DIRECTION AND LINEAR VELOCITY OF FLOW OF CEREBROSPINAL FLUID IN THE SPINAL SUBARACHNOID SPACE

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The direction of flow of cerebrospinal fluid in the spinal subarachnoid space has been the subject of controversy since the end of the last century.

Thus Falkenheim and Naunin [18], Becher [12-14], S. N. Sharavskii [10], Sachs, Wilkins and Sams [22], Hassin [19], I. A. Alov [1], and others deny that there is any flow of cerebrospinal fluod. Jacob [21], Strecker [23], A. D. Speranskii [7], Eichler, Linder and Schmeiser [16, 17], D. A. Shamburov [9], and others maintain that it flows in an upward direction, while Hill [20], Weigeldt [25], N. D. Khodiakov [8], L. L. Papadato [6], D. A. Zhdanov [3], Tubiana, Benda and Constans [24], Becker [15], and others believe that it flows downwards. Finally, Ahrens [11], G. F. Ivanov [4], and others consider that it may flow in both directions, upward and downward.

This conflict of views may to a certain extent be ascribed to the imperfections of the methods applied. Most of the investigators used various dyes, and based their conclusions as to direction of flow on the movements of the dyes from the locus of introduction. Those authors who introduced the dye into the lumbar subarachnoid space, and who then found it in the cranial spaces, concluded that the direction of flow was cranial.

Authors who introduced the dye into the suboccipital cistern, and who later found it to be present in the lower parts of the spinal canal, concluded that the fluid flows caudally. Finally, the authors who injected dyes into both the suboccipital and the lumbar subarachnoid spaces concluded that either the fluid moves in both directions, or that it does not flow at all. These studies did not take into consideration that respiratory and pulse rhythms are of fundamental importance to the dynamics of cerebrospinal fluid. These factors bring about a continuous mixing of cerebrospinal fluid, and are responsible for so-called turbulent diffusion of dyes [2].

Taking into account these features of the hydrodynamics of the cerebrospinal fluid, we came to the conclusion that, in order to be able to determine the direction of flow as shown by movements of diffusible substances, it is necessary to compare the concentrations of such substances above and below the point of introduction. The direction in which the greater part of the indicator substance moves would be that of flow of cerebrospinal fluid, since in that direction the rate of movement of indicator would represent the sum of that of progressive flow of cerebrospinal fluid and of diffusion of indicator substance.

Radioactive indicators are the most convenient for quantitative measurements.

EXPERIMENTAL METHODS

The experiments were performed on cats, under urethane narcosis (1 g per kg body weight). The animals were kept warm by means of electric heaters during the experiments. We performed 8 experiments, including 3 control ones. Radiophosphorus (disodium phosphate containing P^{32}) was taken as the radioactive indicator. We chose this tracer because of the important role played by phosphorus in many of the metabolic processes of the body, so that it is the most physiological indicator. Apart from this consideration, radiophosphorus was the most readily available. We used radiocalcium ($Ca^{42}Cl_2$) in one of our control experiments. We introduced P^{32} at a dosage of 1,000,000 i.p.m. per kg body weight, in 0.02 ml of physiological saline. Suboccipital and lumbar

puncture were performed with the animal lying on its side in a horizontal position, using a fine needle, with a clamp and a fitting for a micropipet. A hole was dripped through the lamina of a vertebra midway between the two punctures (at the level of T-6), and the solution of radioactive indicator was introduced from a micropipet, through a fine straight or bent needle, into the subarachnoid space, taking 10 seconds for the injection, and keeping the pressure as low as possible. The point of the needle was always directed cranially during the injection. After removing the needle, the opening in the vertebral lamina was closed hermetically with a plexiglass plug.

Samples of cerebrospinal fluid (0.01 ml) were taken simultaneously by means of micropipets from the suboccipital and lumbar subarachnoid spaces, after 5, 30, 60, 120, 180, 240, 300, 360, and 480 minutes, and were transferred to aluminum dishes with a filter paper disc attached to the bottom, for ensuring uniform distribution of the sample.

In addition, we measured the activity of the dura mater, caudial and cranial to the point of injection, along the whole length of the vertebral canal. We chose to measure the activity of the dura mater, rather than of the pia mater or the arachnoid, or of medullary tissue, because it is greater than the others (our own observations, and those of N. A. Maiorova [5]). After each experiment the animals were killed by exsanguination. The cavity of the vertebral canal was opened up section by section. We first exposed the spinal cord at the level of introduction of the indicator, and applied a ligature, and then repeated the operation at the level of the first cervical vertebra, in order to prevent any displacement of cerebrospinal fluid during the subsequent trepanation. The next stage was to open up the canal from the direction of lesser to greater activity. During the opening up of the vertebral canal we discarded the instruments after each few manipulations, and cleaned them thoroughly with 10% caustic alkali and copious amounts of water, so as to eliminate possible contamination. After opening up the vertebral canal we took specimens of dura, which we washed with physiological saline for a fixed time, dried with filter paper to the same humidity, weighed on a torsion balance, and distributed 25-mg portions evenly on sampling dishes.

The activity of the dried specimens was measured by means of an end-window counter in a lead chamber, using a Type B equipment. The results were expressed as i.p.m. per 100 mg of fresh tissue or per 0.1 ml of cerebrospinal fluid, applying appropriate background corrections. The relative error of measurement did not exceed 3-4%. Background radiation remained at a constant level during the experiments (about 12-15 i.p.m.).

EXPERIMENTAL RESULTS

After introduction of radiophosphorus into the subarachnoid space at the level of T-6, the activities of cerebrospinal fluid taken from the lumbar and suboccipital subarachnoid spaces were found to vary in accordance with the typical curves of Fig. 1. Activity was zero in the suboccipital cistern after 5 minutes, and had risen after 120-180 minutes to 240-372 i.p.m., falling to 24-44 i.p.m. by the 8th hour. The cerebrospinal fluid of the lumbar subarachnoid space showed a different picture. Activities of the order of 160-840 i.p.m. were found at the end of 5 minutes. The activity rose for 60-120 minutes, to a maximum of 1860-3250 i.p.m. It then fell, amounting by the 4th-8th hour to 990-1020 i.p.m. (Table 1).

We found in the same experiments that the activity of the dura was not uniform along the length of the vertebral canal; it was maximum at the level of the injection, amounting to 99,000 i.p.m. after 4 hours, and to 8,000-13,000 i.p.m. after 8 hours. Parts of the dura cranial to T-6 showed less activity than did those taken caudal to T-6.

The differences in activity are fully significant, since they are many times greater than the mean experimental error. Although the curves vary markedly from individual to individual, they all present the same general picture (Table 2).

The question arises whether these results might not be a consequence of aspiration of cerebrospinal fluid, with production of an artificially directed flow toward the spinal subarachnoid space.

In order to refute this objection we performed 3 control experiments, in which we injected radiophosphorus solution (radiocalcium in Experiment 59), but did not withdraw cerebrospinal fluid from the suboccipital and lumbar subarachnoid spaces. Subsequent measurement of dural activity showed excess activity of caudally located specimens 4 hours after injection (see Table 2, Experiments 52, 56, and 59).

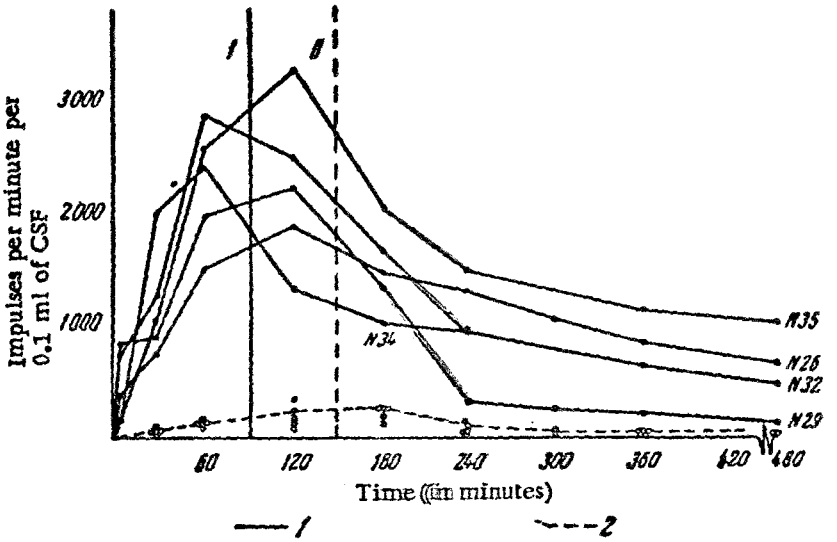

Fig. 1. Activity curves of cerebrospinal fluid taken from the suboccipital and lumbar subarachnoid spaces after subarachnoid injection of radiophosphorus at the level of T-6.
Explanation of curves: 1) activity in the lumbar space; 2) activity in the suboccipital cistern; first vertical line (I) average time needed for development of maximum activity in the lumbar space; second vertical line (II), in the suboccipital cistern.

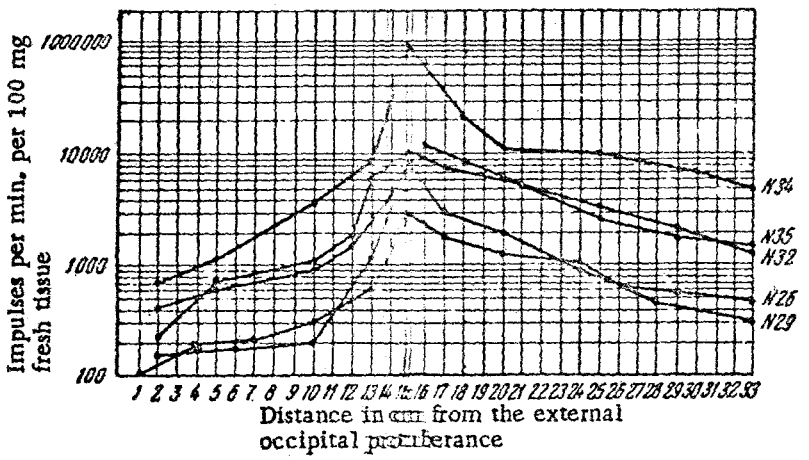

Fig. 2. Activity of the dura mater at different levels of the spinal cord caudal and cranial to the point of injection of radioactive phosphorus.
Explanation of curves: ordinates – activity in impulses per minute per 100 mg of fresh tissue, on a logarithmic scale; abscissae – distance in cm from the external occipital protuberance.

Apart from this, it is noteworthy that the first sample withdrawn from the lumbar space showed a higher activity than did that taken at the same time from the suboccipital cistern.

Our results are in agreement with the view that the flow of cerebrospinal fluid in the spinal subarachnoid space is in a caudal direction, where channels are located for its outflow into the vascular and lymphatic beds. This flow is so slow as to be of the same order of magnitude as is the process of diffusion of radiophosphorus in

TABLE 1

Relative Activity in the Suboccipital and Lumbar Cisterns after Introduction of Radiophosphorus at the Level of T-6

No. of experiment \ Time in minutes	Activity cerebrospinal fluid																	
	in the lumbar cistern									in the suboccipital cistern								
	5	30	60	120	180	240	300	360	480	5	30	60	120	180	240	300	360	480
26	350	740	1 510	1 860	1 450	1 310	1 070	850	650	0	40	84	128	280	92	60	52	24
29	840	940	1 990	2 200	1 390	350	280	240	160	0	12	132	164	264	52	48	40	32
32	720	1 260	2 840	2 480	1 670	950	—	640	510	0	16	136	240	148	104	—	36	28
34	170	2 000	2 400	1 300	1 020	990	—	—	—	0	72	180	372	204	184	—	—	—
35	160	1 020	2 560	3 250	2 000	1 500	—	1 150	1 020	0	24	86	136	284	76	—	60	44

TABLE 2

Relative Activity of the Dura Mater at Different Levels of the Spinal Cord after Subarachnoid Introduction of Radiophosphorus at the Level of T-6 (impulses per min. per 100 mg fresh tissue)

No. of experiment	Duration of experiment \ Distance cm from ext. occipital protuberance	1	2—4	5—7	8—10	11—12	13	14	15	16—17	18—19	20—23	23—24	25—28	29—30	32—33
26	8 hours	100	190	212	300	—	632	—	3 020	1864	—	1 220	1 140	662	572	500
29	8 hours	—	152	184	212	—	1 180	—	8 132	3 000	—	2 104	990	460	—	342
32	8 hours	—	412	640	896	1 580	—	4 152	—	13 420	8 900	6 314	—	3 940	2 120	1 350
34	4 hours	—	716	1 016	3 900	—	8 792	—	99 670	—	22 200	11 750	—	10 060	6 200	4 900
35	8 hours	—	236	752	1 020	1 940	6 825	—	10 150	7 450	—	5 800	—	2 932	1 852	1 600
52	4 hours	—	480	540	756	—	6 542	—	19 620	990	—	8 000	—	4 200	3 120	1 232
56	4 hours	—	284	580	684	—	742	—	5000	17 800	—	6 592	—	3 264	2 000	1 024
59	4 hours	212	—	236	676	912	—	1 184	2756	—	—	2 480	—	2 016	1 968	—

the cerebrospinal fluid, under the given conditions, since radiophosphorus spreads not only in the direction of flow of cerebrospinal fluid, but also in the opposite direction. This is why we found some activity in the cerebrospinal fluid of the suboccipital cistern and in the dura of the cervical spinal cord.

It is possible from our data to make an approximate calculation of the rate of flow of cerebrospinal fluid in the spinal subarachnoid space. If we take the distance from the point of injection to the sites of lumbar and suboccipital puncture as being equal to 15 cm, and the time needed to attain maximum activity of the cerebrospinal fluid as being 96 minutes in the lumbar space, and 156 minutes in the suboccipital cistern, we calculate the linear rate of flow in a caudal direction to be 1.56 mm per minute, and in a cranial direction 0.961 mm per minute. These are not, however, the real values, as they need to be corrected for diffusion. An analysis of the origin of the flow rates in a caudal and a cranial direction permits of an evaluation of this correction.

The observed rate of flow in the caudal direction ($V_{obs.\ caud.}$) is the sum of two rates: diffusion ($V_{diff.}$), and progressive displacement of cerebrospinal fluid, due to its continual resorption from the spinal subarachnoid space ($V_{CSF\ real}$). This relation may be expressed by the following equation:

$$V_{osb.\ caud.} = V_{CSF\ real} + V_{diff.} \qquad (1)$$

The observed flow rate in the cranial direction ($V_{obs.\ cran.}$) is the difference between the rate of diffusion and the actual rate of flow of cerebrospinal fluid downwards:

$$V_{obs.\ cran.} = V_{diff.} - V_{CSF\ real} \qquad (2)$$

We thus have two equations with two unknowns. Substituting the value of $V_{diff.}$ given by Equation (2) in Equation (1) we obtain:

$$V_{CSF\ real} = \frac{V_{obs.\ caud.} - V_{obs.\ cran.}}{2} = \frac{1.56 - 0.961}{2} = 0.299 \text{ mm/min.}$$

Our findings as to the direction of flow of cerebrospinal fluid are in agreement with the observations of Becker and of Tubiani, Benda and Constans. Becker found that a dye (Indian blue) introduced into the spinal subarachnoid space of rabbits was displaced after 2-3 hours 2-3 cm further in the caudal than in the cranial direction, and that the intensity of coloration seemed greater in the lower than in the upper subarachnoid spaces.

According to Tubiani, Benda and Constans, radioactive sodium present in the spinal subarachnoid space of patients under their care diffused faster from above down than from below up.

The practical conclusion might be drawn from our experimental data and from those given in the literature that it is not advantageous to introduce drugs used for the treatment of inflammatory conditions of the brain and meninges into the lumbar subarachnoid space.

Our experimental data are evidence that cerebrospinal fluid flows in a caudal direction through the spinal subarachnoid space. In cats, the mean linear rate of flow in the caudal direction amounts to 0.3 mm/min. Diffusion plays a substantial part in the distribution of substances in the cerebrospinal fluid in the spinal subarachnoid space.

SUMMARY

The direction and velocity of motion of the cerebrospinal fluid in the spinal subarachnoid space was studied in experiments on cats under urethane anesthesia with the aid of radioactive phosphorus (P^{32}). The latter was introduced into the spinal subarachnoid space at the level of the 6th thoracic vertebra. The activity of cerebrospinal fluid was investigated at definite intervals in the suboccipital and lumbar cisterns and it was revealed that it moved in a caudal direction with the velocity of 0.3 mm per min.

Diffusion plays a significant part in distribution of radioactive substances in the spinal subarachnoid space.

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