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THE USE OF IMMUNE SERUM IN THE TREATMENT OF WHOOPING COUGH.*

BY ADRIEN BLEYER, M.D.,

ST. LOUIS.

(From the Pediatric Department of the Medical Department of Washington University, St. Louis.)

VERY satisfactory results with immune serum have been obtained in two diseases of lower animals: in epidemic jaundice the blood of guinea-pigs which have recovered from this disease will inactivate the virus, active blood being neutralized by one-hundredth part of convalescent's blood.^{1 2} In hog cholera immunity is conveyed by injections of convalescent's blood,³ which becomes life-long upon the addition of antigen such as the blood or tissues of an active case.⁴

In no disease in man have such results been obtained with immune blood. In scarlet fever, when used early in cases that have not become septic in type, results have occasionally been obtained; these are not yet consistent.^{5 6 7 8 9 10 11 12 13 14 15 16 17 18} Mixed convalescent's blood has been used in measles.¹⁹ Protective powers have been observed in mumps from small doses (6 to 8 c.c.) injected into muscle²⁰ in an institutional epidemic in which 33 per cent. of (134) susceptible children contracted mumps; no case occurred among those (17 children) treated. The blood of animals (cat) inoculated with saliva from cases of human parotitis is found to modify the course of such inoculations in other animals.²¹ In

* Read at the second annual meeting of the Central States Pediatric Society, in St. Louis, October 18, 1916.

poliomyelitis convalescent's blood will inactivate the virus;²² immune substances have been found both in the blood of monkeys^{21 22 23} and human beings,²⁷ and therapeutic properties were seen when the administration of the serum was made within eighteen to twenty-four hours after the inoculation of the virus into the brain or nose.²³ In a recent summary of this work in poliomyelitis²⁹ it is said that in the case of monkeys in which the virus does not exceed a certain dose the disease can be prevented or the onset of paralysis delayed. Human serum is found effective for monkeys.³¹ A series of 32 human cases in which immune serum from human cases was injected intraspinally is reported;^{31 32 33} there occurred in these about the same incidence of deaths, paralysis, and recoveries as occur among cases not so treated; there is another series of 4 cases with similar results,³⁴ and a report of 2 cases in which serum was used from persons who had recovered years before³⁵ (it is said that the neutralization test remains positive after poliomyelitis for a number of years*).³⁶ Convalescent's blood has been used in epidemic meningitis³⁷ and in pneumonia³⁸ without great success.

Because of these data it seemed worth while to try this method of treatment in whooping cough. It is now usually thought that whooping cough is a specific infectious disease; during the course of the second or third week, antibodies appear which are specific by agglutination³⁹ and by complement tests.^{40 41} For the purpose of determining the value of this method, injections of human blood were carried out in the early weeks of this disease in 45 cases. These were divided into three groups of 15 cases each. In Group A the blood injected was from persons who were convalescent or who had recovered from whooping cough within three months. In Group B the blood was from persons who had had the disease at more remote periods, and in Group C from persons who, so far as they knew, had never had it. Groups B and C were designed as controls to A.

The ages of the children in all groups averaged under three years; in Group A, in which convalescent's blood was used, 5 were in the first half year of life, 1 was five weeks old, and 1 thirty days old. The stage of the disease at which the treatment was given was about the same in the three groups; in Group A it was begun in the first week in 2 cases, in the second week in 5 cases, in the third weeks in 7 cases, and in the fourth week in 1 case. Dosage was gauged in a rough way to body weight of donee, from one-tenth to one-fifth of the computed volume of blood of donee was given; this varied between 40 and 125 c.c., divided into two, three, or four doses and injected into muscle (gluteus). Discoloration often followed the injections in very young infants; in a few there was

* Since this bibliography was prepared, another series of 15 cases has been reported (C. W. Wells: Jour. Am. Med. Assn., October 21, 1916, No. 17, lxvii, 1211).

induration for a day or two; there were no infections, and temperature reactions insofar as could be told in this disease did not occur. The injections in every case were completed within a week in order to avoid hemolytic reactions; reactions to new proteins were not observed. The blood used was from a single donor in ten, from two in four, and from three in one. Blood not used at once was citrated to 1 per cent. (in this amount sodium citrate is said not to affect antibody).⁴² The usual examination of donors, including Wassermann reactions on the bloods of non-relatives, were made.

The results of the treatment in the three groups may be summarized: In Group A of 15 children whose average age was twenty-eight months, who received convalescent's blood during the early weeks of whooping cough, there occurred no deaths and no serious complications; the course of the disease was, however, in no definite way different than is usually seen, and was not appreciably influenced by the treatment except in 3. This is a very small proportion, and it is more than likely that in 15 cases 3 of them might very well run an unexpectedly mild course without attracting a great deal of notice. The blood pictures of 2 of these, however, was interesting: In Case 4, during the third week of the disease, a 50,000 white count came down after 60 c.c. of convalescent's blood to 18,000 and the mononuclear percentage fell from 74 to 50; this drop was coincident with clinical improvement; this was a hand-fed baby of five months who weighed but 3860 grams.

In Cases 8 and 11 a transitory hyperleukoeytosis followed injections of the blood, and was succeeded in each instance by a drop to well below the original counts; changes in mononuclear percentages accompanied these drops. The shortest course of any of these cases was that of Case 11, four weeks; no shortening of the course of the disease was seen in any of the others.

In Group B, in Case 1, in which the blood used was from the mother who had had pertussis twenty years before, quite as satisfactory improvement occurred as in any case in Group A; in this group there were two pneumonias which recovered. There were also two pneumonias in Group C with one death, and in this group there was one case which seemed to have been very favorably affected by the injections of normal blood.

In explanation of these results it may be said that in some diseases injections of normal blood have brought about improvement, and that immunity may be increased at times by injections of normal blood,⁴³ that this has also occurred after injections of other things, such as protease,⁴⁴ lipase, ferments (trypsin), or drugs (kaolin).^{45 46} Hyperleukoeytosis, such as occurred in several cases in this series, has assisted immunity in other diseases (arthritis, typhoid^{47 48}), so for lack of consistency in the results obtained in these cases of whooping cough it is not possible to ascribe any of them to a specific action of the blood injected.

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