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7653 P

### Active Immunization of Children Against Poliomyelitis with Formalin Inactivated Virus Suspension.\*

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In previous communications<sup>1</sup> it was pointed out that definite immunity could be developed against the virus of poliomyelitis using virus rendered non-infective by formalin. However, the amount of formalin used produced considerable skin irritation. Since then it has been shown that virus suspensions inactivated with 0.1% formalin, at incubator temperature, were also antigenic for monkeys, and at the same time, gave practically no skin irritation. The majority of the animals showed both humoral immunity, as tested by the neutralizing power of the serum for the virus of poliomyelitis; and tissue immunity, that is resistance to intracerebral inoculation of active virus.

The inactivated antigen produced no reaction whatsoever, neither symptoms, temperature rise nor cerebrospinal fluid changes developed upon repeated inoculations of large doses given both intracerebrally and intraperitoneally, each dose representing the equivalent of thousands of infective doses of living virus. Moreover, during vaccination the animal suffered no untoward local or systemic reactions, so it was felt that the vaccine could be given to humans with perfect safety.

However, before giving it to children, it was deemed advisable to try it upon ourselves, not that we had any misgivings about the possibilities of infection, but rather to determine whether the vac-

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<sup>1</sup> Brodie, M., *Science*, 1934, **79**, 594; *J. Immunol.*, in press

cine produced any disagreeable local or general reactions. Accordingly, 6 volunteers from the Bureau of Laboratories, Department of Health, New York were given 5 cc. doses of a 10% virus suspension, inactivated with 0.1% formalin for 16 to 48 hours. Three were given one dose, two, 2 doses and the third, 3 doses. The second inoculation was given 11 days after the first, and the third, 8 days after the second. After inoculation there was some soreness at the site of injection, lasting but a few minutes and probably due to the formalin. Three of those injected had some induration, which lasted but a few days and was not painful or uncomfortable. In no instance was there any systemic reaction.

The blood serums of all 6 obtained before immunization were tested for antibody and the amount determined by careful titration. A preliminary test was carried out upon the serums of the 3 who had more than one dose of vaccine and some increase in antibody was demonstrable.

As it was now evident that the vaccine could be administered with perfect safety it was given to a series of 12 children, whose ages ranged between 1 and 6 years. The virus suspension used for preparation of the vaccine was cultured aerobically and anaerobically before it was treated with 0.1% formalin for 16 hours, 12 hours being the time required to inactivate the virus. Five received a single dose of 5 cc., the others were given a second dose, either 11 or 13 days later. One to 2½ cc. was given intracutaneously, the remainder subcutaneously. The material was injected into the skin of the abdominal wall.

The children were carefully observed for local and general reactions and temperatures were recorded 4 times daily. There was no apparent general reaction or discomfort and at no time any febrile manifestations that could be attributed to the vaccine. The local reaction was negligible, consisting only of some induration in those receiving the larger amounts intracutaneously. The first dose did not render the children sensitive to the second dose.

In order to determine the degree of immunity produced by the vaccine, in each instance the antibody or antiviral content of the serum was determined quantitatively, by estimating the number of minimal completely paralyzing (M.C.P.) doses of virus the serum neutralized. The M.C.P. dose representing the smallest amount of virus-containing tissue that will produce a complete and rapid paralysis in a monkey of 2.5 to 4 kg. within 13 days.

All the children showed, prior to immunization, a small amount of neutralizing substance, too little to be of any significance. After

the vaccine each showed an appreciable increase. As far as the tests have been completed the blood serums of 6 children neutralized between 100 and 200 and those of the other 6 between 200 and 500 additional infective doses of virus.

Of course we have no index as to the level of immunity required to protect the children against the natural infection, nor whether the immunity obtained in the present series is sufficient. However, inasmuch as the humans responded better to the antigen than did the experimental animals and inasmuch as the monkeys injected with formalized virus showed a relatively high tissue immunity, sufficient to withstand in most cases intracerebral inoculation of virus, it is quite likely that the humans have an appreciable tissue immunity. By analogy with louping-ill,<sup>2</sup> a disease of sheep that is quite analogous to poliomyelitis, it should be ample to protect against natural exposure to the virus, for formalized louping-ill virus was unable to protect against intracerebral inoculation, yet it did so against the natural disease. However, the ultimate proof of the protective value of the vaccine must be established in a properly controlled series vaccinated in an epidemic area.

## 7654 P

### Vascular Action of Fresh Urine and Extracts Thereof.

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Human urine and extracts of urine have been known for some time to contain both pressor and depressor substances.<sup>1</sup> Attempts have been made to associate them with the presence of arterial hypertension with small success. Since the properties of these substances are little known, we have undertaken a study of them.

Cats anesthetized with ethyl urethane (7-10 cc. of a 25% solution given subcutaneously) or ether were employed as test animals. Blood pressure was recorded from the femoral artery and the vagus nerves were severed. Injections of the warmed fluid were made

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<sup>2</sup> Gordon, W. S., *Proc. Roy. Soc. Med.*, 1934, **27**, 11; *Veterinary Rec.*, 1934, **14**, 1.

<sup>1</sup> Abelous, J. F., and Bardier, E., *J. d. Physiol. et path. gén.*, 1908, **10**, 627; 1909, **11**, 34.