

5. Protein osmotic pressure. Eczema: 32.2; 28.0; 35.9 (mm. Hg.). Controls: 29.0; 25.3; 32.8.

6. Cholesterol. Eczema: 195.7; 187; 139 (mgm. %). Controls: 173.1; 132; 194.

The more striking differences observed were: (1) Marked elevation of the serum albumin, albumin-globulin ratio, and protein osmotic (oncotic) pressure in the serum of the eczema group; (2) Marked elevation of the serum cholesterol in the eczema group, 40% of which showed figures in excess of 200 mg. %; (3) Slight, possibly not significant, lowering of the serum globulin in the eczema group; (4) Moderate elevation of the total protein in the eczema group, due mainly to the high albumin fraction; (5) No difference between the 2 groups in respect to lipoid phosphorus.

The exact significance of the differences noted is not clear. All the children were receiving milk in considerable quantities. In a few instances, precipitin tests for bovine lactalbumin were made on the sera and positive results obtained but these occurred in the controls as well as in the patients with eczema. Even assuming that the increase in serum albumin was wholly due to absorption of undigested lactalbumin—an assumption that is not supported by convincing proof—this might be the result either of increased absorption or from failure to dispose of a normal amount of absorbed protein at a normal rate.

In any case, it may be pointed out that a definite increase, such as has been observed here, in the albumin fraction of human serum is an unusual phenomenon.

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### Experimental Granulopenia.

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The etiology of so-called "agranulocytosis"<sup>1</sup> has not been explained. Kracke<sup>2</sup> has recently produced the disease in rabbits by repeated small injections of benzene, but there is little evidence that such a substance is responsible for the syndrome in man. However,

<sup>1</sup> Schultz, *Deutsche med. Wochenschr.*, 1922, **48**, 1495.

<sup>2</sup> Kracke, *Am. J. Clin. Path.*, 1932, **2**, 11.

certain of the pyogenic bacteria are capable of producing *leucocidin* which is specific and highly lethal for granulocytes. One or more of these organisms is almost constantly associated with focal infections, which in turn are commonly accompanied by leucopenia.<sup>3</sup> A history of focal infection can be elicited from most of the reported cases of agranulocytosis, and their possibility cannot be excluded from the remainder.

Virulent cultures of *Staphylococcus aureus*, *Streptococcus hemolyticus*, *Streptococcus viridans*, and a species *Proteus*, the latter being isolated from the blood and organs of a fatal case of granulopenia, were each sealed into parchment capsules of 5 cc. capacity,<sup>4</sup> and the capsules were placed aseptically in the abdominal cavity of rabbits. Total and differential leucocyte counts were made twice daily both before and after operation. The experiment was controlled by counts on the blood of rabbits which received capsules of sterile broth. The behaviour of the neutrophils is shown by morning

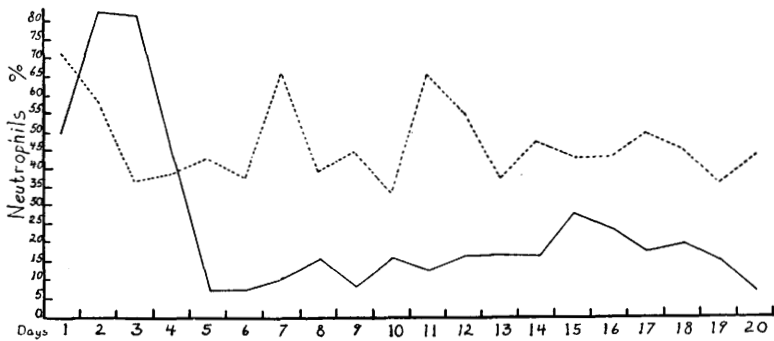


FIG. 1.  
Neutropenia produced by *Staphylococcus aureus*.

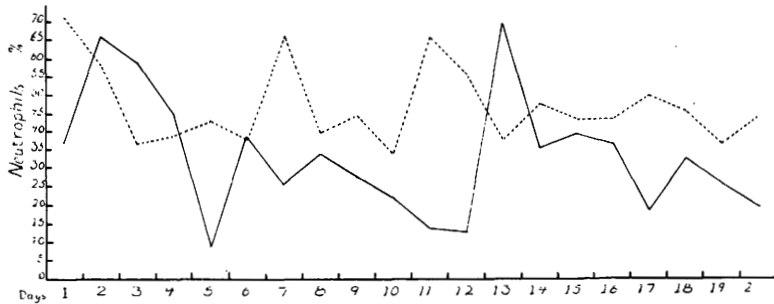


FIG. 2.  
The effect of *Streptococcus hemolyticus* on the neutrophils.

<sup>3</sup> Appleton, *Bacterial Infection* (Lea and Febiger, Philadelphia), 1925, 113.

<sup>4</sup> Dennis, *Science*, in press.

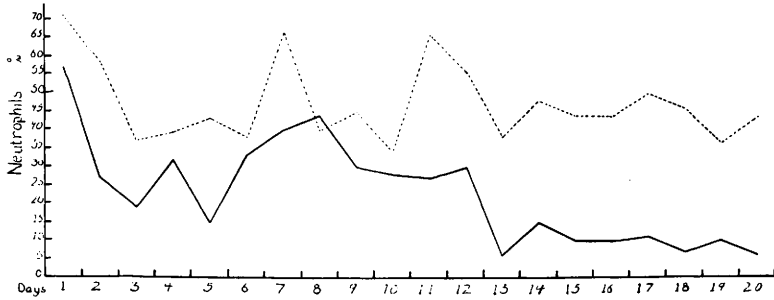


FIG. 3.

Neutropenia produced by *Proteus syriensis* isolated from a case of agranulocytosis.

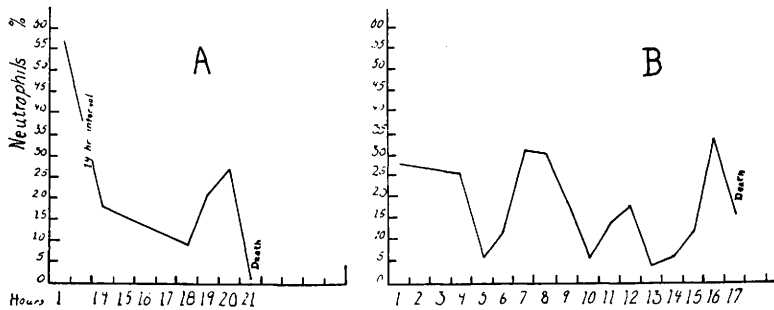


FIG. 4.

Acute leucopenia produced in two rabbits (A and B) by means of *Streptococcus viridans*.

blood counts represented in the accompanying charts, the dotted lines representing the control animals and the solid lines the experimental animals. It is of particular interest that the *S. viridans* was essentially avirulent when injected directly into an animal, yet the results were startling when the above method was used. Both rabbits receiving *S. viridans* had a terminal pneumococcal septicemia.

**Conclusions.** Under conditions simulating a chronic focal infection, *S. aureus*, *S. hemolyticus*, and *Proteus sp.* are capable of inducing a marked neutropenia which has been sustained for 5 months in animals implanted with *Staphylococcus* and *Proteus*. By this method *S. viridans* exhibits a virulence that is not manifested by direct inoculation. It shows a greater toxicity for the bone marrow and the entire leucopoietic system, and the picture produced in rabbits is the same as that of acute "agranulocytosis" in man. The pathogenic factor is a diffusible toxic substance, the specificity of which indicates that it is leucocidin.