

THE VENEREAL ORIGIN OF GRANULOMA INGUINALE*

By T. BHASKARA MENON, M.D. (Mad.)
M.R.C.P. (Lond.)

Pathologist

and

P. NATESAN, M.B.B.S.

Assistant Venereologist, Government Rayapuram
Hospital, Madras

A CAREFUL analysis of the history of cases of granuloma inguinale very often reveals the incidence of a primary lesion on the genitalia in the form of a small pustule. This finally bursts and leaves a small non-indurated ulcer which often heals but breaks down again. One of us (Bhaskara Menon, 1933) has drawn attention to this feature in the history of cases studied in the General Hospital and the Government Rayapuram Hospital, Madras. In a series of patients, the primary lesion was followed by cicatrization and deformity of the prepuce and the patients came into hospital for circumcision. The subsequent history of these cases showed that the circumcision wound did not heal, but continued to break down till all the clinical features of granuloma were reproduced. In other instances, the sore had healed, but had broken down again and the granuloma had developed. The site of the lesion itself is, in most cases, the genitalia, and ulceration of the groin is secondary to spread of infection from the genitalia. It has been argued by Nair and Pandalai (1934) that lack of a primary involvement of the cervix and the vagina is against a venereal origin. But the fact that the organism attacks moist stratified surface epithelium of muco-cutaneous junctions and lives inside epithelial cells is enough to explain this feature. The soft epithelial cells of mucous membranes probably do not afford a footing for the organism.

In sections stained by the Weigert-Gram method, the crowding of the organisms inside the surface epithelial cells can be demonstrated. The implication of the mononuclear cells and intracyclic multiplication is a later stage in the spread of the inflammatory process.

The following three illustrative cases reveal very strong evidence of a venereal origin, besides indicating different stages of the disease:

Case 1.—Mr. A. M. K., a young Hindu of twenty-six years, was admitted to the venereal department of the Government Rayapuram Hospital, Madras, on the 3rd August, 1933, for an ulcer on the penis. The history was that the patient had a sore on the same situation six months previously. It had healed after a month's treatment, but had broken down again previous to admission. There was a definite history of exposure to infection one month prior to the development of the first ulcer. It had started as a small painless boil which had burst and had become

an ulcer. On admission, the patient had two small ulcers, each of the size of a four-anna piece, on the under surface of the prepuce near the frenum (figure 1). The ulcers themselves looked soft and vascular and they bled readily on manipulation. The base was



Figure 1

Case 1.—Showing the primary lesion on the frenum and prepuce. Stage I of granuloma inguinale.

soft and there was no induration. There was little pain and there was not the angry-looking inflamed appearance of soft sore. The glands were just palpable. The dark-ground examination was negative and the Wassermann reaction was also negative. An examination of the smears showed typical intracellular forms of the Donovan body. On treatment with urea stibamine the ulcer completely healed.

Case 2.—Mr. V. S., a young Hindu of thirty years, was admitted to the venereal clinic of the Government Rayapuram Hospital, Madras, on the 15th September, 1934. He was a resident of Nellore and had come down to Madras for treatment. He was married five years ago and his wife Mrs. P. A. was an in-patient in the venereal ward on the 13th October, 1933, and subsequently on the 7th September, 1934, for inguinal granuloma. Her case records show that the Donovan organisms were demonstrated. He himself denied all illicit intercourse. There was a definite history of exposure to infection with his wife two months prior to admission. The present condition developed a month after exposure as a small pustule on the right side of the frenum. This gradually became an ulcer.

On admission the condition was one of paraphimosis, with an oblong granulating ulcer, about 2 inches by 1 inch, extending from the meatus on the ventral aspect of the glans over the paraphimotic prepuce (figure 2). There were a number of small papular elevations all round the ulcer. The ulcer itself was indolent, not very painful, soft to the touch and covered with granulations. There was very little discharge. The groin glands were not enlarged. There were no cutaneous lesions, suggestive of syphilis; there was no discharge from the urethra. The dark-ground examination was negative, the Wassermann reaction was negative, but the Kahn test was positive. A smear from the ulcer showed typical intracellular

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forms of the Donovan organisms. Treatment was carried out by intramuscular injections of a 7 per cent solution of the trivalent antimony compound Fouadin.

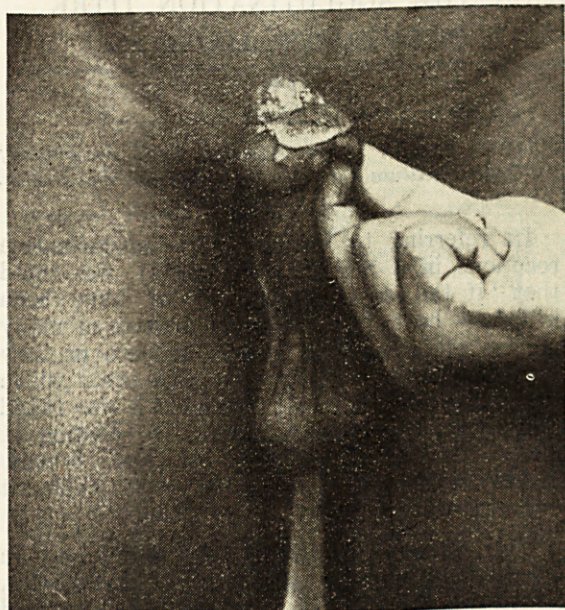


Figure 2

Case 2.—Showing the granulomatous ulcer with secondary nodules all round. Stage II of granuloma inguinale.

The ulcer completely healed after one month's treatment.

Case 3.—Mr. L. N., a young Hindu of the Komati caste, coming from Nellore district, was admitted to



Figure 3

Case 3.—The chronic well-developed lesion—granuloma genito-inguinale. Stage III.

the Government Rayapuram Hospital, Madras, in May 1934, for extensive ulcerating granuloma involving the genitalia and groins. This was of five years' duration. A careful study of the history of this case showed that, five years ago, the lesion started as an ulcer on the frenum ten days after sexual exposure. This had gradually spread around the prepuce. Circumcision was done at the Government Hospital at Ongole as the ulcer in the penis was healing and breaking down again. He remained in hospital for a month and was discharged when the wound had healed. There was a small ulcer which had developed at the root of the penis; and this had not healed. This gradually spread on to the groin on both sides and also on to the skin of the scrotum. He had been under Ayurvedic treatment for the last five years. There was no history of gonorrhœa. *Two other people who exposed themselves to infection with the same woman got similar types of ulcers, but these had healed with Ayurvedic treatment and that was why the patient persisted with this treatment for such a long period.* He was admitted into the General Hospital, Madras, where, under a course of injections, the ulcer had gradually healed but had broken down again, after discharge from hospital.

On admission, the patient had an ulcer on both sides of the groin, extending all round the root of the penis and leaving only a small area of healthy skin on the anterior aspect of the organ. The ulcerated areas in the groin had also spread across two inches above the root of the penis, forming another communicating ulcer. The whole ulcer was $6\frac{1}{2}$ inches long and $3\frac{1}{2}$ inches wide and had an irregular serpiginous margin. The base was covered with protuberant granulations which showed a few bleeding points. There was an oblique scar extending across above the ulcer, $3\frac{1}{2}$ inches long and 1 inch wide. The scrotum was extensively involved, except at the posterior part.

The dark-ground examination was negative, the Wassermann reaction was negative and Frei's test also negative. An examination of the smear showed Donovan organisms.

Discussion

In case 1 we have an instance of the primary lesions which healed and broke down again. In most cases, in our studies, this primary lesion appeared as a small pustule about three to four weeks after sexual intercourse. The pustule breaks down and becomes converted into a shallow ulcer in about a week. There is no induration. There is very little pain and the discharge is only slight, unlike a soft sore. The ulcers are sometimes multiple. In most cases, there is a definite history of healing followed by subsequent breaking down of the ulcer. Very often there is ulceration at the root of the penis or of the skin of the scrotum, probably by auto-inoculation. The involvement of the moist sodden skin of the genito-crural folds is, in our experience, always a secondary event. In earlier studies, one of us (Bhaskara Menon, 1933) raised the question whether granuloma venereum could be regarded as a secondary infection to some other lesion, such as a soft sore on the genitalia; but subsequent work has shown that the primary sore itself is, to some extent, distinctive and could be differentiated from soft sore. The ulcer is indolent in type, there is no angry-looking inflamed base, there is very little pain and no marked involvement of the lymphatic

glands. Examination at this stage has shown that Ducrey's bacillus cannot be demonstrated, but the typical intracellular forms of the Donovan body can be found in smears from the surface, as in case 1, if a careful search is made for the organism.

In case 2 we have an instance of a more advanced type of lesion, following the primary sore. This may be regarded as the second stage of the disease with persistence and chronicity of the penile lesion. The picture here is that of a well-developed granuloma with commencing secondary nodules, all round a chronic granulomatous ulcer confined to the glans and prepuce. The definite venereal history in this case is one that cannot easily be refuted.

In case 3 we have a picture of the well-defined and typical lesion in what might be called the third stage of the disease. Here the granuloma has spread to the groin and there is extensive involvement of the penis and scrotum. The definite venereal history in this case and the history of a similar disease in two other people, though not directly confirmed, reminds one of the case of Mary X, as recorded by Stoddart, when the syphilitic origin of general paralysis was demonstrated.

Summary and conclusions

Our views regarding the venereal origin of granuloma inguinale are re-affirmed. Three illustrative cases are recorded showing the three stages of the disease: a primary lesion, a second stage with the commencement of the granulating lesion with secondary nodules, and a third stage with an established chronic lesion—granuloma genito-inguinale.

In our experience, a careful analysis of the history of cases of granuloma inguinale would reveal a venereal history in a large proportion. In others, there are extra-genital lesions and these can be explained as due to extra-genital inoculations, as in syphilis.

Acknowledgment

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THE EFFECT OF THE USE OF LIVING OR DEAD SUSPENSIONS OF VIBRIOS ON THE AGGLUTINATION TITRE

By RICHARD W. LINTON, Ph.D.

and

S. C. SEAL, M.B.

(Cholera Inquiry, Indian Research Fund Association; All-India Institute of Hygiene and Public Health, Calcutta)

In referring to cholera vibrio agglutination reactions in a recent paper (1935), we stated that 'if the antigens are old or have been killed by heat the agglutination titres of many vibrios are sometimes greatly reduced or may even be absent'. In the case of a strain which we used to illustrate this statement it was found that after it had been killed by heating at 60°C. for half an hour it had become inagglutinable with antiserum with which it agglutinated at 1:1,000 when living.

This observation was of interest not only in its bearing on the structure of the vibrios, which was the point of view from which we had approached it, but also in the practical use of the agglutination reaction for the diagnosis of cholera. We have accordingly studied it further.

Antisera against the following strains were used:—

'Rangoon smooth' and 2027, which are typical vibrios isolated from cases of cholera;

W880, a vibrio isolated from water, which does not agglutinate at all or only very slightly with anti-cholera sera;

El Tor, an agglutinating vibrio of human origin not found in a case of cholera;

and 'Rangoon rough' (2) an extremely rough non-motile variant of 'Rangoon smooth'.

These were set up against the strains named in the table which in addition to those already mentioned comprise:—

vibrios 1617 and 505, which are strains isolated from cholera cases;

'Rangoon rough' (1), a rough vibrio isolated from the same case as 'Rangoon smooth';

and 'Rangoon rough' (2a), a smoother vibrio isolated from the extremely rough 'Rangoon rough (2)'.
(2)'

The killing of the vibrios was carried out by heating them for half an hour at 60°C. in the water bath. The suspensions were of a concentration of approximately 2,000 million per c.cm. before dilution with equal amounts of the diluted antisera. Readings were made after 4 hours at 56°C. and again after the tubes had stood overnight in the ice-box. The titres given represent the dilution in the tube showing at least '1-plus' agglutination; 'plus-and-minus' readings were neglected, as also were titres below 1:50.