showed a greatly reduced but still elevated protein content. The Pandy and Ross-Jones tests were only slightly positive. The cell count was normal.

We have read no reports of spinal fluid examination for heterophile agglutinins in infectious mononucleosis. Serial dilutions beginning with 1:4 concentrations revealed no such agglutinins in our case. Blood and spinal fluid cultures remained sterile.

The chart shows the rapid fall in blood heterophile agglutinins during recovery to an almost insignificant degree just prior to the patient's discharge from the hospital.

Agglutination tests of the patient's serum against Listerella monocytogenes were negative. Throat cultures made on the day of admission showed only alpha streptococci. The urine was constantly normal.

**COMMENT**

This case is almost unique among the cases of infectious mononucleosis which showed involvement of the central nervous system, in that there were no signs and almost no cerebrospinal abnormalities (except for 9 cells in one count) pointing to meningeal involvement. Especially striking was the cell protein dissociation in favor of the protein, which speaks against involvement of the meninges. In the majority of the cases reported there was meningeal involvement with a considerable increase in cell content at least during one phase of the disease, while the protein showed hardly any increase.

Only one case has been reported 6 in which the symptoms (paresis of the left inferior rectus muscle of the eye, highly exaggerated knee jerks, a questionable plantar reflex and entirely normal cerebrospinal fluid) pointed to a purely encephalitic process.

In our case the cerebral involvement was much more extensive. The clinical picture was that of an acute ataxia with outspoken involvement of the cerebellar system.

This is not the place to discuss at any length the question of the localization of the acute ataxia, whether it is produced by the toxi-infectious process of the coordination system (Davidenkoff) or by a circumscribed focus in the hypothalamic region (Margulis). It seems, however, that the pathologic process, whether it is a real "encephalitis," i.e. an inflammatory process, or a "toxic encephalopathy," extends over a rather large area of the brain. In our opinion there cannot be any doubt about the involvement of the cerebellar system. On the other hand there were a number of signs (expressionless face, lack of motor impulse, peculiar kind of somnolence, diffuse perspiration) which make one think of a pathologic process in the gray matter surrounding the third ventricle, the hypothalamic region, so that the possibility of a lethargic encephalitis was considered for a short time.

It is interesting that the lymphadenopathy and palpable spleen, the usual and characteristic signs of infectious mononucleosis, did not appear until the alarming cerebral symptoms were almost gone. We must admit that the diagnosis would have probably been missed except for the laboratory report of positive blood heterophile agglutination, and the case would have been relegated to that wholly unsatisfactory waste-basket category of "aseptic" or "toxic encephalitis." We feel, therefore, that in the presence of acute cerebral symptoms of unknown etiology the heterophile agglutination test should be made.

Several workers have reported isolating Listerella in infectious mononucleosis. Schmidt and Nyfeldt were able to obtain cultures of the organism from the spinal fluid in 4 of 5 cases of the disease, in only 1 of which were cerebral symptoms present. In our case three attempts at obtaining cultures of the organism were unsuccessful.

The spinal fluid in our case was negative for heterophile agglutinins.

**SUMMARY**

1. In a case of infectious mononucleosis symptoms simulated those of encephalitis.
2. The heterophile agglutination test should be used in cases in which acute cerebral symptoms of unknown etiology are present.

**TREATMENT OF PARALYSIS AGITANS WITH VITAMIN B_6 (PYRIDOXINE HYDROCHLORIDE)**

A. B. BAKER, M.D.

**MINNEAPOLIS**

Pyridoxine hydrochloride, or the vitamin B_6 fraction of the vitamin B complex, was first discovered by Gyorgy 1 in 1935 and was first prepared synthetically in 1939 by Harris and Folkers. 2 It consists of 2-methyl-3-hydroxy-4, 5-dihydroxy-methyl-pyridine. It was first used clinically by Antopol and Schotland 3 with beneficial results in 6 patients with pseudohypertrophic muscular dystrophy. These authors expressed the belief that the drug, through its pyridine structure, was involved in the enzyme system concerned in muscular metabolism. Jolliffe, 4 believing muscular metabolism to be involved in paralysis agitans, tested the drug in this condition. He reported its use in 15 patients with paralysis agitans, all of whom had severe involvement. All patients received 50 to 100 mg. of pyridoxine hydrochloride intravenously. Four of the 15 patients showed definite objective improvement. The best results occurred in the idiopathic or arteriosclerotic type of the disease.

Since a considerable proportion of the patients visiting the Outpatient Clinic of the University of Minnesota Hospitals suffer from paralysis agitans, the staff naturally was most anxious to obtain and try any new therapeutic agent that might offer possible aid to these unfortunate persons. A group of 15 patients suffering from paralysis agitans were, therefore, selected for intravenous therapy with pyridoxine hydrochloride.

The type of patient, the amount of treatment and the results of the therapy are shown in the accompanying table. Nine obtained only two weeks of treatment at daily intervals; 6 of these received only 50 mg. of pyridoxine hydrochloride; 2 received 50 mg. for one week and 100 mg. during the second week, while 1 received 100 mg. for two weeks, supplemented by 54 grains (3.5 Gm.) of brewers' yeast. Three patients showed definite objective improvement (in cases 1, 10 and 12). Of these, 1 had idiopathic parkinsonism and 1 had postencephalitic involvement, while the condition

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of the third patient, although she offered no history of any previous illness, suggested postencephalitis, since the age at onset was 39.

Six patients received daily intravenous treatment with pyridoxine hydrochloride for three or more weeks. This treatment was supplemented with the vitamin B complex in the form of 54 grams daily of brewers’ yeast. In 5 of these patients the illness was idiopathic, while in 1 it was postencephalitic. Three patients, all of whom had idiopathic parkinsonism, showed definite objective improvement. Neither the age of the patient nor the duration of symptoms seemed to have any effect on the treatment. Good results were obtained in persons whose illness had been present for as long as fifteen years, while often no improvement occurred in some whose illness was fairly recent. The most favorable results appeared in the idiopathic type of the disease. This is in agreement with the results reported by Jolliffe.4 The nature of the improvement varied from patient to patient. In some it consisted of a drastic reduction in the severity of the tremor; in others the tremor was only slightly affected while the Rigidity improved, allowing the patient more freedom in movement. All the patients benefiting from the drug reported a definite subjective improvement, consisting of a decreased fatigability, better sleeping and increased appetite. A few had mostly choreiform movements rather than a parkinsonian syndrome. Since the involvement probably was arteriosclerotic and also extrapyramidal, it seemed of interest to attempt therapy with pyridoxine hydrochloride. Her improvement was most striking, suggesting the possibility that this type of therapy may be of benefit in other types of extrapyramidal involvement. A brief report of those patients responding to this therapy will aid in evaluating the results.

REPORT OF CASES

Case 1.—E. C., a woman aged 67, first noticed a definite tremor and rigidity of her hands in 1935. The involvement gradually spread to almost all the muscles of her body, including the muscles of the trunk, producing at first a shuffling gait and mild postural changes and finally an almost complete invalidism, the patient ultimately being confined to a wheel chair. She became weak and for years was able to sit up only for short periods. She had difficulty in sitting up in a car during even a short ride. She had been treated with scopolamine hydrobromide but showed no response to this type of therapy.

Neurologic examination revealed no gross involvement of any muscles, except slight impairment of the upper extremities. There was complete loss of facial expression and an absence of blinking. The patient was unable to walk or stand without aid. The deep reflexes were reduced but equal. The rest of the examination gave negative results.

She was given daily intravenous injections of 50 mg. of pyridoxine hydrochloride for one week and 100 mg. for the second week. Improvement became apparent after three weeks. Expression rapidly returned to the patient’s face. Her tremor became reduced and at times would be completely absent, even under emotional excitement. The rigidity also diminished, so that the patient was soon able to sit up for long periods of time and was also able to walk about the house unassisted. Long rides and even the entertaining of company no longer fatigued the patient.

She has continued to maintain her improvement in spite of severe gastrointestinal upsets.

Case 6.—L. S., a man aged 47, a jeweler, in 1935 first became aware of an impairment in speech associated with a generalized bodily weakness. He described this weakness as a general slowing down of all his activities, primarily because of difficulty in using his muscles. Impairment in speech consisted in difficulty in getting words out and a general running together of his words as they came out. The muscular rigidity became more severe, retarding all his voluntary movements. Because of this difficulty he soon became unable to carry on his work as a jeweler. His writing became impaired and his faces expressionless. Continuation of his illness finally resulted in the patient’s complete inability to do any type of work.

The neurologic examination revealed a dystarthritis and dysphonia associated with a masklike facies and a generalized muscular rigidity. Tremor was not present. Laboratory tests all gave negative results. The patient was placed on varying doses of scopolamine hydrobromide, which he continued to take for a period of months with no improvement. He was then given two courses of pyridoxine hydrochloride intravenously, separated by a two week interval. The first consisted of 50 mg. of the drug daily for a period of two weeks, the second of 30 mg. daily for one week followed by 100 mg. doses for the second week. He was simultaneously given 54 grams of brewers’ yeast daily. After the second week of his first course of treatment, the patient began to notice definite improvement in his speech. His voice lost part of its monotonous character and became a little more lively. Improvement continued. The muscular rigidity became so reduced that the patient was able to play ball and perform much of the work which he had been forced to discontinue prior to his treatment. At present he is taking 30 mg. weekly of pyridoxine hydrochloride given orally and has maintained his striking improvement.

Case 7.—A. G., a man aged 54, first noticed a slight stiffness in his left arm and leg in 1927. This rigidity gradually increased, producing a definite difficulty in gait. Three months after the onset of rigidity a coarse tremor appeared in the left hand and soon extended to the entire extremity but has always remained more or less localized to the left upper extremity. One year later there appeared an involvement of the facial muscles and a slight disturbance in speech. There was no history of any severe infectious process antedating the onset of his present illness.

Neurologic examination revealed a slight masking of the facies and a moderate salorrhoea. There was rigidity involving all extremities, being most noticeable on the left side, with a tremor limited to the left upper extremity. The patient had difficulty in performing both fine and gross movements with his hands. Scopolamine hydrobromide, which he had taken for a number of years, had produced but little improvement. During the past eight or nine years of his illness his condition had been little altered.

He was given daily intravenous injections of pyridoxine hydrochloride, receiving a total of four weeks of treatment with 500 mg. of the medication. At the same time he was given 54 grams of brewers’ yeast daily by mouth. After the completion of his treatment, the patient noticed a definite decrease in the tremor of his left upper extremity. His speech was improved. Improvement in speech completely disappeared. Whereas before the patient was able to walk for only short distances without becoming tired, he could now walk with ease for many blocks. He was given 40 mg. of pyridoxine hydrochloride by mouth weekly and in three months showed no recurrence of the involvement.

Case 10.—C. S., a woman aged 54, first noticed a tightness of her legs in 1925. One year later there developed a mild tremor of her right hand associated with definite rigidity. This involvement remained localized to the lower limbs until 1938, at which time it spread rapidly to the other extremities. The progress of the illness had been gradual during the past few years, resulting in a slow and shuffling gait and a severe and annoying tremor in her arms. She had continued to walk and travel about unassisted, although she had refused to go out in company because of her condition. More recently a moderate salorrhoea and some slurring of her speech developed. The patient gave no history suggesting any previous involvement of the central nervous system, although her age at onset certainly was suggestive of a postencephalitic involvement.

Examination revealed the characteristic parkinsonian syndrome. The facies was expressionless, and blinking was infrequent. The impairment in speech was noticeable. There was considerable rigidity of all extremities, associated with a rapid,
shuffling gait. A severe tremor was present in the upper limbs and there were beginning contractions of the hands.

She was given a single course of daily intravenous injections of 50 mg. of pyridoxine hydrochloride the first week and 100 mg. the second week. Along with this medication she received 54 grains of brewers' yeast by mouth. After this was a general slowing up of all her activities, and her gait became shuffling. She found it impossible to do her housework or to carry out her regular activities. At the time of her examination she presented a masklike facies, a staring gaze and a severe tremor and rigidity of all the extremities. She had a definite shuffling gait, walking with small steps and

Summary of Drug Therapy

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Type of Paralysis Agitans</th>
<th>Duration of Disease, Years</th>
<th>Severity of Disease</th>
<th>Intra-venously</th>
<th>Duration of Treatment, Weeks</th>
<th>Type of Medication</th>
<th>Daily Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E. C.</td>
<td>67</td>
<td>♂</td>
<td>Idiopathic</td>
<td>5</td>
<td>Severe</td>
<td>Definitely improved</td>
<td>2</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg. 1 week</td>
</tr>
<tr>
<td>2</td>
<td>G. F.</td>
<td>65</td>
<td>♂</td>
<td>Idiopathic</td>
<td>2</td>
<td>Moderate</td>
<td>Unimproved</td>
<td>2</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg. 1 week</td>
</tr>
<tr>
<td>3</td>
<td>C. M. J.</td>
<td>65</td>
<td>♂</td>
<td>Idiopathic</td>
<td>8</td>
<td>Severe</td>
<td>Unimproved</td>
<td>2</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg.</td>
</tr>
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<td>4</td>
<td>Y. G.</td>
<td>59</td>
<td>♂</td>
<td>Idiopathic</td>
<td>5</td>
<td>Moderate</td>
<td>Unimproved</td>
<td>2</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg.</td>
</tr>
<tr>
<td>5</td>
<td>L. B.</td>
<td>59</td>
<td>♂</td>
<td>Idiopathic</td>
<td>15</td>
<td>Severe</td>
<td>Unimproved</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>100 mg.</td>
</tr>
<tr>
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<td>L. S.</td>
<td>47</td>
<td>♂</td>
<td>Idiopathic</td>
<td>5</td>
<td>Moderate</td>
<td>Definitely improved</td>
<td>4</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg. 3 weeks</td>
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<tr>
<td>7</td>
<td>A. G.</td>
<td>34</td>
<td>♂</td>
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<td>33</td>
<td>Moderate</td>
<td>Moderately improved</td>
<td>4</td>
<td>Pyridoxine hydrochloride</td>
<td>100 mg.</td>
</tr>
<tr>
<td>8</td>
<td>F. Z.</td>
<td>63</td>
<td>♂</td>
<td>Idiopathic</td>
<td>11</td>
<td>Severe</td>
<td>Unimproved</td>
<td>4</td>
<td>Pyridoxine hydrochloride</td>
<td>54 grains</td>
</tr>
<tr>
<td>9</td>
<td>T. M.</td>
<td>71</td>
<td>♂</td>
<td>Senile chorea</td>
<td>4</td>
<td>Severe</td>
<td>Definitely improved</td>
<td>3</td>
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<td>50 mg. 1 week</td>
</tr>
<tr>
<td>10</td>
<td>C. S.</td>
<td>54</td>
<td>♂</td>
<td>Idiopathic</td>
<td>15</td>
<td>Moderate</td>
<td>Moderately improved</td>
<td>2</td>
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<td>100 mg. 2 weeks</td>
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<td>58</td>
<td>♂</td>
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<td>16</td>
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<td>Unimproved</td>
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<td>100 mg.</td>
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<tr>
<td>12</td>
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<td>39</td>
<td>♂</td>
<td>Postencephalic</td>
<td>4</td>
<td>Moderate</td>
<td>Moderately improved</td>
<td>2</td>
<td>Pyridoxine hydrochloride</td>
<td>54 grains</td>
</tr>
<tr>
<td>13</td>
<td>B. H.</td>
<td>38</td>
<td>♂</td>
<td>Postencephalic</td>
<td>5</td>
<td>Moderate</td>
<td>Unimproved</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg.</td>
</tr>
<tr>
<td>14</td>
<td>G. A.</td>
<td>49</td>
<td>♂</td>
<td>Postencephalic</td>
<td>18</td>
<td>Severe</td>
<td>Unimproved</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg. 1 week</td>
</tr>
<tr>
<td>15</td>
<td>L. B.</td>
<td>32</td>
<td>♂</td>
<td>Sprebilitic</td>
<td>4</td>
<td>Severe</td>
<td>Unimproved</td>
<td>2</td>
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<td>54 grains</td>
</tr>
<tr>
<td>16</td>
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<td>60</td>
<td>♂</td>
<td>Idiopathic</td>
<td>3</td>
<td>Severe</td>
<td>Subjective improvement only</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg. 1 week</td>
</tr>
<tr>
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<td>J. C.</td>
<td>60</td>
<td>♂</td>
<td>Idiopathic</td>
<td>2½</td>
<td>Moderate</td>
<td>Subjective improvement only</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>50 mg.</td>
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<tr>
<td>18</td>
<td>J. V.</td>
<td>62</td>
<td>♂</td>
<td>Idiopathic</td>
<td>10</td>
<td>Severe</td>
<td>Unimproved</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>54 grains</td>
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<tr>
<td>19</td>
<td>A. J.</td>
<td>69</td>
<td>♂</td>
<td>Idiopathic</td>
<td>3</td>
<td>Moderate</td>
<td>Unimproved</td>
<td>3</td>
<td>Pyridoxine hydrochloride</td>
<td>54 grains</td>
</tr>
</tbody>
</table>

So what does progressive B6 deficiency look like, the once stable patient finds that symptoms get worse and the patient's daily dose of drugs are increased.
tremor became almost imperceptible. She still has slight diffi-
culty in speech, although this has also improved.

Case 9.—I. M., a housewife aged 71, had been afflicted for
the past twelve years with gross, bizarre, purposeless, invol-
untary movements which began first in the arms and later
spread to the rest of her musculature. For the past three
years this involvement had totally incapacitated the patient.
Walking had been almost impossible, and she had been unable to
feed herself. The patient's mother had been similarly afflicted but
not to the degree to which the patient was involved. The patient has one brother, aged 67, who has
noted similar mild twitchings during the past few years. The
other five siblings are unaffected. She has three daughters who
are at present unaffected. The physical examination, aside
from the normal evidences of senescence, revealed no abnor-
malities. The neurologic examination revealed continuous
involuntary, irregular movements involving the upper portion
of the patient's trunk, arms and head. These choreiform move-
ments also involved, but to a much less extent, the lower
extremities, so that walking was difficult and her gait slightly
bizarre. Laboratory studies all gave negative results. Fluoro-
scopic examination of the chest and a 6 foot roentgenogram
of the heart gave negative results. The diagnosis in this case
was senile chorea.

The patient was given ½ teaspoon (2 cc.) of a concentrated
pyridoxine hydrochloride intravenously daily in 50 mg. doses. The pyridoxine hydrochloride was increased to 100 mg. after the second week. These medications were discontinued after three weeks, and the patient was given 40 mg. of pyridoxine hydrochloride by mouth weekly. After the first few injections of the drug her condition showed improvement, which continued during the
treatment. After three weeks the patient was walking unas-
sisted and with ease, and her gait showed no observable abnor-
mality. She was now able to write her own name. She could
feed herself, but only with considerable difficulty. The chorei-
form movements were greatly reduced, and the patient could
now sit quietly in a chair, whereas previously she had presented
rather a bizarre picture. Subjectively the patient felt stronger.
This manifested itself in an improved appetite and more restful
sleeping.

COMMENT

Fifteen patients suffering from paralysis agitans were
affected intravenously with pyridoxine hydrochloride,
supplemented in most cases by the oral administration
of brewers' yeast. The patients received 50 to 100 mg.
of the intravenous medication at daily intervals for from
two to four weeks. Nine patients had idiopathic or
arteriosclerotic parkinsonism, and of these 4 were
improved. One of these patients had senile chorea
rather than true parkinsonism. This patient showed a
most striking improvement, suggesting the possibility
that therapy with pyridoxine hydrochloride may be of
benefit in other types of extrapyramidal involvement.

Of the remaining 6 patients, 2 showed improvement.
In the latter group 3 had postencephalitic paralysis
agitans and 1 the syphilitic form. In the remaining
2 patients the etiologic factors producing paralysis
agitans were undetermined.

Four patients suffering from arteriosclerotic or idiop-
athic paralysis were treated orally with 50 mg. of
pyridoxine hydrochloride daily for three weeks supple-
mented by 54 grains of brewers' yeast. Two of these
patients insisted that improvement had occurred but in
only 1 was there any objective benefit in the form of
an observable decrease in the tremor and rigidity.

The small number of patients and the inadequate
dosage do not allow any definite conclusions; however,
the results with the oral medication are suggestive and
have encouraged me to undertake further investigations
with this method of administering pyridoxine hydro-
chloride, or vitamin B₆.

THE CEREBROSPINAL FLUID IN
DELIRIUM TREMENS

MILTON ROSENBAUM, M.D.
CINCINNATI

Drainage of the cerebrospinal fluid by means of spinal
puncture as a therapeutic measure in delirium tremens was
introduced by Steinebach 1 in 1915. In that same year Hoppe 2
introduced this procedure in the United States; since then the
treatment has become highly popular. Although it is now
generally assumed that an increase in intracranial pressure occurs in delirium

tremens and that drainage of the cerebrospinal fluid will relieve that tension, few data in support of this hypothe-
sis can be found in the literature.

In a series of 18 cases, Steinebach found 14 patients
(75 per cent) to have an increased pressure of the
cerebrospinal fluid. However, this conclusion was based
on interpretation of any pressure above 150 mm. of water
as abnormally increased, which criterion is not in
accord with that generally employed in this country,
in which the upper limit of normal is usually considered
to be 180 mm. of water. 3 All the pressures observed
in his cases were not recorded by Steinebach and hence
cannot be reevaluated. With no substantiating data,
Hoppe also concluded that the pressure of the cerebro-
spinal fluid is "always increased in delirium tremens." 4
Similar conclusions without supporting data were made
by Goldsmith 5 from his treatment of patients with alcoholic
deliriums and other acute alcoholic psychoses, in which
he claimed that in 48 per cent of his cases the cerebro-
spinal fluid "came out under considerable pressure." 5
Likewise, Levinson 6 stated that in delirium tremens the
"cerebrospinal fluid pressure is greatly increased, run-
ning as a rule from 150 to 300 mm. of water," but gave
no data to support his conclusion. In a similar manner
other authors, 7 in discussing the treatment of delirium
tremens, have expressed the belief that an increase in
intracranial pressure occurs, even though ample demon-
stration of such a phenomenon is still lacking.

The only study on delirium tremens which cast some
doubt on the aforementioned general conclusion was that
of Thomas, Semrad and Schwab. 7 These authors reported
40 cases of delirium tremens in 20 of which spinal
puncture and drainage were done. In only 12 of their
cases were readings of pressure reliable, but in all 12 the pressures of the cerebrospinal fluid were
normal. In view of the small number of cases involved,
these authors could not definitely negate the concept
so generally accepted by others.

In view of the preceding reports, a review of the
results obtained from examinations of the cerebrospinal
fluid of patients with delirium tremens who were treated

From the Department of Psychiatry, University of Cincinnati College of
Medicine, and the Psychiatric Service of the Cincinnati General Hospital.

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the Use of Fluids and Lumbar Puncture in the Treatment of Delirium