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CEREBRAL ŒDEMA.

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CEREBRAL ŒDEMA.[1]

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THE subject of cerebral œdema does not present itself as a distinct entity with constant features, either clinical or pathological. The same laws that apply to the subject of œdema in general, are applicable to cerebral œdema, with the important exception that in the latter case there are certain anatomical peculiarities that greatly modify the conditions under which these laws operate. It is only recently that we have arrived at clearer ideas of the pathology of œdema, and have become dissatisfied with the old mechanical theory of its production. In an interesting paper, by Horsely[2] and Boyce, the following statement occurs: "It is not going too far to assert that the remarkable paper by Tigerstedt and Santesson, disposes once for all, both of the conclusions that have been derived from physical considerations, and of the claim that the process of transudation in the living body is capable of interpretation by the mere variations of pressure on the sides of a permeable membrane." Unquestionably, blood pressure and the rate of flow are important factors in the process, but cannot adequately explain all cases. We know, both clinically and experimentally, that certain states of the blood favor transudation. Again the nervous system exerts an important, though not well understood influence upon the production of œdema, as illustrated by the well-known experiment of Ranvier, of tying the vena cava in the dog, and obtaining œdema of the leg only when the sciatic nerve had been divided.

[1] Presented at the meeting of the American Neurological Association, Washington, D. C., May, 24, 1894.

[2] *Brit. Med. Jour.*, Jan. 25, 1893.

Finally, the condition of the blood vessel wall must be considered, the vitality of the endothelium. Some interesting observations have been made upon this point by Sewall.[3] These laws relating to the general subject of œdema must of necessity undergo some modification, when we consider, first, the number of end arteries in the brain; second, the indistensible venous sinuses; third, the peculiar nature of the lymph spaces and channels. These lymph spaces are of three varieties; first, those of the membranes; second, those of the vessels; and third, those of the cells. All the membranes of the brain are utilized for the purposes of the lymphatic system. The connective tissue meshes of the dura and the sub-dural space, the sub-arachnoid space, and the clefts between the layers of the pia. The sub-arachnoid space is the great lymph reservoir, the other spaces being of little importance in comparison. Owing to the irregular conformation of the surface of the cortex, the arachnoid space is not a uniform cavity, and moreover, at certain places relatively large lacunæ are left, known as the *cisternae arachnoidales.* These lymph spaces, dural, pial, and arachnoid, all communicate with each other, with the lateral ventricles, with similar spaces in the spinal cord, with the perivascular and pericellular lymph spaces, with the venous sinuses, by means of the Pacchionian bodies, with the perineural lymph system, and with the extra cranial lymph system. The arteries in the pia and in the brain lie in a space known as the perivascular lymph space, and this space is often considerably larger than the vessel itself. (Shäfer.)

This is the perivascular space of His. Also between the adventitia and the muscularis is a space known as the adventitial lymph space (Virchow-Robin). Moreover, the cells of the cortex lie in a space, the pericellular lymph space, and these two systems, the perivascular and pericellular communicate with each other, and, as has been seen, also, with the sub-arachnoid space. It

[3] Paper read before 23d meeting of the Colorado State Med. Society.

can thus be seen how wonderfully abundant is the provision for lymph overflow, for comparing the brain with any other tissue or organ, we are forced to the conclusion that this immense area of lymph space is not intended merely for rapid interchange of nutrient fluid or used up material.

Reasoning from anatomical grounds, one function, and perhaps the most important function of this system, must be to equalize pressure in the brain. This organ, enclosed in its bony case, and surrounded by the firm inelastic dura mater, must have some arrangement by which sudden or great influxes of blood, or venous retention can be compensated and the pressure equalized. The soft texture of the brain renders it imperative that local pressure should never be very great, and this provision is met by the arrangement of the lymph spaces. If a certain vascular area be overfilled, the perivascular lymph space stands ready to receive either the increased bulk of the arteries or veins, or their overflow. This overflow is at once distributed to neighboring perivascular or pericellular spaces, and if necessary sent into the great subarachnoid space, or the ventricles. The conservative value of this free interchange between the various lymph spaces, is emphasized by the ill effects which we sometimes see brought about by limited cavities being shut off from communication with the main system.

In looking now for the causes that might be operative in bringing about cerebral œdema, we at once come to the conclusion, that ordinary increase of the force or frequency of the circulation, or even moderate venous obstruction, will not be adequate to explain the condition, since the arteries are allowed room for distention, and the serum that might be forced out by mere mechanical action, as has been shown is not great in amount, and would at once be taken up by the lymph spaces. In some experiments recently made with reference to this point, I found that the internal jugular veins, in dogs, could be clamped, or even tied, without very serious

complications. Clamping for fifteen to twenty minutes produced no appreciable effect, except temporary embarrassment of the circulation and respiration. In animals in whom the jugulars were tied, the symptoms already mentioned were more marked, and in addition, convulsions or spasmodic twitching. One of the animals in whom both internal jugulars had been tied, was allowed to live for more than a week, and after the first hour there were no symptoms other than a certain amount of stupor, the animal remaining in its corner, and with difficulty aroused. In no case, whether after clamping the jugulars for twenty minutes, or tying them and killing the animal twenty-four hours and less afterwards, or in animals in whom the jugulars had been tied and the animal kept alive for a week or more, was there any marked cerebral œdema. In the animals killed a few hours after the operation, there was great congestion and some increase of subarachnoid fluid, but the ventricles were empty. In the animals killed several days after the tying of the veins, the brain was anæmic, and there was no excess of fluid. In one case there seemed to be a dilatation of the aqueduct of Sylvius. Passing over the physical theory as inadequate, we turn to the other most prominent factors, viz., alterations in the blood itself, changes in the vessel wall, or faulty innervation. There is no reason to suppose that these factors are more potent in the case of the cerebral, than in the general circulation, except perhaps it should be taken into consideration that the cerebral vessels have not the same support as vessels elsewhere, but run in lymph spaces. Again, even if there be excessive transudation of serum, the great lymphatic system of the brain rapidly disposes of it. To test this, a dog was trephined and coloring matter injected into the brain, and also coloring material in powder placed under the dura, and in twenty-four hours the animal was killed, and hardly a trace of the large quantity of coloring matter could be found. In order to have cerebral œdema then, it is necessary either that the factors above mentioned be un-

usually active, or that a very large quantity of serum is transuded, so great a quantity, that the lymphatic arrangement of the brain is unable to deal with it, or in the second place, there must be some disturbance of the lymph system. This latter condition is certainly a most powerful factor in the production of cerebral œdema, and acts in two ways: first, a general inflammation of the meninges not only impairs the power of the lymph spaces to dispose of the transuded fluid, but furnishes in its process more or less serum; secondly, inflammation of the membranes, often obliterates the passage of communication between the several lymph spaces, thus preventing the distribution of the fluid. So much for the causes active in producing cerebral œdema. At first sight it might be thought that cerebral œdema ought to be a very common affection; the free and rapid circulation in the brain, the end arteries, the peculiar venous sinuses, all favoring it. On the other hand, however, it is seen that the remarkable lymphatic system more than compensates for these various favoring conditions.

The pathological anatomy of cerebral œdema has attracted little attention. There are certain gross appearances, certain physical alterations, brought about by an excess of fluid in the brain, but no definite structural changes have as yet been discovered. It might be said in passing that we have no method sufficiently delicate to appreciate the changes that theoretically might be produced in the protoplasm of the cells, by an excess of fluid. Again, it must be borne in mind that in cerebral œdema the conditions are very favorable for the action of toxines; the lymphatics are not doing their proper emunctory work, and waste materials may not only be unduly retained, but further elaboration of toxic substances may take place. The microscopic appearances of the brain in cerebral œdema are fairly constant and characteristic. After the removal of the dura the arachnoid is seen more or less tense, with or without milky opacities. The convolutions are widely separated, and in extreme cases are flattened. The ventricles are some-

times distended, at other times apparently not containing even their normal amount of fluid. Both gray and white matter when cut presents a shining, glistening appearance. Even to the naked eye the perivascular lymph spaces are dilated, giving rise to the *l'etat criblé* of the French writers. Under the microscope both the perivascular and the pericellular spaces are dilated. An excess of fluid is common in the brains of the aged, in whom atrophy of the cortex has taken place, the slightly diminished space being filled with fluid. The same thing is occasionally seen in cases of prolonged anæmia. When any local loss of brain substance has taken place, and upon the shrinking of a clot, the space left is filled with fluid. These conditions, however, and also that known as internal hydrocephalus, it is not within the province of this paper to discuss.

Certain of the older pathologists gave a very important place to acute cerebral œdema, as for example, Magendie, Andral, Guersant, Hodgkin, Otto, and Bichat, while on the other hand, few of the late writers on neurology even name the condition. Obersteiner[4] supposes that the intracranial lymph modifies the movements, cardiac and respiratory, of the brain. Richet and Salathé have shown that the amount of cerebro-spinal fluid has a decided effect upon the action of the cerebral arteries. Luys[5] concludes that the presence of the intracranial fluid modifies the relationship between the cranial cavity and the intracranial mass, and he compares the brain and cerebro-spinal fluid to the fœtus and the amniotic fluid. Grasset[6] points out the conservatism of this fluid in meningeal inflammation. Ziegler[7] describes the condition under the headings, œdema of engorgement, hydræmic dropsy, congestive œdema, and meningeal dropsy. As bearing upon the conditions under which cerebral œdema occurs, the following figures may be of

[4] The Anatomy of the Central Nervous Organs,

[5] Quoted by Grasset: Les Maladus du Systeme Nerveux.

[6] *Loc cit.*

[7] Text Book of Pathological Anatomy.

interest. Between five and six hundred records of autopsies made by Prof. Keirle at the Baltimore City Hospital were carefully examined, and the occurrence of cerebral œdema noted. All traumatic cases and cases of gross brain disease, tumor, hemorrhage, etc., were excluded.

Œdema of the brain was found sixty-eight times; the effusion was most frequently confined to the large spaces, particularly the subarachnoid, more rarely the ventricles were involved. Œdema of the brain without other important lesion was found six times; it occurred in nephritis fifteen times; pulmonary tuberculosis six; heart disease four; alcoholism six; affections of the liver four; typhoid fever three; malarial fever three, and once associated with pericarditis, pleurisy, puerperal fever, gastro-enteritis, starvation, and drowning.

It is common to find cerebral œdema, or, at least, an excess of fluid in the brain of those dying insane. Tuke[8] put the percentage at fifty-eight. Spitzka[9] calls attention to the dilation of the perivascular and pericellular lymph spaces in persons dying insane, especially in paretic dementia, epileptic and periodical insanity.

In regard to the conditions in which cerebral œdema is met with, the most important, according to the figures above, is nephritis. Here the œdema is probably the result both of the diseased vessels and the increased tension. It is quite possible, as Traube has suggested, that the uræmic symptoms, at least the milder ones, are due to the effused fluid. In pulmonary tuberculosis, perhaps, the most important factor in the production of the cerebral œdema, is the general lowered nutrition, with more or less anæmia of the brain, or even possible slight atrophy of the cortex and diminution in size. In heart disease and pneumonia the disturbance in the circulation, congestion, and want of compensation are the important factors, while in alcoholism and the fevers, the

[8] Dict. of Psych. Med.

[9] Manual of Insanity.

altered vessels, the state of the blood itself, and, perhaps, certain toxic influences predominate. We know little, either experimentally or clinically, as to the effect of improper innervation upon the production of cerebral œdema, but would expect to find its influence more potent here than in other parts of the body, since both nerve elements and blood vessels are so closely related to the lymphatic system.

We would not expect, *a priori*, any very special symptoms from cerebral œdema, since the involvement of brain tissue is so general. In some cases it would seem that the distended ventricles give rise to certain motor disturbances; in two of the cases reported in which the most important post mortem lesion was the distended ventricles, there was rigidity—one case general, the other of the muscles of the neck, retracting the head. It is possible that the overdistended ventricles press upon and irritate the basal ganglia, and thus cause the motor disturbance. What would be expected in these cases, cases of general acute œdema, would be a general dis turbance of the brain as a whole. The amount of such disturbance would vary with and depend upon the quantity and nature of the effused fluid. Such symptoms are, in brief, general disturbance of intellection, occasional motor disturbances, and in severe cases circulatory, and respiratory disturbances, due to pressure upon the medulla.

In order to illustrate the change that has taken place in our view of the clinical aspect of cerebral œdema, the following quotations are given, one from of old, the other from the new school of neurology; Rosenthal[10] says, "Acute cerebral œdema may cause sudden death by rapid increase of the compression and volume of the brain. It is a matter of experience, that in diseasesof the heart and kidneys, in bronchitis and chronic tuberculosis, sudden fatal cerebral compression may develop. The patient suddenly loses consciousness, falls to the

[10] Dis. of Ner. System.

ground, the muscles are relaxed, spincters paralyzed, reflex irritability considerably weakened, the contracted pupils reacting slightly or not at all. Delirium usually appears, respiration and deglutition become more and more irregular and difficult, and death occurs in coma at the end of a few hours or days."

Compare this what Gowers[11] says. In speaking of the excess of fluid in the brain of the aged, he says: "It was thought to be the cause of the symptoms, and the condition was termed "serous apoplexy," a disease that has no real existence, although the word is still sometimes to be heard at inquests, and to be seen on certificates of death." Both these statements may be regarded as extreme. While on the one hand it is more than doubtful whether acute cerebral œdema ever presents such a distinct clinical picture as the one drawn by Rosenthal, yet, on the other hand, Gowers is rather inclined to deny it any existence, at least so far as its clinical appearance goes. It is highly probable that in a certain proportion of the older observations on this subject, softening from embolism was confounded with serous effusion, and this is rendered the more likely if the statement of Huguenin[12] can be accepted, namely, that effusion, under certain circumstances, is very apt to occur if there exists any disturbance of the intracranial circulation. Most observers who have followed the clinical history and studied the post-mortem appearances of such diseases as nephritis, pheumonia or typhoid fever, will, I think, admit that very often the cerebral symptoms seen in these affections are due, in part, at least, to the abnormal quantity of serum present. Apart from its association with other diseases, cerebral œdema, as has been shown, may occur independently, and may cause death. Reasoning from our knowledge, both of the cause and effect of œdema in other parts of the body, the wonder is that cerebral œdema is not a far more frequent and serious condition than it would

[11] Dis. of Ner. System.

[12] *Lancet*, Sep., 1889.

seem to be, and this can be accounted for only by taking into consideration the very remarkable lymphatic system of the central nervous organs.

The following conclusions would seem warrantable;

1. Cerebral œdema should receive recognition, both from the clinical and pathological standpoint.

2. Œdema of the brain follows the laws of œdema elsewhere in the body, with the important exception that these laws must of necessity be considerably modified by the anatomical arrangement of the lymph spaces of the brain and its membranes.

3. The effused serum may exert injurious mechanical pressure, and also offers occasion for toxic influences.

4. Cerebral œdema would be a much more common and serious affection, were it not for the free communication which exists between the various lymph spaces, as emphasized by the decided symptoms produced when these cavities are isolated by inflammatory adhesions.