WATER EXCHANGE OF CENTRAL NERVOUS SYSTEM
AND CEREBROSPINAL FLUID

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A complete study of each component of cerebrospinal fluid is necessary before its dynamic physiology can be accurately described. This paper presents a study of its largest component, water. Using deuterium oxide (D₂O, heavy water) as a tracer, a general description has been obtained of the water exchange mechanism between blood, brain, spinal cord and cerebrospinal fluid.

The clinical facts of hydrocephalus prove beyond question the necessity of an intact pathway for the passage of cerebrospinal fluid from the cerebral ventricles to the subarachnoid space over the cerebral hemispheres. However, in spite of the apparently conclusive work of Dandy, Weed and others¹.².⁴.⁵.⁷.¹⁵.¹⁶ on the formation and absorption of cerebrospinal fluid, these processes are still imperfectly understood. Though most people regard the choroid plexus as the major site of cerebrospinal fluid formation, evidence that indicates this theory needs revision is steadily accumulating. Wallace and Brodie¹³.¹⁴ have demonstrated that bromide and iodide ions enter the cerebrospinal fluid from the brain substance, and they identify cerebrospinal fluid formation with this process. They stated that cerebrospinal fluid is interstitial fluid from the brain and does not come from the choroid plexuses. Studies with tracer ions have given this idea considerable support. Greenberg et al.,⁸ using a variety of radioactive ions, showed that the ions appeared at separate rates in cerebrospinal fluid continually draining from a dog’s cisterna magna. Such a state is not compatible with production of a completely formed cerebrospinal fluid either by filtration or secretion. This work suggests that each ion is traveling by free diffusion at its own rate.

More recent work with heavy water (D₂O) and radiosodium (Sweet et al.,¹⁹) has shown a difference in their appearance time in cerebrospinal fluid, which is incompatible with the theory of total formation of cerebrospinal fluid by the choroid plexuses.

MATERIALS AND METHODS

Deuterium oxide (D₂O, heavy water), used as the water tracer, was obtained 99.8 per cent pure from the AEC, prepared as 0.8 per cent NaCl, sterilized and stored in ampules of convenient size. The analysis of experimental samples was done by densimetric¹⁰ or mass spectrographic¹¹ methods.

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Studies were made on both humans and animals. All patients studied were from the Neurosurgical Service of the Peter Bent Brigham Hospital and The Children's Medical Center. They included individuals in the normal state as well as those affected by a wide variety of pathological conditions. Monkeys and dogs were used in the animal studies.

The general plan of most of the experiments was an intravenous injection of D₂O as 0.8 per cent NaCl followed by appropriate sampling of arterial blood, superior longitudinal sinus blood, cerebral ventricle cerebrospinal fluid, cisterna magna cerebrospinal fluid, spinal subarachnoid space cerebrospinal fluid and central nervous system tissue (cerebrum, cerebellum and spinal cord). Sampling was always done in such a way with sufficiently small quantities as to maintain a normal physiological state. The amount of D₂O given was approximately 1 cc. per kg., which gave an equilibrium concentration of about 0.15 to 0.25 volumes per cent D₂O.

RESULTS

The Normal State. It is difficult to obtain data on problems of this sort in a normal subject. The cerebral ventricles of most animals are too small to allow adequate sampling, and it is uncommon to find normal persons who require ventricular taps. The "normal" subjects of this study were all patients who had had a unilateral subdural hematoma removed 3 to 6 weeks before the studies were made. At the time of investigation they were considered normal, without evidence of impairment of cerebrospinal fluid circulation.

Following an intravenous injection of heavy water into a normal person, D₂O begins to appear in increasing concentration simultaneously in the cerebrospinal fluid of the cerebral ventricles, the cisterna magna and the lumbar subarachnoid space. However, the increasing concentration proceeds most rapidly in the cisterna magna, with the ventricular and lumbar spaces following more slowly until equilibrium with plasma is reached. There is considerable variation in the time required to reach equilibrium; the younger and smaller the subject, the more quickly equilibrium is reached. Once equilibrium between blood and cerebrospinal fluid has been established, D₂O disappears from both at the same rate. Fig. 1 shows the extremes of the observed normal D₂O appearance curves. The other normals showed appearance curves of similar configuration lying between these two.

A convenient way to consider these data is by the use of the half time for any compartment to reach blood D₂O concentration. This will be designated as the "half time." While the range of half times is large and the data are insufficient to determine the normal variation, the half times appear to increase with age. The spread of half times observed in each compartment over an age range of 6 months to 87 years is: cerebral ventricles, 2 to 37 minutes; cisterna magna 1.5 to 6 minutes; lumbar subarachnoid space 7 to 38 minutes. These half times are in good agreement with those reported by Sweet et al.¹² for 2 adult males with seizures of unknown etiology. Table 1 presents the