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Failure of an Acute Inflammatory Process to Extend into Area Previously Injected with India Ink.

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The observations of Menkin[1] and of Burrows[2] on the failure of the diffusion of trypan blue into areas of inflammation when the dye is injected intradermally near the inflamed site, are interpreted upon the basis of thrombotic occlusions in the lymphatics and on the interference produced by a fibrinous exudate. It seemed of interest then, to study the mechanism of the spread of an acute inflammatory process into the site of a chronic inflammatory reaction. This has been made possible by the intradermal injection of India ink and at subsequent times, by the injection of pneumococci into the adjacent skin.

Preliminary intradermal injections of 0.4 cc of India ink in saline dilutions from 1:4 to 1:50 were made on the sides of white rabbits. Subsequently either .002 cc of Type I or 0.1 cc of Type III pneumococcus 18-hr. broth cultures were injected intradermally 1 to 2 cm above this site. These inoculations were made at intervals from 24 hours to 11 weeks after the ink was injected. Inflammation was also induced in other rabbits by the intradermal injection of 0.2 cc of oil of citronella. This oil produces a more marked induration and a more slowly spreading inflammation than that produced by the pneumococci. A description of the inflammation produced in the skin of rabbits by pneumococci has been given by Rhoads and Goodner.[3] The animals were killed at intervals and sections of the skin were made.

There is present after 24 hours slight hyperemia, edema and leucocytic infiltration in the area of skin injected with India ink. This reaction slowly subsides and after a month there is essentially no cellular reaction at the site of the ink injection. From the site of the inoculation of the pneumococci there develops diffuse edema and hyperemia and rapid spread of the infection downward. The direction of spread is influenced by the lymphatic drainage and by gravity. When the bacteria are injected 2 or 3 cm above the area of India ink the edema and hyperemia pass around but do not pass

[1] Menkin, V., *J. Exp. Med.*, 1931, **53**, 171.

[2] Burrows, H., *Localization of Disease*, Wm. Wood and Co., N. Y., 1932.

[3] Rhoads, C. P., and Goodner, K., *J. Exp. Med.*, 1931, **54**, 41.

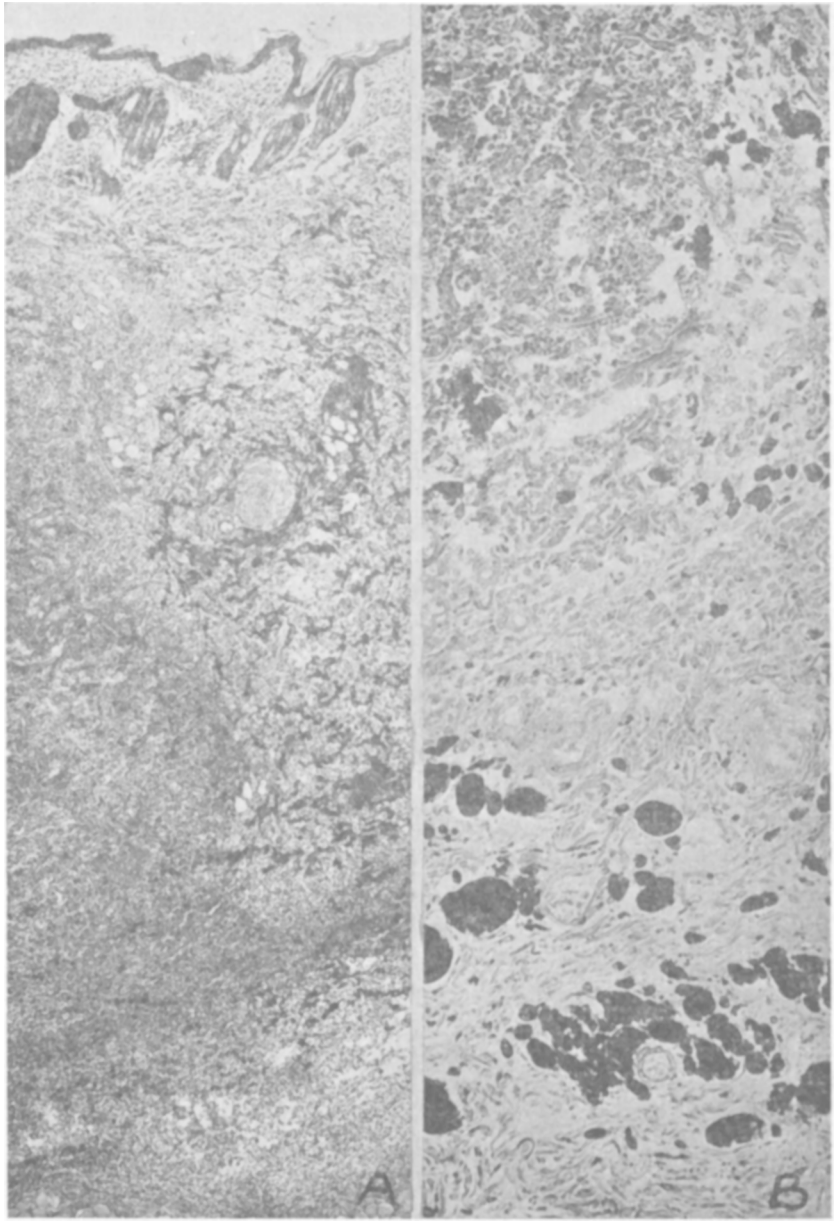

FIG. A.

0.5 cc of 1-4 dilution of India ink injected intradermally 24 hours preceding the intradermal injection of 0.1 cc pneumococci. The inflammatory process produced by the latter does not extend into the area occupied by the ink. H and E × 120.

FIG. B.

0.4 cc of 1-50 dilution of India ink injected intradermally 9 days before 0.002 cc of pneumococci were injected intradermally. There is a zone of tissue separating the inflammatory process produced by the bacteria from the carbon. H and E × 120.

through the pigmented area. (Fig. A.) When the pneumococci are injected 24 hours following the injection of India ink, the area is not so refractory as it is after a period of 11 weeks. At this time there is an area around the site of injection of the ink that is not invaded by leucocytes. (Fig. B.) Similarly the more slowly spreading inflammation induced by the oil injections also did not extend into the ink areas.

Immediately and for several days following the injection of the ink the carbon particles are dispersed throughout the tissue. There are collections of polymorphonuclear leucocytes around the periphery of the blood vessels in these pigmented areas but apparently these leucocytes are not able to wander through the tissue in such areas as readily as they do in the normal skin. There is an increase in the amount of connective tissue around these areas of carbon. A further study of these sections shows that the ink is located in the tissue spaces as well as in the lymphatics.

It is interesting to note that a mild, chronic reaction, such as that produced by the intradermal injection of sterile ink tends to prevent the inward diffusion of fluids, just as Menkin has observed the failure of trypan blue to diffuse into areas of acute inflammation.

If, however, the pneumococci are injected directly into the ink areas, then the inflammation spreads from these sites. This is probably due in part to the disruption caused by the pressure of the subsequent injection.

It is evident from these experiments that skin injected with India ink does not permit the infiltration of bacteria, edema fluid, and leucocytes from an advancing inflammation. The degree of limitation of the spread of the inflammation progresses with the period of time that elapses between the injections of the India ink and the irritant. This process appears to be influenced by scarring, by the plugging of the lymphatics with carbon particles and also by the accumulation of carbon in the tissue spaces. Similar results were obtained when trypan blue in dilutions from 1:50 to 1:500 was substituted for India ink. The change in the consistence of the tissue seems also to contribute to the difficulty of the extension of the bacteria, the infiltration of the tissues by edema fluid and the migration of polymorphonuclear leucocytes into the dye areas.