before and at a higher temperature. The only differences, then, were in the different source of the milk, an element that can not be analyzed, the withdrawal of the Mellin's food and the use of orange juice. Before anything else was given a distinct improvement was obvious, and recovery occurred while on sterilized milk, orange juice, and a small amount of potato and carrot broth. So rapid an improvement, of course, is not at all uncommon, and the change as soon as the orange juice is given, along with the curious avidity with which my patient took it, like so many others, seems to prove that it contains something much needed by the scorbutic body.

Skiagraphy.—My efforts to get an x-ray picture of the affected bones were not successful. It was impossible to make an exposure the first day, when the legs were spontaneously kept still. By the next day there was some motion when the noise and light of the apparatus were perceived, so that it was not possible to make a slow exposure with a soft tube that would show fine differentiation of the soft parts. The pictures, of which my colleague, Mr. V. H. Willey, made a number, show the swellings, as well as the appearances of the bones, but nothing more.

X-ray pictures of infantile scurvy have been published by Ausset, Rotch³ and Lenndorff.⁴ Those of Ausset and Rotch are not very good. Lenndorff's is given in a rather diagrammatic reproduction. The author says there were shadows along the femur and the tibia and fibula, and a clearing up of the bone shadow in all the bones. He explains the findings by assuming that the periosteum had had time to exert its osteogenetic function, a belief that is borne out by postmortem examinations. Lenndorff, however, very properly warns against too much dependence on the skiagraphic diagnosis of infantile scurvy, though it may be of assistance in clearing up some of the anatomic changes.

AN ANTIGONOCOCCUS SERUM EFFECTIVE IN THE TREATMENT OF GONORRHEAL RHEUMATISM.*

JOHN C. TORREY, Ph.D.

Fellow in the Department of Experimental Pathology, Cornell
University Medical College.

NEW YORK CITY.

The following communication is intended merely as a preliminary announcement of the preparation of an antigonococcus serum of therapeutic value. It will be followed shortly by an article in which the character and properties of this serum are dealt with in greater detail.

There are several reasons why an antigonococcus serum has not been used heretofore in the treatment of gonorrheal rheumatism. They may be tabulated as follows: First, there is not the slightest indication of an immunity in man to gonorrheal infection acquired by a previous attack; nor in chronic gonorrhea is the individual any the less susceptible to an acute superinfection. Second, there is no well-established case of an infection in animals with gonococcus. Wertheim, by injecting agar and gonococci together into the peritoneal cavity of rabbits, was able to produce a local peritonitis, but not a real infection. Heller's statement that he has produced an ophthalmic gonorrhea in young dogs by

injecting gonococci into the anterior chamber of the eye has not been confirmed. Third, it is generally supposed that gonococci can not be induced to grow luxuriantly under artificial conditions. Finally, most authorities agree with Wassermann and Nikolaysen in concluding that animals can not be immunized to the toxin of the gonococcus, as it is embraced within the cells and only diffuses into the surrounding tissues on its death and disintegration. In other words, according to their view, it is an endotoxin, a bacterial protein.

Although there was apparently slight chance of success, at the suggestion of Dr. Rogers I prepared a serum for a patient with gonorrheal rheumatism of some 15 years' standing, who had been treated in every other way without result. We were agreeably surprised to find the serum effective, not only in that case, but also in a high percentage of others in which it has been tried. These cases are fully described in the preceding clinical report by Dr. Rogers.

The culture which was originally employed in producing the serum was isolated from an acute case of gonorrhea in a male, who had not been treated. Gonococci were very numerous in the exudate, principally within the leucocytes. Smears were made from the discharge on petri dishes of ascitic agar. After an incubation of 24 hours, an almost pure culture of very small, transparent colonies appeared. These colonies were composed of small diplococci in every respect identical in morphology, staining reactions and cultural features with the characteristics of gonococci. The micro-organisms were negative to Gram's stain, would not grow on ordinary peptone agar or broth (repeated tests have been made extending over several months), and died out even on ascitic media in a short time. On ascitic agar (equal parts of ascitic fluid and 2 per cent. glycerin agar) the colonies are small and tend to remain separate. At first transparent and with regular edge, after four or five days the center of the colony becomes granular and the edge spreads out thinly and irregularly. All the diplococci have died in from six to eight days. In ascitic broth the length of life is much greater, from thirty to forty days.

For purposes of inoculation, a very satisfactory medium has been found to be a mixture of rich ascitic fluid and slightly acid beef infusion peptone broth in equal parts. Tubes of about 12 c.c. of the mixture are heated to 60 C. for several hours and tested for sterility. To obtain the best results, the temperature of the incubator should be between 36 and 37 C. Gonococci are killed at a relatively low temperature (at from 40 to 41 C., according to Scholtz). After from 18 to 24 hours' incubation, a slight granular growth appears near the surface and along the side of the tube. This slowly increases in amount until, after six days, the medium is well clouded on shaking. Other strains of gonococci which have been used form, after four days, a rather thick and flaky pellicle. In all the strains the growth after a time sinks to the bottom of the culture tube.

Various modifications of the proportion of the ingredients in ascitic broth have been tried, such as the presence and absence of peptone, increase in the amount of albuminous matter and ascitic fluid, but no combination has proved, on the whole, more satisfactory than the one which has been described.

It is interesting to note that the strain of gonococcus which was first used, after being cultivated for over a year on ascitic media, grows fully as well and produces as effective a serum as when first isolated. This is in harmony with the well-known fact that gonococci, iso-

3. Medical News, 1903, vol. II.

4. Archiv. f. Kinderheilkunde, vol. xxxviii, 1904, p. 160.

* Read before the New York Academy of Medicine, 1905.

lated from chronic cases, have suffered no loss in virulence or growth energy. Two other strains of this organism, which were kindly given to me by Dr. Elser, have been found to give rise to fully as efficient a serum as the original culture. These were isolated from cases of vaginitis.

Large rabbits have been used exclusively in producing the serum. They were inoculated in early stages of the experiments at intervals of three or four days with about 10 c.c. of the entire culture. It has been found, however, that the results are rather more satisfactory if an interval of five or six days elapses between the inoculations. The animals thrive much better if so treated and bleed more freely. Experiments have been carried on with the idea of determining the most suitable age for the cultures used in inoculations. It has been found that both very young cultures, from two to five days, and old cultures, from twenty to thirty days, produce a serum that is fairly satisfactory. The best results, however, are obtained with cultures from six to fifteen days old. During this period the cell growth reaches its height and the culture contains the greatest amount of toxin. Experiments on guinea-pigs also point to this conclusion. The inoculations are always made intraperitoneally.

According to Wassermann, no immunity can be produced in mice or rabbits to gonotoxin, although these animals may exhibit a slight resistance and adaptation. It has been my experience that rabbits and guinea-pigs show individual differences in their powers of resistance to repeated doses of gonotoxin, and that possibly in no case is there a true prolonged active immunity. The first inoculation always causes in rabbits a great loss of weight, sometimes amounting to one-fourth of the total weight. If the amount of toxin in the first inoculation is not too great and the animal is allowed to recover completely from its effect, the second and four or five subsequent inoculations give rise to only a slight loss of weight and discomfort. After a variable time, however, the majority of the animals reach a condition of hypersensitivity to the toxin and succumb finally to a dose that would never prove fatal to a normal animal. This seems to indicate, as Wassermann and others have pointed out, that the toxin present in the culture is, for the most part, if not entirely, derived from the dead bodies of the cells. When rabbits reach this hypersensitive stage, they refuse to eat and finally die in a greatly emaciated condition.

The rabbits are bled for the first time after they have received six inoculations, or about 60 c.c. of the culture, extending over a period of about a month. The most economical method is to bleed from the ear (which has been carefully shaved, washed with a germicide and finally with sterile normal salt solution) until the animals show signs of becoming hypersensitive, and then from the carotid. Large animals should yield a total of from 70 to 90 c.c. of serum. It is interesting and important to note that serum derived from one of the later bleedings is more potent than that obtained at first, when the animal has received only a few inoculations. Some rabbits, too, produce a better serum than others. It has also been found that the serum loses little, if any, of its power after remaining in the ice box for from one to two months. For distribution, small sealed glass tubes holding about 2 c.c. of serum are used. No preservative is added to the serum. With ordinary precautions it may easily be obtained sterile.

It is obviously a matter of interest to determine to

what factors in the serum its curative properties are due. In inoculating rabbits, whole cultures, both the cells and the filtrate, were used with the hope that a serum might be produced possessing both antitoxic and bactericidal factors. Although the majority of those who have investigated the subject believe, with Wassermann, that the toxin of the gonococcus is not of such a character as to bring about the production of an antitoxin when injected into animals, still one observer, de Christmas, claims to have obtained from old cultures an extracellular toxin, which, when injected into the brain of a guinea-pig, kills in very small doses. He believes that this toxin is produced by a vital process of the cell and is analogous with the extracellular toxins of diphtheria and tetanus. This toxin, however, is produced in considerable amount only when a special culture medium is used, consisting of one part strongly albuminous peptone-free broth and three parts ascitic fluid. By inoculating rabbits and goats with the filtrate of old cultures he apparently obtained a serum with sufficient antitoxic power to neutralize twenty times its volume of toxin. Although I have not found that there is any very decided increase in the amount of toxin produced by the use of the formula of de Christmas, my experiments, so far as they have been conducted, tend to confirm his assertion that it is possible to obtain an antitoxin for the toxin of gonococcus. This seems probable, on the one hand, from the protective power of the serum for guinea-pigs. Two pigs were given 1 c.c. of serum and one pig 2 c.c. Eighteen hours later these three pigs, and also an additional control pig, which had received no serum, were inoculated intraperitoneally with 3 c.c. of toxin. In one hour the temperature of the control pig had dropped over 10 degrees, and in three hours the animal was dead. The three pigs which had been treated with serum suffered only a slight drop in temperature and showed practically no signs of an intoxication. The details of these experiments will be given in a subsequent paper.

The clinical evidence also points to the same conclusion. In some cases there is a decrease of pain in the joints within twenty-four hours after the first administration of the serum. The most reasonable explanation of this result seems to be that some of the gonotoxin, which causes the inflammation and the attendant pain, has been neutralized.

Without doubt, however, the most important permanent relief which the serum affords in most cases is due to a bactericidal activity. In chronic gonorrhea there are comparatively few gonococci, often deep in the tissues, but, as an active immunity never arises in man to gonococcus, the system frequently finds difficulty in disposing of them. It seems possible that the serum supplies enough immune bodies to accomplish this, although too few to bring about the destruction of the great number of gonococci which are present in the urethra in acute gonorrhea. This theory has not been substantiated as yet by complete experimental evidence. The serum, however, has been found to contain both agglutinins and precipitins for the gonococcus.

Honorable Dealings.—It is a question whether the testimony given in suits for damages, against railroads and other corporations, is not at times biased by the knowledge that the physician will get no fee for his attendance, if the patient fails to "recover" for his injury. I was once asked to give a note saying that I was too busy to come to court to testify, because it was known that my opinion would be unfavorable to the cause of the plaintiff. Does anyone doubt that acceding to the request would have rendered the payment of my bill more certain?—J. B. Roberts.