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Soluble substance of pneumococcus origin in the blood and urine during lobar pneumonia.**By A. R. DOCHEZ and O. T. AVERY.***[From the Hospital of the Rockefeller Institute for Medical Research, New York.]*

A specifically reacting substance of pneumococcus origin has been demonstrated in the filtrates of young cultures of pneumococcus, and also in the blood serum and urine of patients during the course of lobar pneumonia. In bacteria-free filtrates of broth cultures of pneumococcus there is present a soluble material which gives a specific precipitin reaction with antipneumococcus serum. The filtrates from the different types of pneumococcus show the same specificity of reaction with immune serum as do the original cultures from which they are derived. The soluble substance present in the filtrates is undoubtedly of bacterial origin. That it is a product of the life processes of the pneumococcus and not due to its disintegration is shown by the fact that it is present in considerable amounts during the early stage of development of the culture when the organisms are growing at their maximum rate and undergoing little or no cell destruction as indicated by their growth curve.

The demonstration of the formation of this soluble substance in cultures of pneumococcus growing actively in vitro suggested the probability of its production in experimentally infected animals and in human beings suffering from lobar pneumonia. If rabbits are infected intraperitoneally with pneumococcus a substance specifically precipitable with antipneumococcus serum can be demonstrated in their blood serum, freed from bacteria by filtration, from within two to six hours following the time of infection. This soluble specific substance is also present in the blood serum during the course of lobar pneumonia in man and gives a precipitin reaction with antipneumococcus serum corresponding in type to the organism with which the individual is infected. This soluble precipitable substance is less frequently present in demonstrable quantities in human serum than in the serum of experimentally

infected animals. However, it has been found both when pneumococci were present in the circulating blood and when, by blood culture, organisms were absent. Complement fixation, as well as the precipitin reaction, may be used for the demonstration of this substance in serum.

The fact that considerable quantities of soluble material formed by the pneumococcus are present in the circulating blood in infection suggested the likelihood of its excretion in demonstrable form in the urine. Study of the urine by precipitin reactions in animals experimentally infected with pneumococcus and in a large series of individuals with lobar pneumonia showed a specifically precipitable substance to be present in almost every instance during some stage of the disease. A positive reaction has been found as early as twelve hours after the initial chill, and has been demonstrated in one instance five weeks after defervescence of fever. The reaction in different urines may vary from a faint cloud to a heavy precipitate. In certain instances the reaction may be negative when whole urine is used but become positive by chemical concentration of the substance in the same urine.

A study of the chemical nature, toxicity, antigenic properties and fate of the soluble substance in normal and infected animals is still in progress. The following facts, however, have already been ascertained concerning its chemical nature. The specific substance is not destroyed by boiling. It is readily soluble in water, precipitable in acetone, alcohol and ether. It is precipitated by colloidal iron and does not dialyze through parchment. Its immunological reactions are unaffected by proteolytic digestion with trypsin and the substance is not split by urease. The determination of total nitrogen and nitrogen partition on the active substance obtained by repeated precipitation with acetone and alcohol, shows this substance to be of protein nature or to be associated with protein.