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An experimental study of the local tissue reactions in the guinea pig to the Bacillus proteus x 19 as affected by the simultaneous injection of carbon.*

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The relation of foreign bodies to the persistence of bacteria in tissues has been repeatedly observed from the clinical standpoint, but few studies of this relationship have been made. Organisms may remain active or latent in an area about a foreign body, or those which have invaded the circulation may localize there, initiating or reviving a suppurative process. The presence of such substances appears to protect organisms in their vicinity from the normal phagocytic activities of the body. The mechanism by which protection is afforded and the response of the organism to this protection, is the purpose of this study. This, in turn, offers a means by which to develop the "hypothesis of Welch", which emphasizes the importance of the changes undergone by bacteria in their conflict with the defensive powers of the host.

This investigation has no immediate relation to the question of the possible etiological importance of *Bacillus proteus* x 19 in typhus fever, but the organism was chosen because of the irregularity of its pathogenicity for guinea pigs, in the hope that conditions might be produced that would control this vagary and enable one to predict with certainty the outcome of a given experiment. The use of carbon was determined upon because of its recognized inert character and ready identification in the tissues. 1 cc. injection units of 10 per cent carbon suspension, bacteria from one-fourth of a 24 hour agar slant suspended in distilled water, or a mixture of the two, each of double strength, were in-

troduced into the loose fascia of the back. The interaction of these two kinds of foreign bodies in the subcutaneous tissues of the guinea pig is outlined in the following summary.

1. Guinea pigs injected subcutaneously with a suspension of carbon show very slight general response and an extremely chronic local tissue reaction, with slow fibrosis of the injection site. Blockade of the lymphatics occurred early; and phagocytosis was moderate in amount, and associated with very little tissue destruction.

2. The injection of suspensions of *B. proteus* x 19 produced little or no reaction, with rapid widespread diffusion of the organisms, invasion of the blood stream and death from septicemia in about 35 per cent of the animals. If the infection were fatal, death took place within 24 hours; those animals surviving that length of time invariably recovered. Organisms were cultivated from the blood stream for two days and from the tissues for four days after injection, the blood thus becoming free from bacteria in a much shorter time. Histologically the bacilli were found in the tissues for at least 10 days, or 6 days after they could be recovered by cultural methods. Some of these organisms were free in the tissue spaces while others were intracellular. The majority of the bacteria were well preserved and displayed no evidence of disintegration. Their presence did not determine a progressively increasing leucocytosis, either locally or generally, during the period of their persistence.

3. Animals injected with carbon and proteus simultaneously, exhibited a local reaction similar to that observed in the carbon-injected animals, and a general reaction more like those receiving the proteus alone. The febrile reaction was a little less marked but persisted longer, and the loss in weight was more slowly made up. The initial death rate was 27.4 per cent, somewhat less than in animals receiving proteus alone, but the cause of death was the same in every case. The presence of the carbon seemed to protect a certain per cent of the animals from an otherwise fatal infection. The local reaction was in some instances more or less definitely inflammatory in character, and the size of the indurated area increased rather than decreased, as it had done in the carbon controls. In some cases the lesion softened and discharged its contents, in the pus from which a pure culture of *B. proteus* was found. Living organisms were thus recovered as long as 40 days after injection.

4. Carbon appears to exert a mild aggressin-like action upon the subcutaneous tissues, making it possible for these bacteria to maintain their existence and multiply locally in spite of the defensive mechanism of the animal body.

5. The serum of the carbon-plus-proteus animals agglutinated the organisms up to a dilution of 1-100, the same as did that from animals receiving the proteus alone, indicating that the presence of the carbon did not modify the agglutinative power of the serum.

6. The method developed has reduced the initial mortality of animals, after injection of *B. proteus* x 19, and has enabled the organisms to resist the bactericidal powers of the body for relatively long periods of time.

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The action of ephedrine, an alkaloid from Ma Huang.

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Ma Huang, identified as *Ephedra vulgaris* var. *helvetica,* has been known to Chinese medicine since about 3100 B. C., when it was one of the herbs tested and approved by Emperor Shen Nung. According to the Pen Tsao Kang Mu (the Chinese Dispensatory, 1596) it improves circulation, causes sweating, stops cough, reduces fever, etc.

Nagai[1] obtained from the plant an alkaloid which he named ephedrine, and which he[2] found to possess a mydriatic effect. Amatsu and Kubota[3] described a rise in blood pressure and relaxation of the intestines after ephedrine. Merck[4] isolated from the European variety of *E. vulgaris* an alkaloid named pseudoephedrine isomeric with ephedrine.

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[1] Nagai, *Pharm. Z.,* 1887, xxxii, 700.

[2] Nagai, *Chem. Z.,* 1888, 755.

[3] Amatsu, H., and Kubota, S., *Kyoto, Igaku, Zosshi,* 1917, xiv, 77, through *Chem. Abs.,* 1918, xii, 2019.

[4] *Merck's Ber.,* 1893, 13.