Herrick (C. L.)

STATE ASYLUM FOR INSANE, COLUMBUS, OHIO.

A. B. RICHARDSON, *Supt.*

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REPORT UPON THE

Pathology of a Case of General Paralysis

BY

C. L. HERRICK,

Professor of Biology in Denison University.

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Note of Transmissal.*

Dr. A. B. Richardson, Superintendent of the State Hospital for the Insane, Columbus, Ohio,

Dear Sir: In pursuance of your suggestion, a microscopical examination has been made of the specimens placed in my hands with results which are detailed beyond. While the history of the case, as you informed me, warranted us in expecting only the usual lesions of general paralysis incident upon alcoholism it was thought worth while to not simply make such examination as should detect the expected lesions but to make the study extended enough to afford a somewhat complete picture of the diseased brain as a whole. Circumstances have prevented the completion of the task in the way at first contemplated. The employment of the slow and tedious fibre-stain methods was rendered impossible by pressure of work immediately upon reception of the specimen. The present paper is devoted almost exclusively to the cells of the various portions of the brain. It is thought that what we now need is the collection of minute, detailed data presenting the facies of a pathological state in its entirety and we have accordingly presented illustrations of the various regions even where involving some repetition and, in order to make the account more generally useful, some historical and physiological suggestions are added. Unexpectedly the distribution of the degenerated structures has thrown incidental light upon an important morphological problem, reenforcing generalizations derived from the comparative realm.

Hoping that the paper, imperfect as it is, may serve its purpose in preparing the way for more systematic and useful work in the same direction.

I am yours respectfully,

C. L. Herrick.

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HISTORY.

Supplied by the Medical Corps of the Columbus Hospital for the Insane.

J—— W. S—— was admitted to this institution June 20th, 1891. He was a native of Ohio, forty years of age, a merchant and a man of good education. He had been addicted to the use of intoxicants for several years but was more temperate within the two or three previous to his admission. There was no history of specific disease and he had been a man of good character in his community and of active business habits. The mental symptoms began about six months previous to admission. When admitted he had delusions of grandeur and was becoming somewhat demented. He imagined he was quite wealthy and was anxious to run for the office of Governor or of President of the United States. His pupils were unequal, there was incoordination in gait and he had the characteristic defect in speech that marks the paretic. There was no history of insanity or nervous disease in his family and the cause assigned was financial trouble, of which he had had considerable. His intemperance was also in my opinion a cause. He continued an inmate of the institution until his death, which occurred Jan. 8th, 1893.

He became rapidly more demented and the paresis increased. His digestion was good during nearly all of the time and only failed him within the last month or two before his death. There was no evidence of focal lesion in a local paralysis and the disease pursued the characteristic history of general paralysis. I regret that the history is so meager, but while we could add illustrations of his delusions they would be of no value in a Pathological Bulletin. The previous history is difficult to secure, but there was nothing very characteristic in his life as far as we can discover. He was a man of active business habits and at one time was worth considerable property, but he lost it all, his reverses, in part at least, being due to his dissipation.

It is further stated that the first symptoms of motor en-

feeblement were a slight speech disturbance, in the nature of a blurring of the articulation, and awkwarkness in the gait that denoted slight incoordination. These facts are significant inasmuch as it will be shown that the most seriously affected cortical areas are those in Broca's region and in adjacent parts, while still more serious lesions are located in the coordinating centers of the thalamus nnd mesencephalon. No sensory aura nor other disturbances, nor any visual, auditory, or olfactory hallucinations were detected. As it was not expected that a careful pathological investigation would be possible, no dynometric or aesthometric tests were made nor were systematic registrations of temperature or urine analyses attempted. *

NATURE OF THE DISEASE.

Mendel says of the etiology of progressive paralysis: "From the results there can remain no doubt that the essential thing is interstitial inflamation. The cell-multiplication, development of spider cells, the increased excretion of intercellular substance, these leave no doubt in this connection, and at the acme of the disease, according to my observation, the evidences of this inflamation are never absent."

"In acute paralysis the nucleary proliferation and the de-

*The following extract from a letter from Dr. Richardson received too late to be inserted in the proper place will be of interest:

"I have just learned a few facts in the history of J. S., whose case you are investigating, which may be of interest in case it is not too late to include them in the record. He was a man of more than usual business activity and conducted a mercantile business in a small town. He was always good hearted and indulgent and inclined for years to the use of intoxicants in moderate amount when with his friends. Through his indulgence to his friends his business became complicated during the years 1888 and 1889, and he was compelled to make an assignment about the close of the latter year. In the spring of 1890 he had an attack of La Grippe and after that never seemed as well as before, and was somewhat despondent. He grew worse that Fall and his disease began to change to a state of exaltation. He became talkative and excitable and enthusiastic over business, until finally, during the winter of 1890 and 1891, his actions

velopment of spider cells is not great while they are replaced by the phenomena of hyperæmia of the vessels or stasis through the collection of blood corpuscles in the adventiva. In the very aged the preceding processes of irritation are only here and there to be noticed, or not at all; the general atrophy extends to include spider cells and granules." "The change in the cell bodies is, so far as our methods show, a secondary process, which in many cases can only be made out by microscopic observation, in a very limited extent, while in other cases, as above shown, producing a very remarkable alteration."

"Changes in the membranes are likewise, in the rule, secondary. . . . The pia as well as the dura, in most cases, is implicated through the disturbances in the circulation in the brain itself which react upon it, as well as through the progressive diseased condition of the vessels, From all these considerations I conclude that progressive paralysis is a diffuse interstitial cortical encephalitis resulting in brain atrophy.

"The beginning of the process is a transmigration of leucocytes and it is accompanied by an increase of the connective elements. The compression of the capillaries and of the small arteries through the accumulations in the adventitious sheath disturbs the regularity of the nutrition of the nervous elements,

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became so unreasonable that he was adjudged insane and sent to the asylum. He remained there until about May of 1891, during which time he became more quiet and was finally taken home on a visit. In June of '91 while at home he had a sudden epileptiform seizure with hemiplegia on the right side, which, though not complete, lasted for about three weeks. His speech was much worse after this than before, and in August of the same year he had an attack of speechlessness lasting for a day or two, during which time he was entirely unable to talk. Soon after this he was returned to the asylum where he remained until his death and did not afterwards have any sudden attack nor any symptons of local paralysis. The history during this time we have heretofore narrated. There is no history of insanity in the family. During the four years previous to his death he did not drink any. In 1888 his only child became lost and the excitement and worry in the search for him was a severe shock to him and his friends were afraid at that time it would cause some mental trouble."

producing degeneration of the latter and finally leads to atrophy and shriveling."

Mendel suggests that the great diversity in the symptomology of general paralysis may be due to the existence of varieties with an interstitial and a parenchymatic origin.

The present case shows sufficiently well that the intensity of the degenerative process varies greatly in various regions. This is sufficient to account for great diversity in the facies of the disease. It would seem that there could be no limit to the range of variation where the slightest change in the seat of disturbance might interrupt a different set of channels of communication. Historically the opinions of the cause of the malady have varied between wide extremes. Meschede, in 1865, considered the alteration in the ganglion cells of primary importance and considered the disease a parenchymatous inflamation. Mangan, in 1866, described it as an interstitial encephalitis, while Rokitansky and, finally, Luys referred the trouble to the neuroglia; the latter called it diffuse interstitial sclerosis of the neuroglia.

It is not unnatural that vaso-motor changes should be appealed to as fundamentally important, as has been done by Obersteiner, Thompson and others, in fact it is difficult to see how the undoubted connection between mental strain on the one hand, and vaso-motor disturbance of alcoholism on the other, with the degenerations of general paralysis is to be explained without admitting, via functional hyperæmia and temporary vaso-moter incordination, the graver and more permanent changes which should make way for morbid nutritive changes in the cells. If metabolism is altered by altered blood pressure it would be natural that other cellular elements besides the cortical cells should be modified. It would seem more rational to suppose that all the cellular structures in the region affected should feel the effects of vascular disturbance and react, each after its kind, while reciprocally modifying each other and thus the course of the disease. Instead then of drawing a distinction between interstitial and parenchymatous phases we may restrict ourselves to such practical classification in accordance

with predisposing cause and the sequence of symptoms as shall most nearly correspond with the requirements of treatment. The prevailing unwillingness to recognize the great influence of alcoholism may account for the failure adequately to construe the influence of slight vascular disturbances if sufficiently long continued.

It will be gathered from our own observations that the facts seem hardly to bear out the statements of Hirt: "This view, according to which the atrophy is the primary process, is in all probability correct, though it is still combatted by many authorities (Mendel), who look upon the death of the nerve fibres as the secondary, upon the increase of the connective tissue, the thickening of the vessel walls and the appearance of spider cells as the primary process ('encephalitis interstitialis')." In the present case, however, the development of the spider cells, upon which Bevan Lewis, Mendel and others lay so much weight, is a very insignificant factor. The most important one seeming to be the involvement of the blood-vascular system and the greatest cellular modifications are seen in the motor co-ordinating centres of the axial lobe. Our case supports the view of Zeigler[1] that the phemomena of general paralysis are not uniformly inflamatory "but not rarely simply degenerative processes in the meninges and the cortex." He says: "Es erscheint danach die gestörte Ernährung und die Degeneration der Ganglienzellen und Nervenfasern als die wesentliche, und die entzündliche Infiltration und die Zunahme der fibrillären Stützsubstanz sind zwar für die anatomische Beurtheilung des Processes, nicht aber für die Krankheitssymptome von wesentlicher Bedeutung."

Mierzejewski and Voisin regard these spider cells and fibrous aggregates, which are not noticeable in some cases, as coagula of fibrin derived from homogeneous masses which may contain nuclei. It may be that diverse structures have been combined under this name. The "spider cells" which were

[1]Lehrbuch der Allgemeinen Pathologische Anatomie und Pathogenese, 4th Edit. 1885, p. 591.

sparingly present in this case may be of the character of a diffuse stroma. Ziegler says that the spider cells are frequently not increased in number but simply more conspicuous because of the atrophy of other parts of the cortex. The fact referred to by Lewis that representativeness is a function early lost in the course of general paralysis may have its anatomical explanation in the fact that slight sporadic changes would interfere with associational tracts (association being intimately connected with representation) before becoming sufficiently pronounced to interfere with the direct presentational processes of perception, etc. In fact, according to Tuczek, there is a marked primary atrophy of the fine medullated nerve fibres, particularly in the outer layers of the cortex, in the tangential "associational" fibres which run parallel to the surface. Friedmann describes four varieties of atrophy of the white matter and others have discovered secondary degeneration in the dorsal columns of the the cord. Our methods were selected with reference to the cells and, whether for this reason or because no genuine degeneration of the fibres had set in, only sparing and unimportant degenerations of white matter were encountered.

In determining the cause and nature of the circulatory changes preceding cerebral degeneration a thorough knowledge of the nature and reactions of the blood and lymph which fill the delicate cerebral organ as fluid fills a sponge is necessary. The brain is almost as really an erectile tissue as the pancreas and we already know enough to be convinced that slight changes in pressure may become the occasion for the rapid proliferation of the corpuscles and that the presence of small quantities of certain substances may greatly change the balance of the fluids in the capillaries, lymphatics and tissues. R. Heidenhain has conducted very elaborate investigations upon the lymph[1] and finds that there are lymphagogues or substances which increase the formation of the lymph. Various extracts of invertebrate muscles, egg albumen, peptone, etc., are

[1]Versuche und Fragen zur Lehreivon der Lymphbilding. *Pflügers Archiv f. d. ges. Physiologie XLIX, p. 209.*

among the lymphagogues.[1] It is shown by experiment that in this case, as when sugar is injected into the veins, the capillaries exert a genuine secretory influence. In the latter case the blood is extracted from the tissues by the dehydrating action of the sugar. It seems probable that alcohol would operate in a similar way. There are many things which suggest that a sort of protoplasm poisoning is an early incident to the development of the circulatory changes preceding paralysis.

One must remember that even in the normal state the variations in metabolism find other expressions than in the form and reaction of the cells. Carazzoni[2] has shown that the ratio of solids in the cerebro-spinal fluids is greater in the morning than in the evening in the percentage of 1.35 to 100 and is more alkaline in the morning also. Substances injected into the abdominal cavity make their way into this fluid after half an hour or more which is, however, more slowly than their entrance into the blood or even the aqueous humor, as would be expected.

The theory that prevails to some extent in this country that the moderate use of alchohol serves to substitute to some extent for proteids in the diet has apparantly been exploded by Minra's researches.[3] A slight increase of albumen is regarded as evidence that alcohol acts like chloroform as a protoplasm poisoning which may be expected as one of the incidents of early stages of the pathological condition now under consideration. (Cf. Heymans. Sur l'action toxique et antiseptique du chloroform etc., *Ann. Soc. med. Gand. 1892.*)

EXTERNAL CHANGES.

Macroscopically there was less alteration than might have been legitimately expected. Plate A. illustrates the appearance of the brain after the removal of the membranes. The membranes were slightly adherent but not closely enough to produce decortication upon their removal. The characteristic

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[1] *Centralblatt f. Phys. 816.*

[2] *Centralblatt f. Phys. VI. 14.*

[3] Ueber die Bedeutung des Alkohols als Eweisssparer in der Ernährung des gesunden Menschen. *Zeitsch. f. Klin. Med. XX, 112.*

opalescence was noticed on the surface of the fresh brain and some hemorrhagic patches along the sulci. The cerebellum was superficially injected but section shows nothing abnormal in its deeper portions. The membranes themselves were thickened but there was no evidence of acute inflamation. The cortex itself appeared nearly normal but the sulci were more conspicuous than would be expected from the age of the subject. The atrophy was especially marked about the insula, fissure of Rolando and the tip of the temporal lobe and not noticeable in the occipital. A wax model made by the method of impregnation of the right hemisphere with Japan wax brought out the atrophy more clearly as the shrinkage incident to the method was more marked in the regions mentioned. The surface of the brain was minutely pitted throughout its extent. The figure sufficiently represents the configuration of the right hemisphere. The weight of the entire brain was about 58 oz., and there seemed to be an abnormal amount of ventricular fluid.

THE MEMBRANES

Circumstances have thus far prevented giving special attention to the meninges but, while somewhat thickened and adherent and while the surface of the brain when removed had the peculiar opalescent character so often described, the most noticeable changes are connected with the vessels. In the sinuses lying in the sulci great accumulation of leucocytes has taken place and the leucocytes fill the considerable space about the vessels and may be readily seen entering the brain and collecting at various levels below the surface. These changes are simply analogous to those which are taking place in the vessels within the cortex and, like the latter, point to an inflammatory condition.

In those regions in which the morbid changes are most marked the blood vessels are also greatly affected. The first characteristic of change is the increased number of white corpuscles and their transmigration into the surrounding tissue. There can be no doubt that normally this transmigration is continually taking place. The large pyramidal ganglion cells almost invari-

ably have a certain number about their bases or active pole. They present a great variety of stages between the full, plump nuclei which have recently reached the cell and the dark, shriveled, exhausted cells which seem to have yielded their nourishment to the nerve cell. Whether as cause or effect, the condition of general paralysis is accompanied by an abnormal collection of leucocytes. These gather in great numbers in the space between the intima and adventiva of the vascular walls and thus narrow the lumen until a partial stasis of the red corpuscles results. Masses of yellow pigment accumulate in the adventitious sheath among the the leucocytes, sometimes in considerable quantities. These hæmatoid granules have been frequently noticed. This yellow pigment which collects in the adventitious sheaths of the blood vessels and elsewhere is doubtless derived from the red corpuscles, which are colorless in these cases. We are reminded of Mühlman's studies on the pigmentary metamorphosis of red corpuscles in the Arachnoid.[1] The yellow grains are found in the walls of the arachnoid vessels. They are not soluble in chlorform but, unlike fat, partially dissolve in sulphuric and nitric acids. Tests with sulphide of ammonia and potassium ferrocyanide demonstrate iron. The author supposes that the pigment formation is due to a state of irritation caused by pressure. They accumulate in the arachnoid because there the texture is so slight as to submit them to pressure. It might be supposed therefore, that the granules found so generally in the clogged capillaries of paralysis are due to a similar irritative cause.

THE CORTEX.

We may begin our examination by glancing at sections from the tip of the temporal lobe (middle convolution). The outer neuroglia layer differs little from that of the normal brain. A careful study shows, however, numerous so-called spider cells or scavengers, which here appear as multipolar bodies staining faintly and lying closely involved in the mesh-work of the neu-

[1]Zur Pigmentmetamorphose der rothen Blutkörperchen. Beobachtungen von der Arachnoides cerebralis. *Virchow's Arch.* (12) *VI, 1. p. 160.*

roglia (Fig. 9, Plate B). Opinion differs greatly as to the nature of these bodies, but from the sections before us one might conclude that they are essentially amœboid and their form depends upon that of the interstices in which they may happen to lie.

In the next succeding layer, that of small pyramids, the changes are not such as to attract the eye but we soon notice that a great number of the small pyramids have undergone more or less pigmentary degeneration. While their processes and form have altered little if any, small areas of degeneration are present in the protoplasm. Sometimes these areas are apparently but an extension of the normal pigmentation near the base and adjacent to the nucleus, but it quite as often happens that the area forms a rather sharply limited cyst in other parts of the cell. The pigmented areas refuse the stain and are recognized by their own brownish yellow color. Fig. 5, Plate B. is a cell from this region. In some cases the degenerated area causes a bulbous protrusion of the cell, yet the nucleus is not at all affected. In the third layer or region of medium pyramids the conditions are not much different but before one reaches the layer of large pyramids it appears that there has been a dispersion of granules which fill the whole field. It is the region of the ramification of small vessels. The larger radial vessels at this point give evidence of important morbid changes; the walls at first seem thickened but we soon see that the inner membrane or intima seems normal, but the outer or adventitious layer is gorged with leucocytes so that it occupies more space than the lumen. One frequent result is that the cavity is more or less occluded and the red corpuscles hence undergo degeneration. Their coloring matter collects among the white corpuscles forming hæmatoid masses. It seems improbable that this leaching is due to the reagents—in fact, this is a well-recognized pathological phenomenon. The smaller vessels are usually empty, as though by the cutting off of the source of supply. Fig. 8, Plate D, illustrates such a vessel as above described. See also Plate E. It will be remembered that Flemming[1] has shown that in the

[1]Ueber Theilung und Kernformen bei Leukocyten, etc. *Arch. für mikr. Anatom.* XXXVII. p 249.

extravascular leucocytes in salamander multiplication is by mitosis or nucleary cell-division. Löwit attempted to distinguish between erythroblastic and leucoblastic nuclei and claimed that mitosis occurs only in the erythroblasts, which are devoid of amœboid movements. Flemming, however, finds that mitosis is common in the amœboid leucoblasts and thus agrees with Müller, Bezzozero and Newmann. The author thinks it probable that fragmentating cells (i. e. amitotic elements) are in a state of decline and are incapable of reproduction. This may be compared with Frenzel's view that the cells reproducing by fragmentation are substituting and not constructive elements, as in the case of those cells in the mucous membrane which are to degenerate in the formation the mucous secretion. The nature of leucocyte proliferation in the brain should have careful study with modern methods.

In the layer of large pyramids the degenerative process is more conspicuous by reason of the larger size of the elements but no more general or relatively extensive. In the radial fibres we encounter here and there a phenomenon of which we find no mention elsewhere. Long deeply staining nuclei, resembling in color the leucocyte or "granule" nuclei, but many times as long as wide lie in the course of the fibre and seem to occupy the sheath. This is probably different from the varicose condition of the apex process sometimes encountered, Figs. 4, 5, Plate B. These bodies at times very closely resemble the nuclei of the intima of the vessels and must be carefully distinguished from these nuclei when greatly elongated in the finest capillaries. The color and appearance and the small diameter as well as the position of these bodies serve to prevent error. We incline to believe them characteristie of the degenerative condition as stated more in detail below.

The innermost cortical layer, that containing multipolar cells, offers no noteworthy peculiarity.

A typical motor region is found in No. 2, from the precentral or ascending frontal convolution. Here the nests of very large pyramids with long processes are eminently characteristic. Fig. 13 of Plate B. gives a good idea of these cells

which are generally, though by no means universally, degenerate. The apical processes do not seem to be degenerate in any case and the atrophy of the protoplasm and fatty pigmentary degeneration at the base are the most malign symptoms. The smaller pyramidal cells of the ectal part of the cortex are generally intact. The usual alteration in the vessels occurs to a moderate extent. We do not encounter the enormous development of spider cells which Dr. Bevan Lewis considers characteristic of the disease.

In the region of Broca (Plate E, Fig. 1, No. 6) we are dealing with a motor area and encounter chiefly fatty or pigmentary degeneration of the cells. This change involves not only the deep pyramids but all the nerve cells to a greater or less extent. Figs. 2, 3, 7 and 12, Plate B., illustrate the varying phases of this degeneration. In Fig. 12 the cells are slightly altered while in Fig. 3. the degeneration appears in various parts of the cell causing a certain amount of deformation. Sometimes it is one of the basal processes while in others the apical process is occupied by the yellowish granular material. The nucleus is scarcely ever implicated. No changes of importance can be detected in the neuroglia or nutritive elements. Rarely we detect a degenerative fiber containing the serpentine bodies described above. Usually where one of a "nest" of motor pyramids is altered all of the cells are involved.

There seems to be no increase in the number of leucocytes about the injured pyramids—if anything, they are fewer than about the normal elements. There can be no doubt that these so-called "granules" are identical with those which under pathological conditions (congestion) pass through the vascular walls in such incredible numbers. It is a question of some importance to decide whether the proliferation of leucocytes take place within the vessels or at large within the brain substance, or whether the multiplication goes on in the usual sources and the accumulation in the perivascular spaces is due to a kind of retardation incident to impaired vitality of the brain. Our own observations thus far point to amitotic proliferation in the adventitions sheaths.

In none of these sections do we find any extensive muliplication of what Bevan Lewis calls the lymph-connective element. The pale corpuscles with flask-shaped faintly staining bodies are no more numerous than in the healthy brain. Occasionally the cell-body is shrunken, as a result of which the processes, which are originally very numerous, became more conspicuous. Golgi staining and our hæmatoxylin process seem to show that these cells are always supplied with an enormous system of processes whose terminal brushes often collect about blood vessels and other cells.

We venture to quote somewhat at length from Bevan Lewis respecting the lymph-connective elements or spider cells, (scavenger cells.)

"The cells which are usually called 'glia cells,' or what we have, in our anatomical section, alluded to as the 'flask-shaped elements' of the neuroglia, undergo a wondrous transformation, the real significance of which does not appear to have been hitherto appreciated. . . . These elements are small flask-shaped cells with a comparatively large nucleus at their greater extremity, which latter stains faintly with aniline-black, whilst the protoplasm of the cell itself remains unstained, and so delicate as to be recognized with difficulty in healthy states. Each has a connection by a delicate process with a neighboring blood vessel, and in frozen sections fresh examined, exhibits several branches so fragile and so excessively delicate, as to be seen only after a keen search, as they remain wholly unstained by reagents. In the morbid change to which we now allude, these flask-shaped cells enlarge very considerably into great amœboid masses of protoplasm, often exhibiting subdivision of the nucleus; and, what is of great import, their protoplasm *now stains deeply* with aniline, though not so intensely as their nuclei. From this extraordinary cell of protean form radiate on all sides numerous branching fibrils, forming an intricate and delicate network around it as a centre, all of which branches even to their most delicate subdivisions are readily stained by the same reagent. These cells have been termed Deiter's cells; they are all characterized by the presence of a

vascular process; but well prepared specimens show not one, but often several, such processes distinguished by their greater diameter, their deep staining, and their termination in a nucleated mass of protoplasm upon the walls of a blood vessel."

The protoplasm of these cells is said to stain in abnormal states but not in normal, because in the former case there is an unnaturally increased vitality. They are said to spread throughout the neuroglia framework and multiply by nucleary subdivision and segmentation of the cell mass. The last stage in the development of these bodies is one of fibrillation in which the cell is exhausted by ramifying into innumerable fibrillary processes. As elsewhere stated, we are inclined to believe that these are truly nervous elements which become more accessible to stain as they shrivel. Proper methods demonstate richly branching processes even during health.

In the region of the hippocampus the evidences of morbid activity are fewer than in cortical motor areas, yet there are regions where profound alterations have taken place. There are many cases where the pigment degeneration is discoverable but the process has not gone far enough to implicate a large part of the protoplasm. The degeneration manifests itself here in the alteration of the fibres. These are large and distinct and even in our somewhat imperfect specimens the apical processes are seen to be shriveled and altered. One evidence of the change is seen in the remarkable vermiform or rod-like granules which lie upon or within the process or in the more distant part of the fibres. These are well-shown on Plate D Fig. 6 and Fig. 7 These vary from short ovoid to rod-shaped or long worm-like. It has not been possible to find a description of these bodies but we venture to suggest that they are the elongated nuclei of leucocytes or scavengers which have penetrated the sheath in pursuit of the decomposing protoplasm of the fibre. The reasons for this asumption are, 1. that the least modified of these bodies closely resemble the phagocytes, 2. no other source for these bodies is suggested, 3. analogy suggests that some means of disposing of the obviously decomposing processes, where as large as in this case, must be found.

Sections have been made from the most caudal part of the occipital lobe and show that, as usual, the purely sensory regions are not implicated. The cortex is almost wholly unaltered and, whereas the sections in the motor regions stained slowly and imperfectly with ordinary reagents, here the stain is well differentiated and uniformly operative.

THE BASAL REGIONS.

The histological changes of general paralysis are typically, if not exclusively, those of the cortex, and particularly of its cells. The references to the degenerative effects in the great ganglia of the axial portion of the brain are, so far as my observation has gone, very scanty. Mendel says: "Aside from the described changes, which occur chiefly in the cortex and adjacent parts of the white substance, which may, however, occur, though to much less extent, in the large ganglia (an atrophic condition is here developed only after paralysis of long duration and extensive laming), there may be observed the greatest variety of focal lesions in paralytics."

The peduncles have been found to be degenerated in a few cases (Huguenin), in one case the gray degeneration of the dorsal fasciculi could be traced from thalamus to the cauda equina and in the motor peduncles and pyramids, extended to the oculomotor region.

A section through the very cephalic portion of the thalamus shows that its small cells are but slightly affected while the somewhat larger multipolar cells scattered in the striatum at the same level are thoroughly implicated. Passing caudad, the thalamus retains the same general character though increasing to form a large quandrangular area (*Fig. 1 a, Plate D.*). Around the margins, near the peduncular fibres there are small multipolar cells which are greatly altered. These cells are like those figured on Plate D, figure 5, which are from *x* in *Fig. 1* of the same plate. They are larger than the cells of the thalamus proper.

For a study of the striatum we may select a portion of a section corresponding to "B" of the Pitres-Nothnagel's series

(Hirt's Diseases of the Brain, p. 197). Ectad of the internal capsule, which evinces no alteration that can be detected by the means here employed, is the head of the caudatum, consisting of a stroma of densely nucleated matter and sporadic fibre bundles. There is almost absolutely no alteration in the substance of either caudatum or lenticulare at this level. We may add that the present tendency to attribute important psychical functions to the striatum has as little anatomical foundation as psychological significance. By far the largest part of the striata is composed of sporadic bundles from the capsule. The vessels of the striatum are nearly normal. The lesion is decidedly cortical. A series of sections through the peduncular region is of special interest as showing that in this segment the degeneration is limited to the motor projection system. The cells of the tectum and niduli of the cephalic quadrigemina, as well as of the ruber, are scarcely modified at all. The nidulus of the oculo-motor is quite unaffected. There are slight changes in the pulvinar and other niduli of the thalamus, but when we turn to the vicinity of the motor peduncle fibres we encounter most conspicuous evidence of degeneration. The large and complicated nidulus niger, including the most remarkable cells of the mesencephalon is almost completely altered. These cells, which hug the ental margin of the peduncles and form the boundary between tegmentum and crusta are not only of enormous size, but by reason of the great extent of their processes they stand out among the elements of the brain. In a series of papers[1] the author has endeavored to follow the homologies of the nidulus throughout the veretebrate phylum. It has proven possible to trace the relation between the pecular cells, which are not easily mistaken for any other cells in the brain, from fishes to mammals. The development of the nidulus niger or Soemmering's nidulus stands in close ratio with that of the cerebellum. In fishes the ventral peduncular fibres, which can hardly be other than the

[1] Contributions to the Morphology of the Brain of Bony Fishes, Journ. Comp. Neurology, Vol. II. Notes upon the Histology of the Central Nervous System of Vertebrates. *Festschrift zum siebenzigsten Geburtstags Leuckart's; Anat. Anzeiger*, VII, 13, 14.

motor tracts, come into intimate association with cells which in form and relations seem to be homologous with the niger cells (i. e., cells in hypoaria). The cerebellar tract also enters into relation with this nidulus. Following this clue we trace the same relation in all the higher groups. It seems safe to affirm that the site of motor association with the cerebellum is in this cell-clustre. It need not surprise us that in a disease which is due primarily to a disturbance of the cortex and notably the motor-cortex, the projection centres of the centrifugal tracts should be especially injured. It seems to amount to an incidental confirmation of our anatomical observation and physiological theory that the nidulus niger is the only region of the mesencephalon in which pronounced indications of degeneration are observed. The nidulus extends from the exit of the third nerve to the point where the peduncles enter the striatum and throughout its entire extent nearly every cell is more or less completely degenerate. In some cases the whole cell body is reduced to a vague patch of yellow granules, while in others bands or stripes of unaltered protoplasm remain. Frequently the incipient stages of decay are seen in a deep pigmentation near the nucleus or one process only is disorganized. The characteristic features of these degenerate cells are best gathered from the figures.

Plate D, Fig. 3, illustrates a niger cell far cephalad near *y* in *Fig. 1*. It well shows the two axis-cylinders of a switch cell. *Fig. 2*, is a portion of the same field with cells in various stages of degeneration. One cell especially illustrates the rare condition where a bulbous swelling occurs upon a process. In some cases the nucleus itself has suffered partial destruction. *Fig. 4*, contains two unaltered cells giving a good idea of the various processes though the finer ramifications of the protoplasmic processes are not bought out. *Figs. 3* and *4*, of *Plate C*, illustrate the changes seen in the same nidulus at the level of the third nidulus.

Figs. 1 are *2* and portions of transverse sections at the level of the pulvinar and third nidulus respectively, for orienta-

tion. Both are figures of actual sections from which *Figs. 3* and *4* were drawn.

THE CEREBELLUM.

The cerebellum, although somewhat isolated from the real centre of morbid activity, might be expected to be involved with other portions of the brain. The vessels of the meninges are only slightly modified and the intrinsic capillaries not at all. The only way in which the extensive changes in the basal ganglia of the fore-brain could react indirectly on the cerebellar structures would seem to be through an atrophy of disuse. While the ganglia in the motor tracts bear unmistakable evidence of extreme degeneration it would seem quite improbable that an extensive atrophy should have had time to develop itself. It will be remembered that (in our view) the axis cylinders of the Purkinje cells passes directly into the restiformia, while the peripheral or protoplasmic processes afford opportunity for association by contiguity with the fibres of the mid-peduncles of the cerebellum which on their part may connect with the cells of the basal ganglia.

Since, then, the relations are very indirect, we should not be surprised to find the cerebellum normal in the absence of irritating causes in the organ itself. The cerebellum can hardly be subject to as rapid alterations in blood pressure as the cerebrum and contains within itself a large stock of reserve nutrient material. Careful examination reveals only a few cases where the cells of Purkinje have some traces of the fatty degeneration seen elsewhere (*Fig. 5, Plate C.*) Most of the lobules are normal, but occasionally there is one of the folia in which there is extensive atrophy of the cells of Purkinje. *Fig. 4, Plate E,* illustrates such an instance. In the sections wherein ordinarily a score or more of cells should stand, only one or two isolated cells remain. There is no notable degeneration in the other structures, but the space which should contain these bodies is empty or contains shriveled remnants. In these cases it might appear that the change was the result of early stages of the disease.

In the unaltered Purkinje's the structure is well preserved

(*Fig. 5, Plate E,*) and the adjacent elements are intact. Although this is perhaps not the place to discuss morphological questions we may call attention to the fact that the radial elements with fusiform cellular dilatations (*Fig. 3 a*) are apparently remnants of the spongioblast system, as may be gathered by a comparison with lower vertebrates.

THE MEDULLA.

It is unfortunate for our purpose that the medulla of the specimen was ruined during removal so that the important question as to the subordinate centres along the motor columns and particularly the condition of the vaso-motor centres remain unexamined.

THE CORD.

For a similar reason the cervical cord is not in a condition to report upon in detail. A number of sections from the cervical region show that the ventral cornua of the gray matter is very largely involved. The large ganglion cells are in some cases intact, but generally are more or less affected by the fatty degeneration. In some cases the entire cell is reduced to a mere sac filled with granules of a honey yellow color. These stages are illustrated in *Fig. 2, Plate E.*

No serious affection of the meninges or blood vessel is obvious from the specimen. If there is any secondary degeneration the only suggestion offered by our sections is a suffused condition of the crossed pyramidal tract of the lateral column. In the same region there is some gorgement of vessels and nucleary proliferation.

DESCRIPTION OF FIGURES.

PLATE A.

Lateral view of the right side of the brain drawn from the fresh specimen corrected by reference to the model subsequently prepared.

PLATE B.

Fig. 1. Pyramidal cortical cell and portion of a capillary vessel from frontal lobe (Plate E, Fig. 1, No. 4. The cell is but slighly altered. The vessel is in the first stage of degeneration. The granules are multiplying and escaping into the perivascular space.

Fig. 2. A group of cells from the layer of deep pyramids in Broca's region. An enormous cyst-like mass of pigmentary degeneration in one of the motor cells.

Fig. 3. Other cases of degenerated cells from Broca's region.

Fig. 4. A case of varicose alteration of the apical process.

Fig. 5. Similar instance from temporal lobe (No. 1).

Fig. 6. Incipient degeneration in a cell of the temporal lobe.

Fig. 7. Striking instance of pigmentary degeneration in Broca's region.

Fig. 8. Incipient degeneration of cell from frontal lobe.

Fig. 9. So-called scavenger cells from temporal lobe. The tangential fibres form the upper margin of the section.

Fig. 10. Deep pyramid of frontal lobe.

Fig. 11. Superficial pyramid of the same region.

Fig. 12. Three slightly altered large pyramids of Broca's region. The sole indication of the lesion is an increase in the pigment.

Fig. 13. Large Pyramids from Precentral convolution. (No. 2.)

PLATE C.

Fig. 1. Part of a transection through the cephalic corpora quadrigemina and pulvinar.

Fig. 2. Part of a similar section through the roots of the third nerve.

Figs. 3, 4. Degenerating cells of the nidulus niger from the sections above indicated.

Fig 5. Slightly altered cells of Purkinje from the cerebellar area shown in *Fig. 6.*

Fig. 6. Apparently normal cerebellar cortex. Compare with *Fig. 4,* Plate E.

PLATE D.

Fig. 1. Transection of left hemisphere through the thalamus and hippocamp.

Fig. 2. Forward extension of the niger beneath the thalamus at *y*, *Fig. 1.*

Fig. 3. Uninjured cells.

Fig. 4. Similar normal cells from the niger farther caudad.

Fig. 5. Smaller cells from dorsal region of the peduncles (*x*, *Fig. 1.*)

Figs. 6, 7. Cells from hippocamp showing certain amount of pigmentary degeneration and vermiform nuclei apparently attacking the fibres.

Fig. 8. A typical case of vascular degeneration. Nuclei accumulating in the adventiva and stasis of red corpuscles.

PLATE E.

Fig. 1. Diagram of front of left hemisphere to locate regions referred to in text. The shaded areas are portions actually sectioned.

Fig. 2. Cells from ventral cornu of the cord.

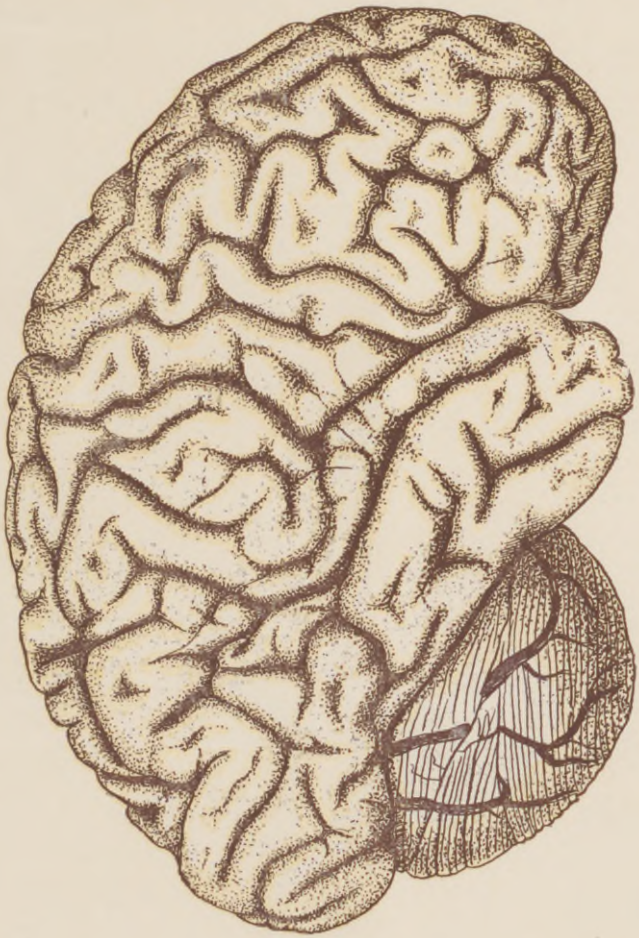
Fig. 3. Normal cells of Purkinje. *a*, spongioblast nuclei.

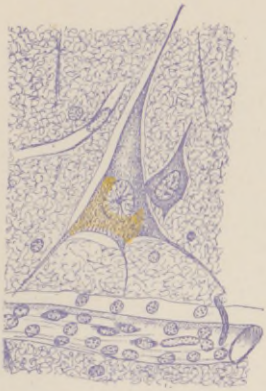
Fig. 4. Portion of cerebellar cortex where the cells have degenerated.

Fig. 5. Degenerate cells from temporal lobe.

Fig. 6. Blood vessel where the intima has separated from the adventiva. The latter filled with corpuscles.

Fig. 7. Diseased cortex cells.





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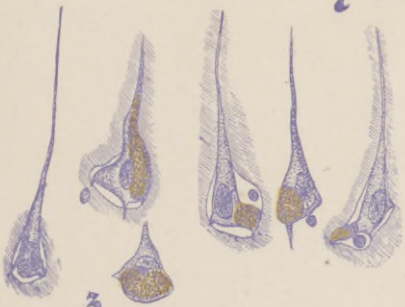

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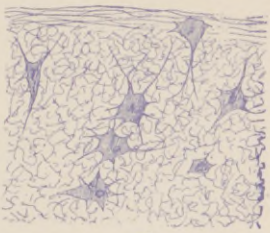

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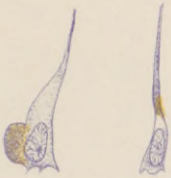

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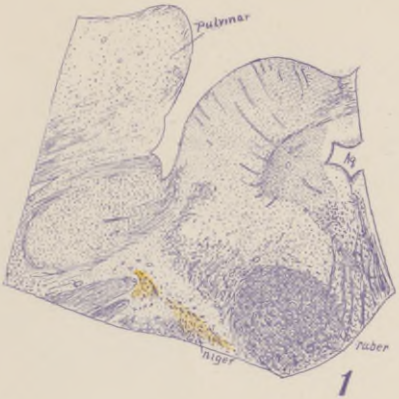

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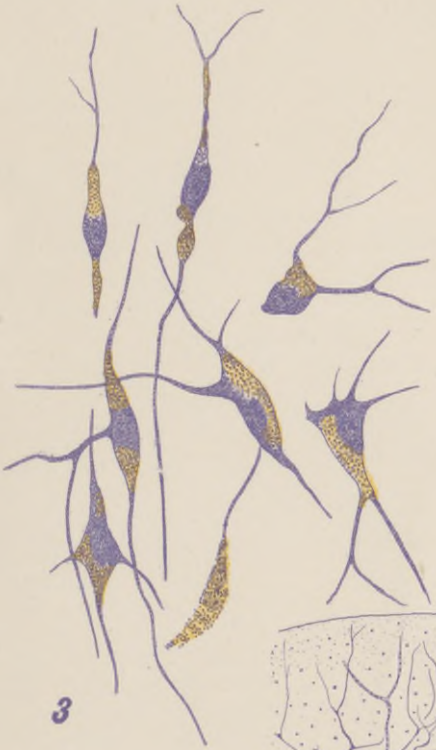

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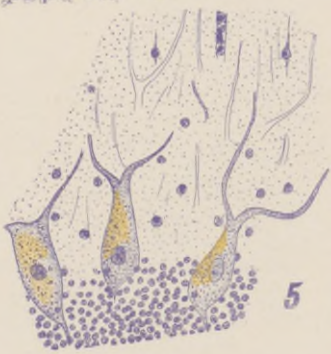

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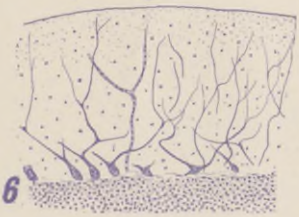

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callosum
fornix
a
thalamus.
x
y
hippocamp
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c.
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b
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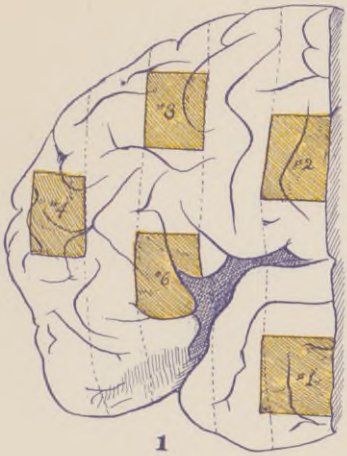
A.



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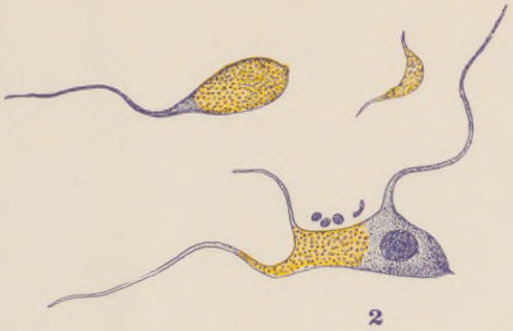
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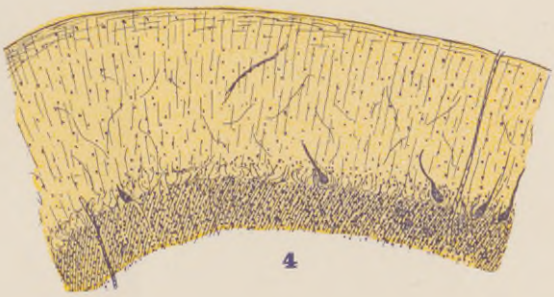
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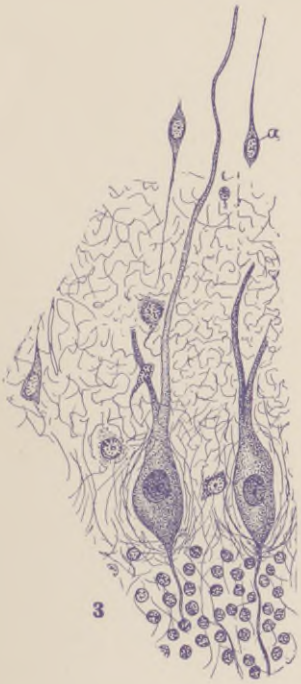


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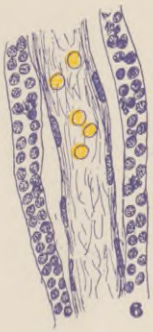
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