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Sputum Studies in Lobar Pneumonia. Phagocytosis and the Effect of Serum Therapy.

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This laboratory is beginning a thorough study of sputum from cases of lobar pneumonia in the hope that the recognized cyclic changes which occur may eventually be correlated with the clinical condition of the patient and thereby become an aid in the therapy and prognosis of this disease. The present communication deals with a few of the microscopic findings which seem to be significant. To the author's knowledge the data herein described have not as yet been recorded in the literature. Most of the sputum studies in lobar pneumonia were made long before the discovery of the various pneumococcal types and are best summarized by von Hoesslin[1] and Clifford.[2]

Methods. The lobar pneumonias included in this series of more than 60 cases were selected in the sense that only typical ones were followed. Thin smears were made directly from representative portions of rusty sputum and treated with Wright's blood stain. Sputum examinations were made at 4- to 12-hour intervals so that 2 or more daily specimens were obtained from each patient until recovery or fatal termination.

The capsules of the pneumococci usually did not stain but were readily visualized as clear or occasionally, when stained, as pink zones around the dark blue diplococci. The size of the capsule corresponded fairly well to that noted by means of the "quellung" reaction and in all cases where no capsules were demonstrable in the stained slide the organisms were not directly typeable. Both the capsules and cell bodies of the pneumococci varied greatly in size, shape and affinity for the Wright stain in the same and different cases infected with a similar type of pneumococcus.

An attempt was made to place the data on a quantitative basis by counting the number of diplococci in 50 or more phagocytizing leu-

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1 Hoesslin, H. von, Julius Springer, Berlin, 1926.

2 Clifford, R., McMillan Co., New York, 1932.

kocytes. Frequently it was difficult to distinguish between disintegrating microörganisms and toxic granulation; therefore the counts included only those diplococci with intact structure and definitely appearing to be in the cytoplasm of the phagocyte.

Microscopic Findings. As has been pointed out by Clifford the phagocytes tend to be more active as the pneumonia progresses. This observation was confirmed by direct counts in some 23 cases of lobar pneumonia. The average number of diplococci per phagocyte in the admission sputa was 5 with variations ranging from 2 to 10. The highest average number at any time during the subsequent course of the disease was found to be 8 with variations ranging from 3 to 16. While this total increase in phagocytosis might be of value in an individual case or even become statistically important when sufficient cases were studied, it was felt that the number of a particular kind of pneumococcus within the cytoplasm of the phagocyte might be even more significant. For this reason the phagocytosis has been divided into 3 types depending upon the appearance of the organisms within the leukocyte. At present these will merely be described and no attempt will be made to correlate them with the clinical condition of the patient.

In the first type of phagocytosis, as illustrated in Fig. 3, the pneumococci within the cytoplasm of the leukocyte are definitely encapsulated. In patients who did not receive serum the number of capsulated diplococci per phagocyte varied from 1 to 5.

A second kind of phagocytosis, as illustrated in Fig. 4, is one in which the capsule is not demonstrable with the Wright stain, but its presence is suggested by the fact that the diplococci within the phagocyte are isolated from each other. Considerably larger numbers of such organisms were phagocytized and while an average of 10 per leukocyte was high, one could find as many as 25 within a single phagocyte.

In the third type of phagocytosis, as illustrated in Fig. 5, clumps of uncapsulated organisms may be seen within the cytoplasm of the leukocyte. The polymorphonuclear cells seem to be able to engulf these diplococci with ease and frequently a single phagocyte contained as many as 25 to 50 such organisms.

Because 40 of the cases of lobar pneumonia studied received serum at some time during their illness, it was possible to follow the effect of the treatment on the pneumococci present in the sputum. Capsulated pneumococci in sputum obtained before therapy was instituted, were evenly dispersed throughout the smear and each diplococcus was isolated from others present in the same field. This is well illustrated in Fig. 1. The first effect of horse or rabbit anti-

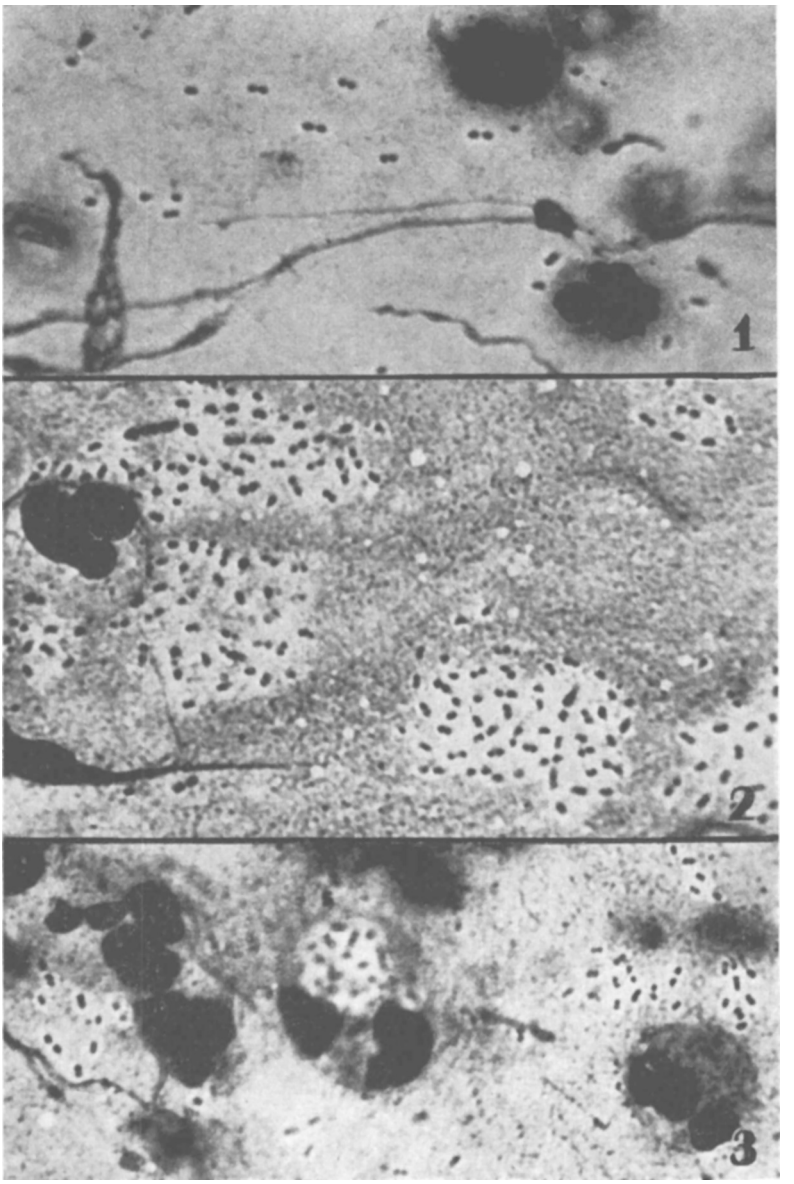

FIG. 1. Virgil Speed, Type VIII pneumonia, 5-6-38, 5 P.M., × 1700. Pre-therapy sputum specimen. Note the capsule halo and that each pneumococcus is isolated from others in the field.

FIG. 2. Virgil Speed, Type VIII pneumonia, 5-7-38, 12 midnight. × 1700. Sputum specimen taken 6 hours after the administration of 120,000 units of anti-pneumococcus horse serum. Note the clumping of extra-cellular capsulated pneumococci.

FIG. 3. Virgil Speed, Type VIII pneumonia, 5-7-38, 6 P.M., × 1700. Sputum specimen taken 3 hours after the administration of 120,000 units of anti-pneumococcus horse serum. Note the phagocytosis of capsulated pneumococci and the clumping of the extra-cellular organisms.

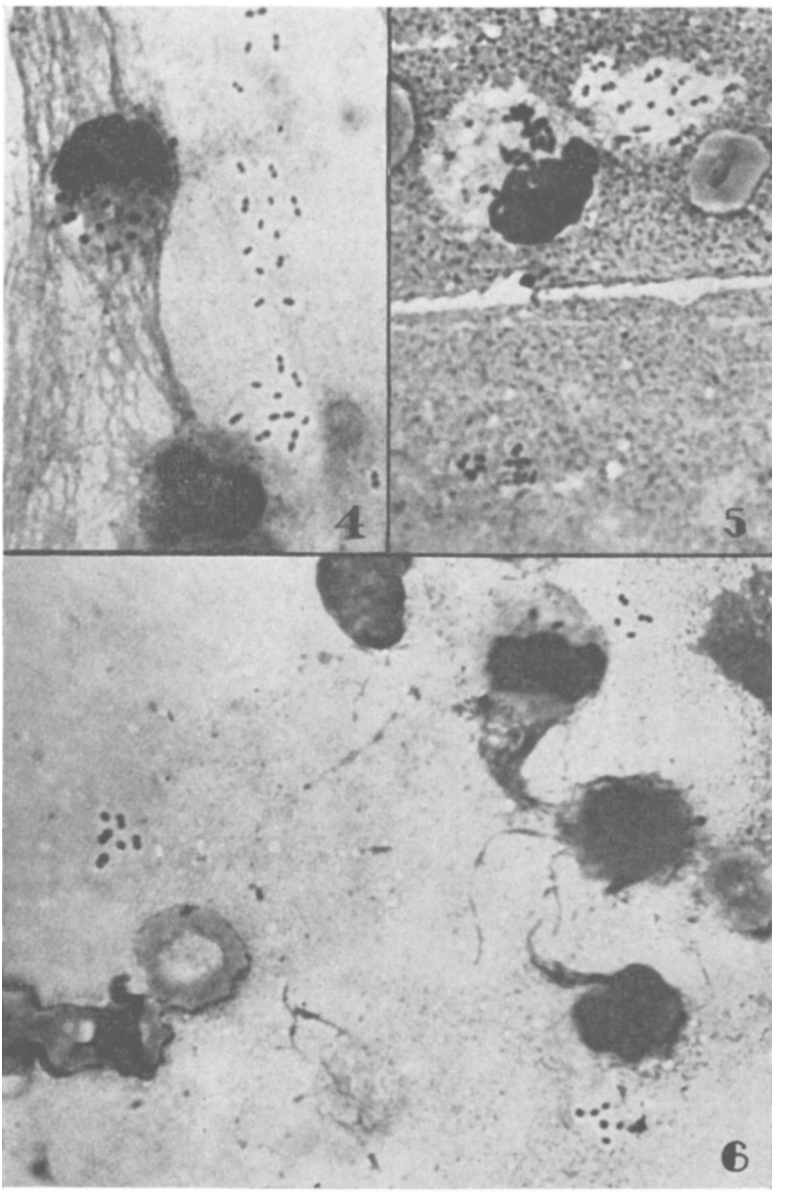

FIG. 4. Virgil Speed, Type VIII pneumonia, 5-8-38, 6 P.M., × 1700. Sputum specimen taken 24 hours after the administration of 120,000 units of anti-pneumococcus horse serum. Note that each phagocytized diplococcus stands out discreetly but that the capsules are not readily visualized. In addition, the individual extracellular pneumococci show less tendency to clump.

FIG. 5. Virgil Speed, Type VIII pneumonia, 5-7-38, 12 midnight, × 1700. Sputum specimen taken 6 hours after administration of 120,000 units of anti-pneumococcus horse serum. Note the clumps of uncapsulated diplococci within the cytoplasm of the phagocyte and also the extra-cellular clumps of both capsulated and uncapsulated organisms.

FIG. 6. David Alonzo, Type I pneumonia of 62 hours' duration. Pre-therapy sputum specimen. Note the clumps of extra-cellular capsulated pneumococci.

(Photographs by C. G. Eddy, Eloise Hospital, Eloise, Michigan.)

pneumococcic serum administration as evidenced in the sputum 3 to 24 hours after treatment with the arrangement of the extracellular capsulated organisms into definite small or large clumps suggestive of agglutination (Fig. 2). At the same time or shortly thereafter, it was often but not always possible to demonstrate an increase in the number of capsulated diplococci per phagocyte as illustrated in Figs. 3 and 4. The capsules of the extra-cellular pneumococci gradually decreased in size and these organisms also decreased in number as the sputum began to lose its rusty character. In most serum-treated cases, however, while the capsulated diplococci decreased, the total number of uncapsulated extra-cellular organisms remained high and in such specimens one obtained marked phagocytosis of clumps of these organisms as illustrated in Fig. 5.

Although clumping of capsulated pneumococci was usually associated with serum therapy, it has also been observed in the sputum of 4 patients who had not yet received treatment (Fig. 6). One of these patients entered the hospital with many Type II and a few Type IX pneumococci in the sputum. On the day of admission his serum agglutinated Type II pneumococcus to a titer of 1:40 but failed to react with Type IX. He recovered promptly without treatment. The phenomenon of clumping has also been seen rather frequently on the sixth to the tenth day of the pneumonia in patients who were under treatment with sulfanilamide but appeared to have no relation either to the dose or to the period of administration of the drug.

Summary. Three types of phagocytosis depending upon the degree of encapsulation of the engulfed pneumococci, have been observed in the sputum of patients suffering from lobar pneumonia. Clumping of capsulated pneumococci similar to agglutination and an increased phagocytosis of these organisms was evident in the sputum shortly after the administration of specific horse or rabbit antibody. Spontaneous clumping of capsulated pneumococci was observed in the sputum of 4 patients prior to therapy suggesting that a similar mechanism is involved in the development of active immunity. Further studies on the relation of the above phenomena to the clinical condition of the patient and the adequacy of serum dosage are now in progress.