THE VACCINE TREATMENT OF GONORRHŒA, WITH NOTES ON THIRTY CASES.

By Captain A. T. FROST.
Royal Army Medical Corps.

The literature on the subject of gonorrhœal vaccination is so contradictory that a trial of this method of treatment was decided on in December, 1910. The various reports on vaccines were consulted, and the following résumé was compiled.

The dosage of vaccine has varied from 500,000 to 1,000,000,000 gonococci in acute and chronic disease respectively. Each bacteriologist prepared the vaccine in his own way, so that there was only an approximate relation between the immunizing power of similar doses in any two vaccines.

The following record of some 300 cases treated by gonococcal vaccine has been extracted from literature.

Hale White and Eyre [1] treated four cases of chronic gonorrhœal arthritis which were unaffected by local or general medication. Opsonic control was employed. In two of the cases four to ten million cocci were injected every seven days; this resulted in cure. Another case had an autogenous vaccine, of which he was given 5 to 25 million cocci with six days interval between the injections. The fourth also had an autogenous vaccine; 100 to 200 million cocci were injected, with complete recovery in five weeks.

Eyre and Stewart [2] published their results in fifty-three cases. The gonococcus was isolated and grown on blood agar. The twenty-four-hour-old culture was sterilized at 50° C. for one hour, and again heated at the same temperature for half an hour, after the addition of ½ per cent trikresol. Three to ten strains were used. After the first few injections, which contained as many as 100 and 250 million cocci, they did not give a higher dose than 25 million cocci.

In acute gonorrhœa, they usually employed a dose of 5 million cocci; this was followed by a negative phase lasting three to four days, after which a strong positive reaction set in. They advise daily opsonic index observations. If the index is variable, they recommend a dose of ½ to 1 million cocci, if it is steady 2 to 5 million cocci are injected. In chronic infections small injections were found to be more beneficial than large ones; the best results were obtained with 1 to 2 million cocci, every three to five days, or 3 to 5 million

every five to seven days, or 10 million with an interval of eight to ten days. In orchitis a small dose is best.

Hartwell [3] in discussing gonorrhœal arthritis, states that of thirty-one subacute cases, twenty-seven made perfect recoveries. In chronic affections vaccines are not of much benefit, especially if ankylosis is present. His vaccine is sterilized at 60° C. for one hour, or kept on ice all night, then lysol added and allowed to act on the organisms for twelve hours. The strength of the lysol is 0·25 per cent. The author did not find any difference between the heated and unheated cultures. The most efficient initial dose for acute arthritis was 10 to 25 million cocci; for chronic cases as many as 600 million cocci have been injected. The interval between inoculations was two to four days in acute cases, and five to seven in the more chronic affections.

Aronstam [4] treated fifty-four patients with stock vaccines, and no local applications. The average time under treatment was three weeks. Three to eight injections were required to effect a cure. He summarizes the results of his experience by stating that recovery from acute gonorrhœa takes place in four weeks, without injections or irrigation, that vaccines act well in epididymitis, and prostatitis. He also observed that latent arthritis became manifest under the vaccine treatment, but was eventually relieved.

Ballinger [5] made use of a mixed vaccine in mixed infections, and a stock culture in uncomplicated gonorrhœa. In addition he had recourse to massage, injections, and irrigation. He considers massage of joints at the same time as vaccination inadvisable, owing to the liability of causing a negative phase. In acute cases he gave from 5 to 10 million cocci, in chronic cases up to 50 million cocci, beginning with a dose of 15 million cocci, and allowing five to eight days' interval between the injections. His conclusions are favourable, if vaccination is only looked on as an adjuvant to local treatment.

Dieulafoy [6] describes the course of a case of gonorrhœal septicæmia, with typhoid symptoms which recovered. He made a culture from the blood in peptone ascitic broth, obtaining a pure culture of the organism in thirty hours. He gave a vaccine containing 5 millions of this organism, after which the temperature dropped to normal. Three days later the same dose was repeated with marked benefit. A third injection of 10 millions was followed by complete recovery.

Carl Mianini [7] reported *in extenso* four cases of arthritis, and showed the interdependence between the opsonic index and the size

of the dose. The first patient had 2 million gonococci injected. His opsonic index before the injection was 0·84; after the injection it fell to 0·42; the fall was accompanied by an increase in all the symptoms. The second dose was reduced to 1 million. Six days later the index was 0·83, and he appeared much better. The joint pains returned after a week's freedom from symptoms, and twenty-six hours after an injection of 200 million cocci again disappeared. A relapse of pain on the seventh day was treated by an injection of 300 million cocci; pain left the joints that evening. His opsonic index at the end of the course was 1·23. The second case received a first injection of 30 million cocci, as he had an index of 0·96; this then fell to 0·73. In five days the opsonic index had risen to 1·42. In all, five doses gradually increased to 350 million cocci were given. The third case had an initial dose of 4 million cocci, followed at intervals of three, five, six, and eighteen days respectively, by 30, 100, 150 and 200 million cocci. The opsonic index varied after the doses thus: at first the index was 0·96; this fell to 0·47. The next index was calculated as 0·54; five days later it was 0·89. On the fourteenth day it was 1·28, and on the thirty-second day it had fallen to 0·68.

Case 4 had an index of 1·12 before the first injection, which contained 250 million cocci. Next day all pain had ceased. On the third day 100 million cocci were given and the opsonic index was 0·78. The daily record showed a lower index each day and an increase in the pains. Two days later 400 million cocci were injected; this was followed by a rise in the opsonic index to 1·04. Seven days after the last injection the patient received another 400 million cocci, and his opsonic index fell to 0·47. There was no relapse from this time, and massage was resorted to.

In conclusion the author is of opinion that the loss of pain is not to be taken as an index of the cure of the disease; it only shows that gonococcal vaccine has a specific action on gonorrhœal arthritis.

Thomas [8] gives three years' experience of specific immunity. He describes the treatment of gonorrhœal vulvo-vaginitis in children, and shows brilliant results from injections of 5 million gonococci. Four joint cases were either cured or improved with a dosage of 50 million gonococci. Autogenous vaccines have given the best results in his hands. Finally, the author states that vaccination is only an adjuvant to local treatment.

Irons [9] made his vaccine from organisms heated to 60° F. for one hour. When a dose of 500 million cocci was experimented

with, the reaction started within twelve hours and persisted for twenty-four hours. With 50 million cocci there was little or no reactive response. In summarizing his results, he comes to the conclusion that the action of vaccine therapy is better in the case of infected joints than in any other form of gonococcal infection.

W. Friedlander and Reiter [10] in discussing the various complications of gonorrhœa say that in acute, subacute and chronic epididymitis, vaccines give the best result. Reiter's preparation was used in doses of 0·2, 0·3, 0·4, 0·6, 0·8 and 1 c.c., each cubic centimetre containing 5 million gonococci. The interval between injections was three days. Infiltration disappeared very rapidly, leaving only a small nodule. Deep lesions appeared to heal before the original focus in the mucous membrane; the urethral discharge remained unchanged.

In acute prostatitis improvement was not noticed. However, in acute and subacute follicular prostatitis both the objective and subjective signs of the disease were quickly ameliorated. Spermocystitis was improved, but not cured. Infection of the ducts of Bartholin's glands was not influenced by vaccination.

Allen [11] has come to the conclusion that in gonorrhœal infections phagocytosis and opsonin formation is not of as much importance as in some of the other vaccine-treated diseases. In support of this, he mentions that two cases of gonorrhœa with equally numerous cocci in the pus leucocytes, give widely different results in culture; thus, one may produce a poor growth, the other an abundant one. He has had very encouraging success in acute disease. As an initial dose, the author recommends 25 million cocci, followed by a similar dose; later doses may be increased up to 50 million cocci. In addition a mild antiseptic irrigation should be carried out at the same time. If the cure is not complete in two or three weeks, as is usual in his cases, the injections are increased, even as many as 1,000 million cocci being given. No secondary complications were met with and he says that in all cases the vaccine should be increased till good results follow.

In reviewing the foregoing work done by various authors the following conclusions have been arrived at. There is unanimity of opinion that vaccine therapy is an advance on the ordinary medicinal method. There is also an agreement on the necessity of high dosage in arthritis of gonorrhœal origin. Acute gonorrhœa may be cured if treated with irrigation; massage of the prostate is required in posterior urethritis, and sounds in the more chronic disease, with or without internal

treatment. The average time in which recovery can be assured is six weeks, provided that the patient begins his course of irrigation, &c., in the very earliest days of his attack. Both Aronstam and Allen have succeeded in curing urethritis with vaccines in three weeks, the former without any other aid, the latter with mild antiseptic irrigation. On the other hand, most of the authors who have tried inoculation for uncomplicated gonorrhœa state that there is not much advantage to be gained therefrom. The general consensus of opinion appears to be that the deeper the lesion the more active is the immunizing power of gonococcal vaccine.

Preparation of Vaccine.—In an article by Martin [12] in the *Journal of the Pathological Society*, on the growth of the gonococcus, he describes a culture medium which has given excellent results in his hands.

Following his procedure a medium was made containing:—

Beef extract broth, to which was added
Disodium phosphate 0·5 per cent,
Witte's peptone 1 per cent,
Agar agar 2 per cent.

When sterilized in test tubes the medium is "slanted" and kept till required. A patient with a gonorrhœal discharge from his urethra, from whom it is desired to make a gonococcal culture, is brought to the pathological laboratory. The glans penis is cleaned with absolute alcohol, and allowed to dry. Two tubes of the medium have the surface of the agar evenly smeared over with about four drops of sterile hydrocele, ascitic or pleuritic fluid. The tubes are now placed in the incubator until they become heated to 37° C. The first part of the urethral discharge is removed from the tip of the penis; two loopfuls of the deeper discharge at the meatal orifice are taken on a platinum needle and quickly transferred to the surface of the agar slope which is marked, and returned to the incubator. A pure culture, or at least isolated colonies, can be subcultured on a similar medium. A large percentage of excellent growths of the gonococcus in pure culture was obtained in this way.

A twenty-four-hour-old culture in 1 per cent sodium chloride is sterilized by heat applied for an hour at 59° C. The vaccine is diluted till 5 minims contain 20 million gonococci. At first three cultures from three cases were mixed, but at a later period, and when better results were got by culture, ten different cultures entered into the vaccine. To keep the vaccine sterile, ½ per cent

lysol was added to the stock, which was stored in rubber capped bottles, 20 c.c. in each.

Of the thirty cases, twelve had a vaccine procured from one of the large manufacturers, the remainder had a vaccine made from a case of gonorrhœa acquired locally as detailed above.

In beginning the systematic vaccination of the thirty cases our idea was to investigate whether the opsonic index could be dispensed with, and whether vaccine inoculation for gonorrhœa could be made a simple clinical method devoid of dangers and capable of employment without the aid of laboratory technique. Gonorrhœa is here meant to include acute, chronic, and blood-stream infections. No attempt was made to select cases. All cases which were admitted into the Royal Infirmary, Dublin, during the period were treated in the same way, with the exception of some cases of mixed gonococcal and other organisms; in these cases cultures of the *Bacillus acidi lactici* were injected into the urethra.

Case 1 had been in hospital since September 5, 1910. He had two or three exacerbations of the disease during October and November. Examination by the urethroscope showed a condition of soft infiltration along the whole of the urethra. A pure culture of gonococcus was isolated from the deep urethra. The first dose of gonococcal stock vaccine was injected on November 29, 1910, dose 5 million cocci. Four days later 50 million cocci were given, and no reaction followed. In forty-eight hours the urethral discharge had ceased for the first time since early in November. The third injection was given on December 10, 1910, as a return of the discharge occurred with threads in the "anterior" urine glass (Thompson's two-glass test). On December 17, 1910, these threads contained a bacillus, but no gonococcus. A culture on ascitic agar of one of these threads produced a diphtheroid organism, and a grey non-liquefying coccus. The *B. acidi lactici* from one of the proprietary tablets "Saurin" was grown on 1 per cent extract of malt in agar. The pure culture incubated for twenty-four hours on the medium just mentioned was emulsified in salt solution and injected into the urethra by means of Ultzmann's instillation syringe. This was followed by an increase of pus for twenty-four hours, and the threads disappeared. The injection was repeated three days later, and an irrigation of permanganate of potash was given next morning. Threads and discharge from the urethra ceased and no further signs of gonorrhœa have recurred.

This patient was one hundred and sixteen days under treatment, but was only forty-five days under vaccine therapy. The gonococcus alone was the pathological factor for ninety-six days, the secondary infection only occurred in the last three weeks.

B. acidi lactici has been the object of some investigations by Cannata and Mitra [13], as to its action on various pathological organisms. The point of interest as regards this paper which was elicited by them, is that the *B. acidi lactici* has a decided bactericidal action on organisms of the typhoid, paratyphoid, and dysentery groups, and also on the staphylococci; while the *B. coli* group, *B. pyocyaneus* and *B. prodigiosus* are practically unaffected by contact with the organisms of the lactic acid family.

Case 2. The next case, also treated by *B. acidi lactici* in addition to vaccines, is of interest owing to the unusually numerous gonococci in the urethral discharge, and the copious growth on the disodium phosphate pleuritic fluid agar. Though the diplococci looked like gonococci microscopically, and were also Gram negative, the appearance on the medium was more like a rather transparent culture of *Staphylococcus albus*. However, no growth could be obtained on ordinary agar, and subcultures on the special medium gave positive results. Three weeks irrigation with permanganate of potash solution did little more than lessen the amount of discharge, but made no impression on the number of gonococci.

To test the effect of *B. acidi lactici* on the gonococci an emulsion of the bacillus similarly prepared to that used in the last case was injected on March 4, 1911; no change was noticed in the urethral discharge, or in the infecting organism.

On March 6, 1911, a second injection was given of *B. acidi lactici;* this was followed by a copious discharge of pus, much pain in the prostate, in fact an acute attack of prostatitis. Two days later permanganate of potash irrigation was resumed. The "local" stock vaccine had now been prepared, and a dose of 50 million was given on March 13, 1911. No reaction followed. Doses of 20 million were injected with weekly intervals. A slight reaction followed the fourth vaccination. At this time the discharge had disappeared and only a slight "haze" remained in the urine, but prostatic pain and frequent micturition were still present. The dosage of gonococci was increased in the following weeks to 35, 40 and finally 100 million; the patient had a slight local reaction after each inoculation; irrigation was continued all through this period. The prostate did not improve to any great extent until sounds and massage were resorted to, when the change was at

once marked. This case was ninety-six days under treatment and neither vaccine or *B. acidi lactici* had a curative effect.

Case 3 had a pure gonococcal infection and a pure culture of the gonococcus was isolated. Potassium permanganate irrigation was begun on admission, but as the urethral discharge did not clear up rapidly another trial was given to the *B. acidi lactici*. One urethral injection was employed on March 4, 1911, on which date gonococci were found in the discharge. Two days later no discharge could be expressed, and a second syringeful of bacilli was introduced high up in the urethra. A third dose was given on the following day. No unpleasant effects followed these injections, and irrigation with Condy's fluid caused the disappearance of the introduced organism immediately. On March 10, 1911, only a faint haze could be seen in the urine. Two vaccinations with his own gonococci with a three-day interval completed the cure of this case. The number of days under treatment was twenty-six. Whether one should attribute the rapid cure of this man to the *B. acidi lactici* or not, is a difficult question to answer, but the fact remains that the discharge from his urethra disappeared and gonococci could not be found within forty-eight hours of beginning the bacillary applications.

From Case 4 a pure gonococcal culture was isolated, and grown to many generations. He had two injections of "manufacturer's" vaccine, of 25 and 50 million respectively at an interval of one week; this treatment was followed by an increase of both the discharge and the number of gonococci. Nitrate of silver was substituted for Condy's fluid as a douche for the urethra, with improvement in the urethritis.

On March 4, 1911, an emulsion of *B. acidi lactici* was injected and also on the following day. No discharge was visible after the second dose, until March 18, 1911. A "local" stock gonococcal vaccine had by this date been made, and five doses were given, beginning at 12 million, while the fifth contained 32 million gonococci. There was a slight reaction after the fourth dose in the form of an increase of discharge; no organisms, however, were found. Before this patient was considered clear he was under treatment for eighty-six days, and a really satisfactory result was not obtained, either with the vaccine or with Massol's bacillus.

The next case (No. 5) was one of anterior and posterior urethritis, with papillomata on the glans penis associated with a septic condition of these warts. Owing to the complication of sepsis on a chronic gleet, this is not a fair test of the time required

for treatment by vaccine. The case is mentioned here to show that the lactic acid bacillus has a decided influence on septic processes. Two injections of 50 million cocci, each at fourteen days' interval, had the effect of eliminating gonococci, but not the discharge; the warts were still in a very purulent state in spite of constant irrigation, and organisms of all kinds were found in the pus. One injection of *Bacillus massol* cleared up these organisms, and the urethral discharge ceased within forty-eight hours.

From Case 6 a pure culture of gonococci was isolated. He had a relapse when one month free from signs of the disease. By means of the urethroscope a small ulcer could be located $2\frac{1}{2}$ in. from the meatus. No curative effect followed eight vaccinations at weekly intervals of a stock gonococcus vaccine containing from 5 to 50 million cocci. Late in the disease an injection of *B. acidi lactici* was tried as there was a Gram positive diplococcus in addition to the gonococcus found in the urethra; it had no influence on the course of the urethritis. Eventually, a cure was effected by silver nitrate applied to the ulcer by Guyon's syringe.

These cases are placed together to show the effect of combined irrigation, vaccine, and *B. acidi lactici*. They were on an average eighty-one days under treatment, the shortest was twenty-six days, and the longest 116. It seems as if the living bacillus has some influence in eliminating a septic infection complicating gonorrhœa. Further work is required on this point before a definite answer can be given.

Gonorrhœal Rheumatism.

Three patients were treated for this complication with vaccines. Two of them suffered from a relapse after vaccination, but were finally discharged from hospital quite cured.

Case 7 had urethritis with pain and swelling of both knees and the left shoulder. On the day following admission to hospital he had 50 millions of stock vaccine. His left knee became more swollen and painful. Five days later 10 million were injected without result. The third dose was 100 million, which caused some reaction for thirty-six hours. No irrigation had been tried up to this date, when 1 in 10,000 solution of permanganate of potassium was used to flush out the urethra morning and evening. A fourth injection of 150 million cleared up the joint pains, but slight swelling still remained. Five days later, 150 million were injected; this aggravated the urethral condition and caused the reappearance of pus with numerous organisms in the cells. The rheumatism disappeared on the twenty-

eighth day, and a final vaccination of 200 million gonococci produced no reaction. The urethral discharge and the threads in his urine disappeared on the next day, and did not recur.

Case 8 had been treated for two and a half months by ordinary methods without success, before coming under observation. In addition to urethritis he had both right and left ankles swollen, also the plantar fasciæ were very tender to touch. He received three injections, each containing 50 million cocci, with an interval of seven days between each injection. All signs of the disease disappeared on the fourteenth day after the first dose. However, in two months a relapse of the rheumatic pains and urethritis compelled this patient to return to hospital. At intervals of three days he had the following quantities of vaccine: 70 million, 20 million, and 30 million. On the seventh day of the relapse the urine became clear and he had no urethral discharge. The fourth injection, 40 million, was given on March 23, 1911, as a slight return of pus was found. As no active signs were present, and it was considered that there was no fear of affecting the urethra at this stage, a dose of 200 million was introduced under the skin of the shoulder, on March 30, 1911, in order to eradicate the rheumatism from his ankles. A marked urethral reaction followed in two days, a large amount of blood and pus also appeared; to control the former tannic acid bougies were necessary. However, the blood and pus cleared up in a week. Two further injections of 150 million on April 6 and 11 were not felt in any way by the patient, and he has not had a relapse of rheumatism for one year. He was in hospital thirty-three days, and free from disease in twenty-eight days.

The relapse in this case was due to insufficient dosage, and during the second admission time would appear to have been lost by giving the small and frequent rather than larger doses at longer intervals.

Case 9 was admitted to hospital with an uncomplicated attack of gonorrhœa on April 11, 1911. He had acute anterior and posterior urethritis. Three vaccinations each of 20 million were given with five days interval between them. At the same time irrigation with silver nitrate 1 in 10,000 was employed. No culture was obtainable, as the gonococci were few in number. On May 17, 1911, no signs of the disease were present and the patient was looked on as cured on May 27, 1911. Two months later, however, he was admitted to another hospital with subacute gonorrhœal rheumatism of both ankles, plantar fasciæ and shoulders. A vaccine

was not given and he was treated by other methods for some months with only partial success. In January, 1912, he was re-admitted with the same condition of his ankles and plantar fasciæ as before. Bier's congestion treatment was tried by means of rubber bands and hot air, but with little result. On February 2, 1912, 20 c.c. of antigonococcal serum was introduced under the skin of the abdomen as an experiment. The effect was most unexpected, for within forty-eight hours the patient could hop on either foot without pain or discomfort, and has been well since that time.

Gonorrhœal Epididymitis.

Case 10 had few gonococci in his urethra as in each of the microscopic fields of a smear of the pus only a few organisms were seen. Irrigation with 1 in 5,000 permanganate of potash was begun from the date of admission. Injections of 20 million "local" vaccine were given on April 30, 1911, and on May 3 and 11. The discharge had ceased by the latter date and only a faint haze was visible in the morning urine; 30 million were injected on May 17. Double orchitis supervened on the 19th. As the urine cleared rapidly a further dose of 30 million was tried; the reaction was slight, and a reappearance of pus from the urethra occurred. In six days there was no further pain in the testicles. On June 13 both urethra and testicles were normal, and no further evidence of gonorrhœa has occurred.

In this case vaccine treatment did not prevent the onset of complications, but that a curative influence was exercised on the course of the disease is shown by the fact that twelve days from the date of onset of orchitis the urethra was clear and the pain and swelling had gone from the testicles.

Case 11. There was acute left epididymitis present on admission to hospital; the patient had been treated for gonorrhœa some months previous to the present attack. Gonococci were very few in number. No culture was attempted. As a routine treatment Condy's fluid irrigation was employed, in a strength of 1 in 5,000. Three weekly injections, 20, 32 and 20 million respectively, of "local" stock were administered; these succeeded in curing the epididymitis, and no further trouble has been noted, nor has a relapse occurred.

A slight testicular reaction followed the first dose, but the others were not felt locally or generally.

Acute Cases.

These are divided into two groups. Nine were treated by a locally made stock vaccine and ten with a "manufacturer's" stock. Of the patients treated by the "local" stock, none had a higher dose than 50 million, the usual dose was 20 million, and the interval one week. The final dose in most of the cases was the largest, but the dose was not varied in a number of the cases, beginning at 20 million and ending with the same quantity. Reactions were avoided as far as possible and only occurred in two of the cases; 20 million appeared to be a medium initial quantity of vaccine, and the average case did not show signs of overdosage. Of course this definite statement only applies to this special vaccine, as it might be an excessive dose for a preparation made with a different technique, or with other strains of the organism. The gonococcus was isolated in pure culture from three cases of this series, and added to the stock emulsion.

The average number of days under treatment was 50·4. The shortest time was 19, and the longest 110 days, but this was an exceptional case which had a stricture in the anterior urethra, and was not in the least benefited by vaccine.

A few other cases may be quoted, first those whom immunization seemed to affect favourably, and also in whom no change could be imputed to vaccination, either for better or worse.

Case 12 was infected on April 24, 1911, and came under observation on May 7. Gonococci were few and cultivation was not successful. Irrigation with Condy's fluid 1 in 5,000 was begun on the first day. A dose of 20 million of a 10-valent vaccine was injected on May 10, 1911, and again on May 17, 1911, and was followed by rapid disappearance of both the discharge and the urinary deposit. There were no signs of gonorrhœa on May 22, 1911, and all treatment was discontinued on May 25, 1911. No relapse has occurred for nine months and no signs could be elicited on examination on March 1, 1912.

Case 13. This was his first attack. He became a hospital patient on February 26, 1911. Examination of the copious purulent discharge from the urethra showed a pure gonococcal infection to be present, very numerous organisms being found both free and in the cells. A culture on the special medium yielded a large growth; this was added to and formed part of the polyvalent vaccine. The urethra was flushed out thrice daily with permanganate solution until March 21; there was no discharge on that

date, though a haze could be seen in both the first and second parts of the morning urine. A dose of 20 million of the above-mentioned stock was given without reaction. Two days later a similar injection did not cause a negative phase, and in forty-eight hours the urine was clear. Irrigation was then stopped, and the patient left hospital on the thirty-first day. No relapse has since taken place.

Case 14. This case was a severe one. He was admitted with a urethral abscess, and a copious discharge containing a large number of gonococci; a pure culture of the organism was obtained on the first examination of the discharge. During the first month he had irrigation with potassium permanganate in very dilute solution owing to pain in the urethra. On March 16, 1911, 20 million gonococci were injected. There was no reaction. Four days later 12 million were injected, and three days later he received a dose of 16 million cocci. At the end of the three injections he still had a discharge containing gonococci. Owing to an anterior urethral stricture sounds were passed daily until Nos. 11 to 13 sounds could be introduced through the narrowed part. Three further doses of vaccine, each of 20 million, at weekly intervals, caused the disappearance of the gonococci from the urethra, and no discharge was to be seen. Four injections of 20 million, with seven days between each of them, completed the treatment.

In this case irrigations were continued throughout the time he had vaccines. Pain was not relieved by the treatment, it disappeared gradually, and the cessation did not seem to be connected with any particular dose of vaccine. Gonococci were found during the first two and a-half months of observation. Perhaps the dosage of the organism was insufficient, as no reaction occurred during the ten vaccinations. It did not appear advisable to give a larger dose owing to the acuteness of the symptoms for a long period.

Ten cases had injections of a stock made by one of the vaccine manufacturers. The quantity most usually employed was 50 million organisms, and varied from 5 to 50 million, the latter dose was not exceeded in the acute cases.

As with the preceding cases irrigation with permanganate of potash and silver nitrate was used in addition to the vaccine. A few typical cases are here quoted.

Case 15 had a copious discharge of pus from his urethra, numerous gonococci were found microscopically, both in the pus cells and free. Five million gonococci were injected the day following his admission into hospital. No reaction resulted. On January 9, 1911, 50 million were given; this was repeated on January

22 and 29. There was a distinct reaction after the last injection, with an increase of urethral discharge, which had previously been getting less. In a few days the condition cleared up very rapidly and no signs of the disease were present in the urethra or urine. The patient was permitted to leave hospital a week later. No relapse has since occurred. The duration of his stay in hospital was thirty-five days; during the last week of this time he was apparently free from gonorrhœa.

In Case 16 gonococcus was the only organism present, but an attempt to grow it was a failure. Vaccination was carried out weekly. The first dose was 25 million, the second 50, the third was also 50 million, and no reaction occurred after any of these, but at the same time there was no appreciable change in the number of gonococci or in the amount of his urethral discharge. The fourth injection was reduced to 20 million; both gonococci and discharge diminished in the course of a week. The disease became quiescent and it was thought that a cure had been brought about. However, in a week both gonococci and discharge reappeared and vaccines were resumed. Two doses, 50 million in each, were given with an interval of a fortnight. No further recurrence has taken place for a year. This case had no other treatment but the stock vaccine. He was under treatment for exactly two months. The next case was treated in a similar manner, inoculation alone being used.

Case 17. When admitted on November 12, 1910, the urine contained much mucus and many threads. Gonococci were found scantily in the threads, but cultivation of the organism was unsuccessful. Urethroscopic examination revealed a granular and swollen state of the whole urethra, as far as could be seen by means of Casper's instrument.

On November 29, 1910, he was injected with a dose of 5 million stock vaccine. There was no reaction. At weekly intervals three doses each of 50 million gonococci were given, and on December 20, 1910, neither urethral discharge nor Thompson's "two glass" test showed any evidence of gonorrhœa. A final dose of 25 million on January 2, 1911, completed the treatment. This case was in hospital for fifty-three days; he was clear of signs in forty days. No other form of treatment was employed in this case, and no relapse has occurred in twelve months.

The other cases do not present points of any special interest. The accompanying table shows the results of this form of treatment.

	Acute Gonorrhœa.	
	No. of cases	Average No. of days in hospital.
Manufacturers' vaccine	10	48·9
Local stock vaccine	9	50·4

For at least one week of this time in hospital there were no signs of disease, as tests were carried out to prove that the gonorrhœa had ceased. By acute gonorrhœa is meant those cases which were treated from the time the men themselves noticed a discharge from the urethra. It is unusual for these men to suffer pain or scalding in the earliest stage of the disease, hence they do not come under treatment till there is a thick yellow discharge of pus from the urethra.

Although these thirty cases were in hospital more than the average time, relapses were below the average, and were quickly amenable to the treatment.

Whether dosage can be laid down is doubtful, for some men could tolerate larger doses of vaccine than others. No true anaphylactic symptoms due to the gonococcus occurred. In some cases a negative phase was observed, but this was due to an overdose.

As in other vaccines too small a dose is to be avoided for it would appear that immunity against the vaccine is the only result, *vide* Case 14.

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