

EXPERIMENTAL STUDIES ON FLOW OF CEREBROSPINAL FLUID IN SPINAL SUBARACHNOID SPACE

By

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I. INTRODUCTION

Production, absorption and flow of the cerebrospinal fluid (CSF) have hitherto been energetically studied by various investigators and much knowledge thereof has been accumulated. Notwithstanding we do not yet have unanimous conclusions on these subjects. In the early years of the present century CUSHING¹⁾, DANDY²⁾³⁾ and others reported the production of CSF at the choroid plexus inside the ventricles, while KEY and RETZIUS⁴⁾, WEED⁵⁾, DANDY⁶⁾ and others described the course of its absorption into the venous or lymphatic system. At present it is popularly believed, as FOERSTER⁷⁾, DANDY⁸⁾ and ARAKI⁹⁾ describe, that CSF is produced in the ventricular system and flows through the cisterna magna to the basilar cistern and further to the subarachnoid space of the cerebral convexity for the most part and partly to the spinal subarachnoid space. However, this theory has by no means been accepted by everyone without objection. For instance, HASSIN¹⁰⁾¹¹⁾ insisted from the pathological point of view that CSF was a kind of tissue fluid in the brain and that the choroid plexus participated also in its absorption. WALLACE et al¹²⁾ threw strong doubt upon ventricular origin of CSF from the standpoint of pharmacology. SCHALTENBRAND¹³⁾ supported an opinion that not only the choroid plexus but also the ependyma and vessels in the subarachnoid space participated both in production and absorption of CSF. Since isotope studies made their appearance in this field recently, results of investigations have successively been reported which make us doubt correctness of the popular view described above concerning production, absorption and flow of CSF. Making use of D₂O and other isotopes, BERING^{14)~16)}, SWEET¹⁷⁾¹⁸⁾, GREENBERG¹⁹⁾, ADAMS²⁰⁾ and others discovered that exchanges of water and electrolytes across the blood-CSF barrier took place at every part of the ventricular system and of the subarachnoid space at an almost identical rate. Disagreement in opinion is especially marked in regard to dynamic state of CSF in the spinal subarachnoid space (SSS). SCHALTENBRAND²¹⁾ supposed that there was a CSF flow in the caudal direction along the dorsal surface of the spinal cord and a flow in the cranial direction along its ventral surface. According to him, there is an anatomical fact supporting his view, i. e. "die Anordnung der arachnoidalen Segel". On the other hand KONNO²²⁾ and MORITA et al²³⁾, using P³² or I¹³¹ as an indicator, obtained a conclusion that there might be little flow of CSF in SSS. Making use of Na²⁴, EICHLER²⁴⁾ attained to a

conclusion that there was a secondary site of CSF production in the lumbar subarachnoid space and that CSF flowed from the caudal to the cranial portion of SSS. Strict and definite verification of the sites of production and absorption of CSF is of course very important, but it is extremely difficult. On the other hand, if we fix our attention to the dynamic state of CSF in SSS, we shall find that the following problem is of no less importance: is there any basic flow of CSF in SSS, if it may be extremely slow, or is there not any basic flow at all? The importance of this problem, in connection with various diagnostic and therapeutic problems, such as etiology and treatment of hydrocephalus, lumbar anesthesia, surgery of the spinal cord, etc., urged me to obtain a correct solution.

As the first step experimentation with a radioisotope has been done to inquire whether the negativistic view on CSF flow in SSS has a correct basis or not. As the next step attempt has been made of experimental direct demonstration of the presence, if any, of CSF flow in SSS in a strict sense. At the same time, influences of various factors on dynamics of CSF and effects of hydrostatic and osmotic pressures on the ability of water absorption in SSS have been examined.

II. MATERIALS, METHODS AND RESULTS

1. Production of chronic and acute blocks in SSS of dogs

Adult mongrels weighing about from 8 to 14 kg were used. Under Ravonal (pentothal sodium) anesthesia laminectomy was performed at the second cervical vertebra (C2), a short longitudinal incision was made at the dura, the spinal cord thus exposed was completely encircled with a strip of gelatine sponge or a string made from arginic acid, and finally sterilized kaolin solution (2g/dl) was injected into SSS in the same region for the purpose of facilitating a formation of adhesion. This kind of operative procedure at such a high cervical level as C2 was apt to produce necrosis of the spinal cord due to compression and there was much fatality from respiratory arrest or general weakness in dogs in which the dura was sutured. To avoid such a risk it was made a routine procedure to leave the dura open and to stuff its defect with muscles, expecting a repair with connective tissues. Its result was found to be excellent. Effects of a gelatine sponge and an arginic acid string as agents producing blocks in the subarachnoid space have already been reported by NISHIMURA²⁵⁾ and TOMITA²⁶⁾. Actual formation of a block in each dog was verified by autopsy. The spinal cord was excised together with the dura for a length of about 10 cm including its blocked portion as well as its cranial and caudal parts, and degree of the blockade was tested by pouring colored fluid into the subarachnoid space. When the blockade was found to be incomplete in a dog, all experimental data obtained in that animal were abandoned.

In a similar way chronic blocks were produced in dogs either at a level of the third thoracic vertebra (Th3), the first lumbar vertebra (L1) or at the caudal end portion of the subarachnoid space.

An acute block was produced as follows. After the dura was exposed by means of laminectomy a No. 6 silk suture was passed epidurally to make a complete turn

around the cord. An acute block of SSS was produced by straining the suture. When this procedure was performed at the level of C2, artificial respiration was carried out combinedly. Since reduction in volume of breathing air induced rapid rise in CSF pressure, much care was taken of maintaining a respiration rate of 24 per minute, or a total breathing volume of about 10 l of air per minute.

In all cases general anesthesia was maintained throughout experimental procedures by means of intravenous and, if necessary, intramuscular injections of Ravonal. Depth of anesthesia was measured according to the method of Magnus-Girndt-Sakamoto, but in reality it was very difficult to keep the depth constantly at the second phase of the third stage and some degree of its fluctuation was inevitable.

2. Preliminary experiments on insertion of a polyethylene tube into the subarachnoid space and on changes in CSF pressure after partial removal of the fluid

In the processes of observing dynamic aspects of CSF and of experimentation with P^{32} , on which description will be made later, it was necessary to conduct CSF outward from SSS, strictly avoiding its leakage. For this end a polyethylene tube was inserted into SSS according to the following procedure. After exposure of the dura in the region of the cisterna magna or of the lumbar cistern, a small hole was produced in the dura with an injection needle and immediately a tip of a polyethylene tube, which had previously been cut sharp, was inserted into SSS expanding the small hole of the dura by force. The tube was then fixed loosely to soft part tissues within the operation field in order to prevent its tip from moving.

If possible flow of CSF in SSS is very slow, any minute leakage of CSF will mislead the conclusion. To exclude such an artefact 0.5% bromsulphalein solution was poured into the polyethylene tube at the end of all experimental procedures and, in bringing the region adjacent to the site of tube insertion to alkalinity, presence or absence of CSF leakage was checked up by means of positive or negative colorization. In case any faint colorization was found all experimental data obtained in that animal were abandoned.

The polyethylene tube used here was about 0.6 mm in its internal diameter and a water column as long as 24 cm was formed by pouring 0.1 cc of water into it.

In order to observe dynamic aspects of CSF by means of such tubing as described above, the tube had to be filled with CSF in the first place. Thus it was inevitable that a certain amount (about 0.5 cc) of CSF was made to flow out at the beginning. However such an outflow may immediately cause reduction in CSF pressure and, furthermore, may strongly influence dynamic state of CSF. For this reason following preliminary experiment was performed.

A polyethylene tube with an internal diameter of 3 mm, to one end of which an injection needle was attached, was used as a manometer. By inserting the needle into the cisterna magna CSF was made to flow out into the tube and time course of recovery of CSF pressure, from a reduced value due to the outflow to the control value, was followed. Results of the experiment are shown in Fig. 1. Both dogs having acute blocks and those having chronic blocks showed initial pressure of about from 50 to 60 mm H₂O. Here the amount of CSF which flowed out into the tube

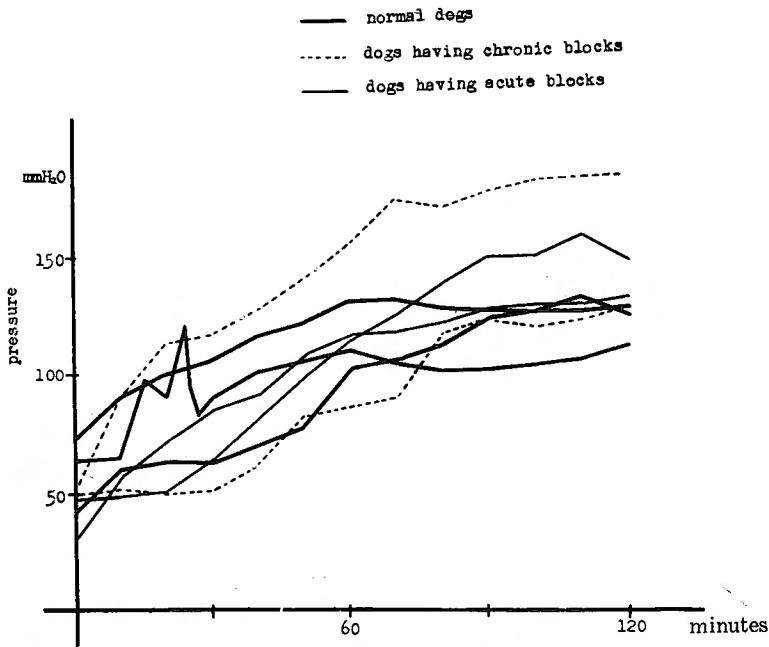


Fig. 1 Changes in CSF pressure.

was about 0.5 cc. This is an amount enough to fill a polyethylene tube (with an inner diameter of about 0.6 mm) as long as 120 cm. The CSF pressure then rose in drawing an arc and reached a plateau in about one and a half hour. As a control similar experiment was performed in normal dogs having no blocks and results similar to those shown above were obtained. Accordingly, in all the experiments in which installation of a polyethylene tube about 120 cm long was done, measurement was started after lapse of a stabilizing period of one and a half hour following the installation.

3. Measurement of the rate of substance exchange across the blood-CSF barrier by means of radioisotope P^{32}

It may be supposed that the attitude of the phosphor ion can never represent the attitude of CSF as a whole. However, in order to obtain a rough information on the rate of substance exchange across the blood-CSF barrier, it is convenient to use P^{32} as an indicator, since it is easily obtainable and its treatment is relatively simple. Thus P^{32} was used in the present experiment and the radioactivity was measured with a Geiger-Mueller probe.

At first P^{32} dissolved in physiological saline solution was injected into a leg vein of each of several dogs having acute or chronic blocks in SSS at a dose of $20\mu\text{c}$ per kg of body weight, for the purpose of examining transference of P^{32} from the blood to CSF. To obtain specimens of CSF two polyethylene tubes were installed according to the method described above, one in the region of the cisterna magna and the other in the region of the lumbar cistern. Two drops of CSF from each of these two sources were obtained periodically as specimens, beginning 5 minutes

after the injection and lasting for from 4 to 6 hours. In order to know changes in P^{32} density in the blood, 0.25 cc of the blood was obtained periodically from a vein of a limb other than that at which P^{32} had been injected. Results of counting in these specimens are shown in Table 1 and Fig. 2. In all the dogs having blocks in SSS, both CSF from the cisterna magna and that from the lumbar cistern showed radioactivity very early after the injection. The density reached a peak from 20 to 30 minutes after the injection, diminishing thereafter gradually. Thus the speed

Table. 1 Transference of P^{32} from the blood to CSF in dogs having blocks at the level of Th3.

B : count per minute in the blood
C : count in CSF of the cisterna magna
L : count in CSF of the lumbar cistern
min. : minute after injection

min.	acute block						chronic block					
	20 μ c/kg			⊙ 20 μ c/kg			10 μ c/kg			20 μ c/kg		
	B	C	L	B	C	L	B	C	L	B	C	L
3		10			10		2970	0		7900		
5	8250		20	5650		30			40		20	10
7		22			30			10			30	10
9	3980			2130		40	1480		60	4100		60
11			40								60	
13												110
15		130	120		120	110	1040	40	100	3300	80	
20		170	180		150						130	140
25	1850			1510		130		40	120			
30		190	190		80	40	500	30	120	870	140	130
40	700			560						650	135	
60	520	80 110	80	380	80	70	430	20	70	500	60 90	70
90	400	50	50		40	30		10		460	40	
120		40		300	40	30	260	20	20	340	30	10
150	370	40	40		30	40		10				
180		40		250	30	20	240	10				
210	320	40	40		30			0				
240		30		260	30	10	240	0				
270	320	30	40		10			0	10			
300		40		240	10	20	240	10				
330	290	20	20		30			10	10			
360		30		230	20	20	210	0				

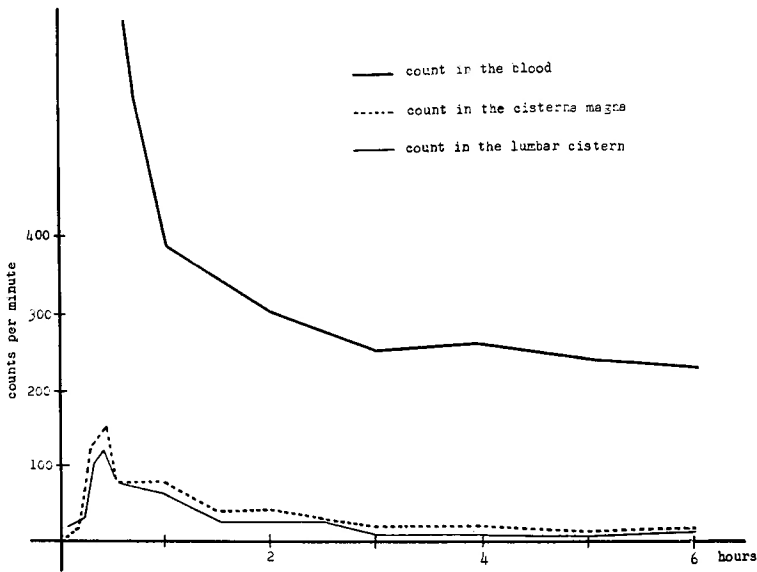


Fig. 2 Transference of P^{32} from the blood to CSF following its intravenous administration at a dose of $20\mu\text{c}/\text{kg}$, in a dog having a block at Th3. (corresponding to the case marked with © in Table 1.)

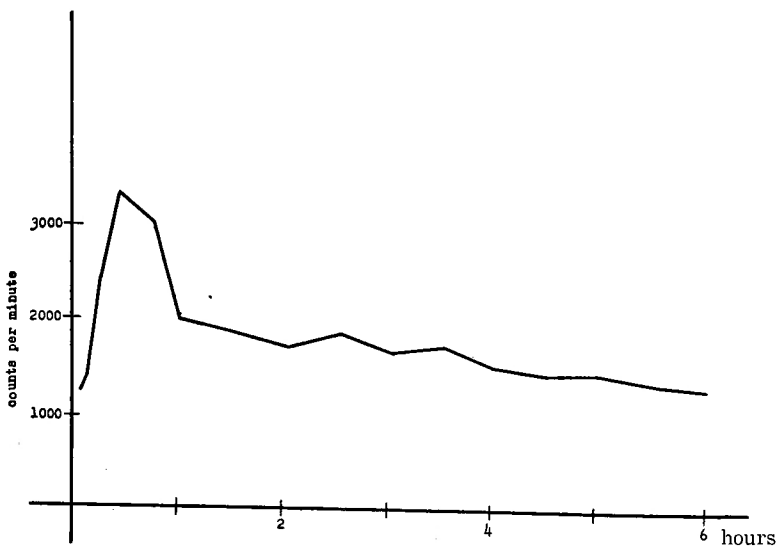


Fig. 3 Transference of P^{32} from CSF to blood following its administration into the lumbar cistern at a dose of $60\mu\text{c}/\text{kg}$, in a dog having a block at Th3. (corresponding to the case marked with © in Table 2.)

of P^{32} exchange across the blood-CSF barrier seemed to be very large both in the CSF space cranial to the block and in the space caudal to it. Already from 20 to 30 minutes after the injection, the density of P^{32} in CSF seemed to equilibrate with

its density in the blood showing a certain constant ratio. Its density in CSF was likely to diminish thereafter in parallel with that in the blood. In dogs with chronic blocks, CSF in the lumbar cistern was small in its total amount and showed the characteristics of "Sperri liquor". Nevertheless, the curves of P^{32} density in CSF in those animals showed similar characteristics to those in dogs having acute blocks (if absolute P^{32} density is not taken into consideration). It is thus worthy of note that P^{32} appears in lumbar CSF as early as cisternal CSF even in dogs with chronic blocks.

Speed of transference of P^{32} from CSF to the blood was next examined. P^{32} dissolved in physiological saline solution was injected into the lumbar cisterns of dogs having chronic blocks at a dose of about $20 \mu\text{c}$ per kg of body weight, and about 0.25 cc of the blood was periodically obtained from a leg vein. Results of counting are shown in Table 2 and Fig. 3. P^{32} injected into the lumbar cistern made an appearance in the blood early after the injection, reached a peak of density from 30 to 40 minutes after the injection and diminished its density gradually thereafter. P^{32} appeared in the blood as early in dogs having chronic blocks as in those having acute blocks

and there was no marked difference in time to peak between these two groups. It is supposed that radioactivity in CSF of the lumbar cistern, into which P^{32} had been injected, might diminish following a logarithmic curve, but its measurement was not performed, because extraction of a little amount of CSF from the cistern where total CSF present was small in amount, would cause a serious change in dose of P^{32} injected. After all, transference of P^{32} from CSF in the lumbar cistern to the blood is also rapid and shows a curve similar in form and in time to peak to that of transference of P^{32} from the blood to CSF until the peak is reached. On the other hand the speed of diminution after the peak is relatively small in the former case as compared with the latter.

In conclusion, it has been verified that exchange of P^{32} across the blood-CSF

Table 2 Transference of P^{32} from lumbar CSF to the blood in dogs having blocks at the level of Th3.

minute after injection	acute block		chronic block	
	$40 \mu\text{c}/\text{kg}$	$20 \mu\text{c}/\text{kg}$	$60 \mu\text{c}/\text{kg}$	$20 \mu\text{c}/\text{kg}$
3	100		1400	
5		140		
7	330		1450	
9	620			210
11				
13	680			
15	790	240	2560	
20	1130			340
25			3260	
30	1150	420		720
40	1080	525	2990	
60	970	370	1960	580
90	870	420	1840	410
120	860	460	1730	550
150	840	470	1820	550
180		400	1620	530
210	830	370	1760	590
240		400	1500	400
270		360	1400	400
300		390	1400	420
330		360	1350	410
360		370	1210	430

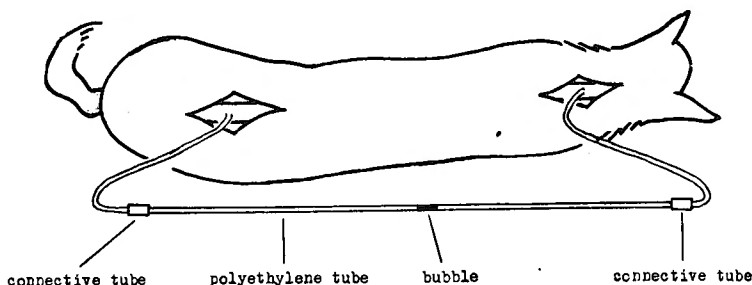


Fig. 4

barrier is rapid and that it takes place at a grossly identical rate on both the cranial and the caudal sides of the blockade, as have already been reported by various authors.

4. Experimental investigation on dynamic aspects of CSF

A dog having an acute or a chronic block in SSS was laid on its side under intravenous Ravonal anesthesia and the cisterna magna and the lumbar cistern were interconnected with a polyethylene tube about 120 cm long, as shown in Fig. 4. Prior to completion of the interconnection CSF in the cisterna magna was made to flow out to fill the tube, of which one end had previously been inserted into that cistern and which had an intervening short rubber tube at the portion about 10 cm distant from the cistern, and the other end of the tube was connected with another polyethylene tube about 10 cm long, of which one end had previously been inserted into the lumbar cistern and which had been filled with CSF, with a help of another short intervening rubber tube. Into the cranially located rubber tube a small amount of air was injected to form a bubble of about 2 mm in longitudinal diameter. This bubble cut the column of CSF inside the tube into two parts, cranial and caudal, and its movements were used as an index of CSF flow. In view of the result of the preliminary experiment that one and a half hour was necessary to obtain the stability of CSF pressure, an air bubble was formed in the tube after lapse of one and a half hour following the installation of the tube. Movements of the bubble were recorded repeatedly with an interval of 10 minutes and from results obtained the speed of CSF flow was calculated.

Results of the observation are shown in Figs. 5 and 6. (In these and following figures a CSF flow in the caudal direction is expressed by a positive value and an expression is used, in the figures and in the text, that the bubble or CSF progresses, while a CSF flow in the opposite direction is expressed by negativity and the bubble or CSF is called as regressing.) In all dogs observed (3 dogs having chronic blocks and 3 dogs having acute blocks) the bubble progressed very slowly but steadily, thus indicating decisively the presence of slow CSF flow from the cranial to the caudal portion of SSS. The bubble used to fluctuate to and fro synchronously with respiration and, to a lesser degree, with pulsation. In several dogs in which blocks in SSS were unsatisfactory neither unidirectional, steady movement of the bubble nor its fluctuation synchronous with pulsation could be observed. Thus it seems that

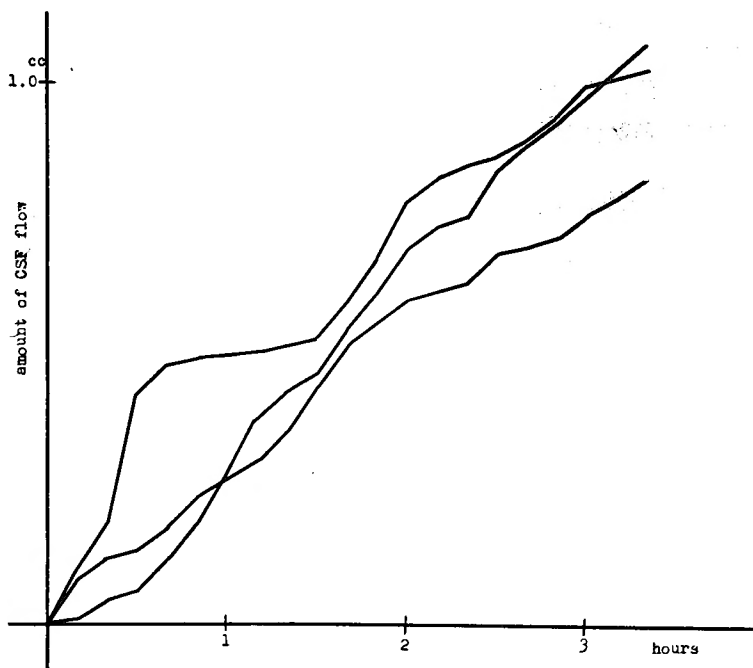


Fig. 5 CSF flow in dogs having chronic blocks at C2.

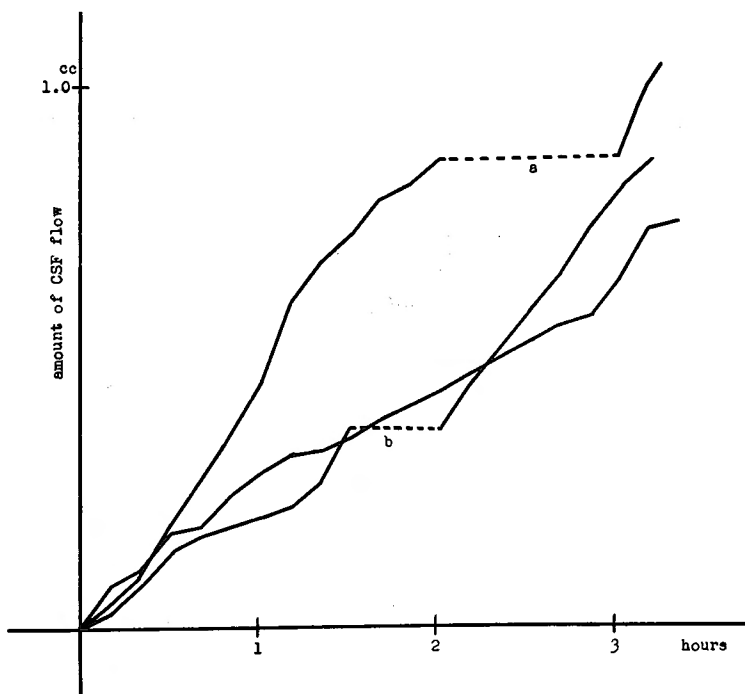


Fig. 6 CSF flow in dogs having acute blocks at C2.

CSF passed in these cases through the incompletely blocked subarachnoid space rather than through the thin polyethylene tube having a large hydrodynamic resistance.

At the portion indicated by a in Fig. 6 the polyethylene tube was occluded for one hour. On recanalization the speed of flow (roughly indicated by inclination of the curve in the figure) was found to be almost twice as large as the value observed prior to the occlusion. This fact suggests that a large difference in pressure between CSF of the cisterna magna and that of the lumbar cistern was produced by occlusion of the tube. At the portion of b in Fig. 6 an acute block in SSS was released by loosening the strain of the silk suture around the spinal cord for a period of 30 minutes. On release of the block the bubble in the tube immediately ceased to move and fluctuations synchronous with respiration and pulsation also disappeared. On resumption of the block inclination of the curve

indicating the speed of flow was almost identical with that prior to release of the block. Thus it is supposed that CSF passed through the subarachnoid space for the period of release of the block.

In some cases too deep anesthesia caused respiratory arrest and on such occasions the speed of CSF flow became from 40 to 50 times as large as the usual speed. In case an artificial respiration was performed on such occasions the rapid progression of the bubble used to cease gradually until at last its regression appeared. The distance of this regression was usually about 10% of the distance of the preceding progression and a new progression took the place of the regression thereafter. In case the animal was left to die without application of an artificial respiration, the bubble which had progressed rapidly began to regress toward the time when the heart action became weak and the regression continued for about 30 minutes after the animal's death. Two representative cases are illustrated in Fig. 7.

As far as there were no such extreme fluctuations in depth of anesthesia as described above the dynamic aspects of CSF were found usually to be in such states as shown in Figs. 5 and 6. Although the amount of CSF flow per 10 minutes showed marked fluctuations, when calculation was made every 3 hours CSF little short of 1.0 cc was found to flow regularly in this period from the cranial to the caudal side. Namely, the amount of CSF flow from the cisterna magna to the

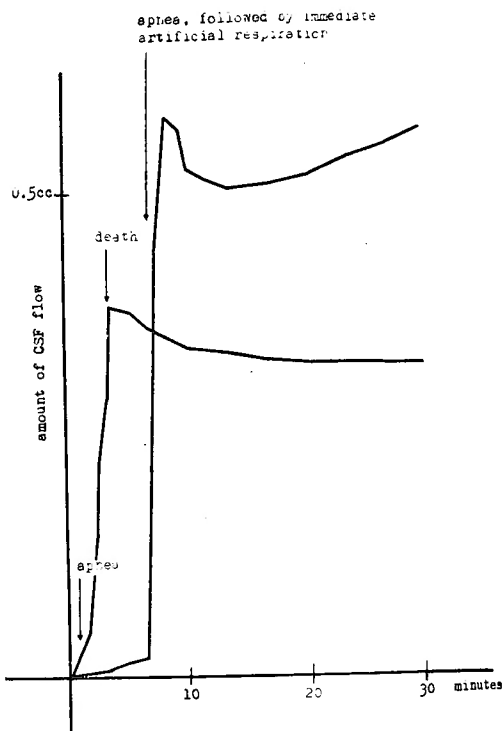


Fig. 7 Changes in CSF flow caused by respiratory arrest.

caudal part of SSS was about 0.3 cc per hour on the average both in animals having acute blocks and in those having chronic ones. The fluctuations in speed of CSF flow with relatively short periods were probably due to small fluctuations in depth of anesthesia, which was difficult to be maintained in a strictly constant condition. The latter fluctuations probably induced those of CSF pressure, which, in turn, seemed to affect CSF flow. Thus next experiment was performed to obtain a correct knowledge on relationship between changes in CSF pressure and the speed of CSF flow.

A polyethylene tube with an inner diameter of 3 mm was attached, as a branch, to the tube interconnecting two cisterns at a point between the cranial end of the latter tube and the cranially placed connection rubber tube (cf. Fig. 4). The former polyethylene tube was used as a manometer. Amount of CSF flow per 10 minutes, value of CSF pressure every 10 minutes and value of its change in a unit period of 10 minutes were continuously measured in 3 dogs having chronic blocks and 3 other dogs having acute blocks. The results are shown in Fig. 8. Although measurement began after lapse of the stabilization period, i. e. about one and a half hour following installation of those tubes, many cases showed gradual rise, accom-

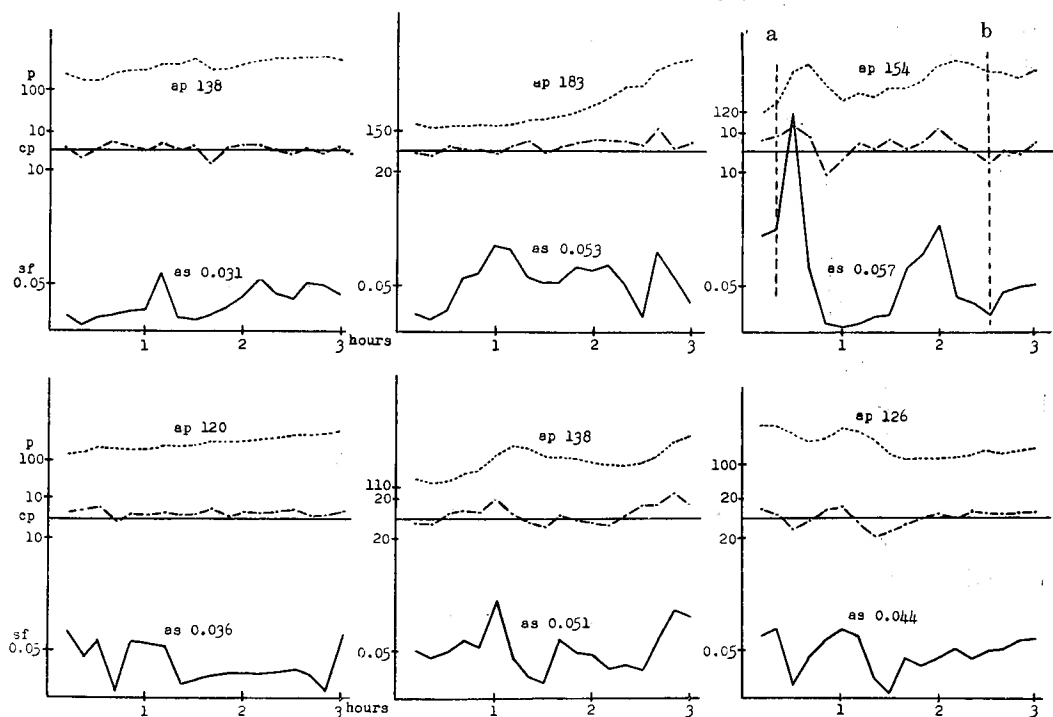


Fig. 8 Relationship among CSF pressure, its change and speed of CSF flow in 6 dogs.

- p, pressure, mmH₂O
- - - cp, change in pressure, mmH₂O/10min.
- sf, speed of flow, cc/10min.
- ap, average pressure, mmH₂O
- as, average speed, cc/10min.

anied by minor fluctuations, in CSF pressure as can be seen in the figure. Against the expectation that CSF flow would increase in proportion to rise in its pressure, parallelism between the two was not always observed. For example, at the point a in Fig. 8 the speed of CSF flow was 0.1 cc /10 min. when its pressure was 128 mm H₂O, while at the point b the speed was 0.02 cc/10 min. when the pressure was 164 mm H₂O. Similar facts were also observed in other cases. Therefore it must be concluded that, when CSF pressure is in a state of fluctuation, there is no direct relationship between CSF pressure and the speed of CSF flow at a certain instant. However, if we pay attention to their average values, appearing in the figure, it will be found that the average speed of CSF flow tends to be large when the average CSF pressure is high. Thus existence of some relationship between the two is supposed. On the other hand, when the speed of CSF flow (indicated by a continuous line in Fig. 8) is compared with the value of change in CSF pressure in 10 minutes (indicated by a broken line in the same figure), we can find a gross parallelism between the two, which suggests an existence of a kind of interrelationship between them. This result may be taken to be an evidence indicating that the change in CSF pressure is a motive power of its flow. Here arise two questions: does CSF flow actually exist if there is no fluctuation in pressure and, if it actually does, is there any definite relationship between the speed of CSF flow and the absolute CSF pressure? To find solutions to these questions following experiments were performed.

Using the same equipment as that in the preceding experiment, a thick injection needle was inserted into the tube used as a manometer at a certain horizontal level

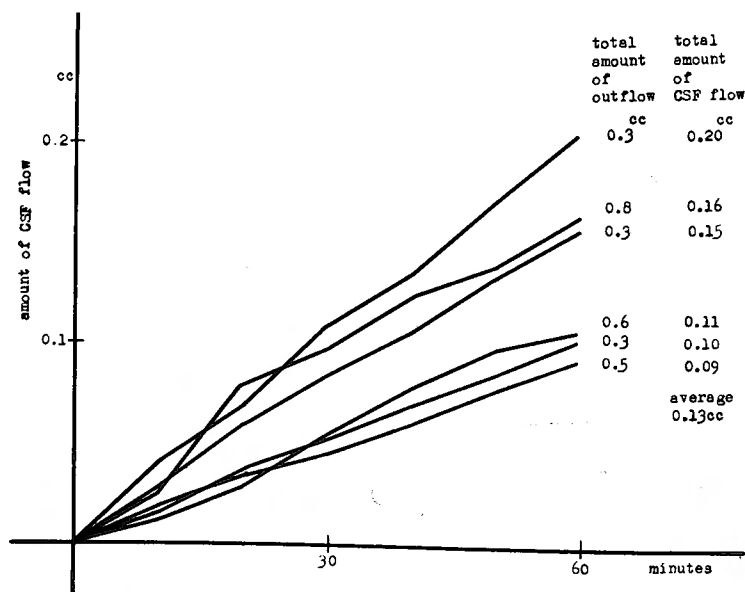


Fig. 9 CSF flow under a constant pressure of 100 mmH₂O.
(in dogs having chronic blocks at C2)

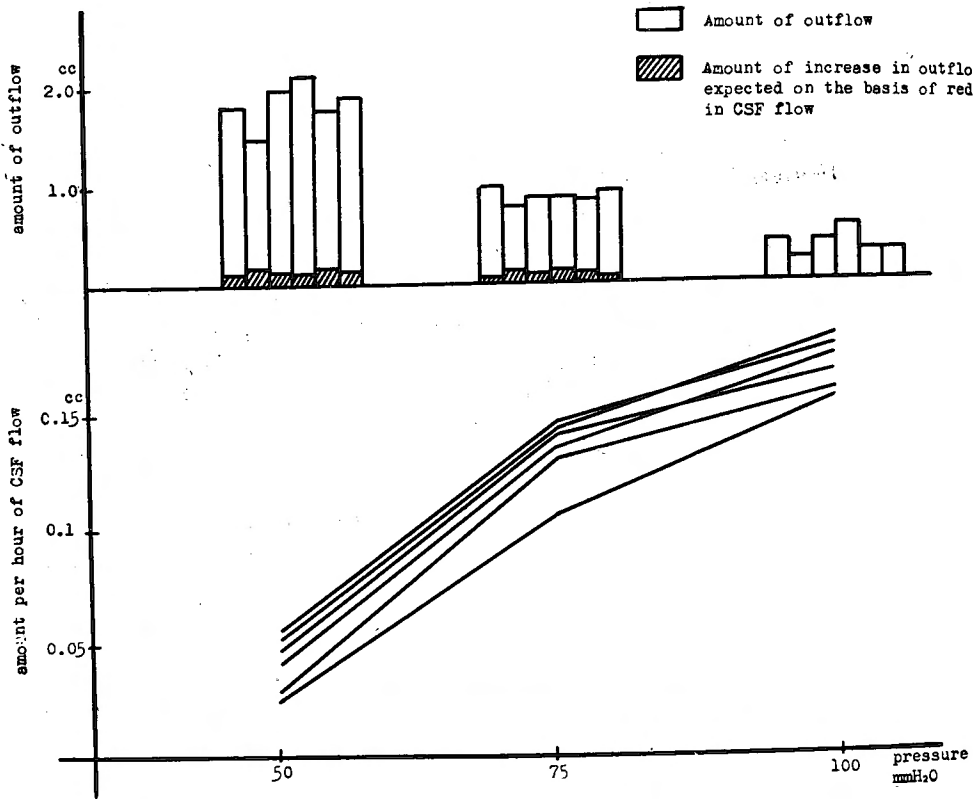


Fig. 11 Changes in amount per hour of CSF flow and in amount of outflow under a constant pressure either of 50, 75, or 100 mmH₂O.

absorbing ability in SSS caudal to the blockade. The increase in amount of overflowing CSF is naturally to be anticipated on the basis of the reduction in CSF flow, but the increase was found in fact to be far more pronounced than that anticipated. This fact is illustrated at the upper portion of Fig. 11. The fact must be explained as follows: the production of CSF in the CSF space cranial to the blockade decreases, when CSF pressure is kept at a high level and its production increases when the pressure is kept at a low level.

As a next step relation of CSF flow to the site of blockade was examined. CSF flow was observed (without attaching the manometer tube to the interconnecting tube), in dogs having chronic or acute blocks in SSS at various levels, i. e. at the level of C2, Th3, L1 or at the caudal end portion. The results are shown in Fig. 12. The speed of CSF flow was found to decrease as the site of blockade approached the caudal end. This fact is seemingly related to reduction in area of CSF absorption in parallel with reduction in SSS caudal to the blockade. However when the length of SSS caudal to the blockade is depicted with a continuous line in the same figure, it becomes evident that, as the blockade approaches the caudal end of SSS, far more amount of CSF flow is observed as compared with the amount anticipated

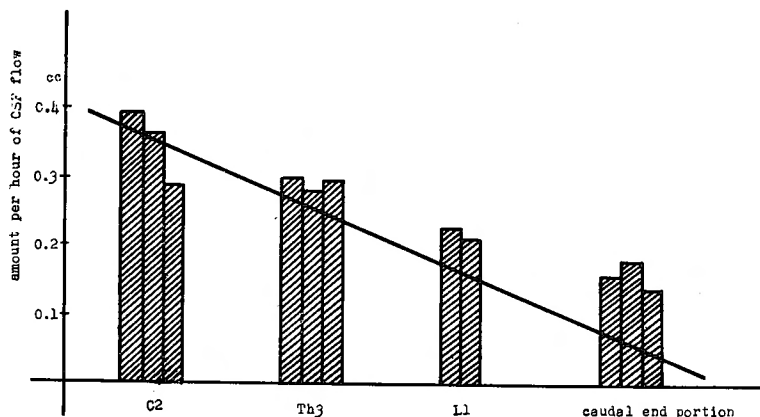


Fig. 12 Amounts per hour of CSF flow in dogs having blocks at different portions of SSS. (Description on the oblique straight line appears in the text.)

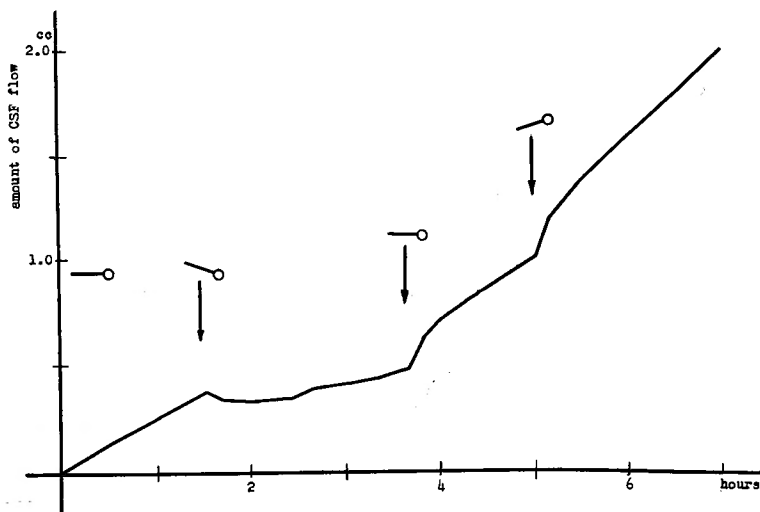


Fig. 13 Changes in CSF flow induced by postural alteration.

on the basis of reduction in length of SSS caudal to the blockade.

5. Experimental studies on influences of various factors, inducing changes in CSF pressure, on CSF flow

Various factors have hitherto been reported which induce changes in CSF pressure. On the other hand, it has been clarified above that changes in CSF pressure induce changes in CSF flow. Among those various factors influencing CSF pressure some were studied in regard to their influences on CSF flow in SSS. CSF flow was measured applying following procedures and the results were compared with the basic CSF flow discovered above.

According to LOMAN⁽²⁷⁾, YOSHINO⁽²⁸⁾ and others, the CSF pressure at a certain point inside the subarachnoid space shows, in case of angular changes in the body

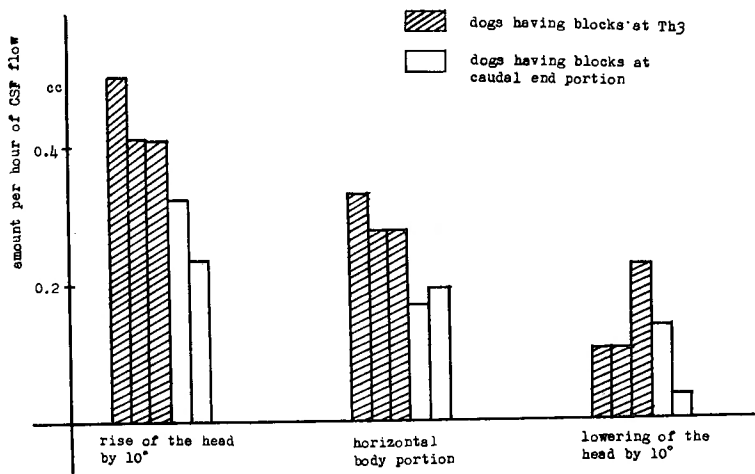


Fig. 14 Changes in amount per hour of CSF flow induced by postural alteration.

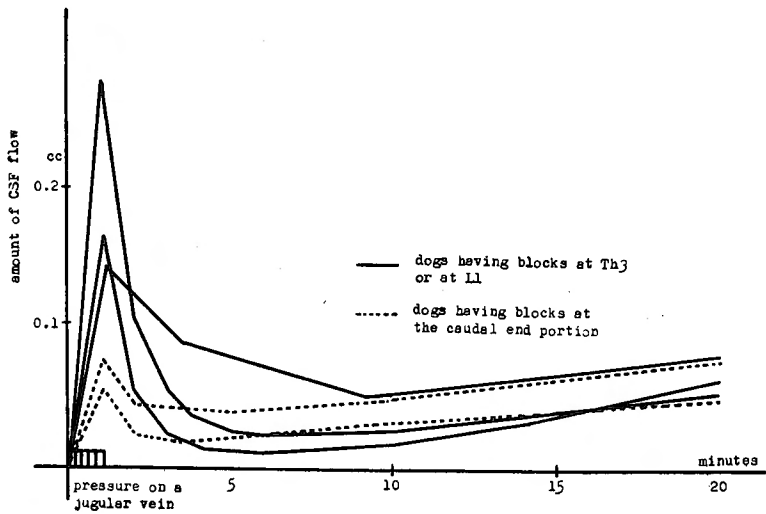


Fig. 15 Changes in CSF flow induced by pressure on a jugular vein.

axi as to the horizon, a tendency to change roughly, but not precisely, in accordance with the law of hydrostatics. The following experiment was performed to observe changes in CSF flow in case of changes in body position. A dog, which had a block in SSS and in which a polyethylene tube had been installed in the ordinary manner, was laid on its side and its body axis was inclined so as to cause an elevation or lowering of its head by an angle of about 10 degrees against the horizon, and changes in CSF flow were measured. Results obtained in several dogs are shown in Figs. 13 and 14. Immediately following changes in body position, CSF flow in the direction of the lower side appeared or increased. After from 30 to 40 minutes, however, the flow reached a state of equilibrium; i. e. in case of elevation of the

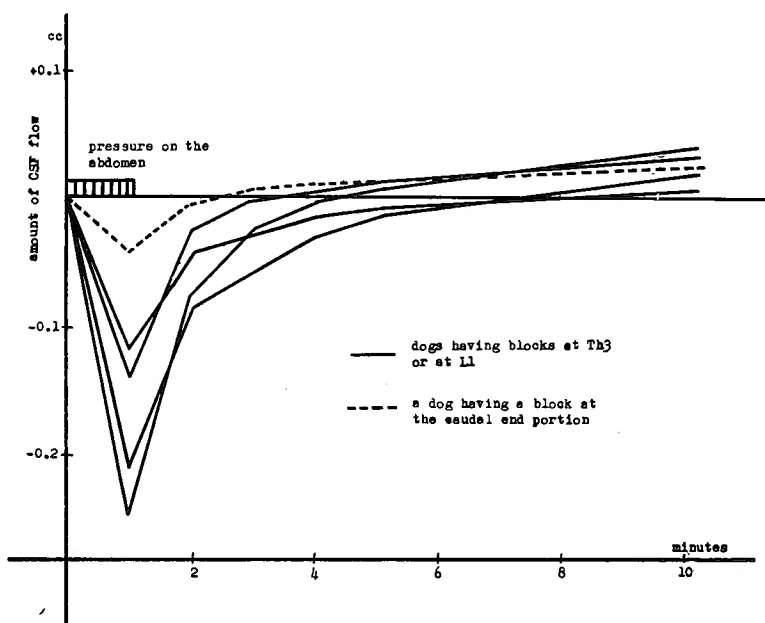


Fig. 16 Changes in CSF flow induced by pressure on the abdomen.

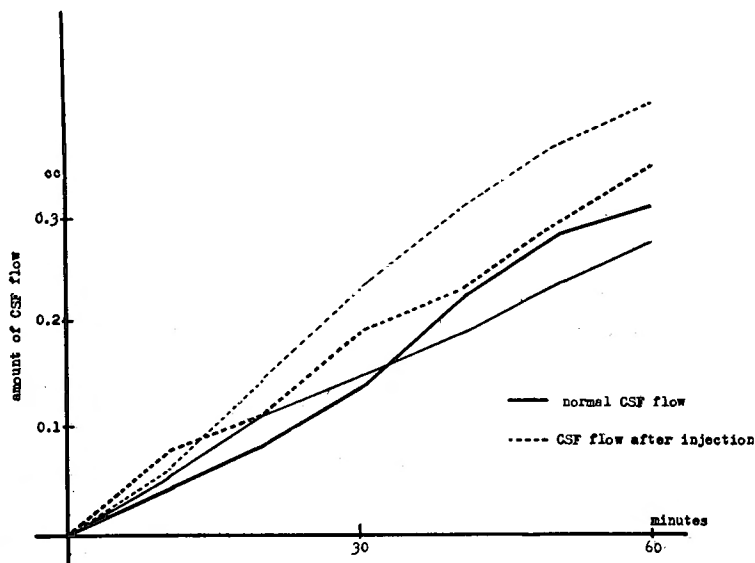


Fig. 17 Changes in CSF flow induced by intravenous injection of 0.5% saline solution. (5 cc/kg)

head CSF progressed more rapidly than in the horizontal position of the body, and in case of lowering of the head CSF did progress (not regressed) definitely but more slowly than in the horizontal position. Fig. 14 illustrates the amount of CSF flow per hour in each case. In case of elevation of the head an average increase in CSF flow by about 53% was observed as compared with the value in the hori-

ontal position of the body, while an average decrease in its flow by about 50% was observed in case of lowering of the head.

In clinical practice we know that application of pressure on a jugular vein or of abdominal pressure induces a rise in lumbar CSF pressure. To investigate changes, if any, of CSF flow caused by these procedures, pressure was applied for one minute to a jugular vein or to the abdomen of a dog having a block in SSS, in which measurement of CSF flow was being performed. Results of the observation in several dogs are shown in Figs. 15 and 16. On pressure of a jugular vein, CSF rapidly progressed and on release of the pressure it regressed for from 5 to 10 minutes, finally resuming progression thereafter. On pressure of the abdomen, CSF rapidly regressed and on release of the pressure it progressed rapidly. The average amount of CSF flow per minute, induced by application of such pressures as above for a minute, was about 0.16 cc in dogs having blocks at the level of Th3. This amount is about 30 times as large as that of the basic CSF flow per minute.

Since it was found by WEED and McKIBBEN²⁹⁾, the fact that changes in the blood osmotic pressure cause changes in CSF pressure has been confirmed by many investigators and is popularly recognized today. WEED et al injected distilled water intravenously in cats and observed a striking rise in CSF pressure. In my experiment 0.5% saline solution was injected intravenously at a dose of 5cc/kg of body weight in dogs having blocks and CSF flow was observed. The results are shown in Fig. 17. A slight increase in CSF flow in the normal direction was seen to be induced by the procedure.

HADEN³⁰⁾ was the first who succeeded in reducing CSF pressure by means of intravenous injection of hypertonic glucose solution. Although untoward effects of the procedure, such as a secondary rise of CSF pressure, have since been discussed,

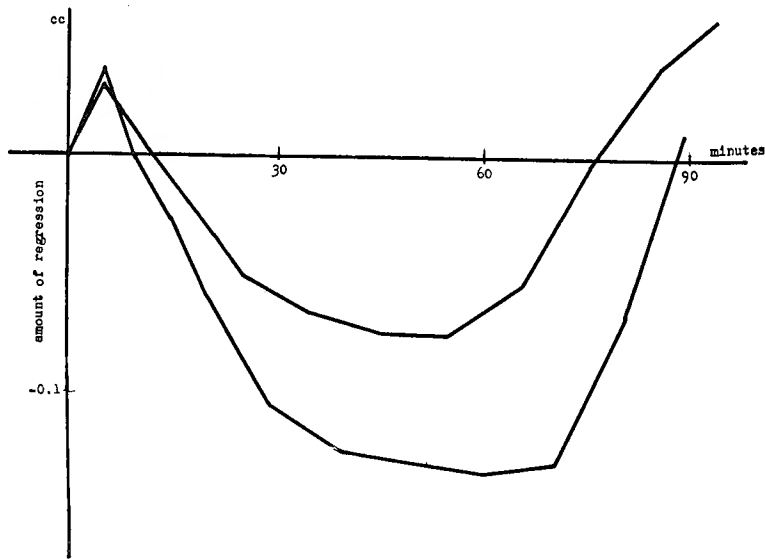


Fig. 18 Changes in CSF flow induced by intravenous injection of 50% glucose solution. (5 cc/kg)

it is at least accepted popularly that CSF pressure decreases for some short period after intravenous administration of hypertonic solution. For the purpose of observing the effect of the procedure on CSF flow, 50% glucose solution was injected intravenously for a period of about 5 minutes to reach a total dose of 5 cc/kg of body weight in dogs having blocks. Fig. 18 shows results of the observation. A comparatively rapid progression of CSF which could be observed during and immediately after the injection, was replaced by a regression 10 minutes after the injection. About 1 hour thereafter, a rapid progression again took the place of the preceding flow. The initial increase of progression might correspond to the initial elevation of CSF pressure according to MASSERMANN³¹⁾. However, it is considered that the hypertonic solution may influence not only the intracranial CSF pressure but also the CSF pressure in SSS caudal to the blockade, and that the amount of CSF flow depends solely upon the difference in pressure on both sides of the blockade. Therefore correct identification cannot be made between the initial increase in progression of CSF and MASSERMANN's initial elevation of CSF pressure.

FREMONT-SMITH et al³²⁾ first pointed out that intravenous administration of urea could reduce CSF pressure and the effect was confirmed clinically by JAVID et al³³⁾. To investigate the effect of this procedure on CSF flow, 30% urea solution was intravenously administered in dogs having blocks by means of drip infusion (with a speed of 60 drops per minute and for a period of about 30 minutes) to attain a total dose of 1 g/kg of body weight. As illustrated in Fig. 19 CSF showed already in early period a rapid regression, which continued for about 40 minutes and was replaced thereafter by a progression.

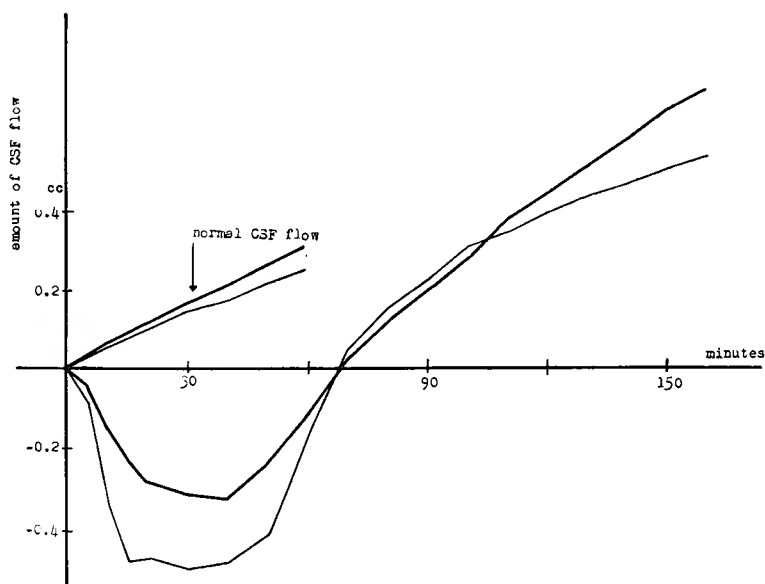


Fig. 19 Changes in CSF flow induced by intravenous injection of 30% urea solution. (1 g/kg in total)
(Thick lines and thin ones are derived from the same dogs respectively.)

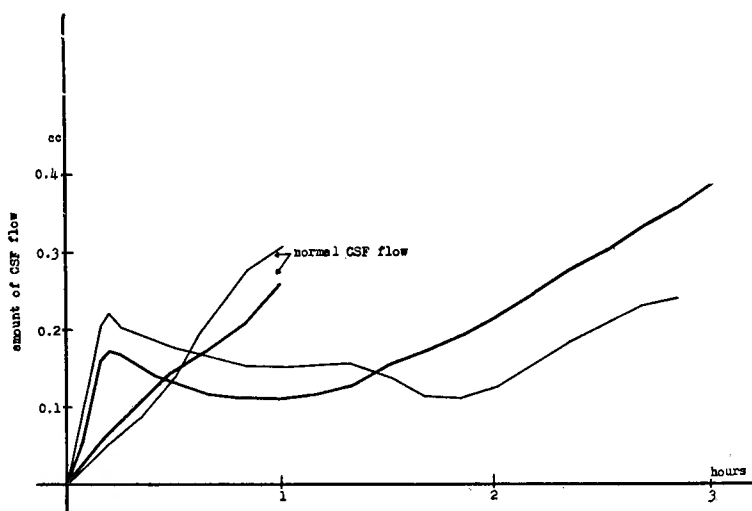


Fig. 20 Changes in CSF flow induced by intravenous injection of Periston-N. (5 cc/kg) (Thick lines and thin ones are derived from the same dogs respectively.)

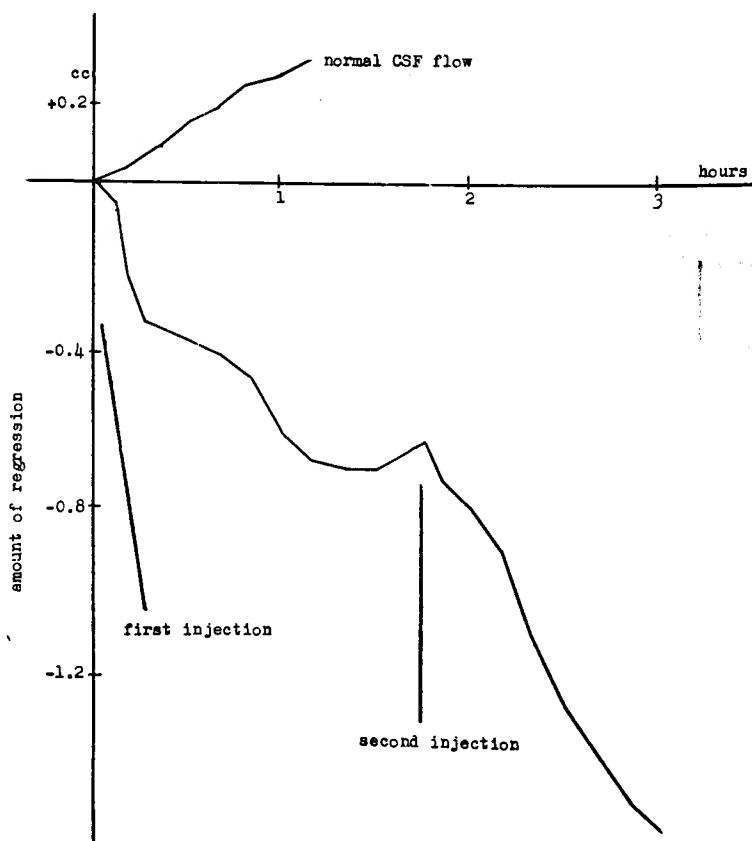


Fig. 21 Change in CSF flow induced by double intravenous injection of 50% glucose solution. (10cc/kg at each time)

A lowering effect on CSF pressure has also been advocated as for polyvinylpyrrolidone (PVP) solution, though TAKAHASHI³⁴⁾ throws doubt upon the effect. At any rate it is supposed that PVP solution may cause changes in osmotic pressure of the blood and thereby cause changes in CSF pressure and, consequently, in CSF flow. On the basis of this assumption Periston-N (Bayer) was intravenously administered in dogs having blocks by means of drip infusion (with a speed of 60 drops per minute and for a period of about 15 minutes) to attain a total dose of 5 cc/kg of body weight, and changes in CSF flow were observed. As shown in Fig. 20 CSF flow in the caudal direction increased for about 10 minutes after beginning of the infusion, to reach a value about twice as rapid as the basic CSF flow. Subsequently slight regression occurred and continued for about one and a half hour, gradually being replaced thereafter by a new progression. After all, it has been confirmed that those agents which cause changes in osmotic pressure of the blood also cause

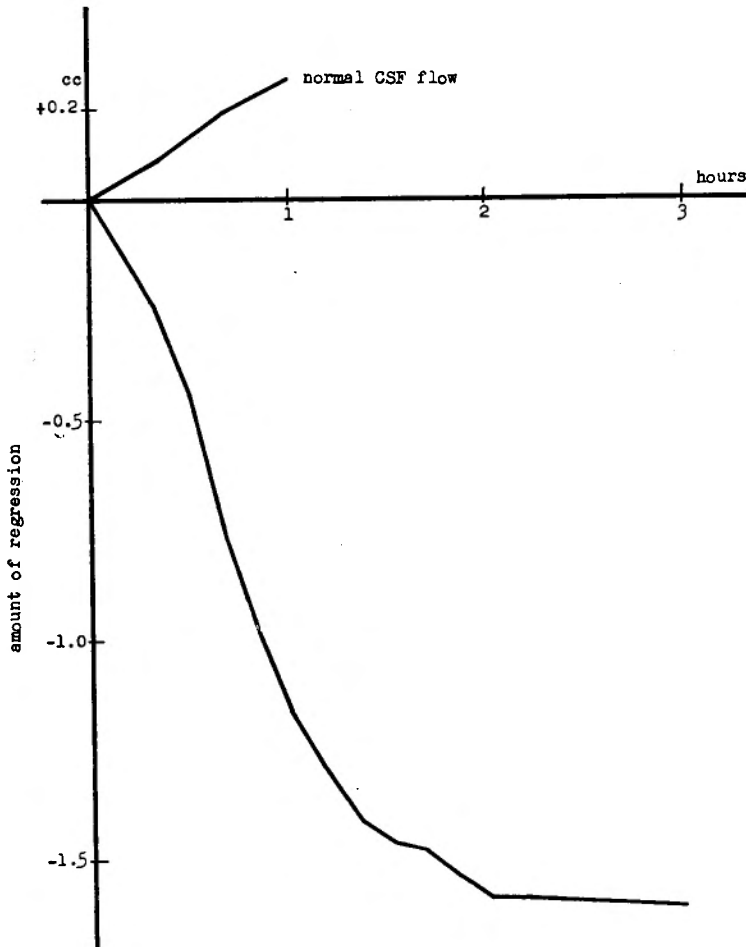


Fig. 22 Change in CSF flow induced by continuous drip infusion of 30% urea solution. (7 g/kg in total)

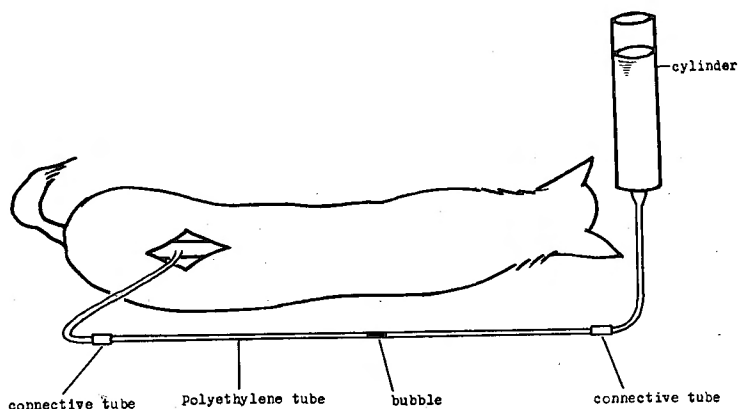


Fig. 23

changes in CSF pressure and, consequently, induce remarkable changes in CSF flow.

If a large dose of such hypertonic solutions as above are injected repeatedly or continuously, dehydration of the animal's tissues will surely occur. To investigate CSF flow in such a condition of strong dehydration, 50% glucose solution was injected intravenously at a dose of 10 cc/kg of body weight in dogs having blocks. It has been described above that regression of CSF occurs after the injection. Toward the time when the regression stopped, i. e. about 1 hour 50 minutes after the injection, 50% glucose solution was injected again at the same dose as above. As shown in Fig. 21 a more strong regression of CSF was induced by the second injection. On the other hand, when 30% urea solution was injected by means of drip infusion to reach a total dose of 7 g/kg of body weight, CSF regressed rapidly as shown in Fig. 22. The fluid that flowed during one and a half hour amounted to 1.5 cc. The regression of CSF continued thereafter for 3 hours, but the speed was slower. In any case, CSF pressure in the cisterna magna showed a negative value of from 50 to 100 mm H₂O after a strong regression had occurred.

In short it has been found that a strong dehydration of tissues due to some drugs can induce CSF flow in the cranial direction for a long period.

6. Studies on absorbing ability of SSS caudal to the blockade

It has been clarified above that there is a very slow flow of CSF in the caudal direction in SSS of dogs, having blocks and kept under general anesthesia. It is considered that this flow is caused by absorption of CSF from SSS caudal to the blockade. To know changes, if any, of CSF absorbing ability in this space in case CSF pressure is changed, following experiment was performed.

Usually it is difficult to maintain CSF pressure, by some means other than infusion of fluid, at a level of 100 mm H₂O or more without giving the animal any modification in its physiological state. Therefore physiological saline solution, instead

of CSF, was infused into the lumbar cistern as shown in Fig. 23, and its flow was observed using a bubble in the polyethylene tube as an indicator just as in the preceding experiments. According to this method any desired strength of pressure could be produced and maintained at a roughly constant level, but when the pressure exceeded 200 mm H₂O leakage of the fluid from the site of insertion was observed. Therefore, amount of the fluid that flowed into the lumbar cistern was measured in keeping the pressure at 50, 100, 150 and 200 mm H₂O respectively in 4 dogs, each having an acute block at the level of Th3. The amount of flow per hour under each of these pressures is shown in Fig. 24. The amount per hour under the pressure of 100 mm H₂O was 0.16 cc on the average. This is roughly equal to the amount of CSF flow per hour under a constant pressure of 100 mm H₂O, which has been described in Section 4. As can be seen in the figure, the amount of inflow increased together with elevation of the pressure. It is to be noted, however, that the rate of increase in the amount of inflow gradually diminished in spite of arithmetical progression of the increase in pressure. It seems from the figure that the maximum amount of inflow per unit time shows individual difference, but there seems to be a common tendency that the speed of inflow comes to show less

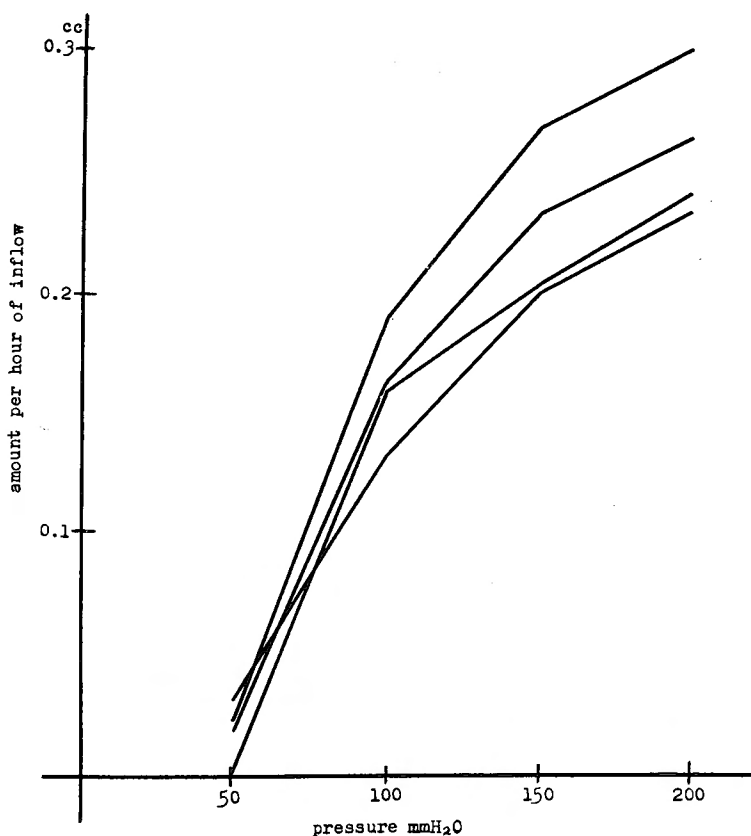


Fig. 24 Relationship between pressure and amount per hour of inflow of physiological saline solution into the lumbar cistern, in dogs having chronic blocks at Th 3.

increase as the pressure reaches 200 mm H₂O, to converge finally at a certain higher value, if the pressure were raised further. It is conjectured from the figure that the pressure, at which roughly maximum speed of inflow would be reached, would be about 250 mm H₂O. On the other hand, when the pressure is lowered toward 50 mm H₂O the speed of inflow rapidly diminishes and the curves tend to cross the ordinate at points corresponding to pressures between 40 and 50 mm H₂O, instead of reaching the origin. They suggest the presence of a minimum value of pressure for the fluid to be able to flow into SSS.

As a next step examination was made on influence, if any, of the presence in SSS of macromolecular substances on the absorption ability of SSS described above. In a dog having a block, CSF caudal to the block was sucked out and replaced with serum of the same dog or dextran solution. After about 5 minutes it was sucked out and replaced this time with physiological saline solution. Then the same solution was infused into the same space under a pressure of 200 mm H₂O according to the procedure described above, and the results of measurement in several dogs were compared with those obtained without infusion of serum or dextran but otherwise under the same situation. In Fig. 25 ratio of values obtained in the present experiment to those obtained in control experiment is shown. As can be seen in the figure, the presence of such a macromolecular substance as serum or dextran, sticking to the whole inner surface of SSS caudal to the block, causes reduction in ability of water absorption in the same space to from 50 to 60% of control values. There seems further to be a tendency that the reduction is more marked in the initial

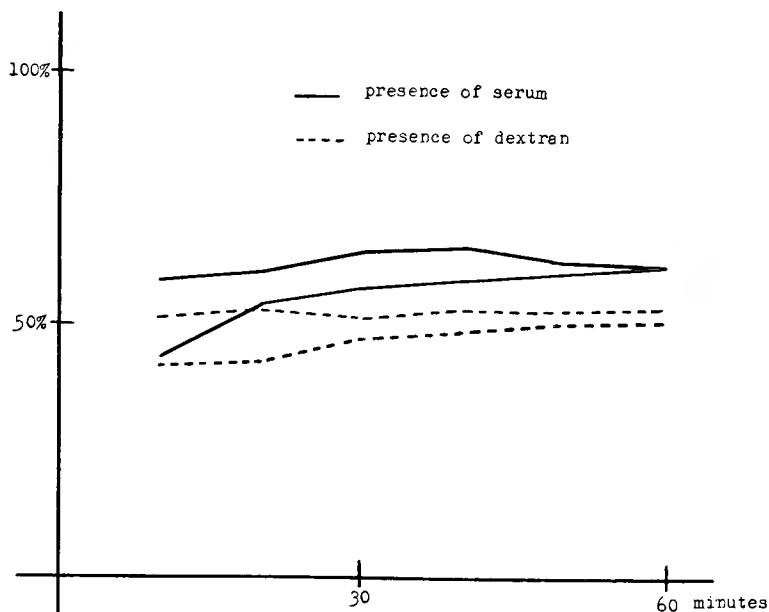


Fig. 25 Rate of decrease in amount of inflow, caused by presence of serum or dextran, of physiological saline solution into the lumbar cistern under a pressure of 200mm H₂O.

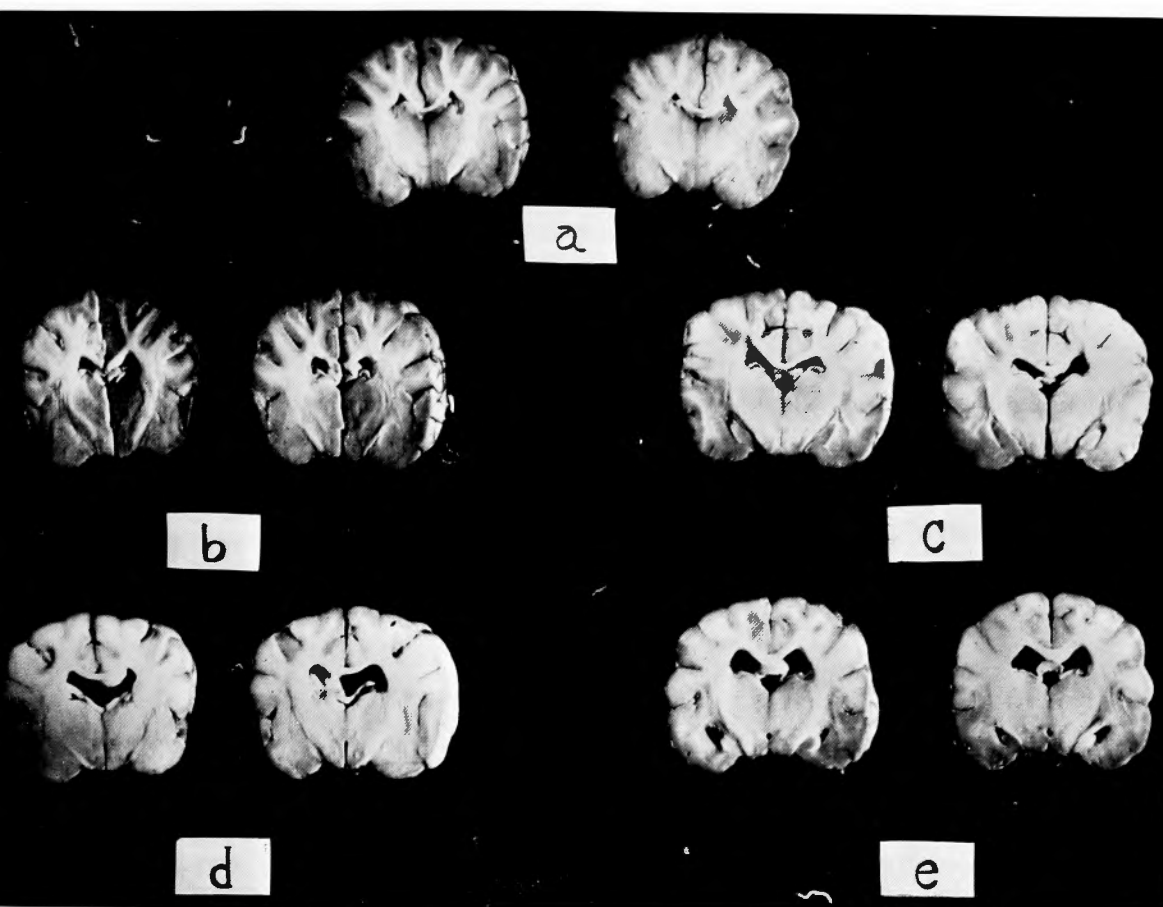


Fig. 26 Specimens of the brains showing ventricular dilatation.

a; normal control b; slight ventricular dilatation c; moderate ventricular dilatation
d; marked ventricular dilatation e; ventricular dilatation in case of blockade at the fourth ventricle

stage of the fluid infusion.

7. Observation on formation of hydrocephalus in dogs having blocks at the cranial portion of SSS

Thirty-two dogs having chronic blocks in SSS at the level of C2 or of Th3 were sacrificed after completion of all experimental procedures and their brains were excised and fixed in 10% formalin. After sufficient fixation the brains were cut on the frontal plane passing through the tuber cinereum, and the size of lateral ventricles was examined. Those dogs had lived for from 1 week to 3 months after formation of the blocks in SSS. The result of the examination is shown in Fig. 26 and Table 3. Moderate or marked dilatation of the ventricles, such as that in b or c in the figure, was observed in 28% of the cases. Thus it is to be concluded that presence of a block in SSS at the level of C2 or of Th3 causes distinct dilatation of the ventricles in relatively small number of cases. No specific relationship was

the former is the passage of a substance from the blood to CSF and the latter is that from CSF to the blood. These terms are contrasted with those in a narrow sense, or in a popular sense. In order that the CSF production in a narrow sense occurs, the CSF production in a wide sense must be larger than the CSF absorption in a wide sense regarding each of various CSF constituents. When the latter is larger than the former the CSF absorption in a narrow sense takes place. In my experiment P^{32} injected into the blood was found to appear in CSF rapidly and there was no marked difference in the situation between CSF cranial to the block and that caudal to it. On the other hand, P^{32} injected into the lumbar cistern of a dog having a block rapidly appeared in the blood, too, showing thereafter a similar change in density to that in the preceding experiment. Thus it is to be concluded that passage of P^{32} across the blood-CSF barrier takes place rapidly, showing a grossly identical change in density, whether it passes from the blood to CSF or vice versa and whether the CSF concerned is cranial to the block or caudal to it. In other words, the production and the absorption in a wide sense occur everywhere in the CSF space, as far as P^{32} concerns, and we cannot postulate a specific locus of the production or the absorption in such a sense. Those results of my experiment coincide with those of SWEET¹⁸⁾, BACKEY³⁵⁾ and others. We are not sure, however, that the dynamic state of P^{32} represents that of CSF to some extent. Even if it were allowed for us to analogize the dynamic state of CSF on the basis of that of P^{32} , we could never attain at once to the conclusion, such as that of KONNO²²⁾, MORITA²³⁾ or others, that the production and the absorption of CSF in a narrow sense occur at an identical rate everywhere in the subarachnoid space and, accordingly, there is no CSF flow in SSS.

It is supposed on the ground of experimental data that the total amount of CSF in SSS caudal to the level of C2 of a dog is about 3 cc. It has been found in my experiments that there is definitely a basic CSF flow in the caudal direction in SSS at a rate of about 0.3 cc per hour on the average. Provided that a similar CSF flow at the same rate as above exists in a normal dog (without a block in SSS), about 10 hours are required for the replacement of total CSF caudal to the level of C2 by CSF flowing down from above. On the other hand P^{32} passes the blood-CSF barrier in several minutes and reaches a state of equilibrium about 30 minutes after its administration. Thus it must be concluded that the use of tracers, such as P^{32} is inadequate to a purpose of examining such a flow of very slow speed as the basic CSF flow found in my experiments.

As has been described in Section 5 of the previous chapter the CSF flow is strongly influenced by various factors. In view of these experimental results and also of morphological complexity of the subarachnoid space (as compared with a polyethylene tube) there are perhaps very complicated flows of CSF in SSS of a normal waking dog. There may be localized flows in either cranial or caudal direction with speeds several times as large as the speed of the basic CSF flow. The object that I intended to examine is not those complicated and localized flows that are evoked by various factors, but is the CSF flow as a whole or of a larger

dimension, which takes place in a certain direction in a relatively steady manner. Heretofore, various investigators have reported on their experiments, in which various pigments, normally absent in CSF, or various isotopes, capable of passing through the blood-CSF barrier rapidly, are injected into the CSF space that has complicated, localized and rapid flows on the one hand and a very slow flow as a whole on the other hand. By means of these procedures they have attempted to examine a basic CSF flow in a strict sense. According to my opinion these attempts can hardly be successful.

No matter how slow the speed may be, the presence of a basic CSF flow from the portion cranial to the block to that caudal to the block definitely indicates that the production of CSF in a narrow sense takes place at the portion cranial to the block and the absorption in a narrow sense does at the portion caudal to the block. If we assume that the production in a narrow sense at the portion cranial to the block occurs at a constant rate irrespective of the absolute pressure, the change (increase or decrease) per unit time in amount of CSF overflowing from the manometer tube, in the experiment described in Section 4 of the preceding chapter, should have been equal to the change (decrease or increase) per unit time in amount of CSF flow in the caudal direction. In fact, however, such a precise relationship could never been found (see Fig. 11). The results obtained must be interpreted as follows: under a relatively low pressure the production of CSF in a narrow sense is relatively large in amount at the portion cranial to the block, while under a relatively high pressure it is relatively small there. The same fact has already been pointed out by Cushing¹⁾ in 1914.

The significance of the absolute value of CSF pressure in the mechanism of CSF flow and the significance in the same mechanism of difference in pressure between the portion cranial to the block and the portion caudal to it, are the problems quite different from each other. When two vessels, which contain the same fluid and in which the height of its surface is different from each other, are interconnected with a tube, it is a physical commonsense that the higher the difference the faster the flow inside the tube. Thus the result of the experiment described in Section 4 of the preceding chapter, i. e. existence of correlation between changes in pressure of CSF and the speed of CSF flow, and also the result of experiment described in Section 5, i. e. the fact that CSF flow is greatly influenced by those factors which cause changes in CSF pressure above and below the block, seem to be little more than that physical commonsense. On the other hand the fact, that CSF flow definitely exists when the pressure is kept at a constant level, certainly indicates that the absorption in a narrow sense occurs at the portion of SSS into which CSF flows. The fact that the CSF flow is faster under a high CSF pressure than under a low one, evidences that the ability of absorption in the lumbar cistern is large under a high CSF pressure. In the experiment, in which physiological saline solution was infused into the lumbar cistern, the attitude of the solution might not be identical with the physiological attitude of CSF, but we can at least conclude that the water is absorbed within the lumbar cistern through some routes. In dogs

having acute blocks, the amount per hour of physiological saline solution flowing into the lumbar cistern under a pressure of 100 mm H₂O and the amount per hour of CSF flow in the caudal direction under a constant pressure of 100 mm H₂O were roughly identical and were about 0.15 cc. This fact suggests that the circumstances in the absorption of physiological saline solution roughly represent those in CSF absorption. The speed of inflow of the solution into the lumbar cistern increases, as described previously, according to rise in pressure, but the rate of increase in inflow gradually diminishes with rise in pressure and the speed of inflow does not seem to exceed a certain limit. In the physiological state of an animal it seems therefore that the ability of absorption in the lumbar cistern cannot increase infinitely if CSF pressure rises more and more. On the other hand, it is considered in view of the result shown in Fig. 24 that the absorption in a narrow sense, in the lumbar cistern of an animal in the physiological state, stops if CSF pressure falls beyond a certain limit. As a matter of fact, if we attempt to measure the upper limit of the speed of CSF flow, we must give up the attempt on account of leakage of CSF and, if we attempt to measure the pressure at which the flow stops, we must also give up the attempt on account of errors due to relative largeness of the hydrodynamic resistance in the tube as compared with relatively small difference in pressure between both ends of the tube. Therefore we cannot help assuming both limits on the basis of the curves in the figure. This assumption, however, well coincides with clinical findings. It is often experienced in clinical cases that, when CSF pressure rises up to a level of from 230 to 250 mm H₂O, symptoms of increased intracranial pressure promptly become marked. This fact makes us suppose that regulation of CSF pressure comes to be difficult as the pressure exceeds the upper limit described above. On the other hand, the fact that "Sperrliques", or CSF in hydrostasis, usually shows a pressure of from 40 to 50 mm H₂O and not a pressure of lower value, argues for the presence of the lower limit mentioned above. I must emphasize here again that the presence of the lower limit indicates the absence below the limit of the CSF absorption in a narrow sense, and that it does not in the least mean cessation of the production and the absorption of CSF in a wide sense below that limit.

GARDNER et al³⁶⁾ stated that increase in protein content in CSF causes a rise of CSF pressure. In my experiment described in Section 6 of the preceding chapter, it was found that the amount of inflow of physiological saline solution into the lumbar cistern under a pressure of 200 mm H₂O decreased to show from 50 to 60% of the original value when the inner surface of SSS had previously been drenched with serum or dextran. This fact indicates that the presence in SSS of macromolecular substances hinders normal CSF absorption. Therefore in discussing ability of absorption in the lumbar cistern, not only the influence of the pressure but also that of osmotic pressure must be taken into consideration.

The ability of CSF absorption in SSS mentioned above is not the same in various parts of SSS. As shown in Fig. 12 it seems to be relatively large at the caudal end portion. This is in accordance with the result of WUSTMANN³⁷⁾, who

studied making use of a contrast medium. It also lends support to BECKER's objection³⁸⁾ against the opinions of EICHLER et al²⁴⁾. This fact does not in the least conflict with a definite rule that the higher the level of the block in SSS the more the absolute amount of CSF absorption below the block. As a matter of fact among dogs having chronic blocks at the caudal end portion of SSS none showed any sign of ventricular dilatation. In contrast, moderate or marked hydrocephalus was found to be produced in about one-third of dogs having chronic blocks at the cranial portion of SSS. Although hydrocephalus was less frequent and tended to be less marked in these dogs as compared with dogs having obstruction at the fourth ventricle or at the cerebral aqueduct (cf. Fig. 26, DANDY²⁾, NISHIMURA²⁵⁾), it is of interest that hydrocephalus did occur as a result of blockade at the cranial portion of SSS. This fact coincides with reports by some authors on clinical cases, in which blocks at the cranial portion of SSS were accompanied by hydrocephalus.

On the basis of his study on hydrocephalus in experimental dogs, DANDY²⁾ considered the choroid plexus as the site of CSF production. Results of BERING's experiment¹⁶⁾ are quite contrasting. Making use of various isotopes he clarified as to ventricular CSF that exchanges across the blood-CSF barrier of water and electrolytes were little affected by plexectomy. This fact indicates, as he correctly stated, that the production of these substances in a wide sense takes place not only at the choroid plexus, however it never evidences that the choroid plexus is not the site of the production of CSF in a narrow sense. Various facts disclosed by recent energetic studies with isotope tracers are certainly true. On the other hand no one can deny the fact that, when the ventricular system is obstructed at some place, the ventricles rostral to the obstruction are usually dilated. In my experiments it has been found that there is a very slow but incessant flow of CSF in SSS from the cranial side to the caudal side. When this extreme slowness of CSF flow and the rapidity with which exchange of CSF constituents occur across the blood-CSF barrier are taken into consideration together, the results obtained by DANDY and others do not seem to conflict with those obtained by BERING and others. Indeed I believe they are certainly compatible with each other.

IV. CONCLUSION

1. Exchange of P^{32} across the blood-CSF barrier in dog is very rapid and it is inadequate to measure CSF flow in SSS by means of such an indicator.
2. In an anesthetized dog there is a very slow but incessant CSF flow in SSS from the cranial to the caudal side. It has been found that the amount of CSF flow at the level of C2 is 0.3 cc per hour on the average.
3. The speed of flow increases with rise of pressure and decreases with fall of pressure. But the rate of increase in speed gradually diminishes as the rise of pressure progresses and the rate of its decrease is gradually promoted as the fall of pressure progresses. The speed of flow is markedly influenced by changes in body position, pressure on jugular veins, pressure on the abdomen, changes in osmotic pressure of the blood and by dehydration.

4. The more caudally located the portion of SSS, the slower the CSF flow inside. However relatively large amount of CSF flow still exists at the caudal end portion of SSS.

5. The lumbar cistern has an ability of water absorption. This ability is regulated by mechanical as well as osmotic pressure inside the cistern.

6. When SSS was blocked chronically at its cranial portion, hydrocephalus was found to develop in relatively small number of cases, but a majority showed no such sign.

REFERENCES

- 1) Cushing, H.: Studies on the cerebrospinal fluid. *J. Med. Res.*, **31**, 1, 1914.
- 2) Dandy, W. E. & Blackfan, K. D.: Internal hydrocephalus. An experimental, clinical and pathological study. *Am. J. Dis. Child.*, **8**, 406, 1914.
- 3) Dandy, W. E.: Experimental hydrocephalus. *Ann. Surg.*, **70**, 129, 1919.
- 4) Key, G. & Retzius, A.: *Anatomie des Nervensystems und des Bindegewebes*. Stockholm 1876 (cited from 5).
- 5) Weed, L. H.: The absorption of cerebrospinal fluid into the venous system. *Am. J. Anat.*, **31**, 191, 1923.
- 6) Dandy, W. E. & Blackfan, K. D.: An experimental and clinical study of internal hydrocephalus. *J. A. M. A.*, **61**, 2216, 1913.
- 7) Foerster, O.: *Handbuch d. Neurologie.*, VII/2, Julius Springer, Berlin, 1936.
- 8) Dandy, W. E.: *Practice of Surgery*. XII, W. F. Prior Co. Inc., Maryland, 1953.
- 9)* Araki, C.: Cerebrospinal fluid in surgical practice. *Geka*, **17**, 79, 1955.
- 10) Hassin, G. B.: So-called circulation of the cerebrospinal fluid. *J. A. M. A.*, **101**, 821, 1933.
- 11) Hassin, G. B.: Cerebrospinal fluid, its origin, nature and function. *J. Neuropath.*, **7**, 172, 1948.
- 12) Wallace, G. B. & Brodie, B. B.: On the source of the cerebrospinal fluid. The distributions of bromide and iodide throughout the central nervous system. *J. Pharmacol. & Exper. Therap.*, **70**, 418, 1940.
- 13) Schaltenbrand, G.: Normal and pathological physiology of the cerebrospinal fluid circulation. *Lancet*, No. **6765**, 805, 1953.
- 14) Bering, E. A.: Water exchange of central nervous system and cerebrospinal fluid. *J. Neurosurg.*, **9**, 275, 1952.
- 15) Bering, E. A.: Water exchange in the brain and c. s. f. Studies on the interventricular instillation of deuterium. *J. Neurosurg.*, **11**, 234, 1954.
- 16) Bering, E. A.: Studies on the role of the choroid plexus in tracer exchanges between blood and c. s. f. *J. Neurosurg.*, **12**, 385, 1955.
- 17) Sweet, W. H., Brownell, G. I., Schall, J. A., Bowsher, O. R., Benda, P. & Stickley, E. E.: The formation, flow and absorption of cerebrospinal fluid. *Res. Publ., A. Nerv. & Ment. Dis.*, **34**, 101, 1956.
- 18) Sweet, W. H. & Locksley, H. B.: Formation, flow and reabsorption of cerebrospinal fluid in man. *Proc. Soc. Exp. Biol. & Med.*, **84**, 397, 1953.
- 19) Greenberg, D. M., Aird, R. B., Boelter, M. D. D., Cambell, W. W., Cohn, W. E. & Murayama, M. M.: Study with radioactive isotopes of the permeability of the blood-cerebrospinal fluid barrier to ions. *Am. J. Physiol.*, **140**, 47, 1943.
- 20) Adams, J. E.: Tracer studies with radioactive phosphorus (P^{32}) on the absorption of cerebrospinal fluid and the problem of hydrocephalus. *J. Neurosurg.*, **8**, 279, 1951.
- 21) Schaltenbrand, G.: *Anatomie und Physiologie der Liquorzirkulation*. *Arch. Ohren-Nasen-u. Kehlkopfh.*, **156**, 1, 1949.
- 22)* Konno, I.: Survey of the problems arising out of the meninges and cerebrospinal fluid. *Jap. Jour. Otol.*, **57**, 1167, 1954.
- 23)* Morita, A.: Studies on the absorption and circulation of the cerebrospinal fluid by means

- of radioactive phosphorus. *Psychiatr. Neurol. Jap.*, **59**, 341, 1957.
- 24) Eichler, O., Linder, F. und Schmeiser, K.: Über die Bildung von Liquor im Lumbalraum, nachgewiesen mit Radionatrium. *Klin. Wchnschr.*, **29**, 9, 1951.
 - 25) Nishimura, S.: The fate of a gelatin sponge introduced into the fourth ventricle, Experiments in dogs. *Arch. Jap. Chir.*, **23**, 310, 1951.
 - 26)* Tomita, T.: presented at 16th annual meeting of Japanese Neurosurgical Association. 1957.
 - 27) Loman, J., Myerson, A. & Goldman, D.: Effects of alteration in posture on the cerebrospinal fluid pressure. *Arch. Neurol. & Psychiat.*, **33**, 1279, 1935.
 - 28)* Yoshino, Y.: Fundamental changes of the cerebrospinal fluid pressure at various points of the cerebrospinal fluid cavity. *Brain and Nerve.*, **1**, 102, 1949.
 - 29) Weed, L. H. & McKibben, P. S.: Pressure changes in the cerebro-spinal fluid, following intravenous injection of solution of various concentrations. *Am. J. Physiol.*, **48**, 512, 1919.
 - 30) Haden, R. L.: Therapeutic application of the alteration of brain volume. *J. A. M. A.*, **73**, 983, 1919.
 - 31) Masserman, J. H.: Effects of intravenous administration of hypertonic solution of dextrose with special reference to the c. s. f. pressure. *J. A. M. A.*, **102**, 2084, 1934.
 - 32) Fremont-Smith, F. & Forbes, H. S.: Intra-ocular and intracranial pressure. Experimental study. *Arch. Neurol. & Psychiat.*, **18**, 550, 1927.
 - 33) Javid, M. & Settlege, P.: Effect of urea on cerebrospinal fluid pressure in human subject. *J. A. M. A.*, **160**, 943, 1956.
 - 34)* Takahashi, K.: Study on dehydration-therapy with the hypertonic solution for the cerebral edema. *J. J. S. S.*, **60**, 188, 1960.
 - 35) Backey, L.: Studies on blood-brain barrier with radioactive phosphorus. IV. Special aspects of phosphate exchange between plasma and brain. *Arch. Neurol. & Psychiat.*, **71**, 673, 1954.
 - 36) Gardner, W. J., Spitler, D. K. & Whitten, C.: Increased intracranial pressure caused by increased protein content in cerebrospinal fluid. *New England J. Med.*, **250**, 932, 1954.
 - 37) Wustmann, O.: Bewegungsvorgänge im Liquorsystem. Ein experimenteller Beitrag zur Vermeidung des postoperativen Hydrozephalus nach Meningozelenoperationen. *Zentralbl. Chir.*, **78**, 1297, 1953.
 - 38) Becker, H.: Erwiderung zur Arbeit von Eichler, Linder und Schmeiser: Erlauben Versuche mit Radionatrium die Annahme einer Liquorbildung im Lumbalraum? *Klin. Wchnschr.*, **29**, 706, 1951.

* Written in Japanese.

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脊髓蜘蛛網膜下腔に於ける髄液循環の実験的研究

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髄液の流れは脳室に発して大槽に達し、大部分は脳底槽を通じて大脳凸部蜘蛛網膜下腔に向い、一部は蜘蛛網膜下腔に向うことは、略ぼ一般に認める所である。しかし此の髄液の循環説は現在に至る迄全く肯定されているものではない。特に蜘蛛網膜下腔の髄液の動態に関しては異論が多く、最近アイソトープを使用して行なつた諸家の実験では、此の部の髄液には一定の流れは無からうと云う結論が多く見られる。各種の臨床診断及び治療手技を行なうにあつて、此の部に髄液の流れが全くないのか、極めて徐々であつても基本的な流れが厳存するのか、の問題は重大な意義をもつものと考えられる。そこで著者はアイソトープによる若干の追試を行なつて、蜘蛛網膜下腔に於ける髄液流否定論に考察を加えると共に、此の部に於ける髄液の厳密な意味での流れの存否を実験的に追究し、併せて髄液の動態に関与する種々の因子の影響及び、蜘蛛腔に於ける髄液の吸収能に関する液圧及び滲透圧の影響を検討した。

実験動物は成熟雄犬を用い、その蜘蛛網膜下腔を各種の高さに於て、慢性或いは急性に完全遮断し、大槽と腰槽とをポリエチレン細管をもつて連結し、此の細管内髄液柱を両断する気泡の移動を指標として、髄液の流動状態を時間的に計測した。

実験結果を要約すると次の如くである。

1) 犬の血液髄液関門に於ける P^{32} の交換は諸家の報告の通り迅速であつて、どちらからも略ぼ類似の経過をもつて通過し、且つ遮断部の上下を問わずほぼ平等に行われている事を確認した。此の様に交換速度の速いものをもつて、緩やかな、しかも局所的には複雑な様相をもつ、蜘蛛網膜下腔の髄液の基本流を測知しようとするのは不適当であると言わねばならぬ。

2) ラボナール麻酔下、安静に横臥させた犬では、髄液は常に極めて徐々に頭側より尾側に向つて流れている。その流量は犬の第2頸椎高で1時間平均0.3ccであり、急性遮断犬と慢性遮断犬の間に大差を見出し

得ない。

3) 此の流量は液圧の上昇と共に増加し、下降と共に減少する。しかし液圧の上昇が進むに従つて流量の増加度は遞減して行き、又液圧の下降が進み、40~50 mm水柱圧に近ずくと流量は激減する傾向を持つ。

4) 又此の流量は髄液圧を変動せしめる各種の因子により大きく影響を受ける。即ち、

i) 体位を変動させると、頭側を約 10° 上げた場合は、水平位にある場合より平均53%流量が増大した。頭側を約 10° 下げた場合は水平位にある場合より、平均50%流量が減少するが、髄液は依然として大槽より腰槽へ流入した。

ii) 頸静脈圧迫を加えると、流量は極めて増大し、圧迫をゆるめると髄液は直ちに頭方へ逆流し、後、基本流に従う緩徐な尾方への流れを認めた。腹圧を加えると上記の流れの変動とは全く対照的であつて、髄液は強く頭方へ逆流する。腹圧を除くと、急速に尾方へ流動した後、漸次基本流に移行する。

iii) 低張液(0.5%食塩水)の静注によつては軽度の流量増大を認めた。高張液(50%葡萄糖溶液)の静注では約1時間にわたる頭方への逆流の後、再び尾方へ急速に流動した。尿素溶液の静注でも同様頭方へ強く逆流した後、再び尾方へ急速に流動した。ベレストンNの静注では短時間尾方へ流量が増大して後若干頭方へ逆流し、以後速度を落して尾方へ流動するのを見た。即ち血液滲透圧の変化は髄液流に複雑な変化を与える。

iv) 高張葡萄糖溶液或いは尿素溶液の大量連続静注によつて、実験動物に脱水状態を起させると髄液は極めて強く頭方に向つて逆流する。

5) 蜘蛛網膜下腔の遮断部位の高さを各種変化して行つた実験によれば、上記流量は蜘蛛網膜下腔の末梢に至るに従い低下するが、尾側端部に於ても比較的多量の髄液の流れを認める。

6) 腰槽には水の吸収能があり、上部より遮断され

た腰槽に生理的食塩水を注入するとき、定圧に於ては一定して流入させる事が出来る。此の吸収能は液圧、滲透圧性に調節され得る。即ち液圧に關しては要約3)の如き傾向をもつており、此の部に高分子溶液が

存在すると、吸収能は減少する。

7) 脊髓蜘蛛網膜下腔を高位に於て遮断すると、32例中10例(28%)に軽度の脳水腫発生を見たが大多数に於ては著明なものは認められなかつた。