
THOMAS H. MILHORAT, M.D., AND RONALD G. CLARK, M.D.

Branch of Surgical Neurology, National Institute of Neurological Diseases and Stroke, and Laboratory of Pathology, Division of Biologics Standards, National Institutes of Health, Education and Welfare, Bethesda, Maryland, and the Department of Neurosurgery, the New York Hospital-Cornell Medical Center, New York, New York

The injection of phenosulfonphthalein (PSP) into the lateral ventricles is followed, usually within minutes, by the appearance of the dye in the cerebrospinal fluid (CSF) of the basilar cisterns and subarachnoid space. Failure of the dye to appear, or any substantial delay in its rate of appearance, may be regarded as strong evidence of an obstruction of the ventricular system. On this basis, the dye has been widely used in the clinical diagnosis of hydrocephalus and has served to distinguish the obstructive and communicating types reliably.1,7

In the current experiment, the circulation of PSP in the ventricles and subarachnoid space of normal and hydrocephalic animals was investigated. A number of observations concerning the normal migration of the dye as well as its altered circulation in obstructive and communicating hydrocephalus have not been previously reported. The significance of these findings is discussed.

Materials and Methods

Rhesus monkeys (macaca mulatta) and purebred beagle dogs were used in this study. The monkeys ranged in age from 1½ to 2 years and varied in weight from 4 to 6 lbs. The monkeys were ostensibly well at the time of the experiment. The dogs, on the other hand, were chosen from a line of purebred beagles in which a high incidence of communicating hydrocephalus spontaneously occurs.6 The dogs ranged in age from 2 days to 4 years and weighed between 500 gm and 40 lbs. For purposes of this experiment the animals were separated into three groups:

Group 1 (Normal). This group was composed of normal rhesus monkeys and normal beagle dogs. In the dogs, pneumoencephalograms had been previously performed to separate the normal animals from those with hydrocephalus. All findings were later confirmed by pathological examination.

Group 2 (Communicating Hydrocephalus). This group was composed of beagle dogs in which severe hydrocephalus had been previously demonstrated by pneumoencephalography and, in some cases, by Pantopaque ventriculography. The communicating nature of the process was suggested by the lack of air over the convexities and by the free passage of Pantopaque from the lateral ventricles into the cisterna magna. The diagnosis was later substantiated by pathological study.

Group 3 (Obstructive Hydrocephalus). Obstructive hydrocephalus was produced in a number of rhesus monkeys by blocking the fourth ventricle and distal aqueduct with an inflatable balloon. This technique has been discussed elsewhere16 and causes advanced ventricular enlargement in a matter of hours.17 Experiments were performed on these animals at intervals between 1 hour and 14 days after obstruction of the ventricular system.

In approximately half of the animals of each group, 0.2 cc of PSP* was injected into one lateral ventricle through a 23 gauge needle.

*In the current experiment, the widely available form of PSP (U.S.P., ph 6.2-7.0) was used. Dandy's original work was done with “neutral PSP” (Dandy's solution, ph 6.0-6.5) which is no longer commercially available.
dle; in the other half a similar dose was injected into the cisterna magna. The animals were sacrificed at intervals ranging from 45 minutes to 5 hours after injection of the dye and perfused with 10% neutral formalin solution via the aortic arch for 45 minutes. Thereafter, the brains were carefully removed and immersed in 1.0 N sodium hydroxide (NaOH) solution to develop the dye which becomes pink when alkalized. Immediate color photographs were taken to document the findings, and routine sections were saved for microscopic study.

Results

Group 1 (Normal): Ventricular Injection of PSP. At 45 minutes after injection of PSP into the lateral ventricles of normal monkeys and dogs, the dye was found diffusely distributed throughout the subarachnoid space (Fig. 1). The leptomeninges of all the major cisterns were deeply stained as were the leptomeninges over the cerebral and cerebellar hemispheres and the leptomeninges of the spinal subarachnoid space. Migration of the dye into the depths of the cortical sulci was evident on coronal section of these brains.

Of particular interest was the finding that PSP leaves the ventricles and subarachnoid space with apparent ease and penetrates the surrounding brain to a depth of several millimeters (Fig. 1 right). The dye was found in the cortical ribbon of gray matter over the hemispheres and was particularly intense at the base of the sulci. Little or no dye was present in the subcortical white matter. Around the ventricles, the dye was observed in a number of periventricular structures. Here, too, the gray matter was selectively stained with a rich uptake in the following structures: the periaqueductal gray, the hypothalamus, the caudate nucleus, and the thalamic nuclei bordering the third ventricle. The septum pellucidum was another richly stained structure, but the midline commissures and other periventricular structures of white matter origin were minimally stained or not stained at all. Examination of brains 2 hours after intraventricular injection of PSP revealed no qualitative differences from the findings at 45 minutes although the migration of dye into the surrounding brain was somewhat increased.

Group 1 (Normal): Cisternal Injection of PSP. Injection of PSP into the cisterna magna of normal animals was followed within 45 minutes by diffuse spread of the dye throughout the subarachnoid space. The pattern of this distribution and the penetration into the surrounding brain were similar to that seen after intraventricular injection. The dye did not enter the ventricular system by retrograde flow, and although the outlets of the fourth ventricle were vitally stained, the cavity of the ventricle contained no dye.

Group 2 (Communicating Hydrocephalus): Ventricular Injection of PSP. Following injection of PSP into the lateral ventricles of dogs with communicating hydrocephalus, the dye was found to pass promptly out of the ventricles into the surrounding cisterns. Within 45 minutes, the leptomeninges of the spinal subarachnoid space were intensely stained as were the leptomeninges of the basilar cisterns, the ambient cisterns, cisterna magna cerebri, and the interpulvuncular cisterna. Dye did not pass over the cerebral convexities but was heavily concentrated over the cerebellar hemispheres where it penetrated the sulcal grooves between the folia. Only a small trace of dye passed into the prechiasmatic and Sylvian fissure cisterns. From these findings it was presumed that the obstruction was the result of obliteration of the subarachnoid spaces over the cerebral hemispheres. This finding was subsequently supported by microscopic findings, which demonstrated a diffuse, non-specific leptomeningitis, most advanced over the cerebral hemispheres.

On coronal section of these brains, it was apparent that a considerable transependymal migration of dye had occurred. The depth of the parenchymal penetration and the intensity of the vital staining were substantially greater than that observed in the normal controls. In contrast to the normal controls, the dye in the hydrocephalic brains had migrated into periventricular structures of both white and gray matter origin, although the latter was preferentially stained. Surface staining of the cerebellum, brain stem, and spinal cord was also evident to a depth of 4 to 5 mm, but no dye was seen in the parenchyma over the cerebral hemispheres owing