Experimental Hydrocephalus Produced by the Subarachnoid Infusion of Silicone Oil*

HENRYK WISNIEWSKI, M.D., PH.D., ROY O. WELLER, M.B., PH.D.,† AND ROBERT D. TERRY, M.D.
Department of Pathology (Neuropathology), Albert Einstein College of Medicine, Bronx, New York

A variety of techniques has been employed experimentally to produce hydrocephalus in adult and infant animals; many of the methods have been reviewed by Pudenz, et al.7 Most successful was the injection of irritants such as India ink into the cisterna magna of rats4 or kaolin into the subarachnoid space of dogs.8 Hydrocephalus also occurs following the introduction of foreign bodies, such as cotton, into the aqueduct of Sylvius in adult dogs,5,6 Trypan blue, when administered to pregnant rats, produces aqueductal stenosis and a high rate of hydrocephalus in the offspring.9 Tellurium in the diet10 of pregnant rats and fetal infection with mumps virus11 may also be followed by hydrocephalus in the newborn.

The technique presented here for inducing hydrocephalus involves the infusion of inert silicone oils into the cisterna magna either indirectly through a polyethylene tube inserted into the spinal subarachnoid space, or by direct puncture of the posterior atlanto-occipital membrane. Wisniewski11 observed, in dogs, that intraventricular infusion of these oils cause little or no inflammatory reaction either of the ependymal surface or within the meninges, even when the contact was maintained for over 6 months. The bland nature of the oils and the distance of the injection site from the lateral ventricles eliminates the complications of mechanical damage and inflammation, thus allowing a more reliable interpretation of histological and physiological data.

Received for publication August 2, 1968.
Revision received November 22, 1968.
* This work was supported by Grants NB-02255 and NB-03356 from the National Institutes of Neurological Diseases and Blindness of the Department of Health, Education and Welfare.
† U.S. Public Health Service International Postdoctoral Fellow No. 3F05-TW-01263-0151. Present address: Department of Pathology, Guy's Hospital, London S.E.1, England.

Material and Methods

Adult New Zealand white rabbits weighing 3 to 4 kg and 2-week-old normocephalic mongrel dogs were used; the former were housed singly in wire cages and fed on rabbit bran, while the puppies remained with their mother. Silicone oil was infused into the subarachnoid space by one of two routes, either through a polyethylene tube in the spinal subarachnoid space, or by direct injection through the posterior atlanto-occipital membrane into the cisterna magna.

Infusion of oil into the Subarachnoid Space of the Spinal Cord. Following the induction of anesthesia, a spinal laminectomy was performed at the lower sacral level (4 to 5 cm above the base of the tail) in the rabbit, and in the mid-lumbar region in puppies. A length of sterile polyethylene tubing was inserted into the spinal subarachnoid space; the internal diameter of the tube used in the puppies fitted over a No. 23 needle, whereas that in the rabbit was a little larger and accepted a No. 21 needle. A free flow of cerebrospinal fluid from the tube was used as an indication that the catheter was correctly inserted into the subarachnoid space. By careful measurement of the animal and the length of the tube inserted, the approximate level of the tip of the cannula could be established. With the catheter in position, the free end was connected by the appropriate needle to a syringe containing silicone oil (Dow Corning 200 fluid) with a viscosity of 3000 centistokes or a 1:1 mixture of 3000 c.s. and 100,000 c.s. oils. Infusions were performed by a mechanical infusion-withdrawal pump at 0.01–0.05 ml per minute. The amount of oil infused varied with the size of the animal and the position of the cannula; 1.5 ml was infused into 2-week-old puppies at 0.02 ml per min, and as much as 6 ml was tolerated by the adult rabbits,
Hydrocephalus Produced by Silicone Oil

especially if the oil were given in divided doses. For this latter purpose the cannula may be left in place by fusing the external end, burying it in the wound, and reconnecting it to the pump some 12 to 24 hours later. The rate of infusion was governed largely by the clinical response of the animal. Adequate infiltration of the operation site with local anesthetic made it possible to insert the cannula under very light general anesthesia. During the infusion any change in respiratory rate, usually an increase followed by slowing and apnea, was an indication of intolerance; in this event the infusion was stopped until the animal returned to a more normal respiratory rate.

Direct Injection into the Cisterna Magna. This method was only performed on adult rabbits. Animals were anesthetized and the posterior atlanto-occipital membrane exposed; thereupon the membrane was punctured with a No. 19 needle. Through this hole, from which cerebrospinal fluid exuded freely, a polyethylene cannula prefilled with very viscous (100,000 c.s.) silicone oil was inserted to a depth of 0.5 to 1 cm. With the tip of the cannula in the cisterna, the distal end was passed over a needle attached to a syringe containing the oil. The infusion was performed by the mechanical infusion-withdrawal pump at 0.02 to 0.05 ml per minute until 1.5 to 2 ml had passed into the cisterna magna. Upon withdrawal of the polyethylene tube, the posterior cervical muscles were drawn tightly together by a purse string suture to minimize the backflow of oil.

Preparation of the Tissue. The animals were killed by perfusion of fixative while under barbiturate anesthesia. Total body perfusion was effected through a cannula in the left ventricle, first with 100 ml of 4% paraformaldehyde then followed by 5% glutaraldehyde in 0.067 molar phosphate buffer at pH 7.3 for 15 min. The brain and the cervical spinal cord were quickly dissected after perfusion, and specimens of tissue from various regions were taken for light and electron microscopy; these results are the subject of a separate communication.10

Results

Hydrocephalus developed in puppies and rabbits following both methods of infusion. However, as the anatomy of the brain and degree of hydrocephalus differs in the two groups of animals, they will be described separately.

Hydrocephalus in Puppies. Infusion of silicone oil into the puppies' spinal subarachnoid space resulted in a marked enlargement of the head over the subsequent 4 weeks, compared with the control litter mate. This enlargement involved the vault of the skull and, although there was delay in closing of the anterior fontanel no separation of the other sutures was detectable. Apart from the enlargement of the head, the hydrocephalic puppies were smaller and less well developed than the controls; they were also ataxic, slightly paraparetic, and displayed a fine oscillatory tremor of the head. At autopsy the brain showed flattening of the gyri and narrowing of the sulci; coronal sections revealed extensive dilation (Fig. 1) of the cerebral ventricles with separation of the corpus callosum from the fornices, destruction of the septum pellucidum, and extensive communication between the third and both lateral ventricles. Around the dilated ventricles, the white matter of the centrum semiovale and corpus callosum was very thin although the thickness of the cortex appeared normal. The silicone oil was located in the cisterna magna and in the subarachnoid space at the base of the brain, around the cerebellum, but not in the ventricles. No thickening or opacity of the meninges in contact with the oil was noted, and no inflammatory reaction was observed microscopically.

Hydrocephalus in Rabbits. Animals that

Fig. 1. Coronal section of hydrocephalic puppy brain 4 weeks after subarachnoid infusion of silicone oil. There is marked dilatation of the posterior parts of the lateral ventricles and of the temporal horns with thinning of the white matter.