VOLUME XIX. SEPTEMBER, 1912. No. 3.

Journal
of the
Royal Army Medical Corps.

Original Communications.

NOTE ON A BACILLUS OCCURRING IN SOME INTRACTABLE VENEREAL ULCERS.

BY LIEUTENANT C. H. H. HAROLD.
Royal Army Medical Corps.

AMONGST ulcerative venereal diseases not the least important is the condition known as soft chancre, a term applied to numbers of non-syphilitic lesions which are usually attributed to infection with Ducrey's bacillus. Clinically these cases present great differences, and it is questionable whether in some of them at any rate another organism is not the chief factor in their causation. Cases of this type of disease may be divided into two main groups.

Group (1)—Soft ulcers which remain in a callous condition for a few weeks and may give rise to a bubo requiring operative treatment. Surgical measures as a rule are quite sufficient to cause healing of these cases in a comparatively short time.

Group (2)—A more eroding type of ulceration, with which this paper is more intimately connected; this form is much more resistant to treatment, spreading in spite of every conceivable surgical procedure, and may destroy considerable portions of the external genitalia. The base of the ulcer is usually soft and covered with greyish granulations which secrete a viscid glutinous pus with a characteristic odour, while its cleanly cut and slightly undermined edges show no signs of reaction. These ulcers frequently cause inflammatory buboes which require

operative interference and the resulting wound exhibits the same ulcerative characteristics as those of the primary ulcer. Some buboes also which depend upon soft chancres of a simpler type than the one just described may take on this character after being opened.

This second type of ulcer is important because of its unsatisfactory response to treatment. The patient remains in hospital for many weeks or even months, being not only inefficient but causing the expenditure of considerable time and energy on the part of his medical attendants.

On account of the unsatisfactory results of purely surgical treatment it was decided to investigate the bacteriological nature of these lesions with a view to vaccine treatment. The following cases in which this was done will illustrate the value of this procedure.

A patient under the care of Major C. W. Profeit, R.A.M.C., was suffering from a slow phagedænic ulceration of the penis clinically resembling the second group of cases just described. Two-thirds of the glans penis had ulcerated away and the remaining third was attached by a small ulcerated pedicle. The ulcer also extended the whole way around the body of the penis and following the course of the urethra had penetrated for some distance into the corpus. The passage of urine irritated the ulcer and gave rise to much pain and scalding. He was also suffering from syphilis contracted at the same time. In another hospital, treatment which included three operations and vigorous anti-syphilitic measures had been carried out for seven months, but had been unsuccessful in arresting the destruction of tissue. After transfer to Rochester Row, he had been treated with salvarsan and mercury and clinically showed no signs of syphilis, while his blood for the last three months had given a negative Wassermann reaction. In spite of all this medical and surgical treatment, however, the ulceration was becoming progressively worse, and as a last resource amputation of the penis was advised; to this the patient cheerfully agreed :—

Before doing this Major Profeit suggested that it might be of interest to make a complete bacteriological investigation of the ulcer with a view to vaccine treatment. The edge of the ulcer was scraped and some of the exuded serum examined by the dark ground illumination, but no spirochætes of any description were discoverable. Some of the exuded serum was sown on several tubes of human serum agar and two kinds of organisms were

recovered from them: (1) a *Staphylococcus aureus;* (2) a short bacillus. A carbolized vaccine prepared from the bacillus was injected into the patient with rather astonishing results.

On the same evening the penis became so swollen and painful that the man was unable to sleep, and on the following day the base and edges of the ulcer had assumed a bright red colour, contrasting with their previous pale appearance, while the dressing showed an increased exudation of pus. There was also a large red tender swelling at the site of inoculation.

From this day onwards the ulceration improved and commenced to heal. The vaccine was repeated after four days and was followed by a reaction of the same type, but not so severe as after the first injection. Repeated doses of vaccine were subsequently given at four-day intervals and within a month the whole of the ulceration had healed with the exception of a small ulcer on the glans penis. The healing of this was probably delayed because the scar tissue at the base of the glans interfered with its blood supply. The patient refused to have this small portion removed, having made such rapid progress under vaccine treatment, and the small ulcer, a few millimetres broad, delayed his discharge from hospital for another month.

A few days after commencing the treatment of this case with vaccine the ulcer was again scraped and tubes inoculated with exuded serum. The same bacillus was recovered, but this time in pure culture.

My next patient was suffering from a chronic ulcerating bubo; he had been in hospital for sixteen weeks and showed no signs of improvement. Following the same method of procedure as in the previous case, the ulcer was scraped and the same organism recovered associated with a diplococcus. The same vaccine was administered and a marked reaction followed. On the night of the injection the man complained of severe pain in his thigh and was unable to sleep. The next day the whole of the groin was swollen and the bubo of a bright red colour, discharging increased quantities of pus; a large localized, red, tender swelling had also formed at the site of inoculation. Similar reactive signs, but of less severe character, occurred after each successive injection of vaccine; the man was discharged cured in less than a month from the time of commencing the vaccine treatment.

The next case clinically resembled the previous one. The patient had been in hospital for six weeks and the ulcerating bubo remained in a callous condition. The same bacillus and the

S. aureus were isolated and injections of vaccine caused the usual reactive signs in the patient, who was discharged cured in five weeks from the time of commencing the treatment.

The last patient was also suffering from an ulcerating bubo which had kept him in hospital for four weeks and bacteriological examination revealed the same organism associated with a *S. albus*. He gave the usual response to vaccine and the bubo is now rapidly healing up. Owing to my unavoidable absence from hospital the patient received one dose of vaccine instead of three in sixteen days, and during that time the bubo showed no signs of improvement.

These cases have all been treated by a vaccine made from the bacillus isolated from the first patient and grown on agar. The vaccine was sterilized by the addition of 0·5 per cent carbolic acid. The initial dose was 15 millions and this was increased gradually to 2,000 millions, the intervals between injections being four days. These have all caused marked local reactions both in the site of infection and in the site of inoculation. They were followed by little or no constitutional disturbance, the temperature of the patient rarely rising more than a degree. When for some reason the injections were withheld, or were not strong enough, the lesions lapsed to the previous callous condition. On these occasions the administration of stronger or more frequent doses of vaccine always produced a beneficial effect.

In none of the cases from which I have recovered this bacillus have I been able to find any organism corresponding to Ducrey's bacillus. The local reaction at the site of the ulcer and the marked benefit which was obvious from the commencement of vaccine treatment are strong evidence that the bacillus in question was the chief ætiological factor in the production of the disease.

Morphologically, it is a short rod-shaped organism 2·5 to 3 μ long and about 0·3 μ broad. In film preparations it is frequently seen lying in parallel rows, giving one the impression of a short palisade. It stains readily with any of the basic aniline dyes and is Gram positive. With all stains, but especially with carbol thionin, it shows marked bi-polar staining with a clear interval between the granules. These can also be demonstrated in many individual bacilli with Neisser's stain. It does not form chains, nor spores. Involution forms are frequent in cultures a few days old, the most frequent variety of these being swollen elongated forms which show no polar staining. Another form frequently seen is somewhat clubbed at one end, which is occupied by a large polar granule.

The organism is strictly aerobic, growing very luxuriantly on human serum agar as well as on 2 per cent agar (+ 6 Eyre's scale). After twelve hours incubation at 37° C., the colonies are the size of a pin's head, moist and heaped up in the centre. By reflected light they appear greyish white and with transmitted light they show a yellow centre with a lighter, well-defined margin. On microscopical examination with the low power they are finely granular with a sharply defined evenly circular margin. The colonies tend to remain discrete; in four days they attain a diameter of **3** mm. and their centres become a deeper yellow colour.

Grown on human serum it forms a grey white deposit and flocculi which sink to the bottom.

It does not liquefy *gelatine;* it grows on neutral red agar, but causes no change in the medium.

In peptone salt solution no indol is formed, while litmus milk is bleached by its action.

It ferments glucose and cane sugar, forming acid but no gas.

In lactose, maltose, dulcite, raffinose, inulin, and salicin no change is produced.

It is non-pathogenic to rabbits when injected into the blood-stream and only causes a local infiltrate when injected beneath the skin of the animal's ear.

In the "Bacteriology of Diphtheria," by Nuttall and Graham Smith, G. S. Graham Smith has collected the observations of numerous workers on the recovery of diphtheroids from the male and female genital tract. The chief varieties with their essential points of difference or similarity are as follows:—

Neisser (1888) recovered from the female vagina diphtheroids which were motile.

Berghy (1898) isolated from the urine and vaginal discharges of certain cases a Gram-positive diphtheroid which differed from the present one by forming a yellow growth on agar, by not liquefying gelatine and by forming a white membrane on broth. It was non-pathogenic to guinea-pigs and did not form acid in glucose.

Foulerton and Bonney (1903) recovered from two cases of puerperal septicæmia and from a case of phagedæna of the penis a Gram positive diphtheroid which showed no granules when stained with Neisser. Stroke cultures had the appearance of ground glass, and when grown in broth it appeared as an evenly staining rod. It did not ferment glucose and was non-pathogenic to guinea-pigs.

Pfeiffer in 1903 isolated Gram negative diphtheroids from normal men and from cases of gonorrhœa.

Graham Smith, Hallé, and Robertson and McRae have also recovered diphtheroids of a more diverse character.

On referring to the original literature I cannot find evidence that any test to prove the pathogenicity of these organisms to man was carried out, or that vaccines prepared from them exercised any therapeutic effect.

In conclusion, I wish to thank Major C. W. Profeit, R.A.M.C., for bringing these cases to my notice, and Major L. W. Harrison, R.A.M.C., for conducting the animal inoculations, and for his valuable technical suggestions.

NOTE.—Since writing the above my attention has been drawn to an article by Herbst and Gatewood, of Chicago, in the *Journal of the American Medical Association* for January 20, 1912. These workers made a bacteriological examination of a series of twenty-six soft sores, and recovered diphtheroid bacilli from sixteen of them, while a doubtful Ducrey's bacillus was found on two occasions only. A vaccine prepared from the supposed Ducrey's bacillus was administered to several patients, but with very poor results. One of the patients became steadily worse and was eventually treated with vaccine prepared from a diphtheroid bacillus and a staphylococcus isolated from the lesion. The result was excellent and subsequently other cases were treated with the same vaccine whenever an autogenous vaccine could not be prepared.

This vaccine gave rise to reactions which were exactly similar to those which I have described in my cases, but the authors do not state quite clearly in how many of the cases beneficial results followed its administration. Altogether they treated thirty-eight cases, of which thirty-nine per cent were benefited by vaccine treatment, but some of the thirty-eight were treated only with the vaccine prepared from the supposed Ducrey's bacillus. They believe, however, that if the diphtheroid or an autogenous vaccine had been used throughout the series the results would have been much better.

Guinea-pigs inoculated with a diphtheroid bacillus isolated from one of the cases developed local infiltrates; on one occasion the axillary glands became enlarged, and on another an ulcerating lesion formed at the site of inoculation from which the same organism was recovered.

They conclude that the diphtheroid bacilli isolated were the

cause of the soft sores in these cases, although organisms which are morphologically identical are commonly present in the urinary tract. They have not, however, detailed the morphological and cultural characteristics of the several organisms they isolated, so that it is impossible to identify any of them with the bacillus isolated at Rochester Row.

It seems probable, however, that the diphtheroid organism from which these workers prepared their vaccine is identical with the one which I isolated. Their methods of isolation, which were similar to mine, demonstrated the persistent presence of a diphtheroid, and the response to vaccine prepared from this micro-organism was the same as in my cases.

Their observations fully confirm those which I have independently made in indicating that soft chancres are not always caused by Ducrey's bacillus, and that the additional work expended in making a bacteriological examination of these cases with a view to vaccine treatment is amply repaid.