prevents denudation is the same as the new factor essential for the growth of rats. Further work is being conducted on this subject.

Pneumonia

Since the opening of the hospital, Dr. Cole and later Dr. Avery and his associates have been interested in respiratory diseases, particularly lobar pneumonia. Much of the fundamental work on this disease has been conducted in the Rockefeller Hospital, and as a result of this activity a method of treating the malady by immune serum was elaborated. At first the serum was made in horses. Later Dr. Goodner and Dr. Horsfall showed that serum prepared in rabbits possessed qualities superior to those of antipneumococcal horse serum. For a few years the treatment of pneumonia by antipneumococcal rabbit serum gave highly satisfactory results and this serum would have been universally used within a short time if it had not been for the appearance upon the scene of sulfapyridine. The relative cheapness of the drug and the ease with which practising physicians can administer it orally made it obvious that within a short time this or some closely related drug would for the most part supplant the use of serum in the treatment of pneumonia. As a matter of fact this has already occurred.

Despite the obvious value of the new drugs, sulfapyridine and sulfathiazole, Dr. Avery and his associates believe that there is still use, under certain conditions, for antipneumococcal rabbit serum, particularly when it is employed in combination with the drugs. Type III pneumonia is one of the most fatal and also one of the most difficult diseases to treat. During the years 1936-38 26 patients with Type III pneumonia were treated with antipneumococcal rabbit serum alone and seven of these died, a mortality rate of 27 per cent. In the past two years only one patient has died

in a group of 20 treated with the combination of serum and sulfapyridine, a mortality rate of 5 per cent.

The introduction of sulfapyridine in the treatment of pneumonia naturally created interest in many centers of research in regard to how this particular drug acts as a curative agent. Does it act directly upon the pneumococcus or indirectly through changes in the physiology of the patient? Dr. Avery and his associates have attacked this problem by gradually acclimatizing pneumococci to concentrations of sulfapyridine that would ordinarily be lethal for these organisms. After this acclimatization has taken place, the pneumococci morphologically, immunologically, and in regard to virulence appear unchanged. On the other hand, it was easily shown that the drug-fast strains had undergone marked physiological alterations in that certain of their enzyme systems (systems having to do with metabolism) had been suppressed.

Almost from the time that sulfapyridine was introduced into the physicians's armamentarium it was noticed that it would not act upon pneumococci in collections of pus in the pleural cavity or in localized abscesses in other parts of the body. A number of explanations have been offered for the inefficacy of the drug under such conditions. Dr. MacLeod on Dr. Avery's service has shown that at least one reason why the drug is impotent under the conditions mentioned is that in purulent materials there occurs a substance which markedly inhibits the bactericidal action of the drug in the test tube. This substance has been isolated and partially purified, but its nature is as yet not known; further work is being conducted along these lines.

When the sulfonamide drugs more or less supplanted the use of immune serum in the treatment of pneumonia, it appeared for a short time that

the work on pneumonia at the Rockefeller Hospital might be forgotten or overshadowed by the striking results obtained with the drug. Fortunately, however, Drs. Dubos and Hotchkiss have kept the Hospital in the front line of chemotherapeutic attack against infectious diseases by the discovery, purification, and crystallization of a new chemical substance capable of attacking all gram-positive organisms so far tested. (The bacterial world is divided into two parts on the basis of the manner in which different microorganisms react to a stain devised by Professor Christian Gram; those organisms that retain the stain are said to be gram-positive, while those not retaining it are classified as gram-negative.)

The substance mentioned has been obtained from a gram-positive soil bacillus; in fact from this soil bacillus there have been extracted several substances which are highly active against gram-positive organisms, e.g., pneumococci, and streptococci, when tests are carried out in test tubes. One of the substances, which has been crystallized and is called gramicidin, kills gram-positive organisms both in the test tube and in mice. These results were quite dramatic. However, when the material was used in dogs, it was soon found that the toxicity of the new chemical for this species of animal was greater than for the mouse, and that experimental pneumonia in dogs could not be successfully combatted by the material in its present form. These findings prevented the immediate use of the drug for the treatment of pneumonia in human beings.

Despite the fact that gramicidin in its present state is not satisfactory for the treatment of pneumonia in human beings, the enthusiasm of the workers has not been dampened, because they realize that they possess a new lead for the chemotherapeutic treatment of infectious diseases in general. This realization has induced them to continue their work on

the chemical structure of the substance, with the result that considerable information concerning the size and constituents of molecules of the material has been obtained. At the present time it is known that gramicidin is essentially a polypeptide to which is linked a fatty acid chain. This knowledge regarding gramicidin has already caused the workers to seek similar substances with bactericidal action, and a number have been found.

Although gramicidin has no immediate value in the treatment of pneumonia, its employment by means of local application may have a widespread use in the treatment of wounds and local infections. Indeed, several workers in this country and abroad are investigating whether gramicidin is of value in the treatment of war wounds. Furthermore, Dr. Dubos and Dr. Little of the Princeton branch of The Rockefeller Institute have shown that gramicidin, when administered locally in small amounts of a bland oil, is valuable in the treatment of mastitis of cows. Dr. John Mohler of the Bureau of Animal Industry, because of results obtained in the Walker Gordon cows, has become interested in this method of treating a disease of great economic importance.

Dr. Goodner, on Dr. Avery's service, has been investigating mechanisms of resistance to infection other than those covered by the term antibody or immune substance in serum. He believes that the physiological state of an animal plays a part in natural resistance and that this physiological state is influenced by diet. By feeding mice unaccustomed diets he was able to show that certain vegetables, fruits, grains and herbs possess something which increases the resistance of mice to pneumococcal infections, while other substances of a similar nature do not. The nature of the substance or substances possessed by the effective foods has not been definitely determined.

For a number of years workers in Dr. Avery's laboratory have been interested in the chemical constitution of the capsule or the covering of the pneumococcus. The capsule is a very important part of this microorganism, because it determines its type specificity and also is essential for its disease-producing characteristics. Information obtained during the course of a number of years regarding the chemical constitution of the capsules of several types of pneumococci has shown that they are composed of complex sugars. The capsule of Type III pneumococcus has been difficult to analyze, but it is believed that during the past year Drs. Goebel and Adams have at last determined its structure.

Rheumatic Fever

Dr. Swift and his associates for a number of years have been endeavoring to find the cause of rheumatic fever and have been collecting data which eventually will permit of an accurate description of the natural history of the disease. Many ideas regarding the cause of this malady have been set forth; the most generally accepted one is that the hemolytic streptococcus plays an important role. Notwithstanding the general belief that the streptococcus is the inciting agent, a number of workers from time to time have sought other agents. For instance, a filtrable virus has been proposed as the cause. Because of Dr. A. B. Sabin's recent work on the occurrence of pleuropneumonia-like microorganisms in mice, which produce in this species a multiple arthritis possessing certain of the characteristics of human rheumatic fever, Dr. Swift and his associates attempted to find out whether a similar microorganism was responsible for the human malady. At first it was believed that it was possible to isolate pleuropneumonia-like organisms from rheumatic fever patients. Much excitement was caused.