

between toxin and antitoxin and not to a combination of other antigens and antibodies. (2) Tetanus toxin adsorbed to collodion particles can be neutralized by high dilutions of antitoxin.

5160

The Experimental Production of Chronic Empyema in Dogs.

W. M. FIROR. (Introduced by Ferdinand C. Lee.)

From the Department of Surgery of the Johns Hopkins Medical School.

In 1929 we became interested in a new treatment for chronic empyema. The procedure, however, was such a radical departure from the accepted ones that it seemed desirable to test its value on experimental animals, rather than on human beings. Chronic empyema virtually never occurs spontaneously in dogs. We found a paucity of literature on this subject; namely, that chronic empyema in dogs is difficult to produce.

We first opened the pleural cavity and injected into it 2 or 3 cc. of fluid abundantly infected with a variety of organisms. To secure the persistence of this infection a bit of gauze was placed in the cavity before expanding the lungs and closing the wound. These animals all died within 48 hours. At necropsy both pleural cavities were found to be heavily infected. In some there was an accumulation of hemorrhagic, purulent fluid which partially compressed both lungs; in others there was a small amount of thick pus covering all the pleural surfaces. A similar result was obtained when cultures of a single pathogenic organism were used in place of those with several types of organisms. It seemed apparent, then, that a possible explanation of the non-occurrence of chronic empyema in dogs is found in the inability of this species to localize acute pyogenic infections within the pleural cavity. The mediastinum in these animals is a thin, filmy structure, and organisms pass with ease and rapidity from one pleural cavity to the other. The pericardial sac is totally different in this respect; in all of our animals this tissue resisted the penetration of the infecting organisms. Another possible explanation for the failure of empyema to occur spontaneously in dogs lies in the fact that these animals seldom have lobar pneumonia.

The next experiments were devised with the idea of securing adhesions between the visceral and parietal pleurae previous to the

implantation of infected material. It was thought that by this procedure one might prevent the dissemination of the infection. A ring of sterile gauze, measuring about 10 cm. in diameter and 1 cm. in width, was spread over the surface of a lung, held in place simply by keeping the lungs expanded during the closure of the thoracotomy wound. In a small percentage of the cases the gauze did not maintain its position, but usually within a week firm adhesions formed around the ring and between the visceral and parietal pleurae. After a month the gauze was not only completely covered with fibrous tissue, but was thoroughly incorporated in it. On a few occasions sterile gauze that had been saturated with bismuth subnitrate was used, with the idea that the tissue reaction might be more intense and the ring would be more readily outlined on x-ray plates. However, the bismuth evoked an outpouring of fluid, which caused a bilateral hydrothorax with sufficient respiratory hindrance to cause death. After varying periods of time, usually 2 weeks, a small opening was made in the center of the thoracotomy wound. By this time the adhesions surrounding the sterile gauze ring prevented collapse of the lung and formed a well walled-off intrapleural pocket, in which cultures of virulent pneumococci were placed. These animals were watched with great care, and at no time were there any evidences of the bacteria having gained a foothold. When, however, a bit of unabsorbable foreign body was added to the bacterial culture, various types of infection resulted. In some cases an abscess would form, which would rupture spontaneously through the scar of the incision, drain for several days, and then heal. In others the infection would become walled off and apparently remain dormant for weeks, without ever communicating with either a bronchus or the outside. In still others the bacteria would spread by way of the interlobar fissure and cause an extensive bilateral pyothorax with death.

None of these results seemed to simulate empyema accurately. Accordingly, a group of animals were prepared in whom sterile gauze rings were carefully placed over the convex surface of the left lung, and in addition strips of gauze were inserted between the lobes. Three to 4 weeks later 3 cc. of a pure culture of pneumococci (Types I and III) were poured into the center of each of these artificially formed pleural pockets. Two days later the wounds were again opened and bits of gauze contaminated with a variety of organisms were placed in the same pockets. The wounds were closed with 2 or 3 deep sutures of braided silk, and with interrupted silk sutures in the skin. Within a few days these wounds formed subcutaneous abscesses

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.

I wish to thank Dr. William M. Millar and Dr. Julian Chisholm for their assistance in the performance of these experiments.

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.

5161

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

L. DIENES.

From the von Ruck Research Laboratory for Tuberculosis, Asheville, N. C.

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.