

With the changes in the smears there occurred subjective improvement, with diminution in the severity and number of hot flushes and headaches, lessened nervousness and depression, increased well-being, and occasionally increased libido.

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Effect of X-Ray on Experimental Encephalitis in Mice Inoculated with the St. Louis Strain.*

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Since perivascular lymphocytic infiltration is the essential lesion in encephalitis and since lymphocytes are highly sensitive to irradiation, it seemed logical that small doses of X-ray should be effective as a therapeutic measure. The treatment by X-ray of 3 cases of encephalitis in human patients has been reported.¹ Since then 4 other cases have been treated. One was an early case and recovered completely in a short time. Two others were more protracted, having had the disease for 3 months before treatment was instituted. In these 2 latter cases various groups of muscles were showing progressive paralysis. The patients showed marked improvement after a series of X-ray treatments and are symptom-free to date. The fourth case, one of 6 months' duration with early Parkinsonian syndrome, is still under treatment but shows improvement.

Although the clinical evidence is very suggestive the findings are empirical and since the clinical studies can not be controlled, it was decided to carry out the treatments under experimental conditions. Mice are known to be highly susceptible to the St. Louis strain of virus.² The infective dose has been standardized and the incubation period is known.³ If mice that were treated with X-ray after inoculation with the virus recovered or had the period of incubation

* X-ray exposures were under the supervision of Doctors C. F. Baker and W. J. Marquis in the Department of Radiology, Presbyterian Hospital, Newark, N. J.

¹ Goldberg, S. A., Baker, C. F., and Hurff, J. W., *Radiology*, 1934, **22**, 663.

² Webster, L. T., and Fite, G. L., *Science*, 1933, **78**, 463.

³ Brodie, M., *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 1227.

or the duration of the disease prolonged, it seemed certain that the X-ray had a definite effect upon the disease.

A series of normal mice exposed to varying amounts of X-ray to determine how much they could tolerate, showed no apparent ill effects after a series of 10-minute treatments (each equivalent to $\frac{1}{2}$ a human erythema dose) given daily for 10 days. Preliminary experiments showed that the small X-ray doses given 48 to 72 hours apart that proved so effective in human beings were not effective in mice because of the fulminating character of the disease. Therefore more prolonged treatments at 24-hour intervals were given. Each treatment was 135 K.V., 5 ma., distance 15 inches, filters 3 mm. aluminum, time 5 minutes, equivalent to one-quarter of a human skin erythema dose.

Two methods of inoculation with the encephalitis virus were employed. In the first, 10 mice inoculated by the intracerebral route were treated daily with X-ray. Untreated controls came down with symptoms on the third or fourth day after inoculation and died in 6 to 12 hours thereafter. Of the treated animals one died on the third day, 8 hours after symptoms appeared; 5 died on the fourth day, two 36 hours and three 12 hours after symptoms appeared; 4 died on the fifth day, one 54 hours and three 15 hours after symptoms appeared. While 3 of these ran a more prolonged course than the controls, the difference was not striking. Therefore this method of inoculation was abandoned in favor of the intranasal route, where treatments could be more extensively carried out.

Inoculated by the intranasal method, mice usually showed symptoms on the fifth to seventh day and died within 6 to 24 hours thereafter. Several series of mice were inoculated intranasally and given daily X-ray treatments until death or up to 12 treatments. The results were as follows: Of the 38 mice thus inoculated and treated 15 survived without any apparent symptoms, 4 survived, having shown symptoms on the sixth and seventh days, of the 19 that died the incubation period varied from 6 to 11 days with an average of 7.8 days; the duration of illness in these 19 was from 1 to 5 days with an average of 2.5 days; the number of days before death in this group varied from 6 to 11 days with an average of 9.5 days. The animals that were ill for several days were unable to take nourishment and their death may have been due to starvation. In all, 53 controls were used and the average day of survival was 6 days with symptoms for 6 to 24 hours. In this control group 8 died on the fifth day, 27 on the sixth, 11 on the seventh and 8 on the eighth day. All the controls died with the exception of one that recovered after a mild attack.

All of these mice received 0.03 cc. of a 1-10 dilution equivalent to about 10-50 infective doses, injected into one nostril. This was based on the following experiment which determined the dosage for intranasal inoculation. Four mice given 0.03 cc. of a 1-100 dilution died in 6 days. Two mice given 0.03 cc. of a 1-500 dilution died in 6 days. Seven mice were given 0.03 cc. of a 1-1000 dilution, 3 died and 4 survived after a mild attack.

Another group of 8 mice was inoculated with a double dose of virus, *i. e.*, 0.03 cc. of a 1-10 dilution in each nostril. Two controls died on the sixth day. In the treated group all showed symptoms on the sixth day. Three of these died on the seventh day, 2 on the eighth day and one on the ninth day.

TABLE I.

Effect in mice of repeated X-ray treatments begun 24-48 hours after intranasal insufflation of St. Louis strain of encephalitis virus.

Dose of virus 0.03 cc. of a 1-10 dilution.

Dose of X-ray equivalent to $\frac{1}{4}$ human erythema dose.

No. of Mice	No. X-ray Treatments	Incubation period days	Duration of illness days	Day of death	Survivors
8	0	5	1	5	0
27	0	6	1	6	0
11	0	7	1	7	0
6	0	8	1	8	0
1	0	6	3	0	1
1	4	6	1	6	0
1	5	6	3	8	0
1	6	6	3	8	0
2	7	6	3	8	0
1	7	6	3	9	0
1	6	8	2	9	0
1	6	7	3	9	0
1	6	6	4	9	0
2	7	8	3	10	0
1	8	8	3	10	0
1	6	7	5	11	0
2	7	10	2	11	0
2	8	10	2	11	0
1	9	11	1	11	0
1	9	10	2	11	0
9	10	0	0	0	9
6	11	0	0	0	6
1	11	6	3	0	1
3	12	6	2	0	3

Because of the small number of animals used no attempt has been made to determine how soon after inoculation X-ray treatments should be started to obtain optimum effects. Taking into consideration the extreme susceptibility of mice to this virus and the fulminating character of the disease, the results must be considered as important. Not only was the life span and the period of

incubation of the treated animals prolonged, but the duration of the disease with symptoms was prolonged to 2, 3, and 4 days. These data indicate that numerous X-ray treatments either prevent or cure encephalitis in a number of mice inoculated intranasally with the virus.

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Nerve Impulses from Receptors in the Cornea.

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The central portion of the human cornea yields, to any form of stimulation, only the sensation of pain. The reactions of laboratory mammals to stimulation of this field recapitulate those of the human. Therefore it may be inferred that the sensation evoked is likewise pain. The site thus offers the possibility of investigating the mechanism of this sense, unconfused by other modalities. To this end arrangements were made to amplify and record action potentials in the long ciliary nerves. In some experiments the active fibers of one of these nerves were reduced to 2 or 3. The animals, cats, were decerebrated, the second to sixth cranial nerves cut, and the ciliary ganglion removed. The stimulators employed included a set of von Frey needles ($\frac{1}{8}$ to 10 gm.), a corresponding set of hairs, a mechanical stimulator delivering prick of variable intensity, and blunt glass rods.

The responses obtained from the cornea using these different instruments were essentially the same—trains of impulses of rapidly diminishing frequency, or occasionally, from the extreme fringe of a fiber's field, a single impulse only. Initial frequency and duration of the discharge were functions, both, of the intensity of the stimulation. In the first hundredth-second frequencies exceeding 500 per second were obtained. Thereafter, with continued stimulation, the discharge fell off precipitately, sometimes to cease entirely in a few seconds, sometimes to establish a sustained activity at one to 5 impulses per second. Removing the stimulus then commonly caused a second small outburst. Not infrequently a single stimulation of the cornea caused 2 fibers to respond, one of which adapted completely, the other, not.