THE RELATION OF THE SPINAL SUBARACHNOID AND PERINEURIAL SPACES*

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The determination of the existence or absence of a direct communication between the spinal subarachnoid space and the perineurial spaces would contribute data regarding the circulation of the cerebrospinal fluid.

Much has already been written in attempts to prove or deny this communication. Key and Retzius (9, 10) were among the first to conclude that pathways existed by which cerebrospinal fluid escaped from the subarachnoid space into the substance of the nerves as well as into the perineurial spaces. They injected gelatin solutions, colored with Berlin blue, into the spinal subarachnoid space of cadavers and found the blue color to extend outward along the spinal nerves for a considerable distance. However, the injections were made under increased pressure (up to 60 mm. Hg) and could certainly have forced the gelatin into the perineurial space by mechanically rupturing a barrier, thus entering potential tissue spaces rather than passively following previously existing anatomical channels. The changes imparted by the high degree of pressure are evident in the sagittal section of the skull, which shows the cisterna magna to be distended with blue gelatin and the cerebellum compressed and pushed upward.

Earlier, Quincke (11) had injected mercuric sulfide repeatedly into the subarachnoid space of living animals and post-mortem examination several days later showed the spinal nerves colored red. He thought this was the mode of absorption of cerebrospinal fluid. However, histological studies revealed that an inflammatory reaction had been produced by the chemical agent with a resultant phagocytosis of particles of mercuric sulfide. The migration, therefore, of such granule-laden cells from the subarachnoid space can hardly be taken as evidence that any pathway for the escape of cerebrospinal fluid exists normally. Goldmann (6), in 1913, repeated these experiments using trypan blue and found the blue color in the spinal nerves at various distances from the spinal cord. As with the mercuric sulfide, trypan blue produced an immediate toxic reaction and later an inflammatory reaction of which the animals died.

Others, who believed that such a communication exists, included Cathelin (2), who thought the peripheral nerves are bathed to their very termination by the same fluid as covers the central nervous system. More recently, Funakda (5) was able to inject 25 cc of dekalin colored with ultramarine into the peroneal nerve of a rabbit and noted the blue dye in the subarachnoid and subdural spaces. In addition, he used a solution of amyl acetate, ether and olive oil colored with dye and observed the same distribution of color as with the dekalin. Unfortunately, there were no measurements of the pressures used for injection. Also, the use of

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fat solvents does not approach the physiological state in which an aqueous solution bathes the central nervous system.

Dyke and Deery (3) reported their observation of apparent passage of lipiodol from the spinal subarachnoid space into the perineurial spaces. Their patient had had 3.5 cc lipiodol injected into the spinal canal between the thoracic 9th and 10th vertebrae. Four years later, the lipiodol on roentgenographic examination was found to be as much as 10 cm outside the vertebral canal. However, before concluding the presence of a direct communication between the subarachnoid and perineurial spaces from this evidence, one should bear in mind the difficulty of spinal puncture in the thoracic 9th interspace and the possibility of lipiodol being in the subdural and epidural spaces as a result of a rent in the arachnoid. In addition, lipiodol has been known to cause an intense inflammatory reaction.

Hassin (7) is today the best-known proponent of the concept of a direct communication. As a result of his anatomical studies, he concludes that “injection of a peripheral nerve brings the injected fluid into its endoneural, perineural and epineurial spaces; from the latter the fluid reaches the spaces around the spinal ganglia, and from there the subdural and subarachnoid spaces of the spinal cord. The cerebrospinal fluid is drained by the perineurial spaces of the cerebrospinal nerves.” However, a photograph of a microscopic section in his textbook (8) shows fusion of all the meninges over the spinal ganglion and no demonstrable anatomical connection with the perineurial spaces beyond this point.

The first to doubt the existence of such a communication were Sicard and Cestan (12). They injected India ink into the subarachnoid space of living animals and on sacrificing them 8 to 9 days later, they found none of the carbon particles beyond the subarachnoid space. In addition they also injected cadavers with India ink under high pressures and again could find no extension into the peripheral nerves. A valid objection to the conclusions reached was that the size of the carbon particles may have prevented their passage through a small potential opening to the perineurial spaces.

Weed (13), in his important studies on the cerebrospinal fluid, used a true solution of potassium ferrocyanide and iron ammonium citrate which is precipitated as Prussian blue granules when acidified. Using animals and attempting to keep the conditions as physiological as possible, he observed that “after a low pressure injection of a true solution of the ferrocyanide, there is an obvious perineural deposit of precipitated granules which can be followed a short distance outward along the anterior and posterior roots. This finding accords with the reported observations of Sicard and Cestan.”

Years later, Elman (4) in the same laboratory repeated these experiments in dogs. After removing 6 cc of cerebrospinal fluid from the cisterna magna, he introduced an equal amount of isotonic potassium ferrocyanide and iron ammonium citrate and precipitated the Prussian blue in situ up to one hour later. In addition he used India ink as his injection medium in other experiments. He observed that there were distinct spaces present about the nerve roots beyond their emergence from the spinal cord immediately beneath their fibrous sheath.
This was true for both the anterior and posterior divisions except that around the spinal ganglia, this space was absent. Thus he concluded that the subarachnoid space forms a closed cavity at the spinal ganglion and is not connected with any space in the nerves beyond the ganglion.

Review of the literature reveals then that the existence or absence of communications between the spinal subarachnoid and perineurial spaces is yet to be clearly defined. Certain deficiencies exist. First, the experiments should be on living human material. In addition the injection medium, in order to pass a minute barrier, must be a true solution and must be nonirritating as well in order to prevent phagocytosis. To simulate physiological conditions, the pressure at the time of injection must be below 200 mm. water and the time interval between injection and observation must be long enough to allow for passage of the substance along a very sluggish circulation.

In order to satisfy these criteria, methylene blue, a nonirritating dye forming a true solution and suitable for intravenous use, was injected into the spinal subarachnoid space of 12 individuals. These patients were ill with a disease of non-neurological character and declared moribund by their attending physicians. In all, 2 cc. of a 1 per cent aqueous methylene blue solution was injected into the lumbar subarachnoid space after removal of 5 cc. of cerebrospinal fluid. Pressures were taken and in all, the readings were below 180 mm. water. Ten of the patients died and permission for post-mortem examination was obtained in six. The two patients who fortunately recovered did not show any ill effects from the methylene blue injections. At autopsy, done one hour up to five days after the intrathecal injection, a complete laminectomy was made on all six patients. The spinal ganglia were isolated and the peripheral nerves up to a distance of 15 cm. were dissected clear. The extent of the blue coloration was carefully observed both on gross inspection and repeated cross-section of the peripheral nerve and ganglion. All observations revealed a constant relationship. The blue color, which had filled the spinal subarachnoid space and had colored the surface of the cord and even the undersurface of the dura, stopped at the proximal end of the spinal ganglion (Figs. 1 and 2). In no instance was there dye beyond this point. Microscopic studies were attempted according to the technique described by Bethe (1), but the specimens were much too large to obtain adequate precipitation of the methylene blue. Thus one must conclude that under such physiological conditions, there is no communication between the spinal subarachnoid space and the perineurial space of the spinal nerves beyond the spinal ganglion.

In order to estimate the importance of the intrathecal pressure in determining the presence or absence of a barrier to the passage of cerebrospinal fluid, segments of human spinal cord and meninges with several pair of spinal ganglia and peripheral nerve segments 5 cm. long were removed within several hours after death. Such segments about 3–4 cm. in length were isolated between silk ligatures and 1 per cent aqueous methylene blue was injected into the subarachnoid space under controlled pressures. When a pressure of 150 mm. of water was maintained for four hours, there was no macroscopic evidence of passage of dye beyond the point of arachnoid-pial fusion just proximal to the spinal ganglion. In three experi-
ments a pressure of 600 mm. of water was maintained and after approximately twenty to twenty-five minutes, the dye became clearly discernible in the peripheral nerve segment just distal to the ganglion. Thus under the pathological condition of increased pressure, solutions may enter the perineurial space from

Fig. 1. Spinal cord and its membranes, A; ganglia, B; spinal nerves, C; 3 days after the injection of 2 cc. of 1 per cent methylene blue into the lumbar subarachnoid space.

Fig. 2. Dissection of the lumbar and sacral spinal cord and its membranes, A; ganglia, B; spinal nerves C; 60 hours after the injection of 2 cc. of 1 per cent methylene blue into the lumbar subarachnoid space.

the subarachnoid space. This would explain the observations of Key and Retzius.

Since the present studies only simulated physiological conditions, it was decided to supplement them with anatomical studies. Serial sections of the spinal cord, nerve roots and peripheral nerves with their respective coverings were made both vertically and horizontally. Our sections (fig. 3) were identical with those in figure 97 in Hassin's textbook "Histopathology of the Peripheral and Central
Nervous System (8).” They showed a fusion of all the coverings at the ganglion with no demonstrable communication between the subarachnoid and subdural spaces on one hand and the perineurial space on the other.

SUMMARY

Methylene blue was injected into the subarachnoid space of 12 humans before death. Post-mortem examination of 6 patients one hour to five days after injection showed the dye confined to the subarachnoid space. This extended to the proximal portion of the spinal ganglia.

Fig. 3. Cross section of spinal cord A, ganglia B and spinal nerves C showing the arachnoid D fusing with the dura E at the point where the posterior nerve root emerges from the ganglia. Note the close apposition of all the layers about the ganglion and nerve root.

Segments of spinal cord, meninges and spinal nerves were isolated and methylene blue injected. When an intrathecal pressure of 150 mm. water was maintained for 4 hours, no passage of dye beyond the spinal ganglia was noted. When the pressure was elevated to 600 mm., after 25 minutes, the blue color was noted distal to the spinal ganglia.

Serial microscopic sections failed to show any communication of the subarachnoid space with the perineural space beyond the spinal ganglia, at which point the meninges fused.

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BIBLIOGRAPHY