passive transfer of immunity to mice, affords little or no protection whatever even against organisms of the homologous type.

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Intracutaneous Vaccination of Rabbits with Pneumococcus. III. Hypersensitiveness.

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In the preceding communications, the intracutaneous vaccination of rabbits with Pneumococcus (S forms) has been shown to give rise chiefly to the formation of the antiprotein rather than the type specific antibodies, and to the development of an increased resistance to infection with organisms of homologous and heterologous types. The present paper describes briefly the development of an altered tissue reaction to Pneumococcus and its protein derivatives in rabbits which have been inoculated repeatedly into the skin with heat killed suspensions of R and S pneumococci.

Mackenzie and Woo[1] have shown that guinea pigs, injected intracutaneously with an alkaline extract of Pneumococcus, develop an allergic reaction in the skin to the bacterial protein; Zinsser and Grinnell[2] have produced allergic sensitization to pneumococcus autolysates in guinea pigs previously injected intradermally or intraperitoneally with the same material. Bull and McKee[3] have recently shown that rabbits, after recovery from infection induced by intranasal inoculation of pneumococci, are highly skin-sensitive to pneumococcus autolysate.

The present observations were made in the course of a study of the antibody response and the immunity developed as a result of intracutaneous injection of rabbits. The intracutaneous injection in normal rabbits of 0.2 cc. of a heated vaccine, representing the bacteria from 2 cc. of broth culture, is followed by the appearance locally of a circumscribed slightly raised and indurated nodule, reddish in color, and measuring about 1 cm. in diameter. Upon repeated injection at weekly intervals the reaction changes in character; the size increases, often reaching a maximum of 4 to 6 cm. in diameter, accompanied by a spreading edema and purplish dis-

[1] Mackenzie, G. M., and Woo, S. T., *J. Exp. Med.*, 1925, xli, 65.

[2] Zinsser, H., and Grinnell, F. B., *J. Bact.*, 1927, xiv, 301.

[3] Bull, C. G., and McKee, C. M., *J. Am. Med. Assn.*, 1928, xci, 396.

coloration. The maximum reaction is generally reached after 6 to 8 injections and thereafter each successive lesion tends to become less intense but to persist longer, often breaking down with the discharge of sterile necrotic material. After healing has taken place, which often requires from 2 to 3 weeks, the animals are sensitive to the nucleoprotein and other protein derivatives of Pneumococcus when tested by the skin and ophthalmic reactions.

Sterile solutions of pneumococcus "nucleoprotein" and bacterial extracts containing the purpura-producing substance, from which the nucleoprotein had been removed by fractional precipitation, were used in the tests for hypersensitiveness. In the doses employed, the nucleoprotein fraction when injected into the skin of normal rabbits gave no local reaction, while extracts containing the purpura-producing material in about 50% of normal animals caused only a faint erythematous blushing of the skin. In the skin-vaccinated rabbits, on the other hand, these protein substances elicited an inflammatory reaction at the point of inoculation which begins to appear in from 8 to 10 hours after injection and fades after 3 days. Protein extracts containing autolytic products cause a similar but often more extensive reaction with purpuric discoloration.

In the eye test in rabbits, the cornea was anesthetized and lightly scarified by the technique described by Derick and Swift,[4] and one drop of nucleoprotein solution or purpura producing extract was instilled into the conjunctival sac. In normal rabbits this procedure causes no visible reaction. In the intracutaneously vaccinated rabbits, on the other hand, a definite reaction appears within 24 hours, which is characterized by congestion of the conjunctiva, the appearance of dilated capillaries at the sclerocorneal junction, followed by turbidity of the cornea, and occasionally by the development of pannus. The reaction may persist for from 4 to 8 days. Of 30 animals immunized intravenously with heat killed pneumococci none gave a positive eye reaction, while all of the 37 animals previously vaccinated intracutaneously reacted positively when subsequently tested with the protein derivatives of Pneumococcus by this method.

This form of hypersensitiveness appears to be limited to the protein substances of the bacterial cell, since solutions of purified type-specific carbohydrates fail to elicit the reactions in sensitive animals. In terms of bacterial specificity therefore, the reactions of hypersensitiveness are species- and not type-specific.

[4] Derick, C. L., and Swift, H. F., PROC. SOC. EXP. BIOL. AND MED., 1927, XXV, 222.

The hypersensitive state induced in rabbit by intracutaneous vaccination with R and S forms of pneumococci may persist for at least 4 months—the longest period so far tested. Moreover, it has been found, in a number of instances, that, after all evidences of the ophthalmic reactions have disappeared, the intravenous injection of nucleoprotein may cause the reappearance of the eye reaction.

A study of the development of hypersensitiveness in animals following experimental infection is in progress. The evidence at present indicates that rabbits surviving a slowly progressive but localized infection in the skin become hypersensitive to pneumococcus protein and that this state may appear as early as 12 days after the onset of the lesion.

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Lactic Acid Content of Blood of Trypanosome Infected Rats.

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Experimental trypanosome infection in rats presents one of the simplest pictures of a protozoan blood infection. After an incubation period of about a week (depending upon the dose injected) there is a period of uncertainty when host and parasite become alternately dominant. Then the trypanosomes become definitely established in the peripheral circulation and increase in numbers progressively until death. Parallel with the increase in the number of trypanosomes there is a progressive decrease in the number of red cells. The significant features of the infection are: (1) An increase of the trypanosomes to a constant number which seems to be characteristic of the species; (2) Anemia, which is variable, ranging between 30% and 50% of the original cell count; (3) Sudden death with symptoms of dyspnea within 10 to 36 hours after the trypanosomes have reached the maximum concentration. There are no toxic symptoms and the injection of large numbers of trypanosomes or a large amount of serum taken from an animal shortly before death do not produce any symptoms of intoxication.

This picture raised 2 problems: (1) The reason for the cessation of the multiplication of trypanosomes; was it due to an inhibiting substance or to exhaustion of the substrate? (2) The actual cause of death. If the cause of death could be ascertained in this simple type of infection, the findings might throw light on the pathology