

(Abstract of paper read by Dr. W. P. Van Wagenen at the New York Meeting of the Harvey Cushing Society, May 19, 1942.)

CLINICAL REPORT ON THE USE OF PANTOPAQUE

(Ethyl Iodophenylundecylate):

A New Contrast Medium for Visualization of the Subarachnoid Spaces

by William P. Van Wagenen, M.D.

(From the Department of Surgery: Neurosurgical Division, School of Medicine and Dentistry, The University of Rochester, Rochester, New York)

This preparation has been used in 30 cases where space-displacing masses within the spinal canal were suspected. The majority of these masses proved to be ruptures of the nucleus pulposus or related lesions. PANTOPAQUE would seem to have certain definite advantages over the use of Lipiodol. First, it is more fluid, more miscible with spinal fluid than Lipiodol. Second, there is little, if any, tendency of the preparation to break up into bubbles and create artefacts. Thirdly, it tends to get into the spaces of Jacot and the various subarachnoid spaces more easily than Lipiodol and there are fewer false and erroneous conclusions regarding space-displacing masses. Fourth, the ease of removal through a lumbar puncture needle is considerably greater than Lipiodol. Fifth, it is a slowly absorbable preparation. Sixth, a lesser amount is needed for study of the subarachnoid space, 2 to 3 cc. being sufficient. We have not as yet asked patients to return for follow-up in order to note the degree of absorbability at this date.

The chemical meningitis created by the presence of this preparation varies a good deal from time to time. It is distinctly the impression that when this preparation is introduced in a closed space, such as created by a spinal cord tumor, that the chemical reaction is fairly great and probably greater than it is with Lipiodol. The degree of headache and other meningeal signs created by this preparation varies a good deal also. A very decided impression is gained that the preparation should be removed in part or entirely after the examination is over. The impression is gained that the increased mobility is a handicap in examining the subarachnoid space for evidences of small lesions in the cervical and thoracic regions. For these regions Lipiodol is preferred.

The technique for use of the preparation is as follows: The patient is placed in the prone position on the tilt fluoroscopic table. A lumbar puncture is done -- usually between L 3 and L 4. At times a blanket is placed beneath the abdomen to give a little added separation of spinous processes. Three cubic centimeters of the warmed preparation are injected after a specimen of spinal fluid has been aspirated. The needle is pushed forward until it appears to lie near the ventral part of the subarachnoid sac. A sterile dressing is placed over the needle, the fluoroscopy carried out and the preparation aspirated at the end of the procedure.

needle with short bevel is pushed through the skin through the ligamentum nuchae and into the cistern. Great care must be taken as the cistern is entered to prevent damage to the medulla. When the subarachnoid space has been entered, the trochar of the needle is removed and a 5 cc. sterile syringe attached. Slightly more spinal fluid is removed than contrast medium to be injected. The pressure within the spinal canal should be sufficiently great to make the removal easy. After the spinal fluid has been removed, the syringe containing it is disengaged and a second sterile syringe containing ethyl iodophenylundecylate or other medium is attached to the needle. The injection is made slowly, the syringe is then disengaged, and the trochar put back in place. The needle is quickly removed and the dog's head extended to aid in preventing escape of spinal fluid from the puncture wound. The animal is then placed for several hours with his head on a support so that it is well above the plane of the body.

Direct trauma of the cord by the needle and escape of spinal fluid from the canal are to be guarded against. Accidental perforation of a blood vessel in the dura frequently occurs and all animals from which a bloody spinal fluid is obtained should be discarded. Similarly, animals in which trauma is suspected should be disregarded. An experienced operator can usually get excellent results in four out of six dogs.

Following recovery from anesthesia the animal should be observed for food consumption, gait changes, evidence of cord bladder, and symptoms of chemical meningitis as evidenced by outcry when the head is quickly bent or the neck palpated. Rectal temperatures should be taken for a period of a week during which the animal should be given opportunity to exercise freely since the maximum effects of a myelographic medium becomes evident only when unrestricted exercise is permitted.

Dogs injected intrathecally with ethyl iodophenylundecylate are usually in better clinical condition than control animals injected with iodized poppyseed oil. This is brought out in the two series of experiments summarized in Tables I and II, the adverse effects of the media, such as gait disturbances, etc., are collectively described under the heading "Chemical Meningitis". Subsequent to those experiments it was noted that although dogs tolerate ethyl iodophenylundecylate better than iodized poppyseed oil in the doses given, nevertheless, ethyl iodophenylundecylate produces a mild fever that is not produced by iodized poppyseed oil. This fever may be as high as 2.0 C and may last for several days. A typical fever curve for a dog injected intrathecally with ethyl iodophenylundecylate is given in Chart I, and typical data showing extent and duration of fever with a group of dogs injected with ethyl iodophenylundecylate are collected in Table III.

Ethyl iodophenylundecylate is absorbed from the spinal canals of dogs in about a year provided the dose is not larger than 3 cc. The rate of absorption appears to be affected by the position that the medium occupies in the subarachnoid space and doubtless is slowest in the region of the cauda equina.

In dogs, both ethyl iodophenylundecylate and iodized poppyseed oil are encysted shortly after intrathecal injection. Because of its greater fluidity, ethyl iodophenylundecylate forms smaller globules in the subarachnoid space, and accordingly the cysts are smaller. The reaction about the two kinds of cyst is essentially that of tissue to a foreign body, but the amount of irritation produced is greater with ethyl iodophenylundecylate. This is seen in the illustrative sections shown in Plate I and II, both of which are selected to show the maximum damage that occurs in dogs. Plate I is a photomicrograph of a section taken from the cord of a dog sacrificed 45 days after injection of ethyl iodophenylundecylate. The cysts are smaller than those shown in

Plate II which is taken from an animal injected with iodized poppyseed oil and killed at 120 days. It is evident that the walls of the cysts in both cases are made up of thin layers of fibrous tissue, in which small numbers of mononuclear cells and phagocytes are present, together with a few polymorphonuclear cells. The detail is shown better in Plate III which is a high power magnification of a portion of a section from the dog injected with ethyl iodophenylundecylate. The dilation of the central canal in the iodized poppyseed oil section (Plate I) is due to a hydrocephalus, two cases of which were seen in a series of nine dogs. One similar case of hydrocephalus has been observed with ethyl iodophenylundecylate in a series of 55 dogs. As the contents of the cysts are absorbed the damaged area becomes smaller and smaller and, with ethyl iodophenylundecylate, are difficult to locate after a period of a year.

The mortality of the experimental dogs was relatively low, both with iodized poppyseed oil and with ethyl iodophenylundecylate. In the poppyseed oil series only one dog out of 14 died, and autopsy showed that a subarachnoid hemorrhage was the cause of death. In contrast, with ethyl iodophenylundecylate 3 dogs died out of the experimental group of 55. One of these deaths was due to peritonitis, but two were referable to damage to the medulla on injection of the contrast medium.

As shown in Tables I-III, the level at which the two contrast media were injected varied from 0.19-0.48 g./kg. or from 7 to 10 times the amount that is usually used in myelography in man. The toxic effects, such as they were, seemed to bear no relation to the dosage; however, a larger series of experiments might bring out such a relationship.

Summary: Intrathecal injection of ethyl iodophenylundecylate in doses up to 0.48 g./kg. in dogs produces a slight fever of short duration, but otherwise does not effect the clinical behavior of the animal. After a short

period of time, the drug is encysted and about these cysts there is a mild foreign body reaction. As the cystic contents are absorbed, the tissue slowly returns to normal in a period of about a year. In contrast, iodized poppyseed oil does not produce fever, but frequently does cause a diminution in the activity of the animal; the drug is encysted and these cysts are essentially unchanged during the life of the animal.

Table I

Intrathecal Injections of Ethyl Iodophenylundecylate in Dogs

Dog. No.	Weight kg.	Dose gm./kg.	Chemical Meningitis	Days Reduced Activity
39-286	17.0	0.30	Slight on 3d day only	2
39-268	15.0	0.34	Slight on 3d day only	2
39-287	18.0	0.28	Slight on 3d day only	2
38-257	13.0	0.39	Moderate on 3d day only	3
39-263	13.5	0.37	None	1
39-293	11.5	0.33	None	3
39-306	15.0	0.34	Slight on 2d day only	34*
39-290	20.0	0.32	None	1
39-313	27.0	0.23	None	1
39- 3	16.6	0.30	Slight for 4 days	4
39- 4	16.7	0.30	Severe for 4 days	12
39- 5	11.3	0.34	Slight for 8 days	8
40- 50	14.2	0.35	Slight for 9 days	9
40- 48	11.4	0.33	Moderate for 6 days	6**
40-51	8.0	0.48	Moderate for 9 days	9

* Distemper

**Died of peritonitis after 24 days

Table II

Intrathecal Injections of Iodized Poppy Seed Oil in Dogs

Dog Number	Weight (kg.)	Dose gm./kg.	Chemical Meningitis
38-201	24.0	0.20	Slight for 2 days
38-332	26.0	0.20	Moderate for 24 days*
37-27	16.9	0.24	Moderate for 14 days
40-12	24.0	0.25	Moderate for 28 days
38-168	13.0	0.28	Moderate for 5 days
38-319	16.0	0.29	Slight for 4 days
38-8	17.0	0.31	Slight for 16 days
40-11	10.0	0.40	Moderate for 14 days
39-1	9.0	0.44	Moderate for 14 days

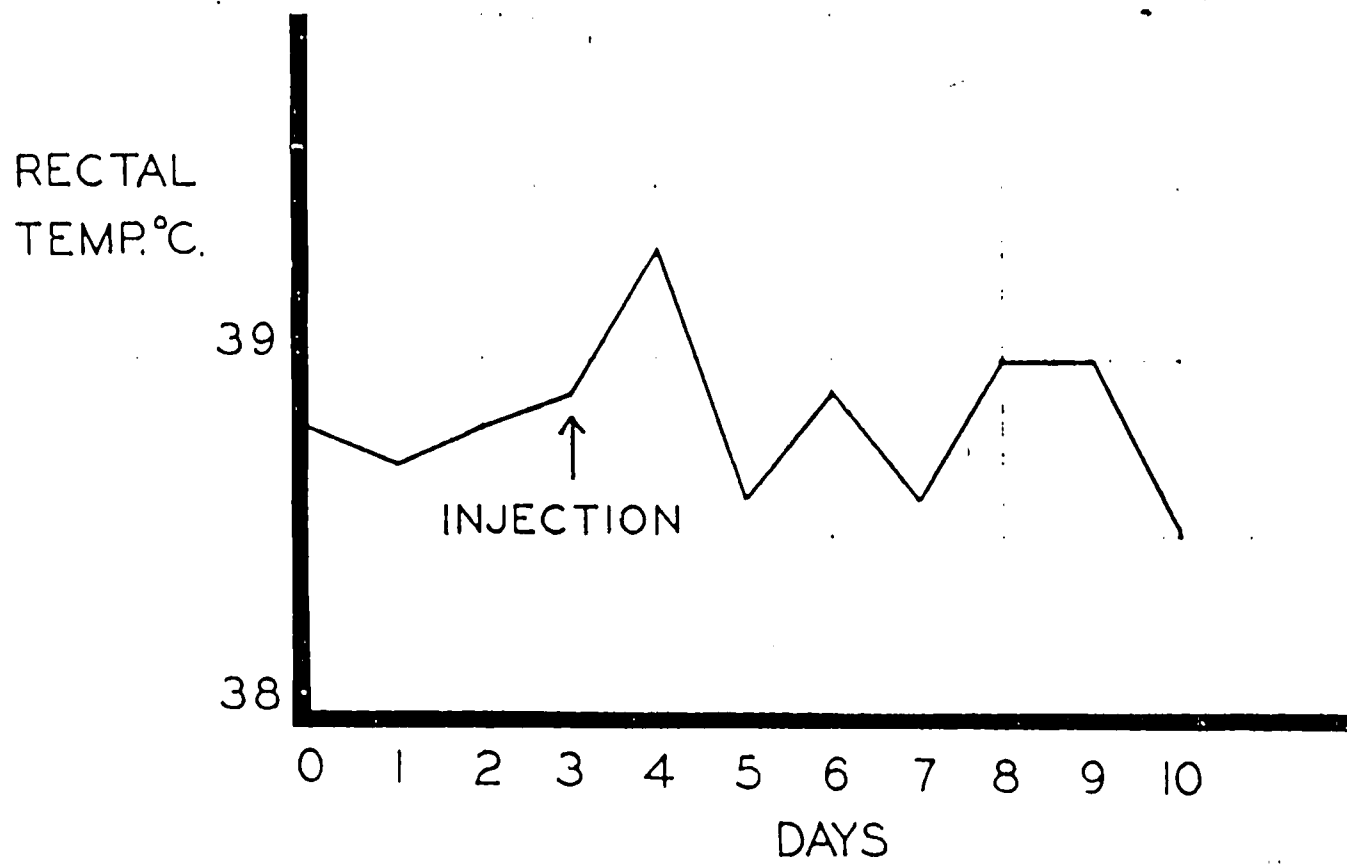
*Died with subarachnoid hemorrhage at the end of 24 days

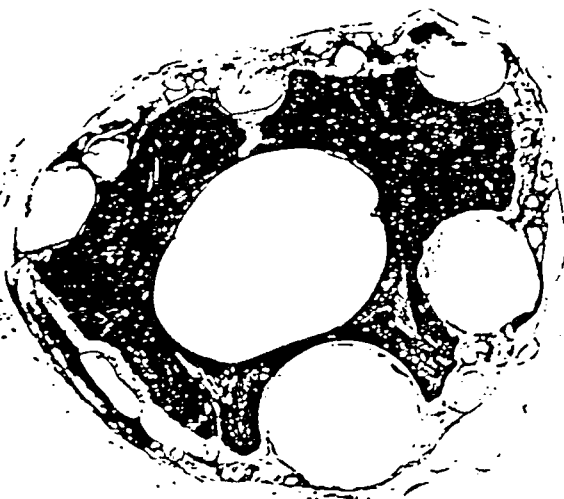
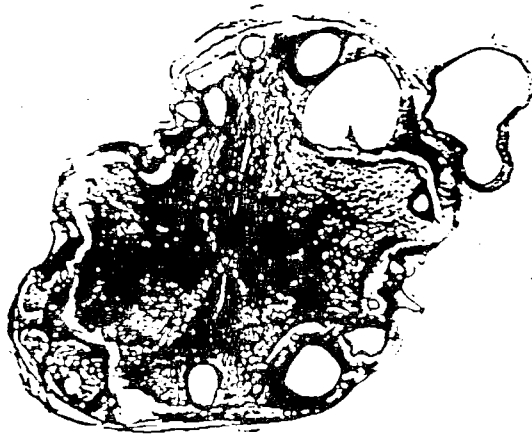
Table III

Intrathecal Injections of Ethyl Iodophenylundecylate in Dogs

Dog No.	Weight (kg.)	Dose (μ ./kg.)	Remarks
759	19.1	0.19	0.5 C. fever for 2 days post injection. Hesitant about lowering head on second day. Otherwise clinically normal during observation period of 60 days.
760	19.0	0.19	0.8 C. fever for 1 day post injection. Otherwise clinically normal for 30 days, after which development of mange obscured study of postural behavior.
767-1	17.4	0.21	1.1 C. fever for 1 day post injection. Otherwise clinically normal during observation period of 7 days.
767-2	15.1	0.24	1.3 C. fever for 1 day 0.7 C. fever for 2 days post injection. Otherwise clinically normal during observation period of 7 days.
758	14.3	0.26	0.9 C. fever for 1 day post injection. Otherwise clinically normal during observation period of 30 days.
757	13.3	0.29	1.3 C. fever for 2 days post injection. Subdued for 4 days and holds head to one side; probably referable to damage during puncture since the spinal fluid was tinged with blood. Subsequently recovered completely.
767-3	13.0	0.28	0.6-1.7 C. fever for 4 days post injection. Otherwise clinically normal during observation period of 7 days.
757-4	8.8	0.42	1.3 C. fever for 1 day post injection. Otherwise clinically normal during observation period of 7 days.

Typical Case Showing Development of Fever in a Dog following
Intrathecal Injection of Ethyl Iodophenylundecylate





SECTIONS SHOWING ENCYSTMENT OF CONTRAST MEDIA

Plate I - Ethyl Iodophenylundecylate after 45 days; Plate II - Iodized
Poppyseed Oil after 120 days (Myelin sheath stain)



Plate III

Reaction at 45 days about a spinal cord cyst due to ethyl iodophenylundecylate (H & D stain). The margin of the cyst is shown in the lower left hand corner.