory disturbances, losses of motor functions, tonic and pain reflexes, exaggeration or absence of tendon reflexes and changes of the cerebrospinal fluid in the form of increased protein with slight or no increase in cell count. Of the less consistent symptoms, the most important are the changes of the blood and general neuropathic phenomena. An analysis of all these symptoms leads one to assume that there is a central component in this disease, and that the primary localization is in the roots. Two forms of the syndrome can be distinguished: (1) the general polyradiculoneuritic type and (2) the encephalomyeloradiculoneuritic type. In the first group, the lesions are chiefly in the roots and peripheral nerves. In the second they are shifted to the central nervous system. Both of the types, however, represent different localizations of essentially the same processes. The author considers the acute ascending paralysis of Landry as belonging to this syndrome. Outside of the acute forms, there are some abortive types of the disease which are characterized by slight sensory or neuralgic symptoms and in which the whole course is very mild. The onset is acute in 71 per cent, and gradual in 29. Whereas the prognosis in all types is good so far as life is concerned, the disease is usually of long duration, and both complications and residual effects are frequent. In some cases relapses were noted after apparent recovery.

MALAMUD, Iowa City.

OBSERVATIONS ON THE TREATMENT OF EPENDYMAL GLIOMAS OF THE SPINAL CORD. HUGH CAIRNS and GEORGE RIDDOCH, Brain **54**:117 (June) 1931.

Two cases of intramedullary glioma of the spinal cord, with successful operative removal, are described. In the first case, the tumor extended from the fourth cervical to the third thoracic segment; in the second from the third to the fifth thoracic segment; both proved to be ependymal gliomas with one or more cavities. In case 1, pain was a relatively insignificant symptom, whereas in case 2 pain of great severity was confined to the right fifth thoracic segmental area and suggested an intrathecal extramedullary tumor. Combinations of physical signs in intramedullary tumors should receive more attention than the symptoms. Signs of a lesion of considerable longitudinal extent in combination with dissociated sensory loss in the areas supplied by the affected segments favor an intramedullary tumor. In both cases an unexplained tachycardia followed the laminectomy, and in case 1, even though the tumor was as high as the fourth cervical segment, there was no serious respiratory disturbance. A considerable degree of gradual recovery of spinal function followed the operations; in case 1, all forms of sensation recovered in an upward direction, and in both cases voluntary power occurred in the extensor muscles before the flexors. From the fortunate experiences of the authors with these two cases, it is urged that operative enucleation of the tumor has its place in the treatment of at least some patients with intramedullary tumor.

MICHAELS, Boston.

THE "PATH" THEORY OF CORTICAL FUNCTION. W. R. ASHBY, J. Neurol. & Psychopath. **12**:148 (Oct.) 1931.

By the "path" theory of cortical function, generally accepted today, is meant the belief that the function of the central nervous system is subserved by strictly constant pathways of neurons which conduct impulses to appropriate end-organs; that learning consists of the opening up of new paths, and that memory consists of the retraversing of some old path by another impulse. This hypothesis arose from the demonstration of established reflex pathways of the sensory and motor spinal nerves and the white matter tracts; there has been no evidence of established gray matter pathways. The author challenges this "path" theory, which is gainsaid

by Lashley's experiments on the maze-habit in rats, from which he developed the concept of the "equipotentiality of the cortex," by Pavlov's failure to determine a definite cortical localization for the conditioned reflex in dogs, and by Marina's experiments on ocular muscle transplantation in apes. An alternative "pattern hypothesis" is suggested: that "the stimuli enter and work themselves out as a pattern of nerve impulses on the cortex or gray matter generally, and that they are dependent on the cortex only in so far as the cortex provides a suitable medium on which the pattern can move and develop."

SPERLING, Philadelphia.

SIX YEARS OF MALARIA THERAPY IN DEMENTIA PARALYTICA. TANCREDI CORTESI, Rassegna di studi psichiat. **20**:770 (July-Aug.) 1931.

The author reports the results of his experience with malaria therapy from 1924 to 1930, and takes into consideration the period of incubation, the type of febrile reaction, the response to malaria, the sensitivity to quinine, the course and complication of malarial therapy, the mental manifestations during the febrile reaction and the result of the treatment. He also takes into consideration the antisyphilitic treatment administered to patients before the malaria.

The conclusions of his observations are that of seventy-six patients with dementia paralytica treated with malaria, 18.4 per cent showed complete remission, 14.4 per cent partial remission, 13.1 per cent slight remission and 26.2 per cent no improvement.

In comparing the results in patients treated with malaria with those in nontreated patients, the author points out that of forty persons with dementia paralytica admitted to the hospital from 1919 to 1924, thirty-three died during the following five years, thus making the percentage of death in nontreated patients 85, as compared with 26.8 per cent in those having received the malarial treatment.

FERRARO, New York.

THE PHYSIOLOGICAL INTEGRATION OF SENSORY PROCESSES WITHIN THE GREY MATTER OF THE NERVOUS SYSTEM: A CRITICAL REVIEW. R. S. CREED, Brain **54**:29 (April) 1931.

Head's concepts of sensation are stressed and elaborated by Creed, who presents evidence from various sources. Interactions at a subperceptual or physiologic level as a result of stimulation of peripheral receptors, whereby alterations are produced in the sensations to which such stimulation gives temporal and spatial summation in the retinocerebral apparatus, are discussed. Experiments of Sherrington and others suggest a physiologic interaction between the two retinocerebral apparatus. Head's experiments on the sensitivity to hot water of the glans penis speak for the theory of inhibition of pain. Foerster supported this concept from his clinical material; however, his claims of descending inhibitory paths to all levels of the nervous system could not be corroborated below the level of the thalamus. The afferent pathway is not to be looked on as a telegraph line; the message ultimately delivered depends on the past and present events in the transmitting system as a whole. The article is concluded with a quotation from Head, "the forms assumed by sensation are ordered and predestined on the physiological level, as the result of innumerable integrations, which take place outside consciousness."

MICHAELS, Boston.

BLOOD GROUPING IN MENTAL DISEASES. I. SOMOGYI and L. VON ANGYAL, Arch. f. Psychiat. **95**:290 (Oct.) 1931.

The authors report an investigation of blood groups in one thousand cases of mental diseases and a comparison of these with similar investigations in normal persons. The grouping was undertaken on the basis of the method devised by Hirschfeld and Dungern. Somogyi and Angyal found that no appreciable difference exists between the blood group distribution in persons with mental diseases

and that of normal persons; that this distribution shows no characteristic features in any of the endogenous psychoses; that in the syphilitic mental and nervous diseases this distribution is also similar to the normal. Investigations of the relationship of blood groups and malarial treatment in dementia paralytica led to the conclusions that this distribution has no important relationship to the period of incubation, the type of reaction or spontaneous cessation of the malarial fever. Contrary to some statements made by other authors, the malarial treatment does not tend to cause any changes in the blood group. The inheritance of blood group characteristics bears no relationship to the inheritance of psychopathic or psychotic traits.

MALAMUD, Iowa City.

ALLERGIC MIGRAINE IN CHILDREN. RAY M. BALYEAT and HERBERT J. RINKEL, Am. J. Dis. Child. **43**:1126 (Nov.) 1931.

This interesting study is based on the authors' assumption that approximately 7 per cent of the people in this country suffer from the symptoms of migraine, and that about 30 per cent of these manifest the symptoms before the age of 10 years, this being equivalent to about 2 per cent of the juvenile population. The hereditary tendency of the disease and its transmission through the maternal protoplasm are stressed. The authors demonstrate the close relationship between conditions due to sensitivity to food, such as asthma, cutaneous visceral reactions and so-called cyclic vomiting, and migraine. They disagree with the usual opinion that migraine is due to a sudden localized vasomotor spasm of the vessels of the cerebral cortex. They offer the premise that it is a condition of vasomotor dilatation, and report that about 15 per cent of all of their patients with migraine obtained relief by the use of ephedrine. Their treatment for the migraine of childhood is based on elimination of specific foods, and their results are encouraging.

LEAVITT, Philadelphia.

MENTAL HYGIENE RESEARCH. C. M. HINCKS, Am. J. Psychiat. **11**:237 (Sept.) 1931.

While improvement in the technic of managing the maladjusted is one of the aims of mental hygiene, this therapeutic purpose is not its most important goal; it is devising procedures to forestall maladjustment and prevent mental disease that constitutes the more significant aim of mental hygiene. Delinquency, dependency, mental disease, inefficiency, complexity of vital problems and unrest generally are all increasing, and this in turn puts increasing demands on students and practitioners of mental hygiene. Hincks pleads for a scientific methodology and lists the contributions to mental hygiene made by other sciences. Psychiatry and psychology, economics and sociology, anthropology and neurology all have their share in building the structure of mental hygiene. Hincks estimates that a hundred million dollars is being spent annually for the treatment and care of the mentally ill, and calls attention to the fact that less than a million dollars of this is devoted to research in mental hygiene. He calls for a larger appropriation for this work, suggesting that an expenditure of five million dollars, constituting only 5 per cent of the total, is well justified.

DAVIDSON, Newark, N. J.

THE STRUCTURE OF CELLS IN TISSUES AS REVEALED BY MICRODISSECTION: V. THE PHYSICAL PROPERTIES OF NERVE CELLS OF THE FROG (RANA PIPIENS). G. S. DE RENYI, J. Comp. Neurol. **53**:497 (Dec.) 1931.

This article is a further study to obtain information concerning the physical condition of surviving nerve cells. Both sensory and motor nerve cells of the frog were studied by microdissection methods. Eighty-five ganglion cells stripped of their capsules were studied. Both sensory and motor nerve cells were found to be composed of a gelatinous substance. This was more or less firm in the spinal ganglion cells, and soft and plastic in the motor cells. Marked individual

variations could be determined in both groups of nerve cells. This, the author suggests, may be explained by the varying amounts of water absorbed by the different cells. In neither type of cell could the nucleus be separated from the cytoplasm by mechanical means. The physical state of the nucleus, according to the author, is practically identical with that of the cytoplasm surrounding it.

ADDISON, Philadelphia.

RELATION OF THE LIVER TO THE BRAIN. B. I. RAPOPORT, Ukrain. Psychoneurol. Inst. **20**:95, 1932.

Histologic studies of the brain were made by Rapoport, in dogs, after desympathization of the liver, after severance of vagi, after ligation of the hepatic artery and after Eck's fistula. The changes observed in the brain were of a general and not of a localized type. The subcortical centers showed graver or milder degrees of involvement, corresponding to the degree of damage to the liver. It was noteworthy that the most pronounced changes were observed in the blood vessels. This corresponded with Levantovsky's finding of permeability of the barrier in the presence of such lesions. It is admissible to speak of a relationship between the liver and the brain only in the sense that the former, when injured, can no longer prevent the passage of exogenous or endogenous poisons. A specific predilection for a definite region of the brain does not exist. Whether or not the so-called hepatolenticular degeneration group of diseases is conditioned primarily by pathologic conditions of the liver is problematic. Only after phosphorus poisoning does one find a simultaneous and similar change in the liver and in the brain.

EDITOR'S ABSTRACT.

AGE INCIDENCE OF SEROPOSITIVE SYPHILIS IN FEMALES. J. ERNEST NICHOLE, Brit. M. J. **1**:749 (April 23) 1932.

The findings in this paper confirm the assertion that syphilis in the female is a different disease from syphilis in the male. In the female the symptoms are much milder and frequently manifest themselves later in life, and treatment, to be efficacious, has to be prolonged. Tests for serologic evidence of syphilis showed a maximum peak just before the age of 50, followed by a considerable drop lasting the next fifteen years and a rise again after 65 in the case of males. In females, however, the results are different. The maximum incidence is delayed until after 65, and there is no peak at the age of 45. From 50 to 60, the curve is still rising without the fluctuation found in the male. These results, the author believes, tend to support the view that the menopause does affect the serologic reactions of females, and it is inferred that something in the female, possibly the lipoid content, coincident with the period between adolescence and the menopause, does have some affect on the serologic reactions of the blood of a syphilitic patient during that period.

FERGUSON, Niagara Falls, N. Y.

RESEARCHES ON THE PRESSURE OF THE CEREBROSPINAL FLUID AND ON THE CEREBROSPINAL FLUID IN CEREBRAL HEMORRHAGE AND THROMBOSIS. KNUD H. KRABB and EINAR GEERT-JORGENSEN, Acta psychiat. et neurol. **6**:529, 1931.

The authors examined the pressure of the cerebrospinal fluid and the fluid itself in 140 cases of cerebral hemorrhage and thrombosis. Autopsies were done in fifty cases. Krabb and Geert-Jorgensen found that a cerebrospinal pressure of over 300 indicated hemorrhage but did not exclude thrombosis. Bloody or xanthochromic fluid was an almost certain indication of cortical or meningeal hemorrhage; such is found in thrombosis only as a result of a hemorrhagic infarct. Increase of albumin in a colorless fluid indicates hemorrhage. The number of cells is not of diagnostic importance.

PEARSON, Philadelphia.

AN OPHTHALMOLOGIC CONTRIBUTION TO THE STUDY OF FEMININE STERILIZATION. M. AVERBACH, Ann. d'ocul. **168**:542 (July) 1931.

The sterilization of women in relation to diseases of the eye has been studied by Averbach. He has attempted to determine the indications which the eye may give for sterilization and what influence sterilization may exert on the eye. In conclusion he says that it is very doubtful that sterilization is the solution of the problem when the ophthalmologist desires to prevent pregnancy because of the danger to the sight of the mother and child. He says that it is hardly to be doubted that sterilization prematurely weakens sexual functions in women. He believes that most ophthalmologists agree that the endocrine system plays an important rôle in the etiology of many eye diseases. He mentions among these hemeralopia, cataract and glaucoma.

BERENS, New York.

THE EFFECT OF LIGATION OF THE VAS DEFERENS ON EPILEPSY AND MENTAL DISEASE. A. KRAPIVKIN, Jahrb. f. Psychiat. u. Neurol. **48**:31 (May 15) 1931.

Ligation of the vas deferens (Steinach's operation) had no effect on the psychotic manifestations in eleven patients with mental disease (seven epileptic, two schizophrenic and two oligophrenic patients). In two of the patients (one epileptic and one an idiot), the operation had a very favorable effect on the excessive masturbation. It is noteworthy that during the first three to five weeks following operation, the epileptic patients either had no attacks of epilepsy or its equivalents, or the number and severity were markedly diminished. Improvement, however, ceased after the five weeks.

KESCHNER, New York.

RETINOBLASTOMA: ITS RECOGNITION WHEN THE FUNDUS OCULI IS OBSCURED. G. M. BRUCE, Arch. Ophth. **5**:890 (June) 1931.

In this article the author discusses the problem of diagnosing retinoblastoma when one is unable to see the fundus with the hand ophthalmoscope. Abstracted, the important observations are: invasion of the iris, pseudohypopyon, the development of ocular hypertension, shrinkage of the globe, with or without perforation, and intra-ocular hemorrhage, especially when connected with hemorrhagic staining of the cornea. These diagnostic points are of great importance when present under the conditions with which this paper is concerned.

SPAETH, Philadelphia.

A CASE OF SCHIZOPHRENIA OF LONG DURATION. L. S. PENROSE, Brit. J. M. Psychol. **11**:1, 1931.

This article contains a detailed description of a case of schizophrenia that lasted over half a century. The fantasy life in the patient is described fully, and the author shows how it occupied completely the intellectual and emotional powers of the patient and kept them alert throughout the entire sickness. The case is discussed with various etiologic theories, including the psychoanalytic, neurogenic and constitutional, and the effect of various precipitating factors and their influence on the contact of the fantasy life are presented.

ALLEN, Philadelphia.

THE EFFECT OF STIMULATION OF THE SYMPATHICUS ON THE RETINA. S. DUCRET and S. KOGE, Arch f. d. ges. Physiol. **227**:71, 1931.

W. R. Hess developed a theory that the vegetative nervous system regulates the excitability of the organs of the somatic system. To examine this theory, the sympathicus was excised in the region of the ansa subclavia. The rods and cones of the retina were studied to determine whether their position is changed after this operation. The authors were not able to show a definite influence of

this operation on these cells of the eye of the frog; however, these cells show a different position if the animals are kept in a dark room or under the influence of light.

VASOMOTOR INNERVATION OF THE LUNG. J. P. FEDOTOW, Arch. f. d. ges. Physiol. **230**:273, 1932.

The vasomotor fibers supplying the lung of the frog leave the medulla oblongata with the vagus; the fibers carried by the nervus sympathicus also enter the nervus vagus. Stimulation of the nervus vagosympathicus produces, as a rule, a contraction of the vessels of the lung. The vasomotor fibers which leave the medulla oblongata are able to produce dilatation as well as constriction of these vessels; the effect of constriction is more frequent. The sympathicus is also able to produce constriction as well as dilatation, but the effect of dilatation is here predominant.

THE INFLUENCE OF THE SYMPATHETIC ON SENSIBILITY. E. T. BRUECKE and E. KRANNICH, Arch. f. d. ges. Physiol. **228**:267, 1931.

The chronaxia of the flexor reflex in frogs was not changed by the severance of the sympathetic fibers to the leg. However, stimulation of the sympathetic, in eight of ten experiments, lowered the chronaxia of the sensory fibers without changing the rheobase. A change similar to that described here in the sensory fibers was found in motor nerves by Achelis and in muscles by Lapicque and Orbeli.

THE SIMULTANEOUS STIMULATION OF ANTAGONISTIC CENTERS. K. GOLLWITZER-MEIER, Arch. f. d. ges. Physiol. **227**:549, 1931.

Intra-arterial or subdural injection of sodium carbonate solutions excites simultaneously the stimulating and the inhibitory centers of the circulation. As long as the vagi are intact, inhibition is stronger. After severance of the vagi, the stimulating effect on the circulation becomes apparent: increase in the blood pressure and in the pulse rate.

PHYSIOLOGY OF THE LABYRINTH IN MAN. P. VOGEL, Arch. f. d. ges. Physiol. **230**:16, 1932.

The author stimulated the labyrinth in normal persons by a direct current. The directions of the falling reactions depend on the position of the head, as described by Bárány. The chronaxia of the vestibular apparatus was determined as between 10 and 20 sigmas.

SPIEGEL, Philadelphia.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

TRACY J. PUTNAM, M.D., *Secretary*

Four Hundred and Second Meeting, Oct. 20, 1932

W. JASON MIXTER, M.D., *in the Chair*

DIFFERENTIAL THERAPEUTIC EFFECTS OF ARSPHENAMINE AND TRYPARSAMIDE (WITH LANTERN SLIDES). DR. H. C. SOLOMON and DR. S. H. EPSTEIN.

It is well known that arsphenamine is a potent spirocheticidal drug, both in vitro and in vivo. Tryparsamide, on the contrary, has little effect on Spirochaeta pallida as it exists in the early stages of syphilis in human beings. On the other hand, whereas tryparsamide has a marked therapeutic effect in syphilis of the central nervous system, arsphenamine, in comparison, has a very low index of efficacy. The mechanism of activity of tryparsamide is not known. The drug was synthesized in an attempt to find an agent having high trypanosomicidal value. As a result of prolonged studies, "tryparsamide" was formed, and it had a high therapeutic index. Lorenz, Loewenhart, Bleckwenn and Hodges found that tryparsamide has a great effect in syphilitic involvement of the central nervous system. Moore and others have showed that tryparsamide has little or no effect in early syphilis or in syphilis with cutaneous manifestations.

The following case shows well the difference in the effect produced by the two drugs: Treatment of a patient was begun during the latter part of the primary period; under conventional treatment with arsphenamine, bismuth and mercury the symptoms disappeared and the Wassermann reaction of the blood became negative. A year after beginning treatment, the patient complained of severe headaches. Examination revealed evidences of syphilitic meningitis. The spinal fluid was strongly positive with each test, and there were approximately 1,000 cells per cubic millimeter. Weekly injections of tryparsamide alone were given. The symptoms promptly receded, and after a few months the spinal fluid became normal. While under this treatment, however, the Wassermann reaction of the blood became positive, and there developed recurrent lesions of the skin and mucous membranes. After a short period of treatment with arsphenamine the lesions all disappeared, and the Wassermann reaction of the blood again became negative.

This case illustrates well the superiority of arsphenamine as regards the effects of syphilis on the skin and mucous membranes, and its relative impotency to affect syphilis of the nervous system. It shows also the much greater effectiveness of tryparsamide in syphilis of the nervous system and the failure of tryparsamide to prevent relapses of the skin and mucous membrane.

The nine or ten years of experience with tryparsamide has so generally indicated its superiority in involvement of the central nervous system that it is unnecessary to give examples. It has been less frequently noted, however, that arsphenamine has much more effect on lesions of the skin and bones than has tryparsamide. The following case exemplifies this: The patient, a woman, aged 46, had typical signs of dementia paralytica. She was subjected to two courses of malaria and to injections of tryparsamide, as well as to a few attacks of fever produced by typhoid vaccine. There was definite mental improvement, and the spinal fluid became normal. However, she continued to have occasional seizures. Subsequent to the fever therapy and while she was receiving tryparsamide, there developed a gumma of the frontal bone. Arsphenamine, in doses of 0.3 Gm., was given weekly. The tumor rapidly disappeared.

Sodoku, or rat-bite fever, like the manifestations of systemic syphilis, responds well to arsphenamine. There is rapid involution of the primary sore. Likewise, the cutaneous manifestations disappear, and the fever is interrupted. If tryparsamide is administered, however, the result is different. The effect on the primary sore is practically identical with that obtained with arsphenamine. But there is little effect on the lesions of the skin, and certainly no beneficial effect as regards the fever. In other words, tryparsamide has a definite effect on the open lesion, stimulating the tissue to rapid repair, whereas the disease otherwise is apparently unaffected. This seems to indicate that while arsphenamine affects Spirochaeta morsus-muris, tryparsamide affects merely the activity of the local tissues about the open sore, stimulating them to heal, without affecting the pathogenic organism itself.

This difference between the effects of arsphenamine and tryparsamide, respectively, is also indicated in malaria. Arsphenamine kills the plasmodia, stopping the fever promptly. Tryparsamide, on the other hand, neither controls the fever nor has any obvious plasmodicidal effect.

In summary: 1. Arsphenamine is more effective in early and late systemic syphilis presenting lesions of the skin, mucous membrane and bones, whereas tryparsamide is more effective when the central nervous system is involved. 2. Arsphenamine cures sodoku, whereas tryparsamide does not, though the latter drug modifies the lesions of the skin and local lesions as effectively as does arsphenamine. 3. Arsphenamine is a plasmodicide and cures inoculation malaria, whereas tryparsamide has no noticeable effects either on the plasmodia in the blood or on the course of the fevers. We conclude, therefore, that arsphenamine is both a spirocheticide and a plasmodicide, whereas there is no evidence that tryparsamide has any direct lethal effect on Spirochaeta pallida, Spirochaeta morsus-muris or the plasmodia of inoculation malaria. The beneficial action of tryparsamide on syphilis of the nervous system must be founded on some other characteristic. The results of our experience with sodoku suggest that there is a stimulation to the local tissues, which heals promptly without destruction of the spirochetes in the blood stream. How this stimulation is produced is not clear. One may be justified in assuming that, as in the case of the local beneficial action in sodoku, so in syphilis of the central nervous system tryparsamide has a local action within the local areas of the nervous system.

DISCUSSION

DR. J. B. AYER: Brown and Pearce advocated that mercury must be used in conjunction with tryparsamide. We seem to get as good results without mercury in early cases, which are the only ones we can follow at the Massachusetts General Hospital.

DR. S. H. EPSTEIN: Your experience is apparently similar to ours at the Psychopathic Hospital, namely, that tryparsamide alone seems to be as effective.

DR. H. C. SOLOMON: In the majority of cases, it does not make any difference whether or not one uses any other drug with tryparsamide.

TUMORS OF THE BRAIN ASSOCIATED WITH MARKED PLEOCYTOSIS IN THE CEREBROSPINAL FLUID. DR. H. HOUSTON MERRITT and DR. MERRILL MOORE.

A marked pleocytosis in cases of tumor of the brain is rare. Ayer examined the lumbar fluid in 67 cases and found more than 10 cells in only 6 cases; in no case was there over 50 cells. Moersch, in 252 cases, found more than 100 cells in the lumbar fluid in only 2 cases. Alpers, in the ventricular fluid in 102 cases, found a slight pleocytosis in 9, from 7 to 20 cells in 7, 73 cells in 1, and 375 cells in another. Spurling and Maddox, in the fluids in 108 cases, reported no cases with over 10 cells. In view of these reports the recent finding of pleocytosis in 2 cases of tumor of the brain was thought significant.

CASE 1.—E. S., a Syrian merchant, aged 62, was admitted to the neurologic service of the Boston City Hospital on Feb. 7, 1929, with a history of mental confusion, drowsiness, severe bilateral temporal headaches, vomiting and incontinence of urine for three weeks. A general physical examination gave negative results. Neurologic examination revealed bilateral choked disk, slight left hemiparesis, with a Babinski reflex and ankle clonus, and slight stiffness of the neck, with Kernig's sign. The urine was normal. There was a moderate leukocytosis. The Kahn reaction of the blood was negative. Lumbar puncture made immediately on the patient's admission showed a pressure of 450 mm. of spinal fluid. The fluid was cloudy and xanthochromic, and contained 2,106 white blood cells per cubic millimeter, 90 per cent of which were polymorphonuclear leukocytes. The total protein content was 216 mg., the sugar 80 mg. and the chloride content 696 mg.; the Wassermann reaction was negative. Cultures of the blood and spinal fluid were sterile. The changes in the spinal fluid were interpreted as indicating a suppurative process within the brain which had not as yet caused a meningitis. The left hemiparesis indicated that the lesion was in the right hemisphere, and from the history of mental disturbance it was thought that the lesion was probably frontal. Therefore the diagnosis of an abscess of the right frontal lobe was made, and the right frontal region was tapped by Dr. Donald Munro on the day of admission. No pus was found, and culture of the bloody fluid obtained on aspiration was sterile. Dr. Munro thought that the brain tissue in the region explored was unusually soft. The following noon lumbar puncture was again performed and the initial pressure was 300 mm. The fluid was cloudy and slightly blood-tinged. It contained 3,000 white blood cells, chiefly polymorphonuclear, and 45,000 red blood cells per cubic millimeter. The total protein was 426 mg. The patient became more stuporous, and he died about twenty-four hours after entry. At necropsy, a large infiltrating tumor was found in the medial portion of the right hemisphere, involving the corpus callosum and extending into the left frontal lobe. The tumor appeared vascular, and there were numerous small hemorrhagic areas. Microscopic examination revealed a glioblastoma multiforme.

CASE 2.—G. B., a white man, aged 50, married, a printer, who was admitted to the Boston Psychopathic Hospital on Oct. 23, 1931, for two years had been worrying about his business and "had not been feeling well." Eight weeks before admission he complained of "nervousness," lost interest in his work and complained of weakness in both legs. One month before admission he had a momentary loss of consciousness while driving a car. After this he had several transient attacks of weakness and fell on several occasions, once falling down a flight of steps. He was in low spirits and was sent to the hospital with a diagnosis of hysteria. Physical examination gave negative results. The blood pressure was 128 systolic and 70 diastolic. On neurologic examination the cranial nerves and the optic fundi were normal. There was no demonstrable paralysis or sensory loss. No psychomotor disturbance or apraxia was demonstrated. The deep reflexes were hyperactive, and there was a questionable Babinski sign on the left. The gait was unsteady. The patient staggered from side to side and required help in getting in and out of bed; in performing these movements he gave the impression that when he cooperated he was able to perform the movements better. He spoke in a whisper, but on encouragement spoke in a normal voice. Lumbar puncture, three days after admission, showed 8 cells, total protein 82 mg., sugar 74 mg. and a gold curve with a midzone rise. Pressure readings were not taken. Six days after entry, the patient sank into coma and had a slight elevation of temperature (101 F.). The neck was not stiff, and the Kernig sign was absent. Lumbar puncture at this time showed an initial pressure of 250 mm. of spinal fluid, with normal dynamics. The fluid was cloudy, and contained 4,000 white blood cells, 70 per cent of which were polymorphonuclear; the total protein was 235 mg. and the sugar 43 mg. Cultures of the blood and spinal fluid showed no growth. In spite of the negative smears and the only slightly reduced sugar content, it was considered advisable immediately to repuncture and administer serum. Later in the same day, a cisternal puncture was done, and an antimeningococcus serum was

given. The cisternal fluid at this time showed 4,800 cells and contained 145 mg. of protein and 62 mg. of sugar per hundred cubic centimeters. After the serum was given there was a temporary rise in the number of cells in the spinal fluid, with a subsequent gradual fall. There was no change in the patient's condition, however, and he died eleven days after entry with the development of no additional neurologic signs. It was thought before death that there was probably either an abscess or a tumor, but in the absence of localizing signs and on account of the poor general condition of the patient operative procedures were thought to be inadvisable. Necropsy, by Dr. Myrtelle Canavan, revealed a large infiltrating tumor involving the anterior portion of the corpus callosum and the adjacent white matter of both frontal lobes. The anterior horns of both lateral ventricles were compressed. The tumor was very vascular in appearance, and in its posterior portion was a fresh hemorrhagic spot, about 2 by 2 cm. in area. No definite line between tumor tissue and brain was found, but the greatest diameters of the tumor were approximately 3 cm. in the anteroposterior direction and 8 cm. in the transverse. Microscopic sections of the tumor showed a glioblastoma multiforme.

The cases are presented to show that tumors of the brain are sometimes accompanied by pleocytosis in the cerebrospinal fluid. Similar cases have been reported by Parker and Moersch. As to the cause of the pleocytosis, Dr. Ayer attributed the cellular response to a low grade meningeal inflammation adjacent to hemorrhagic or softened areas occurring in the tumors. This is supported by recent work by Cone and Barrera, who produced aseptic cerebral emboli in animals and found inflammatory reactions (polymorphonuclear leukocytes) around the infarcted areas. They found also that these cells might reach the cerebrospinal fluid, particularly if the softened area was in relation to the ventricles.

DISCUSSION

Dr. Frank Fremont-Smith: The fact that tumors of the brain may be associated with cells in the cerebrospinal fluid is important. The differential diagnosis from abscess of the brain is always difficult, often impossible. I remember a patient who was at the Massachusetts General Hospital in 1924, a man, aged 53, with some symptoms for six or eight months, and mental changes for two months, who had gradually become stuporous. Four lumbar punctures were made before operation. The first revealed 45 cells per cubic millimeter (no polymorphonuclears); the second, fifteen days later, 9 cells; the third, five days later, 21 cells, of which 5 were polymorphonuclears; the fourth, five days later, 15 cells. There were choked disks and a markedly elevated intracranial pressure, varying from 560 to 240 mm. of spinal fluid. The fluid was slightly yellow and had a protein content on successive punctures of 250, 182, 333 and 333 mg. per hundred cubic centimeters. Because of the increase in cells, particularly because of the presence of polymorphonuclears at one puncture, a diagnosis of abscess of the brain was made. Autopsy revealed a large midline glioma extending deeply into both frontal lobes. The tumor showed considerable degeneration close to and probably involving the wall of the ventricle. It seemed evident that the cells obtained at lumbar puncture had entered the spinal fluid where this area of degeneration approached closely to the ventricular wall. It is difficult to see how a differential diagnosis between abscess of the brain and tumor of the brain could have been made in this instance.

Dr. Merritt and Dr. Moore have shown that an increased cell count in the spinal fluid does not exclude tumor of the brain. The absence of cellular increase, on the other hand, excludes abscess of the brain. I do not know of a case of abscess of the brain without an increase in cells; nearly always a few polymorphonuclears can be found.

Dr. E. M. Cole: In 36 verified tumors of the brain, 6 (16.7 per cent) showed cells in the cerebrospinal fluid. In the cases with cells, the pressure ranged from 100 to 400 mm.; the protein ranged from 35 to 153 mg.; the cells ranged from 13 to 700. In only one case were the cells other than lymphocytes; this exception was in the case with 700 cells, 16 per cent of which were polymorphonuclear

leukocytes. In all of the cases the sugar was normal, and in not more than two were the tumors of the same type. The observations are tabulated in the accompanying table.

DR. H. C. SOLOMON: There is one point of interest in the second case in which there were two punctures. After the first puncture in which there were slightly abnormal observations, a huge hemorrhage probably occurred, and at that point one finds a large number of cells; hence there is reason to suppose that the hemorrhage was the activating agent of the pleocytosis. There had been a large tumor without increased intracranial pressure for a long time. It is also of interest that in this case, in which mental symptoms of a psychoneurotic type predominated, there was a tumor of the corpus callosum.

DR. W. J. MIXTER: I believe that the presence or absence of cells in the spinal fluid, as in these cases, may well be of considerable importance in the diagnosis of tumor of the brain though as yet one is somewhat in the dark as to the cause of the pleocytosis. Did these patients show a leukocytosis?

Observations on the Spinal Fluid in Tumor of the Brain

Case Number		Pressure	Total Protein	Cells	Diagnosis
1		400	...	25 lymphocytes	Cerebellar astrocytoma
2		400	78	67 lymphocytes	Frontoparietal cyst
3		335	75	13 lymphocytes	Glioma
4		100	150	20 lymphocytes	Medulloblastoma
5	9/24/28	180	35	11 lymphocytes	Third ventricle glioma
	9/23/30	240	...	700 16% polymorphonuclears / 84% lymphocytes	
	11/ 9/30	240	153	90 4% polymorphonuclears / 96% lymphocytes	
6	8/20/32	195	48	73 lymphocytes	Metastatic carcinoma of
	9/ 4/32	210	52	22 lymphocytes	cerebellum
	9/28/32	240	46	4 lymphocytes	

DR. H. H. MERRITT: As I recall it, both of the patients presented a slight leukocytosis in the blood. I do not think, however, that the presence or absence of leukocytosis is of any great diagnostic value. Leukocytosis is not found in abscesses of the brain, unless the primary focus is active and is the cause of such a response in the blood. The one point which is of value in differentiating cerebral tumors from abscesses is the presence or absence of a primary septic focus (since abscesses of the brain are always metastatic) such as infected sinuses or mastoids, or abscess of the lungs. One should search carefully for evidence of such foci in all cases in which there are signs of an expanding intracranial lesion.

AN ADDITIONAL CASE OF HEMANGIOMA OF THE RETINA AND CEREBELLUM WITH A NOTE ON LINDAU'S SYNDROME. DR. HENRY VIETS.

In 1926, Lindau described a syndrome of angioblastoma commonly involving the retina, the cerebellum and, more rarely, the pancreas and kidneys. The retinal aspect of this disease had long been recognized by ophthalmologists, for it was described by Fuchs in 1882 and more definitely by von Hippel in 1904. Additions were made to the literature by Czermak, Coats and Brandt. The latter, in 1921, made a postmortem examination in von Hippel's case of seventeen years before, and found, in addition to the retinal changes, a cerebellar cyst and a tumor of the cauda equina of similar character. It was not, however, until 1926 that Lindau first clearly described the complete syndrome, gathering from the literature fifteen

cases. In 1928, Cushing added another case of his own and found four more in the literature. Since that time five or six cases have been reported, and in some of the older cases of von Hippel's disease of the retina the patients have been reexamined and a pathologic process in the cerebellum discovered.

F. L. W., a man, aged 48, entered the Massachusetts General Hospital on May 20, 1932, with symptoms suggestive of cerebellar disease for about four months, particularly dizziness, headache and extreme and continued vomiting. When first seen he was exhausted, dehydrated and in partial coma. The right eye showed a typical condition of von Hippel's disease; this led to an emergency operation on the cerebellum, in which a cyst was found in the right hemisphere. The patient made a prompt recovery and left the hospital within a month. He has been seen a number of times since and appears to be free from cerebellar symptoms. The condition of the eye, in which there is a large cyst, has progressed.

The chief features of Lindau's disease are: the well marked hereditary tendency; the predilection for the angioblastoma to develop in the retina and in the cerebellum; the slow but definite course of the disease, in which the retina may be involved many years before the cerebellum, or vice versa; the rareness of the complete syndrome, there having been only thirty cases reported, and the excellent response to surgical exploration of the cerebellar lesion.

DISCUSSION

DR. W. J. MIXTER: I think that this is about the first time that one of these cases has been completely recognized and operation advised by a neurologist.

DR. DONALD GREGG: Is there any reason why the tumor occurs in the cerebellum instead of the cerebrum?

DR. H. R. VIETS: The cysts are practically always in or near the tonsil of the cerebellum, under the roof of the fourth ventricle. Very rarely a similar lesion is found in the cerebrum or in the spinal cord. Why there is a predilection for the cerebellum and retina is not known.

DR. S. TARTAKOFF: Does a cerebellar syndrome later develop, and will early enucleation of the eye prevent it?

DR. L. EISENHARDT: Many of these tumors were formerly classified as gliomas. They are all cerebellar in our series. Above the tentorium there may be angioblastic meningiomas. I have recently investigated twenty-six tumors of the cord in our collection; two are angioblastic.

DR. C. L. KUBIK: I have seen one hemangioma of the cerebrum. This was partly removed by Dr. John Hodgson at the Massachusetts General Hospital. Subsequent to the operation the patient was given roentgen treatment, and there have been no symptoms of recurrence for about four years.

DR. W. J. MIXTER: There were no optic symptoms in that case.

DR. H. R. VIETS: The cases of von Hippel's disease at the Eye and Ear Infirmary are being followed, but none, as yet, has shown neurologic symptoms. It is well known, however, that there may be a period of fifteen or twenty years between the optic and the cerebellar symptoms. Enucleation of the eye has not succeeded in stopping the disease. On the other hand, cerebellar symptoms may precede the disease in the retina.

There appear to be two kinds of angiomatous tumors arising from blood vessels of the central nervous system; the first has been called by Cushing and Bailey "angiomatous malformations" and the second type "hemangioblastomas." The latter are the true neoplasms, and this is the type found only in Lindau's disease.

DR. W. J. MIXTER: In some of the postmortem studies, are there similar lesions in other portions of the body?

DR. H. R. VIETS: In a number of cases there have been found coincidental hemangioblastomatous cysts of the pancreas and kidney. These lesions, symptomless, were only found post mortem.

DR. W. J. MIXTER: That is part of the syndrome of which I had not heard and which I consider important.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 17, 1932

I. B. DIAMOND, M.D., *Vice-President, in the Chair*

CAUSALGIA: PRESENTATION OF A CASE. DR. HALE HAVEN.

History.—J. M., a white man, aged 21, whose family history was irrelevant was admitted to the Cook County Hospital on Oct. 24, 1932, with the history that, having been well, except for pneumonia two years previously, in the afternoon on August 15, while erecting a radio aerial, he lost his balance and fell from a height of 6 feet. In falling his left arm struck the top of a picket fence, and one of the iron top spikes penetrated the medial aspect of the arm near the juncture of its middle and upper thirds. Immediately after the accident he noted nothing wrong with the hand or arm. There was slight oozing of blood from the puncture wound, which the patient painted with an antiseptic and bandaged. Early that evening, however, he began to feel shooting pain in the whole hand; there was no pain in the arm. A physician prescribed a sedative, which relieved the pain for the next two weeks and permitted normal functioning of the hand and arm. The patient was awakened one morning by pain in the hand of the same character as before, but much more severe. The sedative that he had been taking failed to relieve the pain, which continued until 7:00 p. m., when relief occurred spontaneously, and lasted until early the next morning. The pain continued to occur in the day time for ten days, after which it became sharper, more burning and constant, although it was still limited to the hand. The arm then began to become flexed, as did the hand. The pain became limited to the radial half of the hand, and the patient noticed that the ring and middle fingers were becoming stiff and the skin was becoming glossy. A hot towel placed on the hand gave some relief for the first time in ten days. The patient noticed that moisture lessened the pain, and that he could bear it if the hand was kept damp. The finger-nails began to grow, the hand as well as the arm, became flexed and the skin of the whole hand took on a reddish, shiny appearance. The patient could not bear to have the hand touched. A loud noise, a sudden jarring or anything dry touching the hand would increase the pain. The patient then became supersensitive to a dry object touching any part of the body, as this would immediately cause pain to shoot from the part touched into the left hand. There was constantly present a shooting pain, which the patient recognized as being synchronous with the heart beat.

Examination.—The patient presented an anxious, unkempt appearance. He constantly moaned with pain, would permit no one near him and insisted on keeping the left hand covered with a wet cloth. Narcotics in large doses failed to relieve the pain. The wound received at the time of the accident had healed without evidence of infection. The left forearm was held flexed on the arm and the hand was flexed on the forearm, with the fingers drawn together at the tips in the form of a cone. The nails were long and ridged. The skin of the hand was shiny and opalescent and seemed tightly drawn. Efforts to examine the sensory or motor functions met with such howls of pain that accurate estimation was impossible. It was determined, however, that there was some diminution of sensitivity to pin prick in the center of the palm. Above and behind the scar of the wound was a subcutaneous nodule, palpation of which caused greater pain to shoot down the arm into the hand. A diagnosis of causalgia was made, and it was decided to explore the median nerve.

Operation.—On November 2, the median nerve was exposed. There was much dense scar tissue about the site of the injury. A neuroma-like, fusiform swelling of the median nerve was noted at the junction of the middle and upper thirds of its course in the arm. At this point it was surrounded with scar tissue and was

firmly adherent to the brachial artery, the nerve seeming to pulsate with each beat of the artery. The nerve was freed from the artery by blunt dissection, the neuromatous portion excised and an end-to-end suture made. The artery was extremely small, not exceeding 2 mm. in diameter. A periarterial sympathectomy was attempted, but the wall of the artery was ruptured and ligation was necessary. The suture line in the nerve was protected by a transplantation of free fat, and the wound was closed.

Course.—On recovery from the anesthetic, the patient was free from pain. The next day there was marked amelioration of the trophic disturbances in the hand, which at the time of this presentation, two weeks after the operation, have almost disappeared. Function of the hand is practically normal, except for the lesion of the median nerve.

Histologic Studies.—The specimen removed at operation was embedded in paraffin and sectioned serially. No evidence was found of direct penetration of the nerve sheath. There was marked perineural and intraneural inflammatory reaction, increase in intraneural vascularity, with perivascular round cell infiltration, and a heavy deposit of fibrous tissue around and between the fascicles of the nerve. Myelin sheath stains by Weil's method revealed all stages of demyelinization. Silver stains (Davenport's method for paraffin sections) showed fragmentation of many axons. Both these methods also revealed numerous apparently normal fibers throughout the length of the excised portion, evidence that the lesion at the time of excision was only partial.

Comment.—This is a case of causalgia, corresponding closely to the classic description by Weir Mitchell. Relief was obtained by surgical treatment.

DISCUSSION

DR. G. B. HASSIN: A clinical picture typical of causalgia was caused in this case by an inflammatory process in a peripheral nerve, and not by a neuroma, which is a new growth consisting entirely of nerve tissue. Causalgia, therefore, may be the result of neuritis; I think that Dr. Haven's case is the only one that strikingly demonstrates such a pathogenesis. I believe this case proves that causalgia is due to a lesion of the peripheral spinal nerve, rather than of a sympathetic nerve, in contrast to prevalent teaching, and that findings to this effect can be demonstrated microscopically.

DR. HALE HAVEN: I recall only one reported case of causalgia in which proliferation of the connective tissue was found. I might emphasize the relation of the artery and nerve in the case discussed. One may assume a constant irritation of the nerve at the point of injury, which was continued mechanically by the constant pulsation of the artery. In a brief search of the literature, I have found up to this time only two reports with pathologic studies of the nerve. Both authors reported an intraneural fibrosis.

A CASE OF MEGALENCEPHALY WITH DIFFUSE GLIOBLASTOMATOSIS OF BRAIN-STEM AND CEREBELLUM. DR. ARTHUR WEIL.

This article will be published in full in a later issue of the ARCHIVES.

METASTATIC CARCINOMA OF THE EYE AND BRAIN. DR. ISIDORE FINKELMAN and DR. LEO L. MAYER.

This case is one of metastatic carcinoma of the brain and structures of the eye. The primary site of the tumor was in the breast (inoperable medullary carcinoma). Complete blindness developed in the right eye and mental symptoms appeared. Our interest in the case was first aroused by the fact that the right pupil remained responsive to light, despite the fact that the patient was completely blind in that eye. It was thought that perhaps a basis for this interesting phenomenon, reported by one of us (Gifford, S. R., and Mayer, L. L.: Retained Pupillary Reactions

with no Perception of Light, *Arch. Ophth.* **6**:70 [July] 1931), could be found. However, the enormous involvement of the brain prevented exact localization.

The microscopic findings in the brain were: multiple carcinoma metastases in the meninges, brain and optic nerves. Examination of the structures of the eye revealed metastases in the choroid and optic nerve.

Psychotic behavior in patients with carcinoma may be due to encephalitis (encephalopathy) caused by toxins liberated by cancer cells. Hassin and Singer (Hassin, G. B., and Singer, H. D.: Histopathology of Cerebral Carcinoma, ARCH. NEUROL. & PSYCHIAT. **8**:155 [Aug.] 1922) have described extensive changes in the nerve cells in parts of the brain remote from the metastases.

DISCUSSION

DR. ALEX J. AZAR, Elgin State Hospital: Was the type of carcinoma determined, and if so, was it identical with that in the breast?

DR. G. B. HASSIN: The most interesting feature in this report is the apparently normal reaction around the foci of cancer cells. In many cases of carcinoma of the brain there is no reaction around the foci of cancer cells. When there is a reaction, it is an enormous proliferation of mesenchymal and not of glia cells. The latter die, like the ganglion cells, and cannot react.

As to the cause of destruction of brain tissue, some authors assume a mechanical factor. The cancer cells become so numerous that by mere pressure they actually destroy the brain tissue. In one of my cases it was possible to show the degeneration of the ganglion cells by the invasion of cancer cells, as if the latter ate up the former. In another case it was possible to show the presence of a so-called transition zone, with marked cell degeneration and numerous metastases in the adventitial spaces of the cerebral blood vessels. The brain tissue thus succumbs not to one factor but to a great number of factors. Which factor was predominant in Dr. Finkelman's case is not possible to tell from the few specimens demonstrated.

DR. R. L. JENKINS: Were metastases present in the lung? How did the metastases reach the brain?

DR. J. T. NERANCY: It is of interest that, in spite of complete unilateral amaurosis, the pupillary light reflex was preserved. Behr, Liebrecht and others reported similar findings in congenital and acquired amaurosis, thus adding weight to the theory which postulates the existence of two sets of fibers in the optic nerve. As the case now under discussion came to autopsy, it would appear important to learn whether or not the metastasis had completely interrupted the nerve. It would be unusual if not a single fiber was left unsevered. The multiplicity of the metastases in the brain does not invalidate this point.

DR. I. FINKELMAN: The tumor was a medullary carcinoma, identical with that in the breast. The type of tumor cell may perhaps give a clue to the extent of the toxic encephalitis; a more embryonic type of cell would probably liberate more toxin. In this case we did not find transition zones as described by Dr. Hassin.

There were no metastases in the lungs.

As to the mode of transmission, one can only theorize as to whether the cells traveled along the lymph channels. If so, the cancer cells would travel against the lymph current

DR. LEO L. MAYER: The optic nerve was entirely involved. We have seen this frequently, and many cases have been reported in which there was no response to or perception of light, and yet there was reaction in the pupil. No one has been able to explain this phenomenon. In the case reported, the optic nerve was destroyed entirely by the ingrowth of the cancer cells. There is some reason to believe that there may be stronger fibers of the reflex arc which at times are not destroyed.

Our interest lay in trying to find some center in the brain where the pupillary reflex arc might be found intact, but because of the enormous destruction of tissue this was out of the question.

Another point that I wish to stress is the rarity of the condition. Only 130 cases have been reported; this, I am sure, is due to the fact that the eye is not examined in many cases. I wish to make a plea for an examination of the eye at least at necropsy to discover if the optical membranes are involved.

NARCOSUSTAINED THERAPY WITH DIALLYLBARBITURIC ACID IN PSYCHIATRY. DR. ALEXANDER B. MAGNUS.

Klasi is credited with having systematized in 1929 the method of inducing prolonged sleep which is employed in modern psychiatry. In 1927, Müller reported the intramuscular administration of a soluble preparation of diallylbarbituric acid for this purpose, and shortly afterward Lutz described its use rectally. In the use of this method, the procedure may be divided into stages. In the prenarcotic stage, the patient is prepared as for a major operation and is assured that some important changes will take place after the treatment. One capsule containing 4½ grains of diallylbarbituric acid is given orally, and the dose is repeated every four hours until signs of dimming of consciousness appear. The dose should not be repeated when the patient is drowsy, and swallowing is difficult. There is a decided advantage in giving the initial dose in the evening. At the time when the patient would ordinarily awaken, he may be kept asleep by the administration of smaller doses. When the patient is combative, resistant or negativistic, 2 cc. of the drug, or the equivalent of 3 grains, is given intramuscularly instead of orally. During the stage of narcosis, proctoclysis is at once begun, and about 2,400 cc. of physiologic solution of sodium chloride, in six divided portions, is given every twenty-four hours by the drop method. To three of the feedings a 5 per cent solution of grape sugar is added, one dose of sugar solution being given alternately with one of physiologic solution of sodium chloride. A total of 60 Gm. of dextrose is the average amount used in twenty-four hours.

The patient is kept in a state of narcosis for about ten days. On the third day, the doses of diallylbarbituric acid are diminished, for at this time a rise of temperature usually occurs. Complications have their greatest incidence on this and on the seventh day of the treatment. There is no time schedule for rectal medication, as the manner of response to the drug is surprisingly variable.

The type of sleep is recorded as sound, light, drowsy or wakeful. The quality of sleep, apparently has no bearing on the clinical outcome. A convenient way of measuring the depth of sleep is to compare the patellar reflexes with the biceps jerks. In a lightly narcotized person the knee jerks are sluggish, while the biceps jerks are brisk; in deep narcosis the knee jerks are lost, while the biceps jerks remain sluggish.

In the postnarcotic or amnesic stage, medication is withdrawn. The patient appears wakeful, sits up and calls for food or water. Consciousness is gradually regained. The patient recognizes people about him, but retentive memory is poor. Such a state of amnesia lasts for seventy-two hours or longer. Speech is inarticulate; single words are enunciated with difficulty and are often repeated over and over. Movements are slow and inexact, and the Romberg sign is positive. The picture bears a close resemblance to that of sleep in epidemic encephalitis. Concomitant with the ataxia, the patient appears overwhelmed with uncertainty. He takes note of everything around him and hesitates. Delusional trends frequently follow partial awakening in this stage, often reflecting conflicts vividly. In many patients, a mild toxic state with predominating visual hallucinations and confabulations, is discernible.

Seventy-eight treatments were administered to sixty-seven patients. Among the conditions treated and the number of cases of each were: schizophrenia, eighteen; manic-depressive psychosis, nine; psychoneurosis, four; involutional melancholia, four. Cases of alcoholic and drug addiction have been omitted from this report and will be presented later. With possibly one exception, frankly involutional types did not respond to the treatment. The combined total percentage of cases of recovery and of improvement was more than 60.

The treatment is not without danger, the most important complications being bronchopneumonia, collapse and drug idiosyncrasies. Of lesser importance are dehydration, urinary retention, trauma and gaseous abdominal distentions. The frequency of pneumonia is lessened by adhering strictly to the details of the preparatory stage, by avoiding too deep narcosis for long periods, by changing the position of the body, by allowing daily periods of arousal and by checking tendencies to vomiting. Too sudden and too deep narcosis may predispose to collapse. Drug idiosyncrasies become apparent generally on the day when the drug is given, manifesting themselves by a generalized scarlatiniform rash, accompanied by profuse nasal and pharyngeal mucous secretions. Such reactions suggest the advisability of administering one dose of the drug before the preparatory stage is fully under way. No cardiac complications have been encountered. Kidney conditions, acute or chronic, are contraindications.

DISCUSSION

DR. CHARLES F. READ: I began to follow the subject of sustained sleep therapy by the use of a barbital derivative about ten years ago. After a time it appeared that this drug was too dangerous to use. Recently at the Elgin State Hospital we have used sodium amytal, but only in daily doses. We secured no permanent results. Later, we cooperated with Dr. Magnus, and his report includes the results in thirteen of our cases. The procedure must be carried out carefully. It has rather alarming incidents, chief of which is the fever.

We have been pleased with the results obtained, which will be published later in a communication by Dr. Magnus, Dr. Nerancy and myself. They point to more than a coincidental improvement in the patients. One case was that of a marked depression; after the sleep the patient was much improved, and was sent home. In another case, that of a man with a hypochondriac, involutional type of disorder, the treatment had to be discontinued after the third day because of bronchopneumonia. Yet improvement was marked, and it was later reported that the patient was in good condition.

I think that this contribution is further evidence that sustained narcosis is of decided benefit in many cases, even in some of chronic nature. However, the procedure can be undertaken only with great precaution, as has been outlined by Dr. Magnus.

DR. ALEXANDER B. MAGNUS: There is a certain hazard in most agents that are used in sustained narcosis. Sodium amytal has been reported on extensively. My experience with it is limited. I have concluded that success depends largely on the technic and chiefly on the nurses' efficiency. Patients should never be kept in deep narcosis for more than twelve hours. Avertin is still restricted for use in prolonged narcosis because deaths have been reported by surgeons. It is safe as a hypnotic, but its cumulative action needs further study. Somnifen, used by Klasi, like most derivatives of barbituric acid, when employed for sustained narcosis, tends to cause collapse or bronchopneumonia. These two principal hazards are, however, more evident from the use of somnifen than of some of the other derivatives.

Book Reviews

The Sign of Babinski in Primates. By John F. Fulton, M.D., and Allen D. Keller, M.D. Price, $5. Pp. 165. Springfield, Ill.: Charles C. Thomas, 1932.

This monograph is a painstaking and fulsome account of the extensor plantar response in man and other animals. First described by Babinski in 1896, it has become one of the most important signs in clinical neurology and is recognized as a specific sign of injury of the pyramidal pathways. Temporary suppression of the higher centers, such as occurs in sleep or in Cheyne-Stokes respiration, may also cause a "positive Babinski" sign.

The description of the varieties and the phylogenesis of this sign takes up one hundred and five pages. The work is important and well done. The problem is essentially one of the primate foot. In lower mammals no analogy to the Babinski sign is found. In monkeys, only when the lower lumbar segments are completely freed from higher control is the Babinski reflex found. The baboon (chapter III) is considered phylogenetically higher than the monkeys considered in the previous chapter; in this animal, extension in response to plantar stimulation occurs transiently after spinal lesions and definitely after appropriate cerebral lesions. A new phenomenon called "monoplegic flexion" is described, a peculiarity of the baboon. This occurs after focal removal of an arm or leg area, and is an abrupt flexion of the monoplegic extremity following a nociceptive stimulus to any part of the body. After removal of the cerebral leg area in the gibbon, motor power returns much more slowly than in monkeys or baboons; the Babinski sign was strongly positive for three weeks.

Chapter V considers the chimpanzee; three of these animals were operated on in various ways, and the protocols are given in detail, with twenty-four illustrations. Within forty-eight hours after an ablation of the leg area, a slight Babinski sign is seen, with a later definite digital extension and fanning of the toes following a pinprick to the base of one of the outer toes. There is often "shock," with complete areflexia for twenty-four or thirty hours. Removal of the second leg area causes complete areflexia for a week; the ipsolateral leg again loses motor power, indicating bilateral innervation. Not only is the Babinski reflex found, but also the Chaddock and Rossolimo and Oppenheim signs are fickle, and the Gordon and Schäfer signs are generally absent.

Chapter VI takes up the evolution of cortical dominance. The reflex significance of the normal plantar response is explained as follows: "In the intact primate a nociceptive stimulus applied to the sole causes withdrawal of the extremity and flexion of the toes. Collier pointed out that plantar flexion relaxes the skin of the plantar surface so that a sharp object will penetrate less readily than when the skin is taut. It would appear, therefore, that the normal flexor response of the digits is of obvious functional significance." But, after mentioning untenable theories as to the Babinski sign, the author says "As yet we have no suggestions to offer as to the ultimate atavistic significance of the reflex." The discussion of cortical dominance and the clinical comparisons are not adequate; the conclusions as to cortical dominance are vague. It is difficult to believe the statement on page 138, that "simultaneous destruction of both foot areas is virtually equivalent to spinal transection." Even the author's own experiments seem to be inaccurately quoted on page 136, where he says: "It is true that after a period of several months the chimpanzee develops slight extensor tone, but during the first month after the leg area is destroyed, both leg areas are flaccid." Part of this is evidently misprint, but his tables IV, V and VI seem to show that a few days after ablation of the motor area for one or both legs the knee jerks return and become exaggerated. Moreover, the text of the protocols describes voluntary motion as quickly returning. This is not "flaccid paralysis."

One of the most interesting parts of the book is the brief discussion, on pages 130 and 131, of the uncrossed pyramidal pathways. The generally accepted idea that the uncrossed pyramidal fibers are few and variable and absent below the cervical level is reported. Evidence is given that in chimpanzees, and probably in man, a good sized tract passes uncrossed to the sacral cord. That this is functional ipsolaterally is indicated by experiment 16 (page 113); ablation of one leg area in a chimpanzee caused the expected crossed monoplegia with some subsequent recovery of power and return of reflexes; ablation later of the recovered leg area caused complete flaccid paralysis of both legs.

As a piece of book making this monograph is excellent; the publisher is to be congratulated. But the whole book is exotic; half of the beautiful pictures illustrate nothing significant; twenty pages of good exposition could have told the whole story.

Principles of Mental Development. By Raymond Holt Wheeler and F. Theodore Perkins. Price, $3.75. Pp. 529. New York: Thomas Y. Crowell Company, 1932.

In this book the authors have attempted to develop a text in educational psychology based on the Gestalt theory. In a previous book one of the authors (Wheeler) formulated eight laws based on his ideas of psychology, and these laws are made the foundation of the present work. They are all various expressions of the fact that the change of a part of a mental reaction is not in itself important except as it changes the complete picture of the situation or behavior. An example of one of these laws is the law of field "genesis." It is expressed thus: "This law asserts that wholes are not composed of parts, or expressed by parts, but for purposes of description are reducible to them." Another law is that of "individualization": "The law states that the parts of wholes come into existence through an emergence process called individualization, of structuralization or differentiation." It is unnecessary to give more examples.

The neurologic studies of Child and of Coghill can be made to fit in with the Gestalt theories, and it is on such researches that the authors base their interpretation and description of the function of the central nervous system, describing the embryologic gradients; and, in a number of short paragraphs, they discuss such important groups of facts as: the relation of the size of the brain to behavior, the functions of the brain and the effect on behavior of lesions of the spinal cord. Although there are references to such conservative neurologic concepts as pathways, the authors have dogmatically cast aside any connection between the neuron theory and neurology.

The concept of gradients in development of the central nervous system leads by analogy to similar concepts concerning functional processes. The authors go even further and compare the condition arising in the nervous system at the time of a stimulus with the completion of an electric circuit. All the nervous processes that have built up the background of the individual have caused a change in potential between the various parts of his mind, so that when the stimulus impinges, the individual is prepared to react in a preconceived way. Other mental mechanisms are explained on the same basis. For instance, the process of reaching maturity is merely the result of a large number of changes in potential, each one following the other, so that the child is always prepared for some new experience. When the mind has no gradient arising in it, it is not learning. For this reason the child should be placed in a situation in which he is forced to invent. Such old-fashioned methods of pedagogy as "memorizing" or repetition of past lessons are not justifiable, the authors think.

There is a chapter devoted to animal experiments in order to support the application of Wheeler's laws of human nature and the Gestalt theories. They have little place in a book devoted to pedagogy.

Apparently Gestalt has nothing new to offer to explain general learning ability, for the authors' conclusions in this respect are based on the findings of the older psychologists and the behaviorists to a great extent. The four chapters on the laws

of learning are devoted to selected experiments which, in many cases, do not have specific application to the teaching of children. Much effort is expended throughout the book to present evidence from comparative psychology, and the chapters devoted to this type of material are well documented. The several chapters devoted to the problems of personality and discipline are not, unfortunately, documented, but merely present brief expressions of conservative ideas concerning emotion, will, personality, motivation and discipline, all topics important to teachers.

Space is devoted to the learning of special subjects, the material for which is selected from the more recent literature pertaining to reading, spelling, handwriting and arithmetic. However, one-half chapter on arithmetic would not appear to be adequate. In the middle of the book a simple discussion of intelligence tests and the authors' concept of intelligence appear, although educational tests, which are closely allied to the tests of general intelligence, are left to the last chapter, included under the heading of "New Procedures in Education."

Student teachers will find this book difficult to read because of the complex and didactic style of the authors. If the neurologist or psychiatrist who is concerned with educational problems or child development wishes to make himself acquainted with a phase of the newer knowledge of education, he may obtain information by reading some of the less irrelevant material contained in this book. In a field dominated by convention and befuddled by a multiplicity of problems, this book has one advantage, that of presenting a new point of view.

Let's Operate. By Roy H. McKay, M.D., F.A.C.S., and Norman Beasley. Price, $3. Pp. 361. New York: Long & Smith, 1932.

There are two reasons for writing a book: to amuse or to instruct. The last two hundred pages of "Let's Operate" are instructive to the general public, so thoroughly so that I fear they will not be read. The first fifty pages contain interesting reminiscences. From this point the next hundred pages are the only part of the book from which the name could be derived and the only part referred to on the jacket. The book is not amusing or instructive. It is vicious teaching that there are not nearly as many unselfish physicians as there are incompetent ones. I do not believe it, and have as much basis for my opinion as has Dr. McKay.

The medical profession is made up of human beings with the same proportion of the saint and the scoundrel as is found in any other field of work, be it the ministry or bootlegging. It does not claim perfection. The history of surgery has been written in practically the last fifty years. Before that time surgery was in a prehistoric period. The surgical profession has been trying to digest the tremendous mass of new material brought to it. Being human, its members have felt their lack of ability to keep pace with all the advances and have preferred to limit their field to some one branch, which they can know intimately. This is largely the basis for the rapid growth of specialism. Naturally, it has its weak points as has any new method. The medical profession is spending much time in public meeting and private conference trying to cope with this problem. Its solution is no simpler than that of many of the problems of rapidly growing industrialization. Even if one decides what is ideal, one will still have to be guided by what is practical.

Dr. McKay admits that he tries "to believe that every physician does the best of which he is capable," and then picks out isolated instances of carelessness and incompetence. There is no doubt that these occur, but informing the public cannot prevent them. The careless and incompetent will always be with us, and frequently they will inspire the most confidence and have the most attractive personalities. The educated seem to have fared about as badly from stock market promoters as any other group. One might get the impression from the illustrations that these were everyday occurrences and the rule rather than the exception. I am sure that Dr. McKay does not think this. I do not believe his desire is that the public should think this, but he tells the public no way to distinguish between the good and the bad physician. The medical profession itself wishes it knew

how. Unless one has something constructive to offer, it seems unpardonable to destroy whatever confidence there is.

Undoubtedly too many operations are performed, but, reprehensible as this is, it may be preferable to having a patient delay an emergency operation which means life or death because he has been told that some physicians are too anxious to operate.

Mistakes in diagnosis are made, but not in nearly so large a proportion as a generation ago. Little can be gained by publishing these facts for the layman. The place for this discussion is in the monthly staff meetings which must be held by every hospital recognized by the American College of Surgeons. Here errors in diagnosis are openly discussed. The medical profession has never been noted for charity in its criticism of its confrères' mistakes. The discussions are usually forceful enough so that the same mistake is unlikely to recur for some time.

I cannot concur with Dr. McKay that "a fairly satisfactory level of mediocrity for hospitals" is objectionable. At least that is some progress over twenty years ago, when there were a few good hospitals and many bad ones.

When the leaders of the medical profession can find a slide rule by which they can segregate good from bad physicians, not good or bad handling of a single patient, it will be their duty to pass this on to the public, and they will gladly do so. In the meantime, general publication of medical errors does not fulfil the requirements of either amusement or instruction, but appeals to the same appetite as the daily tabloid.

Recent Advances in Psychiatry. By Henry Devine. Price, $3.50. Pp. 340. Philadelphia: P. Blakiston's Son & Co., 1929.

A book that would record the progress made in psychiatry in the last ten or fifteen years would be extremely useful. It is unfortunate that this volume, which appeared in the excellent "Recent Advances" series, falls so far short of what is needed. Of course, it is scarcely possible to record recent progress in psychiatry so adequately that a critical reader would not be able to point out omissions and what he considers unnecessary overemphasis. But in expressing his disappointment with this book, the reviewer is not referring to this type of minor criticism. The chief thing one notes is that there is no proper background of psychiatric doctrine, against which the advances should be recorded. As a result of this lack, the whole presentation is diffuse and lacking in perspective.

The general classification of the material is neither very logical nor helpful. The introductory part, which is entitled "The Fundamentals of Psychiatry," is highly theoretical and records the views of a motley group of psychiatric and nonpsychiatric authors, from Turro to Briffault. The first part deals with toxic, infectious and somatic factors in the causation of the psychoses. One misses a clear presentation of the views of the more important modern authors on the present-day psychiatric and pathologic problems of the exogenic reaction type. In the brief chapter on the "psychogenic psychoses" in this section, a number of the more important papers on this subject are conspicuously absent. Another chapter, on the confusional syndrome, summarizes work by Mott, Menninger, Strecker (always spelled Strecher), Kirby, Hoch and Bond. In the chapter on psychoses and somatic disease, the survey of progress in knowledge of dementia paralytica is brief and entirely inadequate.

The second part of the book is concerned with "The Effects of Somatic Diseases in Psychotic Subjects." The third part, entitled "The Behavior of the Organism in Mental Disorders," discusses the hemoclastic crisis, basal metabolism and the psychogalvanic reflex. Part four deals with "biopsychic" types. It includes a review of Kretschmer's book "Physique and Character" and a discussion of cerebral pathology which is completely out of date. The last part deals with "Psychology and the Psychoses."

Much of the work that is abstracted in this book might well have been left out, as old fashioned, unproved or disproved. Considerable space is devoted to the mutilation psychiatry of Cotton, and the author reprints statistics and a chart by

Dr. Cotton tabulating the cases of two hundred patients "successfully" treated. On the other hand, a great deal of the actual good spadework that has been done in clinical psychiatry is not pointed out. Recent German psychiatric literature is not adequately covered, and justice is not done to the French literature. It would take another volume to summarize all these omissions.

The Differential Diagnosis of Endocrine Disorders. By Allan Winter Rowe. Price, $4. Pp. 199. Baltimore: Williams & Wilkins Company, 1932.

This charmingly written monograph is a survey of the data obtained from a lengthy and inclusive examination of about five thousand patients over a period of twenty years. The author (who is a doctor of philosophy, not of medicine) has devised a routine of "vital function" tests which with clinical examinations by his colleagues can be concluded in a week's hospitalization in most cases. At the end of this period, he examines the data thus secured and makes a diagnosis. The present publication is an attempt to summarize the diagnostic significance of individual examinations or groups of examinations.

The data are concisely given, much of them in tabular form. There are no case reports, and the methods of arriving at often far-reaching results are rather briefly stated. For more detailed correlation, the reader is referred to previous articles by the author and his colleagues, but he may find himself still unsatisfied. To take a specific instance, one reads on page 117 that "in the writer's experience, the commonest form of pituitary disease is that type of dysfunction in which the anterior lobe is presumptively under- and posterior lobe over-active." As a search for a cleancut statement regarding the functions and abnormalities of the two lobes, respectively, is fruitless, one turns to the bibliography. The only publication by Cushing which is listed is his monograph of 1912, which Cushing himself considers actually misleading, to judge by his more recent contributions. There is no mention of Aschner, Evans or Smith. If one turns to Rowe and Lawrence's special article on the pituitary, one finds a case report of one acromegalic patient who was operated on. The remainder consist of a bizarre group of interesting syndromes the relationship of which to the pituitary gland seems exceedingly improbable in the light of the precise knowledge of the subject which has recently become available. In some instances the diagnosis rests on the effect of anterior lobe by mouth, and this is apparently the basis for the inclusion of the case of a patient with choked disks, homonymous hemianopia and evidences of a pulmonary tuberculosis. Aside from the case of acromegalia, *in not a single case reported was there a histologic examination.*

This appears to be a fair sample of the grade of clinical judgment employed in evaluating and correlating the enormous mass of data obtained. A large part of the contents of the book is not only valueless but actually misleading. Its dangerousness is increased by the easy and plausible style in which it is written, by the precise quantitative statements that glitter on every page and, above all, by the obvious sincerity of the author. When will endocrinology become a part of the science of medicine?

System der Pädagogik in Umriss. By Joseph Göttler. Sixth edition, revised and enlarged. Price, 8.70 marks. Pp. 357. Munich: J. Kösel and F. Pustet, 1932.

This book is a complete and systematic treatise on pedagogy. The modern neuropsychiatrist who has learned that early influences—of which education forms a large part—are of prime importance in the shaping of life patterns will be disappointed that such a representative work remains on such formal ground. There is little evidence, on the part of the author or the many pedagogic authorities he quotes, of a good understanding of the biologic and psychobiologic factors of human behavior.

Some of the chapters are of special interest to the psychiatrist. There is, in the section on "intellectual peculiarity," an interesting enumeration of the various

personality types according to apperception, representation, attention, learning, thinking and judgment. But these types are merely named, and there is no discussion of the psychologic details of their diagnosis and significance. The chapter on emotional peculiarity is strikingly inadequate. The discussion is restricted to the age-old description of the four so-called temperaments, viz., the sanguinic, the choleric, the melancholic and the phlegmatic. The chapter on mentally abnormal pupils is extremely formal and takes no account of modern psychopathology. The author completely omits not only the pertinent data of clinical psychiatry on this subject, but also the many more or less relevant data that are so much discussed in the modern literature on mental hygiene. Finally, the section on sexual instruction is really primitive.

The subject matter is clearly arranged, and there are good bibliographies (of the German literature) after each section. The lack of an index is a great hindrance to the practical value of a book of this type.

Ueber die Schädelperkussion. By Ladislaus Benedek. Price, 6 marks. Pp. 112. Berlin: S. Karger, 1932.

In this monograph Benedek describes a new method of localizing lesions of the brain. He has attempted to differentiate by a most elaborate system and rather complicated apparatus the various notes that may be produced by percussion of the head and be observed by auscultation. He has made a large number of measurements of various points on the skull in order to establish the average thicknesses at each. These are recorded in twenty-three tables. In drawing 19, he then classifies the various percussion notes one may elicit into twelve types.

Benedek has been developing this method since 1917, and he published his first observations in 1923. He cites a number of case histories to prove his thesis that the method makes it possible to diagnose conditions that could not otherwise be recognized. Unfortunately, a number of his cases are not confirmed by operation or autopsy. He records on page 100 a case of aerocele, which certainly should have been illustrated with a good roentgenogram. He does not mention that a picture was taken, but concludes that operative intervention was undertaken because of the abnormal percussion note over the traumatic cyst partially filled with air.

The reviewer thinks that the method does not add anything of great value to the diagnostic armamentarium. Percussion and auscultation of the head, especially the latter, are often neglected in a routine physical examination, but there seems no advantage in resorting to the elaborate technic that has been so painstakingly developed by the author.

The Medical Value of Psychoanalysis. By Franz Alexander, M.D. Price, $2.75. Pp. 227. New York: W. W. Norton & Company, Inc., 1932.

This book is written for the layman and the general practitioner on the subject of the medical value of psychoanalysis. According to psychoanalysts, only those who are properly trained, with the required experience, are now recognized as capable of practicing analysis. In this country the number is gradually increasing, but is not large. According to this concept, most neurologists and psychiatrists know little of psychoanalysis. If this point of view is accepted, then the general practioner and the layman would appreciate the principle of analysis even less. Why therefore this book?

The number of books on psychologic subjects written for the benefit of the general practitioner and public is increasing yearly. If the public, which means the curiosity seeking public, and psychoneurotic persons were to read and understand one tenth of the output, then possibly something would be gained. But, do they?

It would be well if some psychoanalyst would devote sufficient time to analyze the motives that impel some of the authors to write such pseudoscientific literature. It is not difficult to understand why the publishers want to get out such books, for

their business is to sell books, but what about the authors, particularly those who occupy responsible positions and who should and are expected to lead medical thought?

A Handbook of Experimental Pathology. By George Wagoner, M.D., and R. Philip Custer, M.D. Price, $4. Pp. 160. Springfield, Ill.: Charles C. Thomas, 1932.

Some years ago Professor Sherrington in his "Mammalian Physiology" outlined a method of experimental approach. This has served as a model for similar manuals, but up to the present volume no similar work on experimental pathology has ever been issued. The Handbook is based on a course on experimental pathology given to second year students of medicine in the University of Pennsylvania, and while the book demonstrates the more important problems in general and special pathology which are widely known, a large number of experiments are original with the authors. There is first a general exposition of experimental methods and care of animals; then the subject is divided into experiments in general pathology and special pathology. These include all parts of the body except the nervous system. To neurologists and psychiatrists the book is chiefly of interest in that the endocrine system is dealt with to a limited degree. From the general standpoint, however, the subject matter is well set forth, the work is well illustrated, and the book can serve as a guide to all interested in research problems.

Die juvenile amaurotische Idiotie. By Torsten Sjögren. Separat ur Hereditas, XIV. Price, 10 kronor. Pp. 425. Lund, Sweden: Gleerupska Universitäts Bokhandeln, 1931.

This book is an excellent monograph on the subject of the juvenile form of amaurotic family idiocy. It includes a thorough up-to-date and critical review of all previous contributions bearing on this form of heredodegenerative disease, a comprehensive summary of its pathologic anatomy, a competent discussion of the clinical manifestations with highly instructive points of diagnostic significance in the typical and atypical instances and, above all, an important study of the hereditary features of the disease. Of great interest is the account of the ingenious way in which the large material was uncovered and collected in a country where the disease was considered to be rare. The determined search for material led to a thorough genealogic study of fifty-three families and an investigation of over a thousand members of these families. It was rewarded by the discovery of a relatively large number of cases (thirty-nine); eighteen of the cases came to autopsy, and the anatomic observations verified the projected clinical diagnosis. The monograph is richly illustrated, and a great wealth of information is found in abundant genealogic charts and formulas.

Diseases of the Spinal Cord. By Williams B. Cadwalader, M.D. Price, $5. Pp. 204. Baltimore: Williams & Wilkins Company, 1932.

Textbooks limited to diseases of the spinal cord are relatively rare. The present volume follows conventional lines with the exception that there are chapters on progressive muscular dystrophy and Thomsen's disease, subjects that are not usually classed as diseases of the spinal cord, nor is there any intimation in the text that lesions of the spinal cord are responsible. The subject is well and concisely presented; tabes dorsalis, for example, is described in five pages of descriptive text. It is a question whether a book limited to the spinal cord, unless it is a book of reference, is desirable. The average medical student and general practitioner, especially in these times, will more likely buy, at slightly additional cost, one of the smaller textbooks on the whole subject of neurology.

Anatomy of the Brain and Spinal Cord. By William W. Looney, A.B., M.D. Second edition, revised. Price, $4.50. Pp. 370. Philadelphia: F. A. Davis Company, 1932.

The usual method of presentation is adopted. The classification and manner of presentation are good. The illustrations are good, but there are not enough of them. This book, like some similar works recently written by anatomists, suffers from the fact that in an effort to make the subject clearer a clinical discussion is added, usually, as in this instance, inadequately. For example, the motor speech area "is situated in the triangular and opercular portions of the left inferior frontal gyrus in right-handed individuals." One wishes that it were as easy and simple as that.

Jewish Influence in Modern Thought. By A. A. Roback. Pp. 506. Cambridge, Mass.: Sci-Art Publishers, 1929.

This book gives a survey of the achievements of persons of Jewish origin in practically all fields of modern culture. It is written in an anecdotal style and contains much interesting information. A special chapter is devoted to psychoanalysis. There is a good bibliography, and an index of names and subjects.

Nursing in Nervous Diseases. By James W. McConnell, M.D. Price, $1.50. Pp. 143, with 24 engravings. Philadelphia: F. A. Davis Company, 1932.

This book supplies adequately what has long been needed, that is, a safe and sane discussion of nursing in nervous diseases. The subject matter is well presented, and the material covers a sufficiently wide range of nursing in nervous disorders.