toneum against peritonitis. These experiments add to our previously expressed contention[5] that the protective process is not specific in nature. The serum and the peritoneal exudate of the protected animals with peritonitis did not contain humoral antibodies to account for their survival.

The principle of peritoneal protection used in the above experiments was applied to man, prior to abdominal operations requiring resection of bowel. The protecting material consists at present of 50 cc. of physiological salt solution in which are suspended 4 billion colon bacilli (culture 300) and is given in 4 successive daily injections of 5 cc., 10 cc., 15 cc., and 20 cc., respectively.

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Effect of Hyperleukocytosis (Hyperleukocytic Pre-Immunity) on Infection.*

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In the previous article[1] it was demonstrated that a single intraperitoneal injection of heat killed *B. coli* may prevent the death of a dog from an otherwise lethal *B. coli* peritoneal infection. The peritonitis was produced the day after the protecting injection. Four successive injections on successive days resulted in the survival of 65% of the animals. No humoral antibodies were found to account for this protection. In order to determine the rôle played by the cellular antibodies, cell counts of the peripheral blood and of the peritoneal exudate and peritoneal bacterial counts were made hourly during the course of a peritoneal infection in normal and protected dogs. Throughout these experiments, peritonitis was produced by the intraperitoneal introduction of 3 billion living *B. coli* suspended in 40 cc. of a 2½% gum tragacanth.

The peripheral leukocytes of normal dogs dropped rapidly and seldom exceeded the count prior to onset of infection. The leukocytes in the peritoneal exudate were polymorphonuclears and were

[5] Steinberg, B., and Snyder, D., *Arch. Path.*, 1929, **8**, 419.

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[1] Preceding article.

seldom more than 50,000 per cu. mm. The bacteria in the peritoneal exudate were always present in large numbers both free and phagocytosed.

The protected dogs that survived had consistently higher peripheral blood leukocyte counts than the normal animals and the leukocytes rapidly exceeded the count prior to infection. The leukocytes of the peritoneal exudate prior to onset of infection were present in large numbers (232,000 to 546,000 per cu. mm.) and were predominantly polymorphonuclears. After the onset of peritonitis, the number of peritoneal leukocytes dropped considerably and consistently while the total leukocyte counts were higher than in the normal dogs. The bacteria in the peritoneal exudate disappeared rapidly so that in 4 to 5 hours the counts were in thousands instead of many millions as in the normal dogs. The method of bacterial counts employed disclosed the presence of viable organisms whether free or phagocytosed.

The leukocyte counts of the peritoneal exudate of protected dogs that died were consistently lower than those of surviving protected animals but higher than those of normal controls. The cellular response was apparently insufficient to cope with the infection. The bacterial counts, however, in the protected animals that survived or died did not vary. It is assumed that this protective process consists of 2 phases. The first phase comprises the rapid phagocytosis of the bacteria by polymorphonuclears already present at the site of infection. The successful accomplishment of this phagocytosis is the clearing of the first hurdle. The second phase (which is being further investigated) is assumed to transpire at the sites to which the bacteria are transported. The ebb and rise of the peripheral and peritoneal leukocytes probably correspond to migrations of bacteria-laden phagocytes and replacement by new cells.

It is apparent from these experiments that protected dogs respond with a definite peripheral blood leukocytosis upon reinjection of similar living bacteria. The protection may consist of as little as a single injection and the infection may be induced as early as on the following day. The protecting bacterial injection evokes *in situ* a large number of polymorphonuclears. The animal survives largely because of the incidental presence of the polymorphonuclears which phagocytose the living bacteria. The animal is also able to supply rapidly large numbers of new leukocytes to replace those that had been destroyed or that had migrated. This protective process can not be considered either a local or an active immunity in the accepted interpretation of these terms. The animals develop a true

active immunity of a varying degree a number of days following the protecting injections. Because of these factors, the term hyperleukocytic preimmunity is suggested for this process. The question of the specificity of this process will be dealt with in a later article.

Gay and Claypole[2] observed that typhoid immunized animals respond with a peripheral blood hyperleukocytosis upon an intravenous reinjection with living typhoid organisms. They found this hyperleukocytosis to be specific for the microorganism. A typhoid immunized animal did not respond with a hyperleukocytosis to an infection with *Micrococcus aureus*. Gay and Claypole[3] were dealing with a general cellular response in form of an active immunity, since the reinjection was intravenous and was made a sufficient number of days after the first protecting dose to evoke some degree of an active immunity. McWilliams,[4] however, was unable to confirm Gay and Claypole's work neither in regard to the specificity nor to the presence of a hyperleukocytosis. Zinsser and Tsen[5] found a slight leukocytosis in immunized animals but no specificity.

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Absorption of Antigens from Body Surfaces.

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The appearance of agglutinins in the blood 3 weeks after oral vaccination with typhoid antigen was followed in 85 non-febrile dispensary and ablatory patients. Most patients were from orthopedic surgical clinics. One gram of desiccated ox-bile in gelatin capsules was given with a glass of warm water upon rising in the morning. After 30 minutes the typhoid antigen was administered in a glass of warm water. In one series of 24 subjects, 1 cc. of standard typhoid vaccine (Lilly) was administered. In another series 2 cc. of bacteriophage dissolved *B. typhosus* was administered. The meal was withheld from the subjects for 2 hours after the typhoid

[2] Gay, F. P., and Claypole, E. J., *J. Am. Med. Assn.*, 1913, **60**, 1950.

[3] Gay, F. P., and Claypole, E. J., *Arch. Int. Med.*, 1914, **14**, 662.

[4] McWilliams, H. I., *J. Immun.*, 1916, **1**, 159.

[5] Zinsser, Hans, and Tsen, Edgar, *J. Immun.*, 1917, **2**, 247.