lower cord. No attempt was made to correlate these findings with the histological picture in the monkey central nervous system because an attempt to transmit the virus in serial passage through the monkey failed. However, this finding is in keeping with the diffuse distribution of lesions found in the human.[4] The insusceptibility of other laboratory animals to the virus may be explained by a tissue insusceptibility rather than humoral antiviral action.

7515

Production of a Hyperimmune Antipoliomyelitic Horse Serum.*

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It is generally accepted that immune serum is of little or no therapeutic benefit in poliomyelitis, as well as in other filterable virus diseases. However, it may be of value prophylactically, but this has not as yet been fully demonstrated. Successful passive immunization against some virus diseases leads one to suppose that such protection may possibly be afforded against poliomyelitis when an antiserum of sufficient potency is produced. Numerous attempts[1-4] with varied degrees of success, have been made to prepare an effective antiviral serum in large animals. The production of a potent antipoliomyelitic horse serum was first accomplished in 1929 in these laboratories[5] and at about the same time in England.[6] More

[4] McCordock, H. A., *Am. J. Pub. Health*, 1933, **23**, 1152.

* This work was begun by the author in the fall of 1931 with the late William B. Brebner in the laboratories of Dr. E. V. Cowdry at Washington University, St. Louis. Supported by grants from Eli Lilly and Company and the Milbank Fund for the Study of Infantile Paralysis.

† The author wishes to express his gratitude to Dr. Wm. H. Park, Dr. E. V. Cowdry, and Mr. W. A. Jamieson for constant advice and encouragement in this work and wishes to thank Dr. Maurice Brodie for confirming the unusually high titres using a different neutralization test method.

[1] Flexner, S., and Lewis, P. A., *J. Am. Med. Assn.*, 1910, **55**, 662.

[2] Dixon, S. G., and Rucker, J. B., *J. Infect. Dis.*, 1918, **23**, 543.

[3] Pettit, A., *Compt. rend. Soc. biol.*, 1918, **81**, 1087; *Bull. gen. de Therap.*, 1925, **176**, 389.

[4] Neustaedter, M., and Banzhaf, E. J., *J. Am. Med. Assn.*, 1917, **68**, 1531.

[5] Weyer, E. R., Park, W. H., and Banzhaf, E. J., *Am. J. Path.*, 1929, **5**, 517; *J. Exp. Med.*, 1931, **53**, 553.

[6] Fairbrother, R. W., *Brit. J. Exp. Path.*, 1930, **11**, 43.

recently, Howitt[7] and Schultz and Gebhardt[8] have reported exceptional response toward immunization treatment with poliomyelitic virus in the sheep, goat and horse.

These investigators used suspensions of infected monkey brain or cord, as antigen. This was inoculated into the animals frequently and over long periods. A resultant serum, upon clinical trial in the New York poliomyelitis epidemic of 1931, proved to contain a toxic factor (probably a nerve tissue antibody). Toxicity tests conducted by the author upon several such serums showed that 2 of them were highly toxic for monkeys in 10 cc. doses with fatal results in some cases within 8 hours following intraperitoneal injection. The toxic effect of one of these serums was also observed by Kramer.[9]

The obvious need of a protein-free virus extract led to the successful attempt to purify virus emulsions by adsorption and elution.[10] Immunization of horses was then begun with such eluates. Three horses were selected and their serums tested for the presence of natural viricidal substance before treatment was begun. All these serums were negative. The horses were inoculated at weekly intervals by the intrasplenic route, this being chosen on the basis of Brebner's observations on the relation of the spleen to immunity to poliomyelitis.[11] Starting with 20 cc. amounts given weekly, the doses were gradually increased until 200 cc. doses were reached and continued to finish out a 6 month period of intrasplenic treatment. Intramuscular and subcutaneous inoculations given at about weekly intervals were then instituted and continued for another period of 9 months. Bleedings were taken at intervals and *in vitro* neutralization tests, to detect the quantity of antiviral substance, were made. All of these tests were carried out according to the method described by Shaughnessy.[12]

The results may be briefly summarized as follows:

Horse No. 1246—Serum of this horse showed a neutralization titre of 1:5 (serum:virus) after first month of treatment. Failed

[7] Howitt, B. F., *J. Infect. Dis.*, 1932, **50**, 26.

[8] Schultz, E. W., and Gebhardt, L. P., *J. Immun.*, 1934, **26**, 93.

[9] Kramer, S. D., personal communication.

[10] Schaeffer, M., and Brebner, W. B., *Arch. Path.*, 1933, **15**, 221.

[11] Brebner, W. B., *Am. J. Path.*, 1931, **7**, 546; PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 351; and numerous unpublished observations made in conjunction with author.

[12] Shaughnessy, H. J., Harmon, P. H., and Gordon, F. B., *J. Prev. Med.*, 1930, **4**, 463.

to show increase in titre after 4 months of further treatment. Discarded and replaced by Horse No. 1204.

Horse No. 1204—Serum showed an increasing rise in neutralization titre, reaching maximum of 1:40 after 6 months. Subsequent subcutaneous and intramuscular injections failed to increase potency of its serum.

Horse No. 1247—Serum reached maximum neutralization titre of 1:60 after 6 months of treatment. Subsequent intramuscular and subcutaneous inoculations raised the potency of its serum to a titre of 1:100. The concentrated pseudoglobulin of this serum has a neutralizing power of 1:1200.‡

The serum and concentrate is not toxic for monkeys even when given in doses as large as 90 cc.

Preliminary experiments on passive immunization, with the serum concentrate, indicate that it may be of value, since monkeys have been protected against intracerebral doses of highly infective virus for several days.

Two new sets of horses are now being immunized by different methods with the hope of obtaining even more potent products.

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Modification of Vagus Inhibition of the Heart by Quinidine.

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Quinidine acts directly upon the myocardium and is a powerful cardiac depressant. The drug depresses auriculo-ventricular conduction and retards the rate of the sinus node in dogs.[1] Auricular irritability is definitely diminished in the terrapin's heart.[2] However, when applied to clinical cases of hyperactivity of the sinus node as in sinus tachycardia, quinidine does not consistently exhibit its depressor effect. The rate of the sinus rhythm is frequently increased rather than retarded.

‡ This serum is 3 to 4 times as potent, and the concentrate about 40 times as potent as human convalescent serum. The concentrate is at least 10 times as potent as the previous one prepared in this laboratory.[5]

[1] Lewis, T., Drury, A. N., Iliescu, C. C., and Wedd, A. M., *Heart*, 1921, **9**, 55.

[2] Hirschfelder, A. D., and Cervenka, C., *J. Pharm. and Exp. Therap.*, 1925, **26**, 19.