

## **SOME OBSERVATIONS IN THE TREATMENT OF ACUTE ENCEPHALITIS BY ROENTGEN THERAPY AND TYPHOID SHOCK REACTIONS**

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Since the great pandemic of influenza from 1916 to 1920, renewed interest has been shown in the diagnosis and treatment of acute and chronic encephalitis. As experience has increased in the management of this condition we have found that a great many cases do not conform to the classical symptomatology that was first described by von Economo in 1917<sup>1</sup>. While the severe, acute manifestations may consist of "somnolence, ophthalmoplegia and profound asthenia," the onset in most of our cases has not been so typical.

For the sake of accuracy the lethargic type of encephalitis must be differentiated particularly from such conditions as benign lymphocytic choriomeningitis, disseminated encephalomyelitis, and acute multiple sclerosis. Of even greater importance is the necessity for the careful differential diagnosis of spontaneous subarachnoid or intracranial hemorrhage, subdural hematoma, brain tumor, brain abscess, atypical types of meningitis, or hysterical cataleptic states. Likewise, the cerebral manifestations of general disease may simulate acute encephalitis such as diabetic coma, uremia, metastatic brain lesions, or syphilis of the central nervous system. If a careful clinical and laboratory study is made in all cases, the lesion can usually be placed in its proper category.

At the Clinic, among the early acute cases of encephalitis, we have found that the most common symptoms are headache, somnolence, coma, oculomotor disturbances, nausea or vomiting, and fatigue. In certain cases we often find severe vertigo, disturbances of speech, convulsions, monoplegia or hemiplegia. Not infrequently our study of these patients must include not only the usual clinical or neurological examination with various blood chemical and serological studies and the determination of spinal fluid pressures, but in more difficult cases an encephalogram becomes necessary. The subarachnoid fluid is studied for total protein, globulin, differential cell count, colloidal gold, and Wassermann reaction. With the aid of such data, we are able to determine, as a rule, whether the case requires medical or surgical treatment and whether the disease is of virus or bacterial etiology.

When we consider the nature of the neurotrophic virus, we can understand, to some extent, why treatment has been so ineffectual. This pathogenic substance, whether bacterial or chemical, is an obligate parasite which appears to live and reproduce within the grey matter of the central nervous system. Likewise, the cellular protoplasm of the

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host acts as a barrier to viricidal substances such as antibodies and chemicals. It is known that the disease may progress in spite of a high titer of specific antibody in the blood. These observations enable us to understand to some extent why the usual remedies are not specific.

In the second report of the Matheson Commission<sup>2</sup>, we find a discussion of more than fifty different drugs that have been employed in the treatment of acute encephalitis and encephalomyelitis. These include such preparations as salicylates, iodides, arsenicals, silver, antimony, mercury, quinine, methylene blue, strychnine, sulphur, ephedrine, benzedrine sulphate, atropine, scopolamine, pilocarpine, vaccines, convalescent sera, and many other miscellaneous preparations. This large array of medicinal substances bears mute testimony to the fact that, as yet, no specific method of attack has been developed. We have been shooting at a hidden target in the hope that, by controlling symptoms to some extent, we may be able to stay the relentless progress of this disease. While many of the patients with the milder types of encephalitis may recover spontaneously, in many instances the disease progresses to death or to hopeless invalidism.

In the Clinic we have been impressed by the fact that there are two therapeutic procedures which hold considerable promise of success. The first is nonspecific protein shock with intravenous injections of typhoid vaccine which may serve to "shake up" the cells of the body and thus to attenuate or destroy the neurotrophic virus. The second method, deep roentgen therapy, may act in a similar manner. Dr. Portmann believes that it serves to dispose lymphocytic infiltration with the liberation of antibodies as it apparently does in other inflammatory conditions. Both these methods have been used individually or together in a group of selected cases. While our experience in either instance has not been sufficient in number or time to justify a statistical report, the results, in general, have been most gratifying. Further study of these cases is necessary to determine whether the benefit is permanent or whether relapses or postencephalitis complications will appear. We must also take into consideration the knowledge that complete recovery may occur spontaneously in about 25 per cent of the cases, while the death rate is slightly in excess of 38 per cent. In the remaining 37 per cent the complications may be mild or severe<sup>3</sup>.

### TYPHOID SHOCK THERAPY

At present it seems apparent to us that the improvement which may come from typhoid shock reactions will be more striking and more lasting if the patient is seen and treated early, probably within the first week of the disease. On the other hand, we have failed to produce permanent improvement not only in late cases of encephalitis when

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sequelae have appeared but also in most cases of encephalomyelitis or cases that were regarded first as encephalomyelitis and later proved to be acute multiple sclerosis. In general, typhoid shock appears to be most effective when used in conjunction with deep roentgen therapy of the central nervous system.

We employ a modification of the method first employed by Howard<sup>4</sup>. Twenty-five million typhoid organisms from any standard vaccine are diluted with about 10 cc. of fresh sterile normal saline solution and given intravenously. As soon as the temperature is normal for 24 hours, a second dose, double in amount of vaccine, is again given. The third dose is double the second and so on until six reactions of chills and fever have been given. We always wait for normal temperature before administering the next dose. The maximum temperature rise is usually between 101° and 104° F.

### ROENTGEN THERAPY

The use of deep roentgen therapy in the treatment of acute encephalitis is not a new procedure. A few reports have appeared in foreign and American literature, some with favorable and other with adverse comments. Under the supervision of Dr. U. V. Portmann this therapy has proved to be a simple and harmless method of treatment. Amelioration of the patient's symptoms has occurred, often before the full course of radiation has been completed. In some instances two or even three series of treatments have been employed. The number of exposures as well as the dose used is varied somewhat with the type of case and the patient's response to the first few treatments. As will be evident in the case reports, the combination of roentgen irradiation and typhoid shock has been satisfactory. We have no satisfactory explanation for this observation. It may be that the fever and roentgen therapy build up the cellular resistance to the parasite or serve to make antibodies more effective within cells. We have observed no harmful effects from treatment with either x-ray or typhoid shock. The former usually causes depilation of the scalp which is only temporary. The hair returns, usually curly, within a few weeks.

The following case histories, given in tabloid form, will serve to illustrate some of our experiences with these two forms of therapy.

#### POSTINFLUENZAL ENCEPHALITIS. TYPHOID SHOCK THERAPY. RECOVERY

*Case 1:* Woman, 29 years of age, admitted February 2, 1937.

*Complaints:* Sleepiness, headache, staggering.

*History:* "Influenza" in August, 1936, with acute vertex and occipital headache.

Two months later, blurring of vision and slight drooping of eyelids, ataxia, mental depression, sleepiness, and irritability when awake.

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*Significant Findings:* Nystagmus upward and laterally, normal optic discs, slight drooping of eyelids, sluggish mentality, absent abdominal reflexes, ataxic gait.

Sinuses and teeth normal.

Simple hypochromic anemia.

Wassermann reaction and undulant fever agglutination negative.

Spinal fluid pressure normal.

Laboratory tests normal.

No fever.

*Treatment:* Typhoid shock reactions. Good febrile response.

*Results:* Immediate improvement at the termination of the reactions.

Four months: Normal physical findings.

Two years: No recurrence.

*Comment:* It would appear that this patient has responded very well to typhoid vaccine given intravenously. The absence of a recurrence or any sequelae over a two year period is encouraging.

### ACUTE ENCEPHALITIS. ROENTGEN THERAPY. RECOVERY

*Case 2:* Man, 45 years of age. Admitted August 6, 1938.

*Complaints:* Headache, attacks of vomiting, jumbled speech—one month.

*History:* No acute respiratory infection. Gradual onset of increasingly severe headaches, lethargy, vomiting, incoherent speech, and incontinence of urine without fever.

*Significant Findings:* Optic discs normal, lethargy, sluggish deep reflexes, positive abdominal reflexes.

Roentgen Examination of Skull: Pineal calcification in midline.

Spinal Puncture: Pressure 220 mm., clear fluid, 3 cells, negative for globulin, 120 mg. protein, negative Wasserman reaction and colloidal gold.

Encephalogram: No air in either ventricle; cortical fluid pathways normal.

Roentgen Examination of Chest: Normal, no metastases seen.

Laboratory Tests: Wassermann and undulant fever agglutination negative. Urine normal.

No fever.

*Treatment:* Deep roentgen therapy. Nine exposures to right and left sides of skull alternately during a period of 10 days.

*Results:* Six weeks after treatment, normal physical findings.

Patient felt well except slight mental sluggishness.

Ten weeks: Normal except slight urinary urgency.

Five months: Normal.

*Comment:* The acute symptoms in this case were of short duration. The response to roentgen therapy was very striking and satisfactory.

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### ACUTE ENCEPHALITIS. TYPHOID VACCINE AND ROENTGEN THERAPY. RECOVERY

*Case 3:* Woman, 28 years of age. Admitted April 15, 1938.

*Complaints:* Blurred vision, sleepiness, headache.

*History:* "Grippe," fever, and chills, November, 1937.

*Significant Findings:* Normal fundi and visual fields.

Internal squint left eye (paresis sixth cranial nerve, left).

Spinal fluid normal—three separate punctures.

Roentgen examination: Paranasal sinuses normal.

Laboratory tests of blood and urine normal.

No fever.

*Treatment:* Typhoid shock. Six satisfactory reactions, April, 1938.

Typhoid shock, second series, August, 1938.

Roentgen therapy to skull, 4 exposures, December, 1938.

Roentgen therapy, second course, January, 1939.

*Results:* Apparently complete recovery two months after the last treatment.

*Comment:* This patient had had severe symptoms for three and one-half months before therapy was begun. She failed to experience satisfactory relief of her headache and squint until she was given a second course of roentgen therapy. After the first course of typhoid there was a partial remission which lasted for four months. She derived no benefit from the second series of typhoid injections. At the present time she is gaining weight, looks entirely well, and has no complaints.

### ACUTE ENCEPHALITIS FOLLOWING CHICKEN-POX AND MEASLES. ROENTGEN AND TYPHOID THERAPY. RECOVERY

*Case 4:* Child, 8 years of age. Admitted March 29, 1938.

*Complaint:* Coma.

*History:* Five weeks previously, rhinitis, cough and chicken-pox. No fever.

Three weeks previously, measles, slight fever.

Ten days previously, sudden onset of fever to 104° F. with vomiting.

Eight days previously, convulsions, delirium, screaming followed by listlessness, and finally semi-coma.

*Significant Findings:* Dilated, sluggish pupils; fundi normal.

Apathy with no response to mild painful stimuli.

Chewed and swallowed only on command.

Reflexes: Absent patellar and Achilles. Left lower abdominal reflexes positive. Bilateral Babinski.

Paralysis of right eighth and left sixth cranial nerves following spinal puncture.

Urine: Trace of albumin, blood normal.

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Spinal fluid: Pressure, 140 mm. water, clear, 2 cells, 25 mg. protein.

Negative for globulin, colloidal gold, and Wassermann.

*Treatment:* Roentgen therapy: Five exposures in 5 days, March 30, 1938.

Typhoid shock therapy. Five injections with good response, April 14, 1938.

*Results:* Complete recovery with no residuals. Five months.

*Comment:* Symptoms of acute encephalitis rather than of encephalomyelitis developed shortly after the attacks of chicken-pox and measles. Immediately after the x-ray therapy was completed the patient became fully conscious but curious motor manifestations developed which always followed a definite pattern and were repeated over and over throughout the day. Suddenly she would sit up, flop herself down on her right side, then turn over to the left side, and promptly sit up again. The cycle was completed in about one-half minute and was immediately begun again. During meals she could be diverted from these movements and during sleep under sedatives she was quiet. After several days of these distressing symptoms a course of typhoid shock therapy was started. Following the third injection, her motor restlessness disappeared and she made a rapid recovery to normal health. While it is probable that this apparent irritation of the globus pallidus of the mid brain would have responded to a second course of roentgen therapy, she recovered so well after three typhoid chills that this proved to be adequate treatment. This remarkable patient has remained entirely well for five months.

## CONCLUSIONS

The use of deep roentgen and typhoid shock therapy appears to be distinctly helpful and possibly curative in the treatment of acute encephalitis in its early stages. Both Dr. W. James Gardner of the Neurosurgical Division and Dr. U. V. Portmann of the Department of Roentgen Therapy have felt very much encouraged with the results in their cases. Of the two methods, the best results follow radiation. However, observations on a large number of patients over a long period of time is necessary before any positive statements can be made. We do believe that no other form of therapy has been so satisfactory in the treatment of acute encephalitis.

## REFERENCES

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