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Protection of Monkeys Against Intracerebral Inoculation of Virulent Poliomyelitis Virus by Vaccination with Phenolized Poliomyelitis Vaccine.

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Because of the similarity of the pathological changes induced in the central nervous system by poliomyelitis and rabies viruses, and because of the well-known successful vaccination against rabies by means of the Pasteur method, I decided to carry out similar prolonged vaccination of monkeys against poliomyelitis virus, which was kindly furnished by Dr. Simon Flexner, and proved to be highly infectious for *Macacus rhesus* monkeys selected, through the courtesy of the Rockefeller Institute for Medical Research, as proper animals for such observations. The vaccine was prepared according to the Pasteur vaccine technique, by Dr. Herbert Emerson of the University Pasteur Institute, and consisted of a 5% suspension of emulsified cord tissue preserved in 0.7% phenol.

Monkeys were vaccinated subcutaneously by gradually increasing daily doses of vaccine over periods of 28 to 29 days, beginning with 0.10 cc. to 0.3 cc. and ending with 3.5 cc. to 4 cc., which doses in some instances were reached by the seventeenth day and continued at that point for the remainder of the vaccination period. A proved paralyzing dose of Flexner virus was then inoculated into the center of the frontal lobe of the brain either soon after (24 hours) or late after (30 days) the last dose of vaccine was given.

For example, one monkey (V. No. 2) inoculated 24 hours after the last dose of vaccine, developed transient evidences of the disease 23 days after intracerebral inoculation. His gait suddenly became awkward, he was unable to hold a carrot in his hands and easily lost his balance. Six hours later he was apparently normal and the following morning very active and remained so. Another monkey was given a larger dose of the same proved potent virus 30 days after the last dose of vaccine. No recognizable symptoms developed during the course of 3 months. A characteristic protocol is given in Table I.

Of 3 vaccinated monkeys 2 resisted intracerebral inoculation. The monkey that died was inoculated one month after the last dose of vaccine. The 2 vaccinated monkeys that resisted the first intracere-

TABLE I.
Vaccinated Monkey No. 2.

Date of Injection	Amount cc.	Location	Date of Injection	Amount cc.	Location
11-19-31	.10	Arm	12-10	2.25	Arm
11-20	.20	"	12-11	2.50	"
11-21	.30	"	12-12	2.50	"
11-23	.40	Thigh	12-13	2.50	"
11-24	.50	Arm	12-14	2.50	"
11-25	.60	"	12-15	2.75	" Irritable
11-26	.60	Leg	12-16	3.00	"
11-27	.70	"	12-17	3.00	"
11-28	.70	"	12-18	3.50	" Resists. Cries
11-30	.80	Arm	12-21	Has been looking ill since 12-18.	
12- 1	1.00	"	12-29	Has been normal last few days.	
12- 2	1.00	"	12-30	8:15 a. m. Ether anesthesia 1/3 cc. virus into frontal lobe. Wound closed with sterile bone wax, suture, gauze, collodion.	
12- 3	1.50	"			
12- 4	1.50	"			
12- 5	1.60	"			
12- 6	1.75	"	1 -22	Transient evidence of disease. Recovered.	
12- 7	1.75	"			
12- 8	2.00	"			
12- 9	2.00	"			

bral inoculation of virulent virus were inoculated intracerebrally a second time. One (V. No. 2), one month after the first inoculation, was given 0.5 cc. of a very heavy suspension of brain and cord tissue of a control monkey (a proved paralyzing dose) into the opposite lobe. On the third day there was a possibility of weakness of one hand; on the sixth day anorexia, inactivity, stooping forward, headache, watery eyes, slow movements; on the seventh day, progressive paralysis; *i. e.,* left lower extremity, right lower, left upper, complete helplessness, death on the sixteenth day (3-16-32).

The other monkey similarly protected against the first intracerebral inoculation 49 days later was started on a course of subcutaneous injections of living poliomyelitis virus. A 2% saline suspension was used. The injections varied from 0.02 cc. to 0.80 cc. given at 2 to 3 day intervals. A temperature of 105 and a leukocytosis of 10,200 followed the fifteenth injection (0.6 cc.). The animal was perfectly well the next day and remained so for a month following the nineteenth injection of 0.8 cc. The animal was in excellent condition and it would seem that a very high titer of immunity had been attained. So I injected 0.5 cc. of a potent suspension of poliomyelitis virus into the opposite frontal lobe (5-6-32). Nine days later the animal sickened. On the eleventh day he developed a fever of 104.3°F. and paralyses of the hind extremities and on the twelfth day paralysis of all extremities. He was chloroformed on the fifteenth day. One of the 4 control monkeys survived the intracerebral inoculation. There was difficulty in getting the virus into

the brain and there was considerable hemorrhage and escape of fluid through the wound. Possibly some of the virus was washed away.

From these observations it seems that I was able to protect monkeys against an intracerebral paralyzing dose of poliomyelitis virus by prolonged gradually increasing doses of phenolized cord tissue vaccine prepared after the Pasteur vaccine technique method. I was unable to protect them against a second intracerebral injection of the same virus. Autopsies showed typical brain and cord changes.

No evidence of allergy was demonstrated during the progress of the subcutaneous injections of vaccine or by intradermal testing at proper times with virus filtered through a Berkefeld M candle and heated at 57°C. for 30 minutes; 8 to 9 observations in 24 hours.