which opened and discharged pus. This purulent drainage continued for over a year. In none of the cases did bronchial fistulae develop. The persistent infection was accompanied by coughing and, at first, by loss of weight and anorexia. Cultures taken from time to time showed many types of bacteria, with a predominance of hemolytic streptococci. X-ray examinations showed a shadow corresponding to the extent of the disease, which was about the size of the gauze ring. At autopsy heavily infected cavities were found surrounding the gauze ring and the gauze placed in the center of the ring. The diameters of the cavities were from 3 to 4 cm. The parietal and visceral pleurae forming their walls were from 2 to 5 mm. in thickness. The parenchyma of the underlying lung was not involved in the infectious process, nor were there any evidences elsewhere of the extension of the disease.

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Summary. The criteria for the existence of chronic empyema in dogs should be (1) that an infection, localized in the pleural cavity, should discharge pus for at least one year, which represents about one-seventh of the life cycle of the average dog; (2) that the infection should not heal spontaneously; and (3) that the infection should be associated with systemic symptoms. These conditions have been fulfilled by following the procedure outlined in the text.

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Histological Study of Skin Reactions in Anaphylactic and Tuberculin Type of Hypersensitiveness.

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It has been stated that the local inflammatory reaction in hypersensitive animals, at the site of antigen injection, has no morphological characteristics and especially that there are no morphological differences between the local reaction due to anaphylaxis and to tuberculin sensitiveness.[1] We noticed, however, that slight reactions, especially during the first hours after the injection of antigen, show marked morphological differences in the 2 types of hypersensitiveness. It is reasonable to expect that under the conditions men-

[1] Opie, E. L., *J. Immunol.*, 1929, **17**, 329.

tioned the differences are more pronounced than in strong reactions or in later stages of the reactions when the consequences of tissue injury and reparatory processes obscure the original reaction.

We studied the microscopic structure of skin reactions in more than 40 guinea pigs and examined about 180 skin reactions. We compared the different types of skin reactions in the same animal whenever possible. Reactions were examined, 1, 2, 6, 24, and 48 hours after the injection, and different antigens were used, as egg white, crystalline egg albumin, tubercle bacilli and a tuberculin preparation, obtained from the synthetic culture medium (Long) after concentration with ammonium sulphate and elimination of the substances precipitable by acids. For the study of the anaphylactic type of skin sensitiveness we used actively and passively sensitized guinea pigs, both normal and tuberculous. It was necessary to examine tuberculous guinea pigs, as the infection itself exerts under certain conditions an influence on the cellular reaction in the inflammatory processes. We examined tuberculin type of reactions, both with tuberculin and egg white.

The results of these investigations were uniform. Our observations concerning the skin reactions of anaphylactic type, which appears as a quickly developing and transient wheal, correspond to the detailed description given by Gerlach.[2] The development of edema and of the vascular reaction is followed soon by a more or less intense accumulation of leucocytes which in the stronger reactions is well developed one to 2 hours after injection and often is very intense. A slight, in tuberculous animals somewhat more intense, accumulation of mononuclear cells usually follows after the subsidence of the macroscopic reaction. In guinea pigs, we observe necrosis in anaphylactic type of reactions only rarely, even in the cases when a central hemorrhage develops.

In the tuberculin reaction, the sequence in which the different macroscopic and microscopic manifestations of the reaction develop, differs considerably from the above given description. In the slight reactions, often before any macroscopical sign of the reactions is apparent (2 to 6 hours after the injection) we find a strong accumulation of mononuclear cells around the blood vessels. This is the first symptom of the developing reaction, which precedes the symptoms from the side of the circulatory system. After 24 hours, even in very slight reactions consisting of a trace of redness and swelling, we find a strong infiltration with mononuclear cells in the whole area of reaction. Besides these cells in the central area of the reaction we

[2] Gerlach, W., *Virchow's Arch. Path. Anat.*, 1923, **247**, 294.

find more or less polymorphonuclear leucocytes. In the slight reactions, their numbr is small. In the stronger reactions the infiltration with polymorphonuclear leucocytes is intense but, in marked contrast to the reactions of anaphylactic type, it is associated with a strong infiltration with mononuclear cell forms. In reactions where a central necrosis develops, the early stages of the reaction correspond to the above given description. Later, the necrotic area is surrounded by a strong leucocytic infiltration, consequent to the tissue injury. If we produce a skin reaction with tubercle bacilli in the first few hours a strong infiltration with polymorphonuclear leucocytes develops around the bacteria. Adjoining this area we find the infiltration with mononuclear cells characteristic to the tuberculin reaction.

Tuberculous guinea pigs react sometimes to non-specific local irritations by accumulation of mononuclear cells. We observed slight but pronounced reactions of this type after injection of normal saline in the skin. This influence of the infection on the cellular response does not obscure the characteristic differences between the anaphylactic and tuberculin type of reactions, except in very slight reactions of anaphylactic type in which the cellular reaction (consisting of polymorphonuclear leucocytes) is very slight, both in tuberculous and normal guinea pigs.

The anaphylactic type of reaction is characterized besides the symptoms from the side of the circulatory system, which first develop, by accumulation of polymorphonuclear leucocytes. Mononuclear cells take part only later and in slight amount in the reaction. In the tuberculin reaction, the first and, in slight reactions, the predominant symptom is a strong infiltration with mononuclear cells. The symptoms from the side of the circulatory system and the infiltration with leucocytes follow in time the former mentioned reaction, and in the strong reactions it is apparent that they are consecutive to tissue injury. The differences between the 2 types of reactions are certainly not only of quantitative nature, but indicate differences in the intimate mechanism by which the symptoms of the reactions are produced.