immune serum added to an appropriate quantity of virus may render such a virus suspension innocuous immediately after the serum is added. In harmony with the results of other investigators with certain other viruses, we have repeatedly injected monkeys with poliomyelitis virus treated with *undiluted* monkey poliomyelitis convalescent serum immediately before inoculation (that is, without any incubation of the mixtures) without realizing infection. These observations have given rise to the opinion that the immune sera against the viruses may not act directly on the viruses, but in some indirect manner change the susceptibility of the tissues of the host. However, the fact that with dilution of the immune serum, it becomes necessary to prolong its contact with the virus *in vitro* argues distinctly in favor of the opinion that the immune serum *does* act directly on the virus. The relationship between the factor of *time* and that of *dilution* is brought out clearly by Schultz, Quigley and Bullock[14] on the inactivation of bacteriophage. They noted that whereas a serum dilution of 1:128 served to inactivate a given bacteriophage suspension in 30 minutes, a serum dilution of 1:4098 required as long as 8 days to render the same bacteriophage suspension inactive. It appears safe to assume that essentially the same relationships may apply to poliomyelitis and other virus-serum mixtures.

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Immune Serum Production in Poliomyelitis Refractory Animals.*

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Several investigators have reported the production of antipoliomyelitis serum in poliomyelitis refractory animals. Thus, Kraus[1] and likewise Pettit[2] claim to have been able to produce a viricidal serum in sheep, while more recently Neustaedter and Banzhaf[3]

[14] Schultz, Quigley and Bullock, *J. Immunol.*, 1929, **17**, 245.

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[1] Kraus, *Z. f. Immunitätsforsch. u. Exp. Therapie*, 1911, **9**, 117.

[2] Pettit, *Compt. rend. Soc. biol.*, 1918, **81**, 1087.

[3] Neustaedter and Banzhaf, *J. Am. Med. Assn.*, 1917, **68**, 1531.

Pettit,[4] Weyer, Park and Banzhaf,[5] and Fairbrother[6] have reported similar results with the serum of horses immunized with virus material from monkeys. The observations of other investigators (Flexner,[7] Stewart and Haselbauer[8]) have not supported the view that refractory animals are serviceable for the production of antipoliomyelitis serum. We began in 1928 to make a careful study of the capacity of various refractory animals to produce viricidal sera against this virus. The animals used include the guinea pig, rabbit, dog, goat, sheep and horse. These animals received injections of virus material (ground cord and medulla) from poliomyelitis monkeys, administered by various routes, at short intervals of time over periods ranging from several months for some of the animals to more than a year for others (sheep). The sera of these animals have been tested for viricidal properties in the customary manner, except that we aimed to subject the supposedly immune sera to somewhat more severe tests than those described by previous workers. Our method in setting up the viricidal test has been to add to a given volume (1 cc.) of a 5% suspension of virus cord (very finely ground in a machine,[9] lightly centrifuged and filtered through filter paper) to an equal volume (rather than 9 times the volume) of the undiluted immune serum. This mixture was incubated for 2 hours at 37° C. and injected in doses of 1.5 cc. into the frontal lobe of the brain of a monkey. Certain of the immune sera so produced were compared with monkey convalescent serum by titrating them against the same virus suspension. In several of the tests carried out with *undiluted* immune rabbit, sheep, and horse serum, a well defined viricidal action was obtained, but *on diluting these sera, even to a dilution of* 1:2 (after addition of virus suspension, 1:4), *no viricidal action was realized with any of these sera.* A convalescent monkey serum, on the other hand, exercised a viricidal action in dilutions as high as 1:64 under the same conditions. All the tests were controlled with corresponding set-ups made with normal sera. Our results thus far, therefore, indicate that refractory animals are incapable of producing antisera comparable in viricidal activity to monkey convalescent serum.

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[4] Pettit, *Bull. gén. de therap.*, 1925, **176**, 389.

[5] Weyer, Park and Banzhaf, *Am. J. Path.*, 1929, **5**, 517.

[6] Fairbrother, *Brit. J. Exp. Path.*, 1930, **9**, 43.

[7] Flexner, *Lancet*, 1912, **2**, 1271.

[8] Stewart and Haselbauer, *J. Exp. Med.*, 1928, **48**, 449.

[9] Schultz and Banham, *Am. J. Publ. Health*, 1930, **20**, 771.