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Effect of Products of Typhoid Bacilli upon the Tuberculin Reaction.

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In a study of the effect of bacterial products upon tuberculous animals, a filtrate* of a culture of typhoid bacilli, potent in material producing the *Shwartzman phenomenon,* was injected intravascularly into tuberculous guinea pigs which had previously received intracutaneous injections of bovine tuberculin.

Tuberculous guinea pigs were injected with 1-45 to 1-500 dilutions of bovine tuberculin. One or 2 days later 0.5 to 1 cc. of typhoid filtrate was introduced into the blood stream. At the time of the injection of typhoid filtrate, the skin at the sites of the tuberculin reactions was pink or bright red and edematous. One hour afterwards these areas became dull red. About 2-3 hours later a violet or purplish discoloration appeared, and within one day the skin had become obviously necrotic. The extent of necrosis was proportional to the severity of the tuberculin reaction, this relationship being clearly seen in guinea pigs simultaneously injected with a series of 3 different dilutions of tuberculin.

The following is the description of a typical experiment. A guinea pig weighing 450 gm., which had been infected 7 weeks previously, was injected intracutaneously with 0.1 cc. of 1:45 and 1:135 dilutions of old tuberculin. Two days later the reactions at the site of the injections were as follows:

I (1:45) Light redness and edema 10x10 mm. raised 2 mm. II (1:135) Pink discoloration and edema 5x4 mm. raised 1 mm. Immediately after the reading of the skin test 1 cc. of typhoid filtrate was injected intracardially. One hour after the injection the discoloration was dull red and 3 hours later the skin reactions were: I (1:45) Mottled dark purple area 7x7 mm., edema 10x10 mm., raised 2 mm. II (1:135) Dark purple area 4x3 mm., edema 5x4 mm., raised 1 mm. A few dark purple spots about 1x1 mm. were seen around both skin tests. One day later the purple areas described above appeared to be necrotic.

Purple discoloration was not observed in the control guinea pigs which had been infected and tested with tuberculin but had received no typhoid filtrate.

* Received through the courtesy of Dr. Gregory Shwartzman.

In normal guinea pigs, the areas of skin injected with old tuberculin were not affected by a subsequent intravascular injection of a typhoid filtrate. Hence it is probable that the specific inflammation produced by tuberculin in the hypersensitive tissue, rather than products of the tubercle bacillus *per se,* prepared the skin for the action of the typhoid filtrate introduced into the blood stream.

Conclusion. The intravascular injection of a filtrate from the culture of typhoid bacilli produces hemorrhagic necrosis in tuberculous guinea pigs at the site of positive tuberculin reactions.

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Independent Variation of Biological Characters of Bacteria as a Result of Dissociation.

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Numerous observations on bacterial dissociation indicate that the changes occurring as a result of dissociation may involve many of the cultural characteristics. Although alterations in colonial morphology are the most obvious, many other characteristics may also undergo modification. De Kruif demonstrated changes in virulence[1] and acid agglutination optimum.[2] Profound serological alterations have been studied by Arkwright,[3] Schütze,[4] Savage and White,[5] Goyle.[6] The modifying effects of dissociation on many biochemical reactions, including fermentative capacities, have also been reported.[7] In a recent study of the fermentations of variants of *Salmonella schottmülleri,* Nungester and Jung[8] obtained R-variants which formed gas and others that did not; they observed that an S-culture may lose its capacity to form gas without change in colonial morphology. These observations, they concluded, were

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