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On the Prophylactic and Therapeutic Value of Specific Immune Serum in Experimental Poliomyelitis.

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Comparatively few studies have been reported on the protective and therapeutic value of immune serum in experimental poliomyelitis in monkeys. The results vary somewhat, but indicate in the main that specific immune serum, while of doubtful therapeutic value, is of definite prophylactic value. We report observations on *M. rhesus* monkeys injected with immune serum either shortly before or at varying periods of time after inoculation with virus, the latter being administered in most of the experiments by the intranasal route,* the normal route of infection in man. The method of inoculating the experimental animals with virus by the intranasal route has already been reported by us.[1] The method described has yielded infection in about 95% of animals so inoculated. The immune serum employed in most of the experiments was one produced by injecting a horse with poliomyelitis virus over a period of nearly 2 years, at the end of which time its potency was such that 1 cc. of the serum contained sufficient immune substance to inactivate *in vitro* at least 25,000 minimum infecting doses of virus.[2]

Thus far we have carried out 11 experiments on the prophylactic value of immune serum, involving a total of 18 controls and 59 test animals. Convalescent monkey serum was employed in 2 of the experiments and immune horse serum in the remainder. The serums were administered by different routes; the amounts injected varying from a total of 1.75 cc. in one of the experiments to more than 30 cc. in other experiments. In most instances the serum was administered 24 hours prior to the inoculation of the animal with virus.

The results obtained in the individual experiments vary considerably, the percent survivors in the serum inoculated group ranging from 0% in one experiment (1.75 cc. of serum intracranially) to

* All procedures, including intranasal inoculation, carried out under ether anesthesia.

1 Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1010.

2 Schultz, E. W., and Gebhardt, L. P., *J. Immunol.*, in press.

100% in 3 of the experiments. Out of the total number of 58 serum treated animals 20 (or 34%) failed to develop the disease, while among the 18 controls all but one (or 94%) developed poliomyelitis. The average protection is somewhat below that realized in more limited studies by other investigators. Our results do not lead us to believe that pooled convalescent monkey serum is any more or any less effective as a prophylactic agent than the immune horse serum.

The experiments designed to test the *therapeutic* value of immune serum were carried out in much the same manner as those dealing with its prophylactic value, except that the serum injections in the therapeutic series were given 24 or more hours after inoculating the monkeys with virus. Nine experiments, in which a total of 12 controls and 32 test monkeys were employed, have been carried out in this part of our study. In most of these experiments the initial dose of serum was administered within 2 days following the inoculation of virus. The serum was administered by different routes and the amount injected was generally large in comparison with the amount usually administered per unit of body weight in the serum treatment of poliomyelitis in man. This applies also to poliomyelitis convalescent monkey serum, employed in 4 of the experiments.

The results give no indications whatever that serum is of any value 2 or more days after the animals have been successfully inoculated with virus. All of the serum treated animals, save one, developed the disease in about the same length of time and with about the same amount paralysis as the controls. The animal which failed to develop the disease had received 20 cc. of immune horse serum within 24 hours after its inoculation with virus. A companion monkey similarly treated developed the disease.

Our results indicate that once the virus has become implanted in the nervous tissue immune serum therapy is without appreciable effect. They, moreover, suggest that the entrenchment of the virus in the tissues occurs sometime within 2 days after the virus is instilled into the nasal passages of the experimental animal. Should these facts apply also in the natural infection of man, as they may, it would then appear highly improbable that immune serum, whatever its antibody content may be, can be of any appreciable value in combatting poliomyelitis unless it is administered sufficiently in advance of an exposure to the virus to forestall its implantation in the nervous system and at the same time not too far in advance of an exposure to the virus for the passive protection to wear off. This leaves to immune serum a very limited field of usefulness in the control of poliomyelitis.