*Bulletin* of the

University of Minnesota Hospitals
and
Minnesota Medical Foundation



# New Contrast Media for Myelography

Volume XXI | Friday, June 2, 1950 | Number 30

BULLETIN OF THE
UNIVERSITY OF MINNESOTA HOSPITALS
and
MINNESOTA MEDICAL FOUNDATION

Volume XXI | Friday, June 2, 1950 | Number 30

INDEX



Published weekly during the school year, October to June, inclusive.
Annual Subscription Rate - $3.00.



Address communications to: Staff Bulletin, 332M University of Minnesota Hospitals, Minneapolis 14, Minn.

# I. EXPERIMENTS WITH NEW CONTRAST MEDIA FOR MYELOGRAPHY

Osmond J. Baggenstoss
A. B. Baker

Dandy[1] is given credit for the concept of contrast myelography as, in 1919, he suggested the use of air for the visualization of spinal canal tumors and, in 1925[2], reported a number of cases of these lesions in which air myelograms were employed. After this original work, air myelography was temporarily abandoned, probably due to the fact that, in 1922, Sicard and Forestier[3] used lipiodol to demonstrate obstructing tumors of the spinal canal. Lipiodol was then used for this purpose until 1934, when air myelography was again utilized[4,5].

At this time a new lesion of the vertebral column was discovered--the protruded intervertebral disc--which stimulated interest in myelography. Credit for this is given to Schmorl[6], who demonstrated the frequency of the pathology, and Mixter and Barr[7], who realized the clinical significance and developed an operation to correct it.

Although lipiodol was widely used as a contrast media for meylography, there were many objections to its use, the chief of which were:

1. Its non-absorbability or slow rate of absorption.
2. Difficulty in removal.
3. The high viscosity and tendency to globulate.
4. Medico-legal complications because of its non-absorbability.
5. Nerve root irritation, meningeal reaction and encystment.

The last mentioned objection has been minimized by some and probably exaggerated by others. Many early investigators[8,9,10,11], in reporting the use of lipiodol in both animals and humans, reported immediate reactions (e.g., within 24 hours) which consisted of any or all of the following: headache, stiff neck, fever, nausea, vomiting and a slight, moderate and occasionally marked pleocytosis. Pugh[12] and Garland[13] in their reviews of the subject believe that these immediate effects may occur. Walsh and Love[14] stated: "We have seen no clinical reaction to iodized oil that might not have been produced by a spinal or cisternal puncture with the withdrawal of spinal fluid alone."

The late effects of lipiodol in the spinal canal is a more important problem and also a controversial one.

In 1930, Davis, Haven and Stone[15] reported marked changes in the leptomeninges of dogs which had lipiodol injected into the subarachnoid space; these changes consisted of encystment of fat and degenerative changes in the gray matter of the cord. Previous to the injection by cisternal puncture, laminectomy was done on one of the upper dorsal vertebrae and a soft piece of rubber was inserted between the dura and the bony wall of the spinal canal immediately above in an attempt to produce a subarachnoid space block without causing any injury to the spinal cord. Controls were used but microscopic findings on these were not reported.

They concluded that the injection of iodized oil into the subarachnoid space should be regarded as a dangerous procedure. Their conclusions, however, have not been accepted by some investigators because of the fact that an operation was performed prior to the injection of the oil and the microscopic findings were not reported on the controls.

Lindblom[9], working with rabbits in 1926, trephined the skulls and injected one cubic centimeter of iodized oil subdurally and into the lateral ventricles. Microscopic studies revealed a leptomeningitis with infiltrations of leucocytes and lymphocytes. This reaction was at its height at the end of two days; at the end of two to three weeks there was only a slight reaction and after two months there was no evidence of reaction.

Lindblom[16] did some further work with rabbits in 1931, in which he found that

large lakes of the oil were sometimes surrounded and infiltrated with new connective tissue and in some places there was a pachymeningitis reaction which on incision showed droplets of oil. These formations consisted of fatty phagocytes of various sizes surrounded or infiltrated with new grown connective tissue (fatty granulomas). He also found that the amount of irritation of the meninges was directly proportionate to the amount of free fatty acid in the oil.

Garland[13] in his extensive review of the effect of iodized oil states that, "the late pathologic changes consist of small, round cell and fibroblastic proliferation about the oil, especially about the smaller droplets which become shattered along the spinal canal. These small droplets often become encapsulated resulting in miliary nodules on the surface of the cord (pseudogranulomas)." He further states, "It has been emphasized before and should be repeated here that many of the tiny droplets plus their surrounding fibrous proliferations resemble miliary tubercles or granulomas of any type, and at first glance have led pathologists to conclude that some serious lesion of the brain or cord was present. Histologic examination will reveal that the changes are confined to the meninges and that the underlying neural tissues are normal (at least as far as any secondary effect from the lipiodol is concerned)." He believed that the chief drawback to its use was that it remained visible in roentgenograms.

Globus[17], in 1937, reported on 138 patients who had had an intraspinal injection of iodized oil for diagnostic purposes. He concluded that, "iodized oil has no deleterious effect on the lemptomeninges of man, and aside from the hazards of cisternal puncture, its use is not likely to give rise to immediate or delayed disturbance."

Marcovich and his associates[18] reviewed all the cases at the University of Chicago which had had intrathecal injection between 1928 and 1939, of which there were 150 cases. Forty-seven of these patients returned for examination and nine wrote concerning their condition. The oil was not removed in any of these cases. No ill effects could be attributed to the oil except for possibly one case of hyperplastic arachnoiditis, but it is impossible to be certain that the oil was responsible for the arachnoiditis as the patient had an operation for a disc previously. Also, most of the oil was extradural and the pain of the patient was unilateral but the arachnoiditis was equal bilaterally. They also felt that there was a strong psychogenic factor present. Autopsies were performed on three cases at one week, six weeks and ten years after the injection. In the first two cases no operative procedures were performed but in the third a laminectomy had been done and the dura opened. In all three cases fine adhesions were present between the dura and the arachnoid. In this third case, changes were present in the cord, but these were compatible with the severe compression of the cord which the patient had suffered ten years previously.

Bucy and Spiegel[19] report an unusual complication after the intraspinal use of iodized oil. In March 1938, a myelographic examination was performed and it was noted that some of the oil was lodged at the level of the eighth dorsal vertebra and remained there. Late in 1941, progressive symptoms of involvement of the spinal cord developed at that level. On examination in February 1942, an almost complete block was found. At operation on March 10, 1942, two collections of encysted iodized oil in the subarachnoid space and a very much thickened arachnoid membrane were found and removed and the patient made a complete recovery in a few weeks. One cyst measured 1.5 x 1 x 1 centimeter and the other 0.5 centimeters in diameter. He concluded that the patient suffered from a localized adhesive arachnoiditis at the level of the eighth dorsal vertebra and that this caught and held some of the iodized oil which, in turn, stimulated fibroblastic proliferation in the leptomeninges, thus increasing the arachnoiditis and resulting in dysfunction of the cord.

From the investigations which have been reported, the immediate effects of lipiodol offer no valid contra-indication to its use. As to the late effects, the preponderance of evidence is that fibroblastic proliferation with encystments and adhesions may occur. But whether or not these fatty granulomas or encystments have any clinical significance is another question. It appears that in the great majority of cases no ill effects are observed but that the possibility exists. Another detrimental factor is the failure of absorption of the oil which many feel is the chief contra-indication to its use.

As to the use of air or oxygen as a contrast media in myelography, little further will be said except that, in 1937, Reichert, Scott and Young[20] reported its use for visualization of protruded intervertebral discs and it has been used considerably since that time, chiefly because of the possible consequences of the use of lipiodol. The chief disadvantages to the use of air or oxygen are:

1. The contrast is poor.
2. Fluoroscopic verification is not possible.
3. The examination is limited to below the level of the tenth dorsal vertebra unless a complete block is present or unless the two needle procedure devised by Munrow and Elkins[21] is used, and then the entire vertebral canal can be examined with oxygen.
4. Considerable experience is necessary for interpretation even under ideal circumstances.
5. High incidence of positive findings at operation in those who have had a normal pneumospinogram; i.e., a high percentage of negative error.

In 1934, Lucherini[22] described the use of thorotrast (throium dioxide) as a contrast media in myelography, but it was used by some Frenchmen and by Germans in encephalography in 1932--(they had serious reactions and death). Thorotrast was used in this country in 1938, with most of the papers being published by Nosik and Mortenson[23], Bunte[24], Nichols and Nosik[25] and Nichols[26]. Nichols and Nosik advocated using six to ten cubic centimeters of 25 per cent solution with forced drainage afterward. By radio-active measurements they determined that they recovered 70 to 90 per cent of the thorotrast by this method and considered that the amount of thorotrast left in the spinal canal did not have sufficient radioactivity to cause any deleterious effects. The chief disadvantages are:

1. Its radio-activity which necessitates forced spinal fluid drainage and requires several spinal punctures and takes two to three hours.
2. Because of its miscibility its use is limited to the lumbar canal.
3. Fluoroscopy cannot be used to check for defects since the shadow is too faint.
4. It is extremely irritating if an epidural injection is accidentally accomplished.

Arnell and Lidstrom[27] were the first to introduce skiodan (abrodil) for use as a myelographic agent in 1931. They had injected it into rabbits and cadavers and then tried it on a patient with tuberculous meningitis, using 14 cubic centimeters of a 20 per cent solution. Since then it has been used rather extensively in the Scandinavian countries. Lindblom[28] reported the experiences of 721 cases of abrodil myelography which were brought together and discussed at the meeting of the Swedish Society of Radiology in November 1945. Complications were reported in more than 54 cases. As the myelography must be preceded by a lumbar puncture and spinal anesthesia, the complications might be due to either of the aforementioned or to the contrast medium itself. He, therefore, grouped the complications as follows:

1. Headache for some days -- degree of three plus in many cases.
2. Headache and stiff neck for some days -- two cases.
3. Headache and stiff neck and paresis of the bladder for two days -- one case.

These complications, he feels, may be due to the lumbar puncture itself as there was abundant leakage of fluid and in many cases the head was raised for many hours after the examination which facilitated the leakage.

4. Shock within five to 30 minutes -- 22 cases.
5. Shock one to three hours after the myelography -- eight cases.
6. Shock three to 24 hours after the myelography -- two cases.

He assumes the shock to be secondary to an irritation by the contrast medium because of incomplete anesthesia and also the fact that the head of the table was elevated -- sometimes for hours. Most of these cases were prepared with ephedrin.

7. Lumbar pain during the injection of contrast medium -- four cases.
8. Lumbar pain soon after the injection of the contrast medium -- five cases.

These he believes must be attributed to the contrast medium. The anesthetics used were novocain, pontocain or heavy decicain. Sharp pains occurred only in those cases in which the heavy decicain was used. It is believed that the high specific gravity causes a sedimentation in the spinal fluid and the effect is that the anesthesia will not reach as high as the opaque solution.

9. Hyperesthesia and latent spasms three hours after the injection -- three cases -- these lasted a few hours.
10. Manifest spasms in the legs after the myelography -- two cases.
11. Secondary shock and paralysis of the legs and sphincters for weeks -- three cases.

However, in all these cases a wrong contrast medium had been used. In group ten, six to ten cubic centimeters of 35 per cent perabrodil (diodrast) was used, and in group 11, 40 per cent intron was used.

From this study he concludes that in order to avoid complications that:

1. A thin needle should be used for the puncture -- 0.5 millimeter in diameter.
2. The patient should be prepared against a drop in blood pressure; e.g., ephedrin be used and the patient's head elevated only during the examination.
3. The anesthetic solution should not be too heavy. One to two cubic centimeters of a five per cent solution of novocain is recommended.
4. Allergic tests should be made.
5. Only approved radio-opaque solutions, such as 20 per cent abrodil or 20 per cent intron should be employed.

He adds, however, that according to a later report received, a myelographic examination using 20 per cent intron was followed by longstanding pain in the sacral region and paresis of the sphincters.

Odegaard[29] observed the time for absorption using 10 cubic centimeters of a 20 per cent solution of myelotrast (abrodil) (skiodan) in four cases. He calculated that it takes slightly over an hour for the absorption and recommends that the patient therefore lie with the upper part of the body elevated for an hour to an hour and one-half after the examination. The chief disadvantages to the use of abrodil appear to be the fact that:

1. A spinal anesthetic must be used along with the contrast medium.
2. Fluoroscopic verification is not possible.
3. The examination is limited to the lower spinal canal.
4. The rather high number of complications.

Pantopaque was developed by Strain, Plati and Warren[30] and was first used clinically by Garvey and Jones on November 23, 1940. Prior to its clinical use it was tested experimentally by intrathecal injection of animals in a series

of comparative experiments with iodized poppy seed oil by Steinhausen and his associates[31]. They reported that after the injection of three to five cubic centimeters of pantopaque there is a slight fever for one to two days and a fair proportion of the animals may show discomfort for two or three days when the head is bent. With iodized poppy seed oil there was no fever but the period of distress when the head was bent sometimes persisted for 10 to 14 days. Sections taken from the spinal cord of animals sacrificed at varying intervals showed that both agents are encysted after about six weeks, but the size of the cysts produced by pantopaque is considerably less than those produced by the lipiodol. They believe that this is probably due to the greater viscosity of the lipiodol. The response about the cysts of pantopaque is essentially a foreign body reaction. From their experiments they concluded that pantopaque was much easier to handle, produced discomfort of shorter duration, and in most of the animals was almost completely absorbed within a year. They also stated that the clinical results have paralleled those obtained in experimental work.

Ramsey and his associates[32] believe that provisionally the rate of absorption in humans may be set at one cubic centimeter a year. If there is a large degree of globulation and the pantopaque is spread over a large area, they believe the rate of absorption approaches three cubic centimeters a year. On the other hand, if the media is contained in the cauda equina the absorption may be about 0.5 to one cubic centimeter a year. Peacher and Robertson[33] also observed the rate of absorption. They noted that it varied considerably, but appeared to be of the order of 0.5 to one cubic centimeter a year.

Peacher and Robertson[34] report that there is a slight meningeal response following the injection of pantopaque as evidenced by a slight rise in the polymorphonuclear leucocytes and/or lymphocytes and occasionally elevation of the total protein and increased pressure. Usually there was either an increased count or an increase in the total protein, but they were sometimes associated. These changes usually occur in the first week. In a few cases there was elevation of cell count or increased protein more than two months after the examination. The spinal fluid usually remained clear and colorless throughout.

Tarlov[35], in 1945, reported a case of pantopaque meningitis. A lumbar puncture was performed on a 37 year old male through the fourth lumbar interspace and three cubic centimeters of pantopaque injected intrathecally because of symptoms of a disc. Just prior to the injection there was no evidence of block on monometric examination and no cells in the spinal fluid. The globulin was reported as moderately increased and the total protein was very slightly elevated. Approximately 5 hours after the injection, the patient complained of headache and stiffness of the neck. His temperature rose to 100.8° and on the following day to 102°. On the third day (the day of operation) the headache disappeared but there was still some nuchal rigidity and the temperature dropped to 100°. When the dura and arachnoid were opened, considerable whitish, soft stringy exudate, somewhat adherent to the arachnoid and nerve roots of the cauda equina was noted. The pantopaque was removed from the subarachnoid space at this time. Some of the material removed at operation was sent to the laboratory for culture but showed no growth at 48 hours. The remainder of the operative specimen was prepared for microscopic study and showed a meshwork of fibrin strands with numerous embedded polymorphonuclear leucocytes, lymphocytes and plasma cells. The tissue was clearly inflammatory. As the material removed appeared to contain pus, penicillin was administered. The patient made an uneventful recovery and was discharged on the 22nd postoperative day.

Recently Morales and Heiwinkel[36] have published some data on a new contrast media which is a viscous, water soluble substance. As a contrast substance they used umbradil (diodrast) (diethanolamine salt of 3, 5 diodo-4-pyridone-N-acetic acid)

and, to produce the necessary viscosity, sodium carboxymethylcellulose called (CMC). It is a cellulose ether made by the reaction of monochloracetic acid with alkali cellulose. Its sodium salt is easily soluble in water and at concentrations as low as one to three per cent forms highly viscous solutions which are said to be completely clear and colorless. They do not gelatinize, even on storing, and are completely non-irritant.

Some toxicity studies with CMC have been done on rabbits and dogs and it has been found to be relatively non-toxic. CMC with umbradil (diodrast) has been injected into the knee joint of a calk and no irritation was observed. It has been injected intracutaneously, subcutaneously and intramuscularly into humans and also used for bronchography, urethrocystography and also to obtain hystero-salpingograms. The contrast media was noted to absorb in two to four hours. It has been used intraspinally in a corpse, but I know of no instance where it was used on patients.

The contrast media was made up as follows:

35 per cent umbradil (diodrast)
2.5 per cent CMC
0.25 per cent xylocain as an anesthetic

This gives a viscosity of about 500 cps -- which is about the same viscosity as lipiodol. For urethrocystography four per cent CMC has been used giving a viscosity of 5000 cps, which has a consistency comparable to syrup.

In recent years, the Winthrop Company has developed some radio-opaque compounds[37] which they thought might possess the necessary characteristics for successful myelography and have the advantage of being absorbed from the spinal canal. They have as yet not been given any trade names but are designated by numbers and are still considered experimental compounds.

WIN 557 is a colorless oil insoluble in water but soluble in vegetable oils. WIN 557 has a viscosity of 14.8 centistokes at 25° Centigrade and, therefore, has about one-half the viscosity of pantopaque which has a value of 29.5 centistokes at 25° Centigrade. WIN 557 contains 39.6 per cent iodine (theoretical) and pantopaque contains 30.5 per cent iodine.

Preliminary acute oral and intraperitoneal toxicity studies were performed by the Company and these indicate that it is relatively non-toxic. Rabbit eye irritation studies were also performed and they indicate that it is no more irritating than pantopaque. Complete oral and intraperitoneal acute toxicity and subacute oral toxicity studies would be carried out if WIN 557 is well tolerated in the spinal canal and proves to be of further interest as a myelographic medium.

Three dogs and two cats were injected by the Company using one cubic centimeter of WIN 557. Partial paralysis of the hind legs occurred in one cat, possibly due to trauma at the time of injection. No neuromuscular involvement was noted in the others and absorption was complete in 7 to 15 days.

WIN 1756 is a light yellow oil which is soluble in propylene glycol. It has a viscosity of 43.9 centistokes at 25° Centigrade. Pantopaque has a viscosity of 29.5 centistokes at 25° Centigrade. WIN 1756 has an iodine content of 34.85 per cent as compared to 30.5 per cent for pantopaque.

Previous to our intraspinal injections the Winthrop Chemical Company injected 13 dogs with from 0.5 to 1.5 cubic centimeters of WIN 1756 with complete absorption of the medium from 7 to 17 days. Eighteen cats were also injected using 0.5 cubic centimeters with complete ab-

sorption varying from 7 to 23 days. One rabbit was injected using 0.5 cubic centimeters with complete absorption in 10 days. No neuromuscular involvement was noted in any of the animals. Preliminary oral and intraperitoneal toxicity tests indicate that WIN 1756 is quite non-toxic. Rabbit eye irritation studies and intramuscular injections into rabbits indicate that it is no more irritating than pantopaque.

WIN 1742 is a light yellow oil insoluble in water but soluble in propylene glycol. It has a viscosity of 112 centistokes at 25° Centigrade, which is about four times as viscous as pantopaque. The iodine content of WIN 1742 is 33.57 per cent as compared to 30.5 per cent for pantopaque. The Company injected one dog with one cubic centimeter and found complete absorption in 83 days. One cat was also injected with 0.5 cubic centimeters with complete absorption taking place in 50 days. No neuromuscular involvement was noted in either animal. Preliminary oral and intraperitoneal toxicity studies indicate that it is relatively non-toxic. According to rabbit eye irritation studies it is slightly less irritating than pantopaque.

In the dog, the spinal cord fills the vertebral canal throughout its entire length terminating at the level of the sixth or seventh lumbar vertebra. The subarachnoid space appears to vary from one to three cubic centimeters and it is therefore extremely difficult, if not impossible, to introduce a radio-opaque medium into the subarachnoid space and cause it to flow back and forth for the purpose of outlining the anatomy of the spinal canal. The chief purpose of these studies was to observe whether or not there was any immediate or delayed reaction to these new compounds and to observe roentgenographically the rate of absorption from the spinal canal.

Because of the fact that spinal fluid is seldom obtained after inserting a needle into the subarachnoid space, it was necessary to devise a lead protected table and make the injections under fluoroscopic control. After the needle appeared to be in the proper position, a small amount of the media was injected to further ascertain the correct position and then two cubic centimeters of the media injected. Sodium pentothal was used as an anesthetic. In order to minimize any danger of injury to the spinal cord, the interspace between the last lumber vertebra and the first sacral segment was utilized.

Two cubic centimeters of WIN 557 was injected successfully into 11 dogs. Immediately upon injection the material spread evenly caudad through the lower limits of the spinal canal and cephalad to about the midthoracic region, but sometimes as far as the upper thoracic levels. Several attempts were made to make the radio-opaque substance flow into the cervical area or into the lumbar area, but these were unsuccessful. This can probably be explained by the fact that there is very little actual space present in the subarachnoid space, there being normally only one to three cubic centimeters of spinal fluid in the spinal canal.

Of these dogs, two died and one was chiefly an extradural injection. One of these (Dog No. 6) died four days after the contrast media was injected. No neuromuscular changes were evident, but lassitude and a nasal discharge were noted and it was thought that the dog had a respiratory infection. Penicillin and sulfa were administered and the dog seemed to improve. For some unknown reason he was left out on the roof overnight in five below zero weather and died shortly thereafter. The dog was autopsied and grossly the meninges of the cord and brain appeared normal. The liver was ruptured and blood clots and free fluid were present in the peritoneal cavity.

Dog No. 7 died seven days after the injection. No neuromuscular symptoms were noted up to death. At autopsy the

meninges of the cord and brain appeared normal. An adherent mural thrombus was present in the left atrium which extended into the left ventricle.

The day following the injection it was noted that WIN 557 appeared to globulate and accumulate at the root canals, at times often extending out along the nerve roots. This should not be interpreted as a deficiency in the dye, but rather due to the anatomy of the dog. This was also noted in the control dogs in which pantopaque was injected. Films were generally made at intervals of one to two days following the injection until complete absorption. In general it may be stated that one-third to one-half of WIN 557 was absorbed in 24 to 48 hours. The following table gives the time required for complete absorption.

ABSORPTION RATE OF WIN 557

| Number of Dog[1] | Days Required for Absorption |
|---|---|
| 1 | 9 |
| 2 | 7 |
| 3[2] | 7 |
| 4 | 8 |
| 5 | 7 |
| 8 | 11 |
| 9 | 15 |
| 10 | 7 |
| 11 | 7 |

[1]Dog No. 6 died on the 4th day following injection.
Dog No. 7 died on the 7th or 8th day following injection.
[2]Chiefly extradural injection.

The media was absorbed in the majority of dogs in 7 to 8 days. In only 2 dogs did the absorption take over 9 days. In the dog which died on the 4th day following injection, only a few small scattered globules of WIN 557 remained within a few small globules scattered out along the nerve roots. The dog which died on the 7th day showed a few globules in the region of the fore-legs.

After injection of the dye, the animals were sacrificed at periods of from one week to 6 months in an attempt to determine whether this dye produced any pathologic alterations within the meninges or the spinal cord. Changes were found in only two of the animals, both of which had been sacrificed 12 weeks after the injection of the dye. In both these animals there was a mild arachnoiditis, particularly in the lumbar region; the subarachnoid space contained scattered mononuclear cells and a small amount of fibrin. The rootlets showed a very mild edema. The cord was intact. It might be mentioned at this time that none of the animals showed any symptoms suggestive that the dye was irritative in the least.

WIN 1756 was used on a number of animals. Eight animals were successfully inoculated with this radio-opaque material. These animals were followed from a period of 4 to 10 weeks, at which time the animals were sacrificed in order to observe the changes which might have occurred histologically within the meninges or spinal cord. All animals were inoculated with two cubic centimeters of the radio-opaque material under fluoroscopy. Two of the eight animals developed a definite weakness in the hind limbs, developing within 24 hours after the injection of the radio-opaque material. This weakness and stiffness of the limbs persisted for a number of days. The animals apparently suffered considerable pain, since they would resist any movement of the posterior extremities. The weakness and pain cleared up after a period of about a week and the animals showed no further untoward symptomatology until the time the animal was sacrificed. The histologic studies showed definite alterations in all but one of these animals.

ABSORPTION RATE OF WIN 1756

| Number of Dog | Days Required for Absorption |
|---|---|
| 1 | 14 |
| 2 | 11 |
| 3 | 7 |
| 4 | 10 |
| 5 | 9 |
| 6 | 13 |
| 7 | 14 |
| 8 | 14 |

Dog No. 1: Microscopic. No evidence of inflammatory reaction. The anterior horn cells were intact. The rootlets, both anterior and posterior, showed definite alterations. There was marked swelling of many of the axons with a loss of staining properties. The axons often filled the entire myelin sheaths. The myelin was absent. About one-half of the axons, particularly in the lumbar and thoracic regions, were altered.

Dog No. 2: Microscopic. Most of the changes were in the lumbar and thoracic cord. The nerve cells were intact. The axons were definitely swollen in many nerve bundles, particularly in the anterior rootlets. The posterior rootlets were intact. The motor rootlets in the lumbosacral region showed about one-half the axons swollen and often completely filling the myelin sheaths. The myelin was fragmented or absent. The changes were less severe in the lumbar thoracic cord.

Dog No. 6: Pathologic changes were mild. There was a slight swelling of the axons in an occasional fiber. The changes were not severe.

Dog No. 7: There was no cellular reaction. The rootlets of the lumbosacral cord showed marked alterations. The axons were swollen and filled the entire myelin sheaths. The myelin was completely absent in many rootlets. An occasional rootlet was fragmented.

Dog No. 8: There was no gross abnormality of the brain and cord. Microscopically there was a mild cellular reaction in the subarachnoid space. The posterior rootlets in the lumbosacral region showed axonal swelling and complete disappearance of a number of the axons. The anterior rootlets were unaltered. Occasionally anterior horn cells showed chromatolysis and swelling.

It is apparent from histologic studies of these animals that WIN 1756 fairly consistently produced alterations within the rootlets of the lumbosacral region where the radio-opaque material was injected. These changes involved both the anterior and posterior rootlets and consisted primarily of a marked swelling of the axons with partial disappearance of some of the axons and definite alterations within the myelin sheaths. Because of the fairly consistent alterations within the dogs, it was felt that this material could not be used in its present form for a trial in the patient.

WIN 1742 was injected into the subarachnoid space of only four dogs because of the marked toxicity of this substance. It is sufficiently radio-opaque and reacted similar to WIN 557 except in its rate of absorption and as concerns the toxic reactions. Three dogs died of the material. The fourth dog was partially paralyzed in the hind legs within a day following the injection. She was able to walk but slowly and showed evidence of severe pain, particularly when the hind quarters were manipulated. This dog also gave indication of pain when the head was moved from side to side. However, the dog continued to have gait difficulty for the next five days, at which time she was again able to walk normally. By the fourth week the dog appeared to have some difficulty with vision and was finally sacrificed at the end of the 7th week, at which time the dog was completely blind.

Dog No. 1 died 22 days after the injection. Films made 20 days after the injection revealed almost complete absorption, there being only a few small scattered droplets remaining.

Dog. No. 2 showed complete absorption of the media at the end of 14 days and Dog No. 3 at the end of 19 days. Dog No. 4 was observed for 28 days. At the end of that period only two or three small droplets could be identified. This dog was killed. At autopsy it was very difficult to remove the spinal cord, primarily because of its adherence to the dura and to the vertebrae. Microscopic examination showed a very definite cellular reaction in the subarachnoid space. At this stage the rootlets seemed intact. Because of the apparent toxicity of this material, it was felt that further studies did not seem warranted.

Since WIN 557 seemed non-irritative to animals and seemed to produce almost negligible changes even after prolonged periods of observation, it was felt that this dye might be tried in patients.

Four patients were selected for the injection of WIN 557 and were observed fluoroscopically, films being taken at varying intervals. In each case the patients selected already were suffering from a very severe neurological disturbance. The nature of the patient's illness and the course of the dye injection will be described in each case individually.

....., a 37 year old female, had a severe multiple sclerosis. On admission the patient had a flaccid paralysis of the lower limbs and hypesthesia of the second lumbar dermatome. The patient had urinary incontinence. About three weeks after admission three cubic centimeters of WIN 557 were injected intrathecally. This patient offered no complaints or findings referable to the injection of the dye. The patient was observed at regular intervals for the next 22 days. At the end of that period approximately four-fifths of WIN 557 had been absorbed.

, a 62 year old female who was studied at the University of Minnesota Hospitals because of progressive paraplegia developing over a period of two months. Examination revealed a complete paralysis of the lower extremities with secondary sensory level at the second thoracic dermatome. The clinical diagnosis was chronic myelitis of undetermined etiology. One week after admission, 4.5 cubic centimeters of WIN 557 were injected. This patient offered no complaints referable to the injection of the dye. There was no evidence of any irritation, although the patient had constant spasms of the lower limbs and was complaining of pain ever since her admission. After a period of 21 days, only scattered droplets of the dye were visible. This patient was followed for 44 days and at the end of that time only one minute droplet of the dye could be observed.

, a 32 year old female entered the University of Minnesota Hospitals with a paraplegia of some 21 years' duration. This patient began to develop progressive paralysis of both legs at the age of 9 years. She has had complete loss of sensation, motor power, and bowel and bladder functions since the age of 11 years. On admission she showed a spastic paralysis of both lower extremities and had an anesthesia below the twelfth thoracic level. Three weeks after admission, the patient was injected with five cubic centimeters of WIN 557. Prior to the injection of the dye the patient had urinary incontinence. During the ten days following the injection of the dye, the patient developed a urinary retention and required frequent daily catheterization. This cleared up after ten days. No other complaints or evidence of nervous system irritation was apparent, but it was felt that the urinary alteration was definitely the result of the inoculation of the dye. In this patient it was somewhat difficult to tell the time necessary for absorption of the dye since three cubic centimeters of pantopaque had been injected intrathecally about 15 days previously and was not removed. This patient was observed for 36 days and no change in the amount of dye was noted in the last ten days, so absorption of WIN 557 was probably complete or nearly complete at the end of this 26 day period and it was felt that the remaining dye was probably the pantopaque that had not been removed.

., a 34 year old male was injured in an automobile accident in May 1948, at which time he developed an immediate paraplegia. The examination revealed a spastic paraplegia with a sensory level at the tenth dorsal segment. At operation the cord showed a complete transection from the accident. The patient was injected with three to 4.5 cubic centimeters of WIN 557 and it took 27 days for complete absorption of the dye. At the end of that period only two minute particles of the radio-opaque media could be made out in the lumbar area. After two weeks only scattered droplets were visible. For five days after the injection this patient complained of pain in his

lower legs and an increase in the involuntary spasm of these limbs. It was the feeling of the Staff that the contrast medium might be responsible for these mild irritative phenomenon. However, the symptoms cleared up completely within a five day period.

Dr. Alberto Torres[38] of Bogota, Columbia, was visiting the Department of Radiology at the time investigations were being made with these newer compounds and expressed a desire to try WIN 557 on some cases when he returned to his country. He was given some samples and since has briefly reported on four cases.

Case 1. This patient was sent in for a myelogram as he was suspected of having radicular compression. Three cubic centimeters of WIN 557 was injected into the lumbar subarachnoid space. The day following, the patient developed pain in his leg[illegible]nd vesical paralysis which lasted for three weeks. He also complained of pain in his testicles for two weeks. After that the symptoms completely disappeared and the patient was discharged. He was observed roentgenographically for 55 days and at the end of that time only a few minute globules could be made out in the lumbar canal.

Case 2. This patient had signs of cord compression after being shot in the lumbar spine. Three cubic centimeters of WIN 557 was injected. No symptoms due to this were noted and the media was completely absorbed in 34 days.

Case 3. 1.5 cubic centimeters of WIN 557 was used in this patient. An old vertebral fracture had occurred, but there was no evidence of cord compression. No symptoms due to the media were observed and it was completely absorbed within 21 days.

Case 4. The exact amount of WIN 557 injected was not stated, but from the films it appears to be three or four cubic centimeters. No symptoms due to the media were observed. After 24 days only a few small globules were present in the lumbar spinal canal.

## Conclusions

1. In the clinical study of the spinal cord a readily absorbable non-toxic contrast media would be of inestimable value.

2. The best contrast media available at the present time is pantopaque. The big objection to this media is that it must be removed following x-ray studies, this removal being time-consuming and necessitating the leaving of the spinal needle in the patient throughout the x-ray study.

3. In an attempt to find a better medium, three new products manufactured by the Winthrop Company were studied. Of these, only WIN 557 proved to be completely non-toxic to dogs and did not produce tissue changes, even after a prolonged period of six months' study.

4. WIN 557 was then tried in a series of patients. It was absorbed fairly readily, but clinically tended to be somewhat irritating in about one-half of the patients.

5. It is apparent from the above studies that WIN 557 is not quite completely satisfactory because of its irritating qualities but comes very close to fulfilling the criterion necessary for a valuable contrast medium for spinal cord studies.

## References

1. Dandy, W. D.
Roentgenography of the Brain after the Injection of Air into the Spinal Canal.
Ann.Surg.,70:397-403, '19.
2. Dandy, W. E.
The Diagnosis and Localization of Spinal Cord Tumors.
Ann.Surg.,81:223-254, '25.
3. Sicard, J. A. and Forestier, J.
Bull. et mem.Soc.de Chir.de Paris, 46:463, '22.
4. Coggeshall, H. C. and Von Storch, T.J.
Diagnostic Value of Myelographic

Studies of the Caudal Dural Sac.
Arch.Neurol.& Psychiat.,31:611-613, '34.

5. Von Wagenen, W. P.
The Roentgenological Localization of Spinal Subarachnoid Block by the Use of Air in the Subarachnoid Spaces.
Ann.Surg.,99:939-943, '34.

6. Schmorl, G.
Ueber Knorpeknoten an der Hintenfläche der Wirbelbandscheiden.
Fortschr.a.d.Geb.d.Roentgenstrahlen, 40:629-634, '29, Inter alia.

7. Mixter, A. J. and Barr, J. S.
Rupture of the Intervertebral Disc with Involvement of the Spinal Canal.
New Eng. Jr. of Med.,211:210-215,'34..

8. Ayer, J. B. and Mixter, W. J.
Radiography following the Injection of Iodipin into the Spinal Arachnoid Space.
Arch.Neurol. & Psychiat.,11:499-500, '34.

9. Lindblom, A. F.
On the Effect of Lipiodol on the Meninges.
Acta Radiol.,5:129-134, '26.

10. Sicard, J. A. and Forestier, J.
Roentgenologic Exploration of the Central Nervous System with Iodized Oil (Lipiodol).
Arch.Neurol.& Psychiat.,16:420-434, '26.

11. Ebaugh, F. G. and Mella, H.
Use of Lipiodol in Localization of Spinal Lesions.
Am.Jr.Med.Sc.,172:117-123, '26.

12. Pugh, D. G.
The Present Status of Contrast Myelography.
Am.J.Med.Sc.,206:687-694, '43.

13. Garland, L. H.
Effect of Iodized Oil on Meninges of Spinal Cord and Brain.
Radiology, 35:467-476, '40.

14. Walsh, M. N. and Love, J. G.
Meningeal Response following Subarachnoid Injection of Iodized Oil.
Proc.Staff Mtgs. Mayo Clinic, 13:792-796, (Dec.14) '38.

15. Davis, L., Haven, H. A. and Stone, T. T.
The Effects of Injection of Iodized Oil in the Spinal Subarachnoid Space.
J.A.M.A. 94:772 (Mar.15), '30.

16. Lindblom, A. F.
On Effects of Various Iodized Oil on Meninges.
Acta Med. Scand. 76:395-402, '31.

17. Globus, J. H.
Contribution Made by Roentgenographic Evidence after Injection of Iodized Oil.
Arch.Neurol.& Psych.37:1077-1082, '37.

18. Marcovich, A. W., Walker, A. E. and Jessico, C. M.
Immediate and Late Effects of the Intrathecal Injection of Iodized Oil.
J.A.M.A. 116:2247-2254 (May 17),'41.

19. Bucy, P. C. and Spiegel, I. J.
Unusual Complication of Intraspinal Use of Iodized Oil.
J.A.M.A. 122:367-369 (June 5) '43.

20. Young, B. R. and Scott, M.
Air Myelography; Substitution of Air for Lipiodol in Roentgen Visualization of Tumors and Other Structures in Spinal Canal.
Am.J.Roent.,39:187-192, '38.

21. Munro, D. and Elkins, C. W.
Two Needle Oxygen Myelography.
Surg.,Gyn. & Obst.,75:729-736, '42.

22. Lucherini, T.
La Radicolo-Mielografia col Thorotrast.
Riv.Osp.,24:475-484, '34.

23. Nosik, W. A. and Mortenson, O. A.
Myelography with Thorotrast and Subsequent Removal by Forced Drainage: An Experimental Study.
Am.J.Roent.,39:727-730, '38.

24. Bunts, A. T.
Surgical Aspects of Ruptured Intervertebral Disc.
Radiology 36:604-616, '41.

25. Nichols, B. H. and Nosik, W. A.
Myelography with the Use of Thorium Dioxide Solution as a Contrast Medium.
Radiology 35:459-466, '40.

26. Nichols, B. H.
Thorotrast and the Diagnosis of Lesions Involving the Lower Spinal Canal.
Radiol.38:679-685, '42.

27. Arnall, S. and Lindstrom, F.
Myelography with Skiodan.

Acta Radiologica, 12:287, '31.
28. Lindblom, K.
Complications of Myelography by Abrodil.
Acta Radiologica, 28:69, '47.
29. Odegaard, Haakon
The Absorption of Myelotrast (Abrodil) from the Spinal Canal.
Acta Radiologica, 30:'48.
30. Strain, W. H., Plati, J. T. and Warren, S. L.
Jr. Am.Chem.Soc., 64:1436, '42.
31. Steinhausen, T. B., Dungan, C. E., Furst, J. B., Plati, J. T., Smith, S. W., Darling, A. P., Wolcott, E. C., Warren, S. L. and Strain, W. H.
Iodinated Organic Compounds as Contrast Media for Radiographic Diagnosis. III. Experimental and Clinical Myelography with Ethyl Iodophenylundecylate (Pantopaque).
Radiology 43:230-235, '44.
32. Ramsey, G. H., French, J. D. and Strain, W. H.
Iodinated Organic Compounds as Contrast Media for Radiographic Diagnosis. IV. Pantopaque Myelography.
Radiclogy, 43:236-240, '44.
33. Peacher, W. G. and Robertson, R. C. L.
Absorption of Pantopaque following Myelography.
Radiology 47:186-187, '46.
34. Peacher, W. G. and Robertson, R. C. L.
Pantopaque Myelography: Results, Comparison of Contrast Media and Spinal Fluid Reaction.
Jr. of Neuro-surg. 2:220-231, '45.
35. Tarlov, I. M.
Pantopaque Meningitis Disclosed at Operation.
J.A.M.A., 129:1014, (Dec.8), '45.
36. Morales, O. and Heiwinkel, H.
A Viscous Water Soluble Contrast Preparation.
Acta Radiologica 30:257-266, '48.
37. Bulletin from the Sterling Winthrop Research Institute.
Rensslaer, New York. (Mar.24), '48.
38. Torres, Alberto
Personal Communication.

## II. MEDICAL SCHOOL NEWS

### Coming Events

June 12 - Minnesota Medical Alumni Association and Minnesota Medical Foundation Dinner - Spaulding Hotel, Duluth (during annual meeting of Minnesota State Medical Association) -- 6:00 p.m.

June 26-30 - Continuation Course in Ear, Nose, and Throat for Specialists.

* * *

### Notes on the Junior Class

The present Junior Class has an average age of 26 years. The spread is over 22 years, the youngest being 21, the oldest 43. Russell Blanchard is the aged member but still manages to hold his own with his younger classmates. At the present writing, 33 per cent of the class are carrying on work outside of their regular classwork; the majority of these are of the junior internship type, although there are four laboratory technicians, one office worker here in the Hospital, and one person who is an electrocardiograph repair and service man. It would seem that the juniors are entering the omnipresent scramble for liquid assets.

It may be heartening to the administration to learn that at this time approximately 50 per cent of the class intend to become general practitioners. About 35 per cent are still undecided, and the remainder are eyeing the life of the specialist.

In the research for research sake department are Ed Humphrey and Ernie Agar who are working with the Division of Cancer Biology. Ed's work deals with an attempt to find a chemical test for the presence of carcinoma. The test depends on the rate or reduction of methylene blue to its colorless state with the problem at present being the interpretation of the test itself. The basic procedure of the test is old, but Ed is adding new twists.

It should be mentioned that Sanford Bloom has also contributed to the advancement of knowledge in the field of cancer biology. He has added his efforts to four papers in conjunction with other workers. However, his scientific work slowed down somewhat when he became a father this winter. Since that time, Sandy has badgered all who will stop in an attempt to show off his latest baby pictures and to relate what new wonders his offspring can perform. There never was a child quite like the new Bloom baby (unless it could possibly be the latest class addition, William David Weyrauch).

Bob West fills the bill for having

DON'T FORGET THE MINN. MEDICAL FOUNDATION & MINN. MEDICAL ALUMNI ASSN. DINNER -- 6:00 p.m., Monday, June 12, Spaulding Hotel, Duluth

an interesting summer job. In conjunction with Camp Lincoln, he sponsors a trip to the mountains in Montana every summer. He is equipped to handle 10 to 12 boys between the ages of 13 and 18 for an 18-day pack trip into the wild and woolly country. Each boy has his own horse and necessary equipment. The boys live in the open, sleep in sleeping bags, and learn how to handle themselves under outdoor conditions. Bob's biggest problem is discouraging the adolescent boy from climbing a mountain he can't get down from. However, since Bob was reared in the country they travel in and knows every nook and cranny, he is well qualified to do this. The party for this year isn't complete yet so any one interested should get in touch with him.

To return to medical subjects, Bruce Prentice has the jump on everyone in the class by having a series of two cases of measles in his own home. At this time he has seen two more Koplik spots than anyone else. The rest of us are still whizzes in the kala azar department.

-- Jesse E. Douglass, Chairman
Undergraduate Editorial Committee

## Faculty News

Dr. L. J. Wells, Professor of Anatomy, has been invited by the Centre National de la Recherche Scientifique to participate in the International Symposium on "Sex Differentiation in Vertebrates", to be held in Paris, June 5-12. The Symposium, which is being held with the financial assistance of the Rockefeller Foundation, will be attended by 14 Europeans and 5 American scientists.

DON'T FORGET THE MINN. MEDICAL FOUNDATION & MINN. MEDICAL ALUMNI ASSN. DINNER -- 6:00 p.m., Monday, June 12, Spaulding Hotel, Duluth

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

No. 291 June 4 - June 10, 1950

Sunday, June 4

9:00 - 10:00 Surgery Grand Rounds; Station 22, U. H.

10:30 - Surgical Conference; Recent Advances in Antibiotic Therapy; Wesley W. Spink; Todd Amphitheater, U. H.

Monday, June 5

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; M-109, U. H.

10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, Minneapolis General Hospital.

11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.

12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.

12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff; Small Classroom, Minneapolis General Hospital.

1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis General Hospital.

1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.

4:30 - 5:30 Dermatological Seminar; M-436, U. H.

5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss, and Staffs; M-109, U. H.

Tuesday, June 6

7:30 - 9:00 Fracture Rounds; General Hospital.

8:30 - 10:20 Surgery Conference; Small Conference Room, Bldg. I, Veterans Hospital.

9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staffs; Todd Amphitheater, U. H.

10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and E. T. Bell; Veterans Hospital.

11:00 - Contagion Rounds; Forrest Adams; Sta. L, General Hospital.

Tuesday, June 6 (Cont.)

12:30 - Pediatric-Surgery Rounds; Drs. Stoesser, Wyatt, Chisholm, McNelson and Dennis; Sta. I, Minneapolis General Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 102 I. A.

1:30 - 2:30 Pediatric-Psychiatry Conference; R. A. Jensen and Staff; 6th Floor, West Wing, U. H.

1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans Hospital.

3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.

3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.

4:00 - 5:00 Physiology-Surgery Conference; Eustis Amphitheater, U. H.

4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.

5:00 - 6:00 X-ray Conference; Presentation of Cases; Ancker Hospital Staff - Doctors Aurelius, Peterson and Marshall; Todd Amphitheater, U. H.

Wednesday, June 7

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-109, U. H.

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; L. B. Thomas and L. G. Rigler; Todd Amphitheater, U. H.

8:30 - 9:30 Clinico-Pathological Conference; Auditorium Ancker Hospital.

8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans and Bernard O'Loughlin; Room 1AW, Veterans Hospital.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker, Veterans Hospital.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Medicine Case; O. H. Wangensteen, C. J. Watson and Staffs; Todd Amphitheater, U. H.

12:15 - Staff Meeting; Main Classroom, General Hospital.

3:00 - Pediatric Rounds; C. J. Huenekens; Sta. I, General Hospital.

3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.

4:00 - 5:00 Infectious Disease Rounds; Todd Amphitheater, University Hospitals.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; E-101, U. H.

Wednesday, June 7 (Cont.)

5:00 - 7:00 Dermatology Clinical Seminar; Dining Room, U. H.

8:00 - Dermatological Pathology Conference; Todd Amphitheater, U. H.

Thursday, June 8

8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.

11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.

11:30 - Pathology Conference Clinic; Main Classroom; General Hospital.

11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Classroom, Minneapolis General Hospital.

1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.

4:15 - 5:00 Bacteriology Seminar; Cultivation of Virus in vitro; G. Butorac; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.

7:30 - 9:30 Pediatrics Cardiology Conference and Journal Club; Review of Current Literature 1st hour and Review of Patients 2nd hour; 206 Temporary West Hospital.

Friday, June 9

8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - 11:20 Medicine Grand Rounds; Veterans Hospital.

10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - Pediatric Rounds; Erling Platou; Sta. I, General Hospital.

11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser, and Staffs; Minneapolis General Hospital.

Friday, June 9 (Cont.)

11:45 - 12:50 University of Minnesota Hospitals General Staff Meeting; Neomycin: Clinical Investigations; Burton A. Waisbren and Wesley W. Spink; Powell Hall Amphitheater.

12:00 - 1:00 Surgery Clinical Pathological Conference; A. A. Zierold, Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.

2:00 - 3:00 Dermatology and Syphilology Conference; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

3:00 - 4:00 Neuropathology Conference; F. Tichy; Todd Amphitheater, U. H.

4:00 - 5:00 Clinical Pathological Conference; A. B. Baker; Todd Amphitheater, U. H.

4:15 - 5:15 Electrocardiographic Conference; 106 Temp. Bldg., Hospital Court, U. H.

4:30 - 5:30 Journal Club; M-436, U. H.

5:00 - 6:00 Otolaryngology Seminar; Review of Current Literature; H. Frey; Todd Memorial Room, U. H.

Saturday, June 10

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; M-109, U. H.

8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-221, U. H.

9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.

9:15 - 10:00 Surgery-Roentgenology Conference; F. Ruzicka, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - Contagion Rounds; Forrest Adams; Sta. L, General Hospital.