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Selective Susceptibility of the Epithelial Layer of Skin to Certain Bacterial Toxins.

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In connection with the histological study of skin reactions in hypersensitive animals, we studied microscopically the skin lesions produced by the injection of various substances both bacterial toxins and chemical irritants. We noticed an interesting characteristic of the lesions produced by staphylococcus and diphtheria toxins. The epithelial layer of the skin was destroyed early and extensively, out of proportion to the inflammatory reaction in corium, whereas, in the reactions of hypersensitive animals (excepting strong tuberculin types of reactions) and after injection of turpentine or pneumococcus emulsion, although the inflammatory reaction was strong, the epithelial layer was not apparently injured. The skin shows symptoms in several infectious diseases and in the hypersensitive state skin sensitiveness is usually marked. As the cause of this special susceptibility of the skin is not known, it seemed of interest to study a susceptibility which depends probably not on the reactions of mesenchymal but on the reaction of epithelial tissue. The early destruction of the epithelial layer has been known for a long time in lesions caused by the diphtheria bacillus and more recently Parker[1] observed necrosis of the epithelium in the case of staphylococcus toxin.

We examined the histological structure of skin reactions produced by staphylococcus and diphtheria toxins in 7 guinea pigs and 8 rabbits. In every animal several reactions were studied in different stages of development. The staphylococcus toxin, obtained according to the method of Burnet,[2] was quite potent as 0.001 cc. caused necrotic skin reactions in rabbits. After injecting 0.05 cc. of this toxin into the skin of a guinea pig, in a few hours a quite extensive slight swelling developed with moderate hyperaemia. The next day the swelling and hyperaemia decreased. The skin covering the bleb formed by the injection became after a few hours pale with a slight violet hue. Necrosis was obvious to the naked eye in the course of the following days, though in sections made only 3

[1] Parker, J., *J. Exp. Med.*, 1924, **40**, 761.

[2] Burnet, F. M., *J. Path. a. Bact.*, 1930, 331.

hours after the injections, microscopic examination of the epithelium, corresponding to the discolored central area, already showed marked changes. The cytoplasm stained pink with the usual hemotoxylin and eosin stain and the nuclei were shrunken, pyknotic and often surrounded by vacuoles. We found at this stage a moderate edema and infiltration with white cells (mostly polymorphonuclear) in the deeper layers of the skin extending much farther than the area of necrotic epidermis. Six hours after the injection, there was no change in the sections. After 24 hours, the epithelial cells showed marked degeneration and in many places showed infiltration with polymorphonuclear leukocytes. A new layer of epithelium was growing in from both edges below the old necrotic layer. In the upper layers of the corium, adjoining the necrotic epithelium, there were several foci of dense infiltration with polymorphonuclear leukocytes. The epithelial cells of the hair follicles had either disappeared or their nuclei had become pyknotic and the cytoplasm acidophilic. Compared with the 6 hour period, the edema and infiltration of the skin outside of the area of the epithelial necrosis had decreased.

The reactions with diphtheria toxin developed more slowly and the necrosis of the skin was grossly visible only after 48 hours and increased in size in the following days. This destruction was visible microscopically in 24 hours and during the following days strong infiltration with leukocytes developed below the necrotic epithelium. Even with small doses of the toxin, the inflammatory reaction in the corium was stronger than in the staphylococcus lesions. In the sections it was evident that the area of necrosis of the epithelium extended far beyond the zone of marked reaction in the corium.

Our findings in rabbits were essentially the same as in the guinea pigs. The thinness of the epithelium, however, made it more difficult to observe the first alterations.

We call attention to the following characteristics of the histological observations, which are especially apparent in the staphylococcus reactions: The early development of the necrosis of the epithelium, the larger extent of the area of this necrosis than that of the strong reaction in the corium, and the development of marked infiltration with white cells consecutive to the necrosis of the epithelium. These characteristics of the histological picture strongly suggest that the properties of these skin reactions depend largely on the injury to the epithelium and the cause of the special susceptibility of the skin is probably the susceptibility of the epithelial layer.