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Effect of X-Ray on Poliomyelitis Virus in vivo and in vitro.*

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The use of Roentgen rays as an adjuvant in the treatment of human poliomyelitis has been widely recommended by a number of clinicians[1] while others[2] have expressed their doubt regarding the value of this form of therapy. Experimentally, the problem has apparently never been approached save for some earlier work of Amoss, Taylor and Witherbee.[3] These experiments, although originally undertaken for a different purpose, served to demonstrate that monkeys subjected to large doses of X-ray developed a more fulminant type of infection than did the controls.

In view of the conflicting clinical reports and in the absence of pertinent experimental data, it appeared worthwhile to investigate whether poliomyelitic monkeys upon exposure to very small doses of X-ray, such as are used successfully in a variety of acute inflammatory conditions, would not benefit from such treatment. There seemed to be at least a possibility that the quicker regression of paralysis alleged to have happened occasionally in human cases after early treatment with X-ray, might have been due to an acceleration in resorption of the perineuronal edema, mechanical pressure of which is generally conceded to exert a deleterious effect on the ganglion cells long before actual destruction has resulted in permanent damage.[4] At the same time it was interesting to determine whether raying of virus *in vitro* with much larger doses would affect the virulence of the infectious agent.

The experimental data submitted in this paper deal with observations on a total of 12 rhesus monkeys, exclusive of controls, which are distributed over the following 3 groups:

I. Effect of X-ray after onset of paralysis. Seven monkeys

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1 Bordier, H., *Rev. gén. clin. thérap.*, 1931, **45**, 465. Delherm, L., *J. Radiol. et Electrol.*, 1931, **15**, 321.

2 Marinesco, G., Manicatide, M., and Draganesco, St., *Ann. Inst. Past.*, 1929, **43**, 223.

3 Amoss, H. L., Taylor, H. D., and Witherbee, W. D., *J. Exp. Med.*, 1919, **24**, 115.

4 Aycock, W. L., and Amoss, H. L., *Bull. Johns Hopkins Hosp.*, 1923, **34**, 361.

with either incipient or almost completely developed paralysis were subjected to one or repeated X-ray treatments. The rays were directed on the areas corresponding to the cervical and lumbar enlargements of the spinal cord. The factors used were 200 KV, 8MA, 1/2 mm. Cu+1Al filter, TSD 57 cm., fields 6x10 to 6x25 cm. 100 r or approximately 1/6 of an erythema dose was administered for 3 minutes during each treatment. Of the 7 rayed animals 2 were found dead the following morning and 2 others died on the second day after treatment; the remaining animals, with the exception of one, dying at later periods of time. In 6 instances paralysis progressed as usual and histological examination revealed lesions in the cord of almost greater intensity than commonly observed in controls. The one surviving monkey appeared to improve rapidly during the course of further treatments. However, it is more likely that the stated improvement should be attributed to chance rather than to the effect of the X-ray.

II. Effect of X-ray during incubation period. Two monkeys were exposed to X-ray (dosage same as above) during the incubation period of the disease, the first treatment being given on the day of infection over the local area of intracerebral inoculation. This was followed by another treatment, 3 days later, applied to the cervical and lumbar cord. Both monkeys developed typical poliomyelitis within 6 days, leading eventually to complete paralysis and prostration, with no significant difference in the course of the disease from that of an accompanying control animal. It is of interest to note in passing, that after the first exposure to X-ray these monkeys, both of which were immature male animals, showed a peculiar testicular reaction characterized by sudden swelling of the organ and a tendency for descent. This may possibly be interpreted as evidence of action on the pituitary gland.

III. Effect of X-ray on virus in vitro. Three monkeys, in separate tests, were inoculated intracerebrally with 1 cc. of a 10% suspension of poliomyelitic cord, which had previously been exposed to large doses of X-ray. (200 KV, 8MA, 2 cm. wood filter, 50 cm. target distance, 38 minutes.) Two of these monkeys came down with poliomyelitis after an incubation period of 12 and 13 days, respectively, while the third animal developed the disease in a typical manner on the sixth day after inoculation. In all 3 monkeys paralysis progressed to complete prostration. Although the incubation period in 2 of these monkeys was somewhat prolonged over the average seen in controls, it would seem that the variation is still within the limits of spontaneous fluctuation of virulence of the virus.

In concluding it seems safe to assert that under the experimental conditions employed in our work, exposure to X-ray failed to destroy or markedly attenuate the virus *in vitro*. The observations on monkeys suffering from the experimental infection and treated either during the incubation period or with manifest paralytic symptoms furnish no evidence suggesting any benefit from the Roentgentherapy as used. It is difficult to properly evaluate these findings in their bearing upon the usefulness of Roentgentherapy during the course of the human disease. It should be remembered that the infection in the monkey is much more severe and recovery is exceedingly rare after complete paralysis has developed. In the human, on the other hand, paralysis shows a tendency for spontaneous regression in the majority of the cases. The argument therefore is ambiguous, as it may be held in favor as well as adverse to any possible value of X-ray in the treatment of human poliomyelitis.

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Experimental Enhancement of Malignancy in the Brown-Pearce Rabbit Tumor.

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The Brown-Pearce rabbit tumor is a transplantable malignant epithelioma carried in this laboratory for more than 100 generations by intratesticular inoculation. It has been used extensively for the study of animal constitution and it has been found possible to alter the susceptibility or resistance of animals to this tumor by various surgical and environmental procedures. About a year and a half ago attempts were made to alter the resistance or susceptibility of animals to inoculation with this tumor by the use of material derived from the tumor itself. The essential feature concerned the preparation of the material for use in conjunction with a regular tumor inoculation.

The first attempt resulted in a marked enhancement.[1] A rabbit which had died 5 to 10 hours previously of the Brown-Pearce tumor was placed for 2 weeks in the ice-box (26-32°F.) At the termination of this period, a normal saline emulsion of the primary tumor

[1] With reference to enhancing extracts from various tissues and from other tumors see: Chambers, H., and Scott, G. M., *Brit. J. Exp. Path.*, 1924, **5**, 1.