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A Comparison of the Efficacy of Different Methods of Active Immunization in Experimental Poliomyelitis.*

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The difficulties encountered in obtaining protection against poliomyelitic infection in the monkey with any degree of regularity by the various recognized methods of active immunization are sufficiently known to any worker in this field.^{1, 2, 3, 4} In the following paper we have compared the efficacy of different routes of administration of the virus in the production of immunity against intracerebral infection.

A total of 16 monkeys were divided in small groups of from 4 to 2 animals, a different method of immunization being utilized in each instance. Thus, 4 monkeys were immunized intradermally, 3 intrapleurally,⁵ 2 intraperitoneally, and one subcutaneously, while 2 monkeys received the virus intrarectally after thorough cleansing of the colon.⁶ From 2 to 4 injections were given in the various groups, at intervals of 2 to 3 weeks. Live virus was used throughout this work, the size of the dose varying from 1 cc. to 3 cc. of a 20% cord suspension. Taking into account the density of the suspension, considerable amounts of virus were injected in some cases. In a last group of 4 monkeys, collodion sacs containing 3 cc. of virus suspension were inserted into the peritoneal cavity of the animals and left there indefinitely. The sacs, prepared according to the method described by Eggerth,⁷ were sterilized before use in the autoclave (10 min. at 10 lb. pressure). They were roughly tested for permeability with a scale of different dyes of increasing particle size. The sacs which we used retained prussian blue, but allowed the passage of congo red in small quantities and were completely permeable for methylene blue. All animals were tested for immunity about one month af-

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¹ Aycock, W. L., and Kagan, J. R., *J. Immunol.*, 1927, **14**, 85.

² Stewart, F. W., and Rhoads, C. P., *J. Exp. Med.*, 1929, **49**, 959.

³ Rhoads, C. P., *J. Exp. Med.*, 1930, **51**, 1.

⁴ Thompson, R., *J. Exp. Med.*, 1930, **51**, 777.

⁵ Gay, F. P., and Holden, M., *J. Inf. Dis.*, 1929, **45**, 415.

⁶ Hazen, E. L., *J. Immunol.*, 1927, **13**, 171.

⁷ Eggerth, A. H., *J. Biol. Chem.*, 1921, **48**, 203.

ter the last immunizing injection by intracerebral inoculation (1 cc. of a 5% virus cord emulsion), the virulence of the virus being controlled in each instance by simultaneous infection of one normal monkey. Details of experimental procedures and the results are conveniently tabulated in Table I.

TABLE I.
Comparison of different methods of active immunization.

Group	Monkey No.	Route of Immunization	No. of Injections	Amounts of virus injected cc. (20%)	Results during Immunization	Immunity as determined by Intracerebral Infection
I	49	Intradermal	2	7	Polio. 5 days	—
	76	"	2	7.5	—	Polio. 10 days
	77	"	3	8	—	" " "
	90	"	3	9.5	—	No symptoms*
II	101	Intrapleural	3	3	—	No symptoms†
	102	"	3	1.5	—	No symptoms*
	111	"	3	1.5	—	Polio. 9 days
III	170	Intraperitoneal	4	2	—	" " "
	192	"	4	2	—	" 7 "
IV	193	Subcutaneous	4	2	—	" 10 "
V	195	Intrarectal	4	4	—	" 7 "
	198	"	4	4	—	" 8 "
VI	86	Collodion sac	1	3	—	" 10 "
	88	" "	1	3	—	" 8 "
	89	" "	1	3	—	No symptoms*
	122	" "	1	3	—	Polio. 7 days
	135	Control I, II	—	—	—	" 8 "
	182	" III,	—	—	—	" 7 "
	114	" IV, V, VI	—	—	—	" 10 "

*These animals succumbed to poliomyelitis when reinfected one month after the first infection.

†This animal died from tuberculosis before reinfection.

It appears from Table I that one out of 4 monkeys immunized by the intradermal route was protected against the first infection, while one animal developed poliomyelitis during the period of immunization. Similarly, one monkey of 4 which carried virus-collodion sacs in the peritoneal cavity, withstood the first infection without showing any symptoms of the disease. The highest immunity index was obtained in a group of monkeys immunized with small doses of virus in the pleural cavity, 2 of 3 animals thus treated being fully protected against the first infection. Judging from the poor results obtained with intraperitoneal and subcutaneous immunization, it would seem that the success of intrapleural immunization was at-

tributable to the route of administration rather than to the size of the dose employed. As regards the possibilities of intrarectal immunization, with or without previous sensitization with bile, our results clearly indicate the inefficacy of such a procedure. The small number of experimental animals, in part due to intercurrent deaths, precludes the drawing of more definite conclusions at this time.

We wish to state in passing, that 6 monkeys, not enumerated above, which carried collodion sacs with virus in the peritoneal cavity, died with symptoms of progressive toxic cachexia in the course of 2 to 4 weeks. All of these monkeys were awkward in climbing, showing not only marked weakness of the legs and arms but lack of coordination of movements, and in 4 we observed a faint head tremor. The autopsy findings demonstrated the absence of lung infections (tuberculosis, pneumonia) and enteric infection (parasites). In some cases we found a slight congestion of the cord; histological examination however was essentially negative, as was transfer of the cord to a new monkey. The significance of these observations at present is obscure; they are especially perplexing inasmuch as our previous experience indicates that the virus in collodion sacs in the peritoneal cavity of the monkey is not viable beyond a period of 48 hours, contrasted with a survival for 10 days in the rabbit under similar experimental conditions. Work is under way to determine more accurately the actual length of survival and the occurrence of any possible changes in the nature of the virus in such sacs.

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A Critique of Einthoven's Law in Electrocardiography.*

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It is stated in authoritative books on electrocardiography that Einthoven's Law is mathematically exactly true. I wish to discuss this statement and to show that it is not correct. It is true that Einthoven's Law is approximately correct,¹ and that its practical use-

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¹ Pardee, H. E. B., *Clinical Aspects of the Electrocardiogram*, (Hoeber) 1928, 166.