ACUTE INTERNAL HYDROCEPHALUS. A CLINICAL AND PATHOLOGICAL STUDY.[1]

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PLATES XVII AND XVIII.

Clinical History.—W. S., male, white, 33 years old, was admitted to the Philadelphia Hospital on April 15, 1899 complaining of great headache, general weakness and abdominal pain. His family and personal histories were unimportant, possibly except that four years before he had had typhoid fever. On April 13 he stopped work, complaining of violent headache and pain in the back of the neck. The pain continued throughout the night, and the following day he became delirious and was sent to the hospital.

Examination showed a muscular man with flushed face. He lay in bed with the head retracted and the legs strongly flexed upon the abdomen. The temperature was 102° F., pulse 82, and respiration 24. He was stuporous but could be roused by sharp questioning. He would answer a few questions properly and would then become incoherent. Physical examination revealed no abdominal or thoracic disease. There were no palsies. The head was in extreme extension and could not be flexed. Lateral movement of the head was also impossible on account of muscular rigidity. Attempts at passive movement caused severe pain. There was no muscular rigidity elsewhere. Sensation, so far as could be determined, was normal. He was too weak to stand. The tongue was brown, the lips cracked and the abdomen distended. The plantar jerks and knee jerks were absent even with reinforcement. The bladder and rectum were under control. The urine contained a trace of albumin, a few hyaline casts, and had a specific gravity of 1027. The red blood-corpuscles numbered 4,850,000, the white corpuscles 9000, and the hæmoglobin reached 75%. Widal's test was made repeatedly with

[1] Read at the meeting of the Philadelphia Neurological Society, December, 1899.

negative results. Various culture media inoculated with blood remained sterile. The tentative diagnosis was acute meningitis.

On April 22 Kernig's sign was present. Herpes of the lips and nose and a bluish mottling of the skin appeared. The mental state varied greatly. Sometimes the patient was restless and indeed quite violently delirious, at others stuporous, and again he would be almost normal, lying quiet, talking coherently and complaining only of headache and pain in the back of the neck. The pupils were dilated and slight lateral nystagmus was present. Slight deafness appeared. The plantar reflexes returned but the knee jerks remained absent. The eye grounds, examined by Dr. C. A. Oliver, were normal. On May 10 he was stone deaf. For several days he hiccoughed violently. The temperature which ever since his admission had been fluctuating between 101° and 103.4° F. now gradually dropped to normal and he improved greatly in all ways. Pain disappeared and the mind became clear and active. The knee jerks returned. Slight rigidity of the muscles of the neck persisted. His mental state was peculiar. He was perfectly coherent, could talk well and understood all that was said to him, but he was too well content with himself and his surroundings, he had no realization of his being sick and, though really too weak to stand, maintained that he was very well and would be out of doors in a day or two. He was trifling and jocose and, as his sister said, altogether unlike his usual self. He reminded one of a man in the beginning stage of paretic dementia. He gained greatly physically for a month and then the fever rose to 103° and the picture became the same as it was on admission. After a few days the fever again fell, and he again improved but for only a short time. On June 6 the temperature suddenly rose, the old symptoms returned, subsultus was added, nystagmus became marked and on June 9 he died.

Necropsy.—This was made the next day. The calvarium was normal. The dura was tense and elastic. The convolutions were broad, pale and flattened and the sulci were almost obliterated, appearing as lines beneath the pia. About the base over the cerebellum the pia was a little milky. The infundibulum was distended and pressed upon the optic nerves but not enough to distort them. On opening the ventricles a large amount of clear fluid escaped. All were dilated and the aqueduct of Sylvius was much wider than normal. The ependyma was boggy and separated easily from the underlying brain tissue. In the lateral ventricles it was roughened and at the tip of either inferior horn a band of white tissue stretched from the outer to the inner wall. The lining of

the fourth ventricle was somewhat boggy. The choroid plexus of the third ventricle was injected and œdematous, that of the lateral ventricles was rolled up into an oval mass the size of a hazel nut and adhered to the walls. The spinal cord was very wet and in the lumbar region were several small hernia-like protrusions of the white matter into the pia. The dura was a little thickened in the cervical region. The heart and lungs were normal. The right pleura was adherent. The spleen was cirrhotic and the kidneys showed a subacute parenchymatous nephritis.

Histological Examination.—On microscopic examination the choroid plexus of the lateral ventricles showed a small tumor-like mass which on cross-section consisted of a capsule surrounding meshes of blood-vessels. There were a large number of hyaloid bodies (Plate XVII, Fig. 2, A, E, B), often twenty in one field, staining deeply with hæmatoxylin but taking only a faint stain with Lugol's solution. There was marked infiltration of small round cells in the capsule (Plate XVII, Fig. 2, C) and foci of them scattered through the sections. Their nuclei stained deeply and were about half the size of those of the ependymal cells. The vessels were distended with red corpuscles. The choroid plexus of the third ventricle showed similar but slighter changes; that of the fourth was normal.

The ependyma of the third ventricle showed microscopically the same tendency to separate from the underlying tissue as was noted in the gross specimen. A marked ependymal proliferation was present in the lateral ventricles (Plate XVII, Fig. 1). The nuclei of the cells varied in size, shape, and staining properties. The ventricular surface was covered by an amorphous granular layer several times thicker than the ependyma and containing nuclei scattered through it. A golden yellow pigment was present in the ependyma of all the ventricles. The vessels beneath the ependyma to a depth of one-half centimetre were actively congested and were surrounded by round cells (Plate XVII, Fig. 1, D). These cells not only occupied the perivascular spaces but also extended some distance into the surrounding tissue. The greater number of them were small round cells with nuclei slightly smaller than the nuclei of glia cells and surrounded by a narrow ring of cell substance. Though the nuclei of the glia cells within the area of infiltration were swollen and possibly proliferating we feel confident that the larger number of these cells did not arise from the glia. Scattered among the smaller nuclei larger, faintly-staining nuclei resembling very closely those of the endothelial cells of the capillaries were occasionally seen. They were probably endothelial in origin but of this there is no direct evidence. No

polynucleated cells were present in the infiltration. Some of the large pale nuclei were irregular in outline but did not resemble the nuclei of polynuclear leucocytes in any other respect.

The neurogliar cells also showed proliferative changes. The nuclei of those immediately beneath the ependyma were at least twice the normal size and were surrounded by distinct cell bodies from which the processes radiated (spider cells). Further from the surface the nuclei became smaller, the protoplasm less, and the radiating processes finer until at a depth of about three quarters of a centimetre the tissue became normal. The area of change in the glia cells corresponded closely to that of congestion and round-cell infiltration.

The nature of the lesions suggested that they might have been caused by the reaction of the tissues to some toxic or irritative constituent of the ventricular fluid.

The cortical and spinal ganglion cells stained by Nissl's and Weigert's methods and by carmine showed nothing abnormal. The cranial nerves were stained by the Marchi method and carmine. The fourth and sixth showed a few black granules. The eighth pair were very much degenerated; the others normal. The spinal nerve roots showed only a few black granules in the lumbar posterior roots. The white matter of the cord showed no degeneration by the Marchi, Weigert, and carmine stains.

To sum up: A man is suddenly seized with fever, bradycardia, constipation, rigidity of the muscles of the neck, headache, stupor and delirium. After three weeks, during which the intensity of the symptoms varies greatly, he improves very much physically but shows many of the mental symptoms of paretic dementia. A week later fever and the meningeal symptoms return, last about a week, again intermit for four days only to return again and end in death. Post-mortem examination reveals only a moderate internal hydrocephalus, proliferation of the ependyma and ependymal glia, perivascular round-cell infiltration in the sub-ependymal tissues, and sclerotic and degenerative changes in the choroid plexus. What caused the lesions?

Internal hydrocephalus from mechanical causes is quite common, but idiopathic internal hydrocephalus is, or seems to be, rare and has attracted the attention of clinicians and pathologists only in recent years. Before the discovery of the tubercle bacillus it was quite

common to call cases of hydrocephalus tubercular even though tubercles were not present. Barthez and Rilliet[2] separated these from those manifestly tubercular, but the credit of having established idiopathic internal hydrocephalus as a distinct clinical and pathological entity belongs to Quincke.[3] There are two varieties, one acute, the other chronic but often having acute exacerbations.

The acute variety is most frequent in children. In adults it usually follows injury to the head, the infectious fevers, especially typhoid and pneumonia, and acute or chronic alcoholic poisoning. The onset is sudden with headache, delirium, photophobia, vomiting and retraction of the head—symptoms resembling the irritative stage of septic or tubercular meningitis from which affections it may be impossible to differentiate it. Fever, however, may be absent or not so high as in septic meningitis and may either quickly disappear or vacillate with the other symptoms. The headache and muscular rigidity are not so intense nor so constant and the delirium, instead of persisting, alternates with periods of normal consciousness. The intermittency of the symptoms and the early increase of intracranial pressure, shown by choked disc, paralytic mydriasis, and, in early life, enlargement of the head, are characteristic. Examination of the cerebrospinal fluid is important. In tubercular meningitis the bacillus is often, although not always, present in the fluid withdrawn by lumbar puncture, and in septic meningitis inoculations of culture media give characteristic growths, and the fluid is either turbid or distinctly purulent and contains endothelial cells, leucocytes, red corpuscles, and pus microorganisms. In idiopathic hydrocephalus the fluid is under higher tension than normal varying from 150 to 700 mm. (water manometer). It differs but slightly in its constituents from the normal, is clear and transparent, with a specific gravity of 1008 and contains albumin and sugar (?) in small quantities.

The chronic variety often follows the subsidence of the acute symptoms or, in children, may appear only with the increase in intra-

[2] Barthez and Rilliet. Traité clinique et pratique des maladies des enfants. Paris, 1861.

[3] Quincke, Volkmann's *Samml. klin. Vortr.*, 1893, n. F., No. 67, and *Deutsche Zeitschr. f. Nervenheilk.*, 1896, ix, p. 149.

cranial pressure caused by the union of the bones of the skull. A receding optic neuritis may be the only clinical manifestation. In other cases the symptoms may for a long time be vague and inconstant so that mere neurasthenia may be suspected. A large group present the symptoms of brain tumor. Optic neuritis is almost constant and transient or permanent bitemporal hemianopsia caused by varying pressure of the distended infundibulum on the optic chiasm may be present. Headache, vomiting, vertigo and local or general convulsions, and cranial nerve palsies are frequent. Localizing symptoms are almost never present except in the rare cases in which the hydrocephalus is confined almost entirely to the fourth ventricle and causes symptoms of cerebellar disease. The long course of the disease often ending favorably or seeming to do so only to recur, and the good effect of lumbar puncture point to the true nature of the disease, especially if the spinal fluid is found to be under high pressure at the time of puncture.

Our case in the early stages was diagnosed as a meningitis of the convexity and of the cord. Typhoid and spotted fever were both thought of but the continuous absence of the Widal reaction, the absence of spots, the non-enlargement of the spleen, and the clinical course excluded the former and the absence of eruption, of leucocytosis, of spinal-root symptoms, and the negative result of bacteriological investigation made the latter impossible. The peculiar variability of the symptoms, the afebrile intermissions, and the curious mental state made the diagnosis doubtful but it was retained as the best working hypothesis.

There are many points of clinical interest in the case. Kernig's sign which was at one time thought to be pathognomonic of meningitis was present during almost the whole course of the disease. The absence and subsequent return of the knee jerk and plantar reflex is also interesting. Absence of the knee jerk is not very uncommon in brain tumor but its return after an absence of three weeks without any lesion in the cord to explain it must be very rare. The absence could not have been caused by œdema of the cord because at autopsy that was very great though the reflex had returned several weeks before. We can only note the phenomenon, not explain it.

Central deafness with degeneration of both eighth nerves is not mentioned in any other case. It probably was caused by an unusual distribution of the pressure from the ventricles on the nerves at their exits. The optic nerves are most frequently affected and after them the sixth and seventh. In our case the optic nerves were normal save for a small focus of old degeneration near the centre.

The mental state may resemble paretic dementia. Indeed in Prince's[4] cases so close was the resemblance that that diagnosis was held for a time. Jocosity, a total neglect of the relative importance of things, and mild delusions of grandeur were the predominant factors in the mental attitude of our patient.

The pathological findings are interesting because in only a few of the cases heretofore reported have changes in the ependyma and subependymal tissues been described. Quincke[5] explains the absence of inflammatory changes in his cases by the subsidence of the primary hyperæmia subsequent to the occurrence of the hydrocephalus. The membranes of the brain may according to him be the seat of an acute serous inflammation like that which occurs in the pleura and the synovial linings of joints. In other cases the acute onset of the symptoms and their rapid disappearance make it seem probable to him that changes similar to those of angio-neurotic œdema may occur. In our case there were both recent and old changes in the choroid plexus. The proliferation of the interstitial tissue, the dilatation of the vessels, the round-cell infiltration, and the ependymal changes all pointed to an acute inflammation. The encapsulation of the plexus, the adhesions to the ventricular wall, and the bands across the tips of the ventricles indicated an old process. The large number of hyaloid bodies in the plexus of so young a man is evidence of degenerative change in the vessels leading to their obliteration and subsequent change into hyaloid material. All the steps in the process from hyaline degeneration of the media to complete obliteration, fragmentation, and calcification of the fragments are fairly well shown in the sections. That these bodies may have another and very

[4] Prince. *Journal of Nervous and Mental Disease*, 1897, xxiv, p. 473.
[5] Op. cit.

different origin, namely from proliferated endothelial cells blocking up the lymph spaces and undergoing hyaline degeneration, there is abundant evidence in the same sections, but the changes in the blood-vessels are the more important in connection with the other evidences of a chronic and acute inflammation in the plexus.

The changes in the ependyma correspond to those in the choroid plexus. The thickened ependymal membrane and the adhesions and roughened surfaces of the lateral ventricles were of long standing. The acute inflammatory changes were widespread. Some authorities[6] hold that since the ependyma consists only of a layer of cells without blood-vessels it cannot be the seat of acute inflammation, but the distended network of capillaries immediately beneath the ependymal layer, the perivascular round-cell infiltration, the amorphous exudate on the surface and the hypertrophic changes in the glia must be considered to prove the inflammatory nature of the process. The fact that these changes were confined almost wholly to the ependyma and extended only a few millimetres beneath, gives the impression that they were the results of a local reaction of the cerebral tissues to some toxic action of the ventricular fluid rather than an acute primary inflammation leading to a serous exudation. To determine if possible which of these two conditions was present and to discover the effect of toxines and acids on the ependymal membranes we made the following experiments:

Sterilized urine, glycerine extract of the adrenals (P. D. & Co.), tuberculin, hydrochloric and carbolic acid were injected into the ventricles of kittens by means of a large hypodermic syringe.

The three adrenal kittens died within twenty-four hours. A slight increase of the nuclei surrounding the vessels immediately beneath the ependyma and dilatation of the capillaries of the brain substance for a short distance were the only changes noted. In one kitten there was intense dilatation of the vessels of the choroid plexus with hæmorrhages into its meshes.

Three kittens injected with urine were killed after three, six, and ten days. The changes were the same in all, differing only in intensity

[6] Boenninghaus, Die Meningitis serosa acuta. Eine kritische Studie. Wiesbaden, 1897.

(Plate XVIII, Fig. 4). They consisted of a proliferation of the ependyma with an amorphous exudate upon the surface, swelling of the glia fibres which stained deeply, and a perivascular small round-cell infiltration, the whole resembling very much the condition found in the case here reported. In one specimen the layer of cells covering the choroid plexus failed to stain and looked very much like a fatty reticulum. In this specimen also a layer of round nuclei occupied the space immediately beneath the ependyma. Tuberculin gave similar but less marked results.

As dilute hydrochloric and carbolic acids produced the same effect we will describe the former only. The animals were killed at the end of a week. There was no excess of ventricular fluid. The ependyma looked normal and was not boggy or roughened. On microscopic examination (Plate XVIII, Fig. 3) the ependymal layer was intact, but the cells stained very faintly, the nuclei could hardly be seen, and the cell bodies were granular and their margins indistinct. Where this condition was most intense a granular layer covered the ependyma, evidently the debris of degenerated cells. Immediately beneath the ependyma and most marked on the under and inner surfaces of the ventricles a layer of round nucleated cells was present. They were four and five deep in certain areas and in others suddenly disappeared. They had small, round nuclei which stained deeply and were of the same size and character as those surrounding the deeper vessels. No polynuclear cells were found among them. Their probable origin was the network of capillary vessels beneath the ependyma. Columns of small nuclei surrounding the smaller vessels extended from this layer deeper into the brain substance. The glia network within the zone of capillary dilatation and perivascular infiltration was close meshed and had the appearance of a fibrillar structure running parallel to the ependymal surface. The columnar cells of the choroid villi were granular. The superficial cells were mere shadows and often the outer border was absent making the surface of the plexus look frayed. The nuclei were either absent or only outlined and failed to stain. The condition appeared to be caused by a proliferation of the cells; the outer layer becoming degenerated and finally breaking down into an amorphous mass resting upon the surface of the other cells.

We conclude from these experiments that the non-purulent inflammation of the ependyma produced by acid irritants differs only in degree from the reactive changes following the injection of toxines into the ventricles. Changes in the ependyma without changes in

the subjacent tissue probably do not occur. The inflammatory condition experimentally produced, by whatever agent, did not cause any increase in the ventricular fluid and the only evidence of an exudate from the ependyma was the amorphous material which probably was made up of degenerated cells.

The microscopic sections in the toxine experiments resembled the sections from the case reported and to that extent confirm the opinion that the changes found were secondary to a toxic condition of the ventricular fluid. The clinical history offers other evidence in support of this view. For example the mental condition of the patient, corresponding to that seen in other auto-intoxications, would be best explained by a such an hypothesis. The exacerbations which Quincke compares in their sudden development and variability to angio-neurotic œdema appear to us to be rather the manifestations of varying intensity of auto-intoxication, such as occurs in uræmia and syphilis. Finally the hydrocephalus alone by its mere mechanical action, if sufficient fluid is present, can cause many symptoms.

DESCRIPTION OF PLATES XVII AND XVIII.

PLATE XVII.

FIG. 1. Section of the floor of the lateral ventricle. Stained with hæmatoxylin-eosin. The marked irregularity of the floor is shown—caused partly by the folding of the ependyma (*C*), partly by the amorphous exudate on the surface (*B*), and partly by the hypertrophy of the sub-ependymal glia (*A*). The zone of perivascular small, round-cell infiltration (*D*) is seen extending some distance beneath the ventricular surface.

FIG. 2. Section of the choroid plexus of the lateral ventricle. *C*, the capsule very rich in nuclei. Hyaloid bodies in different stages are seen at *A*, where the hyaline change with calcification is beginning in a vessel, and at *B* and *E* has advanced to irregular hyaloid forms. The vessels of the plexus contain many leucocytes which are very rich in a granular pigment (*D*).

PLATE XVIII.

FIG. 3. Showing the reactive changes in the ependyma and choroid plexus of a cat after the injection of hydrochloric acid (5%) into the ventricle. *A*. Granular degeneration of ependymal cells. *B*. Layer of round nuclei immediately beneath the ependyma. *C*. Perivascular infiltration of round cells extending deeper into the brain substance.

FIG. 4. Ventricular surface of the brain of a cat after injection of sterile urine. *A*. Granular degeneration of ependyma cells. *B*. Sub-ependymal layer of round nucleated cells. *C*. A vessel surrounded by an accumulation of round cells. The blood-vessels deeper in the tissue are not affected.

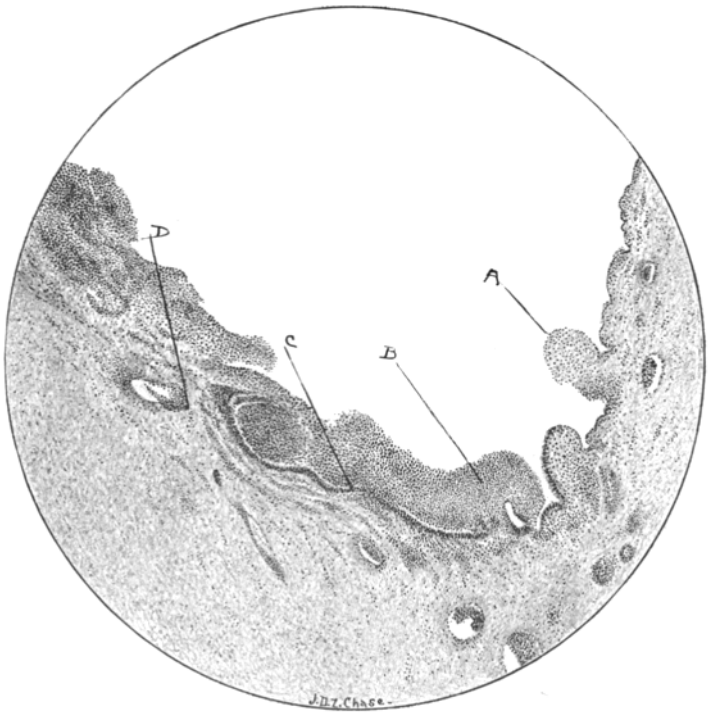

FIG. 1.

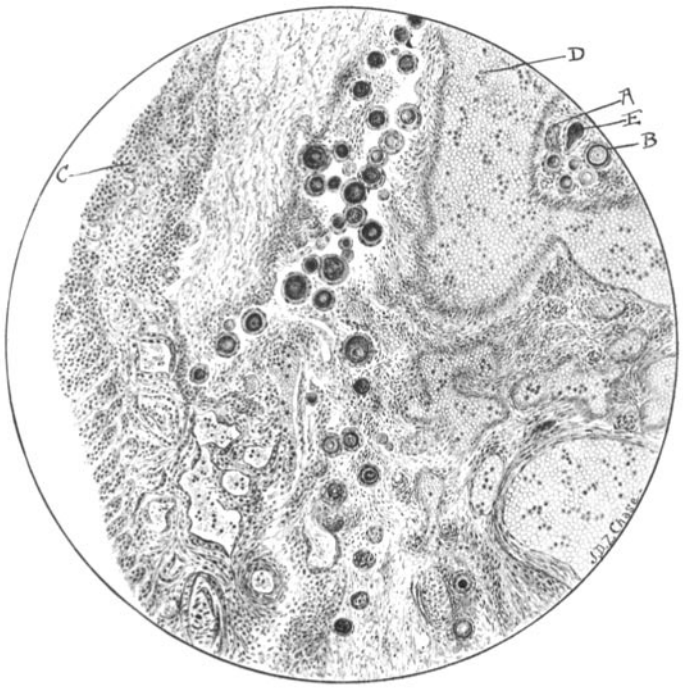

FIG. 2.

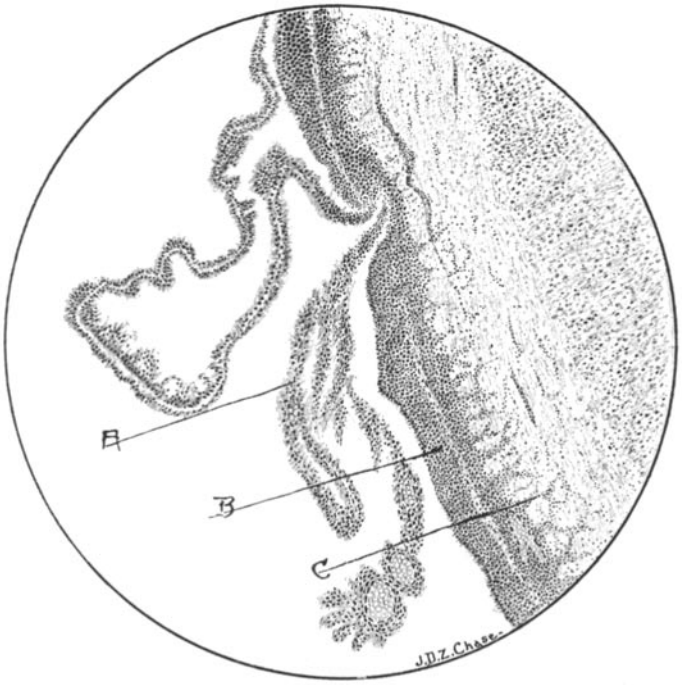

FIG. 3.

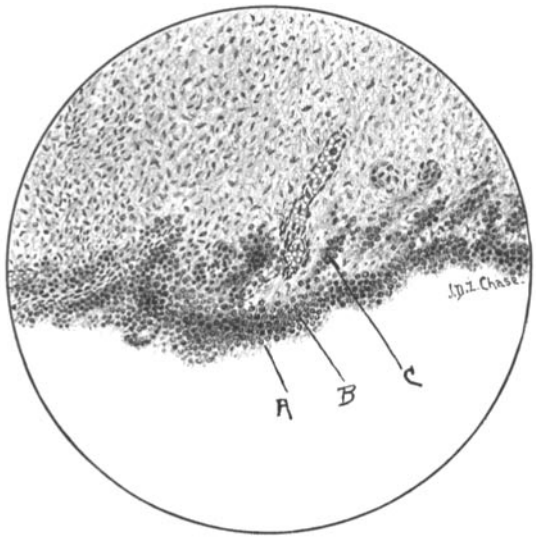

FIG. 4.