

killed pneumococci, when orally administered, were valueless as an immunizing agent and that the living germ was only slightly better. Eguchi finds that *young* mice can be immunized using dead pneumococci.

2958

The histology of local streptococcus immunity.

F. P. GAY and R. W. LINTON.

[*From the Department of Bacteriology, College of Physicians and Surgeons, Columbia University, New York City.*]

The two most significant results of our studies over several years on localized streptococcus infections in the rabbit would seem to be, first: That, under properly controlled conditions, local infection is followed by a local form of immunity;^{1, 2} and second, that local protection in the pleural cavity, whether in a form of increased resistance (broth) or of specific active or passive immunity, is associated with an increase in the number of clasmatocytes or tissue macrophages there present.^{2, 3} A third study would associate clasmatocytes with the formation of antibodies.⁴

Repeated attempts to simulate conditions in the body by the action of clasmatocyte exudates outside the body have been confusing. The transfer of the entire pleural exudate of a clasmatocyte type, from a broth-protected to a normal animal, transfers no protection. Exudates of both polymorphonuclear and clasmatocyte type do not in their entirety destroy even a minimal number of streptococci in the test tube, although it may be shown that the supernatant fluids of both exudates are bactericidal, and furthermore, that the acid cell extracts of both types of cell will destroy streptococcus. (Unpublished observations.) But these extracorporeal phenomena do not account for the occurrences in the animal body, since they are much slower in effect, and, since the polymorphonuclear exudate yields more highly bactericidal

¹ Gay and Rhodes, *J. Infect. Dis.*, 1922, **xxxi**, 101-115.

² Gay and Morrison, *J. Infect. Dis.*, 1923, **xxiii**, 338-367.

³ Gay and Clark, *J. Infect. Dis.*, 1925, **xxxvi**, 233.

⁴ Gay and Clark, *J. Am. Med. Assn.*, 1924, **lxxxiii**, 1296.

substances (owing to the greater number of cells present) than does the clasmatoocyte exudate. The former, however, as it occurs in the body, is associated with no protection of the animal.

When either stock or passage cultures of our streptococcus are injected into the protected pleural cavity of a rabbit, they disappear with great rapidity, and, under proper conditions the cavity is sterile within three hours. This disappearance is judged, not only by a diminished number in cultures but by actual decreased numbers of organisms in smears, when large numbers are used. Drainage from the pleural cavities either of dyestuffs, inert particles, or bacteria, is through the parietal pleura and diaphragm.^{5,6}

We now find that the various degrees of protection, increased resistance and active immunity, are associated with remarkably pronounced changes in the pleura, both visceral as well as in the parietal pleura and diaphragm, but in the latter localities are more marked. The normal parietal pleura of the rabbit measures on the average 27 micra in thickness. Following injection of aleuronat (polymorphonuclear exudate), this thickness is doubled, owing to the infiltration of large numbers of polymorphonuclear cells. Here no protection is evident. Three days after the injection of aleuronat or of broth, the pleura is still further thickened, average 155 micra (x5); the polymorphonuclear cells are replaced by mononuclears, and protection is evident. These mononuclears by vital staining are shown to include a relatively large number of clasmatoocytes as well as fibroblasts. Repeated injections of streptococcus, either in the broth prepared cavity or beginning with a stock culture, still further increases the pleura thickness, so that in one instance it reached over 1100 micra (x40). It presents all the appearances of granulation tissue.

So far as we have gone the degree of protection is paralleled by the increasing thickness of the pleura and increased number of clasmatoocytes. Active phagocytosis of the streptococcus is confined in such tissue to the clasmatoocytes lying under a relatively intact layer of serosal cells, which seems to explain best the mechanism of disposal of microorganisms in this form of localized immunity. We do not for a moment assume that protection even of this local type is entirely accounted for by a mere quantitative increase of the number of cells. There is probably a

⁵ Gay and Rhodes. *J. Infect. Dis.*, 1921, xxix, 217.

⁶ Karsner and Swanbeck, *J. Med. Res.*, July-Sept., 1920, xlii, 91.

specific factor, such as the local formation of antibodies or local mobilization of antibodies which cooperates in the process. This question and many others are being investigated in pursuit of the observations already stated, which we believe offer a most promising and concrete introduction to an histology of immunity.

2959

Active and passive protein sensitization in utero.

BRET RATNER, HOLMES C. JACKSON and HELEN LEE GRUEHL.*

[From the Department of Physiology, University and Bellevue Hospital Medical College, New York University, New York City.]

It seemed probable to one of us that protein sensitivity in certain cases of early infancy might have some relationship to prenatal conditions.

Time does not permit our going into a detailed discussion of our hypothesis, nor can we enter into the clinical considerations, nor historical background for our work. We would merely like to present certain investigations on guinea pigs, which may have a bearing on this problem.

There has been a small but clearly defined amount of work by Rosenau and Anderson,¹ Anderson,² Gay and Southard,³ Wells,⁴ and others, on the passive transfer of antibodies from mother to offspring.

In the study of 29 guinea pig families, in which the mothers had been injected with normal horse serum long before conception, we induced acute anaphylactic death in the offspring born of these mothers, by an injection of normal horse serum within the first twenty-four hours to a few days after birth, thus corroborating the work of others.

* This work is being carried on under "The Crane Fund for the Study of Anaphylaxis."

¹ Rosenau, M. J., and Anderson, J. F., *Hyg. Lab. Bull.*, 1906, xxix, 73.

² Anderson, J. F., *J. Med. Res.*, 1906, x, 259.

³ Gay, F. P., and Southard, E. E., *J. Med. Res.*, 1907, xi, 143.

⁴ Wells, H. G., *J. Inf. Dis.*, 1911, ix, ii, 147.