194 (2717)

The occurrence of antipneumococcus substances in the blood serum in lobar pneumonia.

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With a method[1] previously described for carrying on growth-inhibition tests with the pneumococcus, it was shown that a mixture of serum and leucocytes from naturally resistant animals (cats or dogs) was capable of inhibiting the growth of pneumococci in considerable numbers, whereas a serum-leucocyte mixture from a susceptible animal (rabbit) was found to have no such action. It was possible, however, to passively confer growth-inhibitory and pneumoccidal powers on serum-leucocyte mixtures of the latter animal by adding a very small quantity of a homologous antipneumococcus serum. By comparing different immune sera the degree of growth inhibition thus obtained paralleled closely their protective action for mice. In a subsequent investigation on experimental pneumococcus infection, it was found that recovery was invariably accompanied by the development in the serum of the infected animals of immune substances, which could be demonstrated by the occurrence of pneumococcus growth-inhibition when such serum was added to rabbit serum-leucocyte mixtures. On the other hand, the serum of animals dying from the experimental disease failed to show such immune changes at any time during the course of the infection. This led to the present study of the occurrence of these antipneumococcus substances in the blood serum of patients with lobar pneumonia.

The method employed was briefly as follows: Specimens of patient's serum were obtained from blood taken by vena-puncture on various days of the illness, and kept in a refrigerator until used. The several serum samples, inactivated beforehand, were tested by adding progressive dilutions of them to normal rabbit serum-leucocyte mixtures, which were in turn seeded with a constant small number of pneumococci. The strains of pneumococci used were either those isolated from the patient yielding the test serum or a homologous stock strain. All were virulent for rab-

[1] Robertson, O. H., and Sia, R. H. P., *J. Exp. Med.*, 1924, xxxix, 219.

bits. The small tubes containing the test mixtures were finally sealed with paraffined corks, and attached to a specially devised apparatus which produced constant agitation during incubation.

By the use of this method it was found that in all cases studied the serum obtained at or soon after the crisis possessed the power to inhibit the growth of the pneumococci in the rabbit serum-leucocyte mixtures; the serum obtained before the crisis, on the other hand, either totally lacked this power or showed it to only a very slight degree. The titer of these antipneumococcus substances reached the highest point three to four days following the crisis, then gradually diminished. The length of time before the immune bodies totally disappeared from the serum was not determined. In one patient who recovered spontaneously from a Type 1 pneumococcus pneumonia, the titer of antipneumococcus substances seventy days after the crisis, although markedly decreased, was still demonstrable by this technique. In the cases of Type 1 pneumonia treated with antipneumococcus serum with favorable results, these immune substances were detectable in the patient's serum soon after the intravenous therapy, and with the suspension of the treatment they tended to diminish rapidly, so that by the end of a week immune substances were usually no longer demonstrable in the patient's serum. In one patient with Type 1 pneumococcus pneumonia, however, where the first dose of immune serum was given as early as thirty hours after the onset of the disease, the titer of the anti-pneumococcus substances rose rapidly following the intravenous injections, and diminished very gradually. Thirty-three days after the last injection his serum still gave a fairly high titer of these substances, suggesting the presence of active immunity in this case. With cases that terminated fatally, on the other hand, no such antipneumococcus substances were detectable in the serum at any time during the course of the disease. This included a case of Type 1 pneumonia who died in spite of having received a total of 175 cc. of Type 1 immune serum on the fifth day. His blood serum even immediately after 100 cc. of immune serum failed to show the presence of anti-pneumococcus substances.

These findings add further support to the view that the crisis and recovery from pneumococcus lobar pneumonia are brought about by the development of specific antipneumococcus immune bodies in the blood serum, which, in conjunction with the leucocytes and normal serum constituents, bring about inhibition of growth and final destruction of the invading pneumococci.