STUDY ON THE CONTRAST MEDIUM FOR MYELOGRAPHY

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I. HISTORICAL AND PREFACE

Further development in myelography will depend chiefly upon research for an ideal and suitable contrast medium for myelography. Historically, myelography was originated by P. Krause who instilled Kollargol into the spinal canal as contrast medium in 1912. In 1919, Dandy used air as a contrast medium. Sicard and Forester reported instilling Lipiodol and similar iodized oils into the human cerebrospinal cavity and observing them descend into the lumbosacral sac without any side effects in 1922. In 1923, Berberich and Hirsch used Jodipin in myelography. Later Jodipin was used in Germany and Lipiodol in France and other countries including Japan.

During the period from 1920 to 1940 most research investigated the basic defects of small nonobstructing lesions, multiple tumors and various types of growths. Simultaneously the irritating properties of iodized oils began to be reported during the latter part of this period. In 1935, Lysholm emphasized the irritating properties of Lipiodol on the ependyma and leptomeninges, which were made worse by its remaining for a long period in the subarachnoid space. In 1941, Marcovich described the action of Lipiodol on the leptomeninges and demonstrated its irritating after effects in several autopsies. In 1938, Radovici and Meller used Thorotrast as a new contrast medium in place of Lipiodol. It was abandoned because of the resulting intense meningeal reaction and deposition in the reticuloendothelial system which was thought to act as a carcinogenic agent by its radioactive property. In 1944, Kubik and Hampton recommended “the forced drainage” of all contrast medium from the spinal canal by lumbar puncture. In 1944, Pantopaque was used in myelography by Ramsey, French and Strain. Its irritating properties are very slight but its rate of absorption is remarkably slow which may impede later X-ray examinations. The after effects of Pantopaque, as with previous contrast medium, were reported by many workers to cause meningeal irritation (Tarler, 1945), adhesive arachnoiditis (Erickson, 1953), and multiple extraocular palsies (Nacky, 1954).

The history of myelography parallels the history of contrast media used for it. The development in myelography depends upon finding an ideal and suitable contrast medium. The contrast media which have been used hitherto for myelography remained for a long period after examination and caused...

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many sequelae and impeded further X-ray examination. An ideal and suitable contrast medium should have the following qualities: minimal irritation, rapid absorption and excretion, high contrast, and proper viscosity.

II. ANIMAL EXPERIMENTS

A. Material and method

Urokolin which is used in bronchography has minimal irritating properties to the bronchii and organs in comparison with Lipiodol, and its excretion from the human body is very rapid. Urokolin is chemically 3-acetylamino 2, 4, 6, triiodobenzoic acid, a white crystal powder insoluble in water. I made Urokolin acid crystals finer and suspended them in vegetable oil. There is no limitation of concentration of the preparation because it is used as a suspension. The medium, therefore, is changeable in regard to its concentration, X-ray contrast, specific gravity and viscosity. I used soybean oil as the vegetable oil.

The specific gravity of 60% Urokolin Oil Suspension is 1.35 and its viscosity is 2,540 cps. at 36° C.

In order to examine the contrast figure of Urokolin Oil Suspension, it was instilled in models of various types of spinal canals composed of polyethylene tubes which were filled with Ringer's solution. X-ray film of the contrast figures for the new contrast medium and Lipiodol were taken and compared. When the medium was instilled, it streamed downward on the walls of the models, while Lipiodol fell down as a bolus. The velocity of the descent of this medium was quicker than that of Lipiodol. We could observe the finer structures of the tumors by this medium more clearly than by Lipiodol with same tumor models. The reason for this is due to the lower viscosity and hydrotaxic property of the new contrast medium.

Animal experiments were performed on dogs to determine the rate of absorption and irritating properties of 60% Urokolin Oil Suspension. 1 to 2.5 ccm of the medium were injected into the cysterna magna or the lumbar subarachnoid cavity of dogs under Rabonal anesthesia (Table 1). Dogs were fixed on the abdomen with hyperextended heads elevated above their lower limbs. A hallow at the midline behind the occipital process was palpated and the puncture was done here. The direction of the needle should not be in the rostral direction, or the injected medium may enter the ventricular cavity and intracranial spaces.

To examine the irritating properties when the medium was injected into the spinal cavity, the pulse, respiratory rate, and E.C.G. were recorded periodically. The head of the injected dog was raised to 30 degrees for several minutes after injection. The level of the medium was examined periodically by fluoroscopy. X-ray films were taken antero-posteriorly and laterally to follow the injected contrast medium.

Three dogs were killed by injection of Rabonal and their brain and whole spinal cords were removed and fixed in 10% formol. The tissues were sliced 5 micron thick and stained by Hematoxylin-Eosin and Nissl.
B. Results of experiments

Changes in blood pressure

Blood pressure was recorded by kimography in six of the injected dogs (Fig. 1). Three out of six cases showed no change in blood pressure (Fig. 1). One of the dogs (No. 4) showed a slight decrease in pulse pressure which continued for 15 min. (Fig. 1). Two of the six dogs showed very slight falls in the blood pressure immediately after injection but recovered rapidly (Fig. 1).

Changes in pulse rate

The pulse rate was recorded in all cases by E.C.G. The changes in pulse rate were very slight and variable, and no consistent relation to the blood pressure. In the dogs which showed a change in the pulse rate, the maximal change was observed within 4 or 5 minutes after injection and returned to normal 5 or 6 minutes later. Two minutes after infection, four cases showed decrease in the pulse rate and two cases showed increase of the pulse rate. The other three cases showed no change in the pulse rate.

<table>
<thead>
<tr>
<th>No. of the nations hours ance of the contrast medium</th>
<th>X-ray examinations hours after injection</th>
<th>Disappearance of the contrast</th>
<th>Blood pressure</th>
<th>Pathological examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>0 6 14 90</td>
<td>14–90</td>
<td>No change</td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>0 22 65</td>
<td>No disappearance</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.5</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>0 24 48 72</td>
<td>48–72</td>
<td>Pulse pressure decreased</td>
</tr>
<tr>
<td>5</td>
<td>1.5</td>
<td>0 42 78 92</td>
<td>78–92</td>
<td>Slight decrease</td>
</tr>
<tr>
<td>6</td>
<td>2.5</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.0</td>
<td>0 24 48 66</td>
<td>48–66</td>
<td>Slight decrease</td>
</tr>
<tr>
<td>8</td>
<td>1.0</td>
<td>0 24 60</td>
<td>24–60</td>
<td>No change</td>
</tr>
<tr>
<td>9</td>
<td>1.0</td>
<td>0 17 62 81</td>
<td>62–81</td>
<td>No change</td>
</tr>
</tbody>
</table>

X-ray examination

X-rays of the contrast medium injected into the spinal canals were taken in seven cases. Before the X-ray films were taken all spinal canals were observed fluoroscopically in order to decide the position of the contrast medium.
On each successive day after injection, these procedures were carried out. When thinly spread, the contrast medium disappeared rapidly but in the heavy concentration it was still present on the last films. Three cases which were injected with 1.5 ccm of the contrast medium, the time necessary for disappearance was between from 46 to 85 hours. In three cases which were injected with 1 ccm of the contrast medium, the time for disappearance was between 45 and 81 hours. On the average 1 ccm of the injected contrast medium remained at 46 hours and vanished by 69 hours after injection. During the first 24 hours the contrast did not show any remarkable change but after 24 hours it had either markedly decreased or disappeared (Fig. 2).

Others

Respiration showed no remarkable change in all successful cases. No. 6 dog, which was injected with 2.5 ccm into the ventricular system and cervical space by mistake, showed remarkable salivation and vomiting immediately after injection and later tremor of his trunk.

No. 3 dog, which was injected with 1.5 ccm into the central canal of the spinal cord by mistake, showed an obvious straight narrow shadow of the central canal on X-ray films, and the dog died the night of the experiment.

Pathological study

No. 1, No. 3, No. 7, and No. 8 dogs were pathologically examined by Hematoxylin-Eosin and Nissl stains. No. 3 which was injected with the contrast medium into the central canal, by mistake, showed mechanical destruction of the central canal and the surrounding area. This area showed slight roughness, edema, decrease and swelling of the glia cells, but no infiltration of the leukocytes. We feel that the lesions were mechanical and not caused by the dye (Fig. 3-5, 6).

No. 7, which was killed three days after injection, showed small amount of the injected contrast medium. The meninges showed hyperemia and slight infiltration of leucocytes and separation of the pia mater from the spinal cord. We feel that there was some irritation to the meninges by the contrast medium. The spinal cord showed no pathological changes (Fig. 3-3, 4). No. 8, which was killed ten days after injection, showed no hyperemia and infiltration of leucocytes, but its pia mater remained separated from the spinal cord and the meninges were thicker than No. 7 (Fig. 3-1, 2).

Davis in 1930 described changes of the spinal cord in dogs using Lipiodol, but no such changes were found in our dogs when we used this new contrast medium.

C. Conclusions

On the models of the spinal tumor in the polyethelene tubes the new contrast medium showed higher contrast and finer outline of the tumors than Lipidol. Animal experiments were carried out on nine dogs observing their pulse rate, blood pressure, E.C.G., and respiration. There were no gross changes of the vital signs due to the new contrast medium. By X-ray examination the disappearance of the contrast medium was very rapid.
Histologically the contrast medium caused some irritation to the meninges and pia mater as seen three days after injection but recovery was seen ten days after injection. There was no irritation to the spinal cord.

III. CLINICAL STUDY

In chapter II we concluded from the experimental results on the nine dogs that the medium had enough contrast for use in myelography and no marked irritating properties upon living tissues including the spinal cord. Moreover, the disappearance of the contrast medium by follow up X-ray films is the most rapid of contrast mediums used in myelography.

Clinical studies were undertaken to test the above mentioned properties of the contrast medium in the human body.

The contrast medium was used clinically in 21 myelographic studies. The ages of the patient ranged from one year to 74 years of age. Seventeen cases were male and four were female. The quantities injected into the spinal canal ranged from 1 ccm to 5 ccm. One ccm was injected in 5 cases, 2 ccm in 6 cases, 3 ccm in 5 cases, 4 ccm in 1 cases, and 5 ccm in 4 cases. The disappearance of the contrast medium was followed up in 13 cases rentogenologically by films and fluoroscopy. In all cases, side effects were carefully watched for, in particular headache, lumbago, vomiting, nausea and fever. The medium was injected into the spinal canal by cysternal or lumbar puncture.

The velocity of movement of the contrast medium in the spinal canal by tilting the patient on the fluoroscopic table was faster than Lipiodol. As described previously on the models of the spinal tumors in polyethylene tubes,

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Puncture</th>
<th>ccm inj.</th>
<th>Day X-ray films taken</th>
<th>Disappearance</th>
<th>Headache</th>
<th>Lumbarago</th>
<th>Nausea</th>
<th>Vomiting</th>
<th>Fever</th>
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<tr>
<td>1 Y. Y.</td>
<td>M</td>
<td>74</td>
<td>Comp. myelitis</td>
<td>c.p.</td>
<td>0 3 8</td>
<td>8</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>2 Y. Y.</td>
<td>M</td>
<td>74</td>
<td>&quot;</td>
<td>c.p.</td>
<td>0 3 7</td>
<td>7</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3 E. T.</td>
<td>M</td>
<td>32</td>
<td>Schizophrenia</td>
<td>l.p.</td>
<td>0 2 3</td>
<td>3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4 F. Y.</td>
<td>M</td>
<td>20</td>
<td>Thromboangitis</td>
<td>c.p.</td>
<td>0 1 2</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5 G. M.</td>
<td>M</td>
<td>43</td>
<td>Comp. myelitis</td>
<td>c.p.</td>
<td>0 1 2 3 8</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6 K. K.</td>
<td>F</td>
<td>20</td>
<td>Spondylitis</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>7 H. T.</td>
<td>M</td>
<td>46</td>
<td>Spinal tumor</td>
<td>c.p.</td>
<td>0 2 3</td>
<td>3</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>8 H. S.</td>
<td>M</td>
<td>5</td>
<td>Hydrocephalus</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>9 T. F.</td>
<td>M</td>
<td>22</td>
<td>?</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>10 S. Y.</td>
<td>M</td>
<td>46</td>
<td>?</td>
<td>c.p.</td>
<td>0 3 7</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>11 K. T.</td>
<td>M</td>
<td>43</td>
<td>Spinal tumor</td>
<td>c.p.</td>
<td>0 2 3</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>12 H. N.</td>
<td>F</td>
<td>5</td>
<td>Spondylitis</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>13 M. H.</td>
<td>M</td>
<td>13</td>
<td>?</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>14 A. I.</td>
<td>M</td>
<td>48</td>
<td>Arth. def.</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>15 S. Y.</td>
<td>M</td>
<td>25</td>
<td>Schizophrenia</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>16 A. F.</td>
<td>M</td>
<td>50</td>
<td>?</td>
<td>l.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>17 S. Y.</td>
<td>F</td>
<td>50</td>
<td>Spinal tumor</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>18 F. T.</td>
<td>M</td>
<td>50</td>
<td>&quot;</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>19 M. S.</td>
<td>M</td>
<td>50</td>
<td>&quot;</td>
<td>c.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>20 M. K.</td>
<td>M</td>
<td>5</td>
<td>Spina bifida</td>
<td>l.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>21 A. N.</td>
<td>M</td>
<td>23</td>
<td>?</td>
<td>l.p.</td>
<td>0 1 2 3</td>
<td>3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>
Lipiodol moves as a bolus or large drops but the new contrast medium moves in the spinal canal as a thin layer. This property is suitable for the diagnosis of disc herniation or spinal tumor. The results of 21 cases are shown in table 2.

**X-ray Examination**

Thirteen cases, which were injected with from 1 ccm to 5 ccm of the contrast medium, were followed up rentogenologically. Out of thirteen cases, 4 cases were injected with 5 ccm, 3 cases with 3 ccm, 3 cases with 2 ccm, and 3 cases with 1 ccm.

When 5 ccm of the contrast medium was injected into the spinal canal, the contrast on X-ray film disappeared completely on an average of 7.8 days after injection in 4 cases. When 3 ccm was injected the contrast disappeared on an average of three days in 3 cases. When 2 ccm were injected the contrast disappeared on an average of 2.6 days in 3 cases. When 1 ccm was injected the contrast disappeared on an average of 2.6 days in 3 cases. The average period of time that the contrast was seen on the films was comparatively longer than the other cases because 2 out of the 3 cases where 1 ccm was injected were children.

The average period necessary for the disappearance per 1 ccm of contrast medium was 1.7 days.

**Individual case review**

1. **M. S. 50 year old male** (Fig. 5)
   
   His chief complaint was lumbago on the right side and hypesthesia of both lower extremities. Myelography showed the upper border of a tumor at T-11 dorsal to the spinal cord. Operation revealed an intradural and extramedullar tumor at T-11. The pathological diagnosis was neurinoma.

2. **F. T. 50 year old male** (Fig. 5)
   
   His chief complaint was palsy of both upper limbs and retention of urinae et albi. Myelography showed a contrast defect suggesting a tumor with its lower border at level of T-1. This figure showed the tumor to be extradural. Operation revealed an extradural tumor of thumb-tip size extending from C-7 to T-1. The pathological diagnosis was metastatic cancer.

3. **S. Y. 50 year old female** (Fig. 5)
   
   Her chief complaint was retention of urinae et albi and lumbago. Myelography showed a typical H-form contrast defect at T-8, 9 on the AP views. The lateral view showed a stenosis of the spinal canal. Operation revealed an intradural and extramedullar tumor from T-8 to T-11. The pathological diagnosis was neurinoma.

4. **H. T. 46 year old male** (Fig. 5)
   
   His chief complaint was gait disturbance and sensory disturbance of both lower limbs. Myelography showed an outline of a tumor with its upper border at T-9, 10. Operation revealed an intradural and extramedullar tumor T-9.
Its pathological diagnosis was neurinoma.

5. K. T. 43 year old male (Fig. 5)

His chief complaint was gait disturbance and sensory disturbance of the lower limbs. Myelography showed a tumor at T-12 to L-1, the size of a thumb tip. Operation revealed an intradural and extramedullar tumor at T-1. The pathological diagnosis was meningioma.

Side effects

The side effects in the use of this medium are shown at Table 3.

### Table 3. Side Effects after Myelography

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>(%)</th>
<th>First day</th>
<th>Second day</th>
<th>Third day</th>
<th>Fourth day</th>
<th>Fifth day</th>
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<tbody>
<tr>
<td>Headache</td>
<td>10</td>
<td>48</td>
<td>6</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lumbago</td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>9</td>
<td>42</td>
<td>11</td>
<td>16</td>
<td>13</td>
<td>9</td>
<td>10</td>
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<tr>
<td>Total</td>
<td></td>
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<td>21</td>
<td>29</td>
<td>20</td>
<td>13</td>
<td>12</td>
</tr>
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</table>

One of the side effects was fever with a temperature rise in 9 cases out of 21 cases. The fevers were almost all remittent but some were sustained. They rose promptly after the procedure and showed peaks on the second or third day and fell gradually to normal body temperature within 5 days to 8 days after myelography. There was no case of fever exceeding 39°C. It was noted that temperature was above 38°C in 2 cases on the first day after myelography and above 38°C in 9 cases on the second day. The pulse rate increased and then decreased parallel with the fever in some cases but in most cases the pulse rate did not increase in spite of the increase in the temperature. The fevers were sensitive to antipyretics but not to antibiotics.

There were complaints of headache in 10 cases (47.7%). The headaches were slight and severe headaches were rare. The complaint of headache was almost always on the second day next most common on the first day and decreased gradually after the third day.

The side effects seemed to be minimal considering the amount of the contrast medium injected, especially though a part of the medium was instilled and remained in the intracranial cavity. The description of the lumbago the patients complained of after myelography was pulling pain in the thigh, sciatica and stiffness of the lumbosacral joint. This was present in 3 cases on the second day. In one patient who complained of lumbago before myelography, the lumbago disappeared after the injection of the contrast medium. W. Denk described the disappearance of symptoms after myelography caused perhaps by separation of intraspinal adhesion by the weight of a contrast medium and also by a reactive stimulation of a contrast medium.

Nausea and vomiting were seen in three cases. It is not clear whether
the cause was the contrast medium or the narcotics given as premedication.

As for other side effects, nuchar rigidity was observed in one case, no seizure nor vesicorectal disturbance were observed.

**Findings in C.S.F.**

The results of C.S.F. examinations are shown in Table 4. The pressure was increased slightly in 2 cases. The average increase was 70 mm of water. The cell count increased from the second day to several days later and the peaks were within 2 or 3 days after injection and gradually decreased thereafter. They corresponded to the clinical side effects. Globulin reaction paralleled the increase in quantity of protein as measured by Nissl-Esbach method. The findings in the C.S.F. which paralleled the clinical side effects was the cell count, neither protein reaction nor quantity of protein.

<table>
<thead>
<tr>
<th>No.</th>
<th>Patient</th>
<th>Day</th>
<th>Pressure</th>
<th>Cell count</th>
<th>Pandy R.</th>
<th>Nonne-Apelt R.</th>
<th>Protein; Nissl-Esbach method</th>
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</thead>
<tbody>
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**IV. DISCUSSION**

The chemical, physical and radioactive reaction of many contrast mediums cause meningitis as Odin and Runstrom pointed out about Lipiodol, and Moisky about Throtrast. Moreover, when they remain long in the spinal canal the late side effects are serious. These side effects are manifested clinically as fever, headache, lumbago, vesicorectal disturbances, nausea and vomiting, etc. Odin injected 10 ccm of a contrast medium for myelography but I think adequate studies can be done with less. The more contrast medium that is injected, the more striking are the late effects as shown by clinical usage. Some reports have verified the lesions caused by Lipiodol by post mortem examinations and many reports have proved them by animal experiments as Davis, Haven and Stone, Bruskin and Propper. Peiper and Klose described the lesions in rabbits injected with 2 ccm of Lipiodol. In my study the dogs which were injected with from 1 ccm to 1.5 ccm of the new contrast medium
into the spinal canal tolerated the procedure and showed no remarkable changes physiologically and pathologically. In my clinical study the side effects were comparatively slight though the observation period was not long enough. Side effects are thought to be due to the rapid absorption of the new contrast medium from the spinal canal. By Sicard and Forester the disappearance of 2 ccm of Lipiodol from the spinal canal takes from three to four years. In literature, we find no report of any cases which show the contrast medium completely absorbed from the spinal canal by X-ray films. This new contrast medium showed complete absorption from the spinal canal both experimentally and clinically.

With developments in spinal surgery we need detailed accuracy in myelographic studies. The contrast of a material by X-ray is given in the following formula.

\[ C = Z^dD^l \]

- \( C \) \(
\text{molecular weight of a material}
\)
- \( Z \) \(
\text{density of a material}
\)
- \( D \) \(
\text{thickness of a material}
\)
- \( l \) \(
\text{length of wave of X-ray beam}
\)

In myelography \( l \) and \( D \) are almost constant and the variable factors are \( d \) and \( Z \); \( Z \) is most important factor to determine \( C \) according to the formula. The molecular weight of the new contrast medium is larger than that of iodine itself. Content of iodine in Urokolin is 41.4% in 60% oil suspension. Iodine content of Lipiodol is 40%. The contrast of the new contrast medium is sufficient for myelography and its low viscosity makes instillation and removal easier, and finer structures are demonstrated as described in the above experiments and clinical cases. The late side effects can be determined only by longer follow-up studies.

V. SUMMARY

As a step to an ideal and suitable contrast medium for myelography, I have studied both clinically and experimentally the oil suspension of 3-acetylamino 2.4.6. triiodobenzoic acid.

In the animal experiments the irritating properties as measured by the blood pressure, pulse rate and respirations were examined and seen to be minimal. The disappearance of the contrast medium is very rapid. When 1 ccm was injected into the spinal canal of dog, the contrast on X-ray films disappeared completely 69 hours after injection and when 1.5 ccm was used the average was 85 hours. Histopathologically hyperemia and slight infiltration of leucocytes were observed 3 days after injection and became minimal 10 days after injection. There were no lesions of the spinal cord. Based on the above described experiments, the contrast medium was used clinically in 21 cases. Complete disappearance of the contrast in X-ray films took 7.8 days when 5 ccm was injected, 3 days when 3 ccm was used, 3 days when 2 ccm was used and 2.6 days when 1 ccm was used. As to the side effects of this contrast medium, fever was observed in 42%, lumbago in 7%, nausea and vomiting in
Dog No. 1 Injection | 5 min. | Urination | 10 min.

Dog No. 4 Injection | 5 min.

Dog No. 5 Injection | 5 min. | 10 min.

Dog No. 8 Injection | 5 min. | 10 min.

FIG. 1 Blood pressures at the injection.
FIG. 2. X-ray follow up after the injection.
FIG. 3. Microscopic examination of the spinal cord.
Case No. 3
Just after injection of 5 ccm
3 days after injection
5 days after injection
7 days after injection

Case No. 5
Just after injection of 5 ccm
2 days after injection
3 days after injection
8 days after injection

FIG. 4. X-ray follow up of the contrast after injection.
Case 5

Lateral

Case 4

Case 3

Case 2

Case 1 A.P.

Fig. 5. Individual case review.
StUDY ON THE CONTRAST MEDIUM FOR MYELOGRAPHY

7% and headache in 47.7%. No other remarkable side effects were observed. Examinations of the C.S.F. were performed serially. Cell counts increased maximally on 3 days later and decreased gradually paralleling the clinical side effects.

The contrast figures with this contrast medium were finer and more detailed than with previous mediums.

The author reported the results of this study at the proceedings of the 15th General Meeting of the Japanese Neurosurgical Association.

The author wishes to express his gratitude to Professor Y. Hashimoto for his valuable advice and helpful criticism in this study and manuscript. The author indebted to Dr. Y. Miura and Dr. K. Iwata for their kind guidance and encouragement, and to the other neurosurgical members of the staff for their kind guidance and encouragement.

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