THE CEREBROSPINAL FLUID IN HEALTH AND DISEASE

SUMMARY OF A SYMPOSIUM

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At the XIV Congresso Latino-Americano de Neurocirurgia, an International Symposium was held on March 13, 1971 on "The Cerebrospinal Fluid in Health and Disease". In the opening remarks, the chairman pointed out that although the meninges and spinal fluid had been recognized for centuries, many of their anatomical and physiological features were still poorly defined. Even the mechanism of resorption of cerebrospinal fluid (CSF) is as hotly debated today as half a century ago, when Weed disagreed with Cushing's hypothesis of open channels and stated that CSF resorption occurs by way of membrane filtration.

Arachnoid villi — Shabo and Maxwell (Bethesda, U.S.A.) described their combined light and electron microscopic studies of primate (Macaque) arachnoid villi of the superior sagittal sinus. They found that the villi are entirely invested with an endothelial cell layer, continuous with that of the dural venous sinus, which separates the subarachnoid contents of the villus from the systemic blood. The CSF pathway is interpreted as a filtering mechanism for the fluid en route to circulating blood channels. No endothelium-lined channels or other structures were found which could be interpreted as direct pathways linking the CSF and blood. Consequently, they could not confirm the notion of bulk flow of CSF into the systemic circulation by way of arachnoid villi.

However, other authors were not ready to accept this conclusion. Davson and Segal (London, England) argued that the force permitting drainage of the CSF is the difference in hydrostatic pressure across the arachnoidal villi but the removal of protein from the CSF is achieved by simple flow through large pores. They referred to the work of Welch and associates who perfused particles of varying diameters through excised strips of dural sinus wall and concluded after light microscopic examination that a system of "coapted tubules" (4-12 μ in diameter) exists within the villus which provides an open, direct communication between the subarachnoid space and the dural sinus.

In confirmation of this concept, J. Donald McQueen showed a movie of oil particles exuding from the pacchionian granulations into the dog's longitudinal sinus. He and his associates noted that the arachnoid villus is an obvious site for blockade and they therefore made an attempt to analyze flow through this structure. The clearance of various materials was observed with a binocular dissecting microscope after the superior sagittal sinus of

the dog had been opened in the midline and preliminary intraventricular saline irrigations used the clear residual red cells from the system. Various materials, including saline, mock CSF fluorescein and trypan blue were injected into the ventricle to monitor the flow with the dissecting microscope. Thin mineral oil proved to be the most useful agent. The same general procedure was carried out for the isotope studies except that samples were collected by a catheter inserted into the torcula through a small twist drill opening. Sodium iodide was used with ^{125}I, albumin was tagged with the same tracer and red blood cells were labelled with ^{51}Cr. Samples were collected from the torcula; they were measured with a gamma counter and clearance was expressed as the percentage of activity in this effluent. The passage of saline, mock CSF and fluorescein was readily seen through the villa but was difficult to photograph. Thin, tinted oil proved to be much more easily depicted cinematographically in its transit through the villus. Small droplets formed on the surface of the arachnoid domes, coalesced with other droplets and then disappeared with the irrigating fluid. The isotope studies were performed in an attempt to measure retention. A marked restriction to the passage of blood was apparent. Significant concentration was found in the sinus only with the use of very dilute suspensions at 50,000 cells per c.mm. and a progressive blockade was indicated with heavier suspensions.

The authors concluded that the ready passage of fluid through villi is in keeping with flow through a porous system as originally indicated by Key and Retzius and as later suggested by Welch and coworkers (with tubules) and by Davson et al. The appearance of red cells and spheres within villi suggests a definite filtering action due to the dual effects of bulk fluid flow and retention. This arachnoid blockade as contrasted with a cisternal one occurs primarily in the villi.

Choroid plexus — The structure of the choroid plexus is somewhat better agreed upon. Since the composition of the CSF of the fetus differs from that of the adult, one would expect structural correlates in the morphological development of the choroid plexus. Dr. Virginia Tennyson (New York, U.S.A.) described the evolving plexus on the basis of light and electron microscopic studies.

The initial fold of the telencephalic choroid plexus is covered by a pseudostratified epithelium. It has short, thin microvilli and tight junctions but relatively straight or only slightly folded lateral surfaces near the base of the cell. The myelencephalic choroid plexus, on the other hand, has a tall, columnar epithelium with longer, more polypoid microvilli and similar apical junctions, but more elaborated folded lateral membranes. Glycogen accumulates earlier in the myelencephalic epithelium, but tends to remain in the base of the cell except for scattered particles. The telencephalic epithelium becomes columnar. It amasses large quantities of glycogen, distending the cell and almost obliterating the microvilli and folded cell processes. The nucleus is displaced to the apical region and the organelles are

reduced in number and show ultrastructural alterations. The marked differences between the two epithelia suggest that they are functioning differently during the early developmental period. The telencephalic choroid plexus may have a nutritive function. The myelencephalic choroid plexus also stores glycogen, but it's elaborated membranes and numerous mitochondria suggest that it may be forming cerebrospinal fluid by an active process. Autophagic vacuoles form in the glycogen masses in the later stages. These structures, which appear to be derived from distended mitochondria and associated smooth reticulum, may play a role in the removal of glycogen from the cell.

Formation of cerebrospinal fluid — Davson and Segal noted that the rate of secretion of the CSF is fairly constant being of the order of 0.5% per min. Carbonic anhydrase causes inhibition of secretion of the CSF leaving a residual flow amounting to some 33% of the normal. The only influence that reduces the secretion further seems to by hypothermia. Why a carbonic anhydrase inhibitor should be so effective, remains a physiological puzzle.

So far as practical applications are concerned, only the carbonic anhydrase inhibitors, such as acetazolamide (Diamox) are of likely value in the therapeutic reduction in secretion rate. However, if, as seems very likely, the cause of hydrocephalus in all its manifestations is an obstruction to drainage, then mere reduction in the rate of secretion can only be palliative.

The CSF is much more than a filler of cavities; it comes into close diffusional relations with the central nervous parenchyma, and diffusion between the CSF and nervous tissue, be it across the ependyma or across the pia-glia, is unrestricted. The close relation between the CSF and brain extracellular fluid might suggest a similarity not only in composition, but also in mode of formation; thus, if the cerebrospinal fluid has a low concentration of K^+ by comparison with blood plasma, then the extracellular fluid must also have a low concentration of K^+, and this means an active process operating across the blood-brain barrier.

The evidence on the matter of an actual flow is conflicting. To summarize, the CSF seems to be formed continuously at a rate that is about one half per cent or less of the total volume per minute. The process of formation involves active transport of ions, such as Na^+ and Cl^-, and seems to be analogous with fluid transport processes in the eye, kidney or, gall-bladder. As such, the process is capable of generating, and working against, quite high pressures. There is no reason to doubt that an obstruction to the drainage of CSF could result in the continued formation of fluid with ever increasing pressures.

It is now generally accepted that the major escape route for the secreted CSF is the arachnoid villi. Other sites of drainage have been suggested, such as from the spinal subarachnoid spaces into the large spinal veins associated with emerging nerve roots. There were two physical factors favoring passage from subarachnoid space to vessel lumen, namely the higher hydrostatic pressure in the CSF and the difference of colloid osmotic pressure between the virtually protein-free CSF and the plasma. Whilst

there is little doubt that the hydrostatic difference of pressure is an important factor, the significance of the colloid osmotic pressure of the plasma has been called into question on both theoretical and anatomical grounds.

David Bowsher (Liverpool, England) discussed the mechanisms of production and removal of CSF and the factors concerned with the pressures exerted within the cranium by arteries, sinuses, veins and cerebrospinal fluid.

The total volume of CSF is normally accepted as 140 ml; of this, an average 23 ml, are contained in the ventricles and 30 ml in the spinal subarachnoid space leaving some 87 ml to occupy the cranial subarachnoid space. The glandular nature of the choroid plexuses has been recognized for over three hundred years.

In spite of these early observations, much controversy has raged over the manner by which CSF is formed. An early view regarded it as an ultrafiltrate of plasma, but evidence has been gradually accumulating that the choroid plexuses have an active secretory function. Following the development of a technique for collecting newly-formed fluid from the surface of the choroid plexus, Ames, Sakanous and Endo were able to prove the secretory function of the choroid plexus beyond all possible doubt.

In the first place, it should be noted that the sodium concentration is the same in plexus and cisternal fluid, and higher than that of a plasma ultrafiltrate. The chloride concentration at the plexus is also slightly higher than that of plasma ultrafiltrate. In its passage from plexus to cisterna magna, the fluid gains chloride anions and loses potassium, calcium and magnesium cations in approximately the following proportions: Cl^-: 4.35%; K^+: −10.8%; Ca^{++}; −10.2%; Mg^{++}: −9.5%.

If secretion by the choroid plexus be regarded as the primary source of CSF, exchange (i.e. diffusion) between the neuraxis and the fluid-containing cavities must be regarded as a second source. That this process can take place across the ependyma is not dependent for its proof upon the chemical analyses quoted above, for it was empirically demonstrated long ago by Dandy.

Welch emphasized the capacity of the system to produce fluid by pointing out that the rate of formation "in several instances this has come to an amount of fluid each minute almost equal to the weight of the plexus, a performance which rivals the highest rate of reabsorption of glomerular filtrate by the kidney." Bryan and Coe demonstrated that cryogenic destruction of the choroid plexus of the lateral ventricles reduces CSF flow from the cisterna magna by as much as 26%.

The total extracellular fluid volume is some 150 ml within the nervous tissue — a quantity at least equal to, if not in excess of, that of the CSF. When isotopes of normally-occurring CSF electrolytes are introduced into the isolated ventricles and subarachnoid space of patients with ventriculocisternostomy tubes in whom the fluid pressure is normal, disappearance is seen to be a multiple exponential process. These curves may be resolved into fast and slow components. It seems reasonable to attribute the rapid component to equilibration with extracellular fluid, and the slow component to bulk removal from the craniovertebral cavity.

CSF exerts a pressure which is generally greater than atmospheric. As a base-line, we may take the authoritative study of Spina-França on 1,500 human subjects; he found a mean pressure of 119 mm, with a range from 41 mm to 197 mm.

Regular fluctuations in pressure occur with the arterial pulse and with respiration. Under normal conditions, the CSF pressure is independent of the systemic arterial pressure. In normal dogs for a mean CSF pressure of 98.6 mm H_2O, the mean pressure in small subarachnoid veins is 241.1 mm H_2O, which gives a pressure gradient from subarachnoid veins to intradural sinus of at least 165 mm H_2O. It is easy to demonstrate that an increase in cerebral venous volume, achieved through damming back the outflow, increases the rate of removal of an electrolyte from the CSF. Doubtless the arterial pulse, by causing rhythmic variations in cerebrospinal fluid pressure, also aids in driving substances from the fluid into the veins.

Recent evidence suggests that there is a slowing of bulk removal in hydrocephalus; in many adult cases, this may even be the precipitating factor, due to blocking of the drainage mechanisms by subarachnoid haemorrhage or low-grade chronic arachnoiditis. Shulman, Yarnell, and Ransahoff found that in the normal dog, the pressure in the superior sagittal sinus was about 60% of CSF pressure, while torcular venous pressure (effectively extracranial in the dog) was only 30% of CSF pressure. When hydrocephalus was induced, sagittal sinus pressure rose to a level only about 25% below the CSF pressure, but torcular pressure remained at its normal level.

The question of blood flow is of crucial importance in the progression of hydrocephalus. Häggendal et al. using the krypton elimination technique, showed experimentally that there was no change in cerebral blood flow if CSF pressure ranged from −15 to 100 mm Hg; above this level, however, there was an increase in systemic blood pressure and a decrease in cerebral blood flow. Thus, increasing CSF pressure, probably caused in the first instance by defective absorption in non-obstructive cases, produces increased cerebral venous pressure and decreased cerebral blood flow. The resulting ischaemia causes necrosis first of white matter. Later in the course of the disease, the cortex may be more affected than the white matter.

"Spontaneous arrest" of hydrocephalus occurs in a considerable proportion of cases. This can only occur if the rate of formation is reduced to a level quantitatively equal to what the defective absorptive mechanism can deal with.

In conclusion, Bowsher pointed out that the pathological changes in hydrocephalus which affect the leptomeningeal removal mechanisms are probably irreversible; procedures which partially or totally inactivate plexus secretion by pharmacological or surgical means are the best means of restoring a tolerable balance.

Cerebrospinal fluid pressure — Garcia Austt, Carlevaro, Villar and Arana-Iñiguez (Montevideo, Uruguay) discussed the regulation of the cerebros-

pinal fluid pressure. They pointed out that the system containing the CSF is distensible so that a change in CSF pressure is a function of the volume. The compliance of the system is also a function of CSF pressure or volume. Between 10 and 20 mm Hg pressure, the compliance decreases considerably and in the interval 20-80 mm Hg the changes are discret but after 80 mm Hg the compliance increases rapidly.

The mathematical analysis of the temporal course of the recovery curves of induced hypertension demonstrates that when time tends to be infinite the CSF pressure approximates the basal pressure. However, the capacity to compensate for induced hypertension is not infinite as shown by the slow fall of pressure and the high level at which the pressure may remain.

The elements displaced within the cranium in order to compensate for the added volumes, are still a subject of speculation. The displacement of blood has been the factor most frequently referred to in the literature, despite the experiments of Bradford in the dog, in which ligature of all cranial sinuses failed to eliminate the capacity to compensate for an induced hypertension. On the other hand, the brain, as such, is ruled out as an element subject to displacement. Other possible factors include a decrease of blood supply through an active vasoconstriction of mechanical compression of the vessels. Lastly, an alteration in the balance of CSF production and resorption at the expense of a decrease in the former and an increase of the latter may represent a contributory factor. The non-displaceable volume in the supratentorial compartment tends to shift the brain to the infratentorial compartment so that stresses act upon the brainstem where the autonomic centers are located. Anatomical study of displacements invariably show tentorial herniations of the occipital lobe compressing and deflecting the brainstem.

The existence of a critical threshold value for the displacements is compatible with the rheologic nature of the process, since it is known that the flow of materials which are not merely viscous (newtonians) but simultaneously plastic and viscous, require, before actually occurring, the existence of an effective pressure value, the "yield pressure".

Raised CSF pressure always decreased $p^0 2$. Both curves were similar in shape but opposite in direction. When CSF pressure was dropped to its previous level by abruptly diminishing the volume in the balloon, the $p^0 2$ often attained values even higher (over-shoot) than those it had shown for normal fluid pressure, returning to the latter within a few minutes. The records of oxygen pressure in the brainstem were similar to that described for the cortex during induced hypertension, except that they never returned to the previous levels while the balloon was distended. Therefore, assuming that the systemic arterial pressure and $p^0 2$ remained constant, there are two possibilities to explain the decrease of brain $p^0 2$ observed during intracranial hypertension: (*1*) an increase O_2 utilization; and (*2*) a decrease in blood flow. There is no available evidence to support an increase in cellular consumption. Hence, a decrease in brain blood flow can be assumed. This decrease in flow should tentatively be considered due to direct compression

of the vessels — particularly the veins — with consequent increase of vascular resistance.

Compliance in man is considerably higher than in cats, a feature which tended to return to the value of the basal pressure P_b.

In order to obtain in a simple manner, clinically useful quantitative data, the measurement of the semiregulation time T½ is advocated. This measurement may be accomplished with a manometer and a chronometer, and does not entail a more complex procedure than the routine measurement of CSF pressure. It does, however, yield far more accurate data, for the T½ can be increased during the early stage of an expanding process, when only unspecific focal symptoms are present, without clinical, ophtalmological or spinal fluid evidence of intracranial hypertension. Under these conditions a T½ greater than 60 sec is highly suggestive of a space-occupying lesion.

HYDROCEPHALUS

The second half of the the Symposium on Cerebrospinal Fluid was devoted to the discussion of hydrocephalus. The clinical manifestations of this disorder were much better agreed upon than the pathogenesis of the condition.

Clinical manifestations — C. Carrea and C. Peske (Buenos Aires, Argentina) analysed the clinical features of 577 cases selected from a larger series of patients having various types of hydrocephalus. The great majority of these individuals were seen in the first year of life. The sex distribution was about equal. There did not seem to be a significant increase in malformations in the family as compared to those in the normal population. Even patients suffering from hydrocephalus rarely had other congenital abnormalities. However, the socioeconomic status of the parents of the involved children was definitely lower than average. The delivery was normal in 77% of cases, pathological in 11% and by cesarean section in 12%. Some type of infection preceded the onset of hydrocephalic symptoms in many cases; these involved the central nervous in 10% of the cases, the respiratory system in 4% and other systems less commonly.

The clinical manifestations of hydrocephalus relate to the shape of the head, the size of the anterior fontanelle, the presence of a cracked pot sound and the velocity of head growth. The neurological abnormalities found in patients suffering from hydrocephalus include particularly oculomotor palsies and occasionally convulsions. The intelligence quotient correlates with the thickness of the cerebral mantle and the size of the head. Spinal fluid examinations rarely gives useful information. A comparison of the history of hydrocephalics treated surgically and those not operated upon seems to indicate that the surgically treated patients not only live longer but have a significantly higher intelligence quotient.

Mechanisms of hydrocephalus — S. Hakim (Bogotá, Colombia) in discussing the mechanisms producing hydrocephalus, emphasized that the brain

tissue or parenchyma is subjected to two opposing forces; one produced by the CSF system, tending to enlarge the ventricle, and the other originating from the venous system which tends to reduce the ventricle size.

The force produced by the CSF system is the product of the mean time average CSF pressure and the mean effective surface, related to ventricle area. The opposing force exercised by the venous system is the product of the mean time average venous pressure and the mean effective area of the veins within the parenchyma. Between the venous and CSF systems lies the viscoelastic cerebral tissue. Any imbalance between these forces will manifest itself by stresses and movement of the viscoelastic brain tissue.

Confirmation of the interdependence of CSF and venous systems in hydrocephalus, is that in cases of venous cerebral thrombosis there is an increase in CSF pressure but no enlargement of the ventricles, the effects of increased venous pressure in this case "balancing off" the effects of increased CSF pressure. The main variables influencing hydrocephalus are: *1*) CSF pressure; *2*) venous pressure; *3*) ventricle area; *4*) venous area; *5*) mechanical properties of the cerebral tissue.

The effective force developed on the CSF side of the model is larger than the opposing force generated in the venous side. The mechanical spring-damper system, representing the brain tissue, is therefore displaced due to the imbalance of the two forces. Two important consequences result from this movement; firstly, the effective operational area of CSF piston increases thereby destroying the balance between the two sides; second, the venous system collapses, represented by the piston reaching the end of its travel, in order to accommodate the larger ventricular volume. This condition will continue while the CSF pressure is maintained high, and with the subsequent dilatation of the ventricles, the brain tissue will be stretched while the venous and capillary vessels in the parenchyma are compressed. Once the ventricles have been expanded, they have a tendency to remain dilated and the neurological and mental symptoms remain despite the return of the CSF pressure to normal.

It is surprising to see the clinical and pneumoencephalographic improvement of many cases that have been operated upon after a lengthy period with normal pressure hydrocephalus. The brain tissue recovers its lipids and proteins and the ventricles return to their normal size. In many cases with such patients it is possible to remove the ventriculo-atrial shunt after a complete recovery because equilibrium has been restored between vascular and CSF systems.

T. H. Milhorat (Washington DC, U.S.A.) has developed a simple and effective technique for producing obstructive hydrocephalus in monkeys. It consists of inserting a 8 Foley catheter through the foramen of Magendie until it abuts the caudal end of the aqueduct of Sylvius and the balloon is inflated so as to occlude the 4th ventricle. A highly consistent, but surprising finding was the observation that hydrocephalus can occur as an acute, fulminating process. Acute hydrocephalus may be a possible complication of any of the following conditions: acute head injury, spontaneous

subarachnoid hemorrhage, acute exudative meningitis, intracerebral or intracerebellar hemorrhage, sudden decompensation of tumors bordering the ventricular system, and acute obstruction of functioning ventricular shunts.

The ventricular system enlarges rapidly following complete ventricular obstruction. Within 3-6 hours, however, this rate slows abruptly and continues to decrease, until by 2-3 days, a chronically progressive rate being established. At 3 hours, for example, the stretched and flattened ependymal epithelium developed rents and tears, most apparent at the angles of the lateral ventricles, surrounding the ventricles, and most pronounced adjacent to areas of severe ependymal damage, edema of the white matter was noted. Subsequent to the appearance of edema in the white matter, a progressive loss of white matter occurred which was largely the result of glial cell loss. Axonal swelling and demyelinization were minimal (even up to 3 weeks) suggesting that neurons and their axons are unusually resistant to the combined forces of edema, tissue ischemia, and increased intraventricular pressure.

A significant increase in ventricular permeability was found as soon as pathological changes in the ependyma became apparent (3-6 hours) and the permeability was greatest at points of severe ependymal damage. At the angles of the lateral ventricles, a variety of tracers, normally excluded from the brain parenchyma, penetrated into the dephts of the white matter within 30-40 minutes. These observations suggest that in hydrocephalus, increased intraventricular pressure, acting in concert with the pathological changes in the ventricular wall, results in a flow of CSF out of the ventricles at the points of least resistance. On the basis of the pathological findings just presented, it is apparent that "acute hydrocephalus" and "chronic hydrocephalus" are quite different clinicopathologic conditions. The problem of acute shunt failure is a surgical emergency. The rationale for this approach is to limit, to the extent possible, the rapid destructive changes of acute hydrocephalus. In view of the greatly increased permeability of the ventricular surface in hydrocephalus, it might be asked whether diagnostic techniques that require the injection of foreign substances directly into the ventricles, are altogether innocuous. It would seem that diversion of ventricular fluid into the subarachnoid space would not only bypass the obstruction, but would serve to re-establish normal routes of CSF flow.

Following ventricular obstruction in monkeys, a secondary obstruction of the subarachnoid space rapidly ensued. Within 12-18 hours the cerebral gyri were usually flattened, the cerebral sulci were considerably narrowed, and the surface subarachnoid space was mechanically obliterated. Somewhat later, the basilar cisterns were obstructed by impaction of the temporal lobes through the incisura of the tentorium. Following effective ventricular shunting, considerable re-expansion of the space can frequently be achieved. Prolonged compression of the subarachnoid space, as well as a variety of other insults, can result in a chronic fibrosis of the distal subarachnoid pathways. In both plexectomized and non-plexectomized animals, ventriculo-aqueductal perfusions with C^{14}-inulin were performed with the following results: *a*) the CSF production in bilaterally plexectomized animals was

reduced by 26%; *b*) the composition of CSF in plexectomized and non-plexectomized groups was essentially the same; *c*) it was estimated — allowing that the choroid plexus of the 3rd ventricle produces fluid in proportion to its size and weight — that the combined plexuses of the lateral and third ventricles form less than 1/3rd of the CSF produced rostral to the 4th ventricle. In a large number of plexectomized animals, ventricular obstructions were subsequently performed. Hydrocephalus occurred in all cases, and the extent of the ventricular enlargement was found to be only slightly less advanced than that occurring in non-plexectomized animals with similar obstructions of the same duration. Milhorat concluded therefore, that hydrocephalus can occur rapidly and progressively in the plexectomized ventricular system, and that the choroid plexus is not essential either as a source of ventricular fluid, or as a pulsatile mechanism for expanding the ventricle in hydrocephalus.

Radioactive scanning in hydrocephalus — The value of radioactive scanning in hydrocephalic states was discussed by Giovanni Di Chiro (Bethesda, U.S.A.). For radioisotopic cisternography and myelography, radioactive tracers are injected by lumbar or suboccipital puncture, while radio-pharmaceuticals are introduced directly into the ventricular system for ventriculography. More than 25 different radioactive agents and both rectilinear scanners and cameras have been used for CSF scanning.

The indications of CSF scanning include: (*1*) hydrocephalus in its various forms, communicating (normo- and hyper-tensive) and non-communicating; (*2*) cerebrospinal fluid rhino- and otorrhea; (*3*) leptomeningeal cysts; (*4*) porencephaly; (*5*) *pseudotumor cerebri;* (*6*) patency evaluation of neurosurgical shunts; (*7*) spontaneous ventriculostomy; (*8*) spinal blocks and space-occupying lesions; and (*9*) congenital malformations (Arnold-Chiari, Dandy-Walker).

In the hydrocephalic patient cisternography can offer information regarding differential diagnosis between communicating hydrocephalus and so-called hydrocephalus ex-vacuo.

A wide variety of cisternographic findings are encountered in communicating hydrocephalus. A block, that is, the failure of the ascending radiopharmaceutical to pass beyond the obstructed area, is undoubtedly the most important finding. The block is usually symmetrical, although in some cases the tracer ascends more cranially on one side than on the other. The subarachnoidal spaces proximal to the obstruction are often wider than in normal cases. The block may be total, but frequently it is partial or subtotal. That is, the radiopharmaceutical, after a period of arrest at a certain level, enventually passes beyond the obstruction, moving upward with a somewhat delayed flow toward the convexity of the brain.

A second very important finding is intraventricular penetration of the tracer. As noted above, no intraventricular penetration of the tagged albumin is recognizable in normal cisternograms. Intraventricular penetration may occur together with, but also without, subarachnoid block. A clear-cut

positive radioisotope cisternographic syndrome consists of early (2 to 3 hours) intraventricular penetration of the tracer, with long-standing (24, 36, 48, 72 hours) intraventricular stasis and no passage of the radiopharmaceutical above and beyond the dilated cisterns around the brain stem. The chances that improvement, sometimes dramatic, will follow the establishment of a CSF shunting procedure with the above described cisternographic syndrome, are very good. Occasionally a very slow flow of the radiopharmaceutical may be the dominant or the only pathologic finding. In a few cases, the upward spread of the tracer is totally blocked with arrest in the cisterns around the brain stem and no intraventricular penetration. This last picture is found only in association with increased intracranial pressure and never in normotensive hydrocephalus.

As with other diagnostic methods, the negative cisternogram may be very valuable in the management of the patient. The negative cisternogram rules out the necessity or advisability of a CSF shunting procedure. A patient who presents a characteristic cisternographic syndrome of communicating hydrocephalus, may fail to improve with a shunting because of traumatic involvement or vascular impairment of the nervous system structures.

Communicating hydrocephalus may also be studied by radioisotope ventriculography, since as soon as the tracer that has been injected into the ventricular system flows out of the fourth ventricle, it ascends superiorly in a fashion essentially identical with that observed with cisternography.

Radioisotope ventriculography can offer valuable information in cases of non-communicating (obstructive) hydrocephalus. The anatomic detail that can be visualized by scanning is not comparable with that shown by air ventriculography but the site of the obstruction and the degree of dilatation of the ventricular system are quite satisfactorily demonstrated.

Radioisotope cisternography may also offer useful information in cases of noncommunicating hydrocephalus. Here, one may appraise the patency of the subarachnoidal spaces, which is important in deciding what type of shunting procedure will be most suitable for a specific case.

Di Chiro asks "Why does the tracer penetrate into the ventricular system in certain pathological conditions?" Recent data after experimental and clinical choroid plexectomy would indicate (as it had already been postulated before) that at a certain stage in the development of hydrocephalus, the choroid plexus stops producing CSF and, reversing one of its functions, starts resorbing it. These elements are probably the important factors to explain, possibly on the basis of a CSF gradient, the intriguing phenomenon of the intraventricular penetration.

Shunts for hydrocephalus — Martin P. Sayers (Columbus, U.S.A.) presented his views on shunting for hydrocephalus. He stated that the great hope for a large percentage of the children with obstrutive hydrocephalus lies in finding a successful method of connecting their ventricles with a relatively normal area of absorptive subarachnoid space. A number of investigators have shown that under normal circumstances almost as much fluid is formed in a unit of time in the subarachnoid spaces as in the ventricles.

Thus, in children with obstructive hydrocephalus some degree of extraventricular spinal fluid circulation exists even with basal arachnoiditis or aqueductal stenosis. The institution and maintenance of adequate ventricular shunting seems in most cases to encourage improvement in this external circulation as time passes in that the intraventricular pressure is consistently reduced, thus allowing the brain "to hang slack" and encouraging the subarachnoid fluid to find its way more easily through gradually enlarging subarachnoid pathways, that is, to "force" the subarachnoid space.

Spontaneous compensation occurs after shunt in at least 20% of noncommunicating and 40% of communicating hydrocephalus even without benefit of surgical ventriculostomy. This is of course to be expected particularly in the post infectious and in the post hemorrhagic categories. When discussing treatment for hydrocephalus it is always important to stress that it is not the large ventricles but the *progressive* hydrocephalus which is treated.

Approximately 70% of the proven hydrocephalic children presented for study have been shunted. The major contraindication to immediate shunt has proved to be prior compensation despite large head and/or large ventricles. Many times this judgement requires a period of observation unless the child is obviously in jeopardy due to excessive intracranial pressure. Every neurosurgeon's experience indicates that both neonatal and older children can tolerate relatively elevated intracranial pressure and ventricular distention for short periods without developing detectable brain damage or loss of intellectual potential. Another contraindication to surgery is extreme brain thinning and demonstrable excessive brain damage as manifested by inability to cry or suck, and excessive spasticity or extreme hypotonia. Hydroanencephaly is a contraindication for shunting. In older children it is preferable not to shunt or reshunt and prolong life of a child with no useful intellect, but such shunts may be made at the strong request of sincere families. Spinal fluid and blood infections require delay of surgery until the infection is controlled and the child can be re-evaluated. A final contraindication is the presence of multiple malformations, one or more of which seemed to preclude satisfactory survival.

Ventriculo-vascular shunt is preferred over ventriculo-cisternostomy because: (*1*) higher degree of reliability; (*2*) ease of surgery; (*3*) reduced morbidity; and (*4*) avoidance of arachnoiditis at the critical basal subarachnoid spaces. The Holter valve with very small highly refined silastic cervical and thoracic catheters is mounted high and posteriorly over the parieto-occipital skull to allow a maximum length of very flexibe catheter between the lower end of the valve and the fixation point on the internal jugular vein. The distal end of the catheter is always installed deep in the right auricle, and because of its small diameter causes no demonstrable embolization or tendency to develop pulmonary hypertension. The incidence of septicemia is materially reduced by (*1*) soaking the shunt apparatus in Bacitracin-Neomycin solution for one hour preoperatively; and (*2*) by the reduced intravascular mass of foreign material. Loss of the thoracic catheter into the

mediastinum is prevented by a few millimeters of swedged on 2.4 mm catheter at the point of attachment and entrance into the vein. When thoracic revision of the shunt becomes necessary the right internal jugular vein may be used and re-used as long as possible. The right external jugular vein is then used before the shunt is moved to the left side of the head.

It is not necessary to carry out *routine* shunt revisions. At least 40% of the obstructive hydrocephalics (largely in the myelomeningocele category) do not require a revision after the initial shunt. If there is no revision in a four year period it is relatively safe to assume that the child has become independent.

If a child requires two or more shunt revisions for other than post-operative complications, it is felt that he is and probably will remain shunt dependent unless a new route for spinal fluid disposal can be established; this has been accomplished by anterior and posterior third ventriculostomies on 46 of these shunt dependent children. Since 1968, 28 or more have been performed percutaneously with no operative mortality. Subsequently 2 of these children have died, one from pulmonary embolus after a fractured femur and the other with Arnold-Chiari malformation but without ventricular enlargement or increased intracranial pressure. Just one patient in this series of 43 surviving children has required an additional shunt revision up to the present time.

The key to sucess with this procedure has been a period of successful shunting preoperatively to allow growth of the subarachnoid space and the completion of a successful low pressure shunt just prior to the ventriculostomy. It is relatively easy to keep the fistulas open with the lowest possible intraventricular pressure while the CSF is establishing a new absorptive pathway.

Percutaneous stereotaxic ventriculostomies have the advantage of: (*1*) considerably less morbidity; (*2*) less disturbance of the normal subarachnoid relationships; (*3*) briefer operating time; (*4*) less expense and very small scars. They are made by means of small stab wounds in the scalp and twist drill openings in the skull and dura. Using fluoroscopic image amplification a McKinney leukotome is then introduced through the forehead to the midline lamina terminalis below the anterior communicating artery and into the 3rd ventricle. The loop is opened downward and withdrawn from the ventricle making a 9-12 mm opening in the anterior wall of the ventricle. The leukotome is then reintroduced at a point 2-3 cm to the right of the midline through the skull near the coronal suture so that its course is parallel to the plane of the clivus and directed at the mid dorsum sella. The leukotome slides posteriorly off the dorsum sella, passes through the floor of the 3rd ventricle approximately between the mamillary bodies and into the interpeduncular and basilar cisterns. The loop is then opened toward the dorsum sella and drawn back into the 3rd ventricle, reduced and withdrawn.

Occasionally it is encountered bleeding from a twist drill opening, but Martin P. Sayers has not yet had a return of bloody fluid from the 3rd

ventricle through the leukotome. One child developed a transient lateral rectus eye muscle weakness which subsided in one week. Most children are somewhat drowsy and irritable on the first postoperative day but play in the corridors on the second and go home on the third or fourth postoperative day.

The percutaneous procedure is carried out only on children with moderately large ventricles after careful preoperative localization of the ventricles. The inferior extent of the third ventricle is highly variable, but in most children with moderately advanced hydrocephalus, lies atop of the sella turcica.

The outlook for the patient with obstructive hydrocephalus has improved steadily throughout the first seventy years of the twentieth century. Recent expericence with the later course of children with myelomeningocele and hydrocephalus complicated by late Arnold-Chiari malformation and an overfull posterior fossa suggest the need for very early assistance in regulating the growth of the middle and posterior fossas in the children. Possibly earlier ventriculostomy may help to prevent this very crippling and occasionally lethal malformation.

Anterior and posterior third ventriculostomy can provide a biological substitute for continued renewal of mechanical CSF shunting devices.

FINAL CRITIQUE

E. Bering (Bethesda, U.S.A.) analysed the material presented by the brilliant investigators from all parts of the world. He emphasized the many points which the discussion had clarified. However, it was obvious that the Symposium pointed to the need of further anatomical studies to explain the discrepancies in observations made on different species of animals. Emphasis on enzyme chemical studies of choroid plexus and pacchionian granulations might resolve some of the difficulties for both of these structures require high energy supplies. The biochemical phenomena related to the CSF, thanks to the work of Davson, Pappenheimer and others, seems to be better understood than some of the other aspects. There are many obvious gaps in our knowledge of hydrocephalus, both as to its mechanisms and as to its treatment. The use of radioisotopes has brought out clearly some of our lack of insight into the dynamic changes which occur in hydrocephalus. Cisternal scans, although of considerable diagnostic value, are also, at times, quite confusing and fail to give the crucial information needed for the instigation of therapeutic endeavors. Finally, the mechanisms by which shunts in some cases produce miraculous cures and, in other cases, miserable failures, is quite unknown. Studies of the absorptive capabilities of the arachnoid system, part of a diagnostic workup , probably should be repeated at intervals postoperatively in all cases to determine what the shunt has effected.

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