etc. Three who had responded feebly to the vaccine showed no change. Twenty-four hours later the blood examination showed a marked decrease in titer in all subjects who had previously shown a rise. Subsequent conditioning stimuli again led to a rise.

In a third experiment, 16 subjects were given the same dosage of typhoid vaccine. The conditioning stimuli were not applied until 19 days after the administration of vaccine had been discontinued. Two of the subjects received no further injections and were utilized as controls. Eight subjects received conditioning stimuli alone; 3 received typhoid vaccine in a non-conditioned setting; and 3 received typhoid vaccine with conditioning.

The titers were read 3 times with a 6X magnifier by each of 3 observers, none of whom knew the classification of the subjects. The 2 control subjects showed no rise in titer. Six of the 8 subjects receiving conditioning stimuli alone gave a rise in titer of one tube, and 2 gave a rise in titer of a half tube. Two of the 3 subjects receiving vaccine in a non-conditioned setting showed a rise in titer of 1½ tubes, the third showing no rise. Two of the 3 subjects receiving vaccine with conditioning showed a rise of one-half tube, a third showed a rise of one tube.

Dr. Irving Lorge of Teachers College very generously went over all our data and according to his findings, based on the technic devised by Fisher, in which the 3 observers were differently weighted, there was a rise in titer in subjects receiving conditioning stimuli as compared with their own titers before the stimuli were applied.

It is doubtful from our data that a significant rise in typhoid agglutinins follows conditioning stimuli applied to suitably prepared subjects.

6336

Mechanism of Bacteriophage Action in Staphylococcus Bacteremia.*

WARD J. MACNEAL, FRANCES C. FRISBEE AND ALICE E. SLAVKIN.

From the Department of Pathology and Bacteriology, New York Post-Graduate Medical School and Hospital, Columbia University.

Four young rabbits, 1100 to 1320 gm. in weight, were inoculated intravenously with a suspension of staphylococcus which had been isolated from human bacteremia. Each animal received an intra-

* These studies were supported in part by a grant from the Josiah Macy, Jr., Foundation.

venous injection of 2 cc., equivalent to 5400 million living staphylococci. One rabbit was sacrificed 155 minutes after inoculation. Sections of spleen and liver revealed phagocyted leucocytes and partly disintegrated nuclear granules. Only one pair of cocci was recognized within a Kupffer cell after considerable search. A second animal was sacrificed 238 minutes after inoculation. Sections of the spleen revealed many phagocyted granules and nuclear fragments but no definite bacteria. In the liver, however, there were distinct and definite cocci within the somewhat swollen Kupffer cells. The third rabbit received an intravenous injection of 2 cc. undiluted asparagin staphylococcus bacteriophage 103 minutes after the bacterial inoculation and was sacrificed 131 minutes later, or 234 minutes after the bacterial inoculation. Sections of the spleen of this animal showed numerous phagocyted nuclear granules in the marginal zones about the splenic follicles and along with them poorly differentiated cocci in small numbers. In sections of the liver the phagocyted cocci were very abundant and distinctly differentiated, decidedly more abundant than in the liver of the second animal. The fourth rabbit received a similar dose of bacteriophage 106 minutes after bacterial inoculation and was sacrificed 89 minutes later or 195 minutes after the bacterial inoculation. Sections of the spleen of this animal contained unmistakable groups of micrococci within the reticular cells about the follicles and in some locations these cocci were numerous. In the liver also, the Kupffer cells contained abundant phagocyted cocci. The observations indicate that one immediate effect of intravenous injection of bacteriophage in bacteremia is to favor more rapid phagocytosis of the bacteria which are circulating in the blood.

Another lot of 4 young rabbits, weighing 300 to 400 gm. received similar intravenous inoculation with another septicemic strain of staphylococcus. The dose was 2 cc. of a suspension equivalent to 3500 million living cocci. One animal was sacrificed 203 minutes after inoculation. The blood culture taken at death showed 119,400 viable bacteria per cc. of blood, representing only about one-thousandth part of the bacteria introduced into the blood 203 minutes before. Sections of the spleen and liver revealed phagocyted cocci and also phagocyted red blood cells and leucocytes, especially conspicuous in the Kupffer cells. A second rabbit in this group received 2 cc. of bacteriophage intravenously 130 minutes after the bacterial inoculation and 110 minutes later, or just 4 hours after inoculation with bacteria, this animal was sacrificed. The blood culture at death showed 67,700 viable cocci per cc., slightly more

than half the number found in the first animal. The sections of spleen and liver contained somewhat more phagocyted cocci and there was less evidence of phagocytosis of red and white blood cells. The third animal in this group died 21 hours after inoculation. The blood culture, at necropsy, showed 15,800 viable cocci per cc. of blood or approximately one-eighth the number found in the first animal, which was killed some 17 hours earlier. The spleen and liver contained moderately numerous phagocyted cocci and there were many phagocyted leucocytes in the liver. In the kidney there were many large colonies of staphylococci in the medulla, for the most part plugging the capillary blood vessels in this region. The fourth animal in this group received 2 cc. of bacteriophage intravenously 140 minutes after the bacterial inoculation. The next day it appeared to be in good condition. It was sacrificed 20 hours 45 minutes after the injection of bacteriophage and 23 hours 5 minutes after inoculation with the bacteria. The blood culture at death showed 10 viable cocci per cc. or less than one-thousandth of the number found in the third animal 2 hours earlier. Microscopic study of sections of spleen, liver, kidney and lung failed to disclose any recognizable phagocyted bacteria. Structural alterations in the organs will not be discussed here. The observations on this second group of 4 animals are in accord with those on the first group, indicating that one effect of the injected bacteriophage is the promotion of more rapid phagocytosis of the bacteria by the endothelial cells. There is, however, an additional disclosure, namely that the presence of the bacteriophage tends to restrain the further growth of the bacteria which have lodged in the internal organs and also favors the more rapid and efficient intracellular digestion of the phagocyted bacteria.