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CEREBRAL CIRCULATION

XII. THE EFFECT ON PIAL VESSELS OF VARIATIONS IN THE OXYGEN AND CARBON DIOXIDE CONTENT OF THE BLOOD *

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There is increasing evidence that chemical alterations of the blood, and especially changes of the acid-base equilibrium, have an important regulatory influence both on cerebral circulation and on respiratory movements. In this paper, we shall present observations which are intended to clarify these relationships.

Numerous observers have reported that a dilatation of vessels of the brain occurs during asphyxia.[1] Observations by most of these authors have been by indirect methods, such as measurements of brain volume, of resistance to blood flow, or of the pressure in cerebral vessels. Florey [2] made use of direct observation but did not employ a window.

In the experiments conducted in this laboratory, vessels of the pia were observed directly through a window in the skull, which procedure preserved the normal closed box arrangement. In confirmation of the observations of the previously mentioned authors, it has been our experience that a period of apnea or of asphyxia will be followed by maximum dilatation of vessels of the pia, even in the presence of influences which might be expected to cause contraction of the vessels, such as a severe fall in blood pressure, stimulation of the cervical sym-

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1. Berlin, W.: Schmidt's Jahrb. **69**:14, 1851. Ackerman, T.: Arch. f. path. Anat. u. Physiol. **15**:401, 1858. Mosso, A.: Ueber den Kreislauf des Blutes im menschlichen Gehirn, Leipzig, Von Veit & Cie, 1881. Hürthle, K.: Arch. f. d. ges. Physiol. **44**:561, 1889. Roy, C. S., and Sherrington, C. S.: J. Physiol. **11**:85, 1890. Wertheimer, E.: Arch. de physiol. norm. et path. **25**:297, 1893. Hill, L., and MacLeod, J. J. R.: J. Physiol. **26**:394, 1900-1901. Kahn, R. H.: Centralbl. f. Physiol. **18**:153, 1904. Florey, H.: Brain **48**:43, 1925. Sándor, G.: Arch. f. d. ges. Physiol. **213**:492, 1926. Schmidt, C. S.: Am. J. Physiol. **84**:202, 223 and 242, 1928. Bernthal, T. G.; Bronk, D. W.; Cordero, N., and Gesell, R.: Am. J. Physiol. **83**:435, 1928. Ford, F. R.: Bull. Johns Hopkins Hosp. **42**:70, 1928.

2. Florey (footnote 1, ninth reference).

pathetic or the administration of constrictor drugs. In terminal asphyxia, vasodilatation is always present. Vasodilatation also accompanies severe cerebral anemia induced by clamping of the carotids, by increasing intracranial pressure or by bleeding.

In both of the conditions mentioned, asphyxia and anemia, a number of factors might be concerned in the arterial change observed. In asphyxia, for example, there is an accumulation of carbon dioxide and a depletion of oxygen in the blood and tissues, a shift in the acid-base equilibrium and an alteration of respiration. Although Cow,[3] Landis[4] and Tinel[5] showed that dilatation of arteries accompanied breathing of carbon dioxide, there is need for control of the various factors named, combined with a direct observation of vessels. It was our purpose not only to observe but also to measure and to photograph changes in the size of vessels and to correlate these changes with coincident alteration in the gaseous content of the blood and with the rate and volume of respiration. The fundamental importance of these three physiologic processes to such clinical problems as convulsions, headache, anesthesia, cerebral hemorrhage and artificial respiration is apparent.

METHODS

The method developed by Forbes[6] of observing the vessels of the pia has been followed in detail.

Cats were anesthetized by the intraperitoneal injection of 8 cc. per kilogram of a 1 per cent solution of iso-amyl-ethyl barbituric acid. The skull was trephined, a piece of dura removed by means of a cautery and an air-tight glass window screwed firmly into the opening in the cranium. Air bubbles were removed by introducing cerebrospinal fluid through holes in the metal rim of the window. The operation of removing the dura and exposing the cortical vessels was bloodless and performed with a minimum of trauma. A needle in the cisterna magna permitted recording of the intracranial pressure; a cannula in the femoral artery, that of the systemic arterial pressure. A washout cannula was placed in the other femoral artery and kept filled with mineral oil. One of the openings of this cannula was fitted with a cork, which was pierced by an intravenous needle. Removal of a bull-dog clamp on the artery permitted blood to flow into the cannula from which it was aspirated into a syringe without exposure to the air. The cannula was then washed out with citrate solution and refilled with oil. Seven or 8 cc. of blood was removed at a time. Analysis of this was begun at once. Samples not being analyzed were kept under oil on ice. In order that only a minimum of blood should be withdrawn, whole blood rather than plasma was used, and checks were not run uniformly. It was found that removal of this amount of blood affected the diameter and pressure readings only momentarily, if at all. Blood

3. Cow, D.: J. Physiol. **42**:125, 1911.
4. Landis, E.: Am. J. Physiol. **83**:528, 1928.
5. Tinel, J.: Encéphale **22**:229, 1927.
6. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

gases were measured in the constant volume apparatus of van Slyke.[7] The oxygen content and the oxygen capacity of the arterial blood were determined, the former divided by the latter and the result expressed as the percentage saturation of the blood with oxygen. Likewise, the carbon dioxide content and the carbon dioxide combining power of the whole blood were determined. The gaseous content of the blood was altered by varying the composition of the respired air.

In order to obtain records of the rate and minute volumes of respiration, the gas mixture which it was intended that the animal should breathe was placed in a Benedict-Collins metabolism apparatus, the soda lime container being removed. The animal inhaled this gas through a one-way valve and tracheal cannula, and exhaled into the room. The movements of the bell containing the gas mixture were recorded on a moving drum. Calibration of the bell permitted calculation of the amount of air withdrawn with each inspiration. The composition of the inspired air was measured by means of the Haldane apparatus.

TABLE 1.—*The Diameter of Pial Arteries with Reference to the Gaseous Content of the Blood*

	Gaseous Content of Blood	Number of Experiments	Diameter of Artery in Microns			Arterial Blood: Oxygen, Percentage Saturated			Arterial Blood: Carbon Dioxide Content		
			Before	During	Percentage Change	Before	During	Percentage Change	Before	During	Percentage Change
B	Normal O_2, low CO_2	4	180.0	166.5	− 7	85.0	88.0	+ 3	46.7	38.1	−18
C	Normal O_2, high CO_2	2	201.6	234.0	+16	80.5	82.5	+ 2	40.2	43.7	+ 9
D	High O_2, normal CO_2	5	214.2	209.9	− 2	75.0	95.0	+27	39.8	38.2	− 4
E	High O_2, high CO_2	2	210.6	255.6	+21	82.0	89.0	+ 8	40.6	50.7	+25
F	Low O_2, low CO_2	3	266.4	255.6	− 5	81.3	39.3	−51	39.1	29.5	−24
G	Low O_2, normal CO_2	7	196.2	203.4	+ 3	75.0	39.4	−49	46.4	40.6	−13
	Low O_2, arteries constricted	5	234.6	239.6	−10	80.3	38.6	−50	40.4	33.4	−17
	Low O_2, arteries dilated	4	205.2	223.2	+ 9	89.0	45.7	−48	46.6	40.0	−14
H	Low O_2, high CO_2	3	203.4	250.2	+23	80.0	56.0	−30	47.1	54.7	+16

OBSERVATIONS

A total of thirty-five experiments was made on twenty-six animals. The gaseous content of the blood was measured in all the animals. Graphic record of the respiration was made in sixteen. A good deal of variation in the observations made on different animals was to be expected. In order to treat the material on a statistical basis the experiments were placed in groups and the average changes in the diameter of vessels and the gaseous content in the blood calculated. These results are shown in table 1. The various possible combinations as regards the oxygen and carbon dioxide content of the blood were lettered *A, B, C, D,* etc. The average maximum percentage change in

7. Van Slyke, D. D.: J. Biol. Chem. **73**:121, 1927.

the size of the artery and in the oxygen and carbon dioxide content of the blood during the experimental procedure is shown in figure 1. Each procedure will be described and illustrated by a chart of a typical experiment.

A. Normal Oxygen-Normal Carbon Dioxide (Atmospheric Air).—The bell of the respiration apparatus was filled with atmospheric air, and the cat was required to inhale from this apparatus. Figure 2 shows the constancy in the diameter of the pial artery. The blood pressure was subject to greater variation than the spinal fluid pressure.

B. Normal Oxygen-Low Carbon Dioxide.—Because atmospheric air contains only 0.04 per cent of carbon dioxide, elimination of this

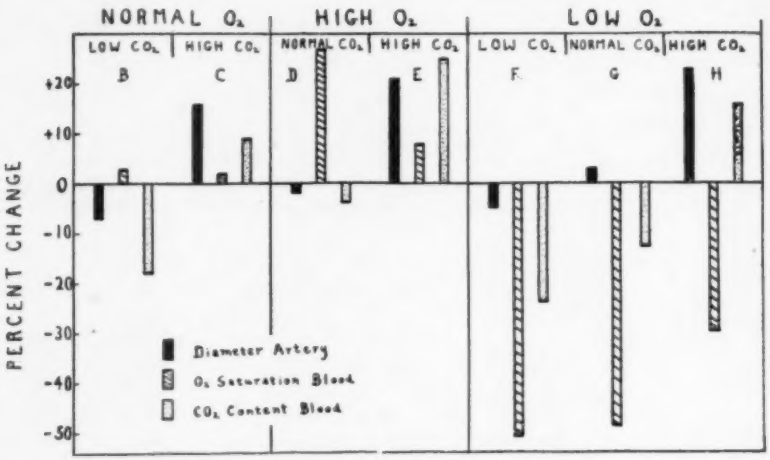

Fig. 1.—Graphic representation of the average percentage change in the diameter of pial arteries and in the gaseous content of arterial blood occurring in various experimental procedures (made up from the data in columns 5, 8 and 11 of table 1). The ordinate represents the percentage change during the experimental period with reference to the preliminary control period. The letters *B, C, D,* etc., indicate the groups listed in table 1 and in the text.

amount from the inspired air is without appreciable effect on the respiratory functions of the blood. It is possible, however, to reduce the concentration of carbon dioxide in the alveolar air, and hence in the blood, by means of overventilation of the lungs. We accomplished this by the squeezing of a hand bulb attached to the tracheal cannula. By this means we doubled the normal respiratory rate and trebled the volume of tidal air, thus increasing the minute volume of respired air approximately six times.

Hyperpnea was continued for approximately ten minutes. Arterial blood drawn at the end of this period showed, as one would expect, a considerable reduction in its content of carbon dioxide, with either no change or a slight increase in the content of oxygen. During hypernea there was a slight decrease in the pressure of the blood and in that of the cerebrospinal fluid. In each of the four experiments (no. 100, 101, 107, 109) there was a decrease in the diameter of pial arteries of from 5 to 11 per cent, the average being 7 per cent. This change usually preceded the fall in blood pressure, and was therefore not due to it.

Following the discontinuance of the excessive artificial respiration, a period of comparative apnea lasting for one or two minutes occurred. At the end of this period, in one instance, the artery under observa-

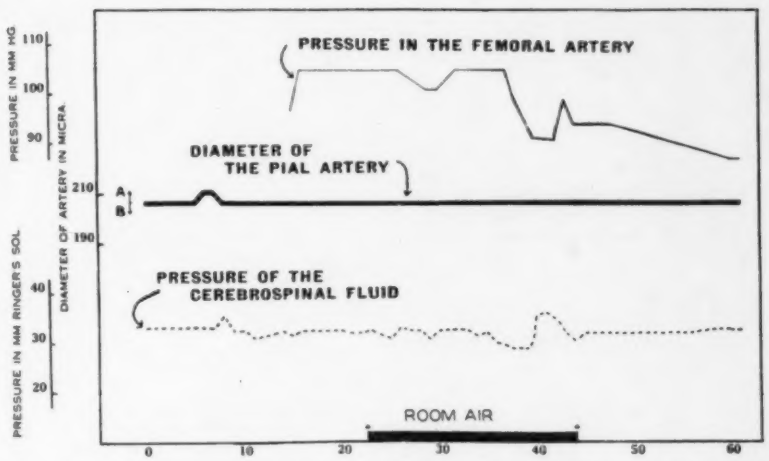

Fig. 2.—Control experiment in which the animal breathed room air from a Collins-Benedict apparatus for the measurement of basal metabolism. In this and similar succeeding figures the abscissa represents minutes. The ordinate represents measurements of the arterial blood pressure in millimeters of mercury, the diameter of the pial artery in microns and the pressure of the cerebrospinal fluid in millimeters of Ringer's solution. The arrow marked *A-B* indicates the limits beyond which measurements of the pial artery are believed to be dependable. A depression of the heavy solid line indicates a constriction and an elevation a dilatation of the artery. The solid rectangle at the bottom of the chart shows the period during which a certain gas was breathed.

tion became cyanotic and momentarily dilated. With the reestablishment of normal breathing the artery resumed its normal color and size. One of the experiments (107) is shown in figure 3. In this experiment there was considerable fluctuation in the blood pressure. The curve representing blood pressure, however, did not parallel that representing the diameter of the pial vessel.

C. Normal Oxygen-High Carbon Dioxide.—In two experiments (80, 91) carbon dioxide was added to atmospheric air. In both instances there was an immediate and marked dilatation of the pial vessels. Coincidentally there was a marked increase in the pressure of the spinal fluid and of the blood. One of the experiments (91) is shown in figure 4. In this experiment the concentration of carbon dioxide in the inspired air was sufficient to cause only a slight increase in the carbon dioxide content of the blood. Yet the artery under observation increased its diameter by 17 per cent.

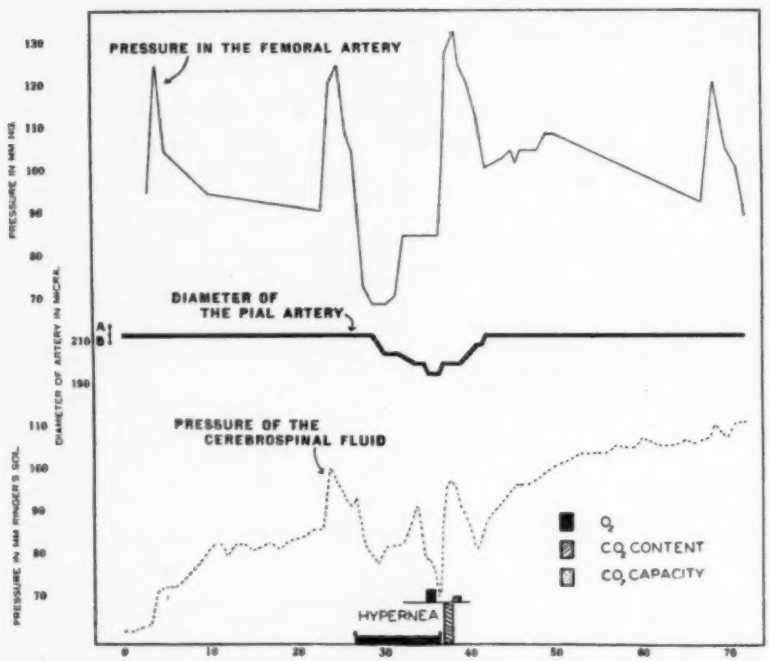

Fig. 3.—The effect of reducing the carbon dioxide content of the blood, accomplished by means of artificial hyperpnea. In this and other charts changes in the gaseous content of the blood from the condition obtaining in the control period are indicated by columns. In this experiment, after ten minutes of overventilation the oxygen saturation had increased 6 per cent, the bicarbonate 3 per cent and the carbon dioxide content had decreased 19 per cent. This alkalosis of the blood was accompanied by an 8 per cent constriction of the pial artery.

D. High Oxygen-Normal Carbon Dioxide.—In these experiments, five in number (74, 75, 90, 105, 106), the animals breathed approximately 100 per cent oxygen. Blood drawn after ten or fifteen minutes in all instances showed an increase in the oxygen content of the arterial blood. Before the inhalation of oxygen the arterial blood of these ani-

mals was on the average only 75 per cent saturated with oxygen. Presumably, the initial low saturation was due to a depression of respiration induced by the anesthesia. During the inhalation the blood was 95.5 per cent saturated, an increase of 27 per cent. The average carbon dioxide content, on the other hand, changed but little, 39.8 per cent by volume before and 38.2 per cent during inhalation. In most instances, also, there was an increase in the minute volume of the respired air. The pressure of the blood and of the spinal fluid became slightly lower in all instances except one. In all experiments except one the diameter of the pial artery became smaller. In this experiment the dilatation

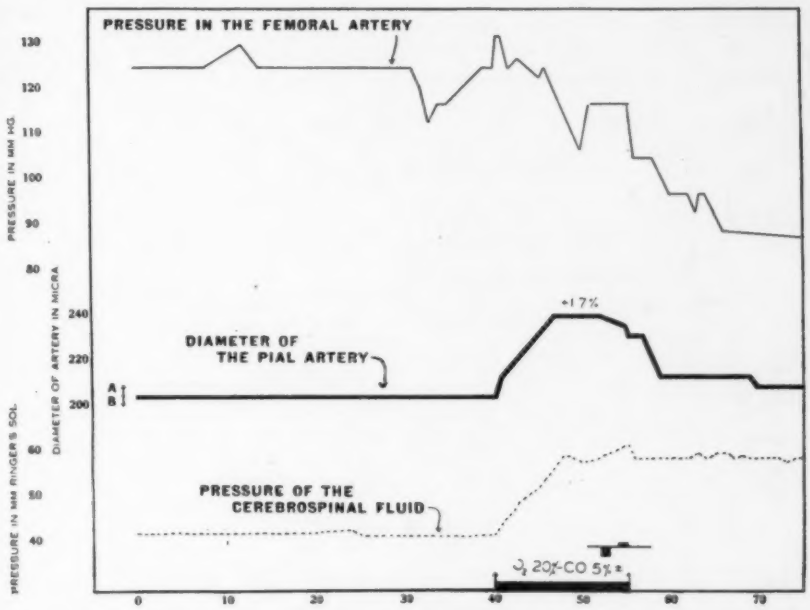

Fig. 4.—The effect of increasing the carbon dioxide content of the blood. In this experiment approximately 5 per cent carbon dioxide was added to room air. Though the carbon dioxide content of the blood was increased only 2 per cent, there was a 17 per cent increase in the size of the artery. The oxygen saturation decreased 5 per cent.

might be explained by an increase in the carbon dioxide content of the blood from 49 to 53 per cent by volume, apparently due to a decrease in the volume of respiration. The decrease in the size of the arteries was slight, from 4 to 8 per cent, the average, including the experiment in which there was expansion, being 2 per cent. In contrast with the almost immediate change when an increased concentration of carbon dioxide was breathed, change with increased oxygen was not apparent until several minutes had elapsed. Figure 5 illustrates experiment 106.

Contraction of the artery did not occur till seven minutes after the breathing of oxygen was begun. In this experiment the augmented respiration resulted in a decrease in the carbon dioxide content of the blood. In other experiments, however, the same contraction of arteries occurred with a constant carbon dioxide factor.

E. High Oxygen-High Carbon Dioxide.—In two experiments (77, 92) the animals breathed a mixture of 90 per cent oxygen and 10 per cent carbon dioxide. In both there was an increase in both the oxygen and the carbon dioxide content of the blood, an increased depth of respiration, a slight fall in blood pressure and a rise in spinal fluid pressure. The increase in the size of the artery was immediate

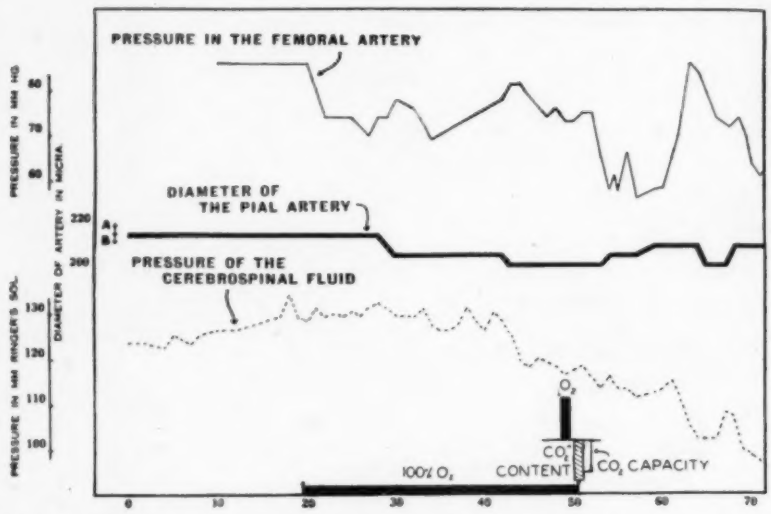

Fig. 5.—The effect of increasing the oxygen content of the blood. In the control period the blood was 84 per cent saturated with oxygen. After thirty-one minutes in which oxygen was breathed the oxygen saturation had increased 9.5 per cent and the artery decreased in diameter 7.5 per cent. The experiment was not clearcut because the carbon dioxide content decreased by 9 and the carbon dioxide capacity by 7 per cent. This slight degree of alkalosis may have contributed toward production of the constriction.

and striking. In the two experiments the average increase in the oxygen saturation of the blood was 8 per cent, in the carbon dioxide content 25 per cent and in the diameter of the artery 21 per cent. Figure 6 illustrates experiment 77. It will be particularly noted that while an increase in spinal fluid pressure closely followed the dilatation of cerebral vessels, the blood pressure suffered an initial fall. In experiment 92, figure 14, the increase in carbon dioxide and the dilatation were less marked.

F. Low Oxygen-Low Carbon Dioxide.—In these experiments atmospheric air was diluted with nitrogen. In some experiments the condition of the oxygen want was induced suddenly, in others gradually. In the procedures which have been named in which there was a normal or an increased content of oxygen of the respired air, it was fairly easy to cause variation in only one of the gases of the blood. When, however, oxygen in the respired air was reduced, there was in all instances a resulting increase in respiration which lowered the carbon

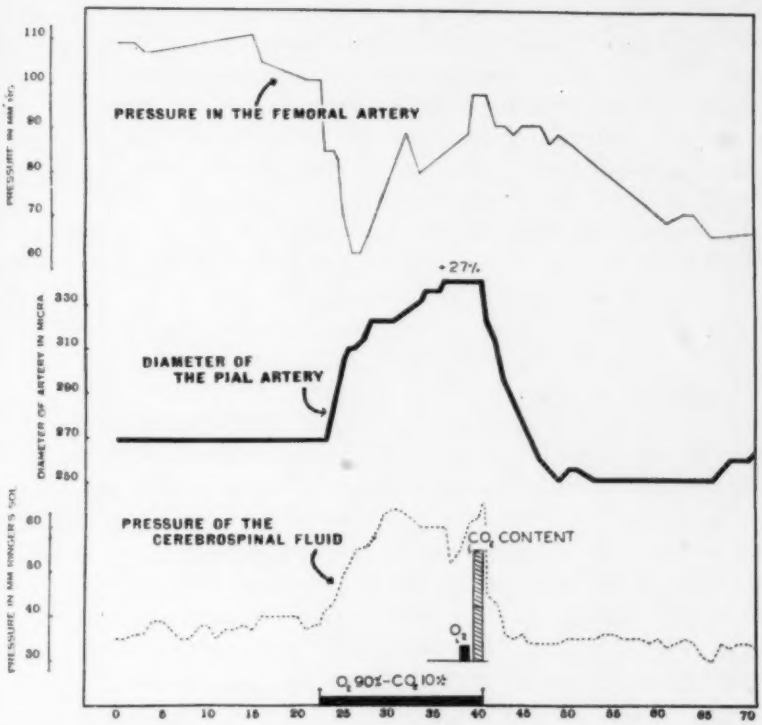

Fig. 6.—The effect of increasing both the oxygen and the carbon dioxide content of the blood. For eighteen minutes the cat breathed a gas which contained 90 per cent oxygen and 10 per cent carbon dioxide. This increased the oxygen saturation of the blood 7 per cent, the carbon dioxide content 25 per cent and the caliber of the artery 27 per cent.

dioxide content of the blood. As shown under *B*, such overventilation would in itself tend to produce a contraction of the artery. Our chief interest in these experiments is in the state of the blood, rather than of the respired air; therefore, we have divided the anoxemia experiments into two groups, those with a marked (*F*) and those with a slight (*G*) reduction in the carbon dioxide content of the blood.

In three experiments (79, 80, 83) the oxygen saturation of the blood fell on the average of from 81 to 39 per cent by volume (a decrease of 51 per cent), and the carbon dioxide content from 39 to 29 per cent by volume (a reduction of 24 per cent). The latter is a greater percentage fall than occurred with the artificially induced hyperpnea. The blood and spinal fluid pressure remained constant or increased slightly. The size of the artery changed little. The average diameter decreased from 14.8 to 14.2 microns, a reduction of 5 per cent. In one experiment the decrease might have been due to a slight fall in blood pressure. What narrowing occurred in these experiments might be explained by the fall in the carbon dioxide content of the blood. That the narrowing of the artery was not greater may have been due to a counteracting effect of the anoxemia.

Figure 7 illustrates experiment 80. At the end of thirty-three minutes, in which the cat breathed air diluted with approximately two parts of nitrogen, the amount of oxygen in the blood (with reference to the amount which the blood was capable of carrying) had fallen one-half. There was no constant change in the diameter of the pial artery under observation. At this time, a gas mixture of opposite composition (high oxygen and high carbon dioxide) was substituted, and immediately there was dilatation of the artery similar to that seen in figure 6.

In another experiment, 103 (fig. 14), in which there was moderate anoxemia and considerable reduction in carbon dioxide, without change in the size of the artery, the addition of carbon dioxide to the respired air in concentration sufficient to raise the carbon dioxide of the blood to its normal level resulted in a 35 per cent increase in the diameter of the artery, with the systemic blood pressure remaining constant.

G. Low Oxygen-Normal Carbon Dioxide.—Because surprisingly small changes in the size of arteries had followed gross changes in the oxygen content of the blood, we did repeated experiments in order to have observations sufficient in number to permit drawing conclusions. In seven experiments (103, 84, 85, 93, 96, 97, 102) the anoxemia was accompanied by a moderate reduction of the carbon dioxide, an amount insufficient to reduce the concentration below a normal value. In these experiments the average oxygen saturation of the blood fell from 75 before the experiment to 40 per cent at its close, the same proportionate reduction as occurred in *F*. The carbon dioxide content fell from 47 to 40 per cent by volume, a decrease of 13 per cent. The blood pressure changed but little, whereas the spinal fluid pressure increased. In contrast with the previous groups of experiments the average diameter of the artery increased slightly (from 109 to 113 microns), an increase of 3 per cent. This slight increase occurred in the face of reduction in the level of the carbon dioxide in the blood.

In figure 8 (illustrating experiment 96) the animal was given a mixture to breathe which contained a constantly increasing percentage of nitrogen. At the end of one hour and forty minutes, when the oxygen saturation of the blood had decreased by 93 per cent, the only change in the artery was a slight dilatation. Fortunately, the carbon dioxide content of the blood changed but little, so that the dilatation which occurred could be ascribed to the severe degree of anoxemia induced. Immediately preceding death there was the customary fall in blood and spinal fluid pressure and resulting constriction of the artery. Other experiments are shown in the first part of figure 14 and in figure 15.

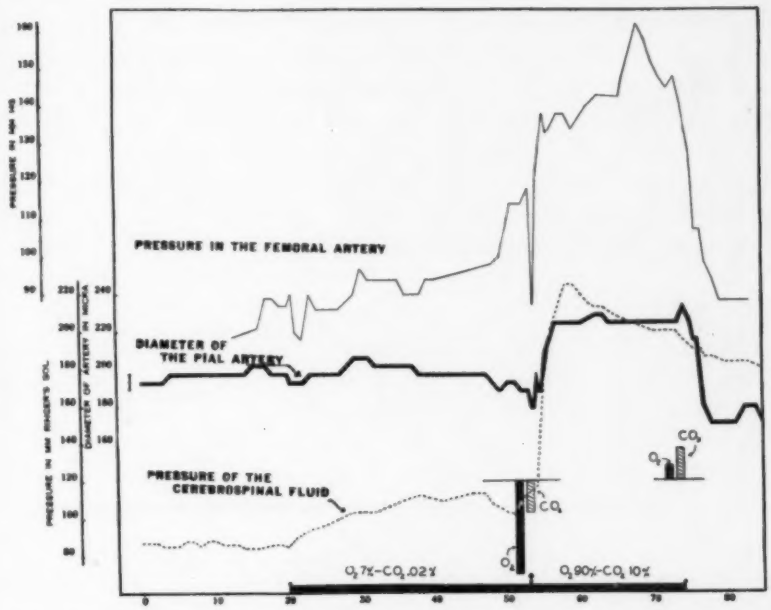

Fig. 7.—The effect of reducing both the oxygen and the carbon dioxide content of the blood. During thirty-three minutes the cat breathed air containing about one-third its normal concentration of oxygen. This changed the oxygen saturation of the blood from 80 to 40 per cent, a reduction of 50 per cent. The resulting hyperpnea reduced the carbon dioxide of the blood 17 per cent. No definite change in the caliber of the artery resulted. Apparently the dilator effect of anoxemia and the constriction effect of reduced carbon dioxide balanced each other. During the next twenty-one minutes a mixture of 90 per cent oxygen and 10 per cent carbon dioxide was substituted. Oxygen saturation increased 8 per cent and carbon dioxide content 17 per cent over the control period. The diameter of the artery increased 15 per cent.

If we rearrange these anoxemia experiments *F* and *G* into groups with reference to whether there was an increase or a decrease in the

diameter of arteries, we find that the two groups showed almost the same decrease in the oxygen saturation of the blood (minus 50 and 48 per cent, respectively). In the five experiments in which there was a constriction of arteries (the average decrease being 10.5 per cent) there was 17 per cent loss of carbon dioxide. In the four experiments in which there was a dilatation of arteries (the average increase being 9.2 per cent), the loss in carbon dioxide amounted to 14 per cent. This difference is not great enough to be significant. It will be noted that in those experiments in which dilatation occurred, the carbon dioxide concentration of the blood was at a higher level (40.6 volumes present)

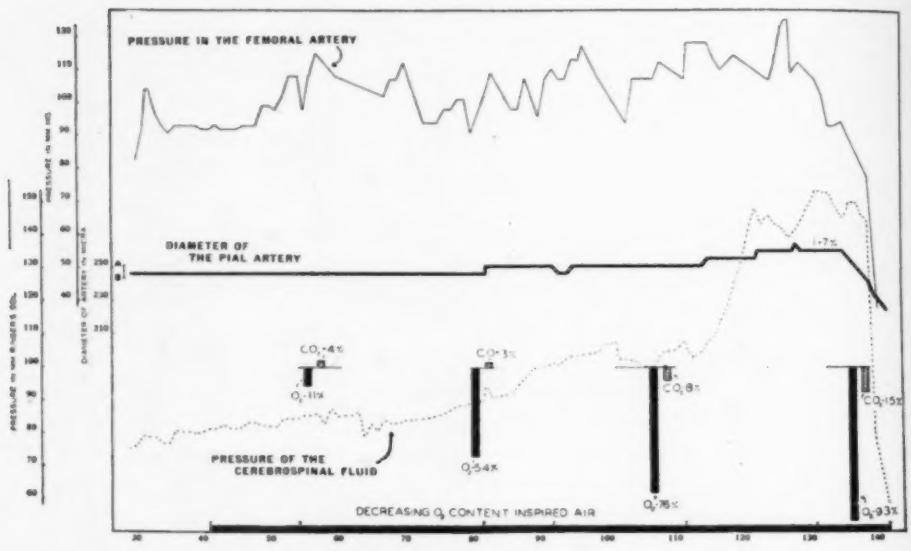

Fig. 8.—The effect of a progressing and finally fatal degree of anoxemia in which the carbon dioxide of the blood was but slightly reduced. During the 102 minutes in which the animal breathed air containing an increasing proportion of nitrogen, the oxygen saturation of the blood fell from 89 per cent (in the control period) to concentrations which were, successively, 11, 54, 76 and 93 per cent less than this. The carbon dioxide content successively increased 4 and 3 per cent and then fell 8 and 15 per cent. Toward the end of the experiment there was a 7 per cent increase in the size of the artery—which took place in the face of a slight decrease in the carbon dioxide content of the blood. The final drop in the pressure of blood and spinal fluid was a terminal affair.

than in the group in which contraction occurred (33.4 volumes present). As we shall mention later, the absolute concentration of carbon dioxide is not so important as the ratio between the acid and alkaline substances of the blood. In figure 15, for example, following the administration

of an oxygen-poor air, the carbon dioxide content of the blood fell 18 per cent. The bicarbonate content had an even greater decrease of 31 per cent, so that the shift of the acid-base ratio was toward the acid side. This would account for the marked dilatation of the artery observed in this experiment.

For the whole group of ten experiments in which there was anoxemia without an increase of carbon dioxide the oxygen saturation of the blood was reduced one-half, and the carbon dioxide content 17 per cent. There was a 3 per cent contraction of the arteries. Because a similar reduction in carbon dioxide in previous experiments, in which anoxemia was not present, had resulted in twice this amount of constriction, we may conclude that the anoxemia present exerted its influence in the opposite direction, i. e., toward a dilatation. Such a conclusion would be in accord with the observation under *C*, that increase in the oxygen content of the blood was associated with a slight contraction of arteries. It is evident that as compared with changes in the carbon dioxide content, gross changes in the oxygen content of the blood have little effect on the size of the arteries. In some experiments, as in figure 8, anoxemia was carried to the point of death without marked effect on the artery until changes secondary to falling blood pressure occurred.

H. Low Oxygen-High Carbon Dioxide.—In this group of three experiments (82, 87, 102) both nitrogen and carbon dioxide were added to atmospheric air. The degree of anoxemia produced was less than in the two previously mentioned groups, the average percentage of oxygen saturation of the blood being reduced by 30 per cent. There was a coincident average increase of the carbon dioxide content from 47.1 to 54.7 per cent by volume, an increase of 16 per cent. The pressure of the blood changed but little, that of the cerebrospinal fluid increased greatly. In each experiment the artery dilated conspicuously, the average increase being 23 per cent. In figure 9 (illustrating experiment 82) a gas was used sufficiently low in oxygen and high in carbon dioxide to reduce the oxygen saturation of the blood by 57 per cent and to increase the carbon dioxide content by 10 per cent. The resulting dilatation was prompt and persisted for five minutes after breathing of room air was resumed. In figure 10 (illustrating experiment 87) the induced anoxemia was less and the increase in carbon dioxide greater. The arterial dilatation also was greater than in experiment 82. The degree of hyperpnea induced was as great as that produced artificially in *B* which resulted in a constriction of the artery.

In order to demonstrate the changes in the size of the artery under observation, photographs made during the course of experiment 102

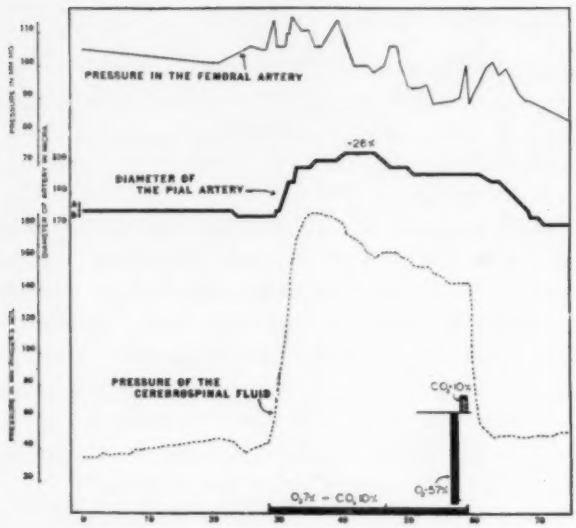

Fig. 9.—The effect of a decrease of 57 per cent in the oxygen saturation and an increase of 10 per cent in the carbon dioxide content of the blood. There was a 20 per cent increase in the diameter of the artery. During thirty minutes the cat breathed a mixture containing approximately 7 per cent oxygen and 10 per cent carbon dioxide. Though the mixture remained constant, there was a tendency for the pressures and the size of the artery to approach the normal control condition.

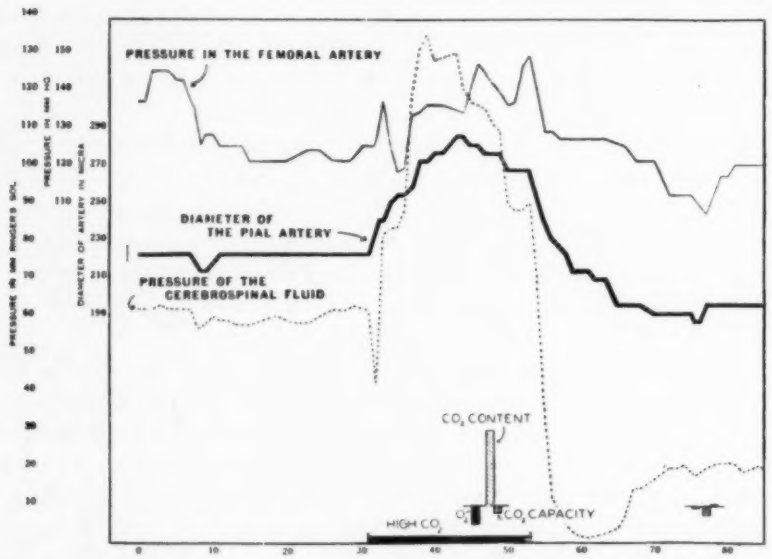

Fig. 10.—The effect of a slight (11 per cent) decrease in the oxygen saturation and a marked (40 per cent) increase in the carbon dioxide content of the blood. A 28 per cent increase in the diameter of the artery resulted.

are shown in figure 11. During breathing of a mixture low in oxygen which resulted in a decrease in both the oxygen and the carbon dioxide of the blood there was a very slight decrease in the size of the artery (middle picture). When, however, carbon dioxide was added to the respired air there was an easily appreciable increase in its size (right hand picture).

These experiments confirm the observation, mentioned in the last section, that variation in the carbon dioxide content of the blood is a much more effective agent in altering the diameter of arteries than is a change in the oxygen content. In the experiments under *E* in which the carbon dioxide content of the blood was increased to an even greater degree (25 per cent) but in which the oxygen content also was increased, the dilatation of the arteries was less than in these high carbon dioxide-low oxygen experiments. This suggests again that the anoxemia tended

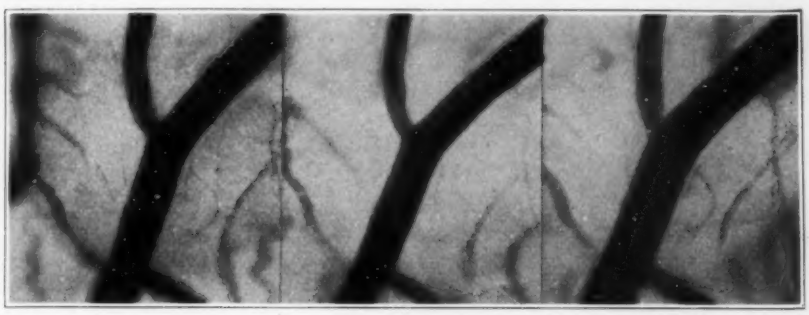

Fig. 11.—The appearance of a pial artery under varying conditions (experiment 102). The left hand figure (normal) shows a control exposure, the middle figure (low oxygen-low carbon dioxide) was taken at a time when the cat's blood showed a decrease of 17 per cent in oxygen and of 12 per cent in carbon dioxide content. The artery was 4 per cent narrower. The right hand exposure (low oxygen-high carbon dioxide) was taken a few minutes later. The oxygen saturation was then 21 per cent less than in the control period, the carbon dioxide content 2 per cent less, the carbon dioxide combining power 4 per cent less (indicating a slight acidosis) and the artery was 17 per cent wider.

to augment the dilator effect of the increased concentration of carbon dioxide. The experiments demonstrate that it is much easier to induce dilatation of arteries, with resulting increase in intracranial pressure, than it is to produce contraction. Comparisons in figure 1 of groups *B* and *H* and of groups *E* and *F* show that a given increase in the carbon dioxide of the blood will cause from three to four times as great a change in the caliber of the artery as the same decrease of carbon dioxide.

RELATION TO ACID-BASE EQUILIBRIUM

In the previous description of results, data have been presented concerning variations in the oxygen and carbon dioxide content of the blood. With changes in the gaseous content of the blood there are coincident variations in the hydrogen ion concentration. With acute accumulations of carbon dioxide there is an uncompensated acidosis, and with rapid elimination of carbon dioxide an uncompensated alkalosis. In a number of the experiments we measured both the carbon dioxide content and the carbon dioxide combining power (the bicarbonate) of the blood. The average results of these measurements are displayed in table 2 and show that in conditions in which the carbon dioxide content was reduced (as in *B, F* and *G*), the reduction was greater than the reduction which took place in the bicarbonate content of the blood. This would produce an alkalosis. When there was an accumulation of carbon dioxide (as in *E* and *H*), the increase in bicarbonate again lagged behind, producing a condition of acidosis. In the experiments which have been presented, a condition of acidosis was accompanied by a dilatation of the pial artery, whereas alkalosis resulted in a constriction. This is in keeping with observations reported by others for vessels elsewhere in the body. As has been suggested, probably changes in p_H of the blood are of more importance than changes in its content of carbon dioxide.

TABLE 2.—*Relation of the Carbon Dioxide Content to the Carbon Dioxide Capacity of the Blood in Various Procedures*

			Arterial Blood					
			Carbon Dioxide Content			Carbon Dioxide Combining Power		
	Gas Mixture Respired	Number of Experiments	Before	During	Percentage Change	Before	During	Percentage Change
B	Normal O_2, low CO_2	4	46.7	38.1	−18	55.3	52.2	−6
D	High O_2, normal CO_2	2	46.3	46.3	0	57.5	55.4	−4
E	High O_2, normal CO_2	1	38.0	47.7	+26	46.9	45.7	−3
F, G	Low O_2, normal or low CO_2	5	48.1	40.1	−17	56.5	53.7	−5
H	Low O_2, high CO_2	2	44.1	56.7	+27	55.4	53.4	−4

INJECTIONS OF ACID AND ALKALI

We wished to determine whether methods of changing the acid-base relations, other than through altering the amount of carbon dioxide in the respired air, would have an effect on the size of the pial arteries. The observations by Gaskell,[8] Leake, Hall and Koehler[9] and by Lan-

8. Gaskell: J. Physiol. **3**:48, 1880.

9. Leake, C. D.; Hall, F. G., and Koehler, A. E.: Am. J. Physiol. **65**:386, 1923.

dis [4] and others on peripheral blood vessels, as well as the experiments of Jacobi,[10] Schmidt [11] and others on cerebral circulation, indicate that alteration of blood p_H from whatever cause would effect the size of the minute vessels of the brain.

After a satisfactory control period, 10 cc. of a 1 per cent isotonic solution of sodium bicarbonate was injected slowly into a femoral vein. In the experiment illustrated by figure 12 there was an immediate sharp constriction of the pial artery. Arterial blood drawn five minutes after the injection showed a 20 per cent decrease in the oxygen saturation, presumably due to dilution of the blood, and a 39 per cent increase

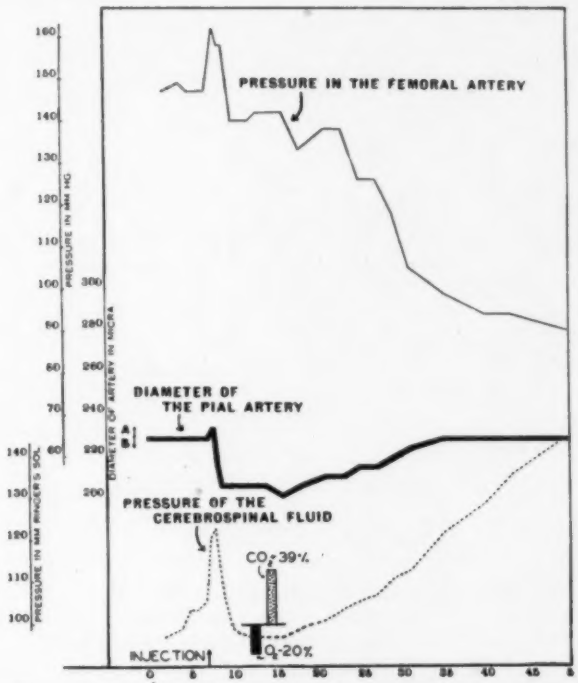

Fig. 12.—The effect of the injection of sodium bicarbonate. The arrow at the bottom indicates the time at which 10 cc. of a 1 per cent solution was injected into the femoral vein. Five minutes after the injection, the oxygen saturation of the arterial blood was less by 20 per cent and the bicarbonate greater by 39 per cent than before the injection.

in the blood bicarbonate. It required twenty minutes for the artery to resume its normal size. During the recovery period the pressure of the blood fell and that of the spinal fluid rose. Control experiments in which Locke's solution was injected showed that the changes were not due merely to the change in blood volume.

10. Jacobi, W.: Ztschr. f. Neurol. u. Psychiat. **102**:625, 1926.
11. Schmidt (footnote 1, eleventh reference).

Figure 13 shows the result of injecting lactic acid. Three intravenous injections of 5 cc. of a 10 per cent solution were made. Following the third injection, there was a 10 per cent increase in the diameter of the artery. The oxygen saturation was not affected, the carbon dioxide content of the blood was decreased 23 per cent by volume and the bicarbonate 17 per cent by volume. That the arterial dilatation was so short lived may perhaps be accounted for by the fact that lactic acid when introduced into the body is quickly oxidized.

Following the intravenous injection of acetone there was also a dilatation of the pial artery. This was repeated several times, but because the necessary examinations of the blood to demonstrate the

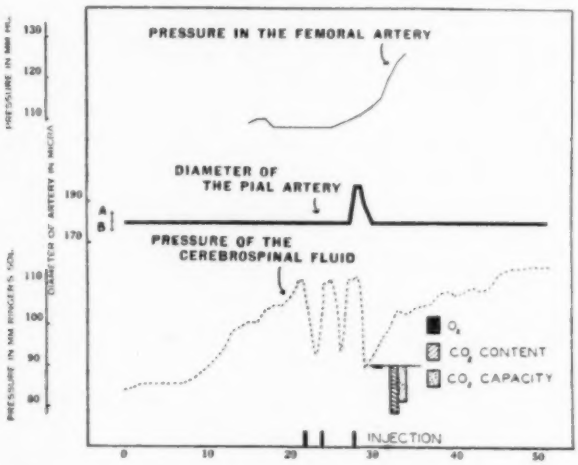

Fig. 13.—The effect of the injection of lactic acid. The columns at the bottom of the charts indicate the points at which 5 cc. amounts of a 10 per cent solution of lactic acid were injected. Following the third injection there was a 10 per cent dilatation of the artery. Blood drawn at this time showed, in comparison with its composition during the control period, a reduction of 1 per cent in oxygen saturation, of 23 per cent in carbon dioxide content and of 17 per cent in carbon dioxide capacity (bicarbonate).

presence of acidosis were not made, these experiments are not described. Because of the few observations, we do not regard these injection experiments as conclusive.

RELATION TO RESPIRATION

In order not to complicate the presentation of data, we have spoken little thus far of the observations concerning respiration. It is of course evident that there is a close reciprocal relation among the elements of the triad—the oxygen, carbon dioxide content of the blood and pulmonary ventilation. Study of the graphic records of air intake

shows that of the various physiologic elements being studied, respiratory movements were the first to change. Only after alteration in respiration was there a perceptible change in the size of the arteries. This applied to experiments in which there were changes both in the oxygen and in the carbon dioxide content of the blood.

Because the total ventilation was not measured in all experiments, the results cannot be treated on a statistical basis. In general, it may be said that changes in respiration occurred before changes in the size

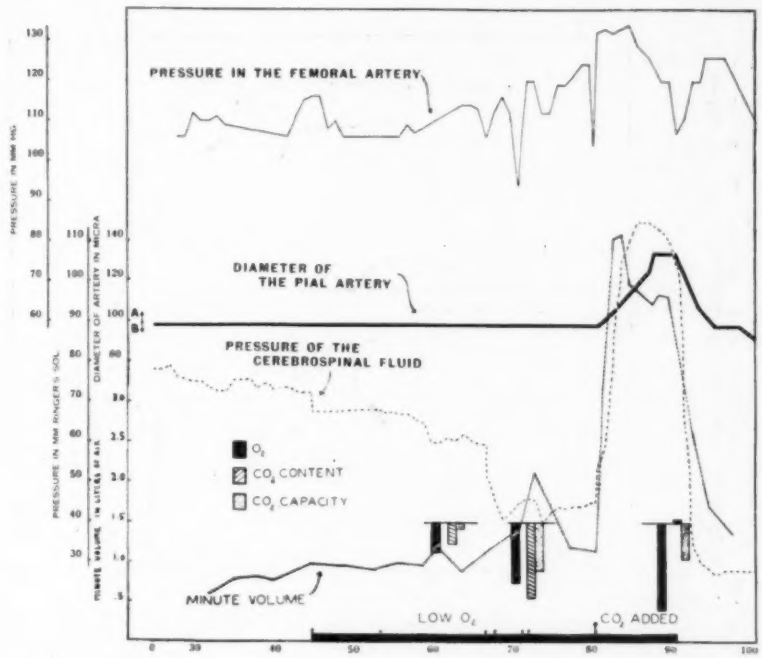

Fig. 14.—The effect of a progressive decrease in the oxygen saturation of the blood with at first a decrease then an increase in its carbon dioxide content. In this and the two following charts the hatched solid line represents the liters of air inspired per minute. During the experiment the oxygen saturation decreased successively 15, 30 and 44 per cent. The carbon dioxide content decreased 11 and 38 per cent, then with the administration of a carbon dioxide increased 2 per cent. The measurements of the carbon dioxide combining power indicated first an alkalosis, then an acidosis. With the latter condition there was a 35 per cent increase in the diameter of the artery. An increase in the volume of inspired air preceded the arterial dilatation.

of vessels and in the pressure of the blood and the spinal fluid, and that there was a reciprocal relationship between the two. Such relationship is shown by examination of the protocols of some of the experiments.

In experiment 103, figure 14, while the animal was breathing a low oxygen-low carbon dioxide mixture the diameter of the pial artery remained constant, but the minute volume of pulmonary ventilation slowly increased. When carbon dioxide was added to the air mixture, the ventilation immediately increased about 400 per cent. At this point the diameter of the artery had increased by only 9 per cent. The artery continued to dilate until its diameter had become 36 per cent greater than during the low oxygen-low carbon dioxide period. Now the ventilation dropped so that it was only 180 per cent greater than

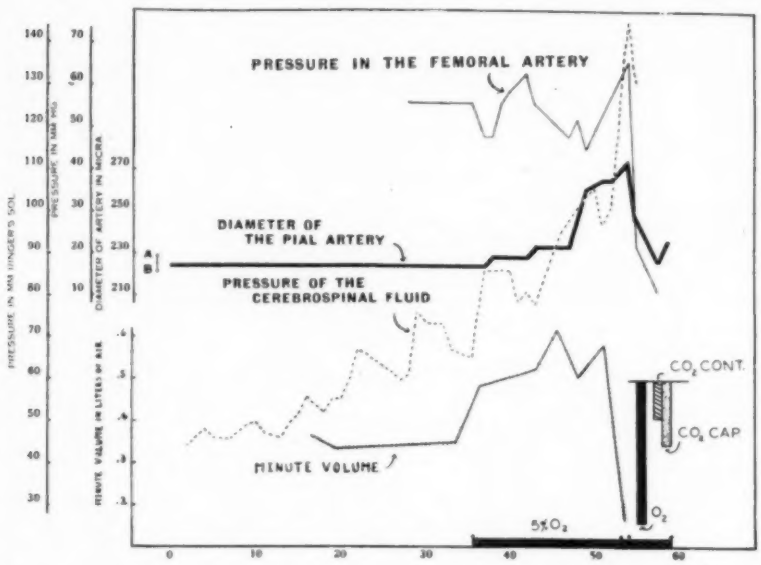

Fig. 15.—The effect of anoxemia caused by breathing a mixture of 5 per cent oxygen and 95 per cent nitrogen for twenty-three minutes. There was reduction of 61 per cent in the oxygen saturation, of 18 per cent in the carbon dioxide content and of 31 per cent in the carbon dioxide combining power of the blood. The 18 per cent increase in the diameter of the artery may have been due in part to the fact that the reduction in the carbon dioxide of the blood did not keep pace with the loss of bicarbonate, due apparently to a depression of respiration. The respiratory apparatus proved more sensitive to the anoxemia than the blood vessels or the blood pressure.

during the preliminary period. During the period of anoxemia and before the artery had dilated, the blood pressure also increased somewhat, and with the dilatation of the pial vessels the blood pressure again became lower.

In experiment 97, figure 15, when the animal first started to breathe the oxygen-poor mixture the ventilation increased 39 per cent. When

it had increased 46 per cent the caliber of the artery was but 2 per cent greater than normal. By the time the artery had reached its maximum dilatation, 18 per cent above normal, the minute volume had dropped to below normal. The blood pressure remained practically unchanged throughout.

In experiment 92, figure 16, when the animal breathed a mixture rich in oxygen and carbon dioxide, there was at first an increase of 180 per cent in ventilation, with a slight dilatation of the artery (5 per cent). For the rest of the experiment, however, the two curves nearly paralleled each other. The blood pressure fell slightly during the height of the ventilation and the arterial dilatation.

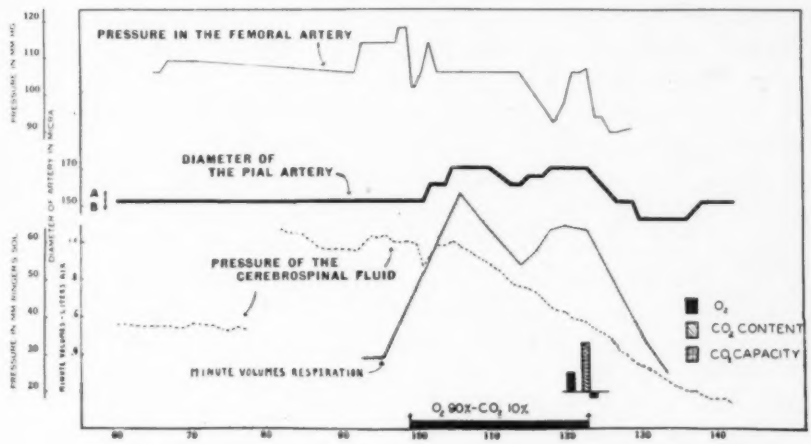

Fig. 16.—The effect of increasing in the blood both the oxygen (by 10 per cent) and the carbon dioxide concentration (by 26 per cent). The carbon dioxide combining power fell 3 per cent. Changes in the volume of respiration preceded other changes. They did not precede breathing of the gas, as the curve with its too scanty points of observation would imply.

Except in very great changes in the composition of respired gases, the variations in the diameter of the pial arteries were not directly dependent on changes in blood pressure. There was usually, in fact, an inverse relationship between the diameter of vessels and the blood pressure. This is apparent when the actual protocols are examined. With two exceptions the pressure of the cerebrospinal fluid varied directly with the diameter of the arteries of the brain.

From these observations one might conclude that in the period in which the oxygen content of the respired air was low the organism first compensated for the anoxemia by an increase in respiration which would increase the percentage of oxygen in the alveolar air and hence

in the blood, and by an increase in blood pressure which would force more blood through the vessels to the tissues. The hyperpnea would result in a "blowing off" of carbon dioxide. The decrease of carbon dioxide in the blood and the resulting alkalosis would tend to maintain constriction of the arteries.

An increased concentration of carbon dioxide in the blood going to the brain, by raising systemic blood pressure and by dilating cerebral arteries, increases the speed and the volume of blood passing through the brain. Venous blood becomes more arterial-like (richer in oxygen and poorer in carbon dioxide). This permits a diminution of respiratory effort, a fall in blood pressure and a decrease in the caliber of cerebral vessels. It is significant that under conditions in which the cat breathes an abnormal but constant gas mixture, it gradually is able to adjust to the new conditions. The blood and spinal fluid pressures and the size of the pial arteries tend to approach the normal control condition.

The mechanism by which variation in the gaseous content of the blood results in changes in the size of small vessels is of great interest. Dilatation, for example, might result from a stimulation of vasodilator nerves. The dilatation of pial vessels which Forbes and Wolff [12] obtained from vagus stimulation was similar in degree to that produced in the experiments described here. The promptness with which dilatation follows cerebral anemia suggests the action of nerve control. On the other hand, there might be a direct action of the chemical substances in the blood on the walls of blood vessels, causing changes in diameter. Both these factors may play a part.

These observations concerning the behavior of vessels in the pia are similar to those made by Krogh [13] and others, that local accumulation of carbon dioxide in muscles causes a dilatation of capillaries with consequent increase in the circulation to the part. The circulation in the brain is under certain restrictions due to its situation in a closed and fairly rigid box. Our observations under conditions which maintain the closed box relations demonstrate that under changing conditions of the gaseous content of the blood, the arteries of the pia act in the same manner as arteries in the muscles or skin. Although hydrostatic and nerve factors undoubtedly play a part in alterations of the cerebral circulation, the factors of chemical and respiratory changes in the blood must be given a prominent position.

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

13. Krogh, A.: Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1922.

These observations have direct clinical applications in that they support the work of Henderson and Haggard,[14] Drinker,[15] and others who have demonstrated the usefulness of altering the composition of the respired air in certain clinical conditions such as carbon monoxide poisoning and in intracranial injuries to infants at birth. Haldane[16] demonstrated that increased carbon dioxide is a much more active stimulator of respiration than is oxygen lack. Our observations prove that the same holds true for the relative effect of these two gases on the caliber of cerebral arteries.

It would seem that the most effective measure for increasing the supply of blood and hence of oxygen to brain tissues is the inhalation of a mixture of 90 per cent oxygen and 10 per cent carbon dioxide. The latter increases the diameter of arteries and by inducing a condition of acidosis increases the dissociation of oxygen from hemoglobin and makes more oxygen available for tissue use. It also stimulates respiration and increases the blood pressure.

In carbon monoxide poisoning, the pial vessels are already dilated to a maximum extent. In convulsions which are precipitated by means of overventilation there are various changes in the physiology of the brain, which may act severally or jointly to produce the fit. The "blowing off" of carbon dioxide induces a condition of alkalosis, a lowering of the oxygen dissociation curve, a constriction of arterioles, a fall of blood pressure and, finally, an increase in the irritability of nerve tissue with resulting explosion. Just as Lennox and Cobb[17] have shown that increasing the content of carbon dioxide, and to a lesser extent of oxygen, in the inspired air decreases the liability to epileptic seizures, it is possible that other symptoms might be influenced by measures which alter the blood supply of the brain. Loevenhart[18] and others have found that certain stuporous psychopathic patients are temporarily released from their stupor by inhalation of air very rich in carbon dioxide. This is explained on the basis of the stimulating effect of oxygen lack, but in the light of considerations which we have mentioned, alterations in cerebral circulation need to be taken into account.

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14. Henderson, Y., and Haggard, H. W.: The Treatment of Carbon Monoxid Asphyxia by Means of Oxygen and CO_2 Inhalation, J. A. M. A. **79**:1137 (Sept. 30) 1922.

15. Drinker, Philip, and McKhann, C. F.: The Use of a New Apparatus for the Prolonged Administration of Artificial Respiration, J. A. M. A. **92**:1658 (May 18) 1929.

16. Haldane, J. S.: Respiration, New Haven, Conn., Yale University Press, 1922.

17. Lennox, W. G., and Cobb, S.: Epilepsy, Baltimore, The Waverly Press, 1928.

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

CONCLUSIONS

Experiments were performed on cats, in which measurements were made of the diameter of pial arteries, the pressure of the blood and of cerebrospinal fluid, the rate and volume of respiration and the oxygen and carbon dioxide content and capacity of arterial blood. These observations were made before and during the inhalation of various gas mixtures, and the injection of acid and alkali.

A decrease in the carbon dioxide content of the blood resulted in a moderate decrease in the diameter of the pial arteries, whereas an increase in carbon dioxide was followed by a very marked increase in their size.

In sharp contrast, an increase in the oxygen content of the blood resulted in a very slight decrease in the diameter of the arteries, and a marked degree of anoxemia had a tendency to increase their size. There was a tendency also for anoxemia to augment the dilator effect of an increased carbon dioxide content of the blood. The influence of carbon dioxide almost completely obscured that of oxygen.

A variation in the ratio of carbonic acid to the bicarbonate of the blood which resulted in an acidosis caused dilatation, and a condition of alkalosis caused a constriction of pial arteries.

Dilatation of vessels was more readily produced than constriction. When the composition of the respired gas was altered, respiration was affected before either the systemic arterial blood pressure or the size of the pial arteries. These mechanisms are so interrelated as to maintain an effective cerebral circulation.

The chemical composition of the blood plays an important part in the regulation of the intracranial circulation.

THE HISTOLOGY OF THE NERVOUS SYSTEM

SOME OBSERVATIONS WITH THE ULTRAMICROSCOPE *

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AND

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PHILADELPHIA

This preliminary report is made on three of the simpler phases of a work which is designed to determine in what manner the methods of biology and physical chemistry can be made applicable to a study of the nervous system:

1. The ultramicroscopic observation of fresh nerve tissue reveals the colloidal nature of the tissue elements. This cannot be observed in fixed tissue with direct illumination.

2. In "swelling" experiments with fresh brain tissue, water is taken up in the proportions that are applicable to colloidal masses in general. The swelling of brain tissue thus follows the same laws as does that of gelatin, for instance. It is important to note that the swelling effects discussed are different from osmotic effects.

3. The effects of the colloidal swelling of the cells and intercellular substance of nerve tissue can be seen with the ultramicroscope. These appearances correlate with the results of the swelling experiments mentioned in the preceding paragraph.

ULTRAMICROSCOPIC OBSERVATION OF FRESH NERVE TISSUE

When fresh brain tissue is examined with the ultramicroscope,[1] one has an unusual picture in three dimensions. The relations are as nearly as possible the same as those in the body during life in the sense that the tissues are studied at once on removal from the living animal, neither fixation nor staining being used. Study of these tissues also represents dynamic histology in contrast to the static histology of fixed and sectioned material. The latter is, of course, a necessity in using a microscope with direct illumination, as is customary in tissue study, since fresh tissue is hardly visible with direct lighting. With the ultramicroscope, on

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1. A cardioid ultramicroscope was used throughout.

the contrary, tissue can be examined at the instant of removal. Its ultramicroscopic form, color and consistence are at once visible, with the added advantage of allowing a study of the presence of brownian motion. There is no distortion or alteration of the tissue due to fixation, embedding and staining.

That consistence can be judged by microscopic study may need a word of explanation for those unfamiliar with ultramicroscopic methods. Chambers [2] said of this means of detecting viscosity: "A valuable adjunct for studying the physical nature of protoplasm is the detection of brownian movement by means of dark-field illumination." The Lewises,[3] in their dark-field studies, said: "Changes in consistency occur during mitosis as evidenced by a rounding up of the cells."

Earlier studies, both by us and by others (Marinesco [4] and Mott), have shown that fixing agents are coagulants of protoplasm at best, and further, that no tissue is stainable until its protoplasm is coagulated. Stains alone, added to fresh tissue, must be sufficiently concentrated to cause coagulation before staining will take place. That coagulation of the essential portion of protoplasm is necessary before staining will take place was recognized in much earlier work. Even in connection with vital staining, Pfeffer,[5] working with plant cells, determined that the ground substance of protoplasm usually remained unstained, the dye being taken up by vacuoles or granules. Heidenhain [6] found that vital staining affects only dead substances in protoplasm. These details are presented to indicate how the appearance of fixed and stained material can differ from that in the fresh state and how the ultramicroscope affords a means of avoiding this condition.

The material on which this study was made was taken from frogs, chickens, albino rats and cats. The frogs were pithed, and the brain substance was removed while circulation and respiration were still active. Frog tissue was examined with the idea that the tissue of a cold-blooded animal might present a different appearance in some way from that of warm-blooded ones. This, however, was not found to be the case. The chicken brains were used immediately after decapitation, while still warm. The rats and cats were etherized, and brain tissue was removed, a fragment at a time, during light anesthesia.

Small pieces of fresh brain tissue, about half the size of the head of a pin, when placed on a glass slide under a coverslip can be flattened to a thin film by gentle pressure. This allows the study of the material without the influence of any foreign substance.

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2. Chambers, in Cowdry, E. W.: General Cytology, Chicago, University of Chicago Press, 1924, p. 239.

3. Lewis and Lewis in Cowdry, E. W.: General Cytology, p. 409.

4. Marinesco: Rev. neurol. **2**:521, 1925.

5. Pfeffer: Untersuchungen aus den Boton, Institut Tübingen, 1886-1888, vol. 2, p. 325.

6. Heidenhain: Plasma and Zelle, Jena, Gustav Fischer, 1911, vol. 1, p. 443.

The most prominent part of the picture seen with the ultramicroscope is the supporting or ground substance of the cortex (fig. 1). The structure of this part of the brain appears entirely different from that seen in stained specimens. Previously it has always been described as a network or reticulum. Held [7] called it a general foundation or supporting network, and described it as close and fine, without question protoplasmic, and containing granules. "Such tissue is not found in any other organ." He considered that it must be concerned with conduction of stimuli and therefore "nervous tissue." As seen under the ultramicro-

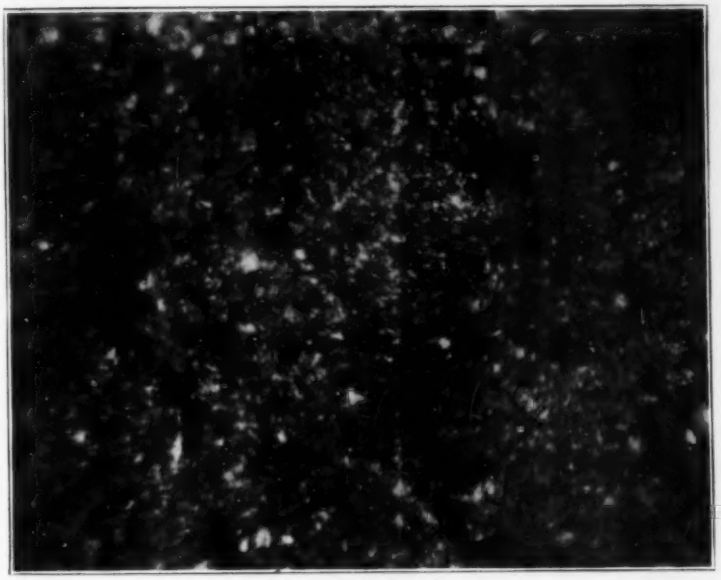

Fig. 1.—The ultramicroscopic appearance of the ground substance of the cortex in fresh brain tissue.

scope, however, it is actually a finely granular mass. As has been described by us elsewhere,[8] it appears like boiled farina—a finely granular, somewhat tenacious substance—eminently suitable for a support or packing for the nerve elements which it surrounds. It is an efficient shock absorber, although its function doubtless is not limited to this mechanical action. It is found in greatest abundance in relation to nerve cells, and possibly its color has given rise to the descriptive name of gray substance. These gray masses, as is well known, represent the areas in

7. Held, H.: Monatschr. f. Psychiat. u. Neurol. **65**:68, 1927.

8. Taft, A. E., and Ludlum, S. DeW.: J. Nerv. & Ment. Dis. **70**:360 (Oct.) 1929.

which nerve cells are present in large numbers. Much less of the granular supporting substance is present among the fibers than among the cells. As Held has pointed out, this substance, which he calls a reticulum from the study of fixed and stained materials, appears in no other organ in the body. A reasonable explanation of this may be that no other cells in the body are final products; that is, nerve cells are generally conceded to be the only cells in the body which do not regenerate when severely injured, and which are not replaced by other cells of their kind when once destroyed.

Fig. 2.—The ultramicroscopic appearance of nerve cells embedded in ground substance in fresh brain tissue.

In addition to this interneuronal granuloplasm, the nerve cells appear as irregular, dark outlines, embedded in the supporting substance (fig. 2). Treatment of fresh tissue with Ringer's solution sometimes causes the cells to be more sharply outlined, as shown in figure 3. They then appear to be made up of very fine, densely packed granules, with a more homogeneous nucleus containing the nongranular nucleolus. The round glia nuclei are also visible. The nerve fibers are prominent, as the myelin sheaths are brilliantly refractile, like lipoid substances in general, and appear like capillary tubes (fig. 4).

Blood vessels with outstanding nuclei are easily seen, and in small capillaries of only one cell layer the individual cells can be made out.

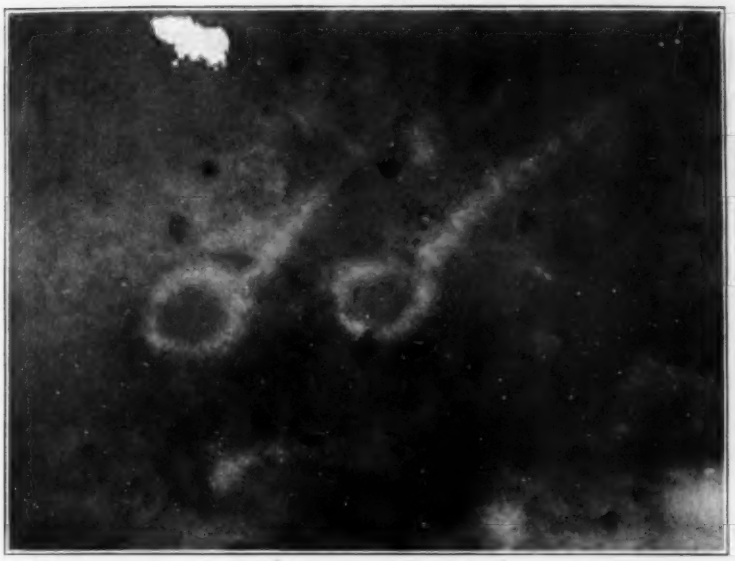

Fig. 3.—The ultramicroscopic appearance of nerve cells embedded in ground substance of fresh brain tissue treated with Ringer's solution.

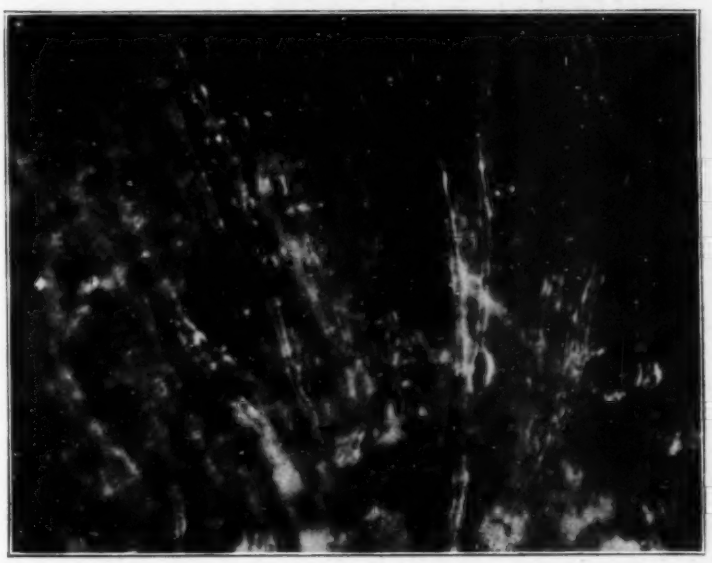

Fig. 4.—The ultramicroscopic appearance of myelinated nerve fibers in fresh brain tissue.

OBSERVATION OF SWELLING DIFFERENCES IN BRAIN TISSUE

According to Heilbrunn,[9] "physiologists are generally agreed that the essential properties of protoplasm are due in large measure to its colloidal nature." Likewise, d'Herelle[10] writes: "Most biologists agree that all living matter exists in the colloidal condition, and that all physiological and pathological reactions occurring in living beings are dominated by the laws of colloid chemistry." Schade[11] believes that the phenomena of life are invariably associated with matter in the colloidal condition, and that nothing injures the ability of cells to function so much as inroads on their colloidal integrity. Schade further says that the vivification of medicine by colloid chemistry justifies us in calling this the beginning of a new era in etiology. He believes that "to complete and extend cellular pathology, which is bound by the limitations of the microscope, future medical research must have as its objective the pathology of the colloidal state, which is found in all diseases."

The foregoing paragraph gives some idea of the importance attached to the relation of colloid science to physiology and pathology. The connection follows naturally when one considers that living matter, included under the general name "protoplasm," is principally a protein-water system, and that nonliving protein-water systems are colloid systems more or less by definition. People started out by saying that the study of protein-water systems should be part of so-called colloid chemistry, which in general is the chemistry of matter in a finely divided state. Many of the most important characteristics of matter in the colloid state arise from the enormous development of surface associated with such division.

Protein-water systems are characteristic of a particular type of colloid system in that the finely divided protein material is associated with more or less water; that is, the protein actually binds a certain amount of water by forces which may be akin to those which bring about ordinary stoechiometric chemical combination. Since protoplasm is a protein-water system, it contains water bound in this way.

The important fact is that in such protein-water systems the amount of water bound in any case depends on the nature and amount of the electrolytes dissolved in the water. It thus depends on the acidity of the solution and on the amount and kind of salts present. Many experiments have demonstrated these general facts in the case of simple proteins. Thus a block of protein jelly containing a certain amount of water may take up more water in certain solutions (swell) and give off water (shrink) in others. Martin Fischer[12] has studied animal tissues

9. Heilbrunn in Alexander, J.: Colloid Chemistry, New York, The Chemical Catalog Company, 1928, vol. 2, p. 451.

10. D'Herelle, in Alexander, J.: Colloid Chemistry, p. 535.

11. Schade in Alexander, J.: Colloid Chemistry, p. 629.

from this point of view for many years, and has announced that their water relations are governed by sets of laws qualitatively and quantitatively similar to those obtaining for simple proteins such as gelatin.

There are various theories as to the reason for this dependence of the water-binding power or state of swelling of protein material on electrolytes. These have been summarized recently by Seifriz.[13] For the purpose of discussion, one may adopt the comparatively simple view that the distribution of water depends on the relative affinities of the salts and protein for water, and that the affinity of the protein for water depends in part on the electric charge imparted to it by the electrolytes. Different salts are known to have different affinities for water and to impart different charges to protein material. The charge on protein material is well known to depend on the acidity (p_H) of the water phase. There is considerable basis for this view, although it is not the whole story. It is known, for example, that Donnan equilibrium effects are operative in certain cases.[14] In any event, regardless of theories as to mechanism, the experimental facts remain.

Comparatively early in the study of the application of these principles to animal tissues, certain opinions arose that they did not apply to nervous tissue. Hooker and Fischer,[15] however, employing the brains and spinal cords of rabbits, promptly showed that they did. More recently, Haldi and associated workers[16] have made further experiments which in general verify the results obtained in the earlier work of Hooker and Fischer. Haldi[17] and Rauth have adopted the general views of Fischer in a specific theory of mental diseases. Ludlum and Taft[18] have emphasized the probable importance of swelling in neuropathology.

Dhar and Chakravarti[19] write: "Every organ has a definite normal fluid content. A healthy plant has a definite turgescence and the protoplasm of a healthy animal a given degree of swelling; every abnormal change in this, signifies illness or even death." Haldi and Rauth take the view that mental pathologies in general may be due to changes in water-holding power of various parts of brain tissue, due to acidity or the salt milieu of the tissue in question. It is conceivable that such changes might occur only within the tissue itself or also in the blood supplying it.

12. Fischer in Alexander, J.: Colloid Chemistry, p. 235.

13. Seifriz in Alexander, J.: Colloid Chemistry, p. 403.

14. Loeb, J.: Proteins and the Theory of Colloidal Behavior, New York, McGraw-Hill Book Company, 1924, p. 240.

15. Hooker and Fischer: Kolloid Ztschr. **10**:283, 1912.

16. Haldi, J. A.; Rauth, J. W.; Larkin, J., and Wright, P.: Am. J. Physiol. **80**:631, 1927.

17. Haldi, J. A.; Larkin, J., and Wright, P.: Am. J. Physiol. **78**:74, 1926.

18. Ludlum and Taft, in Alexander, J.: Colloid Chemistry, p. 695.

19. Dhar and Chakravarti in Alexander, J.: Colloid Chemistry, p. 105.

Different portions of rabbit brain, e. g., cerebral hemispheres, midbrain, cerebellum and medulla, respond differently to conditions.[20] Presumably smaller units within each of these do likewise. Thus any one part of the brain may be specifically affected. It is known that the acidity of brain tissue may increase under certain conditions. Liesegang,[21] in 1910, showed that increased acidity in the brains of thymectomized dogs increased the volumes of the brains to from 86 to 91 per cent of the cranial capacity to from 98 to 100 per cent. Poetzl and Schueller [22] reported lethal brain swelling due to oxygen deficiency. According to Fischer, a 5 per cent swelling of the brain causes coma and an 8 per cent swelling death. McGinty and Gesell [23] have demonstrated the accumulation of lactic acid in the brain as a result of oxygen deficiency.

This type of effect of acidity and salts on the water content of protein materials, such as brain tissue, should not be confused with osmotic swelling and shrinking which result from simple diffusion modified by the presence of some form of membrane. When a plant cell is placed in distilled water, it swells osmotically. Water diffuses in through the cell membrane faster than the cell solutes diffuse in the opposite direction. The swelling of a block of gelatin is different, because it involves no membrane. The results obtained by Weed and McKibben [24] and others [25] with hypotonic and hypertonic salt solutions are presumably osmotic. These workers were able to demonstrate increases in the bulk of the brain when hypotonic solutions were given intravenously or by way of the alimentary canal. With hypertonic solutions this result was reversed.

In any demonstration of colloidal swelling of tissue, possible accompanying osmotic effects cannot be ruled out. In the experiments described subsequently, the degrees of swelling are compared in isotonic solutions, that is, solutions of the same osmotic pressure. In such solutions the osmotic effects should be equal, and therefore any differences observed may be attributed to factors affecting colloidal swelling.

Fischer and Hooker and Haldi and his co-workers used equimolar solutions which are isotonic only in special cases of salts of the same valence type. Thus equimolar solutions of sodium chloride and potassium chloride are isotonic, but they are not isotonic with equimolar solutions of calcium and magnesium chloride.

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20. Haldi, J. A., and Rauth, J. W.: Am. J. Physiol. **75**:294, 1925-1926. Haldi, Larkin and Wright (footnote 17). Haldi, Rauth, Larkin and Wright (footnote 16). Haldi, J. A.; Ward, H. P., and Woo, L.: Am. J. Physiol. **83**:250, 1927-1928.

21. Liesegang: Ztschr. f. allg. Physiol. **11**:347, 1910.

22. Poetzl and Schueller: Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:3, 1910.

23. McGinty and Gesell: Am. J. Physiol. **75**:70, 1925.

24. Weed and McKibben: Am. J. Physiol. **48**:512, 1919.

25. Foley and Putnam: Am. J. Physiol. **53**:414, 1920.

The effect of gross differences in acidity and salt environment on the water content (state of swelling) of nerve tissue is easily demonstrated.

The optic lobes were removed from the brain of a freshly killed chicken. One was placed in 100 cc. of 0.0015 normal sodium hydroxide solution and the other in 100 cc. of 0.0015 normal hydrochloric acid. They were then immediately removed, drained and weighed in a closed weighing bottle. After they were replaced in their respective solutions, the weighing bottle containing the small amount of residual liquid from the tissue was again weighed. The difference between the two weights was taken as the initial weight in each case. At stated intervals the lobes were removed, and their weights again determined in the same manner. The gain in weight at any time divided by the initial weight was taken as a measure of the extent of swelling at this particular time. Figure 5 shows the results of the experiment. The ordinates are percentage increases in

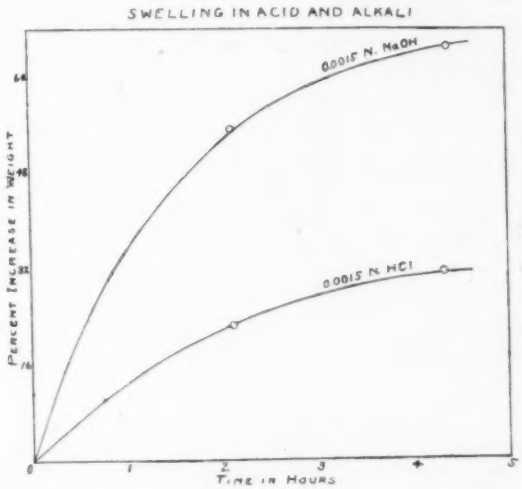

Fig. 5.—The effect of a gross difference in hydrogen ion concentration on the swelling of brain tissue.

weight and the abscissas the times of swelling in hours. After four hours, the lobe in alkali showed a weight increase of more than 60 per cent, whereas that of the lobe in acid was less than half this amount.

A similar experiment was done with two isotonic salt solutions. One contained sodium, potassium, calcium and magnesium chlorides in the proportions used in Ringer-Tyrode's solution with a sodium chloride to calcium chloride molecular ratio of about 75 : 1. The other, although isotonic, had a sodium chloride to calcium chloride molecular ratio of 0.5 : 1. The p_H of the solutions was kept between 7 and 7.5 throughout the experiment by means of the examination of test portions with phenol red indicator and the addition of 0.01 normal acid or alkali as necessary. The brain of a freshly killed chicken was divided symmetrically, and one-half was allowed to swell in each of the salt solutions. The weights were determined as in the previous experiment. After three hours the portion in the solution with the high sodium-calcium ratio had swelled about 20 per cent and the other only about 12 per cent. The results are shown in figure 6.

Perhaps the most striking phenomenon in connection with the swelling of colloidal substances is the different behavior observed in equally concentrated salt solutions. If salts of the same cation and different anions are employed, a regular order of anions is observed (e. g., the Hofmeister series [26]) as between the one that favors greatest swelling and the one that favors least swelling. A similar series of cations is observed when salts with a common anion but different cations are employed. Hooker and Fischer [15] demonstrated such series in the swelling of rabbit brains. More recently, Haldi and his co-workers [16] demonstrated the anion series tartrate, sulphate, acetate, chloride, iodide, and the cation series calcium, sodium, potassium in which the first mentioned ion in each series favors swelling least. Rabbit brains were used in this work also.

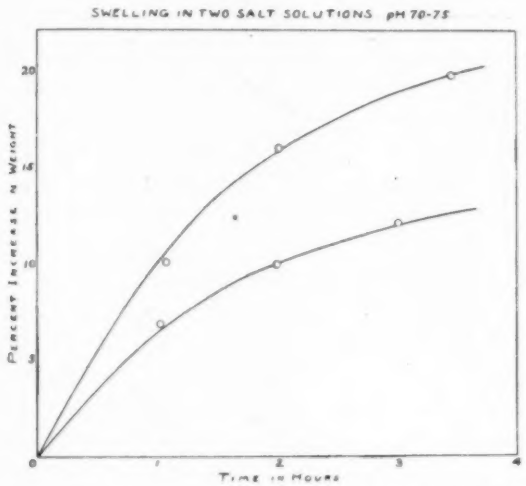

Fig. 6.—The effect of a gross difference in salt ratios on the swelling of brain tissue. The upper curve represents swelling in Ringer's solution. The lower curve represents swelling in an isotonic solution of the same salts, but in which the sodium-calcium ratio is greatly reduced.

In connection with the study of the ultramicroscopic histology of nervous tissue, it was decided to swell brain tissue in such salt solutions and then to examine it for possible characteristic differences in ultramicroscopic appearance.

Half portions of the frontal lobes of the brains of freshly killed chickens were employed in these experiments, the general procedure being that previously described. The salt solutions were all made up to have the same freezing point as 0.9 per cent sodium chloride. They were thus isotonic among themselves and

26. Bayliss, W. M.: Principles of General Physiology, London, Longmans, Green and Company, 1927, p. 97.

approximately isotonic with respect to blood. Their p_H was maintained between 7 and 7.5 as described for a previous experiment, with the exception of that of the aluminum chloride solution and the final points for the other solutions in the cation series.

Apart from the question of ultramicroscopic observation, these experiments present points of interest, since Hooker and Fischer and

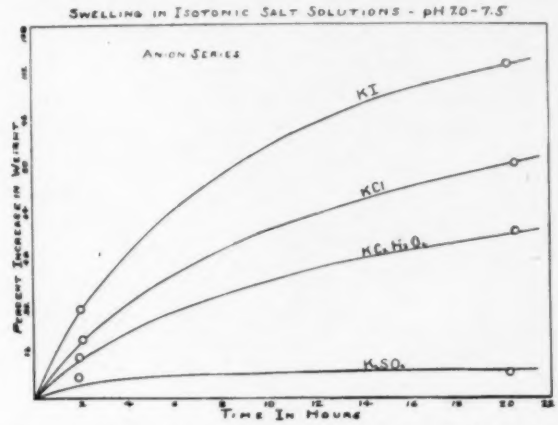

Fig. 7.—The swelling of brain tissue in isotonic solutions of salts with the same cation but different anions kept at from p_H 7 to 7.5.

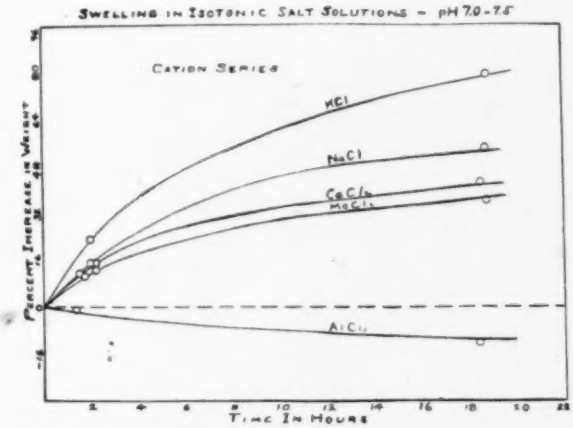

Fig. 8.—The swelling of brain tissue in isotonic solutions of salts with the same anion but different cations kept at from p_H 7 to 7.5

Haldi and his co-workers used rabbit brains and equimolar salt solutions and employed no p_H control. Equimolar solutions of salts of different valence types are, of course, not isotonic. The results are shown in figure 7 (anion series) and figure 8 (cation series). The orders sul-

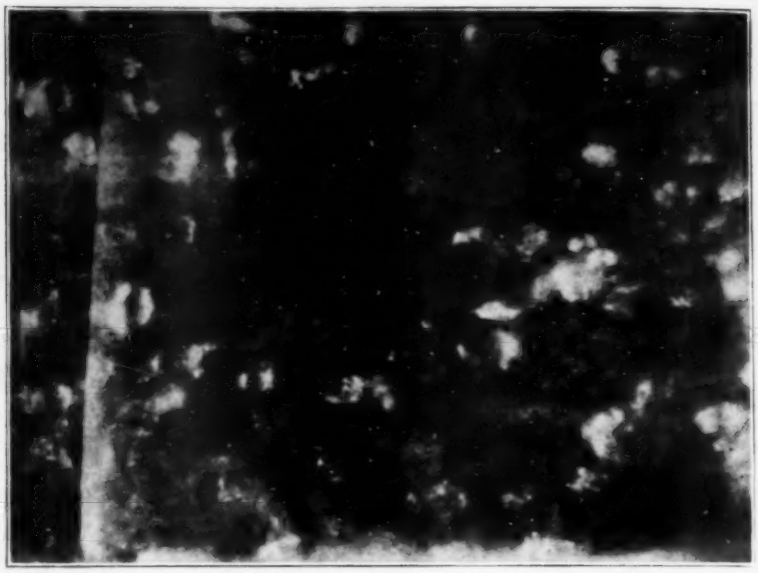

Fig. 9.—The ultramicroscopic appearance of strongly swollen brain tissue.

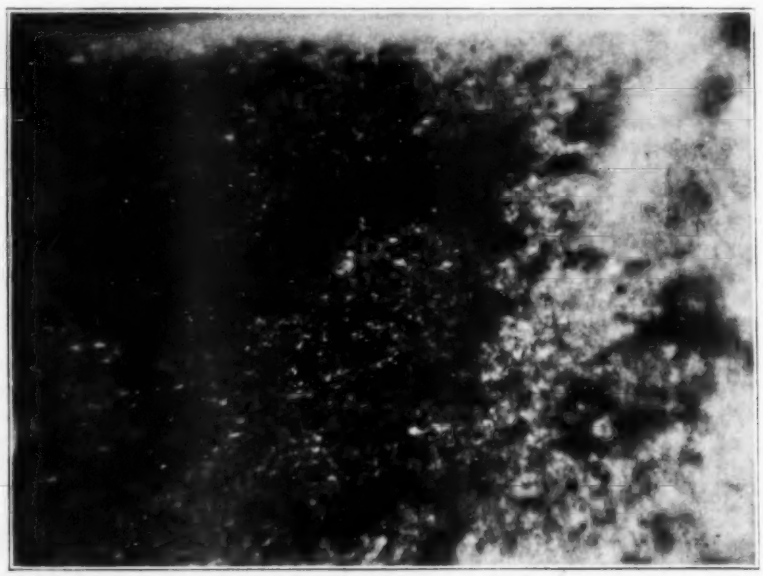

Fig. 10.—The ultramicroscopic appearance of dehydrated brain tissue.

phate, acetate, chloride, iodide, and calcium, sodium, potassium as reported by Haldi and others are apparent. Their results are thus extended to chicken brain and to isotonic solutions kept between p_H 7 and 7.5. The shrinking in aluminum chloride solution is interesting as demonstrating that the normal water content of tissue may decrease as well as increase, depending on its ionic environment.

ULTRAMICROSCOPIC OBSERVATION OF SWELLING DIFFERENCES IN BRAIN TISSUE

In each case in the foregoing experiments, after the final weighing, a small portion of the material was placed on a slide under a cover-slip

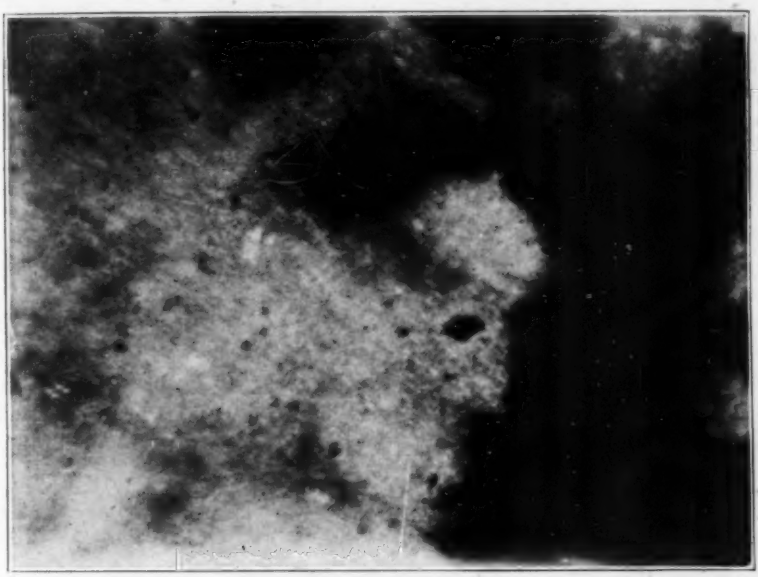

Fig. 11.—The ultramicroscopic appearance of brain tissue treated with aluminum chloride solution isotonic with 0.9 per cent sodium chloride solution.

and examined with the dark-field microscope. The appearance of strongly swollen material is as shown in figure 9, in which the brightest areas are myelin. This tissue swelled in water for twenty hours. The appearance of comparatively dehydrated tissue is as shown in figure 10. This tissue shrank in aluminum chloride solution for twenty hours. The particular preparation shown in the photograph had then stood overnight without sealing. From the point of view of these observations, it may be considered as an example of extreme dehydration. In general, less hydrous material has more definite edges and a more granular appearance than "wetter" material. These general type differences are similar to

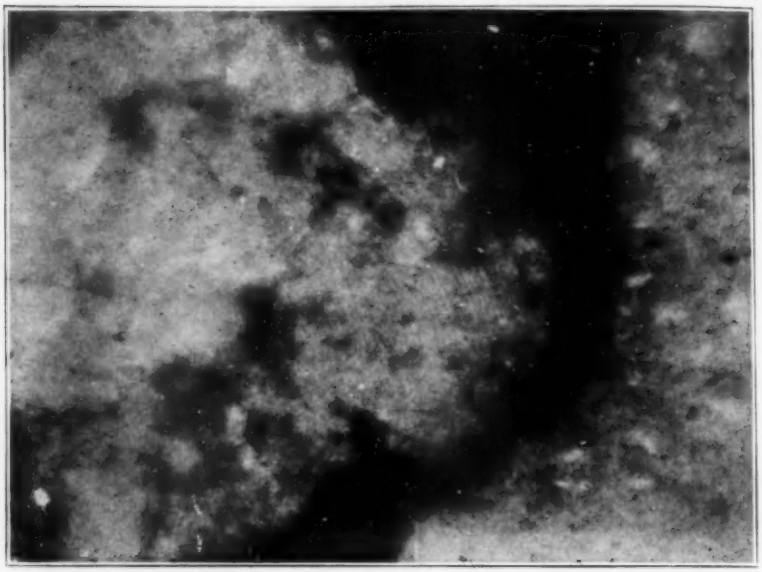

Fig. 12.—The ultramicroscopic appearance of brain tissue treated with magnesium chloride solution isotonic with 0.9 per cent sodium chloride solution.

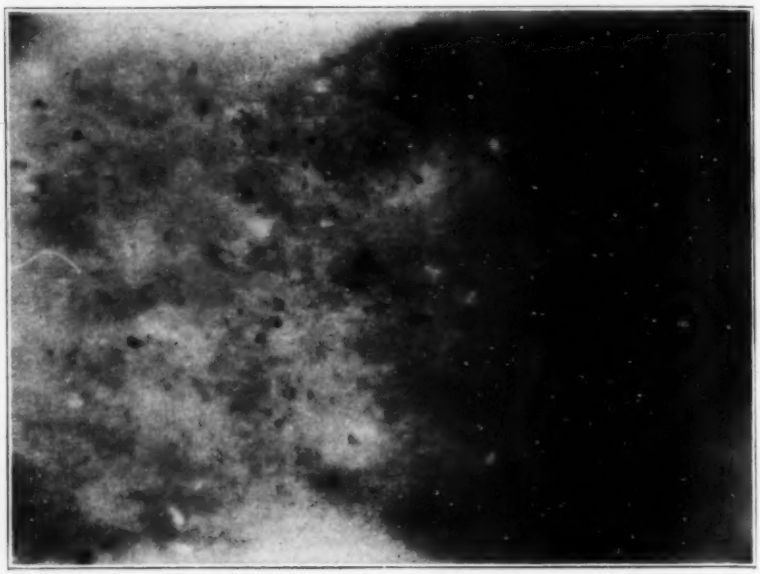

Fig. 13.—The ultramicroscopic appearance of brain tissue treated with 0.9 per cent sodium chloride solution.

those observed by Weiser and Cunningham [27] in the ultramicroscopic study of precipitated sulphur sols.

Given unknown slides of the tissue from either the anion or the cation series, it was found easy to arrange them in the proper order of swelling as between the extreme types shown in figures 9 and 10, when the degree of swelling differed by as much as about 10 per cent. Thus, for the anion series the order, according to ultramicroscopic appearance, was sulphate, acetate, chloride and iodide, and for the cation series calcium-magnesium, sodium and potassium. In making these determinations one person made up the slides for the series, and two others then inde-

Fig. 14.—The ultramicroscopic appearance of the nucleus of a brain cell from tissue treated with 0.9 per cent sodium chloride solution.

pendently arranged them in order of swelling, basing their opinions solely on differences in ultramicroscopic appearance.

Figures 11, 12 and 13 are photomicrographs showing typical preparations from the aluminum, magnesium and sodium chloride solutions of the cation series respectively. Similar fields were chosen under as nearly as possible similar conditions. The gradation of decreasing sharpness of outline and granular appearance from aluminum to sodium is apparent.

The general result is that it is possible to distinguish varying degrees of hydration of brain tissue by simple comparisons of ultramicroscopic appearance. The important possible practical application of this fact

27. Weiser and Cunningham: Colloid Symposium Monograph **6**:334, 1928.

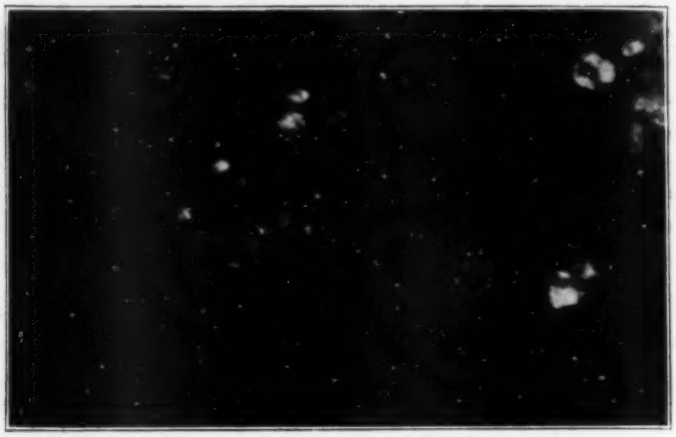

Fig. 15.—The ultramicroscopic appearance of the nucleus of a brain cell from tissue treated with distilled water (middle object).

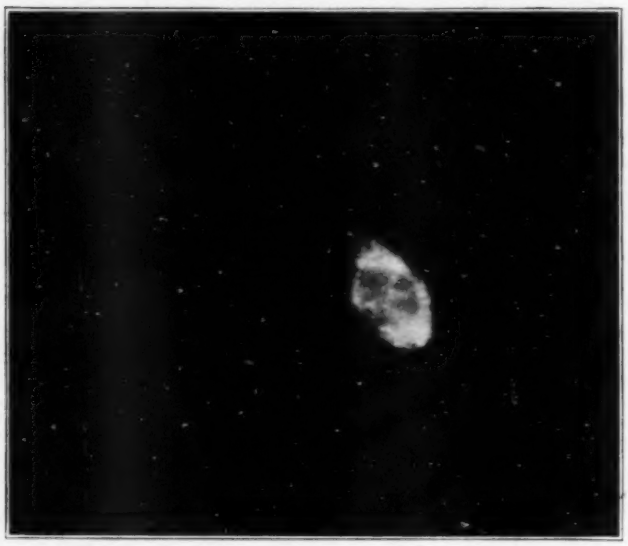

Fig. 16.—The ultramicroscopic appearance of the nucleus and a portion of the cytoplasm of a brain cell from tissue treated with eighth molar magnesium chloride solution.

would be the use of the ultramicroscope in the study of pathologic swelling conditions in fresh brain tissue.

The foregoing observations on tissue apply to the general appearance and make no attempt to describe different effects on different structural units. It should further be remembered that ions have specific effects apart from those on gross swelling.[28] Ionic antagonisms are not explicable on a simple swelling basis so far as is known at present.

Some preliminary observations have been made as to the ultramicroscopic appearance of chicken brain cells from tissue treated with different solutions and observed almost immediately. The results are by no means necessarily related to the swelling results previously discussed. Figure 14 shows a cell nucleus from tissue treated with 0.9 per cent sodium chloride. It approaches normality as to size and appearance. Figure 15 is a similar nucleus from tissue treated with distilled water; it is greatly swollen, presumably due to osmotic inflow of water. Figure 16 shows the nucleus and a portion of the cytoplasm of a cell from tissue treated with eighth molar magnesium chloride solution. The bivalent magnesium ion seems to exert some specific hardening action. It is hoped that work now in progress will serve to elucidate this type of effect.

SUMMARY

Various phases of the application of the ultramicroscope in the study of nerve tissue have been discussed and illustrated with photomicrographs.

It has been demonstrated that different degrees of hydration of brain tissue are differentiable by means of simple ultramicroscopic observation. The possible application of this fact in pathology has been pointed out.

In connection with the preparation of the materials for the observations mentioned in the preceding paragraph, the results of Hooker and Fischer and of Haldi and his co-workers on the swelling of rabbit brains in equimolar salt solutions have been extended to chicken brain and to solutions, isotonic among themselves and with 0.9 per cent sodium chloride, the p_H of which was maintained between 7 and 7.5.

Certain preliminary observations on the immediate effect of different solutions on brain cells are given in conclusion.

28. Zondek, S. G.: Die Elektrolyte; ihre Bedeutung für Physiologie, Pathologie und Therapie, Berlin, Julius Springer, 1927, p. 64.

HUMAN RABIES AND RABIES VACCINE ENCEPHALOMYELITIS

A CLINICOPATHOLOGIC STUDY *

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AND
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Soon after the Pasteur prophylactic treatment for rabies had come into general use, scattered reports were made describing paralyses of myelitic or neuritic type occurring during the treatment. Since a paralytic form of human rabies was known to exist, it was suspected that the postvaccinal paralyses were due to an atypical or modified type of rabies. However, cases were soon observed in which paralysis occurred during treatment, when it was proved either that the patient had not been bitten or that the attacking dog did not have rabies. A lively discussion arose, among the French especially, as to whether the paralysis was due to a rabbit "virus fixé" or to toxic material from the parts of the central nervous system used in the preparation of the vaccine emulsions.

In 1905, Remlinger [1] collected reports of 40 cases of paralysis among 107,712 persons treated, and in 1927 reported 529 cases among 1,164,264 treated from all over the world.[2] Thus, this complication of vaccine administration is extremely rare. He reported some important clinical data.

Nearly all the cases have occurred in adults; in two-thirds the onset of the trouble has been during the treatment, while in the remainder it was shortly after its termination. The time of onset has been from eleven to thirty days after the bite for which the treatment was given, showing that the period of incubation is shorter than that of rabies itself, which is usually from forty to sixty days.

Three clinical forms may be disinguished: 1. The acute ascending paralysis, of Landry's type, in which the onset is sudden, with fever, headache, vomiting, severe backache, insomnia and restlessness. The next day the legs are weak, and in another day paralysis of the legs and sphincters is complete, while the pain in the lower part of the back is less severe. The pain then ascends higher up the back, and the arms

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1. Remlinger, P.: Ann. de l'inst. Pasteur, October, 1905.

2. Remlinger, P.: Les accidents locaux du traitement antirabique, Ann. de l'inst. Pasteur (suppl., Conference Internationale de la Rage), 1928, p. 133.

quickly become paralyzed. This is followed by pain in the face and facial palsy. Bulbar paralysis causes death in one third of these cases, while the remaining patients recover rapidly. 2. Dorsolumbar myelitis, in which the initial febrile reaction is slight and the onset is more gradual. The legs become completely paralyzed and anesthetic, with loss of tendon reflexes, involvement of the sphincters and frequently a positive Babinski sign. Girdle pains in the thorax and lancinating pains in the arms may be severe. The upper extremities are only weakened and bulbar symptoms are absent. Recovery takes place in most of these cases in a few weeks, but infection from decubitus ulcers or ascending urinary infections may cause death in spite of the regression of the paralysis. 3. Neuritic forms, in which after a brief febrile period one or more peripheral nerves, most often the facial, become involved. The oculomotor, vagus, radial, ulnar and sciatic nerves may be affected singly or in various combinations. Rapid complete recovery is the rule.

Of 243 cases with data as to the involvement, Landry's paralysis existed in 39, paraplegia with involvement of the bladder in 68, paresis of both legs with sphincter troubles in 21 and without them in 33, and facial palsies in 58.

The pathologic histology has received little attention, but there have been only a few necropsies. In 1889, Bareggi [3] reported five cases that proved fatal within a week after Ferran's modification of Pasteur's treatment had been instituted. In all cases there were paraplegia, urinary retention and bulbar and ocular symptoms. Unfortunately, the necropsy reports mention only hyperemia of the nerve tissue. Babes and Mironesco [4] related the case of a woman, aged 40, in whom treatment was started six days after the bite of a rabid dog; on the fourteenth day of treatment paraplegia developed. Pathologic examination revealed extensive softening of the lower thoracic and lumbar cord in which gray and white matter could not be distinguished. There were "edematous tumefactions" of nerve fibers in the white matter, swelling and disappearance of axons, rarefied zones about the blood vessels with small elongated cells containing oval nuclei, and proliferated glia and connective tissue. The nerve cells were atrophied and cellular proliferations were found in the spinal ganglia. In the medulla and cerebrum the changes were less severe, and Negri bodies were not found.

In 1911, Borger [5] reported two cases from the Dutch East Indies. Four days after the bite of a dog, Pasteur treatment was begun in a man, aged 25. On the tenth day of treatment pain developed in the head and back, followed by paraplegia, urinary retention, cystitis and death

3. Bareggi: Gazz. med. ital. **48**:217, 1889; cited after Simon, G.: Centralbl. f. Bakteriol. Orig., 1913, vol. 68.

4. Babes and Mironesco: Compt. rend. Soc. de biol. **64**:964, 1908.

5. Borger: Geneesk, Tijdschr. f. Nederl. Indie, 1911; cited after Simon.

in sixteen days. The only histologic report stated that there were hyperemia and edema of the brain and cord with extensive degeneration of the spinal white matter. The inoculation of nerve tissue from this and a similar case did not produce rabies in an animal.

Koch [6] and Jochmann [7] reported the same case, that of a man in whom paraplegia developed on the twelfth day of treatment, with death from sepsis in two months. They found a marked circumscribed serous meningitis and edema of the lumbar cord segments. Softened areas were described about the blood vessels, with slight round-cell infiltrations of the whole transverse area of the cord, and with disappearance and chromatolysis of ganglion cells and degeneration of others. Similar milder changes were found in the cervical cord, while only hyperemia and slight edema of the brain were recorded. No Negri bodies were found. Jochmann believed that the mildness of the pathologic changes explains the recovery in cases in which infection does not cause death.

Fielder [8] recorded seven cases, one with necropsy, the only report with necropsy that we could find in the American literature. Animal inoculations were not made, as the brain had been fixed in formaldehyde by error, but Negri bodies were not found. No essential changes were found in the organs or brain. Because of its inaccessibility, we quote the description of the cord made by the late C. B. Dunlap.

> Sections from the three regions showed the same essential changes varying only in degree; namely, an acute stage of softening involving the fiber systems. This softening appeared first along either side of the various connective tissue septa of the posterior or lateral columns, and spread to involve parts more remote from the septa, and consequently more remote from the larger blood vessels which lie in these septa. The softenings were most extensive in the cervical segments but were quite marked in the dorsal region, where they varied in position in the different sections. They were least extensive in the lumbar segments. The softenings showed as more darkly stained areas or streaks in which the normal structures of nerve fiber and sheath had disappeared, and various types of cells and fragments of necrotic tissue were recognizable. The process in most places was too fresh to present large aggregations of plain granule cells (or "Gitter" cells of the Germans), but in most places scattered cells of this type were plainly visible, and were often loaded with fluid contents and débris. About many of the blood vessels in the softened areas were small round cells, lymphoid cells, which stained deeply; such cells might also be seen at a distance from the vessels; they seemed to be capable of enlarging and of taking up the products of the softening. Neuroglia fibers in the neighborhood of softenings were often abundant and coarse (a condition not well understood, unless explainable by swelling and heightened stainability of preexisting fibers). The Weigert stained

6. Koch, J.: Centralbl. f. Bakteriol. Orig., 1912, vol. 64.

7. Jochmann, G.: Deutsche Ztschr. f. Nervenh. **47**:267, 1913.

8. Fielder, F. S.: Paralysis During Pasteur Antirabic Treatment, J. A. M. A. **56**:1769 (June 3) 1916 (case reports and histologic descriptions in author's reprints only).

sections from the cervical cord, except for slight breaking down due to the softening, were normal. The sections stained with toluidin blue were examined for bacteria, but none were positively identified. The writer has not seen changes, such as are present in this case, explained by the presence of bacteria. The histologic conditions of acute softening suggests the action of a strongly toxic material operating over a wide area in the spinal cord, and probably but not certainly delivered by the blood stream; the location of the earliest visible changes along the course of the blood vessels is not considered proof of such delivery. In postpartum and various other conditions (infections?) similar changes in the spinal cord are sometimes found. Without any experience as to what it is possible for the virus rabies to do in causing spinal lesions, the writer would feel that this case, with its definite pathologic changes would speak rather for the introduction, through the treatment, of some toxic material in a susceptible individual, than for a modified form of rabies, especially in view of the early appearance of symptoms, thirteen days after treatment was begun, and the duration of the process, eleven days.

From Java, van Genderen[9] reported nineteen cases of paralysis in Europeans, with five deaths in from three to ten days. Although twice as many natives received Pasteur treatment, there were only two cases of paralysis among them. Altogether, 13,396 persons had been treated; the incidence of paralysis, therefore, was only 0.157 per cent. Descriptions of necropsy in three cases were not adequate.

Busson[10] reported four cases of ascending paralysis of Landry's type. The material from one patient inoculated into a rabbit resulted in the development of rabies although no Negri bodies were found. Pathologic study of the patient's spinal cord showed large macroscopic softenings in the dorsal and lumbar regions, while the cervical cord and medulla revealed active signs of inflammation. One case which Busson described is important in that the patient, a girl, aged 15, was definitely known not even to have been bitten by an animal, but rabbit inoculation from her nerve tissue resulted in the transmission of rabies. This could have been accomplished only if the virus had been introduced into the patient during the vaccine treatments. The spinal cord revealed softenings, punctate capillary hemorrhages and edema of the brain. Diffuse perivascular hemorrhages were noted in the medulla and cord, but there were only a few scattered infiltrations in the brain. Another patient had perivascular round-cell infiltrations and capillary hemorrhages along the whole length of the cord, but most marked in the lumbar region. There were severe degenerative changes in the ganglion cells. Similar changes, much less marked, were found in the brain, particularly in the basal ganglia. No Negri bodies were seen.

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9. Van den Hoven van Genderen, J.: Ztschr. f. Hyg. u. Infectionskrankh. **105**:427, 1926.

10. Busson, B.: Centralbl. f. Bakteriol., 1926, vol. 99.

The inflammatory nature of the condition was also stressed by Michailov.[11] Stuart and Krikorian [12] reported a case of paraplegia with recovery after the administration of vaccine which had been carbolized, and they found five similar examples on record. They attributed the inflammatory reaction of the cord to the action of the phenol.

We have had the opportunity of studying clinically and pathologically a case of rabies vaccine myelitis and one of human rabies with an exceptionally long incubation period. Comparison of the histopathologic picture in these two conditions and contrast with other diffuse inflammatory troubles of the central nervous system has shed some light on the pathogenesis of the vaccine paralysis.

REPORT OF CASES

CASE 1.—*Landry's type of paralysis in a patient not bitten by a dog, following inoculation with rabies vaccine, and showing perivascular mesodermal infiltrations and softenings.*

Clinical History.—The patient, a previously healthy, unmarried domestic servant, aged 48, had handled a pet dog that developed rabies. She had not been bitten, but because there was a blister on a finger from a previous burn it was thought advisable to give her the Pasteur treatment which was commenced on Sept. 7, 1928. Fourteen equal doses of 2 cc. each of the serum were given on successive days, subcutaneously in the soft tissues of the back and abdomen. Following the injections there was considerable local reaction and after a week a generalized reaction consisting of malaise and a rise of temperature to 102 F. After the thirteenth injection on September 19, she became weak in the legs and went to bed. No more injections were given. The next day, the legs were completely paralyzed and retention of urine necessitated regular catheterization. Moderate weakness of the arms gradually developed, and on September 25, slight respiratory distress became apparent, but there was no difficulty in swallowing. The temperature reached 103 F. on September 26.

Neurologic Examination.—On September 27, the patient was clear mentally. The cranial nerves were normal, except that slightly labored respiration suggested some vagus involvement. The arm movements were very weak but were possible, and the hand grip was almost powerless. The trunk muscles and all those of the lower extremities were paralyzed and flaccid. All tendon reflexes, as well as the plantar and abdominal reflexes, were absent. Sensation was normal in all phases. The respiratory distress and tympanites which had developed subsided in the next few days, but massage on October 1 was followed by delirium, a rapid pulse rate and a temperature of 103 F. At this time, râles developed over the left lung posteriorly, but there was no evidence of pulmonary consolidation. The shoulder group of muscles became stronger, and there were signs of some return of tonus in the legs. Fecal incontinence and urinary retention persisted, however, and severe cystitis developed. Redness over the sacrum was followed by the development of a large decubitus ulcer with extensive burrowing and sup-

11. Michailov, N.: Sovremennaya psichonev **5**:48, 1927; abstr. in Zentralbl. f. d. ges. Neurol. u. Psychiat. **48**:812, 1927.

12. Stuart, G., and Krikorian, K.: Neuroparalytic Accidents of Anti-Rabies Treatment, Ann. Trop. Med. **22**:327, 1928.

puration, but sensation remained normal even on the borders of the ulcer. On October 13, the temperature reached 104 F., and on October 16 it reached 105 F. The pulse rate on October 13 ranged from 90 to 110, and gradually rose to 130. The leukocyte count was 25,300 on October 18, the date of death.

Necropsy.—There were found: extensive gangrenous sacral decubitus ulcers, edema of the subcutaneous tissues over the lumbar vertebrae, hypostatic broncho-

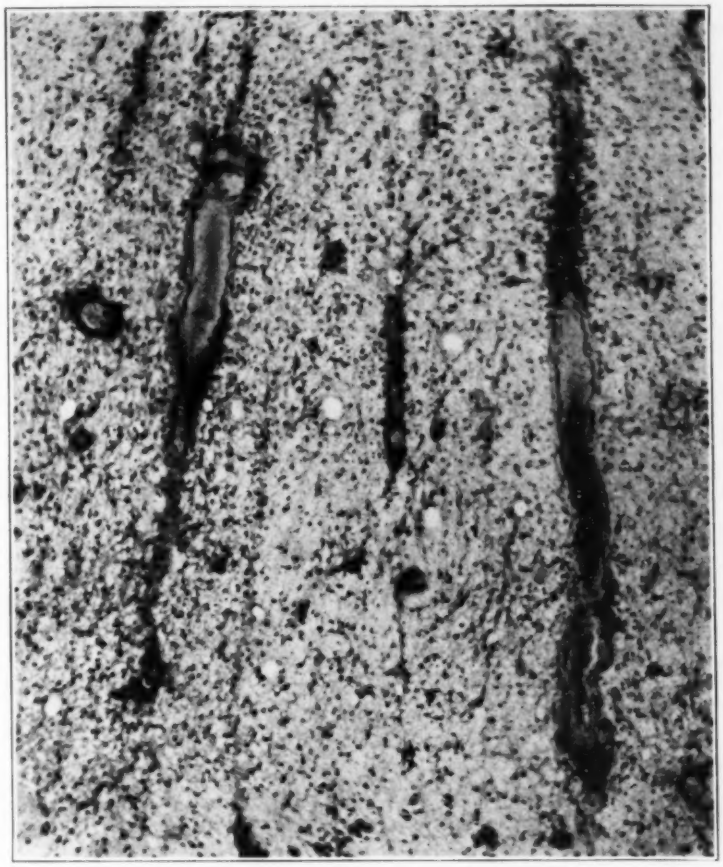


Fig. 1.—White matter of the cervical cord showing the perivascular infiltrations and the diffuse increase of glia cells. Toluidine blue stain; × 80.

pneumonia and edema of the lungs, brown atrophy of the heart, acute splenic tumor and fatty infiltration of the liver.

Microscopic Examination.—The brain and spinal cord revealed no gross abnormality except hyperemia of the pia, the vessels of which were markedly distended with whole blood. There was no thickening or infiltration, but the pia-arachnoidal cells were moderately swollen.

Changes were found diffusely throughout the spinal cord, but reached their maximum in the upper dorsal and cervical regions. The anterior horn cells, and

to lesser degree those of the posterior horn, were ballooned out to from two to three times the normal size. Chromatolysis of the Nissl substance was complete, and the darkly stained, swollen nuclei lay at the periphery of the cells. There was an increased amount of intracellular lipochrome pigment. The number of ganglion cells was definitely decreased, and many were visible only as faint shadowy outlines.

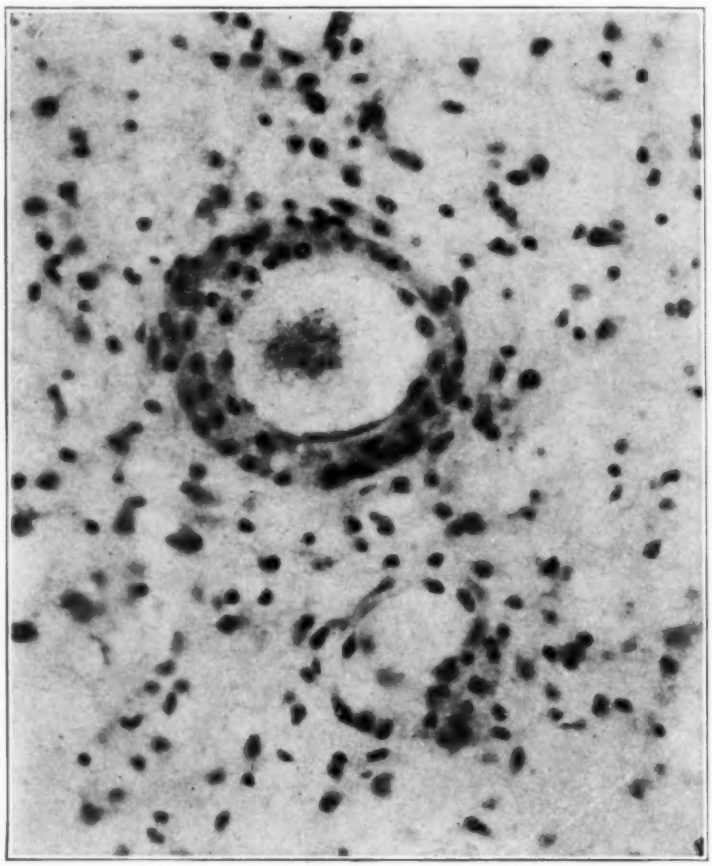


Fig. 2.—Intra-adventitial lymphocytes in an arteriole of white matter of the dorsal cord. Note the absence of lymphocytic infiltrations into the tissue. Toluidine blue stain; × 390.

On lower power examination, the smaller capillaries stood out strikingly, owing to pyknosis of the nuclei of their endothelial lining. The larger vessels and to a lesser degree the smaller radicals showed what appeared to be a perivascular infiltration (fig. 1). This varied in amount in different areas but was present around the vessels of the gray as well as the white matter, particularly about the venules. Closer examination revealed that these cells consisted mainly of proliferated adventitial cells, glia cells and lymphocytes (fig. 2). The relative predominance of glia cells and lymphocytes varied in different vessels.

With myelin sheath stains the blood vessels were clearly outlined because they were all surrounded by a small clear area containing nonstaining material in which demyelinization had become complete (fig. 3). No myelin balls or degenerative changes in the myelin sheaths were found at this time (fig. 4), but a slight impregnation could be accomplished by osmic acid which revealed dark black granules within the vessel walls. However, Scharlach r brought out the fact that the demyelinized areas contained large gitter cells with fat (figs. 5 and 6). Some fat was free in the tissue as small globules, but most of it was intracellular in the perivascular and intra-adventitial phagocyte cells.

These small areas of fatty degeneration were not found around capillaries or in areas suggestive of the blood supply of a small vessel. No large softenings

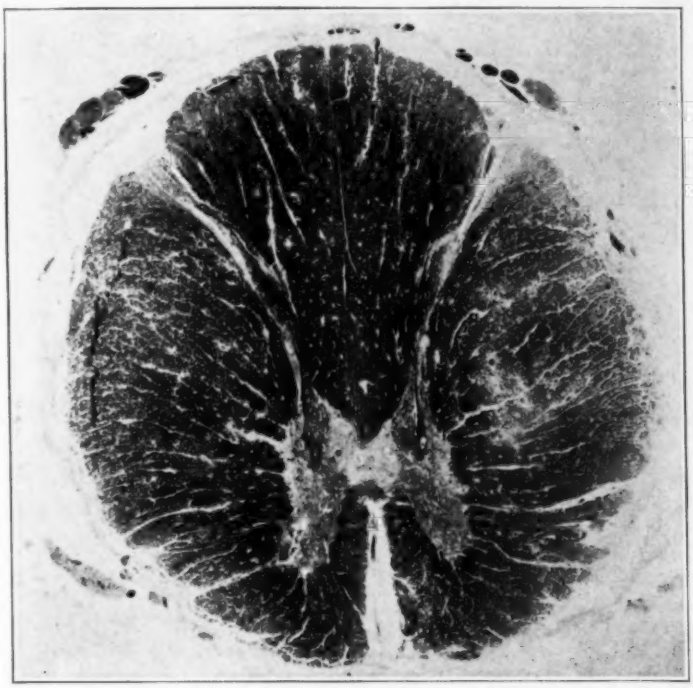


Fig. 3.—Dorsal cord. The blood vessels stand out as white streaks because of perivascular zones of demyelinization. Wright's myelin sheath stain; × 11.

were found. Rather were these changes found in a circular segment of tissue surrounding the venules and arterioles. Where the gitter cells predominated, the lymphocytes seemed to be less in quantity, whereas there was less softening in the vessels where the lymphocytic infiltration was greatest, showing that the latter was not a reaction of the mesodermal elements to the softenings.

Throughout the cord there were a large number of small, darkly stained, oval nuclei, poor in cytoplasm, with fine delicate processes arising from each pole of the cells. These were markedly accentuated in the areas bordering on the perivascular softenings (fig. 7). With silver methods these were seen to be Hortega cells, or microglia, which were diffusely proliferated, especially near the degen-

erated areas. From them typical transitions to the fat-containing gitter cells could be followed (figs. 8 and 9). The nuclei swelled and became more rounded, the cytoplasm swelled, the processes shortened and thickened, and a reticulum appeared within the protoplasm. Finally the nucleus became eccentric, and the cell was filled with lipoid. These changes were frequently and easily seen.

Bielschowsky impregnation revealed swelling and tortuosity of the axons in the demyelinized areas and often fragmentation into an argentophilic débris (fig. 10).

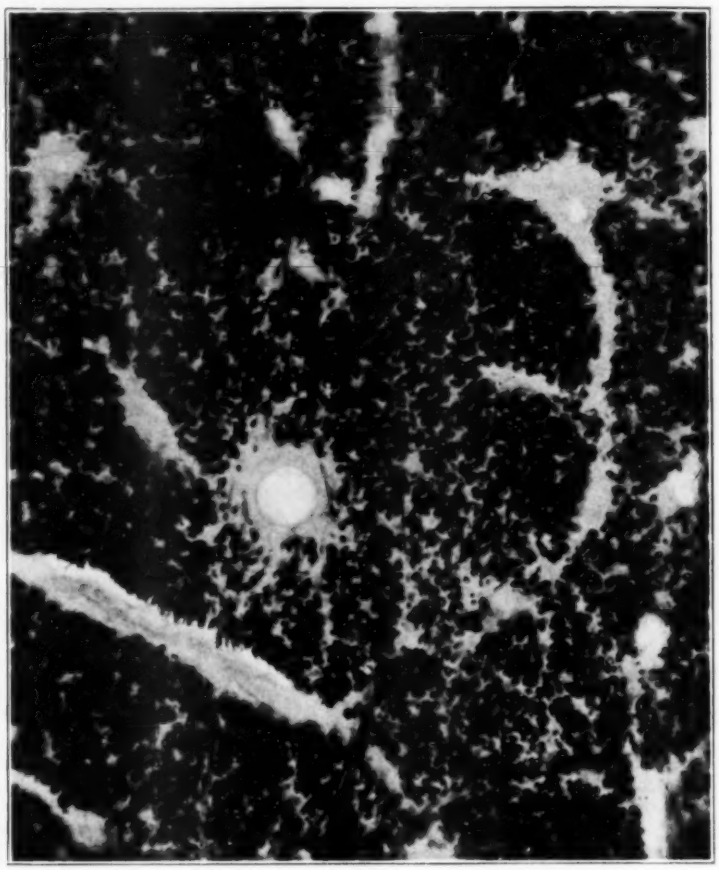


Fig. 4.—White matter of cord. The blood vessels are surrounded by a small zone of completely demyelinized tissue. Wright's stain for myelin sheaths; × 150.

The most complete axonal disintegration was found in the areas adjacent to the vessel walls.

In the brain, careful examination failed to reveal Negri bodies either on smear or in embedded tissue. The ganglion cells were markedly swollen and were associated with an increase of the satellite glia, but revealed no marked regressive changes. The substantia nigra was normal. The cortical architectonic structure was undisturbed. The capillaries were abnormal in that there was a mild swelling

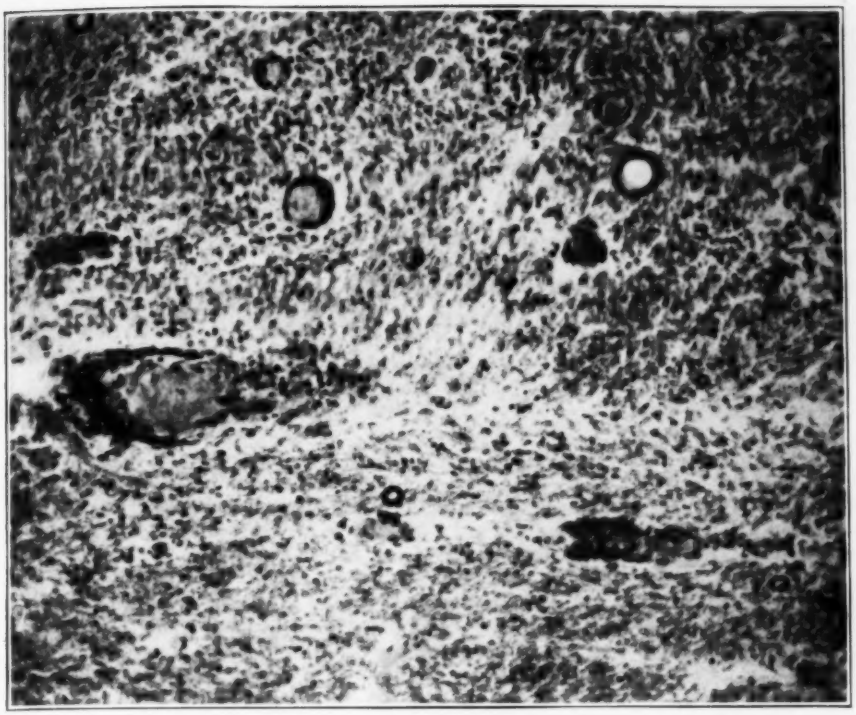


Fig. 5.—Perivascular softenings containing fat-filled gitter cells. Scharlach r stain; × 150.

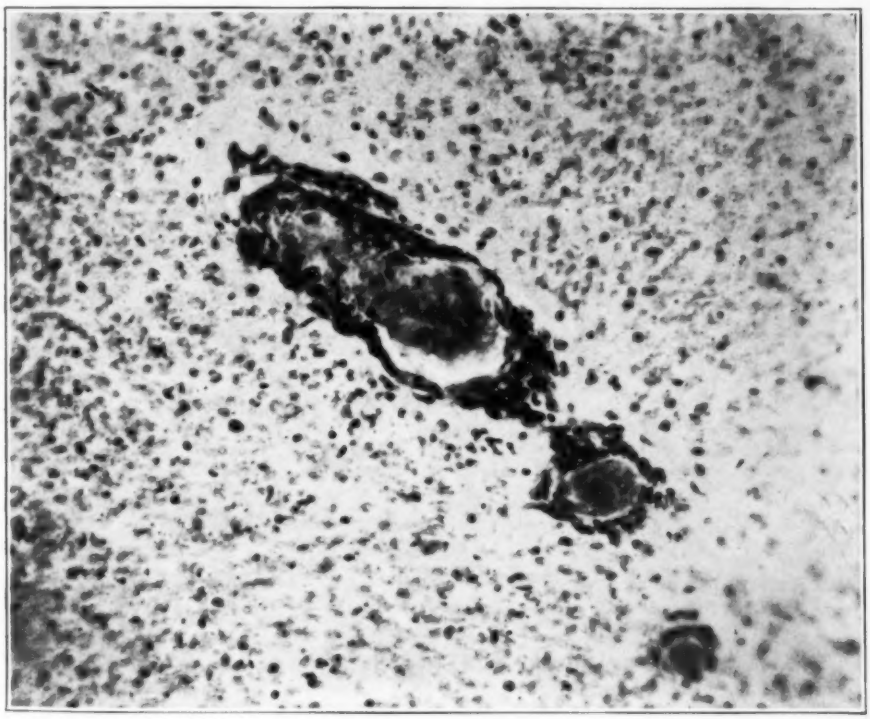


Fig. 6.—The perivascular rarefied zones filled with free and intracellular fat. Many gitter cells in the vessel walls. Scharlach r stain; × 240.

of endothelial cells with a moderate increase in their quantity, at times leading to a capillary obliteration. But no infiltrate or areas of softening, except for a small area adjacent to the fasciculus solitarius in the medulla, were found.

In all the cortical layers, and especially in the cerebral white matter, and throughout the nervous system, there was a marked proliferation of oligodendroglia. These cells had all undergone the typical regressive change called acute swelling. Their processes had disappeared, the nuclei are pyknotic and the cyto-

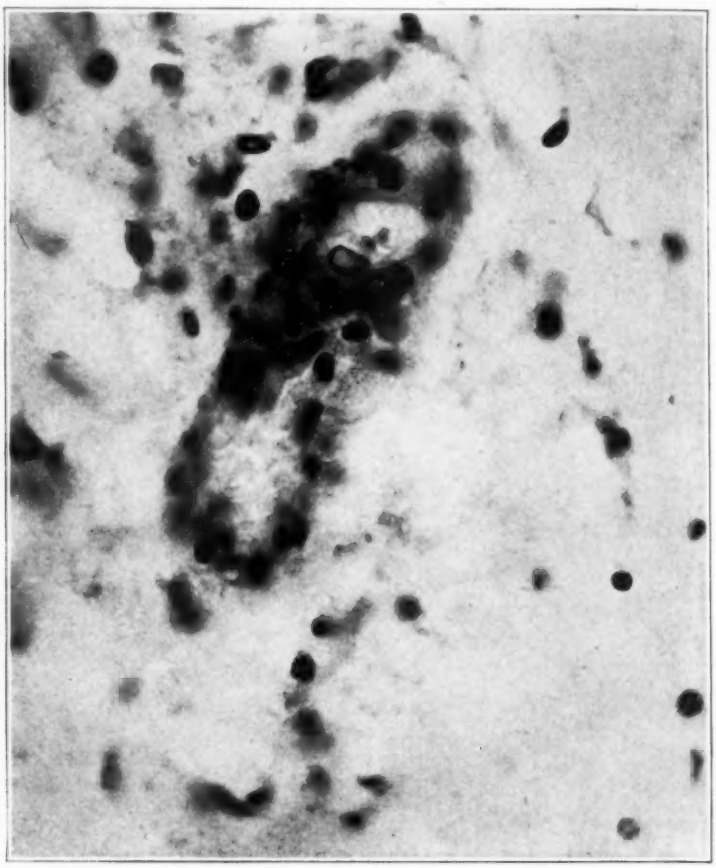


Fig. 7.—Microglia in the softened perivascular tissue in transition to gitter cells. Toluidine blue; × 700.

plasm in the ordinary stains was distended by a nonstainable substance. However, by the use of mucicarmine in either frozen, alcohol or formaldehyde fixed material the clear cytoplasm stained either a faint or a prominent pinkish red (fig. 11). This stainable material was either only perinuclear or filled the entire cell. However, many of the cells still had a clear cytoplasm. The oligodendroglia tended to gather in clumps, and small tissue spaces or holes were seen which were identical in size and shape with the visible cells. From them the nuclei and mucin had completely dropped out.

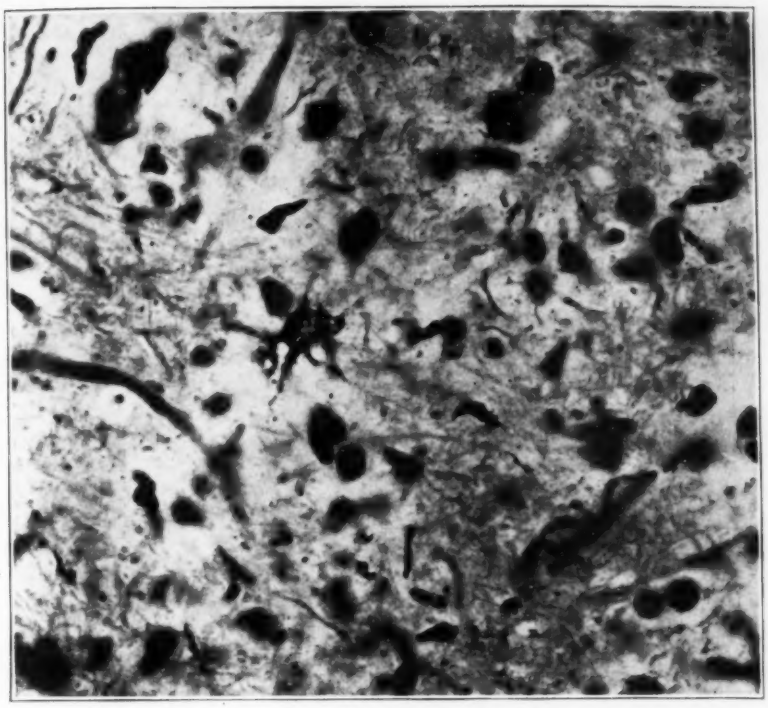


Fig. 8.—A microglia cell in a transition to a gitter cell. The cytoplasm is swollen; the processes are shortened and thickened. Microglia nuclei are abundant. Penfield's modification of Hortega's silver carbonate; × 600.

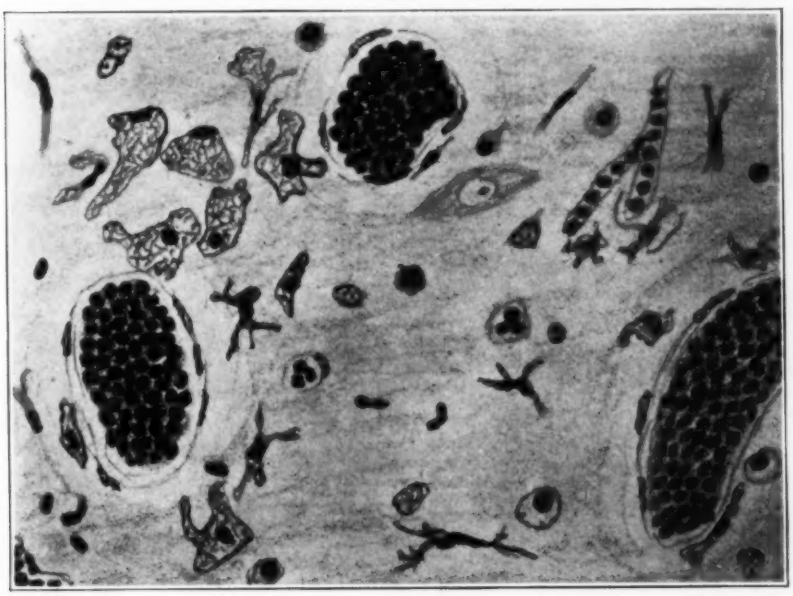


Fig. 9.—Drawing illustrating the transition from microglia cells to fat-containing gitter cells in the spinal cord. Hortega's silver carbonate method; × 800.

There were clumps of mucin-like material free in the tissue, particularly near blood vessels. These assumed a grapelike structure. Within them, mucin-filled oligodendroglia cells could be seen. Some of the material was visible in the adventitial walls of the vessels. This free mucin apparently resulted from the conglomeration of material set free from the degeneration of mucin-bearing oligodendroglia cells. They had no relation to the cord softenings or to any degeneration of ganglion cells, myelin sheaths or axons.

Fig. 10.—Destruction of axis cylinders around vessels. Bielschowsky stain; × 390.

CASE 2.—*Typical clinical syndrome of rabies, one year after a dog bite, beginning two weeks after a trauma to the bitten hand; acute encephalomyelitis with Negri bodies found in the ganglion cells.*

Clinical History.—A man, aged 53, except for the habitual use of alcohol was in good health and worked steadily as a foreman. On or within a day or two of April 8, 1928, while attempting to give a sick dog castor oil he was bitten in the right hand. This dog was known to have come in contact with another dog which

later was pronounced rabic but which in the meantime had been killed and buried. The patient's wound was immediately treated with iodine, but no Pasteur treatment was given. He was in perfect health, but on March 15, 1929, the right hand was injured when a trunk fell on it.

In the forenoon of March 26, the patient felt chilly, but worked the next day and had some teeth extracted in the afternoon. He slept poorly the following night, and on March 28 had difficulty in swallowing either solids or liquids. He

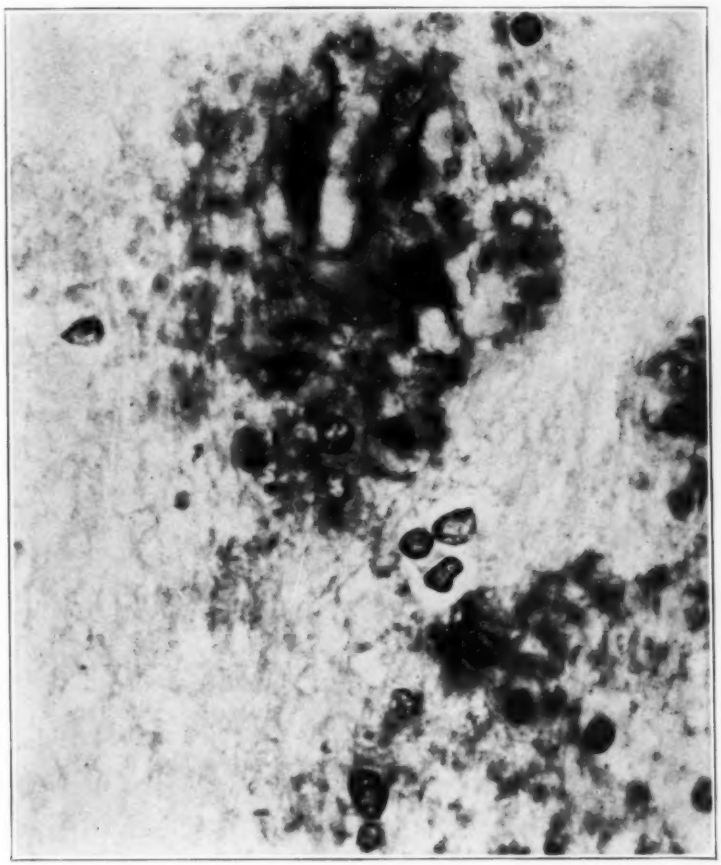


Fig. 11.—Oligodendroglia filled with a stainable substance which is also present around the vessel wall. A clump of three oligodendroglia cells can be seen fusing. Note the mucin free in the tissue of the same shape as the cells. Mucicarmine; × 800.

became more restless and excited and entered the Presbyterian Hospital on March 29. During the night he became more and more restless and salivated. Being unable to swallow the saliva, he constantly expectorated and could not sleep in spite of a hypodermic injection of morphine. He continued restless until 7 a. m., when he became cyanotic, cold and pulseless with shallow irregular respirations, but he was revived by the administration of digifolin. Profuse salivation con-

tinued and the temperature rose to 104.4 F. rectally, the pulse rate to 144 and respiration to 44. On March 30, lumbar puncture yielded clear fluid under a pressure of 80 mm. of water and giving negative Wassermann and Ross-Jones reactions; the cell count was only 5; the Lange curve was normal; the total sugar was 78.1 mg. and the total protein 14.9 mg. per hundred cubic centimeters.

Examination.—Study was difficult because of the extreme restlessness of the patient. There were no ocular or other cranial nerve palsies. There were scars

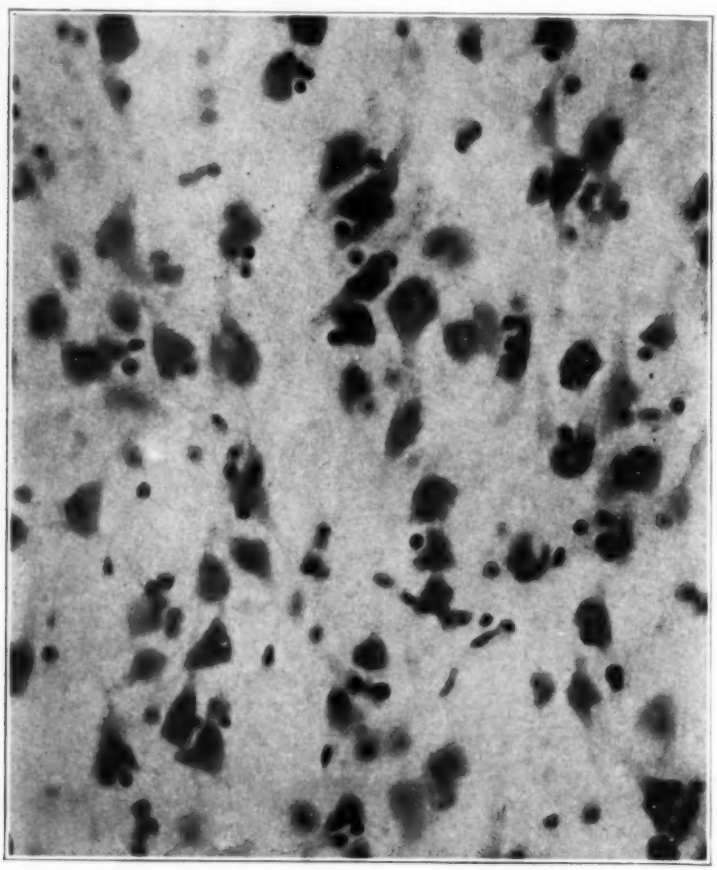


Fig. 12.—Prefrontal cortex, showing the degenerative changes in the ganglion cells and the marked proliferation of satellitic oligodendroglia cells which are acutely swollen. Toluidine blue stain; × 390.

and recent abrasions on the right hand. The mucous membrane of the mouth was dry and beefy red. There was tremor and moderate ataxia of the hands. No tendon reflexes were obtained. The extreme alertness, restlessness and anxious expression of the patient naturally suggested rabies to medical attendants who had seen patients with that disease. The temperature rose to 105.8 F., and the patient died on March 30, four days after the onset of symptoms.

Necropsy.—The pial blood vessels were moderately engorged with blood, but no exudate was present. The cut surfaces of the brain revealed an intense hyperemia of the cortex. The small blood vessels of the white matter were dilated, and about them, especially in the pons, medulla and basal nuclei, were small petechial hemorrhages. There were no areas of softening. The spinal cord was normal grossly.

Microscopic Examination.—The leptomeninges were normal, except about the pons and medulla, where there was a slight thickening with newly formed fibroblasts and only a few lymphocytes scattered in their meshes.

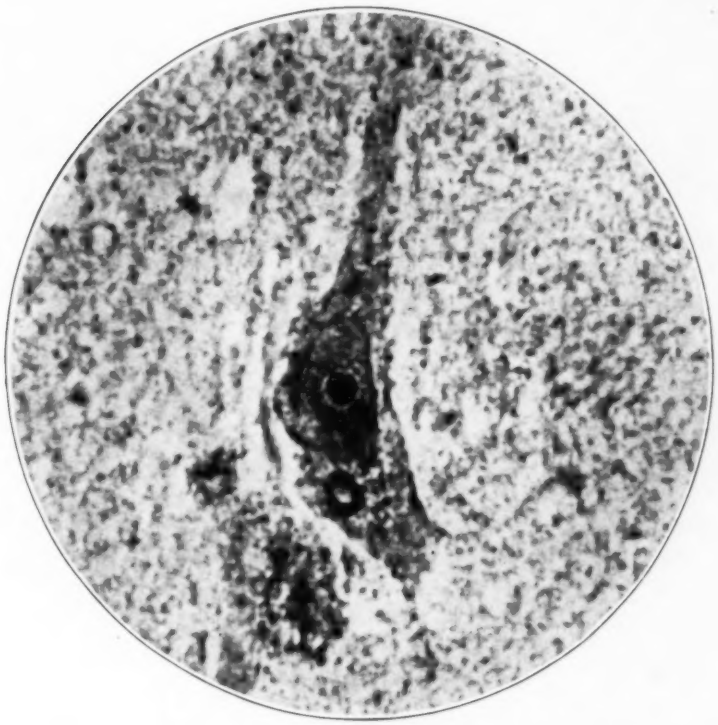
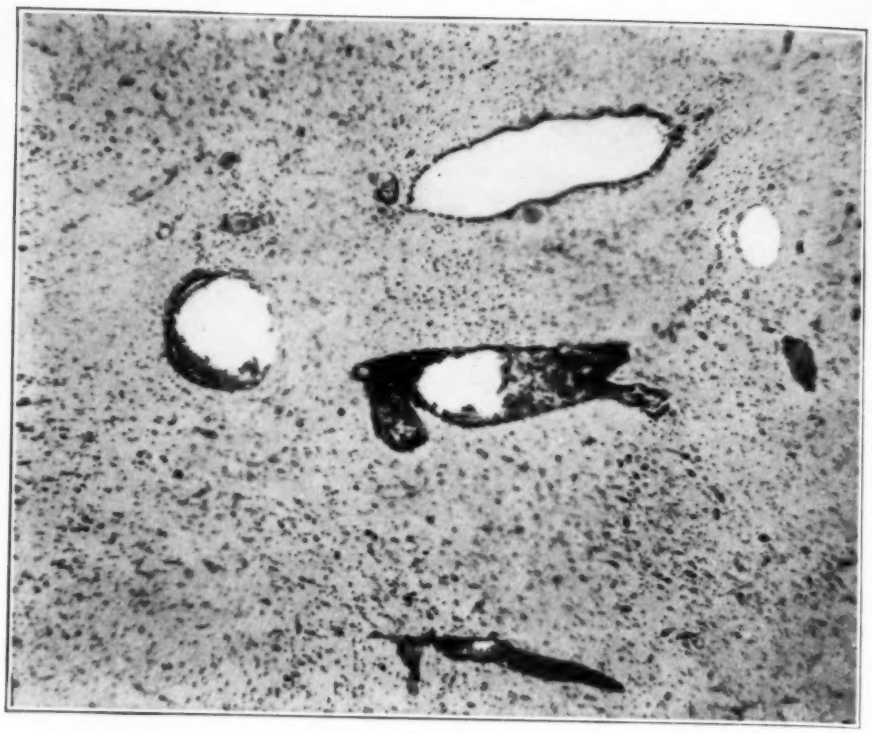


Fig. 13.—Ganglion cell inclusion body (Negri body). Methylene blue-eosin stain.

The spinal cord showed no areas of softening or demyelinization, and the axons impregnated normally. No fat was demonstrable, either free in the tissue or in the perivascular spaces. The ganglion cells of the gray matter throughout the cord were markedly swollen, with eccentrically placed pyknotic nuclei and marked central chromatolysis, but beyond this they revealed no regressive changes. The capillary endothelium contained swollen cells with pyknotic nuclei, but no proliferation could be found. There were only a few lymphocytes in the walls of the larger vessels, and in only one section of the upper cervical cord was an arteriole in the posterior horn surrounded by a fair-sized cuff of lymphocytes. There was a diffuse increase of oligodendroglia throughout the white matter of the cord.



14. Perivascular lymphocytic infiltration in the medulla. Toluidine blue stain; × 70.

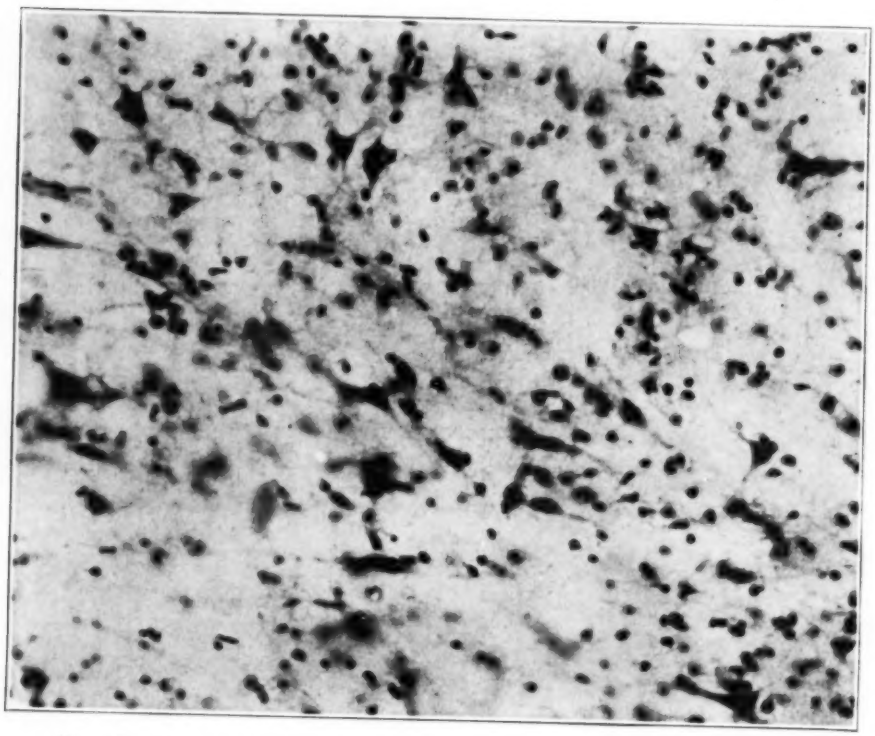


Fig. 15.—Marked degeneration of ganglion cells in the medulla, with profuse glia proliferation. Toluidine blue stain; × 275.

The architectonic structure of the cerebral cortex was everywhere obscured by the marked increase in oligodendroglia cells (fig. 12). These assumed a satellite position about the ganglion cells. Practically no normal nerve cells could be found. All were greatly swollen and showed extensive Nissl body chromatolysis. More severe regressive changes were evidenced by multiple cytoplasmic vacuoles, complete fading of the cell outlines and distintegration of the nuclei. There were many shadows of degenerating cells within a cluster of microglia cells.

Negri bodies were demonstrable with ease in the ganglion cells of the cornu ammonis and adjacent temporal lobe by means of the methylene blue (methylthionine chloride, U. S. P.) eosin technic in paraffin sections (fig. 13). These

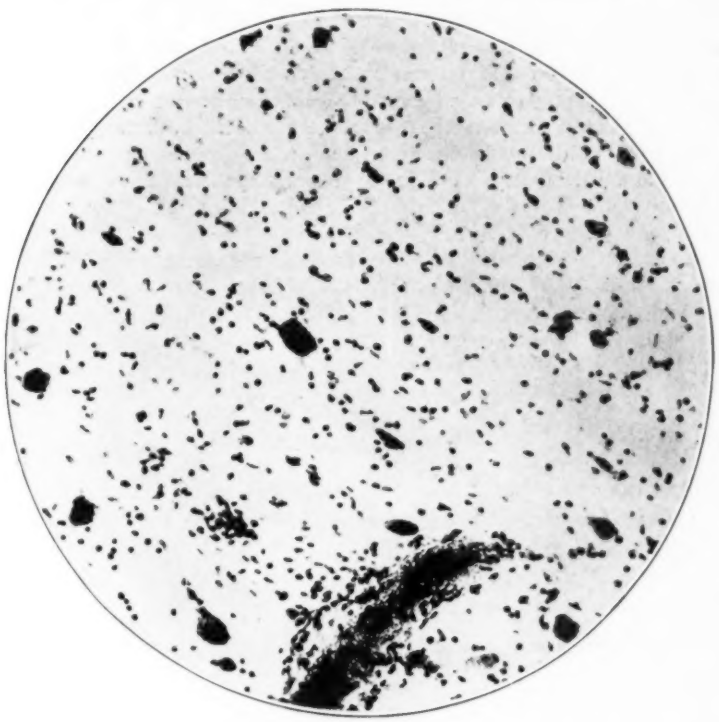


Fig. 16.—A typical Babes nodule in the medulla which consists merely of a cluster of microglia cells. Toluidine blue stain; × 150.

bodies were spherical or oval and were found singly, or less frequently doubly, in the cytoplasm toward the periphery of the cell. They took a dark red stain, and no blue granules could be discerned within them. It is important to note that from the appearance of the ganglion cell containing the Negri bodies no more degenerative changes were associated with their presence than in other ganglion cells.

The cortical capillaries were lined by swollen endothelium containing fat granules. In the vessel walls only a few lymphocytes could be found. In the white matter three was a huge proliferation of the small oligodendroglia cells the round, darkly stained nuclei of which were so abundant, especially streaming along the vessels, as to resemble closely an infiltration. Most of these cells had

pyknotic nuclei, and their cytoplasm was distinctly swollen. Mucicarmine revealed that the swelling of many of these cells was due to a mucin-like material. However, no free mucin could be demonstrated in the issue.

The most severe pathologic process existed, however, in the medulla, with imperceptible merging to a lesser degree into the pons and the basal nuclei. The tegmentum of the pons was more badly damaged than the base, while the striatum was rather mildly involved.

The blood vessels were all widely distended with whole blood, and from some a slight amount of recent extravasation could be seen. The vessels were surrounded by lymphocytes which formed a cuff several times the thickness of the vessel wall (fig. 14). There were very few leukocytes and only an occasional plasma cell in the infiltrate, which was not sharply delimited to the perivascular spaces, as lymphocytes were found free in the tissue but only near the blood vessels. The ganglion cells was all seriously damaged. Many were completely disintegrated, and phagocytosis by surrounding glia had occurred frequently.

The glia elements were markedly increased in number, particularly the oligodendroglia, of which most were acutely swollen. Clusters of cells, which corresponded to the Babes nodules at one time considered specific to rabies, were seen to be only small clumps of microglia (fig. 16). These cells are also diffusely increased, but gitter cells and fat-containing cells were absent.

The substantia nigra was involved, as were all parts of the brain, but the vessels in that region contained no cuffs of lymphocytes, and the cells themselves showed no unusual degenerative changes. This differs decidedly from the picture in epidemic encephalitis in which the vessels of that region are usually markedly infiltrated by lymphocytes, the substantia nigra cells severely degenerated and their pigment granules phagocytosed by microglia.

COMMENT

In the case of rabies vaccine encephalomyelitis (case 1), the important pathologic changes predominated in the spinal cord, where both gray and white matter suffered in equal intensity, especially in the cervicodorsal segments. The noteworthy changes within the cord were definitely related to the perivascular regions and consisted in demyelinization and, to a lesser degree, axis cylinder destruction with "Abbau" attempts by microglia. The liberated simple fats were found free in the tissue and intracellularly in gitter cells and in the fixed vessel wall cells. What appeared as an intensive perivascular lymphocytic infiltration was a relatively mild reaction, most marked in the intra-adventitial spaces of blood vessels surrounded by the smallest softenings. Therefore these lymphocytes were probably not present in response to the liberation of tissue enzymes as a result of the destructive process, but were probably indicative of the inflammatory nature of the trouble.

Most of the perivascular cells were concerned in the Abbau of the destroyed myelin. They were distinctly formed from the microglia cells which were diffusely increased throughout the cord but more particularly in the perivascular regions. The usual transitional stages from the microglia to the gitter cells were seen and described. They differed in no way from those found in the brain. Thus has been overcome

the recent objection of Hassin to the conception of the origin of gitter cells from microglia, which he advanced because microglia have not been demonstrated in pathologic processes within the spinal cord. Our own personal experience has also shown that it is extremely difficult to demonstrate these transitions due to the technical difficulties peculiar to the cord. Microglia transitions have hitherto not been pictured in the cord, but we believe that they are undoubtedly present in abundance as in our case.

In the case in which rabies vaccine was given, another type of change was found diffusely throughout the brain and cord. This was a rather moderate swelling of the ganglion cells, swelling, pyknosis and fatty change in the capillary endothelium and proliferation, acute swelling and mucinoid changes in the oligodendroglia. These changes in the brain were identical with those previously reported in acute toxic encephalitis secondary to various acute infections.[13] The febrile state, the acute generalized reaction caused by the vaccine and the cord condition produced by it, and the terminal pulmonary infection may all have played a rôle in these primarily toxic changes. They give an excellent contrast to essential pathologic process in the cord.

A toxic reaction of the brain and presumably a toxic myelitis act by damage to the capillary endothelium and probably somewhat on the ganglion cells directly. The secondary damage, however, as Winkelman and Eckel [14] demonstrated, results from the toxic reaction of the endothelium progressing to obliteration of many of the capillaries an obliterating endarteritis, and leads to the formation of small foci of softening and atrophy. These are, however, definitely related to the capillary blood supply. However, in case 1 the softenings were in immediate proximity to the venule and arteriole walls, none of which were occluded, and therefore were not caused by a shutting off of the blood supply.

Therefore, the theory that the vaccine encephalomyelitis is due to toxic products within the vaccine, perhaps from the nerve tissue of the rabbit, is not probable. Turnbull and McIntosh [15] and Perdrau [16] showed that similar perivascular areas of demyelinizations and softenings occur in cowpox encephalitis, and Wilson and Ford [17] found them in variola.

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13. Grinker, R. R., and Stone, T. T.: Acute Toxic Encephalitis in Childhood, Arch. Neurol. & Psychiat. **20**:244 (Aug.) 1928.

14. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929.

15. Turnbull, H., and McIntosh, J.: Encephalo-Myelitis Following Vaccination, Brit. J. Exper. Path. **7**:181, 1926.

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

17. Wilson, R. E., and Ford, F. R.: The Nervous Complications of Variola, Vaccinia and Varicella, Bull. Johns Hopkins Hosp. **40**:337, 1927.

In all three conditions there is probably a virus etiology, and in variola no vaccine can be held responsible for lesion. It is remarkable to notice the almost exact identity of the lesions found in cowpox and rabies vaccine encephalomyelitis. Perdrau also compared multiple sclerosis with these conditions and found the perivascular infiltrations and demyelinizations common features. The similarity in the pathologic process does not mean an identity of the causative agents since the pathologic reaction of the central nervous system is rather stereotyped. For example, the close resemblance of Heine-Medin's disease, rabies and epidemic encephalitis pathologically does not mean that the causative virus is the same in all three.

The extensive proliferation and swelling of the oligodendroglia is a common observation in numerous conditions. In fact, this process occurs in so-called "normal" brains as an agonal change or when death is preceded by hyperpyrexia. The frequency of this regressive change associated with loss of processes, nuclear pyknosis and swelling of the cytoplasm is striking. No other regressive changes had been noted in the oligodendroglia. Their transformation into gitter cells containing actively phagocytosed fat, argued for by Ferraro,[18] probably represents only an infrequent degenerative form of the oligodendroglia themselves. Tumors composed of these cells were reported by Bailey and Bucy,[19] but no other progressive form is known. Their function is unknown, although the suggestion advanced by Bailey that they may give rise to astrocytes is worthy of note. Thus, there can be no clue as to the mechanism of the formation of mucin in the swollen oligodendroglia from a consideration of the normal function of the cell. At present it may be stated that mucin [20] arises from no degeneration of the myelin sheath or the axis cylinder of the ganglion cell, as Ferraro [21] thought, but from a change in the swollen oligodendroglia itself. This accumulated mucin is later set free in the tissue by the degeneration of the cells containing it, whence it moves toward the blood vessels.

Case 2 was clinically a classic case of rabies with an excessively long incubation period. The recent trauma to the hand, which was bitten by a dog one year before, probably set free the virus encapsulated

18. Ferraro, A., and Davidoff, L. M.: The Reaction of the Oligodendroglia to Injury of the Brain, Arch. Path. **6**:1030 (Dec.) 1928.

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

20. Grinker, R. R., and Stevens, E.: Mucoid Degeneration of Oligodendroglia and the Formation of Free Mucin in the Brain, Arch. Path. **8**:171 (Aug.) 1929.

21. Ferraro, A.: Acute Swelling of the Oligodendroglia and Grapelike Areas of Disintegration, Arch. Neurol. & Psychiat. **20**:1065 (Nov.) 1928.

latently in the tissues of the hand, for death occurred within two weeks. Incubation periods as long as three years, have been reported, according to Spatz, although Schaffer doubted that these cases are authentic.

The site of the bite usually determines the site of the most marked central lesions. Thus, myelitis must frequently result from a bite on the leg. Correspondingly, our case showed a most marked medullary lesion, tapering off into the cervical cord and pons. The essential pathologic process was that of typical nonsuppurative encephalitis, similar to that found in the epidemic (lethargic) type and differing in location only. There was a tremendous perivascular round cell infiltration extending free in the tissue, a marked proliferative stimulus to oligodendroglia and microglia, and there was severe ganglion cell degeneration without softening.

The ganglion cell change was not limited to the seat of mesodermal infiltration but extended throughout the cortex, thus confirming Schaffer's [22] idea of the dissociation of degenerative and inflammatory change in rabies. Negri bodies were found. They were not present in ganglion cells showing any sign of excessive degenerative change. No clue as to their origin was found, but there was no evidence that they came from a nuclear degeneration. Negri bodies in cases in human beings are relatively rare.

Schurki and Spatz [23] attempted to correlate the pathologic process of the so-called "ganglion cell inclusion diseases," and especially relate the association of rabies with epidemic encephalitis, in their common attack on the substantia nigra. It is definite, in this one case at least, that the substantia nigra was only mildly involved as compared with the illustrated example of epidemic encephalitis.

The so-called typical Babes nodules of rabies are only focal collections of microglia concerned in the phagocytosis of ganglion cells which can be definitely discerned in their midst.

Comparing the pathologic process in these two cases, the rabies and the rabies vaccine lesions, the common denominator seems to be the signs of inflammation, varying in severity and in acuteness. Yet when the rabies is less virulent and partially under control, by perhaps insufficient vaccine prophylaxis, perivascular softenings also occur, the so-called paralytic rabies. Thus, since the rabies vaccine and cowpox vaccine both resemble a nonvaccinal encephalomyelitis found in variola, measles and other virus diseases, it seems likely that we are dealing with an inflammatory disease caused by an attenuated virus.

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22. Schaffer, K.: Lyssa, in Lewandowsky: Handbuch der Neurologie, Berlin, Julius Springer, 1912, vol. 3, p. 980.

23. Schukri, J., and Spatz, H.: Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:627, 1925.

SUMMARY

1. A case of rabies vaccine encephalomyelitis is described revealing perivascular round-cell infiltrations with demyelinization and axis cylinder destruction. A typical toxic reaction was found in ganglion cells, vascular endothelium and oligodendroglia.

2. The Abbau of destroyed myelin sheaths in the spinal cord was accomplished by proliferated microglia which could be demonstrated in transitional stages to the typical gitter cell.

3. Mucocytes, or mucin-containing, regressively changed oligodendroglia cells, were found; free mucin that was present in the tissue resulted from a degeneration of the mucin-containing cells.

4. A typical case of human rabies, with the presence of ganglion cell inclusion bodies (Negri bodies), after an incubation period of almost a year, was stimulated to activity by trauma to the bitten hand two weeks before death.

5. The site of predilection for the rabies infiltration was the medulla, tapering mildly into the pons and cervical cord, although degenerative changes were found diffusely throughout the central nervous system. The substantia nigra was in no way affected as in epidemic encephalitis.

6. The differences between the pathologic process in rabies vaccine lesions and in toxic encephalomyelitis are discussed. The evidences of inflammation, the identity of rabies vaccine, cowpox vaccine, variola and measles, nervous lesions, and the perivascular softenings in subacute rabies suggest that the vaccinal lesions represent an attenuated rabies virus disease transmitted by the vaccine.

THE BRAIN IN BACTERIAL ENDOCARDITIS*

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While neurology is a separate and distinct specialty, one is at times prone to forget that the brain is not an isolated organ but takes part in the pathologic processes to which the rest of the body is subject. On the other hand, internists should keep in mind that in many of the so-called medical diseases there are changes in the brain that are capable of modifying or intensifying the clinical picture. Every one knows the susceptibility of the brain to syphilis and to tuberculosis, and its involvement at times in cancer, but one may forget that in generalized infections the brain may suffer intense damage which may entirely overshadow the clinical picture. Because of our continued interest in these general infections, our attention has been focused on the pathologic changes in the brain in cases of endocarditis that have come to autopsy within the last few years.

REVIEW OF THE LITERATURE

That the brain may suffer damage in disease of the endocardium has long been known, but the older investigators confined their observations mainly to gross changes. It has been only since the World War that any concerted effort has been put forward to investigate this problem in its entirety. So little has been written in the English literature that a review of this kind is deemed timely.

According to Osler,[1] endocarditis has been recognized since the sixteenth century; yet its relation to changes in the brain was not known fully until investigations made at a much later time. The chief complications of endocarditis stressed in the older literature are emboli with their varying symptomatology, dependent on the place of lodgment and the formation of so-called mycotic or embolic aneurysms.

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* From the Graduate School of Medicine of the University of Pennsylvania and the Wards and Laboratory of the Philadelphia General Hospital.

* Read by title before the American Neurological Association at Atlantic City, May 29, 1929.

1. Osler, W., and McCrae, T.: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4, pp. 458, 484.

Among the pioneers to stress the relationship between infection and aneurysm was Church,[2] who in 1870 reported a series of thirteen cases of aneurysm, eleven of which involved the cerebral vessels; all occurred in persons under the age of 20. Ponfick[3] gave careful thought to the embolic formation of aneurysms and held that emboli from the valves of the heart could produce aneurysms by mechanical disturbance of the vessel walls, resulting in calcium deposits and weakening of the wall. Eppinger[4] believed that such a relationship existed. Since then, many papers have appeared on this subject, among them being those of Uebel,[5] Schottmüller,[6] Wickern,[7] Pol,[8] Lubarsch,[9] Lemke,[10] Siegmund,[11] Stern,[12] Shore[13] and Esser.[14]

Schottmüller gave the first good review of the aneurysms resulting from infective emboli. Wickern, after careful study, was not certain as to the absolute relationship between infective emboli and aneurysms. Lubarsch, in a study of 137 cerebral aneurysms, found 5 instances (3.7 per cent) associated with endocarditis. Siegmund (1925) reported in his series of cerebral aneurysms that 20 per cent had occurred in cases with endocarditis lenta. Stern likewise stressed the relationship between infective emboli and aneurysms. Short (1924), in a careful research into the causes of aneurysms, stated that only about 1 per cent of autopsies showed aneurysms of a cerebral vessel. In discussing the causes, he stated that syphilis plays but a small part and that arteriosclerosis plays the dominant rôle. He thought that congenital weakness of the vessel wall and infective emboli from endocarditis or other

2. Church, W. S.: St. Bartholomew's Hosp. Rep. **6**:99, 1870.

3. Ponfick: Virchows Arch. f. path. Anat., 1873, vol. 58.

4. Eppinger, H.: Ueber die Pathogenese der Aneurysmen, Deutsches Arch. f. klin. Chir. **35**:563, 1887.

5. Uebel: Ueber Aneurysmen des Gehirnarterien, Inaug. Diss., Jena, 1896.

6. Schottmüller, H.: Endocarditis lenta, München. med. Wchnschr. **47**:617, 1910.

7. Wickern, H.: Zur Diagnose perforierender Aneurysmen der Hirnarterien, München. med. Wchnschr. **58**:2724, 1911.

8. Pol: Embolisches infectiöses Aneurysma des Arteria Cerebri posterior dextra bei "Endocarditis lenta," München. med. Wchnschr. **69**:417, 1922.

9. Lubarsch, Otto: Einiges zur pathologischen Anatomie und Histologie der Endocarditis lenta, Virchows Arch. f. path. Anat. **246**:323, 1923.

10. Lemke, R.: Arterienveränderungen bei Infectionserkrankungen, Virchows Arch. f. path. Anat. **242** and **243**:52, 1923.

11. Siegmund, H.: Pathology of Chronic Streptococcus Sepsis, München. med. Wchnschr. **72**:639, 1925.

12. Stern, R.: Arterielle Aneurysmen bei Endocarditis lenta, Klin. Wchnschr. **5**:104 (June) 1926.

13. Shore, R. A.: Intracranial Aneurysms, Arch. Path. **6**:181 (Aug.) 1928.

14. Esser, A.: Ueber Hirnarterienaneurysmen, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:208, 1928.

origins play but a small rôle. Esser (1928) reviewed the entire subject carefully and added eleven cases of cerebral aneurysm of his own, among which only one was associated with endocarditis; a second was probably the result of a prostatic abscess rather than from the mild endocarditis associated with that condition. He proposed the theory that if an aneurysm is due to an infection or embolus, it is the result of a panarteritis and not of a weakening of the vessel wall from the infection of the embolus, resulting in calcium deposit and weakness of the wall as proposed by Ponfick. It would appear from the literature that the actual origin of an aneurysm in the cerebral vessels is not yet settled.

Multiple brain emboli resulting in small encephalitic areas were described by Huguenin,[15] and were later confirmed by von Leyden,[16] Cassirer [17] and Fraenkel.[18]

Abscess of the brain resulting from endocarditis was described by von Leichtenstern.[19] Since then a number of papers have appeared in which this complication is discussed. Lemke, Flater [20] and Kimmelstiel [21] all agreed that, in the course of endocarditis, abscess formation in the brain may occur and be located either within the vessel wall or in the brain substance. Similar abscesses may be found in other organs. Diamond [22] described a case of pyemia in which there was endocarditis associated with brain abscess.

Purulent types of meningitis often occur with endocarditis. Many such cases are reported in the literature (Lemke, Flater and Kimmelstiel).

Apart from embolus, meningitis, abscess or infarct formation occurring with endocarditis, certain authors have found that there may be vascular changes in the general arterial system with and without any of the focal manifestations mentioned. Huebner,[23] Wiesel,[24] Frothing-

15. Huguenin: Ziemes spez. path. Anat. u. Therap. **11**:728, 1878.

16. Von Leyden: Verhandl. d. Ver. f. inn. Med. zu Berlin, 1901, p. 103.

17. Cassirer: Arch. f. Psychiat. **36**:153, 1903.

18. Fraenkel, E.: Ueber der Verhalten des Gehirns bei akuten Infektionskrankheiten, Ztschr. f. Hyg. u. Infectionskrankh., 1898, vol. 27; Virchows Arch. f. path. Anat. **194**:189, 1908.

19. Von Leichtenstern, O.: Deutsche med. Wchnschr. **18**:93, 1892.

20. Flater, A.: Endocarditis und Gehirn, Klin. Wchnschr. **3**:2094, 1924.

21. Kimmelstiel, P.: Ueber Viridans-Encephalitis bei Endocarditis lenta, Beitr. z. path. Anat. u. z. allg. Path. **79**:39, 1928.

22. Diamond, I. A.: Changes in the Brain in Pyemia and Septicemia, Arch. Neurol. & Psychiat. **20**:524 (Sept.) 1928.

23. Huebner, O.: Deutsches Arch. f. klin. Med., 1899, vol. 64.

24. Wiesel, J.: Ztschr. f. Heil. **26**:107, 1905; **27**:262, 1905; Wien. klin. Wchnschr. **56**:15, 1906.

ham,[25] Lemke, Rolleston [26] and Istamonowa,[27] in their work on changes in the vessels in infectious diseases, included cases with endocarditis. They found fatty plaques in the intima, occasional swelling of the intimal cells and evidences of endarteritis in some of the smaller vessels of the various organs. Most of their work was confined to the organs of the body rather than to the brain. In some instances they reported the process as one of degeneration of the vessel walls, beginning in the media. Plugging of the vessel, with necrosis in the various organs and at times in the brain, is described. All agreed to the finding of endovascular leukocytic clumping at times; occasionally they found perivascular infiltration with leukocytes and lymphocytes. Some vessels showed perivascular and adventitial infiltration, with closure of vessels from emboli, endarteritis or from swelling of the intima. Istanomowa, however, stated that he found no changes in the small vessels. These investigators described two types of lesions as occurring in the vessels; one produced by the toxins, resulting in productive changes in the vessels, and the other inflammatory with infiltration as the result of the presence of bacteria. Untersteiner,[28] in his work on pneumococcus meningo-encephalitis, described a fibrin exudate found both within and on the outside of a few of the vessels. Kimmelstiel mentioned that he occasionally saw some fibrin in the brain in his studies in cases of endocarditis lenta.

The best general review of changes in the brain produced by endocarditis is that of Kimmelstiel. He stated that any type of endocarditis may produce lesions of the brain or cord. These may be embolic phenomena, aneurysms, thrombi of the large vessels, multiple inflammatory areas, abscesses and ischemic foci. His research was devoted almost entirely to the effects of endocarditis lenta on the brain, and he found a combination of ischemic and inflammatory processes. Many of the vessels were plugged with fibrin and leukocytes, with resulting areas of softening. He also found inflammatory reactions about the vessels with infiltration and abscess formation, glial overgrowth and fibrin exudate. Emboli with degenerative changes in which it is not always possible to find the causative bacteria either in the vessel wall or in the area of softening were noted. Meningitis was also found as a frequent complication.

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25. Frothingham, C.: The Relation Between Acute Infectious Disease and Arteriosclerosis, Arch. Int. Med. **8**:153 (Aug.) 1911.

26. Rolleston, J. B.: Acute Infectious Diseases, New York, Physicians and Surgeons Book Company, 1925.

27. Istamonowa, T.: Histological Findings in Endocarditis Lenta, Virchows Arch. f. path. Anat. **268**:224, 1928.

28. Untersteiner, R.: Pneumococcus Meningo-Encephalitis with Particular Regard to Exudation of Fibrin in the Central Nervous System, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:64, 1926.

REPORT OF CASES

ACUTE BACTERIAL TYPES

CASE 1.—A. G., a man, aged 39, was admitted to the hospital on Oct. 17, 1925, in the service of Dr. Napoleon Boston, with a right upper lobar pneumonia. He developed a systolic murmur at the apex. A blood culture revealed a pneumococcus, type 1. Autopsy revealed an acute vegetative endocarditis of the mitral valve, resolving pneumonia and a congestion and cloudy swelling of the internal organs.

Histology.—The brain weighed 1,250 Gm. Microscopically, throughout the cortex were found numerous small areas of softening of various ages. One noted

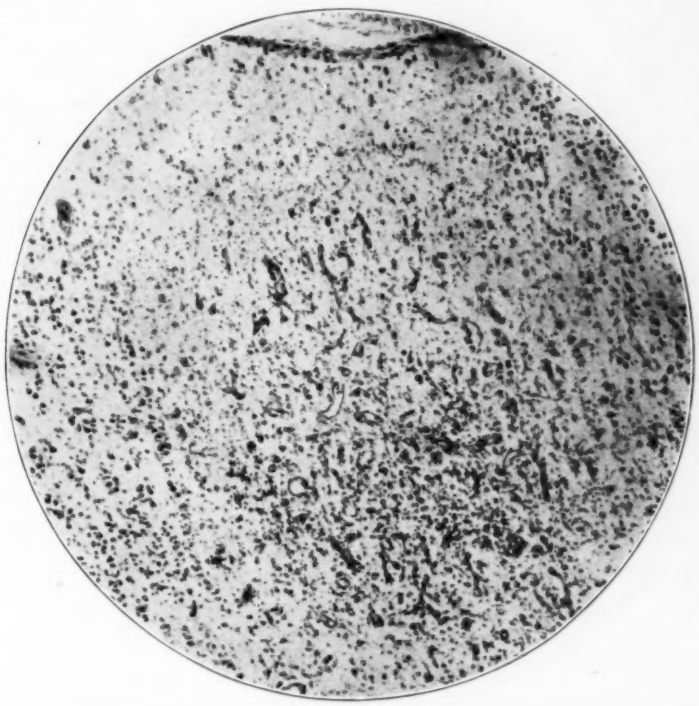

Fig. 1.—Relatively recent area of softening in cerebral cortex with vascularization and gitter cell accumulation.

an occasional area of coagulation necrosis, which, according to the Spielmeyer school, represents a terminal process. Other areas, again limited to the gray matter, showed necrosis with gitter cell accumulation, organization and marked vascularization (fig. 1). There were also areas which represented a process between those previously described. In addition, one or two large foci (Verödungsherde) were seen, limited to the gray matter, in which the architecture was completely destroyed; most of the ganglion cells had fallen out and those that remained showed the most advanced stage of ischemic cell disease with visibility of the Golgi net, or the so-called impregnation of the Golgi net (fig. 2). These foci contained many newly formed vessels, and around them were numerous poly-

morphonuclear cells. The meninges in relation to these foci were hyperplastic and edematous. In relation to one of the foci, a vessel showing marked intimal proliferation on one side of the wall was seen with almost complete occlusion of the vessel lumen. Special glial stains showed marked increase of fibroblastic and protoplasmic macroglia, in many of which degenerative changes were also taking place in the form of clasmatodendrosis (Cajal). Marchi preparations showed a considerable number of fatty granular cells. Universally through the cortex, the small vessels stood out prominently because of a mild yet definite swelling of the lining cells. The medium sized and larger vessels contained clumps of polymorphonuclear cells. Except in relation to the foci, the meninges showed little except

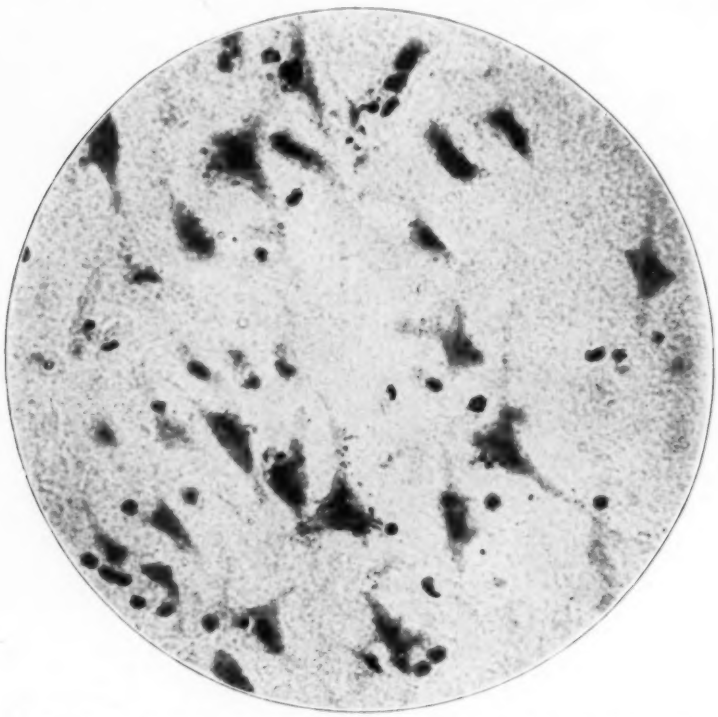

Fig. 2.—Ischemic cell disease with "incrustation of the Golgi net."

edema. One of the larger arteries in the cortex showed almost a complete closure of its lumen by an organized mass, probably an old embolus. No organisms within the vessels were found. The changes were practically limited to the cerebral cortex. The rest of the nervous system showed little of moment.

CASE 2.—F. G., a colored man, aged 25, was admitted to the hospital in the service of Dr. William E. Robertson, on July 8, 1926, giving a history of an illness with a sudden onset one week previously. It began with fever, nausea and throbbing headache, and later there was a convulsion. He gradually became weaker, showed delirium and hallucinations.

Examination revealed a rigid neck and a positive Kernig sign. The spinal fluid was turbid. A culture was sterile on two occasions. The heart presented a soft systolic murmur at the apex. He died in two weeks.

Necropsy.—At autopsy there was a marked vegetative endocarditis of the mitral valve and a coronary sclerosis. There were multiple infarcts of the spleen, liver and kidneys, with marked congestion of the liver and suprarenal glands. The brain weighed 1,450 Gm. Microscopically, in the meninges a definite, though not intense, infiltration with polymorphonuclear cells was noted. The cortex itself showed two general types of lesions: (1) In the frontal area, a comparatively large focus with complete disintegration and gitter cell accumulation. In relation to this area one saw an extremely thick and edematous pia containing, besides the polymorphonuclear cells, pigment-carrying phagocytic cells. (2) Minute collections of polymorphonuclear cells, in many of which degeneration of the constituent

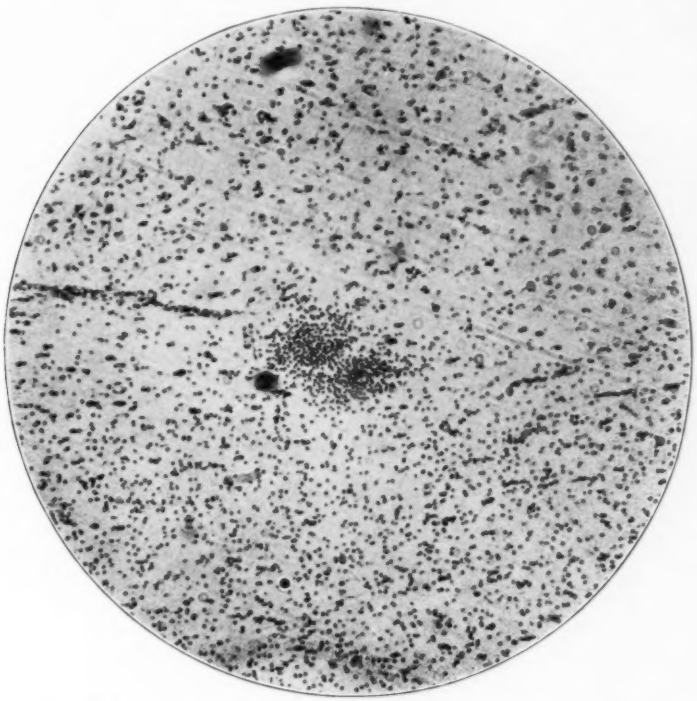

Fig. 3.—Focus of polymorphonuclear cells at the margin of the cortex and subcortex.

elements had not yet taken place (fig. 3). Whole areas throughout the brain showed the ischemic cell changes with beginning disintegration of the cerebral tissue. Nissl bodies were not seen, and the cell bodies appeared swollen. The small vessels showed but a small degree of swelling of the lining cells. No bacteria were found.

Case 3.—H. T., a white man, aged 27, was admitted to the hospital in a state of coma on Jan. 2, 1926, in the service of Dr. Hubley Owen. He had been found unconscious on the floor of his room. No evidence of injury was found. He presented the signs of a left hemiparesis with a positive Babinski sign. On the second day he developed twitching of the muscles of the entire left half of the body and later a series of convulsions, limited to that side. The eyes deviated to the left. He developed pneumonia and died within two weeks.

Necropsy.—Postmortem examination revealed myocardial degeneration and an old valvulitis of the tricuspid valve. There was bilateral pleural effusion and bronchopneumonia. The brain weighed 1,420 Gm. The vessels at the base were in fairly good condition. There was softening from the right frontal lobe to the occipital lobe and from the cortex to the basal ganglia, probably due to occlusion of the internal carotid artery. Through this area were scattered many canary yellow areas resembling purulent collections. Some were also present in the basal ganglia. Microscopically, the area described grossly showed all the signs of a softened brain. There were in the rest of the brain numerous areas of softening of various ages and sizes from small "Verödungsherde," with marked decrease in

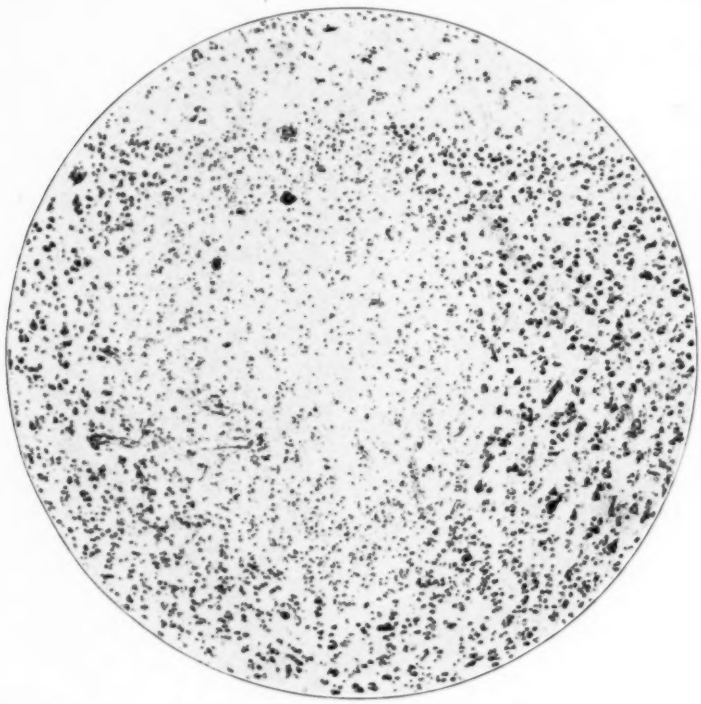

Fig. 4.—Small "Verödungsherde" in second, third and fourth cortical layers, fairly sharply marginated.

the number of ganglion cells and definite increase of glia, mainly of the fibrous astrocytic type, with no phagocytic cells or new vessel formation, to larger areas with marked vascularization and gitter cell accumulation.

In one vessel there was a calcified thrombus or embolus, which reduced the lumen of the vessel at least 75 per cent. In the territory supplied by this vessel were all the evidences of a slow cutting off of the circulation, but much older than in the previous cases, as was shown by new vessel formation and an astrocytic gliosis. The blood stream contained numerous polymorphonuclear cells. Organisms could not be demonstrated. The vessels throughout the brain showed definite hyalinization of the media. Many of the ganglion cells showed chromatolysis.

CASE 4.—D. F., a man, aged 35, was admitted to the hospital in the service of Dr. Napoleon Boston, on March 7, 1926. He had been ill for two and one-half weeks with a "cold in the chest." Associated with this there was headache and pain in the neck. Just before admission he became delirious and had visual hallucinations. The temperature was 104.2 F.; the pulse rate was 140 and respirations 50. He presented the physical signs of bronchopneumonia. He had a rigid neck and a positive Kernig sign; the spinal fluid was turbid and a stain revealed a gram-plus diplococcus. A soft systolic murmur was heard at the apex of the heart. He died within twenty-four hours.

Necropsy.—Autopsy revealed: acute ulcerative endocarditis of the aortic and tricuspid valves, with congestion and edema of the lungs and many areas of lobular pneumonia; congestion of the liver, spleen and kidneys, and purulent meningitis. The vessels at the base were normal. Microscopically, in the cerebellum there was a definite increase in Bergmann's layer, while the soft meninges contained an excess of polymorphonuclear cells. Over the cerebrum the pia was edematous and fibrotic and contained a considerable number of polymorphonuclear cells and many macrophages. The blood vessels were filled with leukocytes. The cortex itself showed a fairly normal structure, but here and there one could make out small areas of coagulation necrosis with loss of ganglion cells and a partial replacement by astrocytic cells, but no vascularization or gitter cell accumulation (fig. 4). The vessels throughout showed rather prominent endothelial cells. The ganglion cells for the most part, except for pallor, were not remarkable. Organisms were not demonstrated either in the subarachnoid space or in the vessels.

CASE 5.—W. W., a colored man, aged 21, was admitted to the hospital in the service of Dr. Napoleon Boston, on April 20, 1926. He had been ill for four weeks, the condition beginning with a severe frontal headache, later chills and fever, and with pain shifting from joint to joint. He was delirious at times. He had a low grade temperature and a soft systolic murmur at the apex. There was rigidity of the neck with a definite Kernig sign. The spinal fluid was turbid and presented a gram-positive diplococcus: pneumococcus, type 4. He failed rapidly after entering the hospital and died within two days.

Necropsy.—Postmortem examination revealed a malignant endocarditis, involving the mitral valve, and dilatation of the left ventricle. The lung showed congestion and edema. The spleen and kidneys were enlarged and showed anemic infarcts. The liver showed cloudy swelling. There was a marked purulent meningitis. The brain weighed 1,300 Gm. The convolutions were somewhat flattened from the increase of intracranial pressure. The exudate was greenish yellow, and the vessels at the base could just be made out through the exudate. The ventricular system was greatly dilated. Microscopically, the important feature consisted of an intense meningeal infiltration of polymorphonuclear cells, which, for the most part, was completely excluded from the cortical tissue in all sections examined. However, there was a much greater infiltration of cells in the ventricles than in the subarachnoid space. In the ventricles there was a breaking through into the subependymal tissue with a marked reaction on the part of the white substance, forming a picture that is well known under the term, "acute ependymitis" (fig. 5), a not infrequent concomitant of meningitis. By diligent searching one found an occasional small abscess within the cerebral substance. The ganglion cells throughout showed cloudy swelling, so often seen in acute infections of the brain. The blood vessels showed but a mild reaction, although some of the medium-sized arteries had hyalinized walls. The rest of the brain was not remarkable. Organisms were not demonstrated in the brain tissue.

Case 6.—S. H., a colored man, aged 21, was admitted to the hospital on the service of Dr. Patterson, on Jan. 13, 1928. He had been ill for three weeks. The illness began with pain in the left shoulder, associated with cough, fever and dyspnea, and later lobar pneumonia on the right side. A blood culture was sterile. The heart presented a definite murmur over the aortic area. He died within twenty-four hours after admission to the hospital.

Necropsy.—Postmortem examination revealed acute ulcerative endocarditis, involving the aortic valve; a culture from the heart blood showed *Staphylococcus aureus* and hemolytic streptococci. There was a large confluent pneumonia, involving both upper and lower lobes on the right side. The spleen, kidneys and

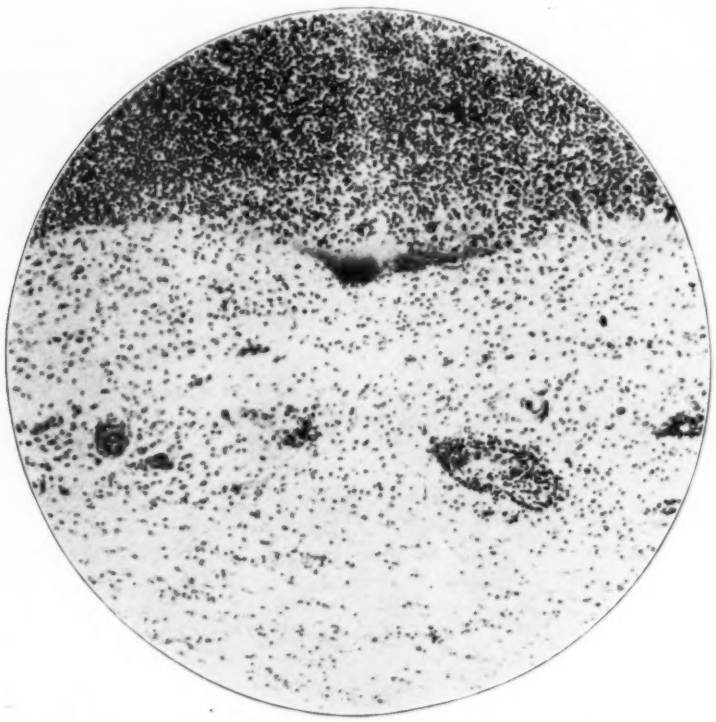

Fig. 5.—Acute ependymitis. Ependymal layer absent at X. Intense polymorphonuclear accumulation in the ventricle and intense subependymal reaction.

liver showed congestion and swelling. There were a small amount of purulent pericarditis and a few small myocardial infarcts. The brain weighed 1,190 Gm. The interpeduncular space was filled with a marked exudate extending backward to the middle of the pons. The pia over the convexity was normal. The hemispheres were normal. The basilar vessels were slightly thickened. There was slight ventricular dilatation. Microscopically, the meninges were definitely edematous and fibrotic with an inflammatory cellular infiltration. For the most part the architecture of the cortex was normal, but scattered throughout were to be seen small "Verödungsherde." These had to be sought for. The small blood vessels were slightly more prominent than normal and were not as involved as in some of the

other cases. They were congested, and many contained polymorphonuclear cells. The ganglion cells showed nothing aside from a mild cloudy swelling. The glia was not increased, except to a moderate degree in the focal necrotic areas. No organisms were demonstrated.

CASE 7.—S. B., a white man, aged 27, was admitted to the hospital in the service of Dr. William Drayton, on Aug. 22, 1928. The onset of the illness was sudden, beginning with confusion and violence; he was brought to the hospital by the police. On admission, his answers were evasive and his voice high pitched. He was easily distracted, and he entertained many delusions of persecution and had auditory hallucinations. The heart presented a soft systolic murmur at the apex. He had a low grade temperature, with some redness of the throat, a culture from which yielded Vincent's organisms.

Necropsy.—Postmortem examination revealed recent vegetations of the mitral and aortic valves. There was congestion of both lungs but no pneumonia. There was a thrombus in the right auricular appendage. The spleen was hyperplastic and congested, and the kidneys showed cloudy swelling. The brain weighed 1,410 Gm. and was somewhat edematous. The dura was normal. The basilar vessels were normal. Microscopically, the soft membranes of the brain showed rather marked edema and fibrosis but without inflammatory exudate, although in places they contained a considerable number of phagocytic cells. The cortex showed a normal lamination, except for the occasional presence of small areas in which the ganglion cells had disappeared (Verödungsherde). The vessel framework and the glia cells still remained. These areas were by no means numerous. The outstanding feature was the presence of swollen lining cells in nearly all the small vessels. The vessels were all congested. They did not contain polymorphonuclear cells or bacteria.

CASE 8.—A white man, aged 31, was admitted to the hospital in the service of Dr. Samuel Lowenberg, on Jan. 21, 1927. He was in a semiconscious state when brought in, and then became delirious. It was learned that he had not been well for a year. He is alleged to have had pneumonia several times. In the hospital he was resistive and delirious and the respirations were deep and irregular. He had hallucinations. The lungs were filled with moist râles. There was a soft systolic murmur at the apex. There was slight rigidity of the neck. A blood culture revealed *Staphylococcus albus.* He died within two days after admission.

Necropsy.—Postmortem examination showed ulcerative endocarditis, involving the aortic valve, plus chronic mitral vegetative endocarditis. There was pneumonia involving the left lower lobe. There were congestion of the spleen, acute nephritis and cloudy swelling of the liver. There were focal areas of necrosis of the heart, with areas of septic myocarditis and an occasional area of hemorrhagic infiltration. The brain weighed 1,400 Gm. Punctate hemorrhages were present throughout the cerebrum, cerebellum and pons. The pia was unevenly thickened. Microscopically, the meninges showed a mild fibrosis with collections of phagocytic cells in places. The cortex showed marked changes. There were multiple areas of degeneration, from small coagulation necrosis to small and large areas with complete degeneration, vascularization and repair. One did not have to search far to find these, so numerous were they. One small vessel in the meninges showed organization of an old embolus with almost complete obliteration of the lumen. The blood vessels for the most part contained polymorphonuclear cells. Areas of softening and hemorrhages were to be found in the cerebrum and cerebellum. No bacteria could be found.

SUBACUTE BACTERIAL TYPES

CASE 9.—E. B., a colored man, aged 23, was admitted to the hospital in the service of Dr. David Riesman, on July 31, 1925, with the complaints of weakness, headache and mental dulness. He had worked to within a few days of admission. There was a low grade fever. There was a murmur over the aortic area. A blood culture revealed *Streptococcus viridans*. He gradually failed and died after an illness of over two months' duration.

Necropsy.—At autopsy the heart showed an acute vegetative endocarditis of the aortic cusps with hypertrophy and dilatation. There were fibrinous adhesions of the pleura. There were anemic infarctions of the spleen. The kidneys pre-

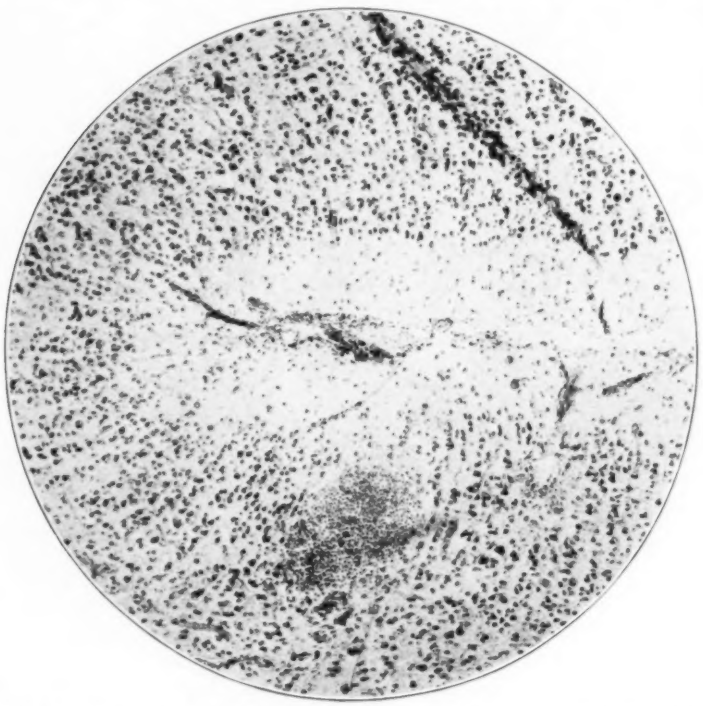

Fig. 6.—Small localized abscess in the upper cortical layers (2.3 Broadmann).

sented nephritis and infarctions. The suprarenal glands showed cloudy swelling, and the stomach acute inflammation.

Grossly, congestion was the main feature in the brain. Microscopically, throughout two different kinds of foci were found: (1) Large and small areas of softening, in various stages from gitter cell accumulation to areas with vascularization and organization. These areas were indistinguishable from the small areas seen in an arteriosclerotic brain as a result of thrombotic lesions. A lamellar situation was seen in some of the foci, taking in the lower cortical layers as a rule. (2) The small abscess. These were found not only in the tissue, which was completely devitalized—the larger ones—but also as minute forms in comparatively normal areas of the cortex (fig. 6). The latter, however, were in the minority. In the blood stream one occasionally observed *Streptococcus*

viridans, which stood out distinctly. These organisms were found to a lesser degree within the abscesses. Contained within one small vessel of the cortex was a small mass of cells (fig. 7), which was probably a piece broken off from an embolus and which practically occluded the vessel lumen. The ganglion cells through the entire brain showed degenerative changes, especially cell sclerosis and ischemic cell disease. The small vessels throughout showed swelling of the lining cells, and in some of the larger vessels hyalinization had already taken place. The glia, as in the previous case, showed not only proliferation to a marked degree, but also degenerative changes. The meninges presented a severe edema with a definite fibrosis, and in relation to the various foci numerous

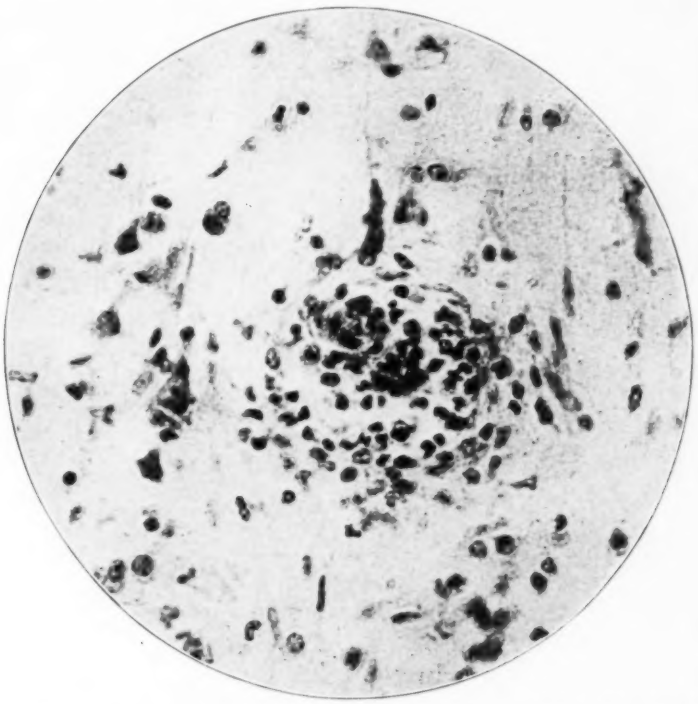

Fig. 7.—Small vessel in deeper layers of cortex containing blood cells and embolic mass of cells.

phagocytic cells were present. The remainder of the brain showed the same changes to a much milder degree; small areas were found in the basal ganglia and in the brain stem.

CASE 10.—J. B., a colored man, aged 49, was admitted to the hospital in the service of Dr. Callahan, on Feb. 2, 1926. His complaint was pain in the left side of the chest associated with a cough. He presented pleurisy at both bases and a loud systolic murmur at the apex of the heart. There was a low grade fever. A blood culture was sterile. The illness lasted five months.

Necropsy.—At autopsy the heart presented a vegetative endocarditis of the mitral valve with a coronary thrombosis. A culture of the heart blood was sterile. The lungs presented infarcts and hemorrhagic pleurisy at both bases. The spleen,

liver and kidneys contained multiple infarcts. The mesentery and small intestines were thickened from multiple infarcts.

The brain weighed 1,380 Gm. and appeared of normal size. Near the center of the left cerebellum was an area of softening, 2 cm. in diameter, which extended to the surface. There was edema of the cerebral hemispheres and the pia-arachnoid was thickened over the entire surface. The vessels at the base contained a few plaques. There was no dilatation of the ventricles. Macroscopic areas of softening were observed in the occipital lobes. Microscopically, the areas of softening were easily found. There were, however, in addition, lesions of a totally different nature. Two rather large vessels were found in which marked

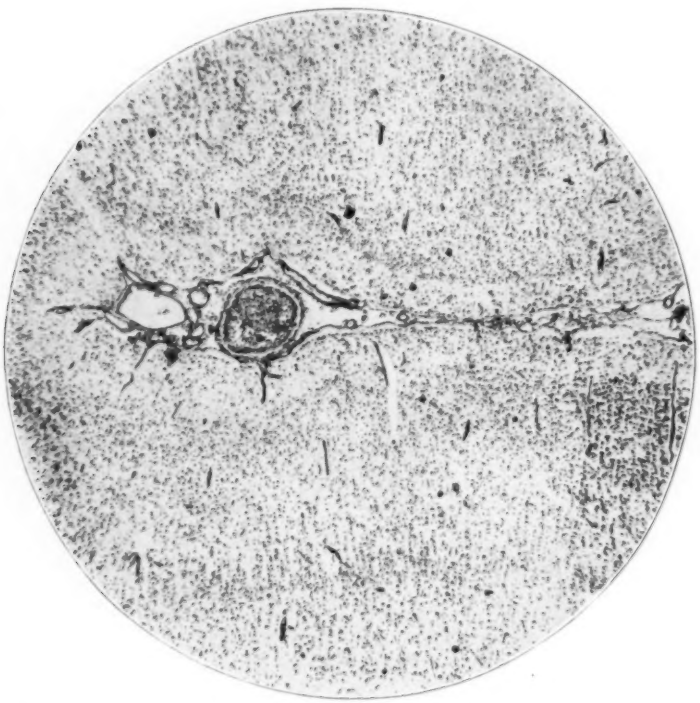

Fig. 8.—Small vessel in the pia showing almost complete occlusion by an organizing lesion with "Verödungsherde" on either side, fairly sharply marginated on the right.

narrowing of the lumen had occurred as a result of the organization of what appeared to be an old embolic lesion (fig. 8). One noted the changes in the cortex that occurred in relation to the slow cutting off of the blood supply, such as marked decrease of the ganglion cells with those remaining showing ischemic cell changes; glial proliferation and degeneration of the macroglia cells; absence of new vessel formation and almost complete absence of gitter cells. Here again, in these foci, one found excellent specimens of impregnation of the Golgi net. No abscesses were to be found. The meninges showed fibrosis; only in the neighborhood of the foci were there phagocytic cells. No bacteria could be found. The small vessels showed mainly hyalinization of the media. The rest of the brain

showed changes of a frank arteriosclerotic nature as well as occasional foci like the one described.

CASE 11.—I. N., a white woman, aged 34, was admitted to the hospital, in the service of Dr. Ludlum, on Sept. 1, 1928. She had been ill for five and one-half months. The illness began with a complaint of indigestion; later she showed mental confusion and had hallucinations of sight. There was fluid in the right side of the chest. During the illness the physical signs of endocarditis developed although a blood culture gave negative results. The patient failed gradually, and died on Dec. 4, 1928.

Necropsy.—Postmortem examination revealed a simple verrucose endocarditis of the mitral valve with myocardial degeneration; there was a fatty liver; the spleen was enlarged and cloudy; there was congestion of the kidneys. A culture of the heart blood was sterile.

The brain appeared normal in size. The vessels at the base revealed no plaques. Microscopically, the meninges showed a definite fibrosis, but without cellular exudation. The cortex showed a few small areas that could be characterized as "Verödungsherde," with absence of ganglion cell elements and with only a moderate glial increase of the astrocytic type, without gitter cell formation but with a definite, though not marked, vascularization. Several vessels were seen that showed practically complete occlusion by hyalinized masses, part of which were covered by endothelial cells producing marked narrowing of the lumen. Some of the smaller vessels contained hyalinized masses which completely occluded them. The outstanding feature in this case was the extreme and intense swelling and proliferation of the lining cells of the small vessels, so that there was a marked narrowing of the vessel lumen. Almost universally throughout was a severe ganglion cell degeneration that at times reached a point of cell sclerosis with tortuosity of the processes. The rest of the brain showed nothing remarkable. No organisms were found.

CASE 12.—D. B., a white man, aged 29, was admitted to the hospital in the service of Dr. Robertson, on June 16, 1924. According to the history he had been ill for four months. There had been pain in the joints and later night sweats. He gradually lost weight and strength. At one time he was thought to have had tuberculosis and was sent to a sanitarium, but was later discharged as nontuberculous.

On admission to the hospital he presented a marked systolic murmur at the apex and a slight swelling of the left ankle. A blood culture was negative. The low grade fever continued. He failed and died on Aug. 4, 1924.

Necropsy.—The brain weighed 1,360 Gm. There was a small aneurysmal dilatation of a vessel in the right parietal lobe and the pia on the left side showed a localized, small collection of greenish-gray material. There were some small whitish spots on the right side. In general, the pia was slightly thickened. There was moderate sclerosis of the vessels at the base. The ventricles were normal. A culture of the heart blood gave *Bacillus pyocyaneus* and *Streptococcus viridans.* There was a subacute bacterial endocarditis of the mitral valve with infarcts throughout the liver, spleen and kidneys, some of which were septic. The lungs presented marked bronchitis, the liver cloudy swelling. Microscopically, the meninges showed definite edema and fibrosis, but with the presence of numerous pigment-carrying phagocytic cells, which at first glance gave one the impression that meningitis was present. The blood vessels throughout showed intense congestion. They did not contain polymorphonuclear cells. The cortex showed the following features: There was prominence of the small vessels because of proliferation of the components of the vessel walls; many showed perivascular collec-

tions of phagocytic cells, at first glance giving the appearance of the cortex in dementia paralytica. There was definite ganglion cell decrease with focal areas of coagulation necrosis. In particular, it was noted that there were areas of softening in the white matter. As in the meninges, the vessels showed intense congestion. Numerous convoluted vessels were present in the cortex, in the formations known as "Paketbildungen." Occasional glial foci could be seen, but they were not so numerous as in some of the other cases. No organisms were demonstrated. For the most part the ganglion cells were extremely pale and without Nissl bodies.

CASE 13.—V. H., a white woman, aged 28, was admitted to the hospital in the service of Dr. Allyn, on Aug. 26, 1920; she died on Oct. 19, 1920. She had been ill about two months. The onset occurred with partial palsy of the right side of the body associated with a low grade fever. A blood culture revealed *Streptococcus viridans*. On admission she presented a right hemiparesis with a positive Babinski sign. There was pronounced secondary anemia. There was a soft systolic murmur at the apex.

Necropsy.—Autopsy revealed subacute bacterial endocarditis of the mitral valve. There was myocardial degeneration. There were infarcts of the spleen and kidneys, with acute septic nephritis and petechial hemorrhages throughout the skin. There were hemorrhagic infarcts of the intestines and cloudy swelling of the liver. The brain was soft and edematous, with much thickening of the pia. The vessels at the base were slightly thickened. Microscopically, the pia-arachnoid showed fibrosis. The vessels showed considerable thickening of the walls, with hyalinization, and were filled with polymorphonuclear cells. The cortex showed no architectural change, except in infrequent areas of softening. The ganglion cells were pale and in places showed severe degeneration. The glia appeared to be in excess. The outstanding feature was the prominence of the small vessels because of swelling of the lining cells and hyalinization of the media. The spinal cord showed exactly the same type of vessel change, with numerous small areas of degeneration and occasional focal collections of glia cells (glial stars) not unlike those met with in the brain in some of our other cases.

COMMENT

In a discussion of a symptom-complex such as endocarditis, one must bear in mind that, while in rare instances it may be a primary disease, in the vast majority of cases it is not an independent condition with a uniform etiology, but is part of a general infectious process. While it is one of the easiest diagnoses to make at times when the condition is absolutely typical, it can be so obscured by overlying conditions that it may be entirely unsuspected until autopsy. Its occurrence in various infections is notorious. No one today would allow the condition to remain undiscovered in the course of an acute rheumatic or choreic condition, but it may occur in tonsillitis, scarlet fever, pneumonia and phthisis, to mention only a few conditions, and in these it may be entirely unsuspected.

According to Libman,[29] the following classification of endocarditis may be used as a working basis: (1) rheumatic, (2) syphilitic, (3) acute bacterial, (4) subacute bacterial and (5) undetermined.

29. Libman, E.: Characterization of Various Forms of Endocarditis, J. A. M. A. **80**:813 (March 24) 1923.

The rheumatic form occurs during the course of an acute rheumatic fever or chorea. When uncomplicated, it produces nodular or warty lesions, usually on the mitral valve near the margins. Ulceration may result, with secondary infection and embolic phenomena throughout the body. Aschoff bodies, when found in the heart muscle, are diagnostic. Before ulceration in the lesions occurs the secondary complications with regard to the central nervous system are due to toxemia. With the occurrence of necrosis in the valve, complications such as emboli, meningitis and abscess occur. We have excluded from our series cases occurring in the course of acute rheumatic fever, since the process here is somewhat different and is to be considered in a separate communication.

The syphilitic form usually is an end-result in the course of a syphilitic infection, and involves mainly the aortic valve. Here again we have excluded this type of case because of the great difference in the pathologic changes.

We have concerned ourselves here mainly with the acute and subacute bacterial types. The former may occur in the course of infection with any of the known bacteria, particularly the pyogenic forms. In this type there is a purulent infiltration over wide areas of the valves with necrosis and ulceration. Vegetations form, and portions are swept off into the general circulation. Any valve may be affected, but the disease by choice invades a valve previously the seat of some other disease or defect. The left side of the heart is particularly vulnerable.

In our series are eight cases belonging to the acute group. Various bacteria were responsible in this group, but the pneumococcus by far predominated. It is possible that the endocardial lesion was secondary to the pneumonic process, but in a few a soft murmur was present at the time of admission of the patient to the hospital, prior to the pneumonia, and became much more pronounced during the pneumonic period.

To some it may seem incorrect to consider this group of changes in the brain as secondary to the cardiac lesion, rather than as part of the general process of a bacteremia. The brain might have been involved even in the absence of the cardiac lesion. With this thought we are heartily in favor; it brings out a fact, which we have stressed in former communications,[30] that the brain is part of the body and takes part in all its pathologic processes. Still, were the brain picture entirely secondary to the septicemia, the changes should be either multiple abscesses or meningitis; yet in some of our cases old embolic lesions were found in the brain, which would substantiate the idea that the

30. Winkelman, N. W., and Eckel, J. L.: Productive Endarteritis of the Small Cortical Vessels in Severe Toxemias, Brain **50**:608, 1927; Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:862 (April) 1929.

valvulitis was responsible partly, at least, for the involvement of the brain. One must also not lose sight of the fact that in many acute and chronic diseases pneumonia is the direct and immediate cause of death; the organisms in the blood stream may overshadow all else, even though the original infection has been some other form. Again one must also realize that the condition may be a meningitis originally with secondary pyemia and subsequent valve involvement. One additional point is that in only a few of our cases was a typical lobar pneumonia present—usually a lobular pneumonia of the type found in any terminal, debilitating disease.

With these basic facts in mind, an analysis of our cases shows:

In case 1 the onset was sudden, six weeks prior to death, with a lobar pneumonia in which resolution was going on. An infection in the blood stream had occurred with acute lesions on the valves, from which emboli were sent to the brain, as was shown by finding an organized embolus in a cortical vessel. Not only did the brain show evidence of the terminal infection but it showed that it had been involved earlier in the process. This case shows also that the brain may be the only organ involved by emboli as the result of an endocardial lesion.

In case 2 the onset was sudden, with headache, vomiting and convulsions and with all the signs of meningitis, in which cultures on two occasions were sterile. A mitral murmur was present. The patient lived eighteen days. It is possible in this case that the endocardial lesion was secondary to the meningeal infection, even though multiple infarcts were present throughout the bodily organs.

In case 3 the illness lasted only sixteen days. The onset was sudden, with unconsciousness; later, a left hemiparesis developed, associated with muscle twitching and convulsive movements limited to that side. A focal lesion was suspected and a decompression was done. Pneumonia developed and death occurred. An old tricuspid valvulitis and bilateral pleural effusion with bronchopneumonia were found. Occlusion of the internal carotid artery was found, as well as "Verödungsherde" in the rest of the brain. A calcified thrombus was noted.

Case 4 is evidently secondary to the pneumonic process, with a meningitis. The brain showed evidence of areas of terminal coagulation necrosis. While in this case the pneumococcus was found in the spinal fluid, it is known that pneumococcemia may occur even without consolidation of the lung.

Case 5 showed a pneumococcus in the spinal fluid, with malignant endocarditis and a lobular pneumonia. Anemic infarcts were present in the body organs. Acute meningitis and ependymitis were the important observations on the brain. The ependymitis here was of interest in that it overshadowed the subarachnoid inflammation.

Case 6 showed lobular pneumonia with a sterile blood culture. Myocardial infarcts were present, and meningitis was the predominating condition in the brain. *Staphylococcus aureus* was found in the heart blood.

Case 7 is difficult to analyze. An acute infection was present which lasted only eight days. No pneumonia occurred. An acute verrucose endocarditis of the aortic and mitral valves was present. No infarcts occurred in the bodily organs. The changes in the brain were entirely those of a severe toxemia.

In case 8 there was a lobular pneumonia with acute aortic ulceration and chronic mitral valvulitis. Clinically, the case was one of lobar pneumonia, the patient dying on the third day. Punctate hemorrhages were universal in the brain. Older areas of partial and complete softening, probably the result of the old valvular condition, were frequently seen. One organized embolus was found as a substantiation of this fact.

Reviewing cases 1 to 8, three pathologic observations stand out: 1. Meningitis predominated, while abscess occurred in only one case, 5. 2. The toxic effects on the blood vessels were uniformly present. 3. Embolic phenomena, the result of a former valvulitis with organized emboli, occurred in cases 3 and 8.

In the second group, that of subacute bacterial endocarditis, the disease again attacked by choice valves that were the seat of a previous lesion, especially rheumatism and syphilis. The left side of the heart again showed frequent involvement.

The symptoms in this group can be considered under two main headings: (1) those the result of the infection itself and (2) those the result of the secondary manifestations. It is to the latter that we shall devote attention and especially the secondary manifestation as regards the central nervous system. Osler stated that they are due to embolism. That this is only partly true will be seen in the review of our cases.

The same process that caused the implantation of the infective agent on the valve can also send its material to the brain and to other organs. In the brain the formation of either multiple abscesses or a frank meningitis may result when the process is early, but after the condition becomes well established on the valve, emboli in the form of clusters of bacteria and portions of the vegetations, infected and noninfected, may ensue, with four different results: (1) multiple abscesses; (2) meningitis; (3) embolic implantation in a vessel, with organization and a gradual decrease in the blood supply to the brain, or a complete and sudden plugging of a small vessel; (4) the effects of an intense toxemia with changes such as we have seen in other forms of severe toxemia or infections.

In case 9, the duration of which was three months, the onset was with headache, weakness and a low grade fever. Syphilis was admitted but serologic tests were negative. Aortic regurgitation and cardiac hypertrophy were present. A blood culture was positive for *Streptococcus viridans*. Aortic valvulitis was present with infarcts in the spleen and kidneys. In the brain were necrotic areas of various ages as well as numerous small abscesses. Streptococci were visible in the blood stream of the brain as well as in one small embolic mass. Acute and chronic toxic changes were found in the small vessels (productive endarteritis of the small vessels).

In case 10 the illness lasted nearly five months, with evidences of a low grade infection not unlike tuberculosis. This case was extremely important from the clinical angle because of the presence of choked disks. Blood cultures were sterile, ante mortem as well as post mortem. Acute vegetative endocarditis of the mitral valve was found. Infarcts were found in the lungs, kidneys, spleen and liver as well as in the brain. Organized emboli were seen in the brain with consequent cortical degeneration. No abscesses were found.

The illness in case 11 lasted five and one-half months, with evidences of a severe low grade toxemia. A cardiac murmur developed during the course of the disease. Blood cultures were sterile. Postmortem, verrucose endocarditis of the mitral valve was present. No infarcts were found in the bodily organs. In the brain, foci of incomplete softening were noted. Old embolic lesions were found within the vessels.

In case 12 the symptoms were present for six months and were those of a low grade infection, for which the patient was sent to a hospital for tuberculosis. Rheumatic pains in the joints occurred. A blood culture was sterile. At autopsy culture of the heart blood showed *Streptococcus viridans*, and subacute bacterial endocarditis of the mitral valve was found with multiple infarcts of the spleen, liver and kidneys, with abscess formation. A small aneurysm was found in the brain. Microscopically, the brain showed the toxic effects on the small vessels with areas of softening, especially in the white matter.

In case 13 a history of rheumatic fever six years previously was elicited. The terminal illness lasted for eight months, of which seven were spent in bed. A low grade infectious syndrome was present. Two months prior to death, a right hemiparesis occurred during sleep. *Streptococcus viridans* was found by blood culture. Postmortem examination showed mitral valve lesions, with infarcts of the spleen, kidneys and intestines, with septic foci; petechiae of the skin were also found. The brain showed infrequent areas of softening with toxic effects on the small vessels. In the spinal cord similar changes were found.

The various types of lesions can best be discussed under four headings: (1) Multiple abscesses. In the subacute group of endocarditis, multiple abscesses of the brain were infrequent, occurring in only one of five cases, and in only one of the acute cases. Injury to the vessel wall, which permits the bacteria to pass through, is probably a requisite to their formation. (2) Meningitis. This did not occur as a complication in the subacute cases, which was in marked contrast to the acute endocardial group in which meningitis was not infrequent. The route by which this infection reaches the subarachnoid space is unknown. One might theorize on methods similar to the dissemination of tuberculosis, cancer and syphilis. (3) Embolic lesions. Three of the five subacute bacterial cases showed organized emboli within the vessels. Two of the acute cases showed a similar condition. As is well known, embolic or thrombotic lesions are not usually met with in the routine study of cases. The fact that they were so easily found in this series makes us believe that they were extremely numerous. The effect on the brain substance was easily demonstrable. As a result of the slow cutting down of the circulation, the changes described in the ganglion cells under the term, "ischemic cell disease" (Spielmeyer) were well portrayed. The absence of phagocytic elements in these areas agrees with the usual observations in similar lesions (Verödungsherde). The effect of a complete and sudden closure of a small vessel by an embolus differs in no way from sudden occlusion from any cause. We thought that the small areas of complete softening (Erweichungsherde) were to be accounted for by this mechanism. (4) Toxic endarteritis. This was invariably of a productive type and was similar to that seen in so many toxic and infectious states; it was practically uniform in every case of the subacute as well as of the acute form. Its significance has been taken up by us in former communications.[30] Suffice it to say here that so great may the swelling of the lining cells be that necrotic foci may result from this mechanism.

SUMMARY AND CONCLUSIONS

1. We have described thirteen cases of bacterial endocarditis in which lesions of the central nervous system were demonstrable.

2. Eight cases belong to the acute bacterial type, mainly the result of pneumococcic infection, and five cases to the subacute variety, in which *Streptococcus viridans* was the causative agent.

3. There is a tendency for both types to attack a valve previously affected through rheumatism or syphilis.

4. Infarction of the body organs is a frequent complication of both types, but occurs more frequently in the subacute variety.

5. The brain can suffer in a variety of ways: Meningitis and toxic vessel changes (productive endarteritis) are the two most common lesions in the acute forms. Organized emboli within the vessel lumen and the secondary changes in the brain (Verödungsherde and Erweichungsherde) are the most frequent and typical secondary results in the brain.

6. Mycotic aneurysms, while described as a frequent complication in the literature, were found in only one case.

7. Multiple minute cerebral abscesses were found in only two instances.

8. Involvement of the spinal cord was found in only one case; it was exactly similar to that of the brain.

OCCLUSION OF THE AQUEDUCT OF SYLVIUS*

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It would not require a very gross disease to occlude the tiny channel of communication between the third and fourth ventricles of the brain. Actually, clinical symptoms and even death may result from a process so minute that it may be impossible to recognize it during the life of the patient, and its identity may be established after death only by use of the microscope. Particular interest, therefore, is attached to such cases because of this difficulty in clinical and in pathologic diagnosis. It is not intended to describe all of the conditions producing occlusion of the aqueduct, but a small group of patients have been selected wherein the difficulties mentioned are exemplified.

REPORT OF CASES

CASE 1.—*History.*—A girl, aged 11, was brought to the Mayo Clinic on Jan. 11, 1918, because of headache, backache and difficulty in walking. Five years before, and for no apparent reason, she had experienced a series of general convulsions, about eight altogether, and these had recurred at intervals of from about six to eight weeks. During the period of the convulsive seizures she had suffered from severe occipital pain, which later was also felt in the thoracic portion of the spinal column. The seizures of recent years had, however, became somewhat less frequent, so that she had had only two attacks in the previous six months. Other symptoms had, however, appeared in these six months, namely, loss of appetite, vomiting in the morning and frequent, persistent, severe headaches. She had gradually lost control of rectal and vesical sphincters in the previous two months, and her gait had become increasingly unsteady. There had been no change in mentality. Ever since birth her parents had noticed a small mass over her spinal column in the midthoracic region.

Examination.—The patient was somewhat obese, but intelligent. She weighed 75 pounds (54.0 Kg.). A meningocele, about 3 cm. in diameter, was present over the seventh thoracic vertebra; the head seemed somewhat larger than the average size for a child of her age. She had marked ataxia on attempting to walk, so that she had to be either carried or wheeled in a chair. Examination of the eyes revealed dilatation of the veins in the fundus, with secondary optic atrophy. Vision, however, was still fairly good; it was 6/15 in the right eye and 6/7 in the left. Roentgenographic studies of the head showed signs of

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increased intracranial pressure, with almost complete destruction of the sella turcica. There was horizontal and vertical nystagmus, with generalized loss of speed in movement and clumsiness of all four extremities. The tendon reflexes were reduced in the left upper extremity and the achilles reflexes were lost. A hydrocephalic percussion note was present on tapping the skull. Sensibility to pain was reduced over the thorax and back, about the level of the meningocele, but thermal and tactile sensibility were preserved. A diagnosis of chronic hydrocephalus associated with meningocele of the thoracic portion of the spinal column was made.

Operation.—The child was operated on on Jan. 19, 1919; a right subtemporal operation for decompression was done, with puncture of the corpus callosum. She died on the following day.

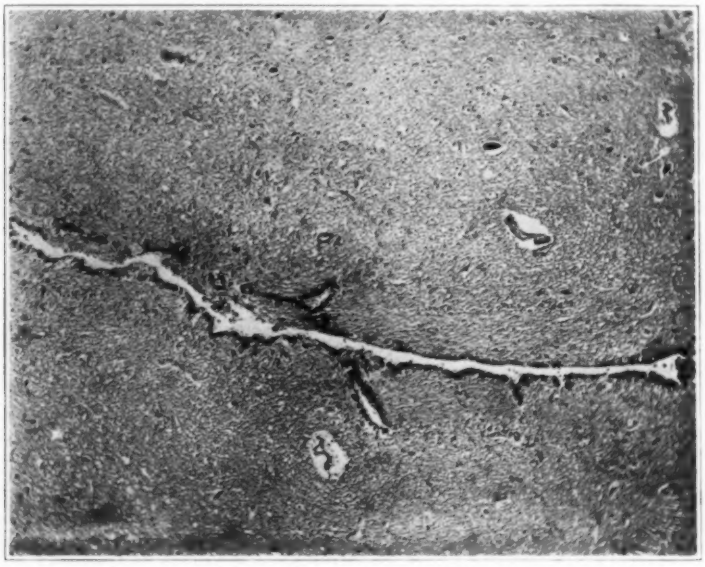

Fig. 1 (case 1).—General architectural arrangement of the aqueduct showing proliferation of subependymal glia, narrowing of the canal and the formation of tubules (× 50).

Necropsy.—On gross examination of the brain at necropsy, the convolutions were found to be markedly flattened. There was no meningitis or arachnoidal thickening except, perhaps, a mild degree of it around the medulla and under the third ventricle, which had bulged markedly. Coronal section of the brain showed marked internal hydrocephalus of the lateral and third ventricles, without any change in the fourth ventricle. The ependymal surfaces were perfectly smooth and glistening to the naked eye; granular ependymitis or exudates of any kind were not present. The aqueduct of Sylvius seemed to be occluded in most of its extent, but complete examination was deferred for microscopic study.

Microscopic Examination.—Histologic examination of the midbrain, with sections across the aqueduct, showed this channel to be an extremely narrow, slit-like opening with small tubules running off laterally and ending as blind pouches. The ependyma lining the aqueduct was only one cell deep and at no place was

there any proliferation. Here and there the continuity of the ependyma was interrupted and the subependymal glia seemed to flow through the interruptions in the continuity of the ependyma. This seemed secondary to definite proliferation of the subependymal glia, especially its fibrillar portions, and there did not seem to be any increase in the nuclear elements. This was particularly true in the case of the layer immediately below the ependyma. In some areas there was edema of the glial tissue surrounding the aqueduct, whereas in other areas there were the small tubules and solid collections of ependymal cells already referred to, but lying at a considerable distance from the main aqueduct. Surrounding these masses of ependymal cells there was some increase in the cellular elements in the adjacent area. Some of these proliferated cells seemed to be ependymal in character, others belonged to the astrocytic and oligodendrogliac group, and occasional cells belonged to the microgliac group. There were absolutely no signs of acute or chronic inflammation in the tissues around the aqueduct of Sylvius, and throughout the ventricles, both above and below the aqueduct, there was no proliferation of ependyma or of subependymal tissues. Neither did sections taken from various portions of the brain, both near and distant to the ventricles, show inflammatory change. The choroid plexuses seemed to be normal, and the meninges also were free from any pathologic changes. Altogether, the main pathologic changes in the brain were confined to the region of the aqueduct of Sylvius and involved chiefly the subependymal glia.

Case 2.—*Clinical History.*—A boy, aged 4, was brought to the clinic on Feb. 7, 1925, because of headaches, vomiting and retraction of the head. He apparently had been in normal health up to eight days prior to examination. At that time rather severe, intermittent, supra-orbital headache developed suddenly, associated with projectile vomiting. These headaches had persisted throughout the following week, and three days before examination they had reached their maximum. The night before the examination he had slept hardly at all and was found moaning and crying with pain early in the morning; this pain had spread into the occipitocervical region. Within a few hours after the appearance of the pain in the neck, the head became retracted and continued so until finally this retraction was of a rather extreme degree.

Examination.—When first examined, the child seemed extremely ill. He lay on the right side with the eyes shut and the face covered. The head was retracted markedly, so that the occiput almost touched the back over the spinal column. The neck was rigid to the degree that movement of the head in any direction was impossible. The knees were flexed, and the Kernig and Laségue signs were strongly positive. There was a marked cracked-pot percussion note on tapping the skull, and right internal strabismus was present. The rectal temperature was 101 F., the pulse rate 110 and rate of respiration 25 each minute. The pupils were greatly dilated but reacted normally to light. There was papilledema of the right optic disk of about 3 diopters, with hemorrhages and exudates. In the left eye there also was papilledema, but only of 1 diopter and without any hemorrhages.

Spinal puncture showed the fluid to be under greatly increased pressure, but it was clear, and contained only twelve small lymphocytes in each cubic millimeter. Following the withdrawal of 15 cc., the patient became somewhat more comfortable, but the retraction continued. He was perfectly rational and conscious throughout the period of observation. The following day, another spinal puncture was done with about the same results, but following this retraction of the head became more marked, the pulse became irregular, and a few hours afterward, while being fed his evening meal, the jaw suddenly dropped, respira-

tion ceased and retraction of the head disappeared. Although the heart continued to beat for five or ten minutes, the heart beat finally ceased and death occurred.

Necropsy.—Gross examination of the brain at necropsy revealed moderate flattening of the convolutions. Very severe herniation of the medulla and cerebellum through the foramen magnum had occurred. The floor of the third ventricle was markedly distended. Coronal section of the cerebrum disclosed a very high degree of internal hydrocephalus of the lateral and third ventricles, but section through the cerebellum showed the fourth ventricle to be normal in size and shape. The ventricular surfaces everywhere were smooth and glistening and without any signs of exudate or proliferation. The choroid plexus seemingly was normal. The aqueduct of Sylvius was dilated in its rostral third but caudally seemed to be completely occluded. Visible changes could not be detected in the meninges.

Microscopic Examination.—Histologic examination of the brain, by sections through the midbrain, showed the aqueduct of Sylvius in its caudal two-thirds to have been almost completely obliterated, in some areas more than others. The essential cause of the occlusion seemed to be a proliferation of the subependymal glia. There were several large as well as innumerable small tubules lined by ependymal cells in this proliferated tissue around the aqueduct. Solid islands of ependymal cells also were present and appeared in some places at a considerable distance from the region of the aqueduct. The increase in the subependymal glia around the aqueduct seemed to consist chiefly of glial elements normally found in that region; the increase was chiefly in the fibrillary portions of the cells, although in some areas there also was increase in the nuclear elements. Throughout the subependymal region of the lateral and third ventricles, there was somewhat similar proliferation, but to a less degree. In a more minute study of the area around the aqueduct, it was apparent that beneath the ependymal layer there was a stratum of proliferated glia comparatively devoid of nuclei. Beneath this fibrillar layer of glia, however, there frequently was another stratum of ependymal cells. These cells sometimes were collected in masses, without any definite arrangement, but sometimes they were aggregated to form tubules. This submerged layer of ependyma was, in some places, many cells thick. The proliferative changes which have been mentioned were absent in the region of the fourth ventricle and there were no manifest signs of inflammation in the brain, ependyma, meninges or choroid plexus.

Comment on Cases 1 and 2.—The essential feature in these two cases was the proliferation of the subependymal glia around the aqueduct which led ultimately to its stenosis or occlusion. The condition seemed to be noninflammatory, since evidence could not be found of any recent or remote inflammation. The small tubules of ependymal cells and islands of similar cells found in the subependymal tissue probably are inclusions in the proliferating glia. In some areas, this process could be seen taking place. The proliferating subependyma penetrated through the gaps in the ependymal lining, spread laterally and submerged the islets and tubules of ependymal cells. This proliferated glia was markedly fibrillar in character; it contained relatively few nuclei and seemed definitely to be simple hyperplasia without evidence of tumor formation. The pathologic changes in these two cases were confined to

the region of the aqueduct and elsewhere in the brain other change could not be found.

Spiller,[1] in 1902, was the first to study in detail this type of occlusion, and reviewing the previous literature on the subject brought it up to date. He also was the first to draw attention to the fact that the changes in the tissue around the aqueduct are similar to the changes occurring around the central canal of the spinal cord under certain conditions. His first patient was a man, aged 19, who had had headaches since childhood. Six months before death, severe symptoms developed, and because of the ataxia, headaches, vomiting and papilledema a diagnosis of cerebellar tumor was strongly suggested. In this case, the same proliferation of subependymal glia and ependymal tubules was present as in cases 1 and 2 reported here. Spiller, at the time, concluded that the aqueduct probably was congenitally small because of the life-long headaches the patient had had, but he considered that the more recent symptoms were due to occlusion of the aqueduct by progressive proliferation of the surrounding glia. In 1907, Spiller and Allen[2] reported a second case, but in this instance there was an extremely narrow canal lined with ependyma and without much, if any, increase in the surrounding neuroglia. It apparently was a case of congenitally small aqueduct, without any progressive changes. Finally, in 1916, Spiller[3] summed up all his experiences and added a study of the normal variations in the aqueduct of Sylvius in thirty-eight brains taken at random. He drew some valuable conclusions from this study. Normally, in fetal life, the aqueduct is large but gradually becomes smaller before birth. This narrowing may be carried beyond the normal degree, so that a congenital type of occlusion may occur, naturally resulting in hydrocephalus of the obstructive type appearing before or shortly after birth. On the other hand, there was evidence in some of the brains which Spiller studied that the narrowing of the lumen may be quite defective, and large canals of various shapes may result. It is also natural to assume that in these cases clinical symptoms cannot result. Between these two types, there was not only an immense variation in the size, shape and character of the lumen, but also some other variations from the normal that have considerable bearing on the problem at hand.

In the first place, the glia beneath the ependymal lining may be of greater density than that a little more remote, hinting no doubt at future

1. Spiller, W. G.: Two Cases of Partial Internal Hydrocephalus from Closure of the Interventricular Passages, Am. J. M. Sc. **124**:44, 1902.

2. Spiller, W. G., and Allen, A. R.: Internal Hydrocephalus: With Report of Two Cases, One Resulting from Occlusion of the Aqueduct of Sylvius, J. A. M. A. **48**:1225 (April 13) 1907.

3. Spiller, W. G.: Syringoencephalia, Syringoencephalomyelia; the Function of the Pyramidal Tract, J. Nerv. & Ment. Dis. **44**:395, 1916.

potentialities of proliferation. The cavity of the aqueduct may be oval in cross-section, with a layer of ependymal cells lining it, and with a few processes extending into the lumen, or at some places small masses of ependymal cells may extend from the ependymal lining into the surrounding tissue. The cavity also may be T-shaped, with two sides of each arm almost touching, and small cavities lined with ependymal cells and resembling a central canal may be found about the aqueduct. A line of ependymal cells, in masses, containing ependymal-lined cavities, may be at a short distance from the aqueduct and may be independent of the ependymal lining of the aqueduct; nests of ependymal cells about the canal are not uncommon. There may be remarkably narrow elongation of the aqueduct dorsoventrally, lined with ependymal cells, and there may be masses of glia cells below the long narrow slit, suggesting that during the closing in of the aqueduct in the developing brain the occlusion was incomplete. A similar process occurs occasionally in the spinal cord, when the central canal extends in a triangular form into the posterior system and is surrounded by masses of glial cells.

All these changes Spiller found in his studies on a series of unselected brains. Again and again he drew attention to the similarity between changes that he found around the aqueduct and changes that may be found around the central canal of the spinal cord, even under supposedly normal conditions. There is the same neuroglial proliferation around the central canal, leading to its occlusion, and similar collections of ependymal cells in masses or in tubules. Haenel [4] has produced some excellent pictures of the cellular proliferation about the central canal, with duplication of the canal, in connection with his work on syringomyelia. The zone surrounding the central canal of the cord is one of considerable cellular activity. Normally, it leads to occlusion of the canal, usually during the first two decades of life, but sometimes abnormal processes such as syringomyelia and formation of tumor may arise as a result of aberrant activity. Considering the aqueduct of Sylvius as a developmental homolog of the central canal, one may readily understand why such similar histologic changes may occur around them. About the aqueduct of Sylvius a process probably occurs which resembles very closely, and which probably is identical with that seen more frequently about the central canal of the cord. If occlusion of the central canal occurs normally, as it does in the first few years of life, wholly analogous processes may, in certain cases, take place around the aqueduct some time after birth and may lead to its occlusion with severe, if not fatal, symptoms resulting from obstructive hydrocephalus. Cases 1 and 2 reported here belong to this class. In the second case nothing

4. Haenel, H.: Syringomyelie, in Lewandowsky, M.: Handbuch der Neurologie, Spezielle Neurologie I, Berlin, Julius Springer, 1911, pt. 2, p. 572.

was found to suggest, clinically, that a developmental anomaly might be present, but in the first the presence of a meningocele certainly gave the impression that something had gone wrong in the patient's development. It is probable that occlusion of the aqueduct, of the type described, may occur at any age after birth. The younger of the two patients was aged 4 years, and Schlapp and Gere [5] published reports of a series of eight cases wherein occlusion apparently was of this type in two, and in these two, death occurred at 3½ years and at 5½ months, respectively. Spiller's patient, however, lived until the age of 19, and a patient described by Friedman [6] lived until the age of 22. The anomalous changes described by Spiller may, however, appear in one form or another at any time after birth and a potentiality toward occlusion always may be present.

Case 3.—*History.*—A girl, aged 10, was brought to the Mayo Clinic on June 7, 1927, because of difficulty in walking. Nothing unusual was described as to her birth and development, and the only illness she had had was appendicitis with the formation of an abscess, for which surgical drainage was carried out two and a half years before. The illness of which the complaint was made apparently had begun about a month after the appendectomy. At that time she had complained of frontal headaches, chiefly coming on in the morning and lasting from one to three hours. At the same time as the onset of headaches, the patient became drowsy and slept a great deal, and her memory began to fail. A year previous to examination, her school teacher had noticed failure in school work, and about the same time she became clumsy in gait and in the use of the hands. This clumsiness and unsteadiness in walking increased to the point that three weeks before examination she had ceased to walk.

Examination.—The patient was obese and was unable to walk, stand or even sit up. She had generalized and severe ataxia and such incoordination of all bodily movements that she was almost helpless. Her memory, attention and cooperation were definitely reduced. Her head was larger than normal, and there was a hydrocephalic note on tapping the skull. Examination of the eyes revealed papilledema of each optic nerve, of about 3 diopters, with hemorrhages. Ocular movements, however, were normal in all directions, and changes in the visual fields were not observed. The tendon reflexes everywhere were exaggerated, and Babinski's sign was present bilaterally. Roentgenographic examination of the skull gave evidence of increased intracranial pressure, with almost total destruction of the sella turcica. A diagnosis of chronic internal hydrocephalus was made, but the cause could not be established by clinical examination. Accordingly, it was advised that an effort be made to find the site of block in the cerebrospinal pathways.

Operation.—On June 16, 1927, Adson established the patency of the communication through the lateral ventricles by the injection of dye into one lateral ventricle and recovering it from the other side. Dye, however, could not be recovered from the cisternal puncture; it was assumed, therefore, that there was

5. Schlapp, M. G., and Gere, Belden: Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus, Am. J. Dis. Child. **13**:461 (June) 1917.

6. Friedman, E. D.: A Case of Chronic Internal Hydrocephalus Due to Blocking of the Aqueduct of Sylvius, J. Nerv. & Ment. Dis. **59**:489, 1924.

blockage at or below the aqueduct of Sylvius. Cerebellar exploration was done then, but nothing abnormal was found in the cerebellum or fourth ventricle. A diagnosis of occlusion of the aqueduct was made and an attempt was made to catheterize the aqueduct. Circulation apparently was reestablished, since dye was recovered through the catheter, and further operative work was not done. Following these operative measures the patient failed to rally; the temperature and pulse rate gradually increased, and she died on the third day following the operation.

Necropsy.—On gross examination of the brain, moderate flattening of the convolutions was apparent. The floor of the third ventricle protruded markedly, compressing and thinning the optic chiasm. On section of the brain, in the sagittal direction, severe hydrocephalus of the lateral and third ventricles could

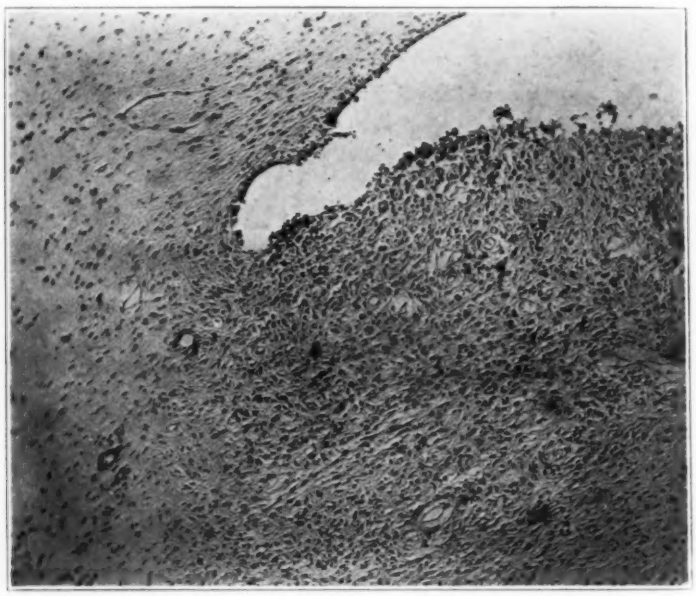

Fig. 2 (case 3).—Very early tumor (astroblastoma) arising in the floor of the aqueduct and growing upward to occlude its lumen (× 75).

be seen, with, however, no dilatation or abnormal change in the fourth ventricle. The ependymal surfaces everywhere were smooth, without granulation or exudate, and the choroid plexus seemed normal to the naked eye. The formina of Monro were markedly dilated, but the aqueduct of Sylvius apparently was occluded in its caudal portion, with dilatation of its rostral third.

Microscopic Examination.—Sections of the mesencephalon showed, as has been mentioned, dilatation of the rostral portion of the aqueduct of Sylvius which, at this place, measured almost 6 mm. in diameter. The ependyma of this portion was flattened and the fibrils of subependymal glia ran in a direction parallel to the course of the aqueduct. More caudally, the subependymal glia had proliferated chiefly on the ventral wall of the aqueduct, so that the ependymal lining was displaced upward, and the aqueduct assumed a crescentic shape. Still more in the caudal direction, this proliferation had become much more marked, the ependy-

mal lining had disappeared, and the aqueduct was reduced to a very small slitlike opening. The ependyma on the dorsal wall was preserved, but was flattened and stretched to the utmost. In the vicinity of the aqueduct, at this point, there were to be seen numerous small tubules lined by ependymal cells. The proliferated subependymal glial tissue was moderately cellular, but the nuclei varied greatly in size and shape. With Orlandi's modification of Bielschowsky's silver impregnation method, it was observed that many of these cells were bipolar, with rather heavy processes at either end. Mallory's phosphotungstic acid-hematoxylin stain revealed that the processes were more abundant and could be demonstrated by the silver stain. These processes were long and wavy and ran a tortuous course. Although most of the cells were bipolar, in some three or more processes emerged from the body of the cell. Cells without processes of any kind were seen, but

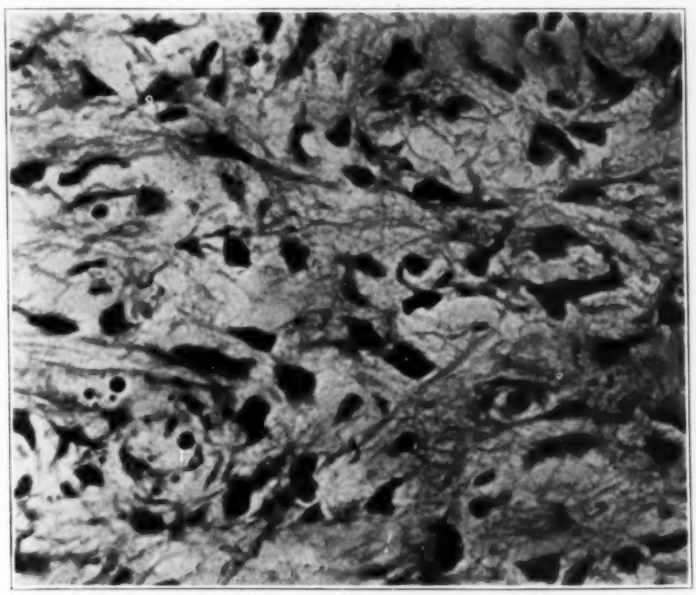

Fig. 3 (case 3).—High power detail of tumor cells (× 350).

they were rare. The blood vessels in this tissue had very thin walls, but perivascular infiltration of lymphocytes or of any other kind of cells could not be seen. The tissues surrounding the lateral, third and fourth ventricles apparently were normal, and signs of inflammation were not found anywhere. The choroid plexuses as well as the meninges were normal.

Case 4.—*History.*—A boy, aged 8, was brought to the Mayo Clinic on June 27, 1928, because of difficulty in walking and failing vision. He had been born prematurely, at 7 months, and had weighed, at birth, 3 or 4 pounds (1.4 or 1.8 Kg.), but his development thereafter apparently had been normal. Four months before visiting the clinic and following an attack of whooping cough, he had severe frontal headaches. With these headaches there was marked drowsiness, so that he slept most of the time for one week; during this time the neck had been rigid and the head retracted. After several weeks, there had been apparent improvement in the headaches and drowsiness and he was able to leave his bed,

but the family noted that he was less active, had less initiative and seemed somewhat shaky and awkward in all bodily movements. About this time, the patient's vision began to fail and the headaches returned; however, the headaches were less severe. He was able to go to school, and apparently he made good grades while he was there. During the month preceding his visit to the clinic, he became more listless and apathetic, and a rather marked increase in weight and a divergent strabismus of both eyes were noticed.

Examination.—The patient's weight was 66½ pounds (30.1 Kg.). The temperature was normal and the pulse rate, 68. The basal metabolic rate on two occasions was —18 and —25, respectively. Examination of the eyes showed vision of 6/30 in the left eye, but with the right eye only moving objects could be distinguished. Perimetric fields showed bitemporal hemianopia for form and color. The pupillary reflexes were markedly diminished, much more so on the right side. Examination of the ocular fundi showed full, pale disks. The ocular movements apparently were normal except that there was complete loss of convergence and persistent divergent strabismus. Roentgenographic studies of the skull showed some evidence of increased intracranial pressure, but the outline of the sella turcica was normal. There was general loss of speed in all muscular movements but no paralysis. The tendon reflexes were somewhat increased generally, more so on the left side; the Babinski sign was positive bilaterally. There was incoordination of the upper extremities, also more marked on the left, and although the patient was able to walk, the gait was both spastic and ataxic. Tapping the skull elicited a hydrocephalic percussion note, and the head in its greatest circumference was 57 cm. A diagnosis of tumor in the region of the optic chiasm was made.

Operation.—The patient was operated on on July 10, 1928, and the region of the optic chiasm was explored through the transfrontal route. On elevation of the right frontal lobe, the chiasm was seen to be compressed by a markedly dilated and bulging third ventricle. This was tapped and about 400 cc. of cerebrospinal fluid was drained. The postoperative course for the first twenty hours was uneventful; then stupor, generalized twitchings and convulsions developed. The temperature rose to 102 F., breathing became rapid and noisy and the patient died on the third day after operation.

Necropsy.—Gross inspection of the brain disclosed moderate flattening of the convolutions. Coronal sections through the brain showed marked internal hydrocephalus of the lateral and third ventricles, with preservation of the normal shape and size of the fourth ventricle. The ependymal surfaces were smooth and the meningeal surfaces were normal. The septum pellucidum was thinned and perforated. There was marked protrusion and bulging of the floor of the third ventricle, with flattening of the optic chiasm. Nothing very striking could be seen on inspection of the midbrain.

Microscopic Examination.—Sections through the midbrain showed that the aqueduct of Sylvius was almost completely occluded, so that only a few small ependymal-lined tubules were left and these were filled with an exudate comparatively devoid of cells. The ependyma lining these tubules was flattened and in some places completely absent. The main cause of the occlusion apparently was proliferation of the glial tissue surrounding the aqueduct. This tissue seemed to be mainly composed of glial cells with an excessive number of fibrils, and in some places the cells were collected in small groups. These cells did not seem to be normal ependymal cells, for the majority were bipolar, with heavy, wavy processes composed of numerous fibrils which were divided and interlaced with

fibrils from adjacent cells. Some of the cells also were multipolar, with three or more processes which were similar to those of the bipolar cells. In the endeavor to identify the type of cell, sections stained with Cajal's gold chloride and sublimate were examined. This stain seemed to show that the majority of the proliferated cells around the aqueduct were bipolar spongioblasts; a few were astroblasts. In the edge of the area of proliferated spongioblasts there was a region of gliosis composed mainly of fibrous astrocytes. These astrocytes seemed to be larger than normal, but their processes were much more delicate. The cellular proliferation around the aqueduct extended for a considerable distance laterad and dorsad into the base of the colliculi, but only to a slight extent rostrad, and not at all caudad into the pons. Mitotic figures were not seen. Occasionally, in some perivascular spaces a few lymphocytes could be seen, but cells of the acute inflammatory type were not seen. In the ependyma of the lateral and third ventricles there were only a few small nodules, such as those found in early granular ependymitis, but except for this there was no proliferation of the subependymal glia. In a few vessels in the subependymal tissue surrounding the ventricles there were small numbers of lymphocytes; this was particularly true in the floor of the third ventricle. The choroid plexuses appeared to be normal and the ependymal tissues surrounding the fourth ventricle were normal. The meninges did not seem to have any pathologic changes, inflammatory or otherwise.

Comment on Cases 3 and 4.—In these two cases the cause of occlusion apparently was a very small and early tumor process. In case 3 the tumor was apparently an astroblastoma; in case 4 it was a spongioblastoma. Death occurred in each case before the tumor had reached any great size. Gross inspection of the specimen obtained at necropsy was in itself insufficient. The diagnosis had to be made by careful histologic study. Cushing [7] illustrated this by a case report and photomicrograph of the aqueduct in a similar case. The patient was a boy, aged 9, who had been nearly blind from obstructive hydrocephalus, thought to be due to a subtentorial tumor. He died several weeks after a negative cerebellar exploration and at necropsy nothing was found to account for the hydrocephalus; it was ascribed to possible ependymitis or arachnoiditis. Reinvestigation of the tissues, with a study in serial sections of the brain stem, disclosed a microscopic subependymal glioma arising in the floor of the aqueduct and occluding its lumen. One patient in Schlapp and Gere's [5] series, a boy, aged 1 year and 3 months, died from what was disclosed to be a tumor of the midbrain, and one of Dandy and Blackfan's [8] series, a boy, aged 5 years, had a similar condition. Both of these tumors, however, were relatively gross and little study was needed to establish the diagnosis. It is, however, manifest in all such cases that the tumor need not be very large in order to occlude the aqueduct and to produce hydrocephalus and death.

7. Cushing, Harvey: Notes on a Series of Intracranial Tumors and Conditions Simulating Them, Arch. Neurol. & Psychiat. **10**:605 (Dec.) 1923.

8. Dandy, W. E., and Blackfan, K. D.: Internal Hydrocephalus, Am. J. Dis. Child. **14**:424 (Dec.) 1917.

As a possible source of origin for these tumors, one is reminded of the ependymal cell nests described by Spiller that lie some distance from the aqueduct in the subependymal glia. In the spinal cord such an origin is not uncommon, but since such ependymal cell clusters are relatively more common around the central canal of the cord, intramedullary glioma, or central gliosis, occurs more frequently than similar processes around the aqueduct.

So far, conditions have been described that have been confined to the region of the aqueduct. Other portions of the brain and its ventricular system were intact and essentially there existed a strictly local and almost microscopic proliferation of the tissues leading to occlusion. A third, and last, group has yet to be described, wherein the changes were more diffuse and involved other portions of the brain as well as the mesencephalon with its aqueduct. In this group the pathologic process was totally different from those hitherto described.

Case 5.—*History.*—A girl, aged 16, was brought to the clinic on July 7, 1925, because of dimness of vision and difficulty in walking. The patient had been born prematurely and was of rather feeble vitality in infancy. At the age of 3, she had had what was diagnosed as scarlatina and meningitis. As a residue from this she always had been somewhat deaf. However, her development and progress following convalescence seemed to have been normal. She had done well in school and had reached the second year of high school. About two years before admission, it had been noticed that she was somewhat awkward in her movements, particularly in walking, and the patient herself complained of a slight feeling of stiffness in both legs. One year before, the patient and her mother had noticed a gradual decline in the quality of her school work. She seemed to be unable to grasp ideas as easily as before; she found that her work was more difficult and that it required more preparation. Seven months before, severe headaches had appeared, coming on chiefly in the morning. They usually appeared before she arose, and disappeared by 11 a. m. At the same time as the appearance of the headaches, there was gradual, progressive failure of vision. In the last few months before admission, the difficulty in walking, visual disturbance and mental deterioration had progressively advanced. There had been a gain in weight of 30 pounds (13.6 Kg.) in one year.

Examination.—The patient appeared to be overweight; she weighed about 140 pounds (63.5 Kg.) and was rather apathetic, with slow and inaccurate mental processes. Intelligence, memory, attention and cooperation were very definitely reduced, so that she was unable to perform simple problems in arithmetic. The basal metabolic rate was —19. There was papilledema of both eyes, with secondary optic atrophy. The disks were elevated 2 diopters in each eye, and perimetric fields showed marked concentric contraction for form and for color vision. Roentgenographic studies of the skull showed complete destruction of the sella turcica. Obvious paralysis was not present, but generalized loss of speed in all muscular movements was observed. The left patellar tendon reflex was a little more active than the right, and Babinski's sign was positive on that side. On walking, the gait was not much affected, but there was slight loss of speed on the left side, apart from general slowness. There was tremor in both hands. A

diagnosis of chronic internal hydrocephalus was made, but the etiology could not be estimated by clinical methods except that possibly the condition was delayed residue from the scarlet fever and meningitis of childhood.

Operation.—A right subtemporal decompression was done on July 18, 1925, but nothing more than marked increased intracranial pressure could be found. Following this operation, convalescence was uneventful until the eighth day, when the temperature rose suddenly and epileptiform seizures occurred. The patient's condition temporarily improved, but later she became stuporous and died on August 12.

Necropsy.—This was performed a few hours after death. Gross examination of the brain showed the convolutions to be markedly flattened, and on coronal section a very severe degree of internal hydrocephalus of the lateral and third ventricles was visible without, however, enlargement or change in the shape of the cavity of the fourth ventricle. On examination of the ependymal surfaces there was obviously very definite thickening of that lining in both lateral ventricles and in the third ventricle. The fourth ventricle apparently was normal, and the aqueduct of Sylvius was occluded by this proliferation, chiefly in its rostral portion, but it seemed to be patent in its caudal portion. This thickening of the ependyma was apparent as a thick, gelatinous exudate, 2 mm. thick, and it was somewhat more marked in the left lateral ventricle. The choroid plexus on that side was covered with exudate. The third ventricle was somewhat less involved than the lateral ventricles. The meningeal surface of the brain did not show evidence of actual meningitis, but there was slight opacity of the arachnoid.

Microscopic Examination.—Sections through the aqueduct showed it to be completely occluded. This occlusion was due to the fact that the aqueduct was filled with a large number of cells that had deeply stained nuclei in a delicate network of fibers. The cell bodies were indistinct and in many places the cytoplasm was either extremely slight or absent. Various types of nuclei were present, suggesting that different kinds of cells composed this mass of tissue. The normal ependymal lining of the aqueduct was, for the most part, absent, but occasionally strips of it were preserved. These ependymal cells were proliferated in places. First it was assumed that this proliferation was responsible for the cell mass within the aqueduct, but in many other places there seemed to have occurred herniation of the subependymal tissues through the gaps in the continuity of the ependymal lining. However, the majority of the cells in the aqueduct resembled ependymal cells more than cells of the subependymal glia. An occasional mitotic figure could be seen among these cells. In spite of the great mass of cellular elements filling the aqueduct, its general contour was intact. The occlusion, therefore, was not due to approximation of its walls and ependymal surfaces, but rather to plugging of the channel with a mass of these proliferated cells. The demarcation of these cells filling the aqueduct from the surrounding tissues was distinct, although here and there a few cells had wandered for slight distances into the adjacent tissues. There was but little sign of inflammation in or around the aqueduct, although occasionally a few lymphocytes could be seen in some of the perivascular spaces. On the other hand, in the walls of the lateral and third ventricles there were abundant signs of chronic inflammation, with proliferative changes of both the ependyma and the subependymal tissue. The ependymal cells in these ventricles were preserved intact; many had retained their normal cuboidal shape, whereas others were elongated and had fibrils projecting into the underlying tissues. Forming the exudate, noted already in the gross examination, there were in many areas masses of cells superficial to the intact

ependyma. Some of these cells were similar to those seen in the aqueduct, but in addition there were many lymphocytes, small blood vessels and proliferated endothelial and connective tissue cells or fibroblasts. Polymorphonuclear leukocytes were not seen. By microscopic examination this exudate was seen to be present over most of the surfaces of the third and lateral ventricles. In the fourth ventricle ependymal proliferation was not present, but in some of the perivascular spaces in the subependymal tissues there were many small collections of lymphocytes. In the choroid plexus of the lateral and third ventricles there were collections of lymphocytes and some polymorphonuclear leukocytes; occasionally a small vessel could be seen to have been the site of thrombosis. However, inflammatory cells were not present in the choroid plexus of the fourth

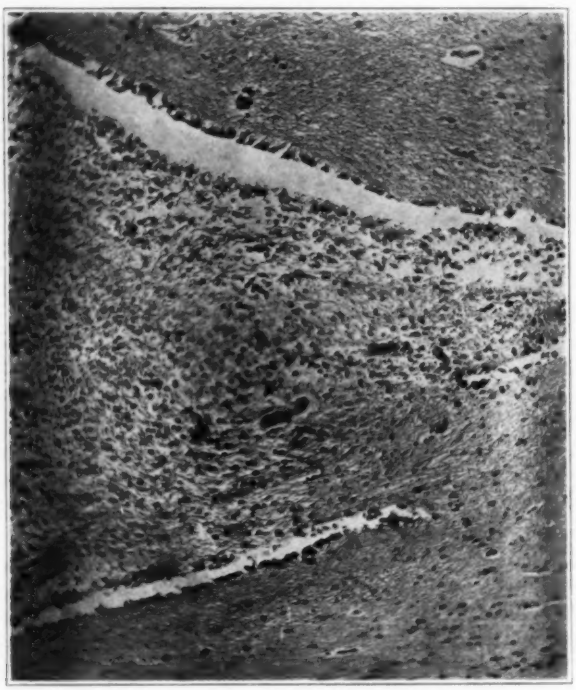

Fig. 4 (case 5).—Occlusion of the aqueduct by chronic ependymitis; aqueduct filled with large mass of cells growing into the lumen from the ependymal glia; preservation of the ependymal lining (× 75).

ventricle. In the subarachnoid spaces there were collections of lymphocytes in considerable numbers; also there were some endothelial cells but no polymorphonuclear leukocytes. The arachnoid membrane was thickened, and the trabeculae of the subarachnoid space were replaced by thickened bands of connective tissue. The inflammatory reaction was more marked around the base of the brain than on its superior and lateral surfaces. Around the base, it was most marked in the posterior fossa and particularly beneath the pons. In the cortex and subcortical tissues, inflammatory reaction was not visible.

Case 6.—*History.*—An unmarried woman, aged 27, came to the Mayo Clinic on Sept. 15, 1926, because of headaches and impairment of vision. Four years

previously she had had an attack of severe frontal headache lasting only a few weeks. Another attack of the same nature occurred two years later and lasted about the same time. She was then apparently well up to nine months before the operation, when again the headaches recurred, associated with constant fatigue and occasional blurring of vision. A month before examination, this headache had increased in frequency and severity so that she was confined to bed, and morphine was required. Spinal puncture with drainage had relieved the pain to some extent. Three days before admission, she had had horizontal diplopia, and during the three weeks preceding her visit to the clinic she had noticed that her vision had become considerably reduced.

Examination.—The patient was well developed and well nourished, not apparently acutely ill and not confined to bed. The basal metabolic rate was —19. Examination of the eyes showed vision in the right eye to be 6/12 and in the left, 6/10. The pupils were large and reacted slowly and inefficiently to light.

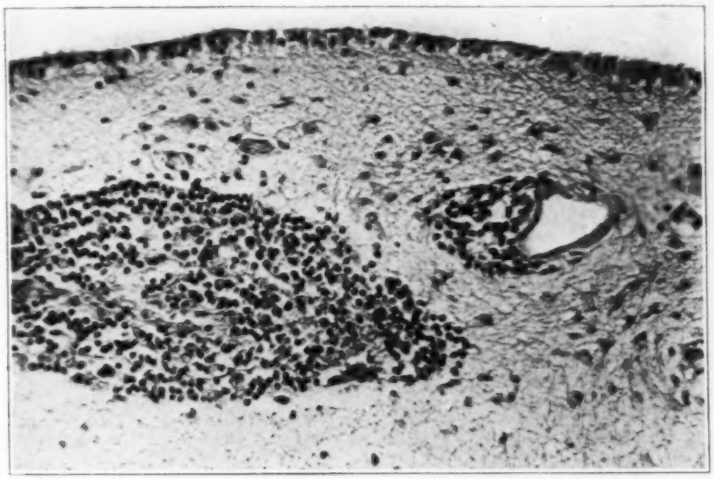

Fig. 5 (case 5).—Section of the wall of the lateral ventricle; adventitial infiltration of the smaller vessels by inflammatory cells; large collections of inflammatory cells in the subependymal tissue; exudate not present in this area (× 150).

The perimetric visual fields were normal. Examination of the fundi disclosed slight blurring of the upper margin of the disk, apparently structural in character, but other changes were not observed. Roentgenographic studies of the skull showed the outline of the sella to be slightly enlarged, and evidence of increased intracranial pressure in the appearance of the bones of the skull. Examination of physical functions showed slight loss of speed and increased tonus of the left side of the body, and on that side the tendon reflexes were increased, with, however, Babinski's sign positive bilaterally. In walking there was slight spasticity of the left leg. Altogether, apart from the observations mentioned, the clinical picture was vague and ill defined. It was not possible to make a more definite diagnosis than that of intermittent attacks of hydrocephalus of unknown cause.

Operations.—On Sept. 4, 1926, an attempt was made to estimate the patency of the channels of communication of the cerebrospinal fluid. Dye was injected

into the right lateral ventricle and was found to communicate freely with the left lateral ventricle. Dye, however, could not be obtained on cisternal puncture, which indicated a block in the pathways of the cerebrospinal fluid in the region of the aqueduct of Sylvius or the fourth ventricle. On Sept. 29, 1926, a cerebellar exploration was performed, but nothing unusual could be discovered in the cerebellum or fourth ventricle, and communication between the third and fourth ventricles was seen to have been blocked. A surgical diagnosis of occlusion of the aqueduct was made. The patient died suddenly on the next day.

Necropsy.—Gross inspection of the brain showed a moderate degree of flattening of the convolutions with marked herniation of the cerebellum and medulla through the foramen magnum, as well as herniation of the brain through the opening of the tentorium. The brain was opened by sagittal incision, and marked internal hydrocephalus of the lateral and third ventricles could be seen without, however, dilatation of the fourth ventricle. There was a slight granular appearance of the floor of the lateral ventricle and also of the third ventricle, and ependymal plaques were present on the floor of the lateral ventricle over the thalamus and caudate nucleus. There was some pouching of the floor of the third ventricle. A few granulations were present on the floor of the fourth ventricle. The rostral portion of the aqueduct cerebri was patent and slightly dilated, but the caudal portion was apparently occluded.

Microscopic Examination.—Sections across the aqueduct of Sylvius showed proliferation of the ependymal cells, but even greater proliferation of the subependymal tissues. Many cells in the subependymal area appeared to be ependymal in character, with long fibrils forming whorls such as are often seen when ependymal cells proliferate. These cells, however, did not have the deeply stained nuclei such as could be seen in those cells that had proliferated from the ependyma of the aqueduct. In spite of this existing proliferation, mitotic figures could not be seen. In many places the lining ependymal cells were pushed into the lumen of the aqueduct because of the underlying proliferation. Occasionally, small tubules had been formed by the ependymal cells in the subependymal glia. Besides this obvious proliferation of tissue around the aqueduct, there was a slight inflammatory reaction, shown in the collection of lymphocytes in the perivascular spaces even at considerable distances from the ependymal surface. Throughout the midbrain, even at some distance from the aqueduct, there was a certain degree of glial proliferation; rod cells were abundant, although with the Cajal's gold chloride and sublimate method some of the proliferated glia cells were seen to belong to the astrocyte group. Besides the perivascular infiltration of the ordinary lymphocytes seen in the sections, there was also some collection of round nuclei in the perivascular spaces of the arterioles and capillaries, and some of these seemed to be the nuclei of oligodendroglia cells. Several small petechial hemorrhages were present in the glial tissue near the aqueduct. In the lateral and third ventricles were also areas of proliferation of the subependymal tissue. This tissue was quite cellular, in contrast to the usual appearance of this zone, and many of the cells seemed to be ependymal in type. The depth of this zone varied much in different places. The ependyma lining these ventricular surfaces was only one cell thick; occasionally it was absent, so that a fibrillar zone of tissue was present without any ependymal covering, the fibrils being apparently in contact with the cerebrospinal fluid. In these regions there were also rows of ependymal cells beneath such areas of the ventricular wall as had been denuded of ependyma. These cells were sometimes arranged in tubules, and sometimes as an irregular layer without any definite architecture. Through gaps in these layers of ependymal cells the subependymal glial tissue flowed toward the ventricular cavity and

became heaped up as a granulation in varying stages of development. Everywhere over the ependymal surfaces of the ventricles, these small nodules of glial tissue projected upward, forming granules, and the apexes of these granules were usually denuded of ependyma. These granules were seen in all stages of formation and represented a very marked example of so-called granular ependymitis. Frequently, in the perivascular spaces of vessels beneath the ependyma of the lateral and third ventricles small collections of lymphocytes were seen. These collections were, however, not numerous and the cells were few in number. In the choroid plexus of the third and lateral ventricles were diffusely distributed small lymphocytes, chiefly in the connective tissue of the choroidal papillae, but thrombosis in the vessels could not be seen and their ependymal lining appeared normal. The ependyma of the fourth ventricle showed proliferative changes that were even more marked than those of the lateral and third ventricles. Many

Fig. 6 (case 6).—Chronic granular ependymitis; early stages of the formation of granulation (× 150).

granulations were seen in various stages of formation, but in at least one place there was marked proliferation of the subependymal tissues consisting of cells that were ependymal in character, with an occasional mitotic figure. Around some of the vessels near the fourth ventricle were collections of lymphocytes, but this perivascular infiltration was not marked and there was nothing to suggest an acute inflammatory reaction. The proliferation in the subependymal region of the fourth ventricle was too superficial to involve any of the nuclei of the cranial nerves. In the subarachnoid spaces of the posterior fossa, particularly around the medulla and the anterior surface of the pons, some lymphocytes were present, but no polymorphonuclear leukocytes. There was no connective tissue, proliferation or thickening of either the arachnoid or the pia mater, and the only evidence of inflammation in this region was the presence of the small number of lymphocytes in the subarachnoid space. Sections of the brain taken elsewhere did not show obvious changes.

Comment on Cases 5 and 6.—The patients in the last two cases presented enough evidence to lead to a reasonable conclusion that they had suffered from a diffuse chronic inflammatory process involving the ependymal lining of the ventricles as well as the subependymal tissue. However, they differed somewhat in character. In case 5 the process was visible grossly as a thick, gelatinous exudate covering the surface of the lateral and third ventricles, and microscopically it was seen to consist of masses of chronic inflammatory cells. The aqueduct was filled with cells arising probably from the subependymal tissues. In case 6 there was diffuse, granular proliferation of the subependymal tissues and instead of a smooth exudate, innumerable small granules could be seen constituting so-called granular ependymitis. The aqueduct in this case was occluded by proliferation of the glial elements as well as the ependyma, but the outline of the canal was lost and its lumen occluded. In both instances there was a certain degree of adventitial infiltration around the smaller and medium-sized blood vessels. Altogether, each case was one of slowly progressive chronic ependymitis. Both patients were considerably older than the others, and clinical diagnosis was extremely difficult. More recently, Globus and Strauss [9] reported a case of subacute diffuse ependymitis and gave an excellent review of the literature on ependymitis. Their patient, a man, aged 42, had an illness characterized by remissions and exacerbations and lasting altogether about ten months before death. Necropsy showed a markedly swollen and thickened ependyma in the lateral ventricles, and in the third ventricle the ependyma and subependyma had separated from the wall of the cavity in the form of a cyst filling the ventricles with its apex inserted into the aqueduct of Sylvius and occluding it. The foramen of Monro was also occluded by the swollen ependymal tissues. The intensity of the inflammatory process varied in different parts of the ventricular system. In the ependymal lining of the aqueduct changes of a more chronic nature had occurred: it was entirely disorganized and was replaced by a wide zone of unorganized necrotic tissue giving the impression of a hyalinized band distinctly separated from the underlying subependyma. The latter showed a wide zone of gliosis. The changes in the walls of the third ventricle were the most acute. Here the ependyma and subependyma had separated from the rest of the wall to form the cyst already mentioned. The wall of the cyst consisted mainly of a narrow zone of necrotic ependyma and a thickened subependyma to which portions of brain were still attached. Numerous infiltrated vessels could be seen. Milder changes were seen elsewhere, so that in some places the ependymal lining was preserved, but beneath

9. Globus, J. H., and Strauss, I.: Subacute Diffuse Ependymitis, Arch. Neurol. & Psychiat. **19**:623 (April) 1928.

it there was mild gliosis of the subependyma and adventitial infiltration of some of the blood vessels. The authors considered it an impossibility to recognize these cases of chronic or subacute ependymitis during life, and indeed such was our experience.

GENERAL COMMENT

From the clinical standpoint, the common feature in the whole group of patients was the extreme difficulty in reaching any accurate conclusions as to what pathologic processes were responsible for the patient's symptoms. It was clearly manifest in all of them that there was an increase in intracranial pressure and probably hydrocephalic distention of the ventricles of the brain. The ages of the patients removed them from the category of patients with congenital hydrocephalus. Most of them had lived apparently normal lives until the first symptoms appeared and definitely suggested a disease acquired after birth. The course was relatively acute in one case (case 2), symptoms having been present only nine days before death, but the patients in the other cases had been ill for periods varying from seventeen months to five years. In one case a mistaken diagnosis of suprasellar tumor was made, an error not infrequently due to the symptoms caused by compression of the sella and optic chiasm by the bulging floor of the third ventricle. In five cases there was a suggestion of hypopituitarism, due, no doubt, to the same mechanical factor and already amply described by Rhein,[10] Friedman,[6] Pollock,[11] Strauch [12] and others. Ataxia was present in three cases; these patients were children aged between 8 and 11 years. This is a period of life when it is notoriously difficult to distinguish clinically between tumor of the vermis and other cause of obstruction of the cerebrospinal fluid pathways. Altogether there was nothing outstanding in the clinical characteristics of the whole group, nor was there anything that would give a reasonable assurance as to the identity of the underlying morbid processes.

From the pathologic standpoint, the six cases fall into three groups of two each. In the first group the condition was confined to the region of the aqueduct, was proliferative and resembled in its general characteristics similar changes that have been found going on around the central canal of the spinal cord. The second group consisted of minute, rapidly growing tumors in a very early stage of formation.

10. Rhein, J. H. W.: Hypophysial Pressure Symptoms Due to Hydrocephalus Causing Cystlike Distention of the Third Ventricle, Arch. Neurol. & Psychiat. **13**:71 (Jan.) 1925.

11. Pollock, L. J.: Hypopituitarism in Chronic Hydrocephalus, J. A. M. A. **64**:395 (Jan. 30) 1915.

12. Strauch, August: Hypophysial Dystrophy in Hydrocephalus, J. A. M. A. **72**:1731 (June 14) 1919.

They were so situated that before they had reached any appreciable size the aqueduct became inevitably compressed and ultimately occluded. In this group also, the changes were confined to the region of the aqueduct. The third group represented a diffuse inflammatory process involving the ependyma of almost the whole ventricular system, with the subependymal tissue. Because of swelling of these tissues, the aqueduct, being the longest and narrowest channel of communication between the different ventricular cavities, necessarily became occluded. In the two last cases it was not definitely ascertained how the infection was acquired, nor was it clear by what pathways such an infection entered

Summary of Clinical Features of Six Cases of Occlusion of the Aqueduct of Sylvius Due to Various Causes

Group	Case	Age, Years, and Sex	Initial Complaint	Course	Duration	Outstanding Clinical Data
Simple hyperplasia	1	11 F	Convulsions	Remittent	5 years	Meningocele; obesity; ataxia; optic atrophy
	2	2 M	Headaches	Progressive (short)	9 days	Retraction of head; rigid neck; papilledema
Formation of tumor	3	10 F	Headaches	Progressive	2½ years	Obesity; ataxia; mental deterioration, papilledema
	4	8 M	Headaches	Remittent	17 months	Obesity; low basal metabolic rate, bitemporal hemianopia; ataxia
Inflammation	5	16 F	Ataxia	Progressive	2 years	Obesity; low basal metabolic rate; mental deterioration; papilledema
	6	27 F	Headaches	Remittent	4 years	Diminished pupillary reflexes; low basal metabolic rate

the ventricular system. The patients in the two cases comprising the last group were much older than any of the others, which may or may not have some significance.

The study covers some of the possibilities that may lead to occlusion of the aqueduct of Sylvius, together with the clinical symptoms so produced. The conditions manifested by the patients could not be differentiated by ordinary clinical methods; frequently gross inspection of necropsy material likewise failed, and in the majority of cases it was a matter of minute histologic study before a satisfactory diagnosis could be made. Nevertheless, the cases represent examples of some of the more interesting pathologic lesions found in the brain of human beings. They are interesting, if not for their intrinsic character alone, then also because of the contrast between their almost microscopic size and the severe clinical symptoms that finally led to a fatal outcome.

INTRACEREBRAL CALCULI

REPORT OF A CASE *

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The presence of intracerebral calculi, demonstrated by the roentgen rays as unchanging in size, situation and consistency during twelve years' observation, presented a problem for diagnosis in a patient who was suspected, owing to the position of these calculi, of having an intraventricular tumor.

Although calcification of one sort or another is commonly seen in tumors, similar examples of "brain stones" had not been observed in this clinic. In this case the question arose as to whether the lesions represented calcification in a granuloma, a hematoma, in areas of degeneration or in a blood vessel abnormality, or two calcified endotheliomas in the right choroid plexus. From their position the last was the favored diagnosis.

As no exploratory operative procedure was carried out in this clinic the answer to the foregoing questions would have remained unknown had not death occurred suddenly and unexpectedly while the patient was at home. The opportunity of examining the lesions was obtained, and the following clinicopathologic report of this unusual case is here presented.

Cerebral tumor suspected in a patient with intracerebral calculi. Epileptic attacks and periods of general weakness and mental anxiety for twenty-three years. Hypertension (vascular). Sudden death. Necropsy.

History.—On July 10, 1916, Philip R., aged 32, was admitted to the hospital because he was suspected of having a tumor of the brain. He had been referred by Dr. A. McAlpin of Detroit. He was readmitted in 1923, and again in 1928, so that a summary of the entire period of observation is presented as a complete history.

For twenty-three years the patient had experienced from one to five epileptic attacks a year. Each attack was preceded by muscular twitchings in the lower part of the left leg. For the past seventeen years he had also been handicapped by periods of weakness in the lower extremities, and by mental anxiety in the presence of people. History of previous injury to the head or of complaints of symptoms of increased intracranial pressure could not be elicited.

The examination on each admission showed the patient to be remarkably well developed, but apprehensive about his condition. Several times while being examined or under observation during the periods of weakness and anxiety, he was

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* From the Surgical Clinic of Dr. Harvey Cushing, Peter Bent Brigham Hospital.

scarcely able to stand or walk. No abnormal physical or neurologic conditions were detected at any period except for a moderate vascular hypertension which was first noted in 1916, at which time the systolic pressure was from 130 to 150 mm., and the diastolic 120 mm. Repeated laboratory examinations of the blood, urine and cerebrospinal fluid showed no abnormalities.

The roentgenograms taken on the first admission, in 1916, showed two dense calcified areas 1.8 and 1 cm., respectively, in diameter lying deep in the right cerebral hemisphere in the vicinity of the ventricles. They remained unchanged in size, position and appearance during the twelve-year period of observation (fig. 1).

In 1916, an exploratory craniotomy was suggested but the patient was apprehensive and he was discharged untreated. From the usual follow-up letters it

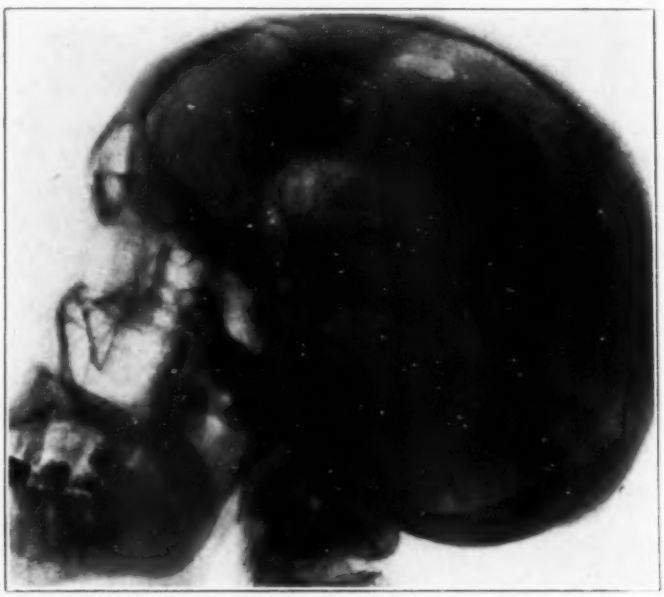

Fig. 1.—Ventriculogram made on Nov. 23, 1928, shows the size and location of the calculi. The residua of the bone flap of 1917 are also apparent. Reduced to one-third.

was learned from Dr. H. Torrey of Detroit that in June, 1917, he had performed a right exploratory craniotomy with negative results. The patient seemed benefited for a short period after the operation, and then the epileptic attacks recurred.

In November, 1923, at the second admission, ventriculograms were unsatisfactory; the patient refused any further procedure and was discharged.

During the five year interval up to the third and last admission in October, 1928, the peculiar attacks of weakness and anxiety increased in severity and in frequency so that permanent hospitalization was being considered. There were no symptoms of increased intracranial pressure. The blood pressure was recorded as from 180 to 190 mm. systolic, and 120 mm. diastolic. At this admission successful ventriculograms showed normal ventricles, and the presumptive diagnosis of intraventricular tumor was made untenable, for the calculi were located outside of the lateral ventricle (fig. 1).

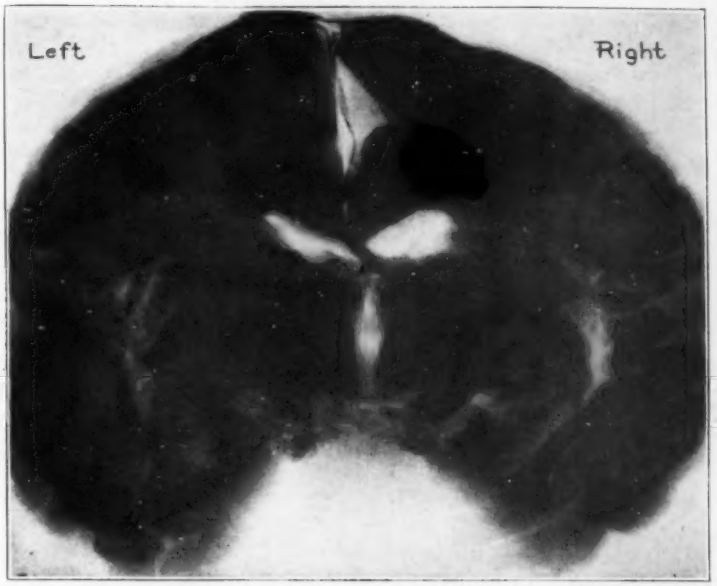

Fig. 2.—Coronal section of the brain shows the larger stone (about one-half natural size).

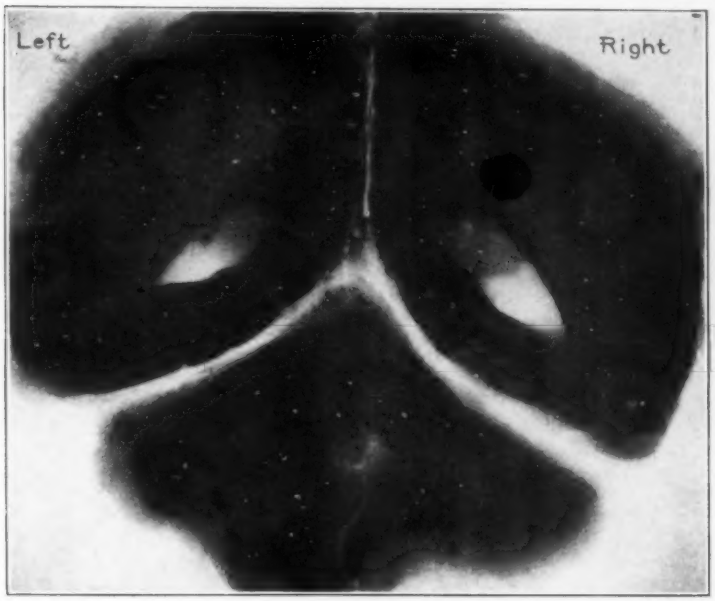

Fig. 3.—Coronal section of the brain shows the small stone in the occipital lobe (about one-half natural size).

There seemed to be no indication for an operation. The patient was discharged on December 2, apparently in excellent condition, with a diagnosis of a "cerebral tumor unverified."

At home he remained active and cheerful although still troubled with "nervousness." He gave no indication then of his unexpected and sudden death on Dec. 22, 1928. Permission was obtained to examine only the cranium and its contents.

Necropsy Observations.—The examination was made two days after death. In situ, the left cerebellar hemisphere appeared larger than the right, and fluid and clotted blood exuded from a rupture in its inferior surface to fill up the basal cisternae. The large cerebral arteries showed no pathologic changes except for an occasional thin yellow plaque. No other abnormality was noted externally.

After fixation, a series of coronal sections were made. A large fresh hemorrhage, about 3 cm. in diameter, was seen in the region of the right dentate nucleus.

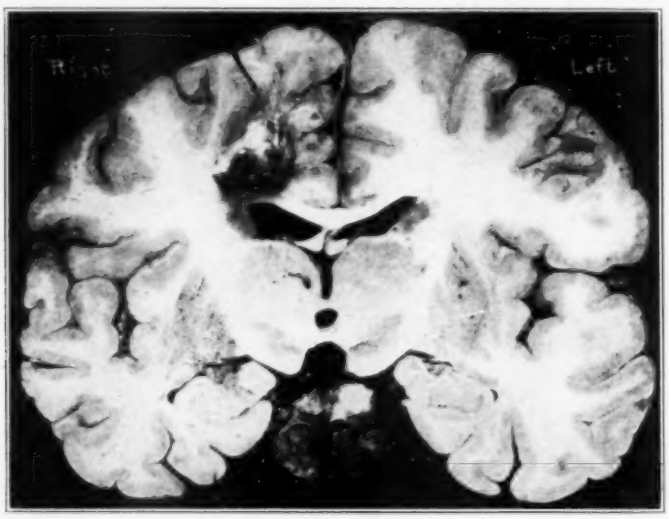

Fig. 4.—Coronal section of the brain shows the larger calculus in situ (about one-half natural size).

A small but recent hemorrhage, about 0.5 cm. in diameter, was found in the basilar position of the right side of the pons. Small cystic areas of degeneration were seen in the right dentate nucleus and the corona radiata. Ruptured blood vessels near the site of the hemorrhage were not demonstrated.

The calculi were found in the white matter of the right cerebral hemisphere. Figures 1 and 2 show the location of the irregular, large stone which measured 1.5 cm. in diameter and weighed 3.5 Gm. It was embedded in a smooth shining cavity and was attached to this wall very lightly at but one point (figs. 4 and 5). The smaller stone was located 1 cm. away from the wall of the occipital horn of the right lateral ventricle (fig. 3). This stone was decalcified and sectioned with the surrounding cerebral tissue (fig. 6). The large stone was sawed through with great difficulty. The small "stone" was sharply marked off from the adjacent normal appearing brain by the dense connective tissue wall. The section of the calculus consisted of a dense blue-staining mass. There was no evidence of bone formation. Tests for iron pigments gave negative reactions.

The wall of the cystlike area containing the largest stone was about 1 mm. in thickness. No cells were seen lining the wall which was made up of a dense mass of collagen fibers with an outer zone of neuroglia fibers and fibrous astrocytes (fig. 7). The astrocytes tended to range themselves tangentially to the wall. The blood vessels in the vicinity of the calculi presented no abnormality. There was no thickening of the leptomeninges seen in the many sections studied.

There was a moderate gliosis with small cystlike areas in the right dentate nucleus, the basal nuclei and pons. There were no evidences of recent softening or hemorrhage near these repaired zones. There was no histologic evidence of a preexisting area of necrosis in the tissues adjacent to the recent hemorrhages in the cerebellum and pons.

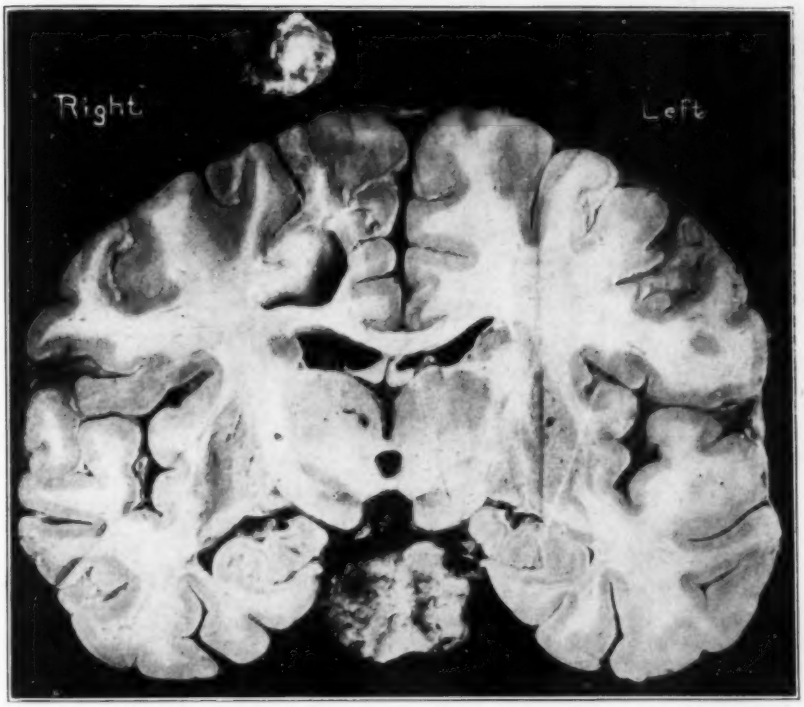

Fig. 5.—Coronal section of the brain with the larger calculus shelled out of its smooth bed.

In the many sections from all parts of the brain there were seen but two small arteries with altered walls; these vessels were located in the pons adjacent to the recent small hemorrhage. In addition to the deposits of calcium in the intima and media, the adventitia was thickened and invaded or surrounded by many small rounded cells with a large round nucleus and little cytoplasm.

COMMENT

Here, then, is a man suspected of having had partially calcified intraventricular tumors for twelve years. An exploratory craniotomy

was done in another hospital without disclosing a lesion. The first attempt at ventriculography in this clinic was unsuccessful and the patient would not allow a repetition of the procedure until several years later. Then successful ventriculograms proved that the calculi were outside the normal-appearing ventricles. Despite the proved vascular hypertension which had existed at least since 1916, this feature of the case was apparently never emphasized as a probable factor in the diagnosis.

The etiology of calculi of this sort is not definitely known. Their occurrence in the brain of this patient who showed postmortem evidence of other healed vascular accidents as well as an acute, fatal cerebellar

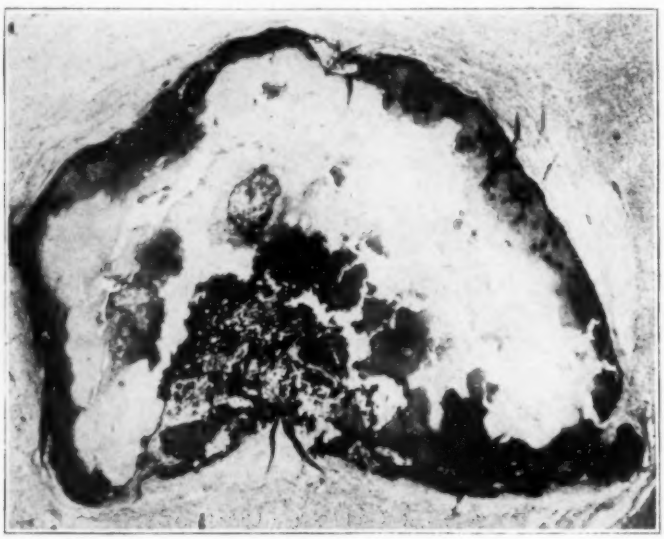

Fig. 6.—A section through the decalcified small calculus to show the sharp line of demarcation between the wall of the cavity and the calculus. Hematoxylin and eosin; × 18.

hemorrhage makes it most certain that they represent the end-result of an area of degeneration or hemorrhage with consequent absorption of the necrotic material and calcium deposition. It is extraordinary, however, in view of the general good condition of the cerebral arteries and in the absence of syphilis, that the patient should have had these multiple lesions. As stated in the protocol, two small arteries in the pons adjacent to the small and recent hemorrhage were the only vessels found to show abnormal changes. The wall of the cystlike structure containing the calculi is similar, histologically and grossly, to those produced by experimental loss of brain substance or a repaired area of softening. The immediate cause of death was the large hemorrhage in the left cerebellar hemisphere.

Areas of calcification are known to occur in many tumors, infections and abnormalities of the brain, the meninges and the blood vessels of the brain. They are also seen in the pineal gland and in the pia-arachnoid. Associated with the calcium there are often deposits of hemosiderin. The mechanism of the deposition of calcium is unknown.

While intracerebral areas of calcification are commonly found, there are few reported verified examples of the formation of actual "calculi" or "brain stones." Certain of the reported cases contained a history of previous cranial injury. In other cases there is no history of cranial injury, but a vascular hypertension has been noted in the observations.

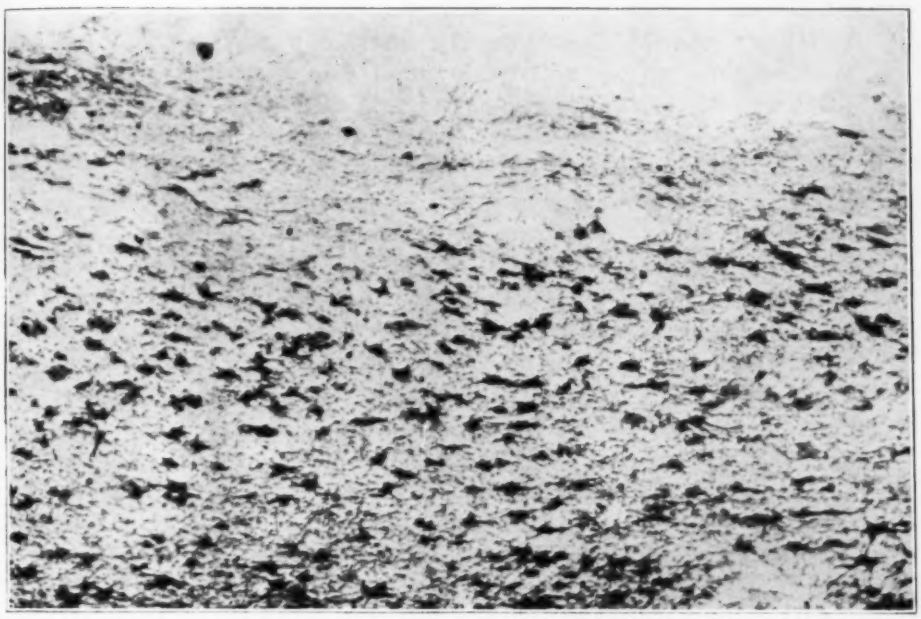

Fig. 7.—A frozen section made through the wall of the cavity seen in figure 5, stained with gold chloride sublimate, shows the dense inner connective tissue layer and the adjacent gliosis; × 165.

Penfield and Geyelin [1] described an unusual family in which the father and four children had multiple intracerebral calcified areas. From the examination of an operative specimen of one of the children the lesion was considered as a degeneration secondary to the obliteration of localized end-arteries, with the degenerated area becoming calcified.

1. Penfield, W., and Geyelin, A. R.: Familial Calcifying Cerebral Degeneration, Arch. Neurol. & Psychiat. **16**:517 (Oct.) 1926.

Levin [2] removed a "spiky" stone from the cerebrum of a young adult giving a definite history of an injury to the head followed by epileptic attacks. The stone consisted of a laminated calcified mass with traces of blood pigment and an amorphous mass with calcifying spicules, like a calcified hematoma. The roentgenograms in his second case showed a similar shadow but he did not consider an operative procedure necessary. Petitpierre [3] described the case of a young adult, with a previous history of cranial injury, who was suspected of having a tumor of the brain. The x-ray films showed cerebral calculi; these were successfully removed. Three large and several small "stones" were found in smooth lined cavities and were readily removed. A dense glial reaction was described in the cerebral tissue attached to the stones.

Miller [4] reported the successful removal of three cerebral calculi lying in smooth walled cavities deep in the brain of a patient who gave no history of injury. However, he had had epileptic attacks for twenty-six years, associated with frequent attacks of weakness and falling when walking. There were no general pressure symptoms. A definite vascular hypertension was noted with a systolic pressure of 170 mm. of mercury and a diastolic pressure of 105 mm. The calculi were grayish-white and "mulberry-like" and were composed of calcium oxalate and decomposed blood. This was the only report encountered which presented a clinical history similar to that described in this report.

O'Sullivan [5] gave additional, but unverified, evidence as to intracranial injury being the etiologic agent in certain examples of cerebral calculi. He presented the roentgen studies of the skulls of three unrelated children, aged 10, 11 and 13 years. There was a history of injury at birth and hemiplegia in each instance. Dense, sharply defined calculi were seen deep in the cerebrum in each case. The author interpreted the calculi as forming from the supposed intracerebral hemorrhage.

The question will rarely arise as to what to do in the case of a patient suspected of having a tumor of the brain, in which actual calculi are shown in the x-ray films. That the calculi can be successfully removed is evident from the reported instances. All of the verified calculi appeared to lie in a smooth lined cavity and should be readily removed if this is indicated.

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2. Levin, J. J.: Intracerebral Calcification, Brit. J. Surg. **14**:215, 1926-1927.

3. Petitpierre, M.: Zur Symptomatologie und operativen Entfernung intracerebraler Kalkherde, Beitr. z. klin. Chir. **140**:532, 1927.

4. Miller, E. A.: Calculi Within the Brain: Report of a Case of Intracranial Calcification with Successful Operation and Recovery, Surg. Gynec. Obst. **34**:786, 1922.

5. O'Sullivan, J.: Some Rarer Intracranial Calcifications and Ossifications, Brit. J. Radiol. **30**:295, 1925.

In the case herein presented, the "stones," in my opinion, were merely the results of old vascular accidents and had no direct bearing on the patient's complaints.

CONCLUSION

Intracerebral calculi are seldom encountered. They may be associated with a previous intracranial injury or with an existing vascular hypertension. They most probably represent the end-result of an area of cerebral hemorrhage or degeneration; as such, the recognition of their nature by roentgen examination is important from a diagnostic standpoint. It is difficult to see how their removal can in any way be therapeutically beneficial.

MEASUREMENT OF CEREBRAL AND CEREBELLAR SURFACES

VIII. MEASUREMENT OF THE MOTOR AREA IN SOME VERTEBRATES AND IN MAN *

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DETROIT

AND

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The work described in the present article is a sequel to that done by Kraus, Ditto, Davison and Weil [1] on the measurement of cerebral and cerebellar surfaces. The total and visible cortical surfaces of man and of various animals having been determined, the problem of the area of various functional regions was attacked. This paper is devoted to an account of the observations for the area containing Betz cells, customarily called the motor area.

Henneberg,[2] in 1910, measured the cortical surface and determined the areas of specific regions. He divided the cortex according to

* Submitted for publication, Dec. 2, 1929.

* From the Laboratory of Neuropathology, Montefiore Hospital.

* This work was done under the auspices of the Hilda Stich Stroock Scholarship.

1. Kraus, W. M., and Ditto, M. W.: A Method of Measuring the Cerebral and Cerebellar Cortical Surfaces, Arch. Neurol. & Psychiat. **17**:193 (Feb.) 1927. Kraus, W. M.; Davison, C., and Weil, A.: The Measurement of Cerebral and Cerebellar Surfaces: III. Problems Encountered in Measuring the Cerebral Cortical Surface in Man, Arch. Neurol. & Psychiat. **19**:454 (March) 1928. Kraus, W. M.: The Measurement of Cerebral and Cerebellar Surfaces: IV. A Technic for Making Endocranial Casts Suitable for the Estimation of the Internal Surface of the Skull Overlying the Cortex Cerebri, Arch. Neurol. & Psychiat. **19**:647 (April) 1928. Weil, A.: The Measurement of Cerebral and Cerebellar Surfaces: V. The Determination of the Shrinkage of the Surface of Different Vertebrate Brains, Arch. Neurol. & Psychiat. **20**:834 (Oct.) 1928. Weil, A.: Measurements of Cerebral and Cerebellar Surfaces: Comparative Studies of the Surfaces of Endocranial Casts of Man, Prehistoric Men, and Anthropoid Apes, Am. J. Phys. Anthrop. **13**:69 (April-June) 1929. Davison, C., and Kraus, W. M.: The Measurement of Cerebral and Cerebellar Surfaces: VII. The Measurement of Visible and Total Cerebral Surfaces of Some Vertebrates and of Man, Arch. Neurol. & Psychiat. **22**:105 (July) 1929.

2. Henneberg, R.: Messung der Oberflachenausdehnung der Grosshirnrinde, J. f. Psychol. u. Neurol. **17**:144, 1910.

Brodmann's classification.[3] He took the region situated between the precentral and central or rolandic fissures (*Ca* in fig. 8) with the lower border as the sulcus callosomarginalis and behind the sulcus subcentralis medialis of Brodmann.

This area was cut into sections of 1 sq. cm. along the fissures and sulci, and these sections were covered with square millimeter paper, and thus the surface was obtained. According to this method, the surface of the motor area in one hemisphere varied from 61.17 sq. cm. in a European brain to 71.77 sq. cm. in that of a Hottentot. The ratio of the motor surface area to the total surface area in the European brain was 5 per cent.

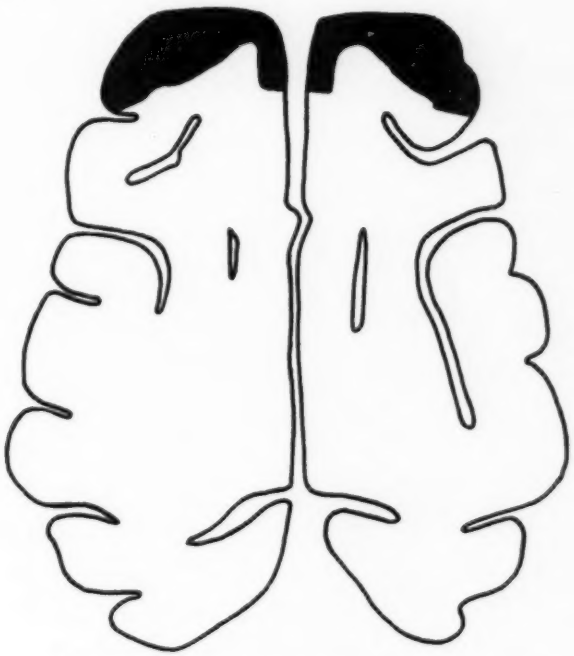

Fig. 1.—Horizontal section of a cat 7 mm. from upper surface. The motor area is shown in black; × 6.

S. Rose,[4] in 1927, measured the surface areas of the divisions of the allocortex in man and other animals. Popoff,[5] in 1927, measured the area striata by a method somewhat analogous to ours.

3. Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, Leipzig, Johann Ambrosius Barth, 1925.

4. Rose, S.: Vergleichende Messungen im Allocortex bei Tier und Mensch, J. f. Psychol. u. Neurol. **34**:250, 1927.

5. Popoff, N.: Für Kenntnis der Grosse der "Area Striata" und die Methodik ihrer Ausmessung, J. f. Psychol. u. Neurol. **34**:238 (Feb.) 1927.

METHOD OF PROCEDURE

Sections from brains of the different animals were prepared according to the method outlined in previous articles.[6] According to the cyto-architecture as outlined by von Economo in his atlas,[7] the limits of the motor area were established microscopically (figs. 1, 2, 3, 4, 5, 6 and 7). Except in monkey and man, little reliance can be placed on the rolandic fissure as a landmark, and in no case was it so used. The occurrence of Betz cells was taken as the indication of the area.

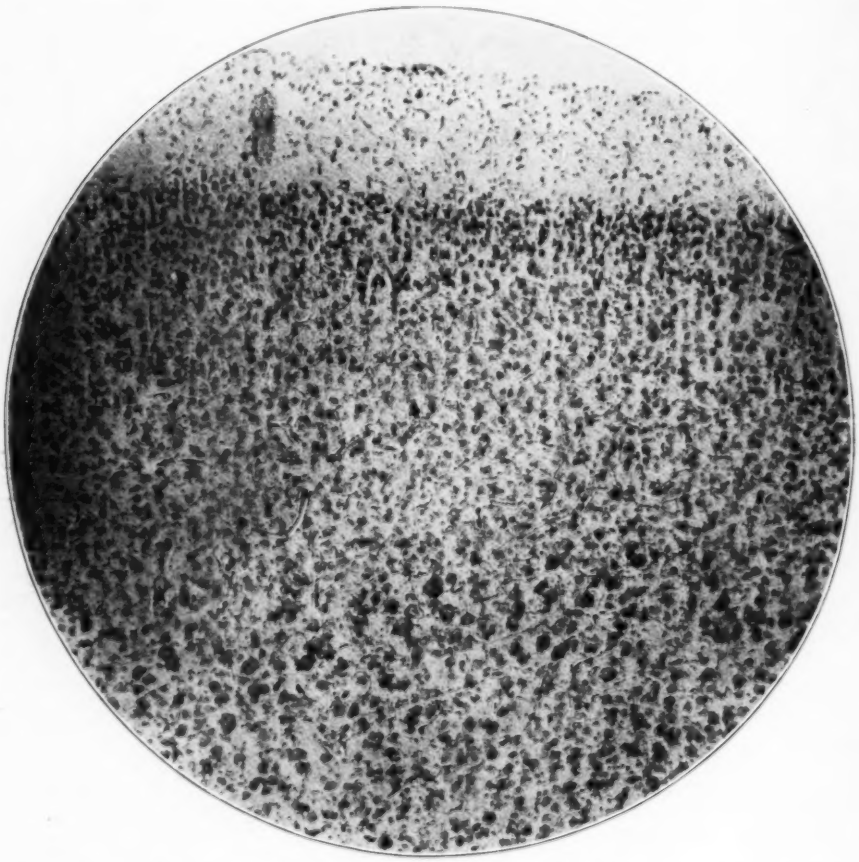

Fig. 2.—Horizontal section of a cat showing the Betz cell area. Cresyl violet; × 30.

According to Campbell,[8] the homolog of the rolandic fissure in the cat and dog is not the sulcus cruciatus, but is an isolated, shallow, insignificant looking fis-

6. Kraus, Davison and Weil (footnote 1, second reference). Davison and Kraus (footnote 1, sixth reference).

7. Von Economo, C., and Koskinas, G.: Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen, Berlin, Julius Springer, 1925.

8. Campbell, A. W.: The Localisation of Cerebral Function, London, Cambridge University Press, 1905, p. 292.

suret, piaced between the cruciate and ansate sulci. The motor cortex of the common members of the carnivore family is in relation to the sulcus cruciatus.

The slides were projected and the perimeters of the motor areas were measured with a curvometer as described in previous papers,[6] including the depths of each gyrus concerned. The sections were enlarged from seventy to eighty times, thus giving a good view of the pyramidal cells. The measurements were then reduced to the actual values.

Calculations.—To ascertain the surface of the Betz cell area, the following steps were used:

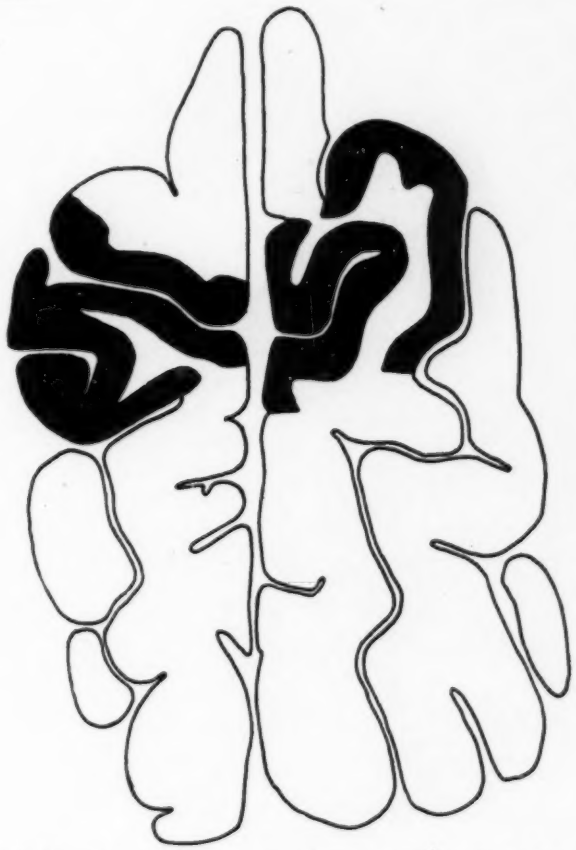

Fig. 3.—Horizontal section of a dog 5 mm. from upper surface. The motor area is shown in black; × 6.

1. The total perimeter of the motor area in each animal and for man was estimated by adding the perimeters of the motor area in each section as illustrated in tables 1, 2, 3 and 4, columns 7 and 8.

2. The total surface area for each section was determined in two steps. First, the total perimeter of a single section was divided by the visible perimeter of the same section. This division gave a ratio:

$$\frac{\text{t. p. (total perimeter)}}{\text{v. p. (visible perimeter)}} = \text{r (ratio)}$$

3. The visible surface area of each section as previously determined (by Davison and Kraus [9]) multiplied by r (ratio) gave the total surface area of each section:

$$v\,s \times r = t\,s$$

4. The addition of the total surface area of each section gave the total surface area for the sections in which the motor area occurred (tables 1, 2, 3 and 4, column 6):

$$t\,s + t\,s, \text{ etc.}, = T.\,S.$$

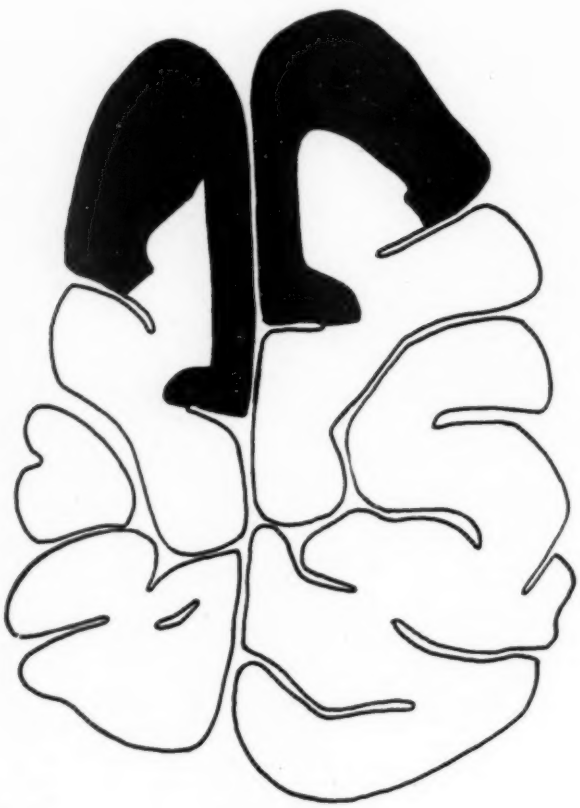

Fig. 4.—Horizontal section from a monkey 4 mm. from upper surface. The motor area is shown in black; × 6.

5. The total perimeters (only of the sections containing the motor area) divided by the total motor perimeters derived in step 1 gave (table 5, columns 1, 2 and 3):

$$\frac{T\,P}{M\,P} = R$$

9. Davison and Kraus (footnote 1, sixth reference).

6. The total motor surface area was obtained by dividing the total surface area (step 4) by ratio in step 5 (table 5, column 5):

$$\frac{T\,S}{R} = \text{M. S. (motor surface)}$$

To determine with certainty that no errors occurred when every twentieth section was measured, every tenth section was measured in one animal, the cat.

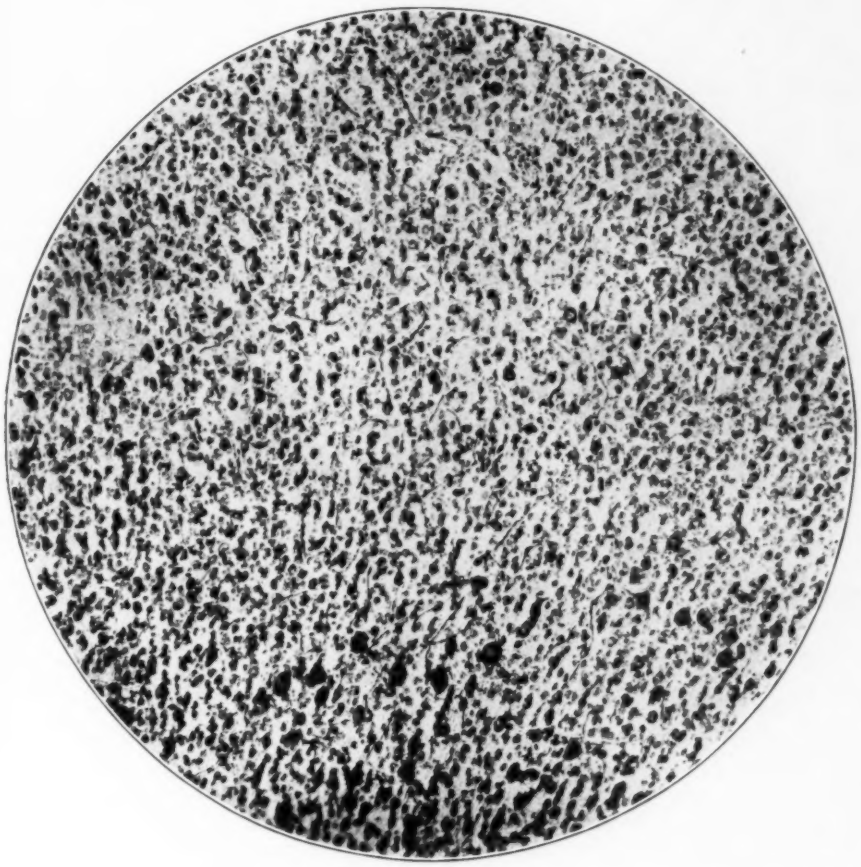

Fig. 5.—Horizontal section from a monkey showing the Betz cell area. Cresyl violet; × 30.

By using every tenth section, the calculated motor surface area was 2.74 sq. cm. (without shrinkage). The calculated motor surface area when every twentieth section was used was 2.79 sq. cm., a negligible difference of 0.05 sq. cm. or an error of 1.8 per cent. In each case an allowance was made for the shrinkage [10] that had occurred during the process of fixing and embedding.

10. Weil (footnote 1, fourth reference).

TABLE 1.—*Motor Area Determinations of Horizontal Sections from the Cat*

Section	Perimeter of the Total Surface	Perimeter of the Visible Surface	Ratio of Total and Visible Perimeters	Visible Surface	Total Surface	Perimeter of Right Betz Cell Area	Perimeter of Left Betz Cell Area
80	21.3200	7.8230	2.720	0.4325	1.1764	0.695	0.735
90	21.5600	8.0250	2.70	0.4675	1.262	0.910	0.796
100	23.2300	8.1450	2.845	0.4285	1.2191	1.151	1.090
110	28.8800	8.2950	3.49	0.4480	1.562	1.240	1.316
120	30.6800	8.5010	3.610	0.5155	1.8610	1.240	1.252
130	27.5400	8.3600	3.29	0.4550	1.490	1.290	1.368
140	26.5150	8.4160	3.143	0.4240	1.3326	1.392	1.430
150	23.7450	8.3510	2.84	0.4245	1.209	1.480	1.507
160	23.7600	8.5300	2.789	0.4850	1.3527	1.710	1.771
170	23.2050	8.5300	2.72	0.4260	1.160	1.582	1.836
180	24.1200	8.7300	2.762	0.5090	1.4059	1.545	1.582
190	23.0750	8.8800	2.60	0.5760	1.500	2.022	2.00
200	22.6050	8.9700	2.520	0.4620	1.1642	1.771	1.542
210	18.7950	8.9350	2.10	0.4750	0.997	1.582	1.456
220	17.5000	8.8800	1.972	0.4810	0.9485	1.330	1.114
230	17.1200	8.7900	1.945	0.4415	0.860	1.280	1.013
240	16.4700	8.7060	1.890	0.4380	0.8288	1.165	0.987
250	16.2750	8.6750	1.875	0.4465	0.840	1.090	0.987
260	15.9150	8.6750	1.835	0.4340	0.7964	1.077	1.077
	422.3100				22.9656	25.552	24.859

TABLE 2.—*Motor Area Determinations of Horizontal Sections from the Dog*

Section	Perimeter of the Total Surface	Perimeter of the Visible Surface	Ratio of Total and Visible Perimeters	Visible Surface	Total Surface	Perimeter of Right Betz Cell Area	Perimeter of Left Betz Cell Area
20	17.765	7.275	2.44	0.3425	0.836	2.91	.....
40	22.825	8.235	2.78	0.9850	0.274	3.77	.....
60	29.600	9.970	2.97	1.4950	4.440	4.35	2.20
80	35.170	10.830	3.25	1.2300	4.000	4.77	4.35
100	45.390	11.830	3.83	1.0495	4.020	4.93	4.76
120	47.930	12.475	3.84	0.9890	3.790	4.85	4.25
140	52.010	12.660	4.10	0.6940	2.840	4.27	3.87
160	53.720	13.615	3.94	1.3840	5.450	3.77	3.38
180	53.620	13.540	3.96	0.6800	2.690	3.39	3.26
200	53.260	13.885	3.84	0.8200	3.150	2.16	3.00
220	53.880	14.210	3.79	0.7710	2.920	1.51	2.95
240	53.210	13.995	3.80	0.7250	2.760	.....	2.78
260	49.070	14.040	3.49	0.7330	2.560	.....	2.65
280	46.900	13.700	3.42	0.7990	2.730	.....	1.76
	614.350		Every twentieth		42.46	40.68	39.21
			Every tenth		84.92		79.89

TABLE 3.—*Motor Area Determinations of Horizontal Sections from the Monkey*

Section	Perimeter of the Total Surface	Perimeter of the Visible Surface	Ratio of Total and Visible Perimeters	Visible Surface	Total Surface	Perimeter of Right Betz Cell Area	Perimeter of Left Betz Cell Area
40	16.695	6.320	2.64	0.7020	1.85	0.768	.....
60	24.490	8.388	2.92	1.2030	3.52	1.950	1.706
80	33.035	9.880	3.35	0.5850	1.96	2.400	2.500
100	36.480	11.195	3.26	1.1460	3.74	3.140	3.120
120	40.575	11.555	3.52	0.5930	2.09	1.989	1.962
140	43.350	12.095	3.58	0.8460	3.03	1.795	1.615
160	46.630	12.590	3.71	0.8915	3.30	0.756	0.705
180	50.300	13.340	3.76	0.9800	3.68	0.513	0.449
	291.555		Every twentieth		23.17	13.311	12.057
			Every tenth		46.34	.....	25.368

COMMENT

The surface areas of the motor area in the brains of the cat, dog, monkey and man were measured (tables 1, 2, 3, 4, 5 and 6). In the cat, the motor area was 3.66 sq. cm., the smallest actual amount of surface area and a relatively high percentage in comparison to the total

TABLE 4.—*Motor Area Determinations of Horizontal Sections from Man*

Section	Perimeter of the Total Surface	Perimeter of the Visible Surface	Ratio of Total and Visible Perimeters	Visible Surface	Total Surface	Perimeter of Right Betz Cell Area	Perimeter of Left Betz Cell Area
500	112.60	34.80	3.24	5.17	16.75	0.45	0.34
520	206.50	35.95	5.75	19.75	113.50	0.69	0.44
540	190.50	32.80	5.80	3.68	21.37	0.63	0.65
560	183.50	30.35	6.05	14.25	86.30	0.58	0.82
580	162.50	33.90	4.80	23.10	110.90	0.83	0.69
600	167.50	35.65	4.70	8.04	37.90	1.21	0.93
620	181.50	34.00	5.34	14.72	78.75	1.25	1.42
640	178.50	26.50	6.75	5.54	37.30	1.21	1.74
660	181.30	24.05	7.54	3.09	23.31	3.26	4.23
680	175.20	25.75	6.82	2.60	17.45	3.62	5.03
700	180.50	25.25	7.14	5.17	35.20	5.82	4.91
720	197.00	21.90	9.00	6.77	60.93	6.25	5.96
740	188.00	20.20	9.30	2.04	18.97	5.95	6.92
760	172.50	21.95	7.85	4.39	34.50	5.84	7.16
780	187.00	25.50	7.34	3.01	22.09	6.42	7.40
800	143.50	24.65	5.82	7.47	43.50	6.32	7.50
820	104.00	21.65	4.8	3.48	16.70	6.92	8.28
840	46.30	17.75	2.61	5.36	14.00	10.85	5.30
	2958.40		Every twentieth		789.42	68.1	69.72
			Every tenth		1578.84	.....	137.82

TABLE 5.—*Motor Surface Areas in Various Mammals Without Shrinkage*

Animal	Total Perimeter	Total Motor Perimeter	Ratio	Total Surface Area	Total Motor Surface	Total Surface Area
Cat	422.31	50.41	8.36	22.97	2.74	55.86
Dog	614.35	79.89	7.69	84.92	11.04	162.66
Monkey	291.56	25.37	11.5	46.34	4.03	142.21
Man	2845.80	137.82	21.46	1578.84	73.56	2656.39

TABLE 6.—*Motor Surface Areas in Various Mammals with Shrinkage*

Animal	Shrinkage, Percentage	Total Motor Surface	Total Surface	Percentage, Motor Surface
Cat	33.4	3.66	74.54	4.90
Dog	29.3	14.28	211.33	6.75
Monkey	19.0	4.79	169.24	2.83
Man	9.0	80.18	2895.46	2.80

surface area, 4.9 (table 6). As a basis for total surface, we used somewhat different figures than in the past. Our new figures included the olfactory area. Furthermore, the fact that every twentieth section instead of every tenth was measured made these figures higher than those of Davison and Kraus.[9] These results will be given in another

paper. The dog showed a larger motor area, 14.28 sq. cm., but the percentage approximated that of the cat, 6.75. Of the four animals measured, the dog has the largest total surface area except man which perhaps may account for the large motor area. In *Cebus hypoleucus,* a low form of monkey, the motor area was 4.79 sq. cm., i. e., relatively small. The percentage ratio was 2.83. Brodmann estimated the pre-

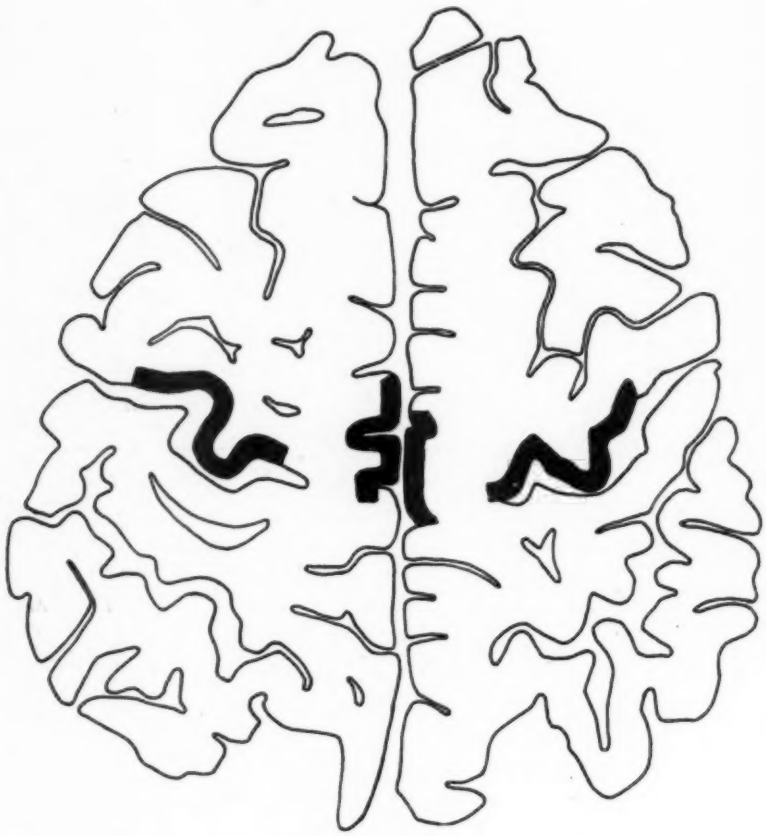

Fig. 6.—Horizontal section from a man 10 mm. from upper surface. The motor area is shown in black; × 3.

central area in lower apes (*Cercopithecinae hapalidae*) and the lemur as about from one tenth to one twentieth of the total surface.

In man, the motor area is the largest, 73.56 sq. cm., with a percentage ratio which is the lowest, 2.8. It is interesting that the percentages of the motor surface area to the total surface area in the cat and dog are much like each other, as is the case for the monkey and man.

Henneberg's figures of 61.17 sq. cm. for the motor area in one hemisphere compared with 73.56 sq. cm. for that of both hemispheres seem high. This can be accounted for only on the basis that we measured the histologic extent of the motor area, and Henneberg seems to have measured the motor area only macroscopically.

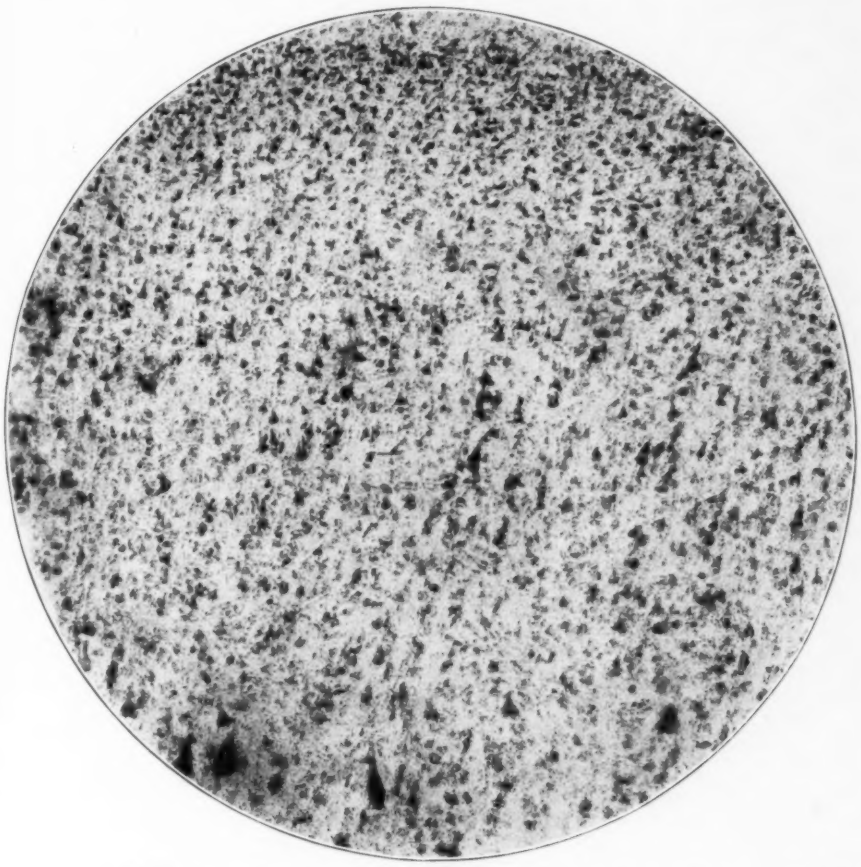

Fig. 7.—Horizontal section from a man showing the Betz cell area. Cresyl violet; × 30.

On examining Henneberg's photographs showing the motor area (*Ca*) compared with Brodmann's field 4, the large difference in extent will be apparent (figs. 8 and 9). Discussing the rolandic fissure, von Economo [7] stated that it is from 10 to 12 cm. in length and from 1 to 1.5 cm. in thickness, and that the anterior wall has a surface of from 1,200 to 1,500 sq. mm. Considering the top of the anterior wall and

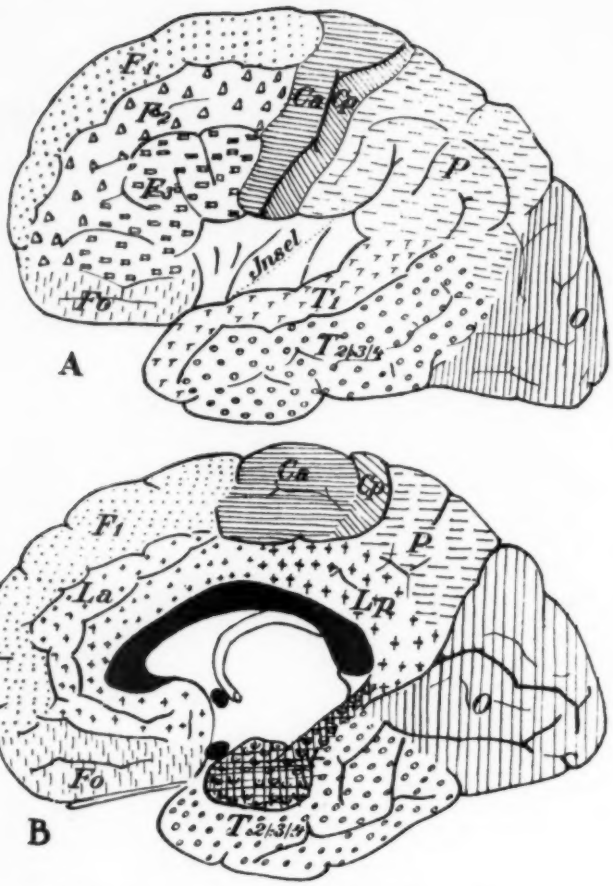

Fig. 8.—Cortical surface as measured by Henneberg. *Ca* indicates the extensive area that was measured as the motor area.

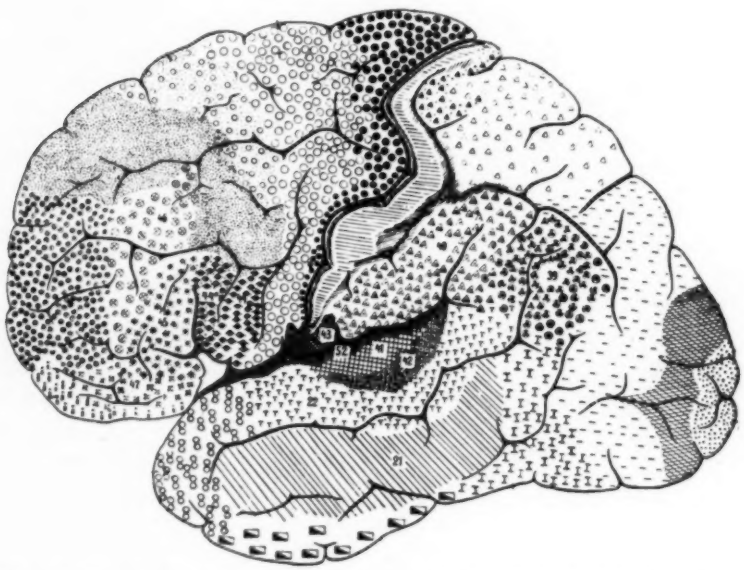

Fig. 9.—Brodmann's new classification, field 4. The shaded dots show the Betz cell area which is about half as large as area *Ca* in Henneberg's illustration (compare with fig. 8).

Fig. 10.—Distribution of the cells of Betz in the human cerebral cortex. The first section (840) is the uppermost. Every twentieth section (100 microns thick) is represented. Section 500 is the lowermost (see fig. 11). This shows that this area does not lie on the visible surface of the cortex except at the upper and lower limits of the rolandic fissure (compare with fig. 12 from von Economo after Campbell).

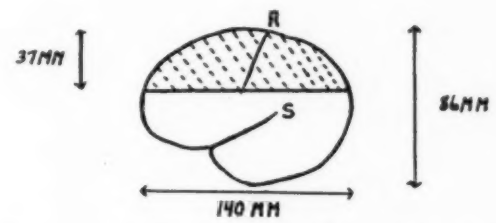

Fig. 11.—A diagram to show the upper and lower limits of the Betz cell area shown in figure 10. The horizontal line beneath the shaded area represents the lower limit.

the paracentral lobule, an area of 2,200 sq. mm. for one hemisphere or 4,400 sq. mm. for both hemispheres is obtained. Considering the surface of the cerebrum as 220,000 sq. mm., the ratio of motor surface to total surface is 2 per cent. Our percentage of 2.8 per cent compares favorably, when our figures for the total surface (Davison and Kraus [9]) of 2,656.39 sq. cm. without shrinkage are used.

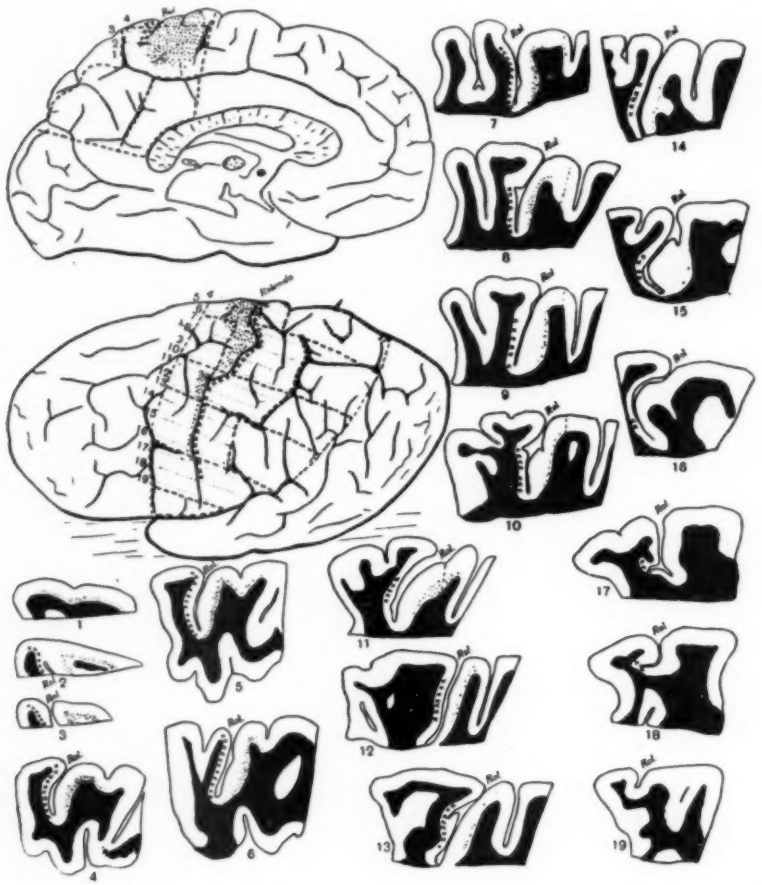

Fig. 12.—Diagram from von Economo (after Campbell) to show the distribution of the giant cells of Betz. In the sectional but not in the surface drawings, each dot represents a cell. Here also the greater portion of the Betz cell area is seen to lie on the invisible surface of the cortex in the wall of the rolandic fissure.

In the study of the human motor cortex, we were impressed by the fact that a great portion of the distribution of the cells of Betz was in the invisible portion of the gyrus along the fissure and not on

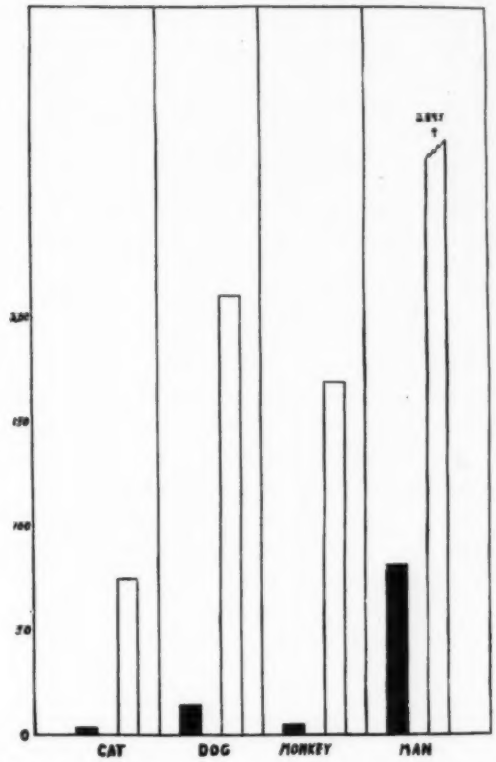

Fig. 13.—Relation of the actual motor surface area in square centimeters (black column) to the total surface area in square centimeters (unshaded column); shrinkage is included.

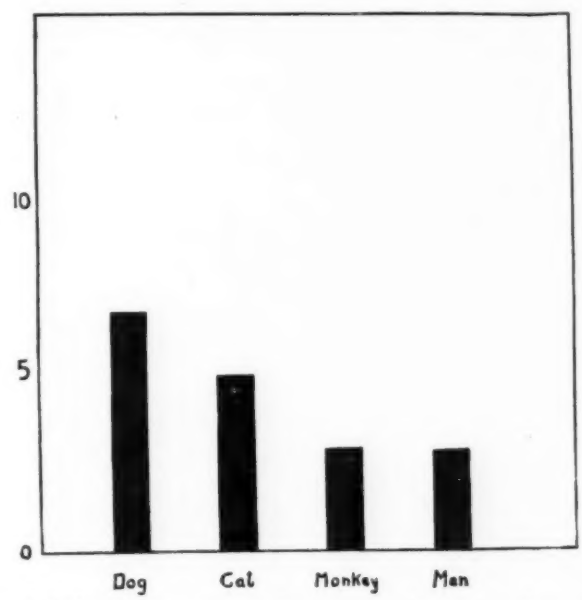

Fig. 14.—Relation of the motor surface area to the total surface area expressed in percentage.

the surface (figs. 10, 11 and 12). Campbell [8] called attention to this when he mentioned that a surface diagram could not give a true idea of the extent of the fields, and the floor, not the lip, is the boundary between the precentral and postcentral fields. Comparing the diagrams from figure 12 (von Economo) and figure 10, the similarity in distribution is apparent.

As we ascend the evolutionary scale of animals, the motor region in comparison to the total surface becomes progressively smaller, as shown in figures 13 and 14, dog and cat, 6.75 and 4.9 per cent, respectively, and man, 2.8 per cent. Sherrington,[11] in discussing the motor area, indorsed the opinion expressed by Beevor and Horsley "that the so-called motor area in the anthropoid brain forms a smaller fraction of the total surface than it does in the lower types of monkey. If it has grown in extent, as undoubtedly it seems to have done, other regions belonging to those so-called 'silent' fields whence electric stimulation excites no obvious response have increased still more." Our estimations offer concrete confirmation of these ideas.

CONCLUSIONS

The motor surface area in the cat, dog, monkey and man was measured. In the cat, the actual motor surface area was the smallest and in man, the largest. In comparison to the total surface area, the motor surface area in man and monkey was low, while in the cat and dog it was high.

This method was a quantitative approach in an effort to determine the size of a specific functional area of the brain.

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11. Sherrington, C. S.: Integrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1906, p. 278.

OCULOGYRIC CRISES

PSYCHOPATHOLOGIC CONSIDERATIONS OF THE AFFECTIVE STATES *

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NEW YORK

In this article I shall focus attention on the thought of the activity of the "organism as a whole," which White and I before and since the first edition of our textbook (1915) have been insisting on if an all round understanding of sick behavior is to be gained; I shall also call attention to the fruitfulness of the conceptions of Freud for psychopathology in other fields than the psychoneuroses, here applied specifically to the positive symptoms (Jackson)—Gestalt (Wertheimer, Goldstein), emergents (Morgan)—of the compulsive phenomena seen in the postencephalitic oculogyric crises.

I make the preliminary statement that irreversible structural changes undoubtedly take place in the central nervous system in epidemic encephalitis. In the language of current pathology, there is an organic disease, although the emphasis on organic after all may mean very little.[4] In other words, the machine, "as a whole," is interfered with in its adaptive capacity to reality. This is a truism so obvious as scarcely to need stating. It is equally true, but not so readily appreciated, that this is only one fragment of the larger situation in which the organism as a whole still functions, in spite of the "monkey wrench" thrown into the machinery. In the terms of Hughlings Jackson's most practical summary, the organism still functions, but functions badly with the well part of its being. The refinements and greater insight into the further elucidation of the phyletic complexities of this situation one owes to von Monakow,[5] Goldstein,[6] Schilder,[7] Hollos and Ferenczi [8] and others,

* Submitted for publication, Feb. 7, 1930.

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

* Parts of this article have been omitted from the Archives, but the entire text appears in the Transactions of the American Neurological Association and in the author's reprints. This omission accounts for the discrepancy in the numbering of the footnotes.

4. The thought closely parallels that of K. Goldstein (Ueber die gleichartige funktionelle Bedingtheit der Symptome bei organischen und psychischen Krankheiten; im besonderen über den funktionellen Mechanismen der Zwangsvorgänge, Monatschr. f. Psychiat. u. Neurol. **57**:191, 1924.

5. Von Monakow treated the subject originally in his "Diaschisis" and most recently in his study with R. Mourgue (Introduction biologique à l'étude de la neurologie et de la psychopathologie, Paris, Félix Alcan, 1928), in which Jackson's integration and disintegration of function in the nervous system are elaborated.

including modestly White and myself,[9] not hypnotized by the etymology of the phrase "organic disease."

It is here chosen, however, in the terminology of Bergson, to look at those functional situations, "the few superfluous recollections which succeed in smuggling themselves through the half open door; the memories, messengers from the unconscious, dimly remind us of what we are dragging behind us unawares." Bergson, quite inaccurately, and grossly so, has called them "superfluous." This is because they were not understood. These "recollections," i. e., disordered bits of behavior it may be, are here regarded as essential rather than "superfluous," because psychoanalysis has shown that the "memories of the unconscious" are a million to one more important than has heretofore been appreciated. In this respect the emphasis on unconscious processes of phyletic and ontogenetic condensation is justified; otherwise no real comprehension of the subtle behavior reaction in disease can be realized.

Is it possible to understand more significantly, and as practical workers in therapy to deal with more successfully, those efforts of the organism, working as a whole, which manifest themselves as bits of behavior which in the present state of understanding—misunderstanding it may be in the future—more closely than any other bits of behavior resemble the "compulsions" which Westphal, among others, first brought into a partial synthesis under this conception?

In the abstract presented before the American Neurological Association, in 1928, the presentation of a complete summary of the available literature of the oculgyric crises following epidemic encephalitis was promised. This has been accomplished and was published in the *Journal of Nervous and Mental Disease*.[13]

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6. Goldstein: Topik der Grosshirnrinde, Deutsche Ztschr. f. Nervenh. **77**:7, 1923; footnote 4. See also later studies on aphasia, particularly Goldstein's handling of the problem from the Gestalt conception of psychology, which is admirable.

7. Schilder, P.: Medizinischer Psychologie, Berlin, Julius Springer, 1927; Lagereflexe, Berlin, Julius Springer, 1927; and also other recent papers.

8. Hollos and Ferenczi: Psychoanalysis and Paresis, Nervous & Mental Disease Monograph Series, 1925, no. 42.

9. Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System, ed. 5, 1929. White, W. A.: The Significance of Psychopathology for Somatic Pathology, J. Nerv. & Ment. Dis. **61**:246, 1925. Jelliffe, S. E.: Postencephalitic Respiratory Disorders, Nervous & Mental Disease Monograph Series, 1927, no. 46; Somatic Pathology and Psychopathology at the Encephalitis Cross Road, J. Nerv. & Ment. Dis. **61**:561, 1925; The Mental Picture in Schizophrenia and in Epidemic Encephalitis, Am. J. Psychiat. **6**:413, 1927.

13. Jelliffe, S. E.: J. Nerv. & Ment. Dis. **69**:59 (Jan.) 1929; **69**:165; **69**:278; **69**:415; **69**:531; **69**:666.

A synthesis of the symptomatology appeared in the ARCHIVES.[14] To this were added some personal, clinical observations and a short discussion of the "anxiety states" which were considered an essential feature of the whole picture of the oculogyric crises if they were to be studied with any degree of completeness.

One fact might be added that was not emphasized; namely, "anxiety states" apparently are not always present. It may be admitted that they may be absent, and for reasons that are possibly understandable. But it is my belief that whereas for the most part such anxiety states do appear in consciousness, it is conceivable that the amount of affect may not be sufficiently great to force them into consciousness, or the repressing mechanisms of the individual patient may be sufficiently operative to keep them unconscious and force an outlet of the libido somewhere else, in accordance with the general law of parsimony (economy of Freud; easiest channel of Goldstein et al.). Although this consideration needs greater elaboration, it is mentioned here as to be thought of in relation to variations in the clinical picture of variable grades of anxiety expression, directly or indirectly in thought, motor action or glandular activity.

Later in the abstract mentioned, it was stated that some approach would be made to a "humanistic interpretation of the phyletic sources of the sense of guilt and its relations to primitive religious anticipation of scientific biologic principles of ethical behavior."[15] In this paper I shall discuss that aspect of the compulsion phenomena of the oculogyric crises seen in the development of anxiety states.

COMPULSION PHENOMENA IN GENERAL

The task of the historical student who would endeavor to trace to its beginnings the Ariadne thread in the domain of the compulsion neuroses is not to be lightly considered. Conventional historians, chiefly Teutonic, have sought to place at Westphal's feet the crown of priority. This is one of those not altogether illusory bits of hero worship that more careful research dispels, while still doing homage to Westphal.

Compulsion neuroses have been present in mankind from very ancient times. As Freud has so ably shown,[16] religious ritual and the compulsion neuroses are twins of prehistoric lineage. Their similarities have been hinted at for centuries. Of recent years, the most thorough discussion of the later history of the conception has come from Bien.[17]

14. Jelliffe, S. E.: Psychologic Components in Postencephalitic Oculogyric Crises, Arch. Neurol. & Psychiat. **21**:491 (March) 1929.

15. Jelliffe (footnote 14, p. 492).

16. Freud: Totem and Tabu, 1912-1913, ed. 2, The New Republic Press, 1920.

17. Bien, E.: Die Lehre von seelischen Zwang in Lichte der Literatur, in Stekel: Zwang und Zweifel, Berlin, Urban & Schwarzenberg, 1927, vol. 10, part 1, p. 557.

Earlier useful guides have been Thomsen [18] (1895), Warda [19] (1905), Löwenfeld [20] (1904) and Schneider [21] (1918).

Even a rapid glance at these sources indicates that brave would be he who would endeavor to digest the voluminous literature and attempt an historical synthesis of this array of studies. "Compulsions," i. e., fixed patterns of discharge, may be seen from the highest social ritualizations of mankind in the mass to the lowest rungs of the physical and chemical ladder. Thus, through physical, chemical, biologic and psychologic to sociologic, fixed (compulsive) reactions may be traced.

Whether one focuses attention on the grosser muscular movements of the extremities, those of the facial musculature, the ocular gyrations, which this study arbitrarily abstracts for observation, the complex subtle movements of developing thought, the mental state in general or the entire individual or group behavior reactions, one striking situation stands out, efforts for the understanding of which have seemed to occupy man's thought as long as any records of these efforts have been obtainable. In present-day psychiatric science this situation has been formulated by Bleuler as "ambitendence" and "ambivalence." This conception so fruitful for understanding, and equally subjected to resistances, is clearly seen, however, in a few fragments of presocratic thought which have come down to the present time.[22]

Anaximander and Anaximenes both spoke of the interaction of opposing bodies; Herakleitus' idea of "flux" envisaged the phenomena; the early Indian philosophies warned one of the "pathway of opposites."

Interestingly enough, as bearing on a later phase of this inquiry, i. e., relative to ritual, religion and ethics, both Anaximander and Herakleitus said that the "opposites are bound to do justice to each other for all unjust encroachments," and Herakleitus is remarkably modern—if I inject my own homologies into his fragmentary statement —when he writes "that if the sun (fire-libido) oversteps his measures, the Erinyes, the assistants of Justice (super-ego) will find him out."

Today it is a commonplace of Newton's first law that "action and reaction are equal and opposite, and always occur in pairs." Equally

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18. Thomsen, R.: Klinische Beiträge zur Lehre von den Zwangsvorstellungen and verwandten psychischen Zuständen, Arch. f. Psychiat. **27**:319, 1895.

19. Warda, W.: Zur Geschichte und Kritik der sogennanten psychischen Zwangszustände, Arch. f. Psychiat. **39**:239, 1905.

20. Löwenfeld: Die psychischen Zwangserscheinungen auf klinischer Grundlage dargestellt, Munich, J. F. Bergmann, 1904.

21. Schneider, K.: Die Lehre vom Zwangsdenken in den letzten 12 Jahren (1905-1917), Ztschr. f. d. ges. Neurol. u. Psychiat. **16**:113, 1918.

22. Scoon, R.: Greek Philosophy Before Plato, Princeton, N. J., Princeton University Press, 1928. Gomperz: Greek Thinkers, vol. 1. Burnet: History of Greek Philosophy, ed. 3. Grote: History of Greece. Diehls: Fragmente der Presokratiker, Berlin, Weidemann.

pertinent possibly is it to be reminded that no electrical engineer could make anything work if the positive and negative forces were not taken into consideration in every problem. Furthermore, not to build up unduly the evidence of the necessity for tracing what is happening to opposites, from physics to sociology, may it not at once be concluded that any interpretation of human behavior that fails to take into consideration these opposing tendencies, from the electron to national rivalries, is bad engineering.

In this discussion, however, I shall not essay to include the universe, even though far-reaching universal factors are always involved in human behavior, but I shall endeavor to build up some insight into certain compulsion accompaniments seen in the postencephalitic state and more particularly in the oculogyric crises and their accompanying mental states. Yet no such discussion could be satisfactory if one did not make some effort to orient the phenomena involved to related occurrences.

Löwenfeld's [20] large and important monograph contains the greatest amount of digested material dealing with the larger problem of the compulsion neuroses. Janet's [23] four volumes on neuroses and fixed ideas, obsessions and psychasthenia present the most detailed case histories extant, but these case histories are extremely wordy; I agree with Kraepelin that they were collected with little clinical psychiatric acumen. Psychasthenia, as outlined by Janet, has been shown to be a very unclinical conception; many of the patients actually described by Janet in their further evolution developed situations into which kraepelinian psychiatry would offer better insight. Cyclothymias, schizophrenias, paranoias, and other types developed in Janet's patients (Jung, Kraepelin, Callin, et al.). A great many of the short descriptions are entirely too fragmentary to be interpreted accurately. The psychasthenia conception, already shown inadequate in the light of the kraepelinian studies, has vanished even more into the limbo of untenable formulations in view of the psychoanalytic psychiatry of Freud, Schilder, and others. The manifest content and rationalizations, however, are given in great detail in Janet's case histories, and they still offer interesting source material. My own impression is that had Janet been able to follow the development of the freudian ideas he could have made some enduring contributions to psychiatry from his elaborate case material. As it is, even in his two latest contributions,[24] one misses the

23. Janet: Névroses et idées fixés: I, Paris, Félix Alcan, 1898; ibid., ed. 2, 1904. Raymond and Janet: Névroses et idées fixés: II, Paris, Félix Alcan, 1898. Janet: Les obsessions et la psychasthénie: I, Paris, Félix Alcan, 1903. Raymond and Janet: Les obsessions et la psychasthénie: II, Paris, Félix Alcan, 1903.

24. Janet: De l'angoisse à l'extase, Paris, Félix Alcan, 1926, vol. 1; ibid. 1928, vol. 2.

penetrating insight into dynamic factors which would meet the present-day inquiries of a concrete psychology. There is charm of description, but it is old-fashioned.

In this study I make no attempt to deal with the larger problem of the compulsion neuroses. Since, however, the phenomena of the oculogyric crises may best be conceived of as belonging more consistently in this general rubric, a general résumé of the compulsion group as of more recent conceptual development seems pertinent.

Without entering into the historical evolution of the compulsion neurosis concept, since Bien has sketched it amply, one may plunge directly into this field by presenting Friedmann's[25] useful outline. Variants and emendations may be offered later, for Friedmann is of the old school that deals with "will," "intellect" and "emotion" as entities, and makes categories which rarely accord with actual situations, except as they may represent temporary cross-sections of events. An enormous number of variations, combinations and permutations develop in almost every case. Few cases of compulsion neuroses begin as or remain monosymptomatic, and none of the earlier students has developed the reasons why as satisfactorily as Freud in his penetrating early and as yet incomplete studies of the compulsive states.

Friedmann's general framework has the advantage of something nosologic to start with, even if it is illusory as to the actual developmental situations.

I. Compulsive Remembering

(*a*) Annoying recalling and repetition of verses, melodies and fantasy thoughts, which appear unwanted and often with painful content.

(*b*) Persistent memories of definite experiences of frightful occurrences (of seeing those who have hanged themselves, of images of dead people, of epileptic convulsions, etc.).

(*c*) Compulsive seeking after some elusive memory, of forgotten names, verses or situations; the compulsion to finish an idea, etc.

II. Mechanical Compulsory Associations

(*a*) Impulses to walk a crack; pedantic spelling; compulsory countings; symbolisms; picking up scraps [paper, orange peel, etc.]; going definite distances, etc.

(*b*) The necessity for certain associative thinking of perceptions and experiences in rare forms, such as certain words coming from the blowing of the wind [like Mark Twain's "Who stole my golden arm?" story] as the trains go by, the images of some one crushed or run over; one's head open on top; how this and that person appears undressed, and seeing a corpse hanging on every tree, etc.

25. Friedmann: Ueber die Natur der Zwangsvorstellungen und ihre Beziehungen zur Willensproblem, in Löwenfeld: Grenzfragen, Munich, J. F. Bergmann, 1920, no. 105.

(*c*) Contrast associations, as for instance the cursing of loved persons; obscene sexual ideas and pictures with holy religious activities; ideas of the mother as a witch; echolalia; coprolalia.

III. Unwished for Compulsive Instinctive Impulses

(*a*) Momentary impulses without preliminary notions, such as to throw oneself out of a window, to shout, to make movements or grimaces, to wish to buy everything one sees [tics of various kinds].

(*b*) Impulses of a more serious and dangerous nature, such as kleptomanias, to mistreat some one, followed by quiet.

(*c*) Feelings of digust and fear of touching things, followed by increased impulses of cleansing.

(*d*) Compulsory inhibitions and shyness without conscious foundation; of going to certain places; to write letters; travel in railroad trains.

IV. Overvalued Compulsory Impulses and Compulsory Ideas on a Primary Affective Foundation

(*a*) Phobias, that is, inhibitory impulses connected with habitual activities —bodily performances, urinary inhibitions, fear of open spaces, closed spaces, the streets, of business activities, etc.

(*b*) Observation and fear of blushing; exaggerated shame feelings; ideas of bodily deformity; etc.

(*c*) Compulsive exaggeration of depressive ideas; affect of disappointment.

(d) Hypochondriac fears.

(*e*) Anxious anticipations of pregnancy, of examinations, of competitions, of punishments; fear of flying, etc.

V. True Compulsory Ideas with Feeling of Strangeness and of Displacement.

(*a*) Rare, groundless, fearful and painful ideas, such as the idea of being attacked by one's wife; fear of the plague, of being buried alive, of hydrophobia, of continuing to feel after death, etc.

(*b*) Foolish impulses of compulsive ideas, such as killing some one (by imitation), doing violence, overprotective impulses, etc.

(*c*) Transformed compulsory ideas through modification of an unsympathetic idea to a new idea.

(*d*) Scrupulosity, such as causing some one else to be sick [Pauline doctrine]: fear of noncomprehension; fear of making mechanical mistakes; not closing doors, etc.

(*e*) Self-accusations because of going to the wrong place, and faults; mistakes of a compulsory character.

(*f*) Compulsory jealousy and passions in general—hate, love, etc. (group IV possibly).

VI. Compulsory Thought Movements and Thought Inhibitions

(*a*) Doubtings, especially of a metaphysical nature.

(*b*) Exaggerated pedantries in thinking; extraordinary exactness in directing, careful regulation, etc. (mania to regulate the future) [complicated rituals, magical, religious, etc.].

(*c*) Doubt concerning responsibility as to marriage, purchase, legal decisions and scrupulosities concerning mistakes.

(*d*) General scrupulosities of the psychasthenic and cyclothymic [Friedmann here mixes categories with symptoms—practically all of the symptoms already noted can be found in cyclothymics and in psychasthenics, whatever these may be].

(*e*) General inhibitions of thinking and doing, as inability to read, write letters, carry on one's work, through dissociation of the thought movement (severe psychasthenia).

As Friedmann noted, there are twenty-six groups, whereas Janet cataloged thirty-two. As one turns over Janet's pages again to see his classifications, one is struck with the futility of all these categories, and the conviction is borne in on the observer that one could make as many classifications along these lines as there are patients—no two will ever be exactly the same, and an infinite variety of obsessive, phobic, compulsive and impulsive situations can be cataloged. Hence one sees the great value of the freudian conceptions of more or less definite mechanisms of conversion, substitution, projection, displacement, introjection, identification, etc. With the understanding of these newer ideas, a certain order falls into the vast chaos of appearances, and, although mixed states are usual, broad outlines of reaction patterns of more fundamental clinical significance commence to appear. In anticipation, it may also be recorded that as even with the newer psychoanalytic ideas many of the phenomena broadly constellated about the substitution mechanism of Freud have remained refractory to treatment, further study will be needed to understand more adequately these obstinate and malignant cases; in other words, deeper comprehension is still lacking, and, although the psychoanalytic conceptions offer a lead in the desired direction, they are in need of more precise formulation, correction or modification.

It is evident that in Friedmann's categories, as well as in those of Janet, one is not dealing even with a syndrome in the kraepelinian sense, but with a rough grouping of symptoms that may be found in a number of disease pictures (dementia paralytica and tumors of the brain, for instance) and in mental syndromes (manic-depressive psychoses schizophrenia, hysteria, anxiety neuroses, etc.).

This may seem unimportant in the main, but one is here much concerned with the emergence of certain symptoms in postencephalitic cases; because they bear such a close similarity to symptoms appearing in neurotic, psychoneurotic and psychotic situations of definitely "nonorganic" nature, the whole problem (possibly a pseudo-problem) of "psychogenic" or "organic" must be touched on. The famous antitheses of matter and motion, body and mind, somatic and psychogenic, after all mean very little. It is here held that the "or," somatic or psychogenic, is largely a pseudo-problem. The careful examination of a symptom is desirable to help locate the place in the structure where the dynamic disturbance takes place.

THE OCULOGYRIC CRISES

Coming closer to the problem, it seems most reasonable to ally the oculogyric spasms with the tics, and yet this is not entirely satisfactory, since the more pronounced protracted cramplike states of the oculogyric crises are extreme drives in one direction, as a rule, and that which stands out in the tiqueur is the short cramp state with more or less rapid ambitendent characteristics. The tiqueur raises and lowers his shoulders, opens and closes his eyes, etc.; the yes-no, in-out, up-down mechanisms follow each other more or less rapidly in the classic tiqueur, with an infinity of variations. Freud has opined that this bipolarity, to use Stekel's more convenient phrase, occurring as alternates, is an essential mechanism in the compulsion neurotic. In the same manner he has defined the conversion mechanism of the hysterical person as carrying out the opposites in a single symptom, simultaneously in space and time. Undoubtedly, many single aspects of the oculogyric crisis attack seem to entitle it to be deemed a conversion phenomenon, and that some energy (libido) discharge through conversion does take place seems probable. Since one swallow does not make a summer, however, so some conversion does not make hysteria. Conversion phenomena undoubtedly occur in patients with dementia paralytica, but that does not make them hysterical. If one studies the various attacks and the varying patients, it may be seen most frequently that alternations in movement are present. Attention has been called to the most frequent up-and-to-right movements, but down-and-to-left may alternate; up-and-down, and right-to-left. The most frequent staring—caught on dead center—lack of movement is classic of the "folie de doute" situation, as was emphasized by the earlier students of this general clinical group, "Le Grand de Saulle," Falret and others.

Certain close relationships to the tonic spasms of the epileptic phenomena have caused the term epileptoid to be used by many students of this problem, and not without reason. But, as already noted, it is a static play to apply "names" to these processes; even to speak of them as belonging in the "compulsive neurosis" group does not escape from this nosologic stupidity unless the fictional functional value of all "names" in the vaihingher, kantian sense is recognized. These problems have received much attention from various sources; Bing, Mayer-Gross and others may be considered later when nosology is discussed. This is not a study of the large problem of anxiety.[26] It deals only with an effort to learn why anxiety is present in those cases of oculogyric crises which, apart from all nosologies, are here viewed chiefly in the light of psychopathologic reactions to traumas of the brain.

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26. Goldstein: Zum Problem Angst, Allg. aerzt. Ztschr. f. Psychotherap. **2**:7, 1929. Jones, E.: Psychopathology of Anxiety, Brit. J. M. Psychol. **9**:17, 1929.

In order, then, to get at the reason for these movements, the study of the mental state seems imperative. If this is seen in the sense of either overdetermination (Freud), positive symptom (Jackson), Gestalt (Wertheimer, Goldstein) or emergents (Morgan), for all of these conceptions are closely related, one can go much further in explaining if not in clearing up the problem of causality than with the worn-out parallelistic conceptions of organic-functional, body-mind formulations.

The outstanding phenomena in the oculogyric crises have been reviewed in a previous section of this study. Attention has been focused on at least four features: (*a*) the crises, (*b*) the thought processes, (*c*) anxiety, (*d*) the state of consciousness. In utilizing dynamic conceptions, it is understandable that varying degrees of intensities may appear in all of these factors. There may be attacks without conscious anxiety, minor oculogyric movements and apparently clear consciousness; at the other extreme, there may be intense anxiety, prolonged, persistent, painful spasms of the eyes and almost trancelike unconscious states. An innumerable series of variants is both observable and conceivable, in the same patient and in different patients. Certain explanations, possibly causal, may be offered later concerning such a gamut of permutations and combinations.

THE AFFECTIVE STATES

This contribution deals more specifically and fragmentarily with the affective states seen in the oculogyric crises. In a former article these were spoken of under the general head of anxiety. In the previous discussion the meager records of the anxiety states were given in detail. Comment was made on the paucity of actual observations made on the emotional content; there are practically no psychoanalytic studies of the anxiety available. It was stated that Stern's contention that anxiety was a primary, unanalyzable state is not tenable and not in touch with the great advances made in the study of anxiety by Freud and others using the psychoanalytic method. Affective situations, of which "anxiety" is a rough and ready term to delimit a small group, are phyletic syntheses of great antiquity and complexity. One may well sympathize with Fabre, who spoke of his observations on insects as hardly more than turning over a grain of sand on the beach of the ocean of life. This individual effort to contribute to the knowledge concerning the anxiety states here reported is thus regarded.

The most satisfactory approach to a more searching analysis of these anxiety states has been made by Freud. "Affective states," he wrote, "are incorporated into the soul life as precipitates of archaic traumatic experiences and are awakened in like situations as memory symbols."

In mankind and the creatures related to him the act of parturition appears to be the first individual anxiety experienced to give the charac-

teristic traits of the expression of an anxiety affect. It is not to be supposed that Rank's thesis is here upheld.

Freud has outlined the fact that most repressions with which one has to deal more particularly in the psychoneuroses are cases of after-repression (i. e., ontogenetic), which presuppose the existence of archaic repressions. He wrote that concerning this background and fore-stage of repression little is known. At present it is impossible to state whether the appearance of the super-ego creates the border between primeval repression and late repression. The first intense outbursts of anxiety in childhood, at any rate, seem to follow the differentiation of the super-ego.

Freud wrote:[27]

> We imagine the Ego as good as powerless against the It, but when it strives against an instinctive process in the It, it needs only to give the signal of pain to attain its objective through the almost omnipotent factor of the pleasure principle.

An illustration of part of this principle appears in G.'s dream, an analysis of which is here given only fragmentarily.

Case 1.—In some place, a crazy man, another man and still another are with the dreamer. The crazy man has attacked and killed one man with a bludgeon, hitting him on the head. It is all bloody. Apparently the crazy man is a brother of the dreamer and while offering aid to the injured or killed man the dreamer would seek to protect the murderer from discovery. The bludgeon is like one of the medieval, clublike affairs with spikes on it.

The situation of the patient was somewhat critical. She was young and unmarried; she stated that she was a virgin and had just passed through the unpleasant experience of a broken engagement with her brother's best friend. In the recovery stage she met a man of overpowering strength and personality. He was twice her age, married but separated from his wife, and for ten years had maintained a very intimate relation with a jealous mistress. The patient's early history shows a tardy narcissistic evolution, with latent and partly overt lesbian situations, beginning at boarding school with an older teacher and emerging partly from this sadistic phase with the engagement, which permitted certain erotic activities.—"necking," etc., "phallic" possession at the oral level.

Analytically, the fiancé was definitely a brother substitute at the narcissistic identification level.

Whence the sadistic, painful nature of the dream? If the bloody bludgeon should represent the taking of her virginity (free association material), then one can see the powerful desire arising from the It that would threaten to throw this young woman of cultivated upbringing into free genital relations with her powerful lover. She is consciously aware of this, but thinks that she can be granted her "three weeks" at a high level of fervid friendship.

Does the dream tell her about the energy borrowed from the death impulse that permits the killing? The man killed (myself, the analyst, through whose confessional situation she must tell her every association)—the father (through

27. Freud: Inhibition, Symptom and Anxiety, translated and published by Clark, p. 8; Ges. Sch., p. 29.

the incest situation)—man old enough to be father—wife (mother) and mistress to be overcome—and the brother (identification with self). "Crazy self" if she permits such an impossible situation to go on; crazy impulse—irresponsible, I want what I want even if I kill to obtain it.

This is but a partial sketch of this young woman's perilous position. Does the dream, "a nightmare" as it was, offer this "pain" reflex, as Freud outlined it, to sidetrack—if even in the dream discharge—the imperious "It"? Here is an inner "Kali-Ghat" sacrificial situation, which through symbolic cathexis may save the patient from a social débâcle and through analytic insight make her aware of the sadistic component of her supposed "love wish."

One can do no better than follow Freud's lead, who in discussing phobias and anxiety (Angst) stated:

> The motif of all later symptom formation is evidently the fear by the ego of its super-ego. The hostility of the super-ego is the danger situation from which the ego must withdraw itself. Here there is no sign of projection. The danger is entirely interiorized. But if one asks oneself what the ego fears on the part of the super-ego, the notion is forced on one that the punishment of the latter is a continuation of the castration punishment. As the super-ego is really the impersonal father (who has been depersonalized) so the anxiety of the threatened castration by the father becomes transformed into indefinite social fears, fears of conscience. But this anxiety is hidden, the ego withdraws itself from it while at the same time it carries out the commands, precautions and expiations laid on it. When these are prevented there develops an extremely painful discomfort, in which one can see the equivalent of anxiety, which the patient himself puts into anxiety. Hence the result runs as follows: Anxiety is a reaction to a danger situation. This is spared if the ego does something to avoid the situation or withdraw from it. One might say that the symptoms are created in order to avoid the development of the anxiety; but that is not perceiving deeply enough. It is more correct to say that the symptoms are developed in order to avoid the dangerous situations which are signalized by the anxiety situation. This danger in the cases hitherto discussed was the danger of castration or of something derived from it.

As the partial study of the phenomena in the oculogyric crises shows, i. e., as far as has been recorded—and knowledge is as yet fragmentary concerning these phenomena, which therefore constitute an interesting field for further study—a certain number of persons show no anxiety in the attack. It seems even that the same person behaves differently in different attacks. Certain attacks are free from anxiety; others show it in varying degrees of intensity. What deductions may be drawn from this if anxiety itself is the complex phenomenon it has been maintained to be following Freud's efforts at its analysis? Symptom formation (i. e., looking away, up, down, sideways) may be, according to these studies, a defensive action to escape the anxiety. The ego would attempt to avoid a dangerous situation; at times successful, again unsuccessful. When the symptom is capable of binding the energy, anxiety will not develop.

Certain preliminary positions may be stated. To many they are obvious. Everything living has an attitude toward its environment. That environment is not alone external. Even in nonliving things, attraction and repulsion, gravity, inertia, etc., may be envisaged as prototypes of such attitudes. From the earliest to the latest living forms, from the lowest to the highest, the external, partly comprehensible manifestations increase in number and variety. Students of lower forms speak a great deal of the fixity of these manifestations; perhaps no one has expressed this general line of thought more clearly than Bergson in showing how a certain release from habitual, reiterated, repetition compulsion (Freud) activity has come about in man through a specialized form of activity, which is called thinking and speech.

The equally obvious formulation is stated that all of these activities, aggressive and passive, may be studied most advantageously as manifestations of the instinctive processes of self-preservation and race propagation (the "Hunger und Liebe" of the poet, Schiller). It may also be remarked that every bit of behavior, internal as metabolism (anabolic or catabolic), external as behavior, contains impulse activities derived from or correlated with these two instinctive drives in varying investment proportions. It may be seriously questioned whether any activity, no matter how trivial or how great, individual or collective, is ever exclusively conditioned through the energy derived through the one instinct channeling. Certainly "eating"—preponderantly, one may say, as nutritive and self-preservative—may easily be shown to be invested, in part, by sexual energy, and likewise, copulation, preeminently adapted for propagation purposes, may be shown to be invested with the energy of self-preservation, or, to use Freud's illuminating conception, with narcissistic libido. A child born to a parent is frequently but an identification—a facsimile for the parent's own self love—self-preservation. Certainly it is of little satisfaction to go more widely into this general truism that the motive powers that underly all activities, and which primarily are derived by and through the capture of the energy in the cosmos, channel or pattern themselves both as organism and as organs of the organisms to carry out the processes or actions adapted to that which has come to be called the instinct of self-preservation and the instinct of race propagation. Only these two instincts are needed; all those of recent positing are deviates, in my opinion; sometimes, as in the nesting instinct, they contain more of one component, the racial and reproductive; in the fighting instinct, more of self-preservation, with variations under differing circumstances.

All that concerns one here is to bear in mind that along such key patterns a partial solution of all bits of behavior may be made.

When Wimmer and many others wrote that the same mechanisms are utilized in hysteria as in the oculogyric crises, and hence that diffi-

culties in differential diagnosis are raised, was that a pertinent way of getting at the situation?

The same mechanisms are used by a workman digging a ditch, plastering a room or driving an automobile as may be used in robbing a bank, setting fire to a house or shooting a suspected violator of the Jones law. Is it not of paramount importance to study motivation, as well as movements? This, it seems, is the gross error of the whole neurologizing tendency, i. e., to neglect in the diagnosis the motive of the movement, its meaning. As already stated, this meaning is always to be interpreted by a consideration of the interaction of the ego, the super-ego and the id. Without such penetration, diagnosis means nothing. As far as material on encephalitis is available, there is excellent ground to support this generalization.

Numerous symptoms may be interposed for the anxiety state. The puffing states of J. F., the patient with postencephalitic parkinsonism, may be utilized as an illustration. In him, anxiety and puffing and, later, anxiety and oculogyric crises occurred. The following dream may be offered as bearing on the motivation and meaning of the mixed puffing and anxiety states.

> I was with another fellow—he lives here in New York (my old friend Jerry). First he said let's go to a $1.00 house. No, I said, let's go to a cheaper one, a 50 cent one. So we went. At the door there was a peculiar device to open the turnstile type of door, a device like a dial telephone disk, yet it was vase-shaped in general proportions. We turned it, a bell rang, and then we entered by a side entrance. The madame of the house was my aunt, and there were two girls in their undergarments, two beds. Jerry was all there, as he took the left hand girl. It took him some minutes, and he puffed and grunted and everything (just like I do). I did not do anything. We paid our 50 cents and got out.

During some of the attacks of J. F., the deviation of the eyes was sufficient to inform the ego of its release from danger. This seems in some way related to the fact, if the danger object is as it were an external one. In this dream (reported in my paper on respiratory disorders and also in the paper on hypervigilance) the presence of "bandy legs" in the girl in the house (uncle-father) prevented the coitus impulse from appearing as puffing for himself, who felt only disinclination for the girl and anxiety—whereas its split-off component, more energized—from the It—allowed Jerry (the disguised self, the poorer super-ego ideals of the boy who taught him all his "bad stuff") to jazz the girl, "puffing thereby." In the conscious the puffing was therefore held to be a coitus equivalent, which releases the It impulse and also saves the patient from an anxiety sufficiently intense to drive him to the feared thing, total castration, i. e., the death wish—suicide. Here the protective mechanism of the symptom and its escape with the ego is fairly clear.

An attempt has been made elsewhere to trace from the physiologic side, the heightened state of vigilance (hypervigilance [28]) which results from the actual trauma of the encephalitic process. Some diaschisis takes place; the repressive mechanism—of cortico-diencephalic or other localization (the innumerable hypotheses are not pertinent here)—is influenced, and the stimulus-response reflex mechanisms of love and hate are heightened. A weakened super-ego, questionably ontogenetically younger at the top and phylogenetically older beneath, is unable to bolster up the ego, and anxiety of different level condensations develops. In many respects, the mechanisms involved in encephalitic persons closely approach those of the traumatic neuroses, especially with reference to hypervigilance.

One case, that of V. L., reported in an earlier communication, has been utilized by Clark as an example of successful treatment by psychoanalysis. It is here partly presented, as taken from the report of the New York Neurological Society, with the comments made at that time. Dr. Clark has promised a complete report later.

The actual report made by me to Clark on Jan. 18, 1929, is as follows:

> Among the many phases through which the L. girl went, some of which I saw, was a distinct respiratory one of tachypnea and brüllen, quite like those reported in my monograph on respiratory disorders (Schuster, and Turner and Critchley).
>
> She would commence to breathe harder and harder and make sounds and noises, and in some of the attacks which I saw she would get up on tip-toe, go about the room with menagerie-like motions, eyes and head to the left in a tonic cramplike position, breathing heavily, and often saying and grunting "don't touch me." The masturbatory implications here were quite direct. This kind of "don't touch me" attack came on after a feebleminded child at "A's" had attempted to masturbate her. This was about a year ago, as I recall it.

The report of the case, quoted from the *Journal of Nervous and Mental Disease,* is as follows:

> Case 2.—A seventeen year old girl came under observation in 1928. Her most marked symptoms were a restless pacing up and down, accompanied by puffing and gasping for breath, and a reeling dizzily and sometimes falling unless caught by someone. She was pale and delicate, and fatigued on slight exertion. She slept poorly and ate her meals in bed. She demanded constant attention and expected nurses and attendants to anticipate her slightest wants.
>
> When Dr. Meagher saw this girl, in 1924, he described the case as a mild attack of encephalitis in which third nerve involvement and lethargy were the prominent features. When she began to exhibit psychopathic reactions after this attack, he referred her to Dr. Jelliffe and the latter describes her respiratory attacks as follows: "She would commence to breathe harder and harder and

28. Jelliffe, S. E.: Paper read before the Association of Research in Nervous and Mental Disease, Dec. 28, 1929, Psychoanalyt. Rev., to be published.

make sounds and noises; in some of the attacks she would get up on tip-toe, go in menagerie-like motions about the room, eyes and head to the left in a tonic cramplike position with heavy breathing, and often saying and grunting, 'Don't touch me, don't touch me.'" [29]

After a few days, analysis was attempted. [For some months she would not listen to any one.] At times she had to be tied in bed. A preparation of sodium bromide combined with bouillon was used. The same restlessness accompanied by puffing and gasping characterized the sessions. For the first few weeks the sessions were short as she quickly tired and would start to pace up and down and go into a respiratory attack. The tantrum phase became so marked as to interfere with the analysis. She became violent toward her nurses, refused to allow them to sleep, screamed at the top of her lungs at any hour of the night, broke windows, slammed doors and tore up her own possessions; in short, she stopped at nothing in venting her temper. The tempers were always worse at night, and at their height from early morning till nine or ten o'clock. She fell down a great deal in her respiratory attacks, suffering bruises from head to foot, yet protesting angrily and threatening violence if anyone tried to help her.

From September till her departure near the end of November, she made great improvement in these behavior reactions. She formed a fairly strong transference. Her physical symptoms, such as the respiratory attacks and sleeplessness, have cleared up almost entirely. She now sleeps without a sedative, eats her meals at regular hours, and during the last month of her stay mingled with the group in all their social activities.

The analysis, which was only properly psychoanalytic for two months, showed an extreme emotional infantility and its sequential narcissism. The autoeroticism was marked, yet a fairly stable transference continued.

I am bound to report here, as in the preceding case, that perhaps as strikingly dramatic recovery, from the neurotic syndrome, was obtained by a treatment that was almost wholly psychoanalytic after all other forms of treatment had failed; at the introduction of psychoanalysis the change was immediate. I have further to state that the patient had begun pubescence for several months prior to her encephalitis process and the most distressing regressions in conduct occurred; at the first induction of psychoanalysis the completion of an arrested pubescence was once more undertaken. The patient began to notice boys, assumed flapper habits and attitudes and the autoerotic needs were once more in evidence. She became more socialized, quieter, and gained many pounds in weight. Was she about ready to undergo this spontaneous recovery? Or did analysis but make the process more easy and rapid? Or is the analysis in such cases more to be prized than some would concede? There is no evidence of there being any purely endocrinic imbalance. I feel certain that only the reaction of further cases can determine the exact rôle of psychoanalysis in such encephalitics. Finally, the so-called specific organic syndromes of respiratory attacks, which are now absent, are shown perhaps to be not a little conditioned upon psychogenic incitation and are not so hopeless of alteration as many suppose. I have several other cases of the striatal types that show similar improvement in their progressive syndrome as well as in their psychotic pictures of depressions and sexual perversions. They will be reported at some future time when we shall be able to more accurately evaluate the different factors in each case.

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29. New York Neurological Society, February, 1929, J. Nerv. & Ment. Dis. **69**:683, 1929.

In discussing this case at the meeting, I said:

The encephalitis case is to me extremely fascinating, because I have seen the patient now on and off for three years. I saw her with Dr. Meagher, who referred her to me. She was then a little devil as well as a saint. I have dodged ash trays and other implements in my office that she threw around the place whenever mother simply wrinkled up her eyebrows in mild reproach. She was so exquisitely sensitized to the slightest thought of what may be called hostility on the part of the environment that she was even affected by the lifting of an eyebrow or the closing of a fist (hypervigilance). The mother, a very charming person, was incredibly stupid from the standpoint of this young instinctual individual. There was a constant fight. Dr. Clark may think psychoanalysis cured her. I give him all the credit he wishes, but if he knew the work which was put upon the mother he might give a slightly different interpretation, but I doubt that he would, because we can shake hands on the situation by saying that it was more or less the psychoanalytic knowledge on the part of the mother that helped her.

The patient [after many vicissitudes] went to a sanitarium where there were a lot of feebleminded boys. One of these boys got to monkeying around with her. She then started this menagerie "don't touch me" activity. Up to that time she had not had any respiratory difficulties. She went through these menagerie movements, and she would grunt "don't touch me," which meant "don't touch my genitals," "don't masturbate me." It was quite plain just what "don't touch me" meant.

She then went to Dr. Jacoby's sanitarium and led them a merry life there. She was still very sick, however, when she went to Stamford. There certain things happened which if Dr. Clark wishes to tell you, he can. These brought out other components to consciousness. Thus from the analytical understanding (there was no psychoanalysis by any "method"), with the analytical wisdom gained by the mother, she no longer struggled to keep this masturbatory situation from coming into consciousness with fear and horror. She accepted it. Then she fell in "love," and that was the beginning of her real cure. She fell in love, paradoxically enough, with at least two individuals in the sanitarium. I think Dr. Clark knows all about it. The transference was very interesting. She had a very fine, religious (super ego) transference on one of the men teachers, and, on the other hand, there was a low, base, vile situation with somebody else in the environment. There the two situations struggled for conscious mastery. Between the two, the whole material, plus the analytic interpretation, plus the knowledge of the environment, slowly came into the field of conscious control, and she was able to accept it all without guilt. I am not prepared to say this is the full explanation of the case. I do believe, however, because I have worked with some respiratory encephalitic cases now for four or five years with very good results, that most of these respiratory cases show a very striking course. At least 15 to 30 per cent of them get well spontaneously, as we say. (See figures of Ziegler, Critchley, Cook, Stern, and others.) Whatever "spontaneously getting well" means, nobody knows. There is really no such thing as spontaneously getting well. There are always a group of factors in the environment as well as internal ones which are of significance in the interpretation of results.

This case history could be much amplified. There is enough to show, however, the early regression to the anal-sadistic level a year or so after the initial insult (traumatic neurosis). The patient had menstruated

at 11 for a short time before the onset of encephalitis. She had eye palsies, facial flattening, lethargy and sleep reversal for one and one-half years. Tantrums, excessive violence and obscenities directed against the mother and a group of anal-sadistic regressive signs indicated the repression of the developing genital organization. Some masturbatory indications of this organization were violently repudiated when Dr. Meagher first spoke of them. These became consolidated at the sanitarium when actual heterosexual fingering took place, with the advent of the menagerie syndrome and the oculogyric crises. This whole sanitarium and another previously was run on the brutality and anal-sadistic system. Evident signs of the father incest situation were apparent and the movements of the eyes and anxiety were implicated in this. Then at Z actual seduction was almost accomplished and the ideal love affair with the teacher plus an artistic outlet and psychoanalytic understanding suddenly released the whole struggle into consciousness. The ego was ready to accept the knowledge of the "It" cravings; her mother was no longer a hated and feared object. A distracted, feared, sadistic father, who had made periodic alcoholic flight adjustments to all these difficulties (sickness, worry, finances, etc.), became more manageable and tenderness took the place of the repressed material. She no longer had a sense of guilt with respect to the mother and father and her instinct cravings. The ego had grown up and the severity of the super-ego abated.

Some final reflections may be offered regarding the sense of guilt and the need for punishment as related to the oculogyric crises and the anxiety states. A full presentation of the movements of the eyes which are utilized as an expression of emotional states, from "anguish to ecstasy," to borrow Janet's excellent phrase, cannot be attempted. In the paper presented a year ago it was suggested that the suppliant expression of the eyes had a meaning, and the biblical phrase "lift thine eyes to the hills from whence cometh thy help" most aptly entered into that meaning.

In more technical metapsychologic phrasing this could be stated by saying that earlier libido stages of instinctual needs, through regression, had to be met by increased repression. The ego had to be spared. The ego, in the mental system, operates chiefly to repress the development of uncomfortable thoughts; as has been stated, anxiety arises to keep out the dangerous (early erotic) situations. Symptoms arise to release the repressed energy and save the individual from further regression which would push the energy back to complete primary narcissistic cathexis. As the stage of the regression contains much energy at oral-anal sadistic levels, such narcissistic investment might lead to complete psychotic regression or to complete defusion and suicide. Either solu-

tion has been found in numerous cases, and continued research will be necessary to determine the relative interrelated dynamics of the somatic insult on the organs of the ego, the formation of the super-ego and the environmental realities.

For the solution found by the oculogyric crises the movements of the eyes offer a part of the release.

It is not without slight significance possibly that in the case of J. F., a certain histrionic attainment registers a stage of his super-ego as well as offers some light on the possibilities of an artistic outlet. J. F. was quite musical and a good dancer; as a youngster, he sang jazz rather well and with much expression. Furthermore, his anal-sadistic organization previous to the encephalitis had begun to show much wit-humor sublimation. Even in the phases of his "degenerate" conduct, as reported by "Dr. Burr," in the midst of his compulsive "obscene expressions," he could "wisecrack" many a broad anal situation.

It is also possibly of significance that as the analysis permitted full recognition of the masturbatory and coitus equivalents (respiratory activities), a period of comparative health followed. Then as actual coitus efforts were carried out and fellatio perversion was indulged in (oral-sadistic phase), the spasms of the eyes arose. A deeper level of infantile fixation material was reached, and the incest situation cathexis was of more significance. Now the sense of guilt, the anxiety and the religious expiatory movements of the eyes began.

It is fairly well agreed, on the double foundations of anthropology and psychoanalytic investigation, that the Oedipus complex is the original source of guilt and of morality. One hardly needs to summarize the evidence from either side. Freud, in his "Totem and Taboo," Nunberg,[30] Abraham, Reich,[31] Reik and numerous others have given much of the evidence.

It is impossible here to prove whether the need for punishment is primary and the sense of guilt secondary, as Freud has later suggested,[32] but it would seem to be so, since, as may be recalled, the attacks of the eyes were extremely painful, and when so there was less anxiety. Milder attacks showed more anxiety, and the obsessive thought arose "rape my mother"—"rape my sister." Nor is it possible to show here, with Nunberg, whether these are two distinct things, other than ambivalents.

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30. Nunberg, H.: Sense of Guilt and Need for Punishment, Internat. J. Psycho-Analysis **7**:420, 1926.

31. Reich, W.: The Source of Neurotic Anxiety, Internat. J. Psycho-Analysis **7**:381, 1926.

32. Freud: Economic Problem in Masochism, Collected Papers, London, International Psycho-Analytical Press, 1927, no. 22.

The argument cannot even be stated that would try out Nunberg's original inquiry whether "the sense of guilt and the need for punishment are not one and the same thing." He wrote:

> Although historically they represent a repetition of the primal deed, as reconstructed by Freud in connection with the primal horde, and in the development of the individual have a common genesis, not differentiated in time, and sometimes cannot be sharply distinguished in their manifestations, yet behind the sense of guilt there is unsatisfied object-libido, while behind the need for punishment there lurks the instinct of destruction, sexualized and directed against the ego. In the sense of guilt we have the attempt to cancel the deed; in the need for punishment the deed is renewed in relation to the subject's own ego. It is true that in the different types of neurosis the relation of the two tendencies to one another differs, but it is of practical importance to differentiate them and to recognize them in every patient.

My material will need more study before I consider this point with reference to J. F. and his painful cramps in the eyes.

As to the anxiety situation, Freud originally showed that it may arise from abstinence or inadequate gratification, and later from trauma. Reich, in his study, further emphasized that "anxiety can arise when the moral ego is not completely successful in repressing a libidinal excitation; the repressed impulse returns in the form of anxiety. Actual anxiety is the core of all neurotic anxieties. There are also birth anxieties, aggressive tendency repression anxieties, and possibly actual gonadal hormone suppression anxieties."

If it may be assumed that the marked masochistic phase of J. F.'s earlier symptomatology was somewhat relieved by the analytic procedure, then with Reich and others it may be assumed that sadistic-aggressive attacks on the environment would bring about increased castration anxiety. This seems to be verified by the outbreak of the oculogyric crises.

The nature of the "ego" then calls for more complete study, especially in its relation to the interrelation of the sexual and the destructive instincts (life and death instincts). Reich emphasized that impulse-ridden character types develop anxiety when they must control their sadistic impulses.

> Anxiety resulting from suppression of aggression is only superficially true. In the first place, if the aggression be carried out it does not disappear, hence it must be true that something else is still behind it. Specific libidinal factors are found to have been freely gratified in childhood. The brutal frustration of incestuous love is severely felt, and frustration of sexual gratification drives into the foreground aggressive impulses which take on an increasingly sexual coloring through fusion with repressed sexual impulses. Here sadism arises. Every frustration of sexual gratification arouses ambivalence.

"Hell hath no fury like a woman scorned" is a classic reminder of this. As is well known, during menstrual periods nearly all women have a tendency to anal-sadistic regression.

It is probably premature, especially in this communication, to attempt to estimate how much of the ego organ has been damaged by the encephalitic process. Just how this can be measured in metapsychologic terms offers a fascinating problem.

With these rather fragmentary bits, this terrain must be left for further elucidation. A closing word, taken chiefly from Reich's study, may help to explain why even with several months of analysis the complete mastery of J. F.'s struggles was not obtained.

> We are inclined to presuppose that this result is a therapeutic success without considering why the same therapeutic process, viz., liberation from anxiety, should produce such opposite results. It is by no means obvious why it should. Further experience, however, shows us: (1) That longing for the mother's womb and aggression persist in spite of analytical understanding so long as castration-anxiety is not analyzed (refractory cases), or that the partly freed libido, after a feeble movement toward the genital position, retreats to earlier fixation-points (relapse). (2) Cases which remain permanently free from symptoms, in spite of the fact that they have not been completely analyzed. In such instances analysis has dealt with genital fixations from the outset and has succeeded in resolving them before the transference-situation could be complicated by deeper fixations. The fact that genital libido was freed from anxiety brought about an automatic abrogation of other wishes. For all practical purposes, relief of libido-congestion by orgasm abolishes the tendency to regress. (3) If genital primacy has never been fully attained in childhood, the "attraction of the womb" or the tendency to pregenital gratification persists in spite of analysis of all sources of anxiety.

In closing, a word may be said about anxiety at the physical level as related to disturbance of gravitational stimulus and response through the temporary disturbance of the vestibular apparatus (van Bogaert, Marinesco and numerous other studies). No attempt will be made to carry this study into this realm beyond the statement that it is fairly conclusive that this level disturbance must be viewed as a positive rather than as an intercurrent sign (Hughlings Jackson) in which there is probably some reduction of the capacity of the somatic arc, thus destroying its hypervigilance (ego; super-ego) and enabling the loss of automatic control to come to consciousness as a part of the anxiety syndrome.

SPECIAL ARTICLE

PROGRESS IN PSYCHIATRY

I. INDUSTRIAL PSYCHIATRY *

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The extension of psychiatric interest to extramural problems has in the last decade led to interesting attempts to apply the methods of psychiatry to problems found in industry in general. Isolated phenomena of behavior problems in direct relation to industrial work have, of course, received a great deal of attention on the part of psychiatrists, such as accidents, the problems of vocational guidance and especially the clinical manifestation of the so-called traumatic neuroses. But only recently have systematic attempts been made to study behavior difficulties in the broadest sense at the place in which the subject actually works, the industrial plant, the store, etc. The appearance of the first comprehensive statement [1] of the results of an intensive psychiatric study of several years' duration furnishes the occasion to sketch in outline some of the developments in industrial psychiatry.

Pioneer attempts to introduce psychiatric methods into the handling of personnel problems of large industrial plants were made by Ball [2] as early as 1916. As a result, a personnel department under psychiatric guidance was established in 1921 by a large oil company. This department functioned for only one unit of this company, namely, the actual production unit in the oil fields. The problems faced by Dr. Ball in the beginning were of two kinds. First, there were the typical more massive occasions for friction and dissatisfaction which characterize any industrial organization, such as "lay-offs, reduction in force, wage conferences, misdirected private detective meddlings, threatened strikes, housing, medical service, employment, petty jealousies etc." Second, there were a large number of individual emotional problems which were treated in repeated psychiatric interviews. The result of one year's work was a general improvement in the health of the workers employed, lowered accident rates, lowered absenteeism and a decrease of 63 per

* Submitted for publication, Jan. 16, 1930.

1. Anderson, V. V.: Psychiatry in Industry, New York, Harper & Brothers, 1929.

2. Ball, J. D.: The Correlation of Neurology, Psychiatry, Psychology and General Medicine as Scientific Aids to Industrial Psychiatry, Am. J. Insan. **75**:521, 1919; Industrial Psychiatry, Am. J. Psychiat. **1**:639, 1922.

cent in the turnover of labor. "Job analyses" and personal examinations were undertaken with a view to a better and more individual handling of the employment, transfer and promotion of workers. This work was later continued in other units of the organization.

Dr. Ball also carried out practical investigations in industrial psychiatry in other industrial plants on a purely research basis. Questionnaire methods, psychiatric examinations and psychologic tests were used in combination. All persons presenting behavior problems were studied, including those graphically designated in their actual working contacts as " 'queer guys,' 'eccentrics,' 'disturbers,' 'querulous persons,' unreliable and unstable fellows,' 'misfits,' 'the irritable,' 'the sullen,' 'socially disgruntled,' 'unsociable,' 'negative,' 'conscientious,' 'litigious,' 'bearing-a-grudge,' 'peculiar,' 'glad-hand,' 'gossipy,' 'roving,' 'restless,' 'malicious,' 'lying,' 'swindling,' 'sex pervert,' 'false accusator,' 'abnormal suggestibility,' and 'mental twist' types!" [3] Ball pointed out, nevertheless, that industrial psychiatry should be considered "not as a 'weeding out' method, but as a method of conservation." [4]

In Dr. Ball's opinion, methods used in the employment bureau are the "keystone to the entire arch of industry." Careful study of methods of employing labor, involving interviews with superintendents, managers, foremen and men, in various large industrial plants brought him to the conclusion that "the turnover in many of our industries is astonishingly and absolutely unnecessary." In the salvaging of much of this human material by eliminating disturbing factors or changing to more congenial or suitable jobs, Dr. Ball found that application of psychiatric principles to industrial purposes should play a large part. He paid special attention to the causes of labor turnover. In a study in collaboration with Edward Williams on causes of labor turnover, the various reasons given for work terminations in a large manufacturing company were analyzed. It was found that a considerable percentage of terminations were due to one "psychopathic foreman." In the reasons for termination given by the company, this was not apparent. Some of the reasons were "discharged as undesirable," "discharged for incompetence," "discharged for disobedience," "disagreement with the foreman." This foreman was an "arrogant, bellicose, carry-a-chip on the shoulder type of foreman who knew nothing about handling men and was constantly swearing at and abusing his men over trivial matters which would easily be settled and smoothed over by a more intelligent and diplomatic type. . . ." He obtained his job as a reward for many years of service, and for no other reason. A psychiatric examination showed mental retardation and an unstable temperament unfitting him for his post.

3. Ball (footnote 2, first reference, p. 555).

4. Ball (footnote 2, second reference).

A great impetus was given to industrial psychiatry by Southard.[5] He pointed out the necessity of psychiatric training for physicians who held industrial positions. In one plant system in which more than twenty-five physicians were employed, he found that not one of them had ever had any training with regard to nervous and mental diseases or lesser personality disorders. His main plea was for an extension of mental hygiene in its broadest sense to the multiform problems of the human material of industry. The essence of the "mental hygiene of industry" was in his opinion not new, but the fresh contribution lay in a systematic attack on industrial personnel problems with "pooling and cooperative combination of expert medical and psychological and sociological interests . . . invoking the aid of all available experts in personality. . . ." [6]

Under Southard's influence interesting investigations, especially from the point of view of psychiatric social service, were undertaken by Jarrett.[7] An important psychologic supplement was added by psychiatric social workers to the efforts to raise efficiency in industry by mechanical means. Powers [8] implied the necessity of such more personal methods when she wrote: "I have often wondered what became of the man Schmidt, whose labor output Taylor, the father of the efficiency movement, raised from something like two to twelve tons of pig iron per day." She herself published a report of some interesting cases showing the economic aspects of the problem of psychopathic employees. One of her schizophrenic patients held 123 jobs in nine years, ranging from manual labor to clerical positions.

Scott [9] published a report on psychiatric work in a large life insurance company carried on over a period of years. She emphasized especially the important prophylactic work that can be done among employees who seek medical aid or come to the attention of their superiors for any incidental reason. She found that factors inherent in the work itself, such as monotony, rarely lead to neurotic disorders. Work situations

5. Southard, E. E.: The Movement for a Mental Hygiene of Industry, Ment. Hyg. **4**:43, 1920; Trade Unionism and Temperament: Notes upon the Psychiatric Point of View in Industry, ibid. **4**:281, 1920; The Modern Specialist in Unrest: A Place for the Psychiatrist in Industry, ibid. **4**:550, 1920; Mental Hygiene of Industry, Industrial Management, February, 1920 (quoted by Ball).

6. Southard (footnote 5, fourth reference).

7. Jarrett, Mary C.: The Psychopathic Employee: A Problem of Industry, Medicine & Surgery **1**:727, 1917; Shell-Shock Analogues: Neuroses in Civil Life Having a Sudden or Critical Origin, ibid. **2**:266, 1918; The Mental Hygiene of Industry, Ment. Hyg. **4**:867, 1920.

8. Powers, Margaret J.: The Industrial Cost of the Psychopathic Employee, Ment. Hyg. **4**:932, 1920.

9. Scott, Augusta: Neuropsychiatric Work in Industry, Ment. Hyg. **7**:521, 1923.

in which psychiatric opinion was sought by the company as a routine were the following: the payment of disability, the question of retirement, the advisability of excuse from overtime work, the changing of vacations after the schedule was once made up, the possibility of cutting down frequent absences ascribed to ill health when there was no physical disease apparent. In her contacts with the working patients, she found that "one must see that there is not too much discrepancy between ambition and capacity for achievement."

Psychiatric studies based on investigations in industries are numerous in a growing literature. Some of them have been summarized by Sherman.[10] (Compare also Adler,[11] Pratt,[12] White,[13] Elkind,[14] Culpin [15] and Smith.[16]) A considerable part of the psychiatric literature on industrial problems, however, is devoted to explaining to the layman who is interested in the industrial field the methods of psychiatry as applied to industry.[17] An especially clear presentation of this type has been given recently by Campbell.[18]

What Dr. Campbell asked for in 1921,[19] in a paper on mental hygiene in industry, namely, that well studied material should be gathered which would allow useful constructive suggestions to be made with regard to the mental health of the industrial worker, bids fair to be furnished by Dr. V. V. Anderson [1] in his book on "Psychiatry in Industry." Dr. Anderson has made the first prolonged systematic study of psychiatric problems in a large department store, R. H. Macy and Company, and has embodied his methods and conclusions in this book.

The history of the development of this important enterprise in applied psychiatry is of considerable interest.[20] In the beginning there was no

10. Sherman, Mandel: A Review of Industrial Psychiatry, Am. J. Psychiat. **6**:701, 1926-1927.

11. Adler, Herman: Unemployment and Personality: A Study of Psychopathic Cases, Ment. Hyg. **1**:16, 1917.

12. Pratt, G. K.: The Problem of the Mental Misfit in Industry, Ment. Hyg. **6**:526, 1922.

13. White, William A.: Psychoanalysis in Vocational Guidance, Psychoanalyt. Rev. **10**:241, 1923.

14. Elkind, H. B.: Industrial Psychiatry, Ment. Hyg. **13**:378, 1929.

15. Culpin, M.: Nervous Illness in Industry, J. Indust. Hyg. **11**:114, 1929.

16. Smith, M.: Some Medicopsychological Problems in Industry, J. Neurol. & Psychopath. **9**:146, 1928-1929.

17. Papers on this subject can be found in the following journals: Industrial Management, Mental Hygiene, Industry, Personnel Journal, Industrial Psychology, Journal of Personnel Research, Hospital Social Service Quarterly, Journal of Industrial Hygiene, and others.

18. Campbell, C. Macfie: Personal Factors in Relation to the Health of the Individual Worker, Ment. Hyg. **13**:483, 1929.

19. Campbell, C. Macfie: Mental Hygiene in Industry, Ment. Hyg. **5**:468, 1921.

20. Anderson, V. V.: Personal communication.

intention of starting what later turned out to be a psychiatric and psychologic department. The primary interest was in improving the technic of employment. For a number of years psychologists had been used to develop tests, but these psychologic tests proved of little practical value, evidently because they were used by themselves to determine the selection of employees, instead of as aids or guides to "interviewers" who were trained in sizing up personalities from a more comprehensive point of view. The work began with interviews with those who left the store, those laid off, those who resigned and those who went to the hospital. The next step was a study of employment technic, followed by surveys of the various departments with the view of determining the conditions that affected unfavorably the ability to work, the attitude toward work and the physical and mental health of the worker. The demonstration that this type of work paid in decreased turnover and increased production led to further employment of psychologists and social workers until within three or four years the present psychiatric department was built up in the store.

In his book, "Psychiatry in Industry," Dr. Anderson summarized the results of application of psychiatric methods in industry over a period of four years. His presentation is concrete and plastic, and refrains deliberately from too far-reaching theoretical generalizations. His chief emphasis is on the need for "individualization of personnel procedure." Anybody familiar with the way in which employment problems are handled in the atmosphere of mass production will realize how revolutionary such endeavors are. The success of this actual working experiment is therefore a milestone in applied psychiatry.

Dr. Anderson believes that the best results can be obtained with what he calls the "mental hygiene unit" composed of a psychiatrist, a psychologist and a psychiatric social service worker. His critique of methods restricted to tests alone is important, especially if one considers that there is at present a widespread trend in the opposite direction.

> Anyone who studies and works with large numbers of actual cases of job failure and job success will find wholly inadequate that conception of vocational guidance that implies the possession, by each individual, of some special ability to do particularly well some one particular task, and that rests the solution of one's work career on the application of certain trick methods to discover these supposed abilities. As a matter of fact, most people can do a great many things well, if they are sufficiently interested, have developed good enough work habits to apply themselves effectively to a task, have a definite appetite for the thing they are doing, know how to work well with people, and have a healthy attitude toward themselves and life's realities. Wherever failure is found, an analysis of its causes will disclose far more complex issues than the mere matter of testable ability to perform the tasks of a given job.[1]

Mental tests, in Dr. Anderson's opinion, should not be given more value than the general physician gives to blood tests, etc. Despite his

optimism and even enthusiasm for the rôle of psychiatry in industry, the author does not go too far, as advocates of applied psychiatry so often do in other spheres. He feels that of course the psychiatrist cannot and should not be the one to take charge of the management of different personnel activities. He should be a "consulting aid for the integration of all diagnostic, adjustment, therapeutic, training and development resources in their bearing on a given case." [1]

"Work failures" are considered first in Dr. Anderson's book. About 20 per cent of employees, by and large, are "problem individuals." They appear as transfers from one job to another, as persons who have resigned or been laid off. Three main causal factors were found for these work failures: a generally badly adjusted personality, special job disabilities and physical disabilities. What the author emphasized with regard to this problem is that the readjustment of these persons is frequently possible; so frequently, indeed, that it "pays," not only from a charitable point of view, but also in terms of financial profit. The actual problems for which cases were referred for psychiatric attention were as varied in the store as they are in the patients in the psychiatric outpatient department of a hospital. For the practicing psychiatrist who frequently has to resort to vocational adjustment in the treatment of persons with mental disorders, it is instructive to see in what form the medical complaint which confronts him in general practice appears in the setting of the place in which the subject works. Some of the reasons for which employees were referred to Dr. Anderson were: "bad attitude," "upsets morale of the department," "poor production," "nervousness," "chronic illness complex," "attendance record," "constant disciplinary problem," "stupid," "error maker," "large shorts in cashiering," "indifferent," "resents authority," "daydreamer," "wastes time," "damages goods," etc.

Coordinating the results of examination and treatment, Dr. Anderson distinguished four groups of cases, all instructively illustrated by abstracts of case records: (1) The group in which the difficulty is more one of personality than any special maladjustment to the job. In these cases adjustment within their own department is attempted by frequent contacts with the psychiatrist and the psychiatric social worker. (2) The inverse group in which misplacement in the job is the main trouble rather than any personality handicap. Therapy consists in finding suitable work in another department and proper training for the new job. (3) A group of persons who are found to be either physically or mentally unable to adjust themselves to the working conditions in the store. The recommendation in these cases is discharge. (4) A final group in which various attempts at readjustment have been made, but in which no satisfactory results could be obtained despite a seemingly good prognostic outlook at the first examination.

Under the heading "selecting executives," another aspect of industrial psychiatry is considered; namely, that of dealing with the exceptionally gifted employee, the group that is considered for promotion. Naturally, a more scientific treatment of this question is indicated only in large concerns in which the necessary acquaintance with these aspirants cannot be gained by daily association. The difference in the treatment of this group and that of the problem employees, discussed before, is the necessity of studying more closely the actual work careers, the "job behavior." Dr. Anderson gives two examples of the type of position to which employees are promoted: head of stock—later leading to a buyer's position—and section manager. The procedure for handling the question of promotions is the following: A detailed study of the duties of the new job to be filled is made. From this is made a list of the qualifications which the holder of the job should have. Such items are included as age, schooling, work history, intelligence, accuracy, speed, personality and physical condition. It was found that study of the applicant against the background of a detailed analysis of the position and its requirements yielded far better results than the usually employed "trial and error" or "personal hunch" method. Out of this study has grown the present service in the store now rendered in the examination of all promotional cases prior to official action by the general manager.

The young employee is of special importance in industrial psychiatry. Failures in work adaptation and continuity, the "turnover" of commercial terminology, are thirteen times as frequent in persons under 20 years of age as would be expected when the turnover of the force as a whole is considered. Of the different departments of junior workers, the messenger boys, stock girls, merchandise checkers, etc., Dr. Anderson reported on his experimentation in one typical "junior" department, that of merchandise checking, in which only girls under 18 are employed. The turnover in this department was greater than in any other department in the store. A study was made of 150 unselected new girls employed as merchandise checkers during a period of four months. The routine followed up to the time of the study was that seniority of service qualified the merchandise checkers for better positions. Under this routine it had been impossible either to develop a stable department or to develop personnel for more important jobs. The more ambitious and promising young people would hold jobs as merchandise checkers only temporarily, to resign as soon as they found better work, because too long a period as merchandise checker was inevitable before transfer. On the other hand, the older employees who had served long as merchandise checkers were rewarded for long service by promotion, although they were "merchandise checker types" and better suited for checking merchandise than for any other type of work.

After a survey of the prevailing conditions and personnel, the psychiatrist advised two changes which were put into practice. First, each merchandise checker could apply for promotion after six months' employment. Second, all the facilities for medical, psychiatric and psychologic study were used to evaluate her capabilities when she did apply. Of 100 applicants for promotion, the psychiatric advice was for promotion in 67 per cent and against it in 33 per cent. Of the 67 per cent who were promoted on psychiatric advice, from 90 to 100 per cent were successful. It is exceedingly interesting to note the changes that took place in this department after one year of the régime under Dr. Anderson's advice.

	Average Age	Education	Intelligence	Turnover
Observations in original study of merchandise checkers	17 years	90% grammar school grades	73% less than average	Very large
Results after one year of the new promotion régime	17 years	54% high school education	58% above average	Reduced to average

Charted by reviewer.

The general results were, in other words, that with the prospect of possible advancement after six months' experience as merchandise checker, the more ambitious young people were content to use that department as a stepping-stone instead of as a stop-gap between jobs; while the girls who were temperamentally and otherwise suitable primarily for this work formed the stable residual of the department, content not to apply for advancement and not "moved up" by any rule regarding seniority of service.

Otherwise Dr. Anderson's book deals mainly with the diffusion of psychiatric methods in industry, comprehensive surveys of whole departments, employment technic, etc. It is interesting that a trained social service worker was more successful in selecting applicants for positions as cashier than the usual employment interviewer had been during the same period of time. As a result of this discovery, an attempt was made to give each "interviewer" some training in psychiatric principles along the line of actual case training, a procedure which led to satisfactory results.

A survey of the psychiatric component in the existing health problems leads Dr. Anderson to the self-evident, but as yet Utopian, postulation that the industrial physician should have training in psychiatry. In a discussion of automobile accidents, Dr. Anderson said that it was found in a study of 450 drivers that of those with "a positive accident tendency" 60 per cent had "sufficiently marked personality disorders to justify our considering them unquestionable risks in driving cars." Application of industrial psychiatric methods to the selection of drivers led to a monthly reduction of accidents of from 50 to 82 per cent.

The problem of the usefulness of psychologic tests in psychiatric work needs a brief discussion. Dr. Anderson's book contains a special chapter by Miss Stella Engel on tests which have been found useful. In Dr. Anderson's view, psychologic tests have been found indispensable, but definitely supplementary. This view was also expressed by Ray,[21] who said that tests "should be considered only as part of the picture that the psychiatric method of study gives of an individual."

The contrast between experimental psychologic and the psychiatric approach which Viteles [22] stressed is perhaps not so far-reaching as some writers assume. It is noteworthy in this connection that experimental psychologists are now putting less emphasis on special aptitude tests, many of which are evidently primarily fine indicators of mild degrees of intellectual debility. The close proximity and with it the great possibility of cooperation between psychologic and psychopathologic methods is evidenced also in an excellent paper by Lorine Pruette and Douglas Fryer [23] on affective factors in vocational adjustment.

An important aspect of psychiatric endeavors in industry, as opposed to the employment of psychologists alone, has been emphasized by Adler:

> I see no rivalry between psychology and psychiatry but think there is one distinction between them which comes out in these industrial relations; in the eyes of the layman the psychologist is a highbrow, and perhaps a paid agent of the employer, whose object it is to take the worker away from his job and analyse him. About this the worker has nothing to say—he passes or he does not. Whether the psychiatrist is employed by the company or not, he is a physician, and that gives him an advantage with the laborer which the psychologist has not. If he uses this advantage he can get a contact with the laborer much like that of the physician in his office with the patient. He is there to help the man, and the employee can look to him for help. This is what stood out in Ball's work . . . he simply managed to sell his work to the workmen. During the very serious disturbance in the oil fields in California after the war, the Shell Company was the only one that did not have a strike; the company officers believe this was due to Dr. Ball's work. . . . Dr. Ball had conferences with both employers and employees, and had in mind what was needed for their welfare.[24]

It would seem that the plea to use psychiatric methods in industry is not so much a demand for highly technical and specialized methods. A great deal can apparently be done with the simplest psychiatric methods if they are applied correctly and in the proper place. "Ventila-

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21. Ray, E. L.: The Psychological Versus the Psychiatric Method in Industry, Ment. Hyg. **11**:140, 1927.

22. Viteles, M. S.: Psychology and Psychiatry in Industry, Ment. Hyg. **13**: 361, 1929.

23. Pruette, L., and Fryer, D.: Affective Factors in Vocational Maladjustment, Ment. Hyg. **7**:102, 1923.

24. Adler, Herman M.: Discussion on Industrial Psychiatry, Arch. Neurol. & Psychiat. **15**:526 (April) 1926.

tion" of problems by a disquieted person is such a method. Dr. Elton Mayo gave an illustrative example of this.[25] He told of a firm "whose workers were given the opportunity to express themselves to selected interviewers as to working conditions, satisfactions and dissatisfactions with the job. The effect was astonishing. Not only was it possible for the firm to establish a far higher level of human happiness and secure improvement in the work, but all kinds of minor ills hitherto unknown and affecting productivity were discovered. There resulted an increasing interest in the human aspects of the shop situation on the part of the supervisors. . . ." It seems to me that one might add that the practicing psychiatrist in giving this attention to the human aspects of the shop situation might gain a great deal of knowledge regarding the shop aspects of human situations, which are often not adequately covered in the study of psychiatric cases. Dr. Anderson's treatment of the problems in the merchandise checking department is a good lesson in this respect.

It would seem that the intricate and often disturbing problems of work adjustment in all its aspects are as a rule not sufficiently taken into account in the study of behavior disorders. Here evidently, general psychopathology may profit from the results of studies in industrial psychiatry as it is defined by Thurstone: ". . . Personnel management might be defined as the attempt to coordinate in some systematic fashion the two realms of working and living. The successful personnel manager is characteristically the man who not only understands thoroughly the effect of living on work as well as the effect of work on living, but who also attempts in a systematic way to bring about conditions which will favor both. It is clear immediately that such a task is also part of the function of industrial psychiatry." [26]

Summing up this survey of recent endeavors in industrial psychiatry, one may say that one part of its importance lies in the fact that a large new field of applied psychiatry is becoming more and more definitely established. There is, however, also a special significance for scientific psychiatry in these attempts. As an increasing amount of well studied material is gathered, the psychiatric study of the individual at work should eventually throw new sidelights on scientific problems of psychiatry. The individual spends no less time at work than he spends sleeping, and since the investigation of dreams has led to important scientific conclusions and outlooks, the study of the individual at work—which has the advantage that it can be objectively observed—may in time add new knowledge to our understanding of psychopathologic behavior.

25. New England Conference on Industrial Mental Hygiene, Ment. Hygiene Bulletin **7**:5, 1925.

26. Thurstone, L. L.: Discussion on Industrial Psychiatry, Arch. Neurol. & Psychiat. **15**:525 (April) 1926.

Abstracts from Current Literature

FEAR REACTION (DAS ZUSAMMENSCHRECKEN). HANS STRAUSS, J. f. Psychol. u. Neurol. **39**:111, 1929.

The acoustic-motor reactions to sudden intense acoustic stimuli (firing of a loud shot from a pistol) were analyzed cinematographically. In healthy normal persons, two types of motor reactions were noted: (1) a primary reaction following the stimulus immediately; (2) a secondary reaction appearing some time after the discharge of the shot. It was found that whereas the secondary reaction is often markedly asymmetric, with the motor pattern varying in different persons, the primary reaction is always symmetrical and of uniform motor pattern in different persons.

The motor reaction is always diphasic. During the first phase, the subject moves the part of the body to which his attention has been focused during the experiment from its normal position to one of maximum deviation. During the second phase, there is a return from the maximum point of deviation to the normal position. The duration of each phase is about the same and is relatively short, never more than a second for both phases and most commonly less than half a second. The motor pattern of the second phase is generally similar to that of the first phase.

In the upright position with the head in the center and arms hanging along the sides of the body, there always occur, regardless of the direction of the sound of the shot, certain definite movements, which may be said to represent the basis of the motor pattern of the first phase. These movements occur in the following order: closure of the eyes, characteristic contraction of the facial muscles, bending forward of the head, elevation and forward projection of the shoulders, abduction, forward elevation and internal rotation of the arm, flexion of the elbow, pronation of the forearm, closure of the hand, forward flexion of the trunk, flexion of lower extremities at the hips and knees with a corresponding movement of the feet, and in the sitting posture adduction and internal rotation at the hips. No movements were observed having a pattern other than that mentioned, in connection with any particular segment of the body.

Marked variations in the reactions were noted in different subjects. The variations noted consisted of changes in the degree of excursion of the different joints, as well as in the participation of a greater or lesser number of body segments in the execution of the motor reaction. It was also noted that whenever there occurred an extensive reaction of the entire body there also occurred an increase in the excursion of movement of the respective segments.

With an increase from a more feeble to a more intense reaction, the effects noted always followed certain definite rules: Closure of the eyes always occurred even though no other movements were observed. With a still further increase of reaction the closure of the eyes was associated with a contraction of the abdominal walls, a movement which does not always accompany closure of the eyes (at least with the author's technic). Other rules were: distal parts of the arm were never moved unless the more proximal parts (shoulders) were also moved; the extent of movements of the more distal segments of the arms always ran parallel to flexion of the head; bending of the trunk never occurred without a simultaneous bending of the head; facial contraction was observed only with severe reactions; in the erect position, the motor reactions in the lower extremities were independent of the intensity of the reaction. These motor reactions were observed not only in the erect but also in the sitting and recumbent postures. Holding the arm in flexion before the shot was fired was never followed by a reaction of extension, but if a movement did occur it was one of further flexion. Similarly, when the head was held in flexion before the shot was fired, the reaction

following the shot was never one of extension of the head but one of further flexion. Closure of the lids before the shot was fired was never followed by an opening of the lids as a motor reaction. Active innervation of a segment of the body was always followed by a failure of the primary motor reaction in that particular segment. When the head was held to one side before the shot was fired, the motor reaction following the firing of the shot was: first, a change in the reaction of the head (modification of the flexion movement, superaddition of turning movements of the head), and second, there occurred changes in the primary reaction of the arm, the latter becoming asymmetric. According to Strauss, these asymmetric reactions correspond to the effects of changes in the tonus of arm muscles in the sense of tonic reflexes.

The later appearing secondary reactions were of three types: "spying," "protective" and "flight" movements. The secondary reaction may appear as an isolated phenomenon after the termination of the primary reaction, or it may merge into it, or it may set in during its progress. With the repetition of the stimuli (shots) there occurred other reactions which Strauss designates as atypical motor reactions, because they appeared, like the primary reactions, immediately after the stimulus, although the pattern of the reaction differed markedly from that of the primary reaction. Inasmuch as these "atypical" reactions were also in the nature of "spying" or "protective" movements, the author believes that they may possibly be premature secondary reactions.

No close relationship could be established between the intensity of the primary reaction and the onset or type of secondary reaction. In the secondary reactions following shots of varying intensity there were sometimes observed in the same subject atypical reactions which often resembled each other. Sometimes there were also observed in the same person great resemblances between the atypical and the secondary reactions. In most of the cases, a repetition of the shots was followed by a gradually progressive diminution of intensity of the primary reaction; at other times, there occurred a delayed diminution and occasionally even an increase in the intensity of the primary reaction.

The intensity of the primary reaction seemed to bear no relationship to the constitution of the subject or, in pathologic cases, to the nature of the disease. The intensity of the primary reaction seemed to depend much more on the ability to arouse the attention of the subject and on the condition of tonus. Age and sex had apparently no influence on the mode of reaction. Marked irregularities in the mode of reaction were, above all, most common in hysterical subjects.

In patients afflicted with disturbances of motility, some of the following phenomena were observed: increase of intensity of the primary reaction; frequent failure of diminution of reaction; markedly intense primary reactions and their slow diminution, especially observed in persons with poor motility but without actual rigidity; feeble primary reaction and progressive diminution in intensity in persons with tremor. Feeble primary reactions were also observed in the affected segments in persons suffering from rigidity. In patients with psychomotor disturbances of motility (catatonia), the primary reactions were feeble and the secondary reactions appeared unusually early. In persons with severe ataxia, the primary reactions were intense and greatly overshadowed by the ataxia.

In persons suffering from various psychopathologic conditions there were noted, among others, the following phenomena: primary reactions varying in the same person from feebleness to moderate intensity; always in paretic patients with euphoria, a progressive diminution of the primary reaction; in cases of lethargy and in diseased states characterized by failure of attention, a complete absence of the primary reactions. This, however, was not the case in patients suffering from delirium tremens.

In nursing infants, the acoustic motor reactions assumed the pattern of a Moro reflex with a play of tonic neck and postural reflexes. Tonic neck reflexes were also observed in the primary reactions of adults.

Strauss is inclined to believe that the primary acoustic-motor reaction is a reflex — "the acoustic-motor" reflex. The substrate of this reflex in the infant he

assumes to be a stimulation of the motor medullary nuclei of the acoustic nerve. He does not believe that the reflex arc extends to the cortex—not even in the adult. His conception of the reflex arc is as follows: Acousticus-nucleus ruber (directly over the lemniscus lateralis, or over the posterior corpora quadrigemina, perhaps also over the optic thalamus) over the rubrofugal tracts. When the pyramidal tracts are intact, they exert an inhibitory influence over the reflex. Biologically, the primary reaction, according to the author, is to be regarded as a reflex of "defense."

The secondary and atypical reactions have their substrate partly in affective impulses and partly in definite voluntary processes. These reactions are motor phenomena, the occurrence of which depends on the cortical auditory centers.

The contribution is concluded with a study of the effect of sudden acoustic stimuli on the vascular system, on the pupils, on pulse frequency, on blood pressure and on respiration. It also includes an investigation of the motor reactions following sudden light stimuli and skin stimuli. Those interested in the subject will be amply repaid by reading this rather lengthy but excellent paper in the original.

KESCHNER, New York.

COMPULSIVE THINKING AS A CASTRATION EQUIVALENT. E. G. HOWE, Brit. J. M. Psychol. **9**:159 (Aug.) 1929.

The author takes as his point of departure the paper by McCurdy on A Hypothetical Mental Constitution for Compulsive Thinkers (*Brit. J. M. Psychol.*, vol. 6; part 3, p. 159). He deduces from this paper that "the motive of compulsive thinking is that it strives to complete the intellectual perfection of an all-important phantasy, at the same time that it satisfies both a grudge against, and an erotic wish towards the mother. Compulsive thinking is a flight from the reality of disappointing infantile experience because only phantasy can give that satisfaction which reality denies." "Compulsive thinking is an escape from a loss: from the loss of the satisfaction of an all-important phantasy, which is safeguarded by flight into compulsive intellectualization." He does not agree with this conception—rather he thinks that "compulsive thinking is an escape by a loss, the escape being from guilt by a process of de-emotionalization and intellectual substitution. The escape from a loss becomes a secondary addition: the original affect is retained by being transferred to the substitute, which is then valued with all the intensity of the original. The motive of compulsive thinking is, on this hypothesis, escape from guilt by a mechanism of castration, the equivalent of which is by de-emotionalization and intellectualization, the one leading inevitably to the other. But having lost the most precious symbol of creation, the genitals, their affect-value must be transferred to their innocuous substitute, which will then be equally or even more precious. That innocuous substitute is the intellect, which then becomes both compulsive in operation, and overvalued in affect. There is, therefore, a secondary motive of escape from a loss: the loss is not felt so long as the genital over-valuation of the intellect is maintained. But the primary motive is escape from guilt, which is obtained by the substitution of a more civilized and socially tolerated process of thought, for the infantile and guilty process of feeling. The guilt from which escape is sought is that derived from the Oedipus and Electra motive, or 'parent fixation.'"

Before proceeding to illustrate this concept by the report of five cases, Howe attempts some theoretical discussion of definitions. The compulsive thinker referred to must be distinguished from the group of obsessional cases in which obsessional thoughts are the most prominent feature; in the former the whole function of thought is compulsive; in the latter, only certain ideas which have a symbolic value. Compulsive thinking is not limited to the neurotic person but is very widespread. In the compulsive thinker, thought may seem to be free and creative but it is not really so. It is essentially an escape activated by fear behind rather than by an ideal in front. The compulsive thinker tends to persist in an apparently unprofitable train of thought. This train of thought appears unprofitable only

if viewed superficially. "But if it is persistent it may safely be assumed that it is profitable to the satisfaction of some unconscious wish."

"The function of thought, viewed from the standpoint of its simplest origin, is to solve the problem of demanding or contending needs. All is simple enough if needs and appetites do not conflict, which they do. Where there is a conflict, the stability of the ego may be preserved in either of two ways: by fight or by flight. And it appears that these two methods of reacting to an emotional problem give rise to two different methods of thought, 'fight thinking' the goal of which is positive and the pursuit of an ideal, and 'flight thinking' the goal of which is negative and the escape from a difficulty. The common emotional conflict from which flight is made is that of infantile emotional relationships with parents and parent substitutes." The second type of thinking "is equivalent to an attempt at emotional repression, or de-emotionalization: and that the consequent intellectualization assumes the value of the all-important genital primacy."

In order to clear himself of the imputation that all motive and symbolism are phallic, the author states that he regards both phallus and castration as simple symbols of great ideas — the phallus not merely of genital significance, but of the eternal onward drive of all creative power in life; castration as its negative signifying escape, fear and death. From a study of his cases he concludes: "The symptom complex of the compulsive thinker is suggestive of the dementia praecox type: namely, an escape from reality into 'thinking' of a compulsive character, emotional regression and sexual maladjustment, isolation, martyrdom, self-punishment, castration symbolism and suicidal tendencies. It may also present to a greater or lesser degree obsessional characteristics, but in their most subtle forms these may be no more than a striving for logical perfection and systematic completeness. The 'inviolable personality' is a very marked feature of the compulsive thinker and is due to the transference of genital value to the thinking process. Thinking is all in all to the compulsive thinker, and his thoughts are cherished as if they were himself. For the same reason he is extremely resistive to criticism and shows the rigidity of character. He is primarily self-centered and self-seeking, and if he leads, must lead from a distance, his leadership being autocratic and not cooperative, and itself more important than the cause.

"Psychotherapy is peculiarly difficult, for the following reasons, amongst others: (a) The critical faculty is itself involved in the compulsion. (b) The inviolable personality must be violated, and when threatened always tends to revert again to defend itself by compulsive thinking. (c) Fear of emotional reality, which is the foundation of and motive for the whole scheme, is so strong as to cause fear of recovery, and sanity to be feared as being itself insane. This would again be utilized and exaggerated by a masochistic factor. (d) The subtlety and widespread character of the process make analysis peculiarly difficult."

Compulsive thinking is more than a problem in individual psychopathology, for its principle permeates the foundations of society and threatens it with suicide, through the underlying castration motive. Compulsive thinkers tend to become the teachers of the race. The result is the dogmatic commendation of over-intellectualization, emotional maladjustment, mechanization and a confusion of precept that threatens the root of the true principles of education, religion and sound psychologic development, which must be emotional freedom and growth. In a scientific method, reason and mathematical accuracy are not enough, for the motive of each may be unconscious and compulsive, seeking an escape from the problem which they seem to try to solve.

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EMBRYONAL AND POSTEMBRYONAL DEVELOPMENT OF THE HUMAN CEREBRAL CORTEX. I. N. FILIMONOFF, J. f. Psychol. u. Neurol. **39**:323, 1929.

In the sixth month of fetal life, the cortex in the region of the area striata shows distinct stratification. The area striata is easily distinguished from the area occipitalis, because the latter is considerably less stratified. The areas in the region of the fissura centralis are still less stratified. Even at this age there

is a greater cell density in the gyrus centralis posterior than in the gyrus centralis anterior, and the differentiated cells (the future Betz cells) can already be made out in the gyrus centralis anterior.

In the seventh month of fetal life, all areas examined were distinctly stratified and many showed peculiarities in stratification that could be regarded as characteristic for certain individual areas. The area striata is already divided into its ten layers (I, II, III, IV a, IV bα, IV bβ, IV c, V, VI, VII), is rich in cells, and has a wide IV layer but a narrow III layer; its VI layer is dense and dark, and in marked contrast to the VII layer. The area occipitalis is characterized at this stage by intense stratification of its upper (II, III and IV) layers and relatively poorer stratification of the lower (VI and VII) layers. The area gigantopyramidalis is characterized by the extensive width of its cortex, the transition of its layers into one another, a relatively narrow IV layer, and a wide V layer with its characteristic subdivisions into V a r, Vγ and V b r. In this stage, the area postcentralis tenuigranularis is already characterized by its relatively wide III and relatively narrow IV layer. The area postcentralis supragranularis is characterized by its intense cell density, slight differentiation of the upper layers (II, III, IV) and unusually well differentiated lower layers, which are separated from the former by a pale V layer. Finally, the area postcentralis eumacropyramidalis shows a typical seven-layer stratification which is exceptionally well marked in the upper, as well as in the lower, layers.

At this age, as well as later, the area striata shows by far the most characteristic stratification. Changes in stratification after the seventh month of fetal life occur chiefly in layer II. First, it merges gradually into layer III, and second, it becomes narrower at the expense of the latter. In the adult, the III layer is developed not only at its own expense but also at the expense of the tectogenic ground layer of the II layer. At birth, the narrowing of the II layer reaches its full and definite degree of development. Beyond this, the alterations in stratification are insignificant. An exception to this rule is observed only in the area gigantopyramidalis. Layer IV, which is already well indicated at the end of fetal life in this area, disappears completely first in the process of postembryonal development. For a long period after birth there is found between III^3 and V a r a band which on structural grounds cannot be designated as a genuine IV layer, because it consists to a considerable degree of well differentiated cells which, owing to the dense distribution of the latter, can readily be distinguished from its adjacent layers. This remnant of the IV zone is designated as (IV)—the parenthesis indicating not only its origin (its separateness from III and V) but also its nongranular character.

Whereas the differentiation of the layers, with the exception of the IV layer of the area gigantopyramidalis, is practically complete at birth, cell differentiation to any considerable extent does not begin to take place till the postembryonal period. The differentiation of the various kinds of cells of the cerebral cortex occurs during different periods. In this respect, the large cells of the V layer far exceed all remaining cells. In all the areas examined by the author, these cells were already well developed in the seventh, and in the area gigantopyramidalis in the sixth month of fetal life; i. e., at an age when the remaining cellular elements still have their neuroblastic character, the former are already well formed and of relatively large size, though not so large as in the adult. The remaining cells are first differentiated later, but even in these, the differentiation is already in full progress at birth. In this connection, it must, however, be emphasized that during this process of differentiation the development of the size of the cells is relatively independent of the time at which the development begins. This is best illustrated in the area postcentralis supragranularis. In this area, in the adult, the large cells are only rarely found in the V layer, and during the process of embryonal development their size and number are not so great as those of the corresponding cells of the other areas. Here one is dealing apparently with a postembryonal arrest of development.

It must also be pointed out that there is no reason to speak of this phenomenon as an arrest of development in the strict sense of the word. These cells are

merely retarded in their growth: whereas during an early period of development these cells may be regarded as large cells, in the adult brain, unless they keep on growing further, they must be regarded as small cells.

The tempo of differentiation and development of the cells, both of which are rapid during embryonal and postembryonal development, becomes rapidly slow during further postembryonal development, so that in a child aged 3, cell differentiation has reached a high degree, and in a child aged 8, the cells of the cerebral cortex differ little from those of an adult.

The differentiation of the various kinds of cells of the cerebral cortex assumes different characteristics for each type of cell. The cells of the II and III layer go through the early stage of pyramidization: a wide triangular cell with a large nucleus so situated that the protoplasm of the cell is visible only in the margins of the triangle. The spindle cells never go through this stage; they always assume the shape of a bipolar cell. The cells of the IV layer and the star-shaped cells of layer IV b in the area striata show early in their differentiation a perinuclear arrangement of protoplasm in which the nucleus is surrounded on all sides by a more or less uniform deposit of protoplasm.

These are, in the main, the general characteristics of embryonal and postembryonal development of the areas examined. The author states that present methods of investigation and especially methods of brain fixation do not permit more detailed conclusions.

KESCHNER, New York.

CEREBRAL CENTROLOBAL SCLEROSIS OR SCHILDER-FOIX DISEASE. JULIEN MARIE, Ann. de méd. **26**:162 (July) 1929.

The attempt was made to give a description of the clinical course of the different types of encephalitis periaxialis diffusa based on the study of cases which had been published. Most of the acute types of the disease had been reported in children, occasionally in adults with a maximal age of from 20 to 30 years. The course resembles very much the clinical picture of a rapidly progressing brain tumor. The acute type is characterized by three main groups of syndromes: disturbances of vision, of motion and of the psyche. The order of sequence is usually in the order cited, though it may vary in rare instances. The visual disturbances are manifested by a diminution of vision, hemianopia or a concentric diminution of the visual fields, loss of color vision and papilledema. Within from fifteen days to three months after the preliminary period, convulsive crises may occur which are followed by paralysis and finally total blindness. The psychic disturbances consist in a loss of concentration and apathy. The motor troubles are hemiplegia, or more frequently triplegia and tetraplegia, with rapidly developing contractures. In the foot, the pes equinovarus is seen very early; in the upper extremities, adduction with flexion of the arms and hyperflexion of the thumb. Spastic convulsions occur which are very painful and usually end with a fixed posture of the extremities involved, like elevation of the arm with adduction and flexion of the lower arm or with forced flexion of the leg at the hip. The psychic disturbances, which usually are the last of the triad to appear, consist in diminished concentration, apathy, indifference and inactive behavior. In addition, one finds disturbances of speech, which is slow, indistinct and dysarthric. Disturbances of hearing, taste and smell are finally added. Sensory disturbances are difficult to diagnose with the diminished mental response of the patient. Sometimes ataxia and tremor have been reported. The papilledema, which is present in 50 per cent of the cases together with the other neurologic observations, usually leads at first to a diagnosis of a brain tumor.

The chronic type shows a development somewhat similar to that of poliomyelitis. Three phases may be differentiated, the acute attack, the regression and the sequelae. The first attack is usually characterized by the rapid development of a spastic paralysis with early contractures. Sometimes convulsions and sensory disturbances may precede this first phase, which is at its maximum after a few weeks. It remains stationary for some weeks or months, then a slight improve-

ment sets in with amelioration of speech, motion and vision. Approximately from one to one and one-half years after the first appearance of the disease, a gradual return of the syndrome of the first attack sets in, which leads finally to complete spastic paralysis with marked contractures, blindness and mental deficiency.

As to the differential diagnosis of the acute cases, the papilledema in nearly all cases leads first to a diagnosis of a brain tumor. But the mild edema, which remains stationary, and the rapid onset of the paralysis with signs pointing to bilateral involvement of the hemispheres soon call for a correction of the first impression. If the early blindness is not accompanied by papilledema, a diagnosis may be made of retrobulbar neuritis following disseminated sclerosis, epidemic encephalitis, syphilis or sinus infection. The abundance and bilateral occurrence of neurologic symptoms, the absence of objective sensory disturbances, the rapid development of the disease, the extraordinary intensity of the contractures, the absence or unimportance of cerebellar symptoms and the profound change of the psyche help to differentiate this disease from multiple sclerosis. The anatomic differentiation is sometimes more difficult than the clinical, and many observers have thought that "cerebral centrolobal sclerosis" is an infantile form of disseminated sclerosis. The examination of the cerebrospinal fluid and of the blood serum will help in establishing a differential diagnosis with epidemic encephalitis and with syphilis of the central nervous system. In the chronic form, the differentiation from the latter disease is extremely difficult. Again, in the absence of cerebellar symptoms, the rapid onset with triplegia and tetraplegia may help to establish the final diagnosis. Bilateral softening of the brain following thrombosis is much more rapid and develops to its full height within a few days with a deep coma or with the other extreme of regression, but never with the slowly progressive course seen in the disease under discussion. Infantile paralysis with abolition of reflexes and radicular distribution of the lesions may also easily be excluded. The same is true of syphilis in its chronic manifestations. The differential diagnosis is most difficult in young children, in whom different encephalopathies may simulate the cerebral centrolobal sclerosis — Tay-Sachs' disease, tuberous sclerosis and diffuse gliomas should present no difficulties in being recognized. The extreme intensity of the early contractures, if encountered in infantile cases with doubtful diagnosis, should always make one think of the disease described.

As to etiology and pathogenesis, four theories have been advanced: neoplasm, degeneration, infection and intoxication. The occurrence of large, monstrous astrocytes has been cited in favor of a neoplastic disease. Similar forms are encountered, however, in pseudosclerosis and in tuberous sclerosis; besides they occur only in the acute stage of the disease, disappearing in the chronic stages. Furthermore, the confinement to the central white matter and the adult character of the fibrous glia formation speaks against a neoplasm. The assumption of a primary degenerative disease seems the least probable. The idea of a toxin acting destructively on the myelin sheaths and irritatively on the glia is shared by Schilder, Barré, and others. Collier and Greenfelt's idea is cited and rejected — that it is a specific disease of the glia of the central white matter which differs from the glia of the rest of the central nervous system. The author adopts the theory of Foix, which assumes an infectious disease. A summary of the clinical and anatomic reports of selected cases from the literature is added.

WEIL, Chicago.

TREATMENT OF SUPPURATIVE MENINGITIS AND HYDROCEPHALUS BY MEANS OF TEMPORARY SPINAL DRAINAGE. N. I. KRASNOGORSKI, Jahrb. f. Kinderh. **124**:245 (July) 1929.

In a patient with severe hydrocephalus a fistula developed from repeated lumbar punctures, through which the spinal fluid flowed freely. This produced such favorable results that the patient recovered in a short time. The author then constructed a thin silver syringe pipe, which, by means of the trocars contained therein, could be introduced into the subarachnoid space. On the outer end

of the pipe a discus was attached with four openings, which could be fastened to the skin with four silk threads. Outside the discus was the thick end of the pipe and to this the rubber tube was attached for draining away the fluid. A series of such pipes of different lengths and thicknesses was made, so that the length of the pipe from the discus inward was from 2 to 4 cm. and each following pipe was 1 mm. longer than the preceding one. The thickness varied accordingly from 1 to 2 mm. with distances of 0.2 mm.

The application of these pipes in children produced free flow of the fluid and the compression phenomena disappeared; sometimes when the pressure got too low there was great restlessness, flushing, then pallor and vomiting. Therefore, to control the outflow, the author, with Dr. I. K. Panferof, constructed a regulating apparatus which is illustrated and described in detail.

The apparatus is applied as follows: the child lies in the side position. After disinfecting the skin, the usual lumbar puncture is made and the distance from the skin to the subarachnoid space carefully determined; the appropriate sized syringe pipe is then selected and inserted by means of a guide in the same spot. The guide is removed and the syringe pipe connected with the pressure regulating apparatus. The place of entry of the pipe under the discus is covered with xeroform and the discus fastened down by means of four ligatures which pass through the four holes in the discus and are fastened to the skin with adhesive tape. The area around the apparatus is protected by a ring of soft material which is placed to the right and left of the rubber pipe that carries away the fluid.

This method has enabled the authors to keep the apparatus in place for some length of time in pressure cases of long duration. The lumbar syringe makes it possible to investigate systematically the outflow of the cerebrospinal fluid as well as the physiology of its contents. It has been used in the treatment for the acute stages of epidemic meningitis and in hydrocephalus.

It was found that the smaller the pressure, the greater was the fluid outflow; e. g., with a pressure of 150 mm., in one hour 12.9 cc. of fluid flowed out, while with a pressure of 50 mm., 44.5 cc. flowed out. It appeared that the decrease of the pressure in the ventricular system is a natural incentive to production of the cerebrospinal fluid flow. This was of great value in suppurative meningitis. Here the flow was so reduced that the outflow was accomplished without causing pathologic phenomena of intracranial decrease of pressure.

Use of the apparatus in patients in acute stages of epidemic meningitis showed a great flow of fluid containing pus, bacteria and toxins. While the pressure was being reduced over a number of days, from 150 to 200 cc. and more of purulent fluid was withdrawn. Reduction of pressure produced a strong outflow of fluid, which washed away the inflammatory products. No unfavorable manifestations were noted in children even when the pressure was reduced over a period of many hours to 50 mm. In the first part of the drainage time the fluid was thick and contained flocculus, then it became clearer every day. The outflow of the fluid was least during sleep and strongest in crying and during excitement; e. g., in sleep 0.3 cc. flowed out in five minutes, while awake 1.2 cc., and while crying 4 cc. By systematic checking up of the outflow of pus, bacteria and toxins, particularly favorable conditions were established in fighting the disease.

As a consequence of overcoming the compression, good circulation in the brain was established. The whole procedure is, so to speak, a physiologic flushing of the subarachnoid spaces. In the treatment for the acute stages of epidemic meningitis it is an important consideration that the child absorbs a great deal of cerebrospinal fluid, so that it is necessary to increase its production. It is now a common thing to influence the cerebrospinal fluid production by giving the patient coffee, caffeine, urea, solution of potassium acetate, etc.

Favorable results were obtained by the use of the syringe apparatus, which was followed by marked improvement of the general condition and gradual disappearance of the meningitic symptoms. The children were quieter and began to eat, and the sleeplessness disappeared. Up to the time of writing, this method had

been tried in nine cases without serum therapy and not a single child died. Of course, in severe cases after long drainage, serum may also be used either intravenously or intramuscularly. The drainage must be continued until the fluid is clear.

Favorable results have also been obtained in hydrocephalus; in one case the choked disk disappeared after seventy hours of drainage. In all cases the compression signs disappeared, the circumference of the head was reduced, the child could hold its head erect, the exophthalmos disappeared, and the child became gradually well. In these cases periodic systematic drainage was done. Theoretically, the drainage might be regarded as a means of infection, but this has never occurred so far, probably because the steady outflow of fluid prevents the possibility of infection.

The author has reported this method even with comparatively so little material because of the extraordinarily favorable therapeutic results obtained.

SACHSE, Philadelphia.

ALTERATIONS OF THE SELLA TURCICA FROM VENTRICULAR DISTENTION CAUSED BY REMOTE CEREBRAL TUMORS. G. MARINESCO, DRAGANESCU and J. DUMITRESCO, Rev. d'oto-neuro-opht. **7**:245 (April) 1929.

The use of roentgenography, with or without injection of air or iodized oil gives the greatest help in the recognition of alterations in the sella. The sella can be changed by both intrasellar and extrasellar tumors. Adenoma of the pituitary produces a uniform circular dilatation, a thinning of the wall and a mosslike appearance of the clinoid processes. At times the enlargement of the sella is not present and the roentgenogram will show other changes in the skull indicative of acromegaly. Deformities of the sella do not always mean hypophyseal tumors. In tumors of the brain producing internal hydrocephalus, important changes are found in the sella.

Two cases are reported. Case 1.—A woman, aged 45, was brought to the clinic in November, 1928, showing visual difficulties, functional impotence of the limbs and somnolence with crises of sleep, which dated from September, 1926, at which time there were intermittent headaches. In May, 1927, glycosuria was found, and in the following January, a left hemiplegia with convulsions involving especially the right half of the body appeared. Vision now began to fail, and a bilateral papillary stasis was noted in March, 1928. Crises of sleep, lasting several hours, came on and continued to the date of admission. The vision was reduced to light perception.

Neurologic examination revealed ocular paralysis with horizontal nystagmus to the right, left facial paresis, left hemiplegia and a slight right-sided hemiparesis; the tendon reflexes were slightly increased and Babinski's sign was positive on the left. There was slight obnubilation. After each convulsive attack the temperature was elevated. Urinalysis revealed 5.8 per cent of sugar and no acetone or diacetic acid; the blood sugar was 0.99 per cent.

Puncture of the ventricle and injection of air and iodized oil, followed by a roentgenogram, showed disappearance of the clinoid processes and the floor of the sella with narrowing of the sphenoidal sinus. A tentative diagnosis of hypophyseal tumor was made. Death occurred in two weeks. Autopsy revealed a rounded tumor in the right retrothalamic region between the knee of the corpus callosum and the limbic convolution above and the cerebral peduncles in front, which compressed the posterior wall of the third ventricle and obliterated the aqueduct of Sylvius. The peduncles, especially the right, were compressed and deformed. There was dilatation of the lateral and third ventricles. The hypophysis was flattened, and the bony floor of the sella was very thin and the bone in places almost destroyed.

CASE 2.—A man, aged 18, was admitted on Dec. 6, 1928, complaining of headaches, vertigo, tinnitus aurium, diminished vision and muscular weakness. The

illness began in January, 1925. The headaches, at first intermittent, had been constant for nine months. Vomiting appeared in the spring.

Examination revealed slight left facial paresis, very slight reduction of hearing in the right ear and paresis of the left extremities. The tendon reflexes had almost disappeared but the cutaneous reflexes were present. A slightly positive Babinski sign was present on the left side. Ocular examination revealed a bilateral diminution of vision and papillary stasis. If the patient stood up and walked unaided, there was total loss of vision for a few seconds and the tinnitus and vertigo were increased. The observations pointed to an endocranial hypertension probably from tumor but with no localizing signs. Vestibular examination showed lateral nystagmus to both sides with some vertical nystagmus and deviation of the left arm. Reactions from the horizontal canals were normal but there was loss of the reactions of the vertical canals. A roentgenogram of the skull showed decalcified areas in the frontal bone, and complete disappearance of the sella and clinoid processes and part of the body of the sphenoid bone. Lumbar puncture yielded only 1 cc. of liquid with a pressure of 35 cc. of water in the lateral decubitus. Death occurred three days after admission.

At autopsy there were found edema of the brain and dilatation of the third ventricle in the infundibulotuberian region, forming a cyst the size of a nut. The tuberian wall was reduced to paper thinness; the interpeduncular space was enlarged, and there was much distention of the lateral ventricles. The aqueduct of Sylvius and the upper part of the fourth ventricle were compressed by a tumor of the left lobe and posterior part of the vermis of the cerebellum, situated just beneath the dura. The hypophysis was flattened and the floor of the sella was much thinned by absorption of the bone. The mucosa of the sinus was inflamed.

Similar cases have been reported by Souques, Vincent, Bernard and Darquier, de Martel, Beclère, Cushing, Schüller, Schnitzler, Stenvers, Cassirer and Lewy, Lysholm and Olivecrona.

DENNIS, Colorado Springs, Colo.

PATHOLOGIC STUDIES OF THE BRAIN IN UREMIA. K. UCHIDA, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **31**:37, 1929.

Three cases were investigated; two of these were of genuine uremia and one of amyloid kidney; both presented manifestations resembling uremia during life. Uniform pathologic changes that Uchida believes are of greatest significance in uremia were found in all three cases: 1. Every one of the cases showed a chronic severe meningofibrosis. The condition was undoubtedly the result of a chronic inflammatory process. The severest change in the meninges was in the nature of arteriosclerosis which involved all coats of the vessels leading to a widening of the wall of the vessel with swelling of the cells of the intima. It was noteworthy that destructive changes were hardly noticeable. The meningeal involvement was not generalized, the brunt of the lesions being in the membranes covering the frontal lobe, the central convolutions, temporal lobes, to less extent the parietal lobes and still less the occipital lobe where the pia seemed to have been entirely normal. That the meningeal changes were not wholly due to the vascular condition is proved by the fact that the meninges over the occipital lobe also showed diseased vessels. 2. It is obvious that with such severe meningeal involvement the molecular layer of the cerebral cortex must also be involved, and this was actually the case, this layer showing undoubted manifestations of sclerosis; here the pia showed a coarse glial network but no proliferation. It is also noteworthy that in spite of this coarse glial network the tangential fibers in some areas were unusually well preserved. The normal relationship, however, between the supraradial and tangential fiber layers had disappeared. 3. The next characteristic lesion was a predominatingly perivascular edema. The cortical vessels showed the same type of involvement as in the pia. In some areas the perivascular edema produced disintegration of the tissue. There was no diffuse edema in the cortex, although the former was more marked in the cortex than in the white substance. Here and there, some venous stasis was observed; this, however,

was not a uniform observation. Similar lesions, including disintegrations (perivascular), were also found in the basal ganglia and in the thalamus.

Besides these three types of lesions there were also found changes in the ganglion cells; these, however, were only swollen and showed no evidences of destruction. The appearance of the glial reaction and the occasional neuronophagia near the ganglion cells was indicative of an old irritative process. The nerve fibers seemed also to have participated in the process, especially the delicate fibers on the surface of the brain, but the involvement of these seemed to have been due to the pial and glial reaction in the outer layers of the cortex. The glia cells of the cortex showed three types of reaction: sclerosis of the outer layer, perivascular glial reaction and ameboidosis of individual glia cells. Another interesting observation was the presence of peculiar "Drusen"-like deposits in the cortex. The significance of these deposits is not discussed by the author. The entire pathologic process of the brain in uremia is summarized by Uchida as a meningo-encephalopathy with perivascular edema and parenchymatous disintegrations, the precise nature of which is yet to be determined.

KESCHNER, New York.

THE PHYSIOLOGIC BASIS OF REPRESSION AND DISSOCIATION. R. G. GORDON, J. Neurol. & Psychopath. **10**:106 (Oct.) 1929.

This is an endeavor to explain the mechanisms of repression and dissociation by substituting psychologic equivalents for physiologic facts. A common ground of expression is conceded in the concept of a strict correlation between patterns of behavior and patterns of neuronic activity. The integration of coordinated action would seem to take place in the frontal lobe. If an impulse is prevented from leaving any set pattern form there can be no spread to other pattern forms and compulsive reiterations occur, such as are found in obsessional neuroses. The author cites Sherrington's concept of reciprocal innervation in order to demonstrate his theory of repression. Reciprocal innervation also prevails in the physiologic activity of the vegetative system. In the emotional life, reciprocal activity is present but is less perfectly integrated. It is commonplace to find indecisive actions due to a conflict between curiosity and fear, fear and anger, or more complex patterns which are called self-assertion and self-abasement.

Pathologically, in the sphere of voluntary muscular activity, hysterical paralysis is considered. In the rigid hysterical limb the extensors and flexors are in action at the same time and completely cancel each other. On the other hand, if the cancellation is incomplete, tremor or, better, oscillation occurs. The physical accompaniments of anxiety are similar, for there is an incomplete balance of sympathetic and the parasympathetic function.

The nature of repression is the failure of proper cortical integration for complex patterns, which in themselves are antagonistic in the end they serve. These patterns cancel themselves either perfectly or imperfectly as do the patterns of muscular and vegetative action. Minor cancellations and oscillations appear as symptoms of repression such as pathologic doubts and anxiety. One side may give way partially with a subsequent increased activity of the opposite pattern which results in a new symptom, such as an obsession. If cancellation is complete, there may be a sudden terrific emotional outburst. Gordon analogizes this condition with two wrestlers locked in a clinch. They must turn toward each other or at least be interested in each other at all times; in other words, they must find constant contact. This interlocking of two opponents, in terms of neuronic patterns, means repression. On the other hand, if the two persons fail to come in contact and continually turn their backs on each other, this would represent, when translated into terms of neuronic patterns, the state of dissociation.

The introvert, being concerned with his own subjective reactions, tends to get his patterns into conflict with resultant subsequent repression. The extrovert is concerned with objects in his environment and his adjustments to them. If these objects are incompatible and the higher levels of cortical function fail, dissociation is bound to occur.

There is excellent, thoughtful analysis in this paper but the free substitutions of dissimilar terms make the conclusions rather weak. It is, however, a splendid attempt and shows the possibilities in this type of reasoning.

BECK, Buffalo.

ETIOLOGY OF ENCEPHALITIS AFTER VACCINATION. D. WIERSMA, Acta psychiat. et neurol. **4**:75, 1929.

Wiersma adds two more cases of encephalitis following vaccination in children to those he has reported previously (*Acta psychiat. et neurol.* **2**:167, 1927). In the first, encephalitic symptoms appeared suddenly fourteen days after vaccination and disappeared within a few hours. In the second, the rarer meningeal symptoms were most prominent. He also reports a case of encephalitis, not of the epidemic type, which occurred spontaneously without any previous infectious disease, to show that perhaps the vaccination is not directly responsible for the condition in the two cases first cited. He also describes the pathologic observations in the brain from one case reported previously. The outer surface of the brain was normal, except for hyperemia, but on section the whole substance showed numerous minute red spots. On microscopic examination these were found to be the cut ends of hyperemic vessels. Perivascular infiltrations with microglia and a few polynuclear leukocytes were present, mostly in the white matter, but were distributed irregularly. (Large areas of the brain and the entire cerebellum were free, but in the region of the basal ganglia they were found in large numbers in the gray matter as well as in the white matter, contrary to the author's previous experience.) The ganglion cells, both of the cortex and the basal ganglia, showed mild pathologic changes.

The author discusses at length the possible reasons for the increase in incidence of this condition. He does not consider that the encephalitis is caused directly by any increase in the neurotropism or virulence of the vaccine itself. Nor does he agree with Pondman that there is any reason for supposing that vaccines produced in the same way for a number of years should have become infected suddenly with a still unknown invisible virus which produces encephalitis in susceptible persons. The fact that encephalitis has followed inoculations with absolutely sterile vaccine seems to rule out the possibility that bacteria or their toxins (which until recently have been present in nearly every sample of vaccine) are responsible for the outbreak of the infection. Cramer's supposition that the albumin of the vaccine may have undergone some physiochemical change, the products of which produce an intoxication of the brain, is a more intriguing hypothesis, but the author thinks that the irregular distribution of the lesions in his case, with autopsy, indicate the probability of an infection rather than an intoxication. On the basis of his third case and similar ones reported by other authors, he thinks that there may be a large number of children infected with some micro-organism which is harmless usually, but which becomes pathogenic if activated by vaccination or some other cause which diminishes the resistance. There is the possibility, however, that the resistance against diseases of the central nervous system may be less now than in previous years. If this is true, the encephalitis may be due to any usual vaccine, either directly or as a result of its infection with micro-organisms of a previously harmless type.

PEARSON, Philadelphia.

ON THE ARRANGEMENT OF THE GANGLION CELLS IN THE ANTERIOR HORN OF THE LUMBAR ENLARGEMENT. YANNI TSIMINAKIS, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **31**:188, 1929.

The apical group of cells in the anterior horn of the lumbar enlargement consists almost entirely of large cells. Small cells are found only up to the middle of L 1. This group is most uniform in the second half, from L 2 and L 5; it is also most marked in this area. Here and there in almost every segment no

cells can be seen, especially in the lower half of L 3 and in the entire segment of L 4. The laterodorsal group in L 1 consists exclusively of small cells of uniform development. A few small cells forming this group may also be seen at the beginning of L 3. This group is unusually well developed and uniform in L 4 and extends to L 5, disappearing only at the termination of this segment. The external lateroventral group consists throughout its entire extent of large cells with only slight deposits of small cells. Up to L 4 this group is well, or moderately well, developed, reaching its greatest development at L 5 but diminishing in volume toward the end of this segment. The central group shows a vicarious arrangement with the internal lateroventral group and is developed irregularly. The same is true of the size of the cells in this group. It is most uniform at L 2. The internal lateroventral group is almost completely absent at L 1 and L 2, beginning its development first at L 3. This group consists in some areas of large cells and in others of small cells. Its greatest development is found at L 4, and at L 5 it is barely recognizable. The greatest development of this group is found where the mediodorsal group is least developed. The mediodorsal group consists, except for a few large cells in the first half of L 1, chiefly of small cells. Of all cell groups this one is least developed, and is almost completely absent in L 4 and L 5. The medialis intermedia group consists only of small cells. Owing to its irregular development, little can be said about it. It is only of interest to note that this group is best developed where the mediodorsal and medioventral groups are least developed, namely, at L 4. Just as the preceding group, so this one is almost completely absent at L 5. The medioventral group begins at L 1 with its greatest development which is uniform and consists of large cells. At L 2 a series of sections may be seen in which this group of small cells is beginning to intermingle with the large cells. As one descends there is a gradual increase of the small cells so that at L 4 these constitute almost exclusively the cellular content of this group.

The vicarious arrangement of cells in the various groups is striking and as marked as in the cervical enlargement which the author had previously studied and reported on.

KESCHNER, New York.

SOCIAL FACTORS INVOLVED IN PERSONALITY INTEGRATION. J. S. PLANT, Am. J. Psychiat. **9**:113 (July) 1929.

In the development of mental hygiene and child guidance clinics, the claim is made that psychiatrists are interested primarily in the integration of the personality. They call themselves synthesizors, particularly in comparison with specialists in other fields of medicine, in that the attempt is made to emulate the old "family doctor" in dealing with the personality of the patient rather than ignoring the feelings of the man while treating a particular organ or disease. The marked difference in the social situation in an existing highly industralized area from that in the pre-industrial area is contrasted by illustrating in the latter, the child's interests, activities and entire personality as definitely oriented to his family; his social structure, earning capacity and learning are all closely interlined in the family, making total personality integration easier, with the needs not geographically or socially separated. The family of today is described as showing: dissipation of interests and activities, with the time spent in traveling to and from them; inroads made by apartment life and the incessant migration of families, more than 78 per cent of the population changing address in a five-year period.

Hence, the family of today can no longer be an arena for all the various needs for all its members; as a social institution it has withdrawn from other social institutions, a form of specialization, just as is shown in medical specialization and in the school. Industry has specialized in caring for the earning and productive capacities of the worker, but this has not met the needs of the total personality; mass production has meant automatization, leaving increased outside hours to be spent intensely in a search for emotional satisfactions; the development of huge combines threatens individual initiation. The church also plays a small part. The

effort is being made to integrate personality when the total condition of social life is essentially analytic. The writer concludes that the orthopsychiatrist needs to attack certain social problems rather than to occupy himself with persons who have failed — he must act as synthesizor and become a social psychiatrist.

IRISH, Philadelphia.

DISTURBANCES OF THE RESORPTION OF THE CEREBROSPINAL FLUID IN PSYCHOSES. LUDWIG GUTTMANN, Arch. f. Psychiat. u. Nervenk. **88**:211 (Aug.) 1929.

The author reports investigations of the resorption of cerebrospinal fluid in fifty cases of dementia praecox and in forty cases of neurosyphilis (mostly dementia paralytica). He used the sodium iodide method of Foerster, which is carried out as follows: Several cubic centimeters of cerebrospinal fluid are obtained by lumbar puncture. To 8 cc. of this fluid, 2 cc. of a 10 per cent solution of sodium iodide is added and the whole is slowly reinjected into the canal. For the first one and a half hours following this, catheterized specimens of urine are examined every quarter of an hour for iodine. Following the first positive result, the urine is collected and hourly specimens are examined quantitatively for iodine. This is carried out until the urine becomes negative to iodine reaction for three consecutive examinations.

In the schizophrenic patients, he found that twelve of fifty cases showed a normal rate of resorption, two a high normal and thirty-six a pathologic slowing of the process. These pathologic values were especially numerous in cases of catatonic stupor. The slowing affected not only the first appearance of iodine in the urine but also in most cases the length of time required for the complete disappearance of the iodine. In a high percentage of the cases that showed pathologic slowing of the process, there could also be demonstrated the occurrence of pathologic quantities of proteins according to the method of Kafka. In the forty cases of paresis, twelve showed a normal reaction, five a high normal, eighteen were slowed and in five there was an increased rate of resorption. Here, too, there were some correlations with the Kafka protein reaction. The author is of the opinion that investigation of the resorption of the cerebrospinal fluid is of distinct use in the study of mental diseases and along with the Kafka reaction, as well as the permeability tests of Walter, should be further investigated; attempts should be made to correlate these with the clinical pictures. So far, however, no definite statements can be made as to the relationship between these and differential diagnostic or prognostic criteria.

MALAMUD, Iowa City.

FLACCID PARAPLEGIA FOLLOWING ANTIRABIES TREATMENT. L. BABONNEIX and J. SIGWALD, Ann. de méd. **26**:114 (July) 1929.

A man, aged 31, who had been bitten by a cat which ultimately turned out not to have rabies, had been treated at the Institut Pasteur with injections of glycerinated spinal cord emulsions. After ten injections, a complete flaccid paraplegia of both lower extremities developed, preceded by dysesthesias, and accompanied by vesicular and rectal retention and a temperature of 39.5 C. (103.1 F.). The spinal fluid contained 160 lymphocytes and 0.8 mg. of albumin per cubic centimeter. After the injection of 50 cc. of poliomyelitic serum intraspinally, a gradual improvement set in ten days after the onset of the disease and after two months led to complete recovery.

Though other people who had been treated with the same vaccine (including the wife of the patient) did not show any neurologic manifestations, the transverse myelitis had to be attributed to the antirabies treatment. A review of similar cases from the literature is given with a description of other types of complications following this treatment. One was that of an ascending Landry's paralysis, and a second a peripheral neuritis.

Many theories have been advanced to explain these accidents. One theory assumes that the myelitis is a manifestation of rabies produced by a virus which has been weakened by animal passage. Another assumes that toxins have been produced during the process of drying and glycerin preservation of the spinal cords of the laboratory animals, either by the action of the virus itself or by autolysis and putrefaction of the rabbits' spinal cords. To these theories the authors add one of their own which assumes that treatment with fixed virus stimulates the action of a micro-organism which is already present, though latent, in the central nervous system of the patient and which has "biotrophic" affinities to the nervous system. They compare this action with the encephalitis following vaccination against smallpox, which, according to Levaditi and Nicolai, makes the nerve tissues more sensitive to the invasion of the virus of herpes encephalitis.

WEIL, Chicago.

TESTS OF REACTION-TIME AND MOTOR INHIBITION IN THE PSYCHOSES. ELEANORA B. SAUNDERS and SCHACHNE ISAACS, Am. J. Psychiat. **9**:79 (July) 1929.

The article contains a discussion of the adaptability and supplementation of psychiatric clinical observation by psychologic experimental methods, with the varying opinions, from entire lack of acceptance to an optimistic attitude that more complicated forms of reaction tests will give direct results in diagnoses. Investigators conclude generally that in the psychoses, the average reaction time is lengthened, that the variability is greater or lengthened in type from the normal and that the instability of performance in psychotic subjects is to be considered primarily as an attentional disturbance.

Patients, including schizophrenics, manic-depressives, both excited and depressed, psychoneurotics and those with organic brain disease, were tested by means of various forms of apparatus that are described, to determine the diagnostic value in average reaction time difference, whether there was a significant difference, and in the degree or type of variability in the reactions. The history abstracts with the varying results are shown in the form of tables and the reasons for differences in individual cases are given.

The conclusion offered was that the particular tests used were not sufficiently positive to be recommended as standards for diagnosis, but that the application of tests for this purpose is not to be regarded as hopeless, as shown by "condition measurement" rather than by the various capacity tests used. The results of these tests were useful in an investigation of the effects on the aviator of oxygen deficiency in high altitude, and coincide with the "two factor theory" on the nature of dementia, which is attributed to "a general impairment of a diffuse character or a lowering of the whole intellectual level," conditioned physiologically by the efficiency of the entire cortex; hence, they offer a field of usefulness in the study of the psychotic person who may be able to execute satisfactorily specific tasks even though there is sufficient disturbance of attention and coordination to prohibit a daily practical routine of adjustment.

IRISH, Philadelphia.

NOTES ON PERIPHERAL FACIAL PARALYSIS. F. J. Collet, Rev. d'oto-neuro-opht. **7**: 81 (Feb.) 1929.

These notes concern three observations made in cases of facial paralysis: (1) A diagnostic sign of very early or regressive paralysis, which is elicited by having the patient open and close the eyes rapidly for a few seconds. One observes that the eye on the affected side opens more quickly and more completely than its fellow and remains more widely open in these alternate movements. This sign is not apparent and is not needed in developed cases. Its value is in early cases in which the ordinary methods reveal nothing and in cases in which the paralysis has apparently disappeared. This was exemplified in a case of a patient, aged 13, who had had a facial paralysis eleven years previously. Following

exposure to the heat of the sun there was great restlessness, fever and paralysis of the left side of the face and limbs. At the time of examination almost every vestige of paralysis had disappeared; the grip in the left hand was much weaker and the labial commissure deviated to the right, but the left eye closed well. The etiologic factor was probably one of the peripheral forms of epidemic encephalitis. The paresis of the lower branch of the facial nerve was evident but the involvement of the upper branch would have not been perceived without the maneuver suggested. (2) Synkinesis in peripheral facial paralysis. This is illustrated by a case of left facial paralysis from a gunshot wound. While rapidly opening and closing the eyes, the left, which remained immobile, shows a slight movement of the lid when the right eye is closed and at the same time the left labial commissure deviates slightly. This is not seen when the opening and closing movements are made slowly. (3) Multiple recurrences of facial paralysis in the course of a chronic otorrhea. The case concerns a patient, aged 35, who had had a right otorrhea for six years. A right facial paralysis in 1919 was relieved by syringing cholesteatoma from the ear. Recurrences occurred in 1924, 1926 and 1927. The last attack disappeared in three months, after treatment of the ear. The patient refused to permit an operation on the mastoid.

DENNIS, Colorado Springs, Colo.

ORGAN NEUROSES IN THE LIGHT OF NEWER POINTS OF VIEW. ERNST HOFFSTAEDT, Berl. Klinik **35**:388 (April) 1928.

From a purely clinical standpoint the neuroses are divided into psychoneuroses and organ neuroses. In the latter, the symptoms are limited to the vegetative organs and their functions; they are further subdivided into vasoneuroses, secretion neuroses and dyskinetic neuroses. The terms organic and functional as alternatives are regarded as unnecessary, because psychic influences can produce organic changes, and organic diseases often contain neurotic components. The organ neurosis begins when the psychovegetative reflexes show exaggerated reactions to minimal stimuli, leading to a disturbance of equilibrium in the vegetative system. In the same way that long forgotten experiences leave traces in psychic structure, there is also an organ memory whereby an organ that has once been diseased always tends toward abnormal reactions, even after complete recovery in the clinical sense. Thus, in many cases, the choice of organ neurosis is determined on purely somatic grounds, being the expression of a latent organ inferiority. However, the author believes that in all cases the manifestations of the neurosis are ultimately brought about by unconscious tendencies.

While recognizing the fundamental importance of prolonged psychotherapy in uncovering the psychogenic factors responsible for the neurosis, the author believes that a great deal of benefit is often derived from physiotherapeutic measures, such as local applications, diathermy and natural and artificial light therapy. He believes that, in individual cases, resort to pharmacologic measures is often justified, although he emphasizes their temporary effect. He regards a combination of calcium and vitamin D therapy, together with a vegetarian diet, as beneficial in some cases of urticaria, migraine and asthma.

ROTHSCHILD, Foxborough, Mass.

THE DIAGNOSTIC SIGNIFICANCE OF WALTER'S PERMEABILITY REACTION. FRIEDRICH VON ROHDEN, Arch. f. Psychiat. **87**:797 (July) 1929.

The author reports investigations of the permeability in 800 cases of mental and nervous diseases in which he has made 1,250 separate determinations. The material includes reports on a great variety of mental and nervous diseases and on a group of thirty-five persons whom he designates as normal subjects. The latter, as a matter of fact, were patients whose cases were diagnosed as psychopathic personality, psychoneurosis and latent syphilis. He describes in detail the technic of the test and the possible sources of error, and he discusses the literature

on the subject. He comes to the following conclusions: The bromide method of Walter is of distinct value in the diagnosis, prognosis, treatment and investigation of the pathogenesis of the psychoses. It is an objectively demonstrable reaction. It is not as simple and easily acquired a method as is deemed by some, because there are numerous sources of error which must be taken into consideration before definite conclusions can be reached.

The results of his investigations lead him to take sides with the conclusions that have been reached by Walter, and he is of the opinion that four distinct types of permeability can be established: (1) Normal permeability. By this he means quotients that range between 290 and 330. They occur in "normals," neuropathic, hysterical and psychopathic persons and in manic-depressive psychoses. (2) Increased permeability. By this is meant the group in which the quotients are below 290. They occur mostly in exogenous psychoses, such as symptomatic psychoses, paresis, intoxication psychoses and senile dementia. (3) Decreased permeability. Here the quotients are above 330; they occur in schizophrenia and metencephalitis. (4) Indifferent permeability. In this group are placed diseases in which the quotients may be either increased, decreased or normal. To this group belong paranoia, epilepsy and congenital mental defect.

MALAMUD, Iowa City.

THE ENHANCEMENT OF CENTRAL ACTIVITY BY A SUBSTANCE THAT STIMULATES THE CENTRAL NERVOUS SYSTEM. E. STEINACH (With the assistance of H. Kun), Wien. akad. Anz., July 4, 1929, no. 17.

This article is a preliminary communication in which the author, by injecting a watery extract of the central nervous system into frogs, demonstrates that it contains a substance which acts as a stimulus to reflex activity. (A slightly fuller version appears in *Med. Klin.* **25**:1273, 1929, an abstract of which follows.)

A SUBSTANCE THAT STIMULATES THE CENTRAL NERVOUS SYSTEM AND ITS FUNCTIONS. E. STEINACH and H. KUN, Med. Klin. **25**:1273 (Aug. 16) 1929.

Watery extracts of the central nervous system are shown to contain a substance capable of stimulating reflex activity. The extract was injected into frogs, and numerous indifferent substances were used in control animals. Over 800 animals were tested by means of graduated chemical stimuli, and an increase was observed of from 400 to 600 per cent in reflex activity as compared with control animals. Attempts were also made to estimate more general performances by the experimental and control animals by observing their ability to catch flies in a closed chamber, with the result that in most cases the former showed the greater activity. The active substance, to which the author gives the name "centronervin," is not limited to any one portion of the nervous system or to any one species of animals; the same results were obtained with material prepared from the gray matter, white matter and spinal cords of frogs, rats, dogs and human beings. It is thermolabile and probably hormonal in nature. The author supposes that it guides the activity of the central nervous system, and he raises the question whether mental retardation, psychic anomalies and some diseases of the nervous system may not be due to insufficient or abnormal formation of this substance.

ROTHSCHILD, Foxborough, Mass.

VAGOTONIA AND CORTICAL EPILEPSY. D. SANTENOISE, P. VARÉ, H. VERDIER and M. VIDACOVITCH, Encéphale **24**:605 (July-Aug.) 1929.

Experimental facts demonstrate that there can exist a relationship between vagal tonus and the epileptic predisposition. This relation appears to be established through action of the psychomotor centers. The vagus influences the production by the thyroid apparatus of a hormone which exerts a powerful action on the chronaxia of these psychomotor centers. The chronaxia is low in experimental

monkeys that are markedly vagotonic, and high in hypovagotonic animals. Specifically, in tests on the sigmoid gyrus of 150 monkeys, it was observed that the injection of eserine produced a rapid fall of chronaxia; this was not true for atropine. In fact, eserine often caused partial or generalized convulsions. Section of the vagus above the plexiform ganglion always provoked, at the end of a certain time, a marked elevation of chronaxia; low section produced only unimportant changes. In the former case, usual modes of stimuli failed to evoke convulsive crises. Faradic excitation of the thyroid branches is followed by considerable lowering of the chronaxia of the sigmoid gyrus; section of these fibers is followed by the reverse.

Thyroid extracts obtained from vagotonic animals induced significant lowerings of the chronaxia; those secured from hypovagotonic animals little or none. Many times, after the injection of thyroid into animals spontaneously vagotonic, or rendered so by eserine, there occurred convulsive seizures. All these facts lead the writers to conclude that hypervagotonia corresponds to the hyperproduction of a thyroid hormone capable of considerable excitation of the psychomotor centers and hence of sensitization to epileptic manifestations. The frequency among epileptic patients of hypervagotonicity is in line with these observations.

ANDERSON, Los Angeles.

EXPERIMENTAL MANGANESE POISONING. A. M. GRÜNSTEIN and N. POPOWA, Arch. f. Psychiat. **87**:742 (July) 1929.

The authors report the results of clinical and anatomic observations of rabbits subjected to the effects of powdered manganese. They begin with a discussion of the literature, which they sum up as follows: In the reported cases of manganese poisoning in man, the clinical picture consisted of muscular rigidity, masklike facies, compulsive laughing and crying, increased salivation, tremors and disturbances of gait. These symptoms altogether usually presented a parkinson-like picture, so that it could be assumed that the pathologic process would be mainly localized in the globus pallidus. So far, however, no anatomic observations in such cases have been reported. Experimentally, observations of this type have been studied in animals of different types (Mella in this country studied the effects of manganese poisoning in monkeys).

The observations of the authors are essentially similar to those of other observers, and the results are summed up as follows: Clinically, the symptoms varied from episodic paralyses of the hind legs to general weakness of the musculature without any definite neurologic changes. Anatomically, marked changes of the central nervous system were found in the form of advanced degenerative phenomena of the nerve cells. These were particularly intense in the small cells of the caudate nucleus and putamen, but were observed also in the pallidum and in some parts of the cortex. In some cases there were, in addition to these changes, proliferations of the neuroglia and lesions in the walls of blood vessels, as well as degeneration in the cells of the choroid plexus. There were marked degenerative lesions in the liver, spleen, heart, kidneys and suprarenal glands.

MALAMUD, Iowa City, Ia.

THE VEGETATIVE NERVOUS SYSTEM AND THE INFLUENCE OF PHARMACOLOGIC SUBSTANCES IN CATATONIC PATIENTS. T. GORDONOFF and F. WALTHER, Klin. Wchnschr. **8**:1179 (June 18) 1929.

Examination of the blood of various catatonic patients showed a normal calcium content. The normal variation of calcium in the blood is from 8 to 10 mg. per hundred cubic centimeters. The potassium content was extraordinarily increased. Thus, while the normal percentage varies from 18 to 20 in catatonic patients, it may be from 23 to 24 and higher. In one severe catatonic condition the content was found to be 240 mg. per hundred cubic centimeters. The authors found a definite increase in the potassium content of the blood with a corresponding increase

in the catatonic symptoms. They found an increase of from 2.4 to 2.6 in the potassium-calcium quotient. This increase in the potassium of the blood the authors associate with an increased sympathetic excitability; the influence of certain pharmacologic substances, such as epinephrine and atropine, were studied in these cases. It was found that epinephrine caused a fall in the potassium-calcium quotient while there was a rise in the quotient of normal controls. The potassium content of the serum in catatonic patients decreased after epinephrine. In general, they seem to be less susceptible, however, to this drug. In normal persons atropine leads to transient and slight decrease in blood pressure and pulse frequency following an increase in both these functions. In many catatonic patients there was an increase in blood pressure and pulse frequency but the potassium content decreased after atropine as well as did the potassium-calcium quotient. These showed no alterations in normals. Acetylcholine was found to produce the reverse effect of atropine in catatonic patients.

HART, Greenwich, Conn.

THE HEREDITARY FACTOR IN ALLERGIC DISEASES WITH SPECIAL REFERENCE TO THE GENERAL HEALTH AND MENTAL ACTIVITY OF ALLERGIC PATIENTS. RAY M. BALYEAT, Am. J. M. Sc. **176**:332 (Sept.) 1928.

Balyeat shows how heredity and environment play interesting rôles in patients with allergic diseases. In a previous article, in a group of 1,000 cases of atopy (hay fever and asthma) he found that 58.6 per cent of all patients with a bilateral family history manifested clinical symptoms of specific hypersensitiveness in the first decade. He also concluded that the development of sensitivity to a particular protein is dependent on the extent to which a person is exposed to that protein. Patients may be born specifically sensitive to a substance and there is a possibility of this developing in utero. As in so many other diseases, it is not the specific sensitivity that is inherited but the predisposition; the transmission of this follows Mendel's laws. In the linkage, eczema and migraine are interchangeable with hay fever and asthma, and hence may have a common cause.

In the histories of patients with hay fever, asthma and allied conditions it was found that 74.9 per cent develop a general resistance to infectious diseases which is far above normal. Patients with hay fever and asthma are less likely to become insane than normal persons when the insanity is a result of pathogenic organisms. The school records of allergic children were much superior to those of the average child. In intelligence tests, 37.5 per cent of all allergic students fell in the classification "very superior," while only 5 per cent of the nonallergic students fell in that class; only 30 per cent of the allergic students fell in the normal class while 80 per cent of the nonallergic students fell in that group.

MICHAELS, Detroit.

A CASE OF RHIZOMELIC SPONDYLOSIS. SWYNGHEDAUW and E. GAUDIER, Arch. franco-belges de chir. **30**:855 (Oct.) 1927.

The authors describe a case of rhizomelic spondylosis in a man, aged 29, a carpenter. During the past year he had slowly developed pain in the left hip and thigh. Three months later, there was pain localized in the lumbosacral region; any movement of the back was painful. A slight kyphoscoliosis developed. On examination he showed complete immobility of the head and spinal column; to turn his head it was necessary to rotate the entire body, while to pick an object from the floor it was necessary for him to get down on his knees. The spinous processes were painful to pressure, particularly the fifth and sixth cervical. The large trunk muscles attached to the spine were atrophied, with slight contracture of the trapezii. There was no loss of power, atrophy or contracture of any of the extremities. No sensory disturbance was noted. An ocular examination gave entirely negative results. Radiologic examination of the spine showed calcification involving practically the entire vertebral column with atrophy of the intravertebral disks. The articular facets seemed uninvolved by calcification. Complete

ankylosis of the intervertebral column had resulted. No focus of infection could be discovered. Serologic examination gave negative results. The possibility of treatment in these cases is discussed and a review is given of the literature on the etiology and frequency of the condition.

GRANT, Philadelphia.

LIGHT AND COLOR CELLS IN THE BRAIN. S. E. HENSCHEN, Hygiea **91**:705 (Oct. 31) 1929.

The discovery of the visual center in the calcarine cortex has been histologically established. This center surrounds a narrow region of the stria gennari which appears to be of specific structure and composed of eight different layers, of which the fourth or visual layer is divided into three parts. From the retina there is an organized projection, e. g., the macula is represented at the pole, while the periphery of the visual field is represented more frontally. The position of light and color representations were disputed for a long time. In studying numerous animals the author finds that the visual cortex of nocturnal apes has one kind of cells, whereas all apes with daylight habits have two kinds—those possessed by night apes, and certain small cells with large nuclei besides. Homologous with the cells in the human being are two types of cells in the day apes with variable distribution. Henschen identifies the larger cells as light cells and the smaller as color cells, for apes have color vision. Whether or not there are different cell forms for different colors cannot be determined. The color sense cells always are limited to the calcarine fissure. The light cells in the center or deep portion of the calcarine fissure are more numerous, hence the author finds sharpness of sensory impression expressed anatomically in a number of cells.

HART, Greenwich, Conn.

SURGICAL TREATMENT OF TUMORS OF THE SPINE. Y. DELAGENIÈRE, Arch. franco-belges de chir. **30**:741 (Sept.) 1927.

The indications for and the operative technic in surgical removal of spinal tumors are described. The article is well illustrated with cuts of the operative technic. The results are given in a series of fifty-two cases of tumors of the spinal cord in which the patients were subjected to operation. The mortality was 7.4 per cent. Intramedullary tumors and tumors of the lumbosacral region have the highest mortality. The importance of early operation is shown by the fact that in cases in which operation was performed before complete paralysis developed, there were no operative deaths; all of these patients were relieved completely of symptoms. The results in the entire series showed 75 per cent of marked relief from symptoms, and 63.1 per cent of complete cure.

GRANT, Philadelphia.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, Oct. 18, 1929

EVERETT S. BARR, M.D., *Vice-President, in the Chair*

POSSIBLE ABUSES OF THE USE OF HYPNOTICS; WITH SPECIAL REFERENCE TO ALLONAL. DR. PAUL SLOANE and DR. LAUREN H. SMITH.

Allonal as a drug for clinical usage has been in existence scarcely more than ten years, and has been in general usage in the various branches of medicine little longer than five years. Burns (1922) was evidently the first to present its values as a sedative, hypnotic and analgesic drug. This study was presented largely from the psychiatric and neurologic point of view, but he recommended usage and further investigation of this drug in other specialties also. Two years later, the same author reviewed the subject again, and added more data and cases that established still further the usefulness of the preparation. By this time, it was being used by many practitioners in various conditions. Kuh and Gerty (1923) used it in the Cook County Psychopathic Hospital and found it satisfactory in various psychiatric conditions. They mentioned that their patients experienced "few after-effects even with a single dose up to twenty grains." The after-effects mentioned in these cases were dizziness and drowsiness. Bryant (1924) was more critical of the use of allonal and questioned its unlimited and general use, emphasizing the fact that "toxic and cumulative tendencies are characteristic of the urates, at least so in the case of allonal." He pointed out that allonal belonged in the "urea class of drugs — they have an affinity for the cholesterin and lecithin in the nerve cell, and the change in the cell may account for the persistent dizziness and grogginess that so frequently follow the administration of the urates." The previous authors were inclined to discount toxic or cumulative effects of this drug. Saenger (1925), who used from one-third to one-half a tablet three times a day in pediatric cases, found no bad effects. Heufelder at the same time reported its use in surgical cases, from one to four tablets a night, and had no bad results. Stix reported the case of a patient with acute articular rheumatism, in whom subnormal temperature, signs of severe general collapse and active hallucinations developed after taking four tablets. Wolf (1925) had a patient who took thirteen tablets within one and one-half hours. After two hours, the patient showed unfavorable reactions, consisting of dilated pupils, marked hypotonia, diminished tendon reflexes, weak pulse, deep respirations, marked pallor and a deeply comatose condition. The patient came out of this state (after stimulation) during the second day, but was weak and without energy for several days, with some disturbance of motility. The subjective symptoms noted were: great drowsiness, apathy, dizziness, visual disturbance and a feeling of coldness. Haegi and Huyssen, (1926) used allonal in postoperative cases, from two to four tablets in a night, and found no cumulative effects or untoward results. Burckhardt (1926) reported its successful use as a sedative in cough, and found no ill results. In a study of 150 cases (1927), von Seemen found no ill effects, habit formation, cumulative action or after-effects even with a dosage of four tablets. One contraindication for its use in cases with high fever and vasomotor weakness, is the occurrence of a sudden drop of temperature with profuse perspiration. Hippe used allonal in cough therapy, and found good therapeutic results and no ill results or after-effects. Jenny treated eleven children with whooping cough, all less than 2 years of age, with a dosage of from one-half to one tablet three times a day, and found no ill results; the drug gave the children rest and relieved the frequency

of the cough. Lange treated about thirty patients with sciatica, using from one to two tablets nightly. He stated that the pain disappeared in from three to eight days. In two cases he had to stop the drug on the third day because the patients developed fatigue. Otherwise no ill effects, except sleepiness, were found, but he mentioned that one must watch out for idiosyncrasies (narcosis, exanthemata, etc.). Gutman reported a case of attempted suicide by allonal, the patient having taken thirty-six tablets (96 grains!). The patient, however, awakened the next morning (no mention is made of the treatment instituted). The respiration and pulse were slow and regular; the tendon reflexes were diminished, and the pupils were one-half dilated and responded to light. Eighteen hours later, the patient recovered sufficiently to pass urine and to drink coffee. Marked weakness persisted for thirty-six hours. There were no renal signs, and she did not vomit. Exner and Viditz (1928) found no ill effects in the general usage of the drug. Several others have used it generally for insomnia and pain, and report favorable and satisfactory results. In 1926, the council on Pharmacy and Chemistry of the American Medical Association (*J. A. M. A.* **86**:1853 [June 12] 1926) reported allonal not acceptable for publication in "New and Nonofficial Remedies" because (1) the therapeutic claims advanced are deemed unwarranted by the facts; (2) the name is not descriptive of its composition, and (3) there is no satisfactory evidence that the administration of allylisopropylbarbituric acid and amidopyrine is rational. From a practical clinical standpoint, this view seems rather extreme and theoretical, as the use of allonal is largely one of general application with no specific effects expected on either pain or insomnia singly. Undoubtedly, having perhaps two "types" of allonal would be worthy of trial, with the relative proportion of the two components changed, according to whether more analgesic or more hypnotic effects were desired.

These reports and opinions have unquestionably established the value of this preparation as a sedative, hypnotic and analgesic drug, and as an agent for other special uses. Certain of these citations suggest only the possibility of toxic or cumulative effects or idiosyncratic reactions of the drug. Practically no mention is made of the possibility of drug addiction, except to state that such a tendency was not observed. With the advent of every new clinical preparation of this type, the favorable signs and developments are usually the first to appear, and it holds true in this instance also. Finally, unfavorable reports appear, but they do not necessarily affect the true merits of the drug. In recent years, the use of allonal has been extremely common. Dentists and physicians find it effective for toothache and pains in the head. The drug is used by lay people, without securing prescriptions. Younger physicians are becoming careless in prescribing it for many conditions and in extreme dosages. The general impression is that the drug is nontoxic and "practically harmless." As a result, bad effects are now more frequently noted, and we are presenting the need for conservative control in using this preparation. We shall report two cases in particular in which untoward effects followed the use of this drug. It is believed that these cases are the first to be reported that show such definite and extensive untoward results of this particular nature.

Case 1.—The patient, a woman, aged 35, had had several abdominal operations during a period of seven years, consisting of an Alexander operation, dilatation and curettage, trachelorrhaphy, anterior colporrhaphy and perineorrhaphy, appendicostomy, and cholecystogastrostomy. Following this she developed a large ventral hernia and appendiceal fistula. After this condition had existed for several years, her physician referred her to the Pennsylvania Hospital for further surgical intervention. For about from one year to eighteen months, she had been using allonal (at least four tablets a day) to relieve her of abdominal discomfort, pains and cramps. Previous to this time she had never shown any signs of mental or nervous disease; recently she had commenced to show nervous symptoms which were thought to be due to an abdominal condition. At the hospital she showed marked mental symptoms, with active hallucinations, disorientation, general excitement and definite neurologic signs of such extent that a provisional diagnosis of

dementia paralytica was made. At the Department for Mental and Nervous Diseases all laboratory examinations, including Wassermann tests of the blood and spinal fluid, gave negative results. Physical examination gave negative results, but a neurologic examination showed flattening of the right side of the face, unequal pupils with poor reaction to light and in accommodation, poor coordination of the upper extremities, limited rotation of the eyes to the left and active deep reflexes throughout, slightly more so on the left side. Mental examination showed slight memory defect, deficiencies of judgment, difficulty in thinking, overapprehensiveness, inadequate emotional reactions and a deterioration of general abilities. Little improvement, mental or physical, occurred during the four weeks she was in the hospital. She returned home and immediately resumed taking the drug. It was finally necessary to send her to a state institution, where she has since remained, and during the last two years no marked improvement has occurred. The following are portions of two letters written by the husband in answer to special queries concerning her use of allonal. "Regarding the use of allonal by my wife, I can only approximate the time, making it possibly a year and a half before the bad effects were noticed. She was alone most of the time, my daughter being at high school, and so no particular attention was paid as to how much she used. We learned later that she would have people get it for her — she was taking it right along after she left the hospital — three tablets in the morning and three at night. It gets her 'off' — of that there can be no question. She demanded it, and became extremely violent if she did not get it. She would go to almost any means to procure the drug. If she didn't have it she raved and cried for it. My daughter and I certainly had a bad time with her for months, until we could no longer stand it. She was 'sore' on our daughter, whom she had previously loved very deeply."

This case seems to be one of definite addiction, beyond reasonable doubt. There also appear to be organic effects in the central nervous system, judging from the positive neurologic and psychic changes. All other etiologic factors were ruled out by careful study. Repeated laboratory and neurologic examinations gave no evidence of any other organic disease of the brain that could possibly explain the observations in the course of the case. A follow-up report (March 11, 1929) from the State Institution in which the patient is, stated that "she shows no essential change since admission. She is now paranoid. A positive Romberg sign is present."

CASE 2.—The patient, a woman, aged 39, developed a severe peritonsillar abscess, and for three weeks prior to admission (June 16, 1926) suffered severely from the pain. She refused to have it lanced, and the nurse reported that the patient had taken large quantities of allonal throughout the illness; later, she took large doses of a preparation containing morphine. In two weeks the abscess broke, and soon thereafter the patient began to show active mental symptoms. These increased until her admission to the Pennsylvania Hospital, one week later.

On admission, she was confused, apprehensive, terrified at times, clouded, excited and reacted to auditory hallucinations. A physical examination gave negative results except for neurologic signs (marked Romberg sign backward and to the right, staggering gait, deviating usually to the right, slight incoordination in the finger-to-nose test, and slight nystagmoid movements on lateral rotation). She complained of soreness in the right parietal region. Mental examination showed marked fear, rambling speech, visual, tactile and auditory hallucinations, disorientation and mild confusion. She improved rapidly and was taken home in two weeks, without the approval of the staff. At the time of discharge she was still ataxic and appeared to have a defect which would indicate organic damage. A follow-up note from the family physician one year later stated that she was in excellent health; a recent checking on this (February, 1929) verified the continuance of her good health.

The psychosis in this patient may have been due to the peritonsillar abscess on an infective—toxic (or postinfective and toxic) basis. On the other hand, the heavy dosage of allonal used (it was known to be excessive, without supervision of a physician, although the amount was not determined) may have been an added

etiologic factor. In either case the point must be considered that the psychosis was too severe and the organic neurologic picture too marked to be due entirely to a focus of infection such as a peritonsillar abscess. In addition, the mental phase of the illness came following a rupture and subsidence of the active infection. The patient continued to take the allonal during this time, up to the date of entry to the hospital, and the psychotic symptoms increased in intensity and extent. As soon as the ingestion of allonal was stopped, she began to make rapid improvement. The final diagnosis made was "psychosis due to drug (allonal)."

Such an effect will, of course, be rare and unlikely in ordinary cases. But it must be kept in mind that this bad result may occur, and the lay person must be warned against using allonal freely and without medical supervision.

Dr. Wilson, of Philadelphia, in a personal communication, mentioned three cases in which he had found untoward effects as a result of using allonal. The first case was that of a man, aged 36, who suffered from a true trigeminal neuralgia. He took from two to three tablets a day, for about a week or ten days, for relief from the neuralgia. One day he left the hospital in which he worked to drive into the center of the city. On a busy thoroughfare he apparently became unconscious and drove up on a sidewalk. In the second case, a man, aged 46, a dentist, had been taking from one to three tablets a day on account of pain and insomnia from sinus disease. In the midst of some dental treatment on one of his patients he put on his hat and coat, walked out of the building and "came to" at two or three squares distance from his office. In neither case was there any cerebral disease or tendency to hysteria or similar attacks. Dr. Wilson believes that the difficulty in each of these cases was due to the idiosyncratic effect of the allonal. In the third case, that of a woman, aged 66, four tablets a day were taken for relief from sciatica. Gradually this was reduced to from one to two tablets every other day. The patient insisted on having it, even in preference to a combined dose of barbital (10 grains) and codeine sulphate (½ grain) as she said that nothing helped her but the allonal. In the latter case Dr. Wilson believes that the condition approaches almost an addition to the drug.

Summary.—The foregoing review of the literature and case reports emphasizes a few points concerning allonal. First, it is an efficient sedative, hypnotic and analgesic drug, if used properly by physicians. Second, definite untoward results may be associated with its use. These untoward results may be toxic effects, cumulative effects, idiosyncratic reactions, and even possible addiction to the drug. Such bad effects may come from overdosage, improper continuance in use of the preparation or from unusual reactions. The proper dosage must be determined by watching the individual result in the case. Probably it is unwise to continue using this drug over a long period of time. Experience alone can indicate how high a dosage may be given, but the indications are that the smaller doses (from one to two tablets) should be adhered to in all but unusual cases.

THE PERMEABILITY OF THE HEMATO-ENCEPHALIC BARRIER AS DETERMINED BY THE BROMIDE METHOD. DR. SAMUEL T. GORDY and DR. STEPHEN M. SMITH.

This article will appear in a later issue of the ARCHIVES.

DEPRESSIONS OF LATER LIFE. DR. JAMES J. WAYGOOD.

Many classifications of functional nervous and mental diseases have been provided from time to time for the guidance of the physician and psychiatrist and for the preparation of hospital statistics. In spite of these many attempts at clarifying this matter of diagnosis, one has only to sit through a hospital staff conference or examine hospital statistical records to see the difficulties and confusion that still exist in the matter of diagnosis and consequently prognosis. If, in order to avoid discussion of the great number of cases grouped as dementia praecox and allied states, one considers here only the illnesses occurring from 45 years of age and after, in which depression of varying degree is a cardinal

feature, one finds that they are placed mainly in three classifications, manic-depressive depression, involutional melancholia and arteriosclerotic and senile dementia. The diagnosis of pronounced or clearcut cases in these three divisions is fairly easy and from long series of cases one can say with fair accuracy that the manic-depressive patient will recover, that the patient with involutional melancholia has about an even chance of recovery and that the chances for the arteriosclerotic and the senile patient are nothing. Even in this limited field of these depressions of middle life and beyond, one finds that hospital statistics show large groups of cases that are evidently not clearcut syndromes, but are grouped as symptomatic depressions, undifferentiated depressions, allied to manic-depression and even merely unclassified. If this is the case in a mental hospital with patients whose symptoms are so pronounced that hospital residence is deemed necessary, one can see the possible confusion as to diagnosis and prognosis and the futility of such classifications of disease in the office of the private practitioner, where, for every patient who shows sufficiently pronounced symptoms to warrant reference to a hospital, there are a half dozen or more who, if classification were attempted, would have to be placed in an allied or unclassified grouping.

There are, for example, depressions shown by the tired and overstrained business man, by the wife who has become bored with her husband, by persons who are troubled with queer sex ideas, by the more pronounced neurasthenic patients, and by those suffering from circulatory disorders and the effects of long-standing focal infections. Any one of these patients may show ideas of hopelessness or delusions of poverty, or may show the retardation of a manic-depressive depression or the agitation of involutional melancholia, and yet the outlook may be a satisfactory one.

Dreyfus reported a study of a long series of cases of involutional melancholia and came to the conclusion that the behavior in this disease was much the same as that in the depressive forms of manic-depressive psychoses, and that patients failed to recover only in the instances when the melancholia passed over into arteriosclerotic or senile dementia.

Hoch and MacCurdy, in 1922, studied the symptoms shown by a group of patients who had recovered from involutional melancholia, and compared them with symptoms shown by a group which did not recover. They concluded that deep depression and the delusions of poverty and death which accompanied 75 per cent of these cases did not have any true bearing on the outcome, but that bizarre and absurd delusions regarding food and body organs, delusions of a schizophrenic nature, were of grave portent. These, with loss of emotional reaction, evidenced deterioration and general senescence.

(Several cases were detailed of depression of a degree sufficiently grave to necessitate hospital treatment, which were intended to show that not the depth or the type of the depression but rather the ability or the inability to correct the discovered causative factors, were the determinants in the recovery or chronicity of the cases.)

Variations of emotion, mood and temperament are seen in normal persons in average good health, even to a fairly marked degree. Depressive moods of longer or shorter duration, of greater or less degree, are seen in every person in his reaction to his every-day environment.

From observance of normal persons and the study of cases such as those which have been detailed, we can come to the conclusion that depression, its depth or its duration, is, of itself, of no diagnostic or prognostic value. Depression bears much the same relation to mental disease that fever does to infection. In infections it is the micro-organism, the streptococcus, the bacillus that is sought for, that gives the disease its name and that is attacked by therapeutic agents. In the depressions, it is the underlying etiology, namely heredity, lifelong habits, psychogenic factors, physical factors, endocrine dysfunction, focal infection, organic decay that should form the basis of differentiating the types of the disease and the indications for prognosis and treatment. This view encourages a more thorough medical and psychologic study of the patient as an individual, rather than as a member of a large group whose symptomatic appearances are somewhat similar. Its result should be a more exact prognosis and a better system of therapy.

DISCUSSION

DR. JOSEPH C. YASKIN: I was particularly impressed by the importance of the rôle played by arteriosclerotic changes in the depressions of later life. Dr. Waygood aptly stressed that the prognosis in these cases depends on the changes in the cardiovascular apparatus. In an interesting case that I studied last year, there was a poor family history. One brother died in a state of depression; a sister committed suicide at the age of 50, and another member of the family committed suicide at about the same period of life. My patient was depressed and agitated and had a great many somatic symptoms. Although he was close to 60 years of age, the general examination revealed no evidence of any acute arteriosclerotic changes and the kidney function was good. He made a good recovery in about six or eight months. This case illustrated well the importance of organic changes as playing an important rôle in the depressions of middle life.

Regular Meeting, Nov. 8, 1929

W. DUFFIELD ROBINSON, M.D., *Vice President, in the Chair*

THE HISTORY OF A HOMOSEXUAL PERSON; HIS DIFFICULTIES AND TRIUMPH. DR. ALFRED GORDON.

The sexual abnormality commenced several years before the patient came under my observation. He was unusually bright and accomplished. When gratification could not be obtained, there was either marked depression or exaltation, which found its outlet in music or in literary work. The patient's childhood was most unfavorable in regard to sexuality. The parents were extremely strict and persistently kept the boy from any association with children of the opposite sex. When treatment was commenced, effort was made to demonstrate to the patient the direct connection of his present abnormality with the unwholesome training in childhood. After many months of training, success was finally obtained.

Gordon discussed the problem of sexuality in general. He made a plea for a scientific study of homosexuality. The latter should not be regarded as a mere perversion and ignored. The victim demands thoughtful management, which can be accomplished successfully only by a sympathetic attitude and understanding. The conventional point of view concerning homosexual conduct is unreasonable. The problem of homosexuality forms a chapter of preventive medicine and belongs to mental hygiene.

DISCUSSION

DR. EARL D. BOND: During the reading of this interesting paper I noticed that Dr. Gordon kept his finger on the really abnormal person, the mother of the patient. Because of this recognition of the source of the trouble, the treatment had good results.

DR. MAX LEVIN: I do not believe that Dr. Gordon mentioned anything about the physical habitus of the patient; whether he had a masculine or a feminine physique. I think that this is an important point in determining to what extent the homosexuality was due to faulty training. Some homosexual males have a normal masculine physique and others a feminine physique. The feminine type of physique suggests a constitutional rather than an environmental basis for the homosexuality. The presence or absence of evidence of deep-seated constitutional alterations may determine whether the homosexuality is ingrained and chronic or superficial and temporary.

DR. ALFRED GORDON: I wish to lay special emphasis on the possibility of recovery in acquired forms of homosexuality. Unfortunately, treatment requires

a long time. The unusual opportunity found in the case presented demonstrates the necessity of persistence. The analytic method of treatment is particularly stressed. Homosexuality is not a mere perversion. Its victim demands thoughtful attention accompanied by a sympathetic attitude.

ACUTE PARANOID EPISODES ASSOCIATED WITH CARDIAC DYSFUNCTION. DR. B. L. KEYES.

Clinical History.—Mrs. G. T. P., aged 60, was admitted to St. Agnes Hospital under the care of Dr. D. J. McCarthy on Oct. 23, 1915, and died there on April 16, 1929, at the age of 74, after a hospital residence of nearly fourteen years. The family and personal history is negative for any significant illness. The patient was always considered healthy. She was an unusually intelligent woman, interested in all that went on in the world and she had traveled considerably. She was a social as well as an intellectual leader in her community. Her home life was of the best American type, and she raised a normal son and daughter. She was widowed about the time when these children became fully grown.

At about the age of 58, two years prior to admission to the hospital, an infection of the upper respiratory tract and of the throat developed, complicated by a low grade toxic nephritis and a myocarditis, from which she never fully recovered. She was bedridden for some weeks and her convalescence was gradual. Soon she developed signs of a mild decompensation, an extreme irritability and a paranoid attitude toward her family. With difficulty she was put to bed and kept there. Under suitable treatment, the circulation became rebalanced, and the nervous symptoms faded out; she showed a complete insight into the paranoid ideas she had expressed.

Again, after a quiet and comfortable convalescence, she was permitted to be up and about, but again signs of early decompensation and an associated violent paranoid outbreak quickly developed. Rest in bed and suitable treatment soon rebalanced the circulation, and during the same period the psychosis faded out. This series of events was repeated several times.

The patient's insight into this condition was so complete that she finally refused to leave her bed, insisting that it was preferable to be bedridden with a normal mind than up on her feet and insane. The household was so regulated that she was able to remain in bed and indulge in all of her intellectual pursuits and her contacts with those who would and could come to her. No further evidence of decompensation occurred, nor was there any evidence of mental symptoms.

She finally decided, however, that she was creating an abnormal home condition, and after the marriages of her son and daughter, she considered it best to go to a hospital and simplify her existence.

Condition on Admission and Course.—She was admitted to St. Agnes' Hospital. There she was able to continue her correspondence and reading and was able to receive visitors. She was quite content with the arrangement.

As she improved physically, attempts were again made to get her up and about. These efforts, however, were unsuccessful; she again manifested very definite, almost violent paranoid attacks in association with the extra work thrown on the circulation. The violence of her anger nearly endangered her life in the presence of so delicate a myocardium.

She again insisted that she would not submit to further experimentation, realizing that her ideas at such times were unreasonable and that her mental reaction to them was entirely beyond her control. During these episodes she showed no insight; but afterward there was complete insight, and she was at times deeply mortified in realizing the experiences.

Efforts to get her out of bed, therefore, were discontinued, and she existed comfortably as a bed patient, inventing many new and useful bedside comforts, especially from the nursing standpoint.

After a time a fear of fire gradually developed; special bells were installed so that she could summon instant aid, and her room was changed to open onto a fire escape from the second floor. This fear was intensified by a fire in her vicinity and the realization that she was unable to help herself.

Several times during the next four years, several mild, upper respiratory and throat infections developed and an occasional mild cystitis. Each time when these additional circulatory and renal periods of stress occurred there was a tendency to swing back to a paranoid psychosis with suspicions and accusations of negligence against physicians, nurses and family, and extreme irritability, but always with complete reasoning and insight after recovery.

At the age of 67 (1922), a small mass was noticed in the left breast and a diagnosis of early carcinoma was made. Radium was used; then the breast was amputated, and the axilla resected. Radium was again administered.

She tolerated the operation very well, though she again showed signs of a borderline paranoid psychosis for the first few days after the operation.

Four years later, a recurrence of the carcinoma was noticed in the left axilla, and a secondary operation was performed, this time under local anesthesia.

She behaved wonderfully well during and immediately after the ordeal, but the following day and for several days afterward she was irrational, angry and abusive of the physicians and nurses and made many scathing remarks, even refusing certain of the staff admission to her room. As the condition progressed, she readmitted those who had been excluded, but never quite regained her former confidence in them.

About the same time her daughter's husband of whom the patient was very fond died. Within a short time, the daughter remarried against her mother's wish and advice. This brought about a change in attitude toward the daughter, from which the patient never recovered; hence it was always necessary for the daughter to visit only when accompanied by some other person. This rule was instituted at the urgent request of the patient, for she realized that on one or two occasions when her daughter had visited her alone, she had quickly become tired, then exasperated and then so angry that she said things for which she was sorry later.

Gradually a carcinomatosis developed involving the lungs and other organs, and the patient died with a decompensation precipitated by a pulmonary metastasis.

Necropsy.—Metastatic carcinomas were scattered throughout the lungs, especially in the upper part. The heart showed: arteriosclerosis with calcareous plaques in the aorta; slight calcification of the margin of the aortic cusps; normal mitral and myocardial valves; tremendous hypertrophy of the chordae tendineae and papillary muscles; left ventricle 2 cm., right ventricle 1.5 cm. thick; small size as compared with the normal for the size of patient; distinct brown atrophy.

The brain showed: arteriosclerosis and plaques on the basal vessels; external hydrocephalus and atrophy of the cortex, especially of the frontal and parietal margins; flat carcinoma nodules on the anterior part of the falx; a nodule (1 cm.) within the squamous portion of the left temporal bone.

IDENTICAL TWINS WITH IDENTICAL PERSONALITIES. DR. CHARLES W. BURR.

Biologists accept as proved the occurrence of monozygotic (identical) twins; i. e., twins from one egg enclosed in one chorion and with a single placenta. Much has been written about the occurrence of the same physical diseases in such twins, the existence of similar susceptibilities and their equal powers of resistance to external morbid stimuli. Only recently, my associate, Dr. F. H. Leavitt, reported the occurrence of cerebellar tumors in a pair of such twins.

Francis Galton was the first man of science to study exhaustively mental inheritance and to investigate carefully mental likeness in twins. During the last few years the problem of mental likeness has interested an increasing number

of writers, for example, Dr. G. R. Murry, who published a scholarly paper in the London *Lancet* (March 14, 1925), Alfred Gordon and D. A. Johnston. The French and German literature is large. Benjamin Rush was the first American authority who described mental similarity in twins. Of course, he knew nothing of the biologic aspect of the question. The cases I report illustrate how close the likeness may be.

Family History.—The paternal grandfather left Pennsylvania, where his forefathers, of English stock, had lived for several generations, having settled there as farmers soon after Penn's founding of Philadelphia. I know nothing of his wife, save that her people had treked from Massachusetts, where they settled after leaving England. The grandfather prospered and became a large landowner. I know but little of his intellectual, moral and emotional makeup. But it is safe to assume, since he withstood the hardship of pioneer life, lived to old age, and was successful in a worldly sense, that he was a normal man.

I know little of the parents of my patients. The father, one of four children, inherited a large tract of land in a growing city of the middle west, which, being developed by him, made him wealthy. He died in early middle life, while his twin sons, his only children, were still small. He drank heavily at times and apparently was very ugly in conduct when drunk. He had periods of depression which caused him to seek relief in drinking. He was not a social, but a solitary, drinker. This, I believe, is always pathologic. He was financially shrewd, not highly educated, of few intellectual interests, not oversexed, and a good husband. The mother lived until her sixty-sixth year and died from apoplexy, probably a cerebral hemorrhage. From what I have been able to learn, she was a good mother, sensible in her attitude toward life, and religious in a wholesome way. She certainly realized the value of education, because she gave her sons every opportunity.

Life History.—The twins at birth, and indeed throughout life, were indistinguishable. When I knew them in their last years (from 62 to 65), I could not tell them apart. Even the intonations of speech were the same. I never saw their handwriting, and know only from hearsay that the brothers wrote in a similar way. This may have been the result of training in the same standardized style, one of the few standardizations in education which is harmless.

I know nothing of their childhood, except that they were bottle fed, well cared for in a material way, had no childish diseases, and even as boys quarreled with each other continually. This quarreling developed into lasting hate, and, from the fourteenth year, when they were sent to different boarding schools, they had no intercourse with each other save on matters of business. After they grew to manhood this was always carried out by agents. They never met, save casually, after they went to college, and rarely even casually.

They did their lessons at boarding school fairly well. Indeed, they learned with ease, but soon began to get into trouble. Because of misconduct, they were expelled from school after school. They entered different colleges at the age of 19 years. Both were expelled in their freshman year for misconduct concerning women and drink. At about the age of 21, each went into the real estate business in different towns.

This was largely, if not entirely, the result of environment. Both inherited much land in several towns, and they had heard much about real estate matters. Neither was a success in business, largely because they gave so much time to pleasure that business was neglected. Each of them held on to most of his properties and grew richer from the so-called unearned increment. Neither was financially dishonest; indeed, both men had excellent reputations for business integrity.

Both married. I do not know the exact time, but one brother took a wife two or three years after the other. They chose different types of women, and a curious result followed. One, Charles, married a prostitute (a woman about ten years younger than himself), who stood by him until his death (many years after) and had peace only in her older age. The other (John) married a gentlewoman,

well off and well educated, and about his own age. She divorced him for infidelity and brutality, not the technical brutality of the law courts but actual physical injury, after five years. Neither woman had any children. I do not think they were ever pregnant. The brothers retired from active business at the age of 40. Each had repeated attacks of gonorrhea in adolescence, but neither was syphilitic. The history was unimportant and the clinical examination and laboratory tests (blood and spinal fluid) gave negative results.

I have said that at school and college both learned easily and quickly; but soon they lost all interest in intellectual things and cared only for bodily pleasure. Their lives were altogether useless. At 60, both began, at first slowly, to become demented. They became forgetful, lost judgment and were depressed, with occasional spurts of silly happiness. At 62, which was the age at which I first saw them, both had cardiorenal-vascular disease, with high blood pressure, and were depressed. At 63, after they had been removed from my care, Charles committed suicide by jumping out of the window in a Detroit hotel, and John by jumping from the window on the upper floor of a sanitarium in a town in California. The two deaths occurred in the same week. Neither brother had known anything of the other for several years. The parallelism in their lives was remarkable. One case does not prove anything, but it does create a presumption. Accident might have caused some of the coincidences of their lives, but such a series of coincidences as they showed was too remarkable to be explained on that ground. People who knew them well, and who had no biologic theories to support, spoke often of their likeness in temperament, character and intellectual qualities.

The hate they bore each other is unusual in twins. Popularly they are thought to be always friendly and sympathetic to each other. The explanation of the hate in my patients was their intense selfishness.

DISCUSSION

Dr. James Hendrie Lloyd: One statement in Dr. Burr's paper strikes me as especially interesting, and that is the aversion these twins had to each other. I have always thought that identical twins were attached to one another. Dr. Benjamin Rush refers to a strikingly similar case to that of Dr. Burr. It was the case of twin brothers who were so nearly alike that their own relatives could hardly tell them apart. They were both officers in the Revolutionary War. Later in life they settled in New England, 100 miles apart. When past middle life they both developed the same mental disease, and both committed suicide.

Dr. Burr has referred very properly and clearly to the subject of heredity. There is a tendency to belittle the importance of heredity. Behaviorists seem to think that the cortex of the brain of a new-born child is like a blank page. One can write anything on it, and the child will develop accordingly. But one cannot ignore heredity. The only safe way is to recognize environment on the one hand and heredity on the other. It is the joint action of these two that counts.

Dr. Alfred Gordon: Some German authors, under the term "Zwillingirresein," and some French authors, under the term "folie gemellaire," speak of a special "twins psychosis." What particularly suggested the idea of a special psychosis to those writers is the simultaneous occurrence and development of psychotic disturbances in twins who live apart, so that there can be no question of induced mental manifestations. In spite of the similarity of the clinical pictures, one must bear in mind the conditions and circumstances in which the patients live and which might induce a psychosis in any other person, if there is a morbid heredity. Similarity in the course of a well known mental condition does not render it specific. As for the question of heredity, one may say that if the predisposition to mental disorders in many instances presupposes a congenital morbid organization of the nervous system, the rôle of heredity finds its strongest corroboration in cases of psychosis in twins. As to the nature of double conception, one sees in it an inferior mode of procreation, which is observed not only in man but also in animals. It is frequent in syphilitic persons, and in a large per-

centage of twins who died early, syphilitic livers were found. Fournier had great opportunities to observe and record double births when the parents had hereditary syphilis.

CHILDREN'S DREAMS. DR. GERALD H. J. PEARSON.

In order to understand the etiology of the problem behavior of children, and to be able to apply adequate treatment to the factors that are hampering the development of a mature personality, it is necessary to understand, not only the situation in which the child lives, but his feelings about that situation, and the individuals in it and himself. For many reasons it is difficult to elicit this information from the child, and any means that helps in understanding his emotional life is of value. Dreams are important psychic phenomena, and as such are useful in ascertaining the personality trends, the conflicts and emotional difficulties of the child. A series of dreams of one child, aged 10, gives plain evidence of the personality type of the dreamer. Many children's dreams are simple wish fulfilments, but a large number show various degrees of an attempt to disguise the wish because it is unpleasant to the waking child. The interpretation of the simple wish fulfilling dreams presents no difficulty. The more complex dreams contain both a manifest and a latent content. Often in the dreams of children the manifest content can be interpreted as a wish fulfilment without a great deal of difficulty. This applies particularly to dreams of relatives. In others, it is impossible to interpret the dream without investigating the latent content by the free associational method. Particularly burglary and kidnaping dreams disguise the real content, so that interpretation is difficult. Children's dreams are similar to those of adults. All are wish fulfilling; but in some the meaning is undisguised, in others the disguise is easily penetrated, and in still others the wish is completely concealed. Study of the dreams of children is as important and valuable a method for investigating the mental life of a child as is the study of adult dreams.

DISCUSSION

DR. ALFRED GORDON: Speaking of children's dreams, conduct and behavior, I do not find any difference between them and those of adults. They are all dreams of emotion, fear, etc. One phase of that study is important. In trying to separate the dreams of fears and the dreams of wishes, the author in the last analysis brought the whole subject to one point, namely wish fulfilment; I believe that he is right. Fear is an attempt to run away from an unpleasant situation, which is, after all, a wish.

A girl, aged 14, was highly sexual. A cousin with whom she had sex relations lived in the same house. One night she awakened and began to scream. She had dreamed that her cousin had tried to assault her. She screamed, although she wanted to be seized. She was very fond of him.

DR. LEVIN: Dr. Pearson has called attention to a very important topic. I have had occasion in the last two years to listen to the dreams of many children, and I can say that if one understands the child one can in most cases see some sort of wish in the dream. I find that the dream often consists of the death of the opposite parent. Today I examined a girl, aged 15, who has not been getting along well with her mother. She dreamed that her mother was drowning. A boy had a hatred for his father and dreamed that he was choking his father to death; he described vividly how his father was struggling. A boy, aged 15, lived for the first nine years of his life with his mother in Europe. The father was in America. At the age of 9 the boy came to America. His mother had then to give some of her love to her husband, and the boy was quite unhappy. He told me that a couple of years ago he had a dream in which he was crossing a bridge made of logs, and he recalled that one day at the age of 7, while moving from one city to another, he and his mother had to cross a small stream on such a bridge. I think this dream expresses a wish that he were back again in the earlier situation, when he had more of his mother's love.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 22, 1929

C. A. PATTEN, M.D., *President, in the Chair*

CEREBELLAR ABSCESS. DR. FRANCIS C. GRANT.

D. H., aged 9, was admitted to the University Hospital from the Children's Hospital on Aug. 1, 1929, complaining of headache, weakness, convulsions and ataxia. Five weeks before presentation, the child became listless and seemed drowsy. A week later, she began to complain of headache and pain in the neck. Twelve days before admission, she had a general spastic convulsion and was unconscious for sixteen minutes. During her stay at the Children's Hospital her condition became worse. She had convulsions of a severe spastic nature, beginning on the right side and spreading to the left, being more intense on the right. Apparently these convulsions commenced abruptly with seizures of the right arm and right leg and then spread to the left arm and left leg. Involvement of the face was doubtful; at least it was much less affected than arm or leg.

Horizontal nystagmus developed which was more extreme to the left. Hypotonia of the left arm and leg and ataxia were observed. When the patient walked she staggered to the right. She never complained of dizziness, tinnitus or deafness. Her mentality was unimpaired. She did not seem to remember the convulsions. In the last two weeks before the operation, definite blurring of vision developed.

The child lay in bed and was unable to sit up. She tended to keep her head turned to the right. A cracked-pot sound, suboccipital tenderness and some rigidity in the neck were observed. At intervals she seemed to become oblivious to her surroundings; her eyes were turned up and to the left; her mouth opened widely and deviated to the left, and she screamed shrilly as though in pain. The position of the extremities varied; at times they were spastically extended, but at other times one arm would be held rigidly extended while the other was rigidly flexed. She was as likely to flex or extend the left arm as the right. There did not seem to be any fixed position for the arms. The legs were usually in fairly rigid extension. During these attacks she made a curious irregular, sucking movement with her mouth. After the attacks disappeared she did not seem to remember any pain and was oriented and intelligent. She talked well and understood what was said to her.

There were no pathologic symptoms in the frontal lobe. There was definite weakness of the left extremities, the face being much less involved than the arm or leg. There was no sensory disturbance of any type. The child was almost blind. The visual fields seemed grossly normal.

There was marked ataxia and dysmetria in the left extremities. Nystagmus to the left and adiadokokinesis on the left were noted. There was hypotonia at all joints. There was visual loss, with 7 diopters of choked disk in both eyes. There was a questionable weakness of the left side of the face.

All reflexes were diminished equally; there were no pathologic reflexes.

The diagnosis was between a right frontal and a left cerebellar lesion. General convulsions and weakness of the left extremities suggested the diagnosis of a tumor in the right part of the motor cortex. The shortness of the history of the case, the degree of choked disk, the nystagmus, the cracked-pot sound, the suboccipital tenderness, the ataxia and dysmetria in the left extremities with a condition of hypotonia, the diminished reflexes and the lack of pathologic reflexes favored the diagnosis of a left cerebellar lesion.

It was obvious that an operative procedure had to be carried through promptly, if at all, as the child was becoming more drowsy. In order to make a differential diagnosis between right cerebral and left cerebellar tumor, the right lateral

ventricle was tapped and found to be dilated. Inasmuch as this condition practically precluded the possibility of a cerebral lesion, a suboccipital craniectomy was performed.

Exposure of the cerebellar hemispheres made it obvious at once that there was a lesion in the left cerebellum, for this hemisphere bulged much more than the right. The cortical veins were clipped and an incision was made in the hemisphere with the Bovie knife. What was thought to be a fairly well encapsulated tumor was found at once.

As I was separating the brain from the capsule it suddenly ruptured, flooding the wound with pus. The lesion turned out to be a cerebellar abscess and not a tumor. With the posterior fossa widely opened it did not seem possible to avoid contamination of the wound. However, the pus was carefully sucked up with an aspirator, the cavity opened widely and the remaining pus removed. With the Bovie knife I then cut away the capsule, hoping thus to sterilize the bed of the abscess. The abscess cavity was washed out with alcohol and mercurochrome-220 soluble, a little mercurochrome being left in place. Since a careful history of the case had failed to reveal the presence of otitis media on either side, I hoped that the abscess might be sterile, at least the active organisms much attenuated.

I determined, therefore, to close the wound tightly; after careful hemostasis, this was done by the usual technic. Immediate postoperative recovery was uneventful. Smears of the pus showed pneumococci, so I gave the child 50 cc. of Huntoon's polyvalent antipneumococcic serum with 2 cc. of 1 per cent ethylhydrocupreine into the right ventricle after withdrawing 75 cc. of fluid.

Five days after the operation Dr. Gardner took charge of the patient. To reduce tension and for the purpose of drainage, lumbar and ventricular punctures were done every day for three weeks after the operation. The child had a temperature varying between normal and 101 F., during this time. The wound was dressed and the stitches were removed. The wound was in good condition.

The child's condition was much improved; the convulsions had ceased and cerebellar symptoms were less distinct. The only unfortunate complication was a complete loss of vision, although the choking of the disks had diminished to less than 1 diopter. The nerve heads were white with poor vascularity.

Three weeks after the operation, the child suddenly developed a temperature of 103 F. Examination of the wound at this time showed infection with a cerebrospinal fluid leak. On the following day, Dr. Gardner made a midline incision running up to the lower edge of the wound and evacuated considerable pus. It was obvious that unless the cerebrospinal fluid leak could be controlled, meningitis was sure to occur. Seven hundred and fifty mg. of sodium iso-amylethyl barbituric acid was given by rectum. The nasal catheter was introduced to feed the patient and she was given 600 mg. of additional iso-amylethyl barbituric acid through the nasal tube. The drug put the child to sleep for practically seventy-two hours. During this time a lumbar puncture needle was kept in place and continuous drainage of spinal fluid instituted. At the end of the seventy-two hours, the cerebrospinal fluid leak had stopped and the wound apparently had healed by first intention. At first the fluid from the lumbar puncture needle was cloudy but it gradually became clear. When the child showed evidence of recovering from the effect of the drug, the lumbar puncture needle was withdrawn and daily lumbar puncture instituted. Cerebrospinal fluid again commenced to leak from the wound but this was practically stopped by a secondary suture. Cultures of the spinal fluid were at all times negative, although the fluid contained between 12,000 and 15,000 leukocytes per cubic millimeter. The child's condition rapidly improved and she was discharged from the University Hospital on Sept. 15, 1929.

Neurologic examination, three days before presentation, showed that the child had recovered sufficient vision to read fine newspaper print with the right eye; the left eye showed less recovery. There were no residual cerebellar symptoms. The decompression was flat and the wound well healed. This case is reported because it affords an example of cerebellar convulsions.

THE IMMEDIATE EFFECT OF RHIZOTOMY ON SPASMODIC TORTICOLLIS. DR. CHARLES H. FRAZIER.

In presenting this case I shall not attempt to give a classification of the disease; suffice it to say that it concerns a form in which the contractions were violent, painful and of unknown origin. My object primarily in selecting this case for demonstration was to establish the merits of a different surgical principle in the treatment of this disease, a method which interrupts only the afferent impulses.

The patient, referred to me by Dr. Spiller, was well until the winter of 1928-1929, when she complained of generalized weakness and loss of appetite, together with a dull ache in the left shoulder. The latter was relieved by massage. The aching spread to the back of the neck and head, apparently leaving the shoulder, and lasted all spring. In May, she noticed that the muscles of the neck began to jerk, pulling the head backward and to the right, the jerking occurring when she used her arms in sewing, washing dishes or eating. The condition progressively became worse. No additional muscles were involved. In June, she began a series of chiropractic treatments, which lasted until August. She grew worse during these treatments. In August, her physician advised rest. This did not improve matters. Later a roentgen examination of the teeth showed six infected teeth. Three were removed on about October 1, and immediately the condition seemed to get worse; the jerking became continuous and more violent, lasting all day but disappearing when she went to sleep. Injections of magnesium sulphate were recommended, and one injection was given. On admission the patient believed that the jerking was a little less intense and the drawing sensation not as intense. For the five days before the operation the patient had been confined to bed, the jerking continuing even when she was reclining.

For six years the patient had been engaged in the work of assembling porcelain electric light sockets, inserting from 1,500 to 2,000 screws a day. In her work she inclined her head slightly to the right, using a screw driver in the right hand, the socket gripped tightly in the left. She worked for nine and one-half hours a day, five and one-half days a week, and felt that this was a severe strain.

Before the operation there was no question as to which sternocleidomastoid was at fault in the spasmodic movement, but Dr. Spiller and I were not altogether in accord as to the side on which the posterior group of muscles were at fault. However, I acquiesced in Dr. Spiller's opinion, cut the first, second and third cervical anterior roots on the left side, but crushed the second and third cervical posterior roots on both sides, at the same time dividing the spinal accessory nerve on the left side within the spinal canal.

The results have been eminently satisfactory. There have been no spasmodic movements since the operation and the patient is able to maintain the head erect in the sitting posture.

Preliminary to discussing the various operative procedures, I shall refer to the movements involved in spasmodic torticollis. There is the action of one sternocleidomastoid muscle, which inclines the head toward the affected side and directs the chin upward and to the contralateral side. This movement is easily recognized and one can readily select the offending muscle. A second movement is rotation of the head to the right or left, a movement occasioned by the rectus posticus anticus major and minor. Obviously, one can neither see nor feel these muscles in spasm because of their location, covered as they are by other large muscles which are often in a state of contraction. Third, there is the action of the trapezius, the splenius capitus and the complexus, the semispinalis capitis, the rectus capitis and lateralis, and the longissimus capitis. These muscles incline the head backward and toward the homolateral part of the shoulder. As a rule, the sternocleidomastoid muscle is affected on one side and the posterior group on the other. This combination does not always prevail, as in some cases the anterior and posterior group may be involved on the same side, and again in others the posterior group on both sides.

The difficulty in planning the operation arises chiefly with the latter group. One group of posterior muscles, contracting more violently than the other, masks

the action of the lesser of the two offenders. Such a situation was experienced only a few weeks ago in a patient in whom Dr. Spiller and I were jointly interested.

The second aspect of the problem, how to relieve the spasm in this form of torticollis, is more fundamental. Shall the anterior roots alone, the anterior and the posterior roots on one or both sides, or the posterior roots alone be divided? I shall not discuss here the propriety of attempting to relieve a condition which may be of central origin by interruption of peripheral impulses. To divide the anterior or efferent fibers implies an attempt to arrest the spasmodic movements by paralyzing the affected muscles. Should this be the objective? Obviously, one could not apply this principle in a case in which the muscles on both sides were involved. The resulting paralysis of the muscles of both sides would interfere with the maintenance of the head in the erect posture.

In 1924, McKenzie of Toronto (*Surg. Gynec. Obst.* **39**:5, 1924) described the beneficent effects of intrameningeal division of the spinal accessory and of the roots of the upper cervical nerves in the treatment for spasmodic torticollis. Both the anterior and posterior roots were divided. In that contribution he suggested that spasm might be effectively relieved by interruption alone of the afferent fibers. Certainly there is ample evidence from the work of Sherrington in the laboratory and Foerster in the clinic that muscle spasm may be controlled by interruption of afferent impulses. According to Sherrington (*Proc. Roy. Soc. Med.* **16**:337, 1907), the rigidity of the muscles immediately ceases on severance of the spinal afferent roots. Section of the posterior roots for relief of spastic rigidity was advocated by Foerster many years ago and I have recorded my own experience in the case of a patient with spastic paraplegia (*Univ. Penn. M. Bull.*, January, 1910). From these observations, from the results obtained in the case presented here and from my experience in other cases, I have concluded that to relieve the spasm of spasmodic torticollis it is necessary only to arrest the function of the afferent impulses. There is an apparent inconsistency in this position if one recommends section of the spinal accessory nerve as well. I acknowledge this, because I have had no experience in cases in which this nerve has not been cut. But it may be that this is not essential. At all events, I shall in the future cut, tie or crush the second, the third, and possibly the fourth cervical afferent roots, always on both sides, and leave the efferent roots alone.

The operation itself is not difficult and should be free from any inherent hazards. Certainly it reduces the treatment to surgical simplicity, exactness and safety.

DISCUSSION

Dr. Cadwalader: Dr. Frazier's suggestion of cutting the second and third posterior cervical roots of each side for the relief of spasmodic torticollis seems to me a logical procedure. In cases of torticollis the muscles of both sides of the neck are hypertonic. Hypertonia is a manifestation of increased reflex activity. Normal muscle tone is dependent on the integrity of the posterior spinal roots; therefore, cutting the cervical roots should diminish the muscular spasm of torticollis. Cutting the posterior roots is capable of diminishing the hypertonicity or spasticity that occurs in the lower limbs in cases of lateral spinal sclerosis.

Dr. C. K. Mills: Spasmodic torticollis was discussed in one of my earliest papers. Spasmodic torticollis was never cured by any operation of the kind reported tonight. It may sometimes be improved temporarily. Spasmodic torticollis and facial tic are of cerebral origin and the only way to get at their source operatively is to operate on the cerebrum. This was suggested by Sir Victor Horsley. The cerebral operation would be no more difficult than the list of operations reported tonight. I will ask Dr. Frazier: "Does he know of any case that has been cured by operations like those reported this evening and that has remained cured after a period of six months?"

Dr. Frazier: I recognize the propriety of Dr. Mills' criticism as to the attempt to control spasticity of central origin by peripheral operations. I have never taken issue with Dr. Mills in a discussion of any neurologic problem as his

experience is so much vaster than mine. But I only venture to remind him that the same principle I have advocated as applicable to spasmodic torticollis has been applied with advantage in cases of cerebral spastic diplegia. May I, in concluding, merely restate the purpose of this presentation: to advocate section of afferent fibers alone as a means of controlling the spasms of this distressing disease, spasmodic torticollis.

Two Cases of Hereditary Ocular Nystagmus. Dr. W. B. Cadwalader.

Two brothers, one aged 2, the other 8, were in perfect health, except that each had ocular nystagmus, chiefly lateral, but partially rotary in type; in other respects, the ocular examination gave negative results. The reason for reporting these cases is to call attention to the fact that nystagmus may occur in more than one member of a family without other evidence of disease. It was stated that in this family there had been one aunt, a grandmother, a greatgrandmother and one first cousin with nystagmus. In each instance it appeared to be transmitted through the female line. The father of the two children presented was normal. Each case of nystagmus was recorded only in the mother's family.

Nystagmus as an isolated manifestation of disease has been reported from time to time in different members of the same family. It is regarded as a defect in development, which may be transmitted and may recur in successive generations.

Discussion

Dr. Yaskin: At the Orthopaedic Hospital there is a family of two children, one of whom showed nystagmus since the age of 3 months; the other, 2 or 3 years of age, had developed nystagmus about six months before admittance. It would be interesting to know just what type of nystagmus was present in Dr. Cadwalader's cases. Are they of the horizontal type and are they to be accounted for by changes in the refractive or the retinal components of the eyes?

Treatment for Acute Cerebral Trauma Showing Various Phases of Intracranial Pressure. Dr. Nicholas Gotten.

In the following case of cerebral trauma there was a marked increase in intracranial pressure complicated by subarachnoid hemorrhage. This was controlled by limitation of fluid taken in by the mouth and spinal drainage; recovery occurred. A secondary period of stupor, due to the uncontrolled ingestion of a large amount of water, followed.

M. A., a man, aged 21, an Italian, was admitted in an unconscious condition to the Samaritan Hospital, on the service of Dr. Temple Fay, on Sept. 30, 1929. He had been struck by an automobile a few minutes before admittance. There was a deep laceration, about 1½ inches (3.8 cm.) long, in the occipital region. The patient was in a condition of moderate shock. Examination showed no evidence of a depressed fracture.

The patient was not aphasic. He responded well to painful stimuli. Ocular movements were normal. There was no facial weakness. The reflexes of the upper extremities were absent; in the lower extremities there was a slightly increased patellar reflex on the left. There was an abortive clonus on both sides. No Babinski sign was found.

The patient reacted well under treatment for shock, so that within a few hours he was in suitable condition for suturing the scalp. At this time the patient showed evidence of beginning cerebral edema as evidenced by a pulse rate of 70 and a pulse pressure of 65 with a respiratory rate of 14. A spinal puncture revealed intensely bloody fluid under moderate pressure. The patient was given 50 cc. of 50 per cent dextrose and was placed on a fluid restriction of 26 ounces (768.8 cc.) every twenty-four hours.

Following this procedure, the pulse rate rose to 75 and the pulse pressure was 62. Thereafter, daily spinal punctures were done, with withdrawal of from 30

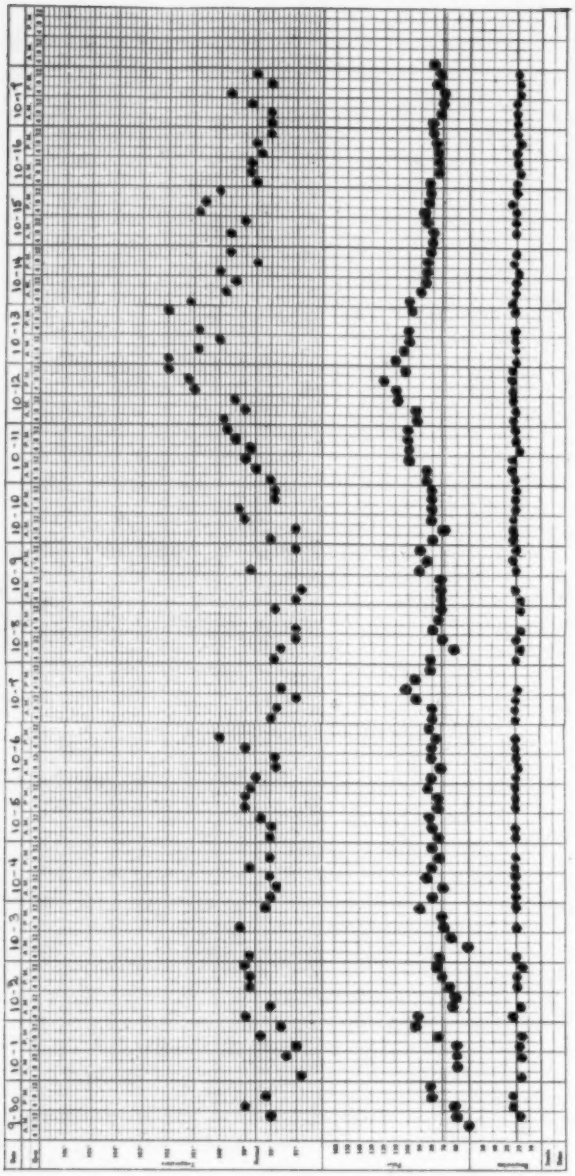

Chart 1.—Observations on patient with acute cerebral trauma: temperature, pulse rate and respiration.

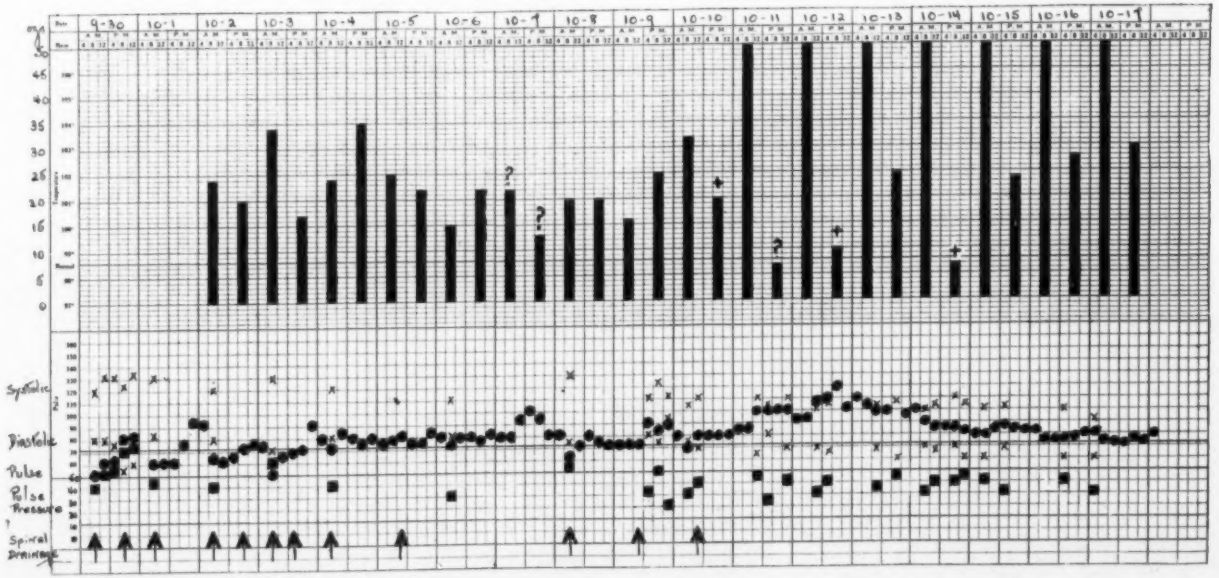

Chart 2.—Intake and output of fluid, blood pressure and spinal drainage. Under each date at the top of the chart the first black column indicates intake, the second output, of fluid.

to 40 cc. of bloody spinal fluid at each puncture. The patient reacted well. There was no evidence of increase in the intracranial pressure. He was bright and alert and was easily controlled, with the exception of a continual desire for water.

On the eighth day after admission, the patient arose from bed, went to the bathroom at 1 a. m., and drank a large quantity of water; the amount could not be determined. On the same day, at 8 a. m., the respirations were of the Cheyne-Stokes type, and the respiratory rate was 16; the pulse rate, 64; the pulse pressure, 57, and the patient was stuporous. A spinal puncture was immediately done and fluid obtained under pressure; 35 cc. was withdrawn. He was given 50 cc. of 50 per cent dextrose and 1½ ounces (44.3 cc.) of magnesium sulphate. In the course of an hour, the patient was alert and no longer in a state of stupor. It was necessary to restrain him in order to prevent him from getting out of bed. Lumbar punctures were repeated daily. No further difficulty was encountered in handling the intracranial pressure phases in the case. Thirteen days after admission, the patient became incontinent, and a slight cystitis developed. The total fluids were then increased to 50 ounces (1.4 liters) with careful observations of the output and of the pulse pressure in order that there should be no recurrence of the former condition.

The patient made an uneventful recovery and was discharged twenty-one days after admission. He returned to the dispensary recently and reported that he was back at work and was apparently in good condition.

Laboratory examinations of the spinal fluid showed that the content of red blood cells ranged from 6,000 per cubic centimeter at the time of admission, with subsequent daily decreases in the number until ten days after admission. At the time of the last puncture the cells were 13 per cubic centimeter.

Increased intracranial pressure after trauma usually begins within a few hours after the period of shock is over. It is caused by cerebral edema; the pathologic and physiologic factors are similar to those which occur following an injury to tissues in any other part of the body, except that the skull is an unyielding container and the escape of spinal fluid may be impaired by blood. Histologically, there are intensely dilated pericellular and perivascular spaces, with dilatation of the subarachnoid spaces due to an overaccumulation of cerebrospinal fluid. When a subarachnoid hemorrhage is combined with these conditions there is usually a more intense reaction, with a tendency to persist for a much longer period of time than in the usual cases of cerebral edema following states of contusion or hydration. This is due to the irritative action of the blood in the subarachnoid space (Weed, Bagley, Winkelman), and also to clogging of the cerebral exits for fluid (pacchionian bodies) in the region of the longitudinal sinus.

The index to the amount of cerebral edema cannot be determined by observations of blood pressure, temperature, pulse rate or, more especially, spinal fluid pressure readings. Respiratory rates often give a clue, and also spinal punctures, with increased pressure readings, may indicate the presence of edema; but I have found cerebral tissue edema without increase in spinal pressure.

The patient improved so that he was allowed out of bed during the first seven days until the fluid intake level was suddenly upset by his theft of water. There was a resultant immediate increase in intracranial pressure, followed by stupor, which required emergency measures of dehydration and spinal drainage to save his life and undo what hydration had done in a few hours.

The treatment in cases of intracranial pressure and subarachnoid hemorrhages is based on dehydration (Fay's method), with lowering of the intracranial pressure —removal of all cerebral spinal fluid, if bloody, that can be obtained by drainage at the time of each puncture, and the careful restriction of fluid intake. Punctures should be repeated in the early stages as often as three or four times a day for the removal of the blood, and as often as is indicated by clinical signs for the relief of cerebral edema. At the same time, fluids should be given in small quantities and an accurate intake and output chart kept as an index of how the patient is handling fluids. Fifteen-minute temperature, pulse and respiration readings are recorded, and the blood pressure is taken every half hour. During the acute stages

of intracranial pressure, magnesium sulphate may be given if the patient is out of shock (by mouth if the patient is not stuporous, by bowel if necessary); 50 per cent dextrose intravenously is also recommended when shock and rising pulse pressure demand a quick therapeutic result.

Fluids should be restricted to 1,500 cc. during the three months following discharge from the hospital to prevent post-traumatic symptoms, convulsions and brain atrophy as pointed out by Fay (*J. A. M. A.* **94**:245 [Jan. 25] 1930).

DISCUSSION

DR. TEMPLE FAY: I asked Dr. Gotten to present this record. The case shows clearly that a patient who has received a severe head injury and has been brought to the hospital in stupor, after careful control of the intake and output of fluid with restriction of fluid to 24 ounces in twenty-four hours, responds promptly from the increase of intracranial pressure. The use of additional dehydrating factors, such as spinal drainage (especially as there was bloody fluid in this case) and the use of magnesium sulphate and 50 per cent solution of dextrose intravenously, show that operation is no longer necessary to control the intracranial pressure. The hospital days are greatly decreased and the patient returns home with few post-traumatic sequelae. The record shows that as long as the fluid intake is controlled during the first few days following the trauma, the patient is apparently normal so that he may be out of bed after the third day and, aside from headache and thirst, convalesces rapidly. In this case, on the night of the seventh day following the trauma, the surreptitious ingestion of a large amount of fluid was responsible for a prompt reappearance of symptoms of stupor, rise of pulse pressure and fall in pulse rate, so that it was necessary to reinstitute spinal drainage and dextrose by vein and to cut the fluid intake sharply. Uncontrolled fluid intake is extremely dangerous to patients in this type of case during the first ten days. After the tenth day, in cases in which the spinal fluid is bloody, there is readjustment of cerebrospinal fluid circulation so that the patient can safely take large quantities, and one sees in this patient's chart that 50 ounces of intake was possible without disturbance of the pulse rate or the pulse pressure after the tenth day.

DR. ROSS THOMPSON: What do you consider the relative values of magnesium sulphate and hypertonic solution of dextrose? When do you use magnesium sulphate, and when do you use hypertonic dextrose intravenously in these cases?

DR. TEMPLE FAY: Dr. Thompson has raised a most important consideration; the dehydrating effects of the two solutions are entirely different in that magnesium sulphate draws fluid rapidly from the intestinal vascular bed into the gastrointestinal tract and eliminates it by this means. The depletion of the vascular volume will eventually decrease cerebrospinal fluid pressure as Weed and others have shown, but it is not to be used when the patient is in shock, for in this condition vascular volume is already depleted and magnesium sulphate increases the shock. It should be used when the patient is entirely out of the period of shock. Its action is more prolonged; the fluid depletion is primarily of the vascular volume and secondarily of the tissue edema.

On the other hand, 50 per cent dextrose, when given intravenously, draws the fluid from the tissues into the blood vessels and thus depletes cerebral edema both, from the tissue side and from the cerebrospinal fluid side, by increasing the elimination of cerebrospinal fluid, as well as by preventing its subsequent production. In this way it immediately offsets both shock and increased intracranial pressure, so that it is the ideal method of treatment in a case in the early stages following trauma. If one desires to give magnesium sulphate after the period of shock has been thus controlled, it will subtract the fluid from vascular volume created from the tissues by the 50 per cent dextrose and effectually eliminate it from the entire system. The combination of these two solutions, when properly used, will produce the desired relief of pressure. The repetition of one or the other of these solutions or their combined use from time to time gives the desired effect and makes possible an efficient nonoperative method to control intracranial pressure.

DR. GRANT: I am extremely interested in the suggestion of Dr. Gotten that it is an advantage to increase dehydration by limiting the patient's fluid intake following cranial trauma. In the past, I considered dehydration with dextrose or magnesium sulphate and direct removal of fluid from the brain by lumbar puncture sufficient to keep the intracranial pressure within the proper limits. This treatment has worked so satisfactorily that I wonder whether further dehydration by restricting fluid intake is absolutely necessary.

It would seem, as in the case presented, that dehydration carried to this extent may work considerable hardship on the patient. Dr. Gotten's patient suffered so much from thirst that he got out of bed and drank sufficient water to make him comfortable. As a result, he over-flooded his system with water and produced a marked increase in intracranial tension. This certainly seems to show that he had been thoroughly dehydrated. But are the results to be obtained by complete dehydration worth the discomfort the patient must suffer? Of course, I realize that fluid penned up in the subarachnoid spaces may possibly cause atrophy of the brain as can apparently be demonstrated later by encephalography. However, I do not think that it is proved that many of these patients did not have the brain atrophy prior to their injury. It seems to me that a certain amount of apparent cortical atrophy can be demonstrated by any encephalogram if a sufficiently vigorous effort is made to remove all the fluid from the cortical subarachnoid spaces.

Another factor to be considered in arriving at a conclusion concerning the value of intensive dehydration following cranial trauma is the fact that spinal fluid in the subarachnoid space may actually be of benefit rather than the reverse. Bagley (*Arch. Surg.* **17**:18, 1928, and **18**:1078, 1929) has shown recently that blood in the subarachnoid space sets up an irritative reaction. In another paper on the clinical treatment in cases of cranial trauma, the same author stated that he believed that the way in which blood in this locality is taken care of is by sufficient dilution with cerebrospinal fluid so that the cells can be resorbed with the fluid. It has occurred to me that the superdehydration suggested may so limit the amount of cerebrospinal fluid that blood in the subarachnoid spaces cannot be properly diluted and removed. This might well lead to the formation of adhesions and an irritative process. While this suggestion of Dr. Gotten is interesting, the results with methods working less hardship on the patient have been so satisfactory, that further evidence must be presented as to the necessity for limitation of fluids by mouth before I adopt it as a routine method of treatment following cranial trauma.

DR. TEMPLE FAY: Dr. Grant must be aware of the fact that dehydration by either magnesium sulphate or dextrose solution is impossible when fluid intake is not controlled. He should not be content with halfway measures in a condition that promotes intracranial pressure and that prolongs cerebral pressure merely because the patient may complain of thirst. It is not enough that the patient merely survives when sufficient spinal drainage and dehydration are accomplished to maintain respiration and other cerebral vital functions. If one is to return the patients in traumatic cases to economic activity, it is necessary to do more than save their lives; the duty of the physician today is to retain, if possible, the mechanism that will determine that person's health and mental activity, otherwise there can be little satisfaction in saving his life only to condemn him to years of mental deficiency under institutional care.

The objections that Dr. Grant raises regarding the discomfort of the patient are trivial indeed when compared to the long histories of post-traumatic sequelae secondary to prolonged manifestations of increased intracranial pressure so frequently seen on services that have no regard for the physiologic factors involved. Thirst requires no control other than proper sedatives and, if necessary, appropriate gargles. Dr. Grant asks whether the results obtained by complete dehydration are worth while to the patient. I would answer by stating that the five or ten days of discomfort are nothing as compared with the forlorn picture of mental inadequacy so often seen in cases that have been handled by halfway methods toward control of cerebral pressure.

Dr. Grant is apparently not familiar with encephalography to a sufficient degree or he would not ask the question regarding the cerebral atrophy prior to the injury. A study of the case history would indicate clearly that signs of cerebral atrophy were not present before the injury and that they are promptly induced by periods of intracranial pressure applied to the frontoparietal regions of the brain through the hydraulic mechanism during the first five days when the patient lies unconscious after a cerebral injury. If Dr. Grant will study the observations of the commission appointed by the American Roentgen Ray Society as to the technic of encephalography and cortical fluid pathways considered to be normal, he will find that there is no possibility, under the standardized conditions, of demonstrating "apparent cortical atrophy . . . if a sufficiently vigorous effort is made to remove all the fluid from the cortical subarachnoid spaces." Dr. Grant is probably familiar with the fact that Weed was the first to show reactions in the subarachnoid spaces in the presence of washed red blood cells and that Bagley later confirmed his work. It remains for Dr. Grant to prove that the cerebrospinal fluid absorbs the red blood cells present following subarachnoid hemorrhage.

Hematolysis is not a function of the cerebrospinal fluid or of the red blood cell per se, but is probably secondary to other cellular physiologic and hematolytic substances. Superdehydration, therefore, has nothing to do with the question of the red blood cell, hematolysis or the reestablishment of cerebrospinal fluid circulation; it is merely the best protection that one can offer the patient in a period of intense cerebral edema that may leave in its wake widespread cortical atrophy and changes in mentality that may be avoided by relief of intracranial pressure. It seems to me that the burden of proof lies with Dr. Grant to demonstrate that his series of patients with post-traumatic injuries to whom sufficient fluids were given to make them comfortable, are better off clinically, or encephalographically, at the end of a year than the cases in which dehydration has maintained a relief of the intracranial pressure from the earliest stage in the case. In my own experience, covering over 700 such cases, I have long abandoned the methods of empiric treatment for those of rational physiology, and I have been impressed with the fact that during the past two years those patients who have received consideration from every angle of pressure-producing mechanisms made a more rapid recovery, had less post-traumatic sequelae and became of economic value within a shorter period of time than the earlier series before strict control of fluid was maintained. Furthermore, the mortality in a consecutive series of cases of severe cerebral trauma (in which the patients survived the first three hours after admission) during the past six months is approaching 10 per cent, which is the best result that I have ever been able to obtain, and I know of no other series of similar cases with such a low mortality.

SPONTANEOUS SUBARACHNOID HEMORRHAGE WITH LOCALIZING SIGNS. DR. E. L. CLEMENS.

A white woman, aged 35, while sweeping the pavement before her home, fell, was picked up unconscious and brought immediately by neighbors to the accident ward of the Samaritan Hospital and was admitted to the medical ward at 5:45 p. m., Oct. 19, 1929.

The patient was in a fair state of nutrition and weighed about 90 pounds (40.8 Kg.). The temperature was 100.2 F.; the pulse rate, 100; the respirations, 25, and the blood pressure 95 systolic, 70 diastolic. General physical examination gave negative results save for a slight abrasion of the left side of the anterior part of the tongue. Neurologically, there were: rigidity of the neck, bilateral Kernig's sign, and apparent subjective pain in the region of the back of the neck and base of the skull. Mentally, the patient was confused and incapable of giving a history. On lumbar puncture, extremely bloody spinal fluid was obtained; on repeated puncturing, twice daily it became less and less colored.

On the day after admission, the patient recovered sufficiently to give a history. The family, personal and previous medical histories were not significant in regard

to the present condition. For about six months prior to admission, she had suffered from headaches and occasional vomiting on rising in the morning. She had noted some blurring of vision, but no diplopia. For some time she had had pain in the left eye, with a sensation of the left eyeball being larger than the right. She had had a sensation as though the pavement were moving under her feet. For about two months before admission, she had dizzy spells almost every day and some staggering in walking. She was irritable and had noted fine tremors of her hands. Other occasional symptoms were "hot flashes," dyspnea and palpitation on exertion, with marked fatigability and frequent precordial pains. A general physical examination gave negative results. There was a moderate Kernig's sign, bilateral, with some rigidity of the neck. The pupils were unequal, the left being smaller, but both reacting to light and in accommodation. The left palpebral fissure was narrower than the right, with a suggestion of enophthalmos. Convergence was defective. The left cornea was anesthetic. The tendon reflexes were present and equal in the upper limbs, but absent in the lower limbs with the exception of the left ankle jerk. The superficial reflexes were present and normal. Sensation to touch, pain, position and vibration was unimpaired.

Subjectively, the patient complained of pain in the left eye and of a feeling of enlargement of the left eyeball (as before coming to hospital), and of weakness physically and of stupid and heavy mentality.

The patient remained in the hospital until November 8. The signs related persisted, with some variation in the size of the left pupil and in the width of the left palpebral fissure and apparent enophthalmos. On November 7, it was found that the reflexes in the lower limbs had returned in the preceding twenty-four hours, the knee jerks being moderately active and equal; the left ankle jerk was slightly more active than the right. The ocular signs were present as before.

Subjectively, the patient said she felt well. Pain in the left eye had disappeared. She was discharged on the following day.

Laboratory tests, including spinal fluid and blood examinations, urinalysis and roentgenograms of the skull gave normal results.

The diagnosis was spontaneous subarachnoid hemorrhage with an aneurysm in the region of the left internal carotid artery.

DISCUSSION

DR. J. C. YASKIN: It is difficult to conceive that a woman, aged 35, without a history of hypertension, goiter or infectious disease would have an aneurysm that would account for the hemorrhage in the middle fossa. It would be much more desirable to find a simpler explanation for the subarachnoid hemorrhage in this case. The absence of the knee jerks after any hemorrhage can be readily explained by the shock to the nervous system. They are absent for a number of days and then usually reappear when the period of shock wears off.

CEREBELLAR DYSFUNCTION. DR. ALFRED GORDON.

A. S., aged 19, a clerk, up to the age of 16 had been perfectly well. He took part in games, and had intensive training in baseball and football. Three years before presentation, he noticed on several occasions that when walking on the street he would stumble without the presence of any obstacle in front of him. This condition gradually increased and he observed an awkwardness in going up and down stairs. Soon he noticed that he could not run and would sway on the street so that strangers would consider him intoxicated. At no time did he experience pain or present any other disturbance. The condition progressed so that the following picture was presented.

He could not stand still even with his eyes open. He had to stand with his feet wide apart. It was impossible for him to maintain equilibrium with open or closed eyes. The body swayed from side to side, and the swaying was transmitted even to the head. The same swaying was observed even when the patient was walking. He lifted his feet high off the floor and dropped them with all force.

At times the toes scraped the floor as in cases of foot-drop. The trunk was bent forward in walking because the patient was in constant fear of falling.

Inspection of the body showed uneven development of the musculature of the legs; the left was somewhat thinner than the right. The gluteal muscles were distinctly flattened on both sides in their upper and external portions. There was no impairment of motion; the patient could move his legs in every direction. The knee jerks were present, the left being somewhat more marked than the right. Ankle clonus was absent on both sides; the plantar reflex occurred in extension. The achilles reflex was obtained only by reenforcement. The cremasteric and abdominal reflexes were normal on both sides. The sensibility of the patient was intact according to all tests. The sphincters were not involved. The upper extremities were normal. The pupillary reflexes were intact. The eyegrounds showed no abnormalities. The patient's blood and spinal fluid were normal to all tests. Blood count and urine studies gave negative results.

The ataxia of gait and station and Romberg's sign directed attention to tabes dorsalis, but the preservation of the tendon reflexes, the presence of the extensor plantar reflex, the absence of other characteristic symptoms—subjective sensory disturbances, disturbance of the sphincters and ocular symptoms—all spoke against a true case of tabes. The presence of ataxia of station and gait, and of extensor plantar reflexes favored the diagnosis of combined sclerosis, but the absence of increased tendon reflexes, of spasticity and of ankle clonus militated against this diagnosis. In subacute degenerative changes of the sensory and motor tracts, spasticity sets in late, but the duration in this case was sufficiently long to produce rigidity which, on the other hand, is totally absent in subacute degeneration; there is rather a certain degree of hypotonia. Subacute degeneration of the type observed in cases of anemia could not be entertained, since the patient's blood picture was perfectly normal.

Finally, a cerebellar involvement was considered: The oscillation of the body, the forward inclination of the latter in walking or standing, the slight hypotonia of the lower extremities, the ataxia of the lower limbs, the asynergia of the trunk and lower limbs were all indications of a disturbance of cerebellar function. The lesion was probably localized in the midportion of the cerebellum, because there was no preponderance of the disorder on one special side; there was a complete asynergia, but not a hemiasynergia. It might be localized in the vermis or in the projection fibers of the superior cerebellar peduncles at their level of penetration into the pons to form the decussation and then reach the red nucleus, which could explain the presence of the extensor plantar reflex. This rubral tract forms a link in the mechanism coordinating the movements of locomotion. The nature of the lesion was difficult to determine. The gradual development of the ataxia precluded an infectious process of an acute onset; the patient did not recall being ill at any time preceding the present condition. He was an energetic youth, aged 16, indulging in dancing and sports even of a strenuous character. He never sustained a trauma during these activities. Perhaps by reason of strong physical efforts while playing football or baseball, some vascular disturbance occurred at any of the levels in the vicinity of the cerebellum, insufficient to produce an immediate dysfunction of his sensorimotor pathways but sufficient to produce a gradual disturbance of the tracts that play an important rôle in coordinating the movement of locomotion. Systematic exercises and antisyphilitic treatment improved the condition, but this improvement was extremely slight.

SPINAL CORD TUMOR. DR. FRANCIS C. GRANT.

The patient complained of aching pain in the left leg. In September, 1921, he fell on his back. In July, 1922, pain began in the left side of the back at the level of the crest of the ilium and radiated down the left leg into the groin. The pain was made worse by jarring. He was constipated. Roentgen examination showed a pathologic condition in the lumbosacral part of the spine. In October, 1923, loss of sensation in the calf of each leg and weakness in both knees was

noted. In March, 1924, there was marked loss of power in both legs, numbness of the left leg and loss of sexual power. There was dribbling from the bladder and constipation. A fusion operation on the lumbosacral part of the spine relieved the condition. In June, 1924, the pain subsided. Power returned to the extent that the patient could move his toes. From June, 1924, to February, 1929, he was pushed about in a chair most of the time, but he could walk with crutches. In February, 1929, there was recurrence of pain; it differed from the previous pain on the left side of the pelvis, in that it proceeded from the left groin and left buttock, down the left thigh. Weakness in the legs increased, and the lower extremities became more numb, especially on the left side. There was an increasing loss of urinary control.

Various diagnoses were made during this period, including alcoholic neuritis and lumbosacral sprain.

Neurologic examination revealed a sensory level at the level of the second lumbar dermatome for light touch, pain and temperature. Motor examination showed weakness and spasticity of the legs, particularly on the left, with a bilateral Babinski sign. There was bilateral increase of all reflexes in the lower extremities, with bilateral ankle and patellar clonus. On roentgen examination, the lumbar spine appeared normal. Spinal puncture revealed xanthrochromic spinal fluid and there was evidence from the Queckenstedt test of complete block.

A diagnosis was made of spinal cord tumor at the level of the second lumbar segment.

Operation revealed a tumor extending from the third lumbar segment down to the tip of the conus. The tumor lay entirely to the left of and posterior to the cord and the cauda equina. The tumor was cystic and seemed to lie between the dura and the arachnoid. It was completely removed.

The pathologic report was that the tumor was a meningioma.

After a stormy postoperative convalescence, the patient made a satisfactory recovery. When last seen he had recovered sphincter control and had regained power in the lower extremities enough to discard crutches and go about with only a cane.

The case is reported because of the puzzling picture and extremely slow progression of symptoms, probably due to the position of the tumor low down in an area where the cauda rather than the solid cord itself was involved.

Book Reviews

UEBER EINIGE NEUEVE DIAGNOSTISCHE UND THERAPEUTISCHE VERFAHREN IN DER NEUROLOGIE. By DR. EUGEN VON THURZÓ. Pp. 77. Berlin: S. Karger, 1929.

This pamphlet is a report of some of the neurologic work carried on at the University of Debreczen. There are six articles with the following headings: (1) the diagnostic importance of spastic reflexes: abduction reflex of the toes; (2) the use of spinal and suboccipital pneumography; (3) infection therapy and improvement of the spinal fluid in neurosyphilitic patients who have had a natural malarial infection; (4) pseudoneurotic forms of chronic epidemic encephalitis; (5) report of a case of epileptic palilogia with paligraphic symptoms; (6) the Sicard-Haguenau colloidal gold reaction.

(1) In this article, the importance of spastic reflexes as a sign of disturbance of the pyramidal tract is fully discussed. It is pointed out that each reflex has an optimum point of stimulation and that under varying conditions the reflex may be markedly altered. Benedek noted that small doses of scopolamine will incite a latent Babinski sign and in larger doses will produce a positive reflex even in healthy persons. Physostigmine produces the reverse action, abolishing a positive Babinski sign. These reactions are stated to be central, but the Babinski sign may also be influenced peripherally; if an Esmarch bandage is placed above a spastic limb, a Babinski reflex will be abolished.

Since Babinski first reported his observations on the plantar reflex in 1896, much speculation has existed as to the exact factors involved. In discussing the various types of spastic reflexes, the writer points out that none of them are constant and that even the Babinski reflex cannot be fully relied on. In attempting to find some differential point between a true and a spurious Babinski reflex, the fact has been observed that if the patient is in a prone position the Babinski sign remains constant if a mild stimulus is applied to the sole. In functional conditions, if the patient is placed in the prone position, the spurious Babinski sign disappears and one obtains a defense reaction.

It is Thurzó's opinion that in spastic conditions of the lower limbs, the flexors are mainly affected, while in the upper limbs the extensors show the greatest change. It is this observation which leads him to the conclusion that the Babinski reflex is the most important spastic reflex of the lower extremities, while the radial reflex is the most important in the upper limbs.

In addition to an extensive discussion of the various spastic reflexes, the writer adds another reflex which he terms the abduction reflex of the toes, which is obtained by stroking or striking the inner border of the tibia, especially in its lower two-thirds.

(2) Besides its value in the localization of tumors of the brain, pneumography is also a help in the diagnosis of internal hydrocephalus, meningeal adhesions and cystic formations. The method of air injection is the problem that the author attempted to solve. Three special questions presented themselves for investigation: 1. Which method gave the best picture? 2. Which method is the simplest from a technical standpoint? 3. Which is the safest procedure?

The report consists of the results of 124 pneumographic studies; 68 were suboccipital and 56 were spinal. The ventricular method, especially in tumors of the posterior fossa, is the safest. Dandy reported 3 deaths (1920-1925) in 187 pneumographies, the deaths occurring in the first 50 cases, during which period the technic was not standardized.

The writer believes that the suboccipital route is usually the route of choice. He describes his technic, which is essentially as in spinal pneumography. The

meningeal reaction, as indicated by the spinal fluid cell count, the colloidal reaction and the temperature curve are very much less in suboccipital than in lumbar pneumography. The author comes to the conclusion that the suboccipital route is by far superior to the lumbar method, and that only in suspected lesions of the posterior fossa or lesions of the occipital lobe should the ventricular method be employed.

(3) This article is a review of infection therapy in late syphilis of the central nervous system. The writer reports five cases of dementia paralytica and four cases of tabes, in which the patient, during the metasyphilitic period, passed through a natural malarial infection. Taking these cases as a basis for study, he concluded that the occurrence of malaria, either in the secondary stage or in the latent period, had no apparent effect on the development of tabes or dementia paralytica. It is interesting, however, that in both the tabetic patients and those with dementia paralytica who have had a natural malarial infection, the prognosis is very much better when they are placed on antisyphilitic treatment. It has also been observed that in this group of patients, the spinal fluid is more easily influenced by treatment.

(4) As has been noted by many observers, the epidemic of encephalitis has changed the general conception regarding many of the so-called functional conditions. In this article the author attempts to show that many of the functional disturbances which have heretofore been classified as neurasthenia or hysteria are now to be considered organic in character. Among some of the interesting phenomena that he describes under this heading are the oculogyric phenomena, palilalia, anxiety states, etc.

Thurzó also reports an interesting case of epileptic palilogia with paligraphic symptoms.

(5) The final contribution is a discussion of the Sicard-Haguenau gold reaction, in which the writer believes that they have a more staple solution to work with, that the reaction may be read immediately and, finally, that the technic is markedly simplified since the numerous dilutions that are required by the Lange colloidal gold reaction are unnecessary.

PSYCHIATRIE DU MÉDECIN PRACTICIEN. By M. DIDE and P. GUIRAUD. Tenth edition. Price, 45 francs. Pp. 466. Paris: Masson & Cie.

Dide and Guiraud are both excellent practitioners in psychiatry and have written a book serviceable to the practitioner, cleancut, lucid and without being too schematic. After a fairly full chapter on the "unconscious psychisms," affectivity, activity and intelligence, the authors deal with: arrested development; the psychopathic constitutions; the essentially instincto-affective syndromes, manic-depressive, progressive-delusional and hebephrenia; the instinctive-affective syndromes with open cause; confusion and dream-states; the syndromes of chronic mental enfeeblement (organic), arterial, focal, senile, arteriosclerotic, syphilitic, general paralytic, encephalitic, alcoholic, post-traumatic, epileptic, from cerebral diseases and "post-confusional." This is followed by a chapter on the examination and therapeutic disposal and medicolegal problems.

The book has the clearness of French thought, with a liberal eclecticism, including psychoanalytic and bergsonian concepts and those of von Monakow and Mourgue, without surrendering the basic tenets of French clinical nosography and the easy grouping of the data. Well chosen pictures of patients are rendered in eight plates.

To enter more closely into the spirit of the book would lead one too far. It claims to start on an anatomoclinical basis, much less by hypothesis than by dogmatic conviction. It quotes G. Dumas as saying that there is nothing more organic than emotion, as if that would prove their case. Then it proceeds to give an outline of freudian terminology, after a frank identification of psychic or mental with the "social order of causes," and the emphasis on mental contagion similar to the epidemics in the Middle Ages. It sensitizes the reader for the

"exterior causes" (auto-intoxications, colloidoclasia, exo-intoxications, physical agents and traumatisms, neoplasms, infections, with a promise of surprises perhaps, especially from protozoa and filtrable viruses) and causes resulting from deficient vitality of the nerve tissue (poor germ plasm, abiotrophy and hereditary transmission of anomalies including intermittent psychosis, emotivity and obsessions — excessive emotional sensitivity or prolonged reactions, disequilibrium of the encephalic vegetative centers, etc.). The nosography of the authors is that of Morel, Magnan and Kraepelin. The mental phenomena are the direct product of the nerve centers and the changes in the latter are the necessary and sufficient conditions of morbid mentation (pensée morbide), which "has not its essential cause in previous mental stages." With this declaration of allegiance to anatomy and physiology, the authors plunge into the "psychisme inconscient," so as not to have any quarrel with the recent swing toward psychoanalysis in France, but on a very special acceptance of "ergo-genetic" and "teleformative" conceptions, a conservative and a reproductive instinct, etc.

From this one can see readily that, while the book is written for the practitioner, it is by no means colorless from a general point of view, but on the ground of a conviction without discussion of other points of view.

DEGENERATION AND REGENERATION OF THE NERVOUS SYSTEM. By S. RAMÓN Y CAJAL, M.D., F.R.S., Director of the Instituto Cajal, Madrid. Translated and edited by Raoul M. May, Ph.D., D.es Sc., Paris. Pp. 769. New York: Oxford University Press, 1928.

In 1913, there appeared a Spanish edition of this work but practically all the copies were distributed to physicians of the Argentine Republic, who, following the award of the Nobel prize to the author, persuaded this eminent Spanish scientist to publish a book at their expense. This work, however, has been lost sight of, partly because it was in Spanish and partly because of the incidence of the World War. The book has now been translated by Dr. Raoul M. May and has become available to English speaking neurologists.

Originally, the work consisted of a revision of all the investigations previously published and a special study of many doubtful or uncertain points, the book constituting an extensive monograph, original in large part. The 1927 translation has been completely revised by the author, who has supplemented it with additional notes which follow each chapter and which are in effect a discussion of the literature of the particular subject under consideration. Cajal states that he would have made it more extensive and detailed had he not feared to add unduly to an already extensive work which represented eight years of patient study.

The subject matter is divided into two volumes. The first considers traumatic degeneration and regeneration of the nerves; the second, degeneration and regeneration of the nerve centers. The first volume is divided into sixteen chapters and begins with the discussion and history of the degeneration and regeneration of nerves. These views are of course well known and need not be referred to in this review.

The second volume is divided into four parts: The first deals with degeneration and regeneration of sensory and sympathetic ganglia; the second, degeneration and regeneration of the spinal cord and nerve roots; the third, degenerative phenomena consequent on cerebellar traumatisms, and the fourth, traumatic degenerative processes of the cerebral cortex.

In the history of every specialty there appears in each generation an outstanding figure whose achievements are epoch-making. This was true of Hughlings Jackson. Cajal, in his own particular field, easily ranks with the English neurologist, for there is no one who has approached him in the brilliance of his efforts and the excellence of his results. In the last few years an increasing number of neurologists from all over the world, particularly from America, have journeyed to Spain to learn from this master. It was a happy thought, therefore, which led Sir Charles Sherrington, an equally brilliant figure in the realm of

neurophysiology, to cause this book to become available in the English language. These two volumes should be in the hands of every neurologist.

THE AUTONOMIC NERVOUS SYSTEM. By ALBERT KUNTZ, Ph.D., M.D. Price, $7. Pp. 576. Philadelphia: Lea & Febiger, 1929.

In the last decade more attention has perhaps been paid to the autonomic nervous system than to any other branch of neurology and, as would necessarily follow, more books on the subject have appeared than perhaps in the previous four or five decades. There has been considerable advance in knowledge of the anatomy and physiology of the autonomic system, but less progress has been made in the pathology of this subject. In the clinical field, while a great deal has been published, little real progress has been made, although from a casual reading of the literature one would infer that the clinical types described by some endocrinologists have a sound anatomic, physiologic and pathologic basis.

This book, although written by a professor of anatomy, discusses the autonomic nervous system not only from the anatomic standpoint, but also from its developmental and general physiologic relationship to the cerebrospinal nervous system, and gives as well as it can the more important pathologic and clinical data bearing on the functional relationship of this division of the nervous system in disease.

The book contains about 500 pages divided into twenty chapters which are treated under the following headings: (1) Morphology and Distribution of the Autonomic Nervous System; (2) The Autonomic Ganglion Cells; (3) Central Autonomic Centers and Conduction Pathways; (4) General Physiology of the Autonomic Nervous System; (5) Development of the Autonomic Nervous System; (6) Innervation of the Heart; (7) Innervation of the Blood Vessels; (8) Innervation of the Respiratory System; (9) Innervation of the Digestive Tube; (10) Innervation of the Biliary System; (11) Innervation of Glands; (12) Innervation of the Urinary Organs; (13) Innervation of the Sex Organs; (14) Involuntary Innervation of the Eye; (15) Autonomic Innervation of Skeletal Muscle; (16) Pathology of the Autonomic Nervous System; (17) Visceral Sensitivity and Referred Pain; (18) Vagotonia and Sympatheticotonia; (19) The Autonomic Nervous System in Disease; (20) Surgery of the Autonomic Nervous System.

The reviewer knows of no book in the English language which presents the subject so adequately. It is up to date even in the discussion of the surgical intervention of the autonomic nervous system. The illustrations are uniformly excellent. A valuable addition is a bibliography which is divided according to chapters under discussion.

LE TRAITEMENT DE LA PARALYSIE GÉNÉRALE ET DU TABES PAR LA MALARIA PROVOQUÉE. By A. FRIBOURG-BLANC. Price, 15 francs. Pp. 120. Paris: Masson & Cie.

The material in this book would hardly justify the form it takes if published in America. The material on which it is based consists of thirty-three cases of paralytic dementia and three cases of tabes in which the patients were treated by the malarial method. The results obtained are similar to those reported in the general literature. The author has no new ideas to enunciate, but attempts rather to give a running review of the literature.

Possibly this last statement should be modified by saying that he suggests a method by which the malarial blood may retain its potency for a matter of two or three days. The method is as follows: 10 cc. of pure sterile gelatin is liquefied in a water bath at 30 C. and is mixed with 2 cc. of malarial blood. The mixture is allowed to solidify, either by being left for fifteen to thirty minutes at room temperature or for a few minutes in an icebox. For injection, it is allowed to liquefy at 28 C., thoroughly shaken and then injected.

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