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THE CEREBROSPINAL FLUID AS A PROBLEM IN INTRACRANIAL SURGERY *

CHARLES H. FRAZIER, M.D., Sc.D.
PHILADELPHIA

The rapid strides that have been made in the evolution of modern civilization are almost past man's understanding. To the casual observer, the progress of recent times is attributed hastily to the material contributions of the master minds of the industrial world; but a more careful analysis will lead the seeker after truth out of the turmoil and the noise and bustle of the busy centers of population into the seclusion of the laboratory, where, in the quiet of their academic atmosphere, the chemist and the physicist, the geologist and the agriculturist, the psychologist and the pedagogue, the bacteriologist and the physiologist are working out the problems which make it possible for the human race — men, women and children — to live where conditions compel them to work, and not be mowed down by the cruel operation of the law of the survival of the fittest.

Would it ever have been possible to combat this law of Nature were it not for the accomplishments of the scientist? Could the spirit of the philanthropist embodied in the social worker have made the congested districts inhabitable, had it not been for the science of preventive medicine? The application of scientific principles to agriculture will alone make it possible to feed the ever increasing population from the products of the soil. Was it the builder or contractor, or a disciple of the Taylor system of scientific efficiency that revolutionized the bricklaying industry, which had changed not one iota in all the centuries that have elapsed since the building of the pyramids until the present decade? Who would have dreamt at the time of the Spanish-American War that the dreadful sacrifice of countless lives might have been avoided by vaccination, or that the mortality of the infested zone of the Isthmus of Panama could be reduced below that of the wholesome surroundings of the rural districts of more northern climes?

Scientific discovery, the product of research, is the guiding-star in our modern civilization in matters of health and happiness, in conservation and productivity, in social welfare and social uplift. And what is true of all these is true, also, of the progress of surgery. It is not so long ago that the practical surgeon so-called looked with pity, if not with scorn, at the

surgeon who endeavored to work out problems in the laboratory and not in the clinic. But who is there among you to-day that does not look with admiration and appreciation on the addition to knowledge that has been derived from the laboratories of Halsted, of Matas, of Crile, of Cushing, of Carrel and of Sweet? Through blundering errors and at the cost of human life the clinician may hit on truths which might have been solved at less cost in the experimental laboratory. Surgery has won its place as a scientific branch of medicine, and the hidden truths, on which will depend the progress of surgery as of all other human attainment, will be the product of the surgeon in his rôle of trained investigator.

The subject taken for the topic of this address is the cerebrospinal fluid as a factor in the problem of intracranial surgery. This topic is one of absorbing interest, as well as of great practical moment. It is one with which the surgeon must reckon in the diagnosis, the prognosis and the treatment of most intracranial lesions, and cannot be disregarded in any operative procedure. I shall present facts gleaned in part from literature, but in large measure from personal observations in the clinic and experimental laboratory.

Meningitis.—Illustrative of the part played by the cerebrospinal fluid in intracranial lesions, let us cite, for example, meningitis: its pathologic factors and its clinical syndrome. In meningitis there are two pathogenic factors: first, infection through the invading micro-organism, and, second, the increased intracranial tension. The increased tension in its clinical expression is analogous to the increased tension of sources other than infectious, as in cases of intracranial trauma and tumors. Whatever may be the nature of the infection or its effect on the meninges and cortex, there does exist a resulting increased tension in the cerebrospinal fluid and ultimately disturbance in its circulation and absorption. In their series of experiments, Kopetzky and Haynes demonstrated the analogy of experimentally induced increased intracranial tension and that due to infection of the meninges by pathogenic micro-organisms. While it is true that the fatal outcome of many cases of meningitis is due to the metabolic action of the particular micro-organism on the meninges and cortex with the production of certain toxins and ptomains, it is also true that in cases of otitic meningitis the progress of the disease has been arrested after drainage by ventricular puncture or lumbar puncture when the examination of the fluid failed to demonstrate the existence of micro-organisms.

In meningitis, then, there is an increase in cerebrospinal fluid and edema of the brain. There results an

* Chairman's address, read before the Section on Surgery at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, June, 1914.

increase in pressure which so interferes with the blood-supply that the function of the vasomotor, respiratory and cardiac centers is disturbed, and the alarming picture of intracranial pressure asserts itself. It is significant that this increased pressure is the determining factor, as often perhaps as the specific action of the bacteria. The part played by the cerebrospinal fluid in meningitis is, therefore, a major one and the treatment of meningitis should comprehend some means of controlling the intracranial pressure as well as the microbic activity.

Hydrocephalus.—The study of the physiology of the cerebrospinal fluid in relation to congenital hydrocephalus offers another fruitful field for study. In the two thousand years which have elapsed since Hippocrates first tapped the ventricles, not a substantial contribution has been made to the etiology of hydrocephalus. The question whether or not hydrocephalus is due to a lesion of the absorptive mechanism is, even to-day, absolutely in the domain of speculation. We are told that it may be due to traumatic or psychic disturbances during pregnancy, to toxic or infectious disease of the parent, such as alcoholism, tuberculosis or syphilis, or that there may be a degenerative process of the capillaries in the ventricular wall (Weber); but there has never yet been revealed by necropsy or otherwise a constant pathologic factor which gives us a clue as to the etiology, prevention or treatment. Despite the seriousness with which the originator of some new method of treating hydrocephalus takes himself, we feel almost like apologizing for the multiplicity and variety of surgical procedures that have from time to time been recommended, so many have been the disappointments, so many the failures.

Brain Tumors.—Again, the relation of cerebrospinal fluid to brain tumors is an absorbing topic. We attribute to the new growth those symptoms of brain tumor which are the result of increased intracranial tension, but, as a matter of fact, in most instances the increased intracranial tension is the result of the excessive accumulation of cerebrospinal fluid in the ventricles, in the basal cisternae, or throughout the subarachnoid space. Evidence of intracranial tension is absent when there is no excessive accumulation of fluid in the distended ventricles or the basal cisternae. I supported this statement with numerous illustrations from my clinic in a paper presented to the Philadelphia Neurological Society.¹ This general rule holds good whether the tumor be a glioma or an endothelioma; whether it be cortical, subcortical or basal. What is true of pretentorial lesions is true also of subtentorial lesions. The truth of this statement is readily demonstrated on the operating-table. If, with pretentorial tumors, there is excessive tension, the tension will subside when the cerebrospinal fluid is withdrawn by tapping directly the ventricles, or by lumbar puncture. Similarly, in posterior fossa tumors, the evacuation of fluid from the basal cisternae is invariably followed by the immediate decrease of tension.

The extraordinary rapidity with which the cerebrospinal fluid reaccumulates after evacuation is worthy of mention. I had an opportunity in a case of tumor to tap the ventricles through an opening in the skull on several occasions when I withdrew from 60 to 150 c.c. of cerebrospinal fluid, from two to five times the normal content of the ventricles, only to find the

fluid replaced within the space of twenty minutes. Palliative treatment in the case of brain tumors becomes then a problem of dealing with the excessive accumulation of cerebrospinal fluid, and the important question at once arises: Shall temporal decompression as a palliative procedure be altogether supplanted by the Anton puncture of the ventricle through the corpus callosum? This method at once strikes at the root of the trouble and offers an outlet and an area of absorption for the fluid in the distended ventricles. In this manner, tension is relieved and a definite method adopted to prevent its immediate recurrence.

The cerebrospinal fluid was mentioned first by Colugno in 1764, who thought it present only after death, and later Haller found it in the spinal cord, but without realizing that there was any relation between the fluid in the cord and that in the ventricles. It was not until 1840 that the connection between the ventricles and the subarachnoid spaces was revealed by Magendie through his description of the foramen which bears his name.

Well known as are the physical characteristics of cerebrospinal fluid in health and their variation in disease, we are still in the dark as to its function, and as to the manner in which the secretory and absorptive balance is maintained in health, and is disturbed in disease. The cerebrospinal fluid has no analogy in the body; it is wholly different on the one hand from lymph and on the other from the liquid found in serous cavities, as of the pleura and peritoneum. Because of the communication between the perivascular sheaths and the pericellular and perineural spaces, there are some who believe that the cerebrospinal fluid plays a part in the nutrition of the brain cells.² Some regard it as a means whereby the delicate balance of intracranial pressure is preserved; others, again, as Dixon and Halliburton, believe that it affords the central nervous system an additional mechanism for eliminating carbon dioxide from the brain: as urea increases the renal flow, so carbon dioxide increases the cerebrospinal secretion. While we know that the cerebrospinal fluid is a secretion, we have at the same time found from repeated examination of fluid discharged in large quantities that the solids in the fluid diminish materially in quantity, so that there is reason for suspecting that under abnormal conditions the fluid may be of the nature of a transudation.

The cerebrospinal fluid fills all the space of the cranial cavity not occupied by the vessels and nerve-tissues; and, by equalizing pressure, adjusts the mechanism of the circulation of the nerve cells. Under normal conditions, we find the pressure registers 100 mm. of water, or with the mercury manometer, which I prefer, about 6 mm. Natural variations from the normal occur during inspiration and expiration, the former lowering, the latter raising it, as the blood is dammed back from the right auricle and vena cava into the cerebral sinuses. The pressure is believed by some to be equal to or a little greater than that of the venous pressure. This relation of cerebral venous pressure to the pressure of the cerebrospinal fluid, we have been able to demonstrate a number of times in our experiments. On clamping one internal jugular vein, there is no change in pressure, but when both veins are clamped, the pressure rises 20 mm. in five seconds. When both internal

1. Frazier, C. H.: New York Med. Jour., June 27, 1914.

2. This is still open to question, as His, Sicard and others believe that the true lymph channels of the brain are separate from the perivascular sheaths. (Ferrier: Lancet, London, Oct. 18, 1913.)

jugular veins are closed, and first one external jugular and then the other is clamped, the pressure rises 10 mm. and 40 mm., respectively, within ten seconds. This bald statement on the relation of the venous to the cerebrospinal pressure is of considerable import when taken in relation with the problems of absorption and confirms the observations which have been and are being made to prove that the greater part of the fluid is taken up by the venous, rather than by the lymph, channels.

THE PRODUCTION AND ABSORPTION OF THE FLUID

Every pathologic state of the cerebrospinal fluid implies an increase in quantity. So far as we know, there are no pathologic conditions in which the symptoms are the result of a diminution in quantity of cerebrospinal fluid, whereas, as we have already shown, there are many diseases in which the increase in fluid is a dominant factor. Any increase in fluid above the normal implies a disturbance of balance between absorption and secretion, so that an understanding of these two processes is essential before it will be possible to adjust the disturbed balance.

By the injection of various dyes into the subarachnoid space, we have been able to demonstrate positively that the lymphatic system plays a very insignificant part in the problem of absorption of the cerebrospinal fluid. One may trace the avenue of absorption through the nerve-sheaths, chiefly of the olfactory and optic nerves, thence to the posterior part of the eyeball, and to the mucous membrane of the turbinates and septum, to the posterior lymph-nodes of the nasopharynx, to the parotid and deeper cervical chain and thence to the thoracic duct. Usually, it took twelve hours for the stain to reach the lower glands. While, therefore, absorption does take place by the lymphatics, the course is roundabout and the process relatively slow.

A better method of studying absorption, we found in the use of phenolsulphonephthalein (an observation confirmed by the work of Dandy and Blackfan) which, when injected into the ventricles, appears in the torcular herophili in two minutes and in the veins in five minutes. As it takes almost twelve hours for the stained fluid to reach the cervical lymph-nodes and only five minutes for phenolsulphonephthalein to reach the veins, one sees that the cerebrospinal fluid is absorbed chiefly by the blood-channels.

Our studies of the process of absorption and secretion have been greatly facilitated through our producing an artificial hydrocephalus by blocking the fourth ventricle. If phenolsulphonephthalein is injected into a blocked ventricle, absorption is practically inhibited; even after two hours there appears only the slightest trace and this is not constant, whereas in the unobstructed ventricle the drug is recovered from the veins in five minutes. Furthermore, we have shown that from 50 to 60 per cent. of the amount of phenolsulphonephthalein injected may be recovered from the veins in two hours. Hence it is fair to assume that an equal quantity of cerebrospinal fluid may be absorbed in the same time.

While, therefore, it is an established fact that the cerebrospinal fluid escapes chiefly through the venous channels, one is still in doubt which of the veins or sinuses play the most important part. Key and Retzius asserted that the pacchionian bodies acted as filters, and, while this theory is not generally accepted because these bodies do not exist in very young children, the fact that hydrocephalus is more prevalent in infancy is

at least suggestive to me that the pacchionian bodies play some part, be it large or small, in the absorptive process. Hill believes that the cerebrospinal fluid makes its escape from the veins opening into the longitudinal sinus between which and the subarachnoid space Adamkiewicz claims there is a free communication. In relation to the part played by the longitudinal sinus, we found experimentally that when fluid was introduced under pressure into the cisterna magna of the posterior fossa, none of the fluid reached the cerebral cortex, and we attributed this phenomenon to the blocking of the isthmus of the tentorium cerebelli when the midbrain was forced upward by the artificial pressure. In this phenomenon, I take it, is an explanation of the greater frequency with which we find signs of increased intracranial tension in tumors of the posterior rather than of the anterior fossa. It is not of necessity the obstruction of the ventricles that causes their distention (for frequently the outlet to the ventricles is not blocked); but the distention is due to the interference with absorption that follows when the passage of the cerebrospinal fluid from the posterior fossa to the cerebral cortex is obstructed because the isthmus of the tentorium is blocked. Furthermore, the improvement which follows puncture of the corpus callosum, permitting the escape of cerebrospinal fluid directly from the dilated ventricle to the cerebral cortex, may be due to the greater facility with which the fluid may reach the longitudinal sinus.

The control of the production of cerebrospinal fluid is pregnant with possibilities, and the study of the formation of cerebrospinal fluid offers a fascinating problem for experimental research. Up to the present all therapeutic efforts have been directed toward finding an artificial outlet for the excessive fluid which accumulates in such diseases as serous meningitis, brain tumors and hydrocephalus. The meager results we know. I believe that the future may bring forth remedies which will deal with the problem of cerebrospinal fluid at its source, and control its output.

It is no longer a matter of speculation that the cerebrospinal fluid is the output of the cubical cells of the choroid plexus and is found within the ventricles, lateral, third and fourth. That it is a secretion has been proved by the histological evidence of Cavazzani, Mott and others, and is confirmed by the experimental data which I shall present.

Is it not true, then, that the choroid plexus must be looked on as a gland subject to a variety of influences like other glandular structures, some now well known, others to be revealed by continued research? The choroid has been described by Mott as a gland with an external secretion but with an internal destination—a mixed type of gland intermediate between a ductless gland and a gland with a duct; its formation being affected in an inverse manner, epithelial invagination for a gland with an excretory duct, ependymal invagination for the choroid plexus.

The suggestion of Stiles that ligation of the common carotid is an effective way of dealing with hydrocephalus implied that the activity of the choroid plexus or choroid *gland*, as I shall now call it, is diminished by limiting its blood-supply. If an analogy can be drawn between the thyroid and the choroid gland, Stiles' suggestion is not wholly illogical, since the control of hyperthyroidism by ligation of two thyroidal vessels is an undisputed fact. Unfortunately, however, this analogy of the two glands is not borne out

by either our laboratory or our clinical experience. We have been able to obtain readings of the normal flow of cerebrospinal fluid by a suitable apparatus, attached to a cannula introduced into the subarachnoid space through the occipito-atlantal ligaments, and with these as controls, observed the effect of various circulatory disturbances, clamping first one, then both common carotids, one and both internal jugular veins. Curiously enough, this interference with the larger vessels of the cerebral circulation had absolutely no retarding influence on the rate of secretion. This experimental evidence alone would seem sufficient to prove that the function of the choroid gland cannot be controlled by ligation as is that of the thyroid gland. But, as further evidence, I may refer to a clinical experience in the case of inoperable brain tumor with enormously distended ventricles. Decompression had failed to compensate for the tremendous increase in tension due to the distended ventricles, and an attempt was made prior to our laboratory investigation to influence the accumulation of fluid by gradual interruption of the carotid circulation. The ventricle was tapped before each ligation, and the time required for it to fill was noted. These observations were repeated after ligation, and the results were practically negative, in that after the withdrawal of from 100 to 150 c.c. of fluid before ligation and after ligation, the time required for the ventricle to refill was practically unchanged.

Further, continuing our search into the factors influencing the secretory activity of the choroid gland, we investigated the physiologic action of the saline extracts of certain glands, including the pancreas, spleen, kidney, testes, ovary, thymus, adrenals, liver and brain. Nearly all these, especially the spleen, liver, kidney and pancreas caused a greater or less fall in blood-pressure, and, coincident with this, a marked increase in the rate of flow of cerebrospinal fluid in proportion to the quantity of extract injected. Amyl nitrite produced a similar fall and a similar increase in the outflow of cerebrospinal fluid. Frequently, after this temporary increase, the rate of flow became slower or ceased altogether. This increase in the secretory output must be the result either of direct stimulation of the choroid gland or of the disturbance in blood-pressure. The fall of arterial pressure causes an increase in pressure and dilatation of the cerebral sinuses, which in turn forces the cerebrospinal fluid out of the ventricles. Further observations tended to confirm the latter theory rather than the theory of hypersecretion.

Some interesting facts have been brought out recently by Dixon and Halliburton,³ who, with us, have been studying the effect of various substances on the cerebrospinal secretion. They found, for example, that pilocarpin caused a genuine increase in secretion, although they were doubtful whether it acted directly on the choroidal epithelium or its nervous mechanism. A slight increase followed the injection of brain extracts, but the most interesting of their observations was on the effect of an extract of the choroid gland. This caused a uniform increase in the cerebrospinal secretion. This increase is not due to altered vascular or respiratory conditions, but rather to the specific action of some substance on the secretory cells of the choroid gland. The precise nature of this substance is still undetermined, although, as Dixon and Halliburton

suggest, it may be due to a hormone product of brain metabolism.

In beginning our experiments, we hoped to find a tissue or an extract which, when injected into the circulation, might have a retarding influence on the activity of the choroid gland. But, until recently, with all the substances investigated, the effect was a hypersecretion rather than a hyposecretion. It was not until we began to study the effects of the thyroid gland extract that we discovered a substance which had a specific inhibitory action on the choroid gland. When injected in sufficient quantities, the thyroid extract caused a temporary fall in blood-pressure, with the usual transitory increase in outflow of cerebrospinal fluid; but the significant and altogether unique effect was the prolonged period of decreased outflow which followed, for three or four hours, that is, to the end of the experiment. Even when such small doses as to cause little, if any, change in blood-pressure are injected, the diminution in the rate of choroid secretion is marked, so that we are led to the conclusion that the thyroid gland extract, when injected intravenously, has a specific inhibitory action on the choroid gland. We will continue these studies on the thyroid gland to determine which of its constituents is the responsible factor.

The cerebrospinal fluid, then, has an absorbing interest for the clinician. Not only must he reckon with it in the diagnosis of many intracranial diseases, but also he cannot ignore it when his constructive ingenuity may be taxed to devise measures of relief for such diseases. Of equal interest, however, are the problems of research for those who would reveal the secrets of the function of this fluid in which our brain cells are forever bathed.

1724 Spruce Street.

THE TREATMENT OF PLACENTA PRAEVIA *

EDWARD P. DAVIS, M.D.

PHILADELPHIA

In the advance which the science of obstetrics has made in the last fifteen years, this serious condition with others of like importance, has received new consideration, and some changes have been suggested in its treatment.

At present we recognize that septic infection is quite as important in causing the death of the mother as hemorrhage or shock. It has also been repeatedly demonstrated that placenta praevia causes such a vascular condition of the cervix and lower uterine segment that forcible dilatation or vaginal cesarean section exposes the patient to great danger from hemorrhage and infection. Furthermore, so grave a complication as placenta praevia demands hospital facilities and the skill of experienced hospital operators.

My experience leads me to agree with the conclusions just stated, and I desire, in addition, to present this subject to you from the following point of view: Logically, placenta praevia is a variety of ectopic gestation. The normal location of attachment of the impregnated ovum during its greatest period of devel-

* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

3. Dixon and Halliburton: Jour. Physiol., 1913-1914, xlvii, 213.