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Phenomenon of Local Skin Reactivity to Culture Filtrates of Various Microorganisms.

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In previous communications a new phenomenon of local skin reactivity to *B. typhosus* culture filtrates in rabbits was described.[1] The local skin reactivity was induced by skin injections of the filtrate. If 24 hours later the filtrate was injected intravenously into the locally prepared rabbits there appeared extremely severe hemorrhagic necrosis at the site of previous skin injections 4 to 5 hours after the intravenous injection. There were observed certain features which considered together distinguished this phenomenon from the known manifestations of bacterial hypersusceptibility and the Arthus phenomenon. These features were: the local reactivity, the short incubation period necessary to induce the local reactivity, the short duration of the state of reactivity, the ability to induce local reactivity by a single skin injection, the severity of the reaction and the necessity to make the second injection of the toxic agent by the intravenous route.

The factors inducing the local skin reactivity were termed skin preparatory factors and those injected intravenously were called skin reaction factors.

The *B. typhosus* skin preparatory factors were specifically neutralized by immune anti-typhoid sera. Normal and non-related heterologous sera failed to neutralize these factors.

Further studies representing attempts to reproduce the described phenomenon with culture filtrates of microorganisms other than *B. typhosus* are reported here.

The mode of preparation of filtrates and the technique of the experiments were the same as described before.[1] The phenomenon could be reproduced with the culture filtrates of the following microorganisms: *B. coli, B. paratyphosus A, B. paratyphosus B, B. enteriditis, B. dysenteriae Y, Z, Mt. Desert, Shiga* and *Flexner, B. avicida, 5 strains of Streptococcus non-hemolyticus (gamma) isolated in this laboratory from blood cultures of acute rheumatic fever, one strain of Streptococcus viridans (alpha) isolated from a pelvic abscess, one strain of Streptococcus hemolyticus (beta) isolated from a case of mastoiditis, with Pneumococcus types I, II, and III, and*

[1] PROC. SOC. EXP. BIOL. AND MED., 1928, XXV, 560; *J. Exp. Med.*, 1928, xlviii, 267.

several strains of meningococcus. (The mode of preparation of the pneumococcus and meningococcus toxic substances was somewhat different.)*

The reactions were fully developed 4 to 5 hours after the intravenous injection. They were severely hemorrhagic and necrotic. A certain percentage of rabbits proved resistant to the phenomenon and this percentage seemed to vary with the microorganism employed.

There was no relation observed between the intensity of the erythema produced by the skin injection of the filtrate alone and the intensity of the local reaction which followed the intravenous injection of the filtrate into the same rabbits. Rabbits which showed an extensive erythema after the skin injections alone at times, remained resistant to phenomenon, and *vice versa,* rabbits in which the skin injections yielded no erythema whatsoever frequently developed locally severe hemorrhagic necrosis after the intravenous injection.

24 hour interval between the skin and the intravenous injections was sufficient for the uniform reproduction of the phenomenon with the culture filtrates of above enumerated microorganisms.

With the following microorganisms neutralization of the skin preparatory factors by homologous sera was obtained, namely: Pneumococcus types I, II and III, 3 strains of *Streptococcus non-hemolyticus* isolated from blood cultures of acute rheumatic fever patients, *Streptococcus viridans* isolated from a pelvic abscess, *B. paratyphosus A, B. paratyphosus B, B. Shiga, B. Flexner, B. dysenteriae Y, B. coli and meningococcus sera.*

Normal horse serum failed to neutralize the *B. coli, paratyphosus A, B. shiga, Streptococcus non-hemolyticus* isolated from a case of rheumatic fever (one strain), and *Streptococcus viridans* (one strain) skin preparatory factors.

Scarlet fever serum failed to neutralize the *paratyphosus A* and *B. coli* skin preparatory factors.

Studies on the effect of specific sera of other microorganisms as well as the effect of various batches of normal and heterologous sera are under way.

Work is also under progress to determine whether the described phenomenon could be advantageously applied to diagnostic, prognostic, preventive and therapeutic studies on diseases in which the above mentioned microorganisms play a pathogenic rôle and also to the studies on the etiology of certain diseases.

* This phenomenon of local skin reactivity to pneumococcus and meningococcus will receive special consideration in a future communication.