epidermis, marked increase in the depth of the papillae and abundant pigmentation in the deeper portions of the corium where many chromatophores have wandered into the deeper strata. The cutaneous lesions are identical with the microscopic picture of the skin in human pellagra.

These experiments would indicate that pellagra may be transmitted to the monkey (*Macacus rhesus*) by means of a Berkefeld filtrate derived from the tissue of the human subject; at least, the animals develop all the essential clinical signs and symptoms together with the pathologic picture discerned in the disease in man. Furthermore, they suggest that the etiology of pellagra is a filterable virus or a micro-organism capable of passing through the pores of certain Berkefeld filters. The details of this work and the further experiments which have been undertaken with a view of determining the nature of this filtrate and other phases of the problem will appear in a subsequent publication.

For many suggestions during the progress of this work I wish to extend thanks to Prof. C. W. Duval in whose laboratory the work was carried out.

SPECIFIC AND EXTREME HYPERLEUKOCYTOSIS FOLLOWING THE INJECTION OF BACILLUS TYPHOSUS IN IMMUNIZED RABBITS*

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In a previous note¹ dealing with induced variations in the agglutinability of the typhoid bacillus, we have indicated a method for testing the protection of animals that have been immunized by various preparations of the typhoid bacillus. This method consists in employing the typhoid-carrier state in rabbits, which, under proper conditions, may be produced regularly in control animals. This carrier state, which is usually followed by the death of the animal in from five to twenty days, does not occur in animals that have been properly immunized against the typhoid bacillus. In a further study of the mechanism by which the injected bacteria are disposed of in the immunized animal, an apparently unrecognized and significant phenomenon has been observed which further emphasizes the importance of polymorphonuclear leukocytes in disposing of bacteria.

The preeminent importance of leukocytes of the polymorphonuclear type in taking care of bacterial infections has been amply determined by the work of Metchnikoff and his followers. We know that these cells dispose of bacteria either through direct phagocytosis or indirectly following the action of tropic substances in serum on the bacteria. Further evidence that indicates the importance of leukocytes is their response to the injection of any foreign protein substance, particularly to bacteria, by an increase in number (hyperleukocytosis). So far as we are able to determine, no distinct evidence has been brought forward that hyperleukocytosis occurs to any greater extent in specifically immunized than in normal animals.

We find that the injection of living typhoid bacilli, grown on rabbit-blood medium, directly into the circulation of normal rabbits produces first a hypoleukocytosis, which may fall to from one-fourth to one-eighth of the original count, and which is followed by a hyperleukocytosis reaching its maximum in from sixteen to twenty-eight hours. The average maximum in five observations in which the maximum was almost certainly obtained is 46,000 leukocytes to the cubic millimeter (lowest count 34,000; highest count 56,000). This fluctuation is due entirely to variations in polymorphonuclear leukocytes, which disappear almost entirely from the peripheral circulation during the stage of hypoleukocytosis.

In typhoid-immunized animals the response is enormously increased over that obtained in normal animals. The hypoleukocytosis occurs somewhat earlier than in the normal animals (from about one and one-half to three hours), although it does not reach any remarkably lower grade. The count has returned to the normal usually in about six hours, whereas it does not return in the normal animal until about fourteen hours. The maximum in immunized animals, which is also reached earlier than in normal animals, was found to vary from 80,000 to 274,000, with an average in five cases of 138,000. Owing to the fact that observations were not taken at sufficiently frequent intervals, there is no certainty in many of these cases that the crest of the curve of hyperleukocytosis was actually obtained. The figures are, however, perfectly comparable with those obtained in normal animals and show on the average a leukocytosis that is three times as great. It is further to be noted that this response of leukocytes in typhoid-immunized animals is specific for the typhoid bacillus, as such animals are found to respond no better than normal animals to injections of the *Micrococcus aureus*.

It is evident, therefore, from this observation that the activity of polymorphonuclear leukocytes in immunized animals may be not only qualitatively but quantitatively increased. We are engaged in extending these observations to other types of immunity.

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EPIDEMIC OF TYPHOID DUE TO MILK

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Indiana Harbor, a city of 10,000 people, in Lake County, Indiana, in common with the other cities about the southern end of Lake Michigan, is accustomed to have a rather high death-rate from typhoid during August, September, October and November. During the month of October, 1912, however, the number of cases was unusually high.

November 8, 1912, we visited Indiana Harbor. Thirty-two cases of typhoid had been reported to the town health-officer. Of the patients twelve were men and twenty were women and children. The water-supply for Indiana Harbor is taken from the same source and pumped through the same mains as that for East Chicago. There was not an unusual number of cases of typhoid in East Chicago. This fact, along with the age

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¹ Gay, Frederick P., and Claypole, Edith J.: Induced Variations in the Agglutinability of *Bacillus Typhosus*, THE JOURNAL A. M. A., April 12, 1913, p. 1141.