Intrathecal Injection of Ethyl Iodocephylundoclylate in Dogs

In the development of ethyl iodocephylundoclylate as a contrast medium for myelography, upwards of 150 dogs have been injected intrathecally with different types of liquid iodorganic compounds. Through this large experience, which has extended from 1936 until the present, the procedure has been standardized somewhat. It is essential that the dogs be free of distemper, or any suspicion of distemper, and that the operator be experienced before the results are significant. The animals used in the assay should be held under observation for at least three weeks and should preferably weigh 15-20 kilograms. Rectal temperatures should be taken daily for three days prior to the injection, or until the temperature is constant. The reading on the last day is taken arbitrarily as the reference temperature.

Prior to the injection, the dogs are anesthetized either by intraperitoneal injection of Vipital or by intravenous injection of Nembutal. The hair is closely clipped over a wide area of the back of the skull and the cervical spine. The clipped area is then thoroughly scrubbed with soap and water. Next, using sterile technique, the prepared site is cleansed with 70% alcohol, painted with tincture of iodine, and again cleansed with 70% alcohol. The prepared area may, if desired, be draped with sterile towels.

An assistant, gripping the nose of the dog, sharply flexes the head on the chest. This maneuver makes the cisterna magna more accessible by widening the distance between the aulas and the foramen magnum. Observing sterile technique, the operator then determines the location of the occipital protuberance and the position of the spine of the second cervical vertebra. At a point midway between these two landmarks a 20-gauge lumbar puncture
needle with short bevel is pushed through the skin through the ligamentum
mammas 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 trocher 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 methyl iodophylumidate or other medium is attached
to the needle. The injection is made slowly, the syringe is then disengaged,
and the trocher 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 its 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 cistern 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 cyanosis when the head is quickly bent or
the neck piped. 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 un-
restricted exercise is permitted.
Dogs injected intrathecally with ethyl iodocephylundecylate are usually in a better clinical condition than control animals injected with iodoised 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 gastric disturbances, etc., are collectively described under the heading "Chemical meningitis". Subsequent to these experiments it was noted that although dogs tolerated ethyl iodocephylundecylate better than iodoised poppyseed oil in the doses given, nevertheless, ethyl iodocephylundecylate produces a mild fever that is not produced by iodoised poppyseed oil. This fever may be as high as 2°C and may last for several days. A typical fever curve for a dog injected intrathecally with ethyl iodocephylundecylate is given in Chart I, and typical data showing extent and duration of fever with a group of dogs injected with ethyl iodocephylundecylate are collected in Table III.

Ethyl iodocephylundecylate 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 iodocephylundecylate and iodoised poppyseed oil are evacuated shortly after intrathecal injection. Because of its greater fluidity, ethyl iodocephylundecylate 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 extent of irritation produced is greater with ethyl iodocephylundecylate. 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 iodocephylundecylate. The cysts are smaller than those shown in...
Plate II which is taken from an animal injected with iodized poppyseed oil and killed at 100 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 damped 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 iodophenyl undecylate in doses up to 0.48 g./kg. in dogs produces a slight fever of short duration, but otherwise does not affect the clinical behavior of the animal. After a short

\[ \text{in CSF} = \text{CIDR} \]
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, iodised 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 Iosphenylundecylate in Dogs

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Weight (kg)</th>
<th>Dose (gm/kg)</th>
<th>Chemical Meningitis</th>
<th>Days Reduced Activity</th>
</tr>
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<tbody>
<tr>
<td>39-285</td>
<td>17.0</td>
<td>0.30</td>
<td>Slight on 3rd day only</td>
<td>2</td>
</tr>
<tr>
<td>39-288</td>
<td>15.0</td>
<td>0.34</td>
<td>Slight on 3rd day only</td>
<td>2</td>
</tr>
<tr>
<td>39-287</td>
<td>16.0</td>
<td>0.29</td>
<td>Slight on 3rd day only</td>
<td>2</td>
</tr>
<tr>
<td>39-283</td>
<td>13.0</td>
<td>0.39</td>
<td>Moderate on 3rd day only</td>
<td>3</td>
</tr>
<tr>
<td>39-293</td>
<td>13.5</td>
<td>0.37</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>39-306</td>
<td>11.5</td>
<td>0.33</td>
<td>None</td>
<td>3</td>
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<tr>
<td>39-229</td>
<td>18.0</td>
<td>0.34</td>
<td>Slight on 2nd day only</td>
<td>3</td>
</tr>
<tr>
<td>39-513</td>
<td>22.0</td>
<td>0.32</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>39-3</td>
<td>27.0</td>
<td>0.25</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>39-4</td>
<td>16.6</td>
<td>0.30</td>
<td>Slight for 4 days</td>
<td>4</td>
</tr>
<tr>
<td>39-5</td>
<td>16.7</td>
<td>0.30</td>
<td>Severe for 4 days</td>
<td>3</td>
</tr>
<tr>
<td>39-6</td>
<td>11.3</td>
<td>0.34</td>
<td>Slight for 8 days</td>
<td>9</td>
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<td>40-50</td>
<td>14.2</td>
<td>0.35</td>
<td>Slight for 9 days</td>
<td>9</td>
</tr>
<tr>
<td>40-48</td>
<td>11.4</td>
<td>0.33</td>
<td>Moderate for 6 days</td>
<td>8</td>
</tr>
<tr>
<td>40-51</td>
<td>8.0</td>
<td>0.48</td>
<td>Moderate for 9 days</td>
<td>9</td>
</tr>
</tbody>
</table>

* Distemper
** Died of peritonitis after 24 days
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.
Please note the first slide refers to Pantopaque taken after 45 days whilst the poppy seed oil was taken after 120 days. Question, what would have been the damage of Pantopaque after 120 days? Much worse I expect, furthermore, if you look carefully, the cysts of the poppy seed is within only, whilst the Pantopaque cysts are also outside the cord.