LYMPHOGRANULOMA INGUINALE (TROPICAL BUBO)

BY

F. A. R. STAMMERS, Ch.M., F.R.C.S.

Brigadier, A.M.S.; Consulting Surgeon, Western Command

With men of the Services scattered throughout the world it is certain that some tropical diseases will be met with increasingly in the United Kingdom. In times of peace small numbers of cases have always been encountered at seaports, but they are now arriving at inland hospitals; and some of the less-well-known ones will at first puzzle those whose lot it is to treat them.

One of the diseases very common among the natives of West Africa is tropical bubo, or lymphogranuloma inguinale ("L.G." for short), and as it also affects Europeans, though in smaller numbers, it will from time to time appear in hospitals at home. Having recently returned from a continuous service of 20 months in Sierra Leone, during which time my colleagues and I saw well over 300 cases of this disease, including about 30 in Europeans, a brief description of it based on this experience may be of help to those meeting their first few cases.

Aetiology.—It is a virus disease of venereal origin, occurring in the Tropics. It affects both sexes—the men by a primary lesion on some part of the genitalia, followed by enlargement of the glands in the groin; the women by vulvovaginitis, esthiomene, and proctitis, the last-named leading to stricture of the rectum, of which I saw very few cases, and these only while working for three months at Colonial Medical Service hospitals during 1941. Only as the condition affects the male will it be discussed here.

Symptoms

The primary lesion—in the form of one or more very small vesicles, pustules, or ulcers, rather like herpes, usually on the glans and inner surface of the prepuce, but also sometimes on the body of the penis—develops within a few days of intercourse, and unless complicated by superimposed infection is of fleeting duration. It causes little or no discomfort, and the patient scarcely ever presents himself at this stage. A few weeks later—3 to 8 weeks—a gland in one or both groins enlarges, usually at the inner end, though not uncommonly at about the middle, and on two occasions I saw the outer ones involved. By this time the primary herpetiform lesion has usually cleared up, though where the glands have enlarged early several minute scabs may remain as evidence; but, as has already been said, the primary lesion is essentially fleeting, and more often than not is entirely unnoticed by the patient, and therefore denied. This may be because, in the uncircumcised, if the prepuce is long and tight, where washing facilities are restricted owing to water shortage, or when the man has never been taught the wisdom of keeping himself clean, it is not uncommon to get a mild balanitis, so that the man thinks the primary of L.G. the same thing. However, L.G. is not confined to the uncircumcised.

It is therefore almost invariably for the enlargement of the glands that the patient seeks advice, and this rarely less than three weeks, and usually around six weeks, after the risk of infection. At first it may be entirely painless, in which case the patient either reports in order to find out the significance of the swelling, or not at all. Later on, however, pain develops. The condition then progresses through such constant phases that definite stages may be recognized: I have described these in official reports, and I repeat them here since the classification is a useful one upon which to base treatment and prognosis. It was described in 1942 in the *West African Military Medical Journal*, in collaboration with Major W. A. Law, R.A.M.C.

Stages of the Condition

Stage I.—A solitary, elastic, freely movable gland, adherent to neither skin nor deeper structures. Little or no constitutional disturbance. Rarely tender, but physical activity may cause pain.

Stage II.—The solitary gland becomes adherent to the skin and deeper structures, and there is a tendency for surrounding glands to enlarge, becoming fused with the original one. In Europeans it is common for the glands along the external iliac

artery to be involved, sometimes forming a large mass above Poupart's ligament, and later spreading up to the common iliac and even aortic glands. In some instances there is a brawny mass in the groin, with *peau d'orange* appearance of the skin. The mass is tender and painful but non-fluctuant, and the constitutional upset considerable: temperature up to 103° F., pulse around 100, malaise, anaemia, bronchitis, jaundice, etc. This constitutional disturbance is always more pronounced in the European than in the native. A section of the original glands at this stage has a very characteristic appearance, looking like a gland packed with tiny abscesses.

Stage III.—The original mass, be it large or small, softens in one or more places, and fluctuates, and the general condition of the patient improves. I have never seen the glands along the external iliac artery break down. On section the softened area consists of a cavity broken up by interlacing trabeculations of fibrous tissue and containing sterile, glairy, sticky fluid that adheres to the knife, the whole process being the result of coalescence of the earlier tiny points of necrosis.

Stage IV.—Spontaneous fistulation has occurred and secondary infection quickly follows.

Comments on Diagnosis

It is, of course, essential to examine thoroughly for any other source of infection. Ulcers are so common on the legs of natives that doubt may arise as to the true nature of the glands. In the same way abrasions on the skin, chafing by the boot, athlete's foot, etc., may be a source in the white man. The Frei intradermal test will here be of great help, and gives a reliable result in 90% of cases. Small lesions in the urethra have been described, but none was seen in a series that we urethroscoped. General congestion of the urethra, on the other hand, was common.

In brief, it may be said that a mass confined to one or both groins, conforming to any of the four stages described, in the absence of any other possible source of infection and with a positive Frei test, spells lymphogranuloma inguinale. The condition most likely to be confused with it in Europeans is tuberculous glands, and we made this error in our first European case. However, the Frei test was not then available, but is the differentiating point.

Treatment

There is no doubt that among natives a number of cases never pass beyond Stage I, and subside spontaneously without the men ever reporting sick. It is an observed fact, too, that in some of those reporting in Stage I and put to rest in their billet for a few days the condition subsides spontaneously. But the difficult case is the Stage II one that in spite of rest shows no improvement but rather a worsening. It is to such cases that this communication especially draws attention, since the European behaves in this manner—hardly ever clearing up spontaneously, even in the rare event of not progressing beyond Stage I; the vast majority pass well into Stage II with marked constitutional effects. The various lines of treatment available are as follows:

1. Rest in Bed.—Local applications of heat to the glands by fomentation, antiphlogistine, or radiant heat and infra-red lamp.
2. Intramuscular injections of anthiomaline (10 to 20 injections), an antimony preparation, as described by Major W. A. Law in the paper already quoted.
3. Intravenous injections of sodium antimony tartrate.
4. Large Doses of Sulphonamide.—We began with sulphapyridine, giving as much as 96 g., spaced over 3 to 4 weeks, in three courses. Careful watch on the white cell count must be kept. Later on, because of the higher price of sulphapyridine, we ran a series on sulphanilamide, using about the same amount, at roughly one-third of the cost. Later on still, we treated some natives with intramuscular injections of a suspension of sulphapyridine in water. This requires about one-quarter of the above amounts, and was seemingly just as successful. The method was a natural sequel to the highly successful treatment of gonorrhoea in this way by Capt. England and others on the West Coast. Care has to be taken not to inject the drug near a large nerve root, as cases of permanent interstitial neuritis have been reported, though no accident occurred at a general hospital where this work was carried out. In order to avoid the risk of such a catastrophe the vastus externus muscle is the site of election.
5. Injections of triple typhoid vaccine (T.A.B.) 50 millions intravenously—about six injections at three-day intervals.

6. Surgical Excision.—We tried a small group of cases by this method. Those in Stage I do well, healing by first intention and requiring about ten days' hospitalization followed by a week's convalescence. Early Stage II cases can be treated by excision too, but the wound is liable to become moist, and in the brawny stage surgical intervention is contraindicated, the wound always breaking down.

Comments on Treatment

The untreated Stage II case will never resolve spontaneously—it tends to linger in Stage II for weeks and then the mass breaks down. Treatment by local heat hastens this breaking-down process but rarely encourages resolution. The various drug methods, on the other hand, cause a large proportion to resolve—often quite quickly; but even where this does not occur the mass breaks down quickly, and so in either event a prolonged Stage II is avoided. The majority of cases treated with anthiomaline, sodium antimony tartrate, sulphonamides, or T.A.B. are cured, apart from a little residual thickening in the groin, and fit to return to their units in 3 to 4 weeks; anthiomaline is perhaps the best by a few days, but it is expensive. Its chief advantage is that, where constitutional reaction is not great, it can be given to the man in his unit M.I. room, whereas the others require bed treatment. However, as most Europeans do get a marked constitutional disturbance, the point is not so important.

Stage III has been treated in many ways, and there is a natural temptation to incise the fluctuating swelling. This, however, is the worst possible treatment, for experience shows that secondary infection rapidly develops and the wound continues to discharge for weeks. All are agreed that under no circumstances should incision ever be practised. The best treatment is aspiration, which may have to be at several points because of the tendency to loculation, and it may have to be repeated once or twice. It must be carried out with aseptic precautions, and the punctures should be covered with a patch of sterile gauze and elastoplast. Another method is to use a seton, and a piece of silkworm-gut transfixing the cavity serves well, though the device is not so satisfactory as aspiration.

The treatment of Stage IV is really the treatment of the secondary infection; a combination of dry heat and sulphonamides, with rest in bed, is necessary, and is eventually effective.

Recurrence.—A small proportion of our 300 cases showed recurrence of the glandular swelling, but this soon subsided under the influence of a second, shorter, course of the original treatment.

I should like to acknowledge the work of the various officers who successively took charge of the V.D. Department, and to express thanks to Colonel L. A. Harwood, T.D., the commanding officer of this unit, for permission to publish these cases.

ARSENICAL ENCEPHALOPATHY A COMPLICATION OCCURRING DURING THE TREATMENT OF SYPHILIS

BY

R. B. NELSON, M.B., D.P.H.

C. McGIBBON, M.B., Ch.B.

AND

F. GLYN-HUGHES, M.D.

The results obtained from the adequate treatment of syphilis with arsenical compounds are among the most gratifying in medicine. Most of the lesions disappear rapidly, and in the primary and secondary stages the Wassermann reaction is quickly reversed to normal, while subsequent treatment in these stages invariably results in a complete cure. The treatment, however, is not without the risks attendant on the administration of a powerful drug, and the toxic effects of arsenical therapy are many and varied. Fortunately the vast majority are mild, and the more severe types, such as deep jaundice and exfoliative dermatitis, are relatively uncommon. But it is to one of the rarest and most fatal complications, haemorrhagic encephalopathy, that we wish to draw attention.

During the past 18 months we have had opportunity of witnessing four cases which we consider typical of this condition. These patients were admitted to the wards after treatment as out-patients at the local clinics, and they are the first cases recorded during the nine years' existence of the wards.

Case I

A man aged 50 first attended the out-patient department on Nov. 21, 1940, with lymphopathia venerea. A positive test to Frei antigen was obtained. A Wassermann test was made as a routine measure; the result was doubtful. Four days later the test was repeated, and a strongly positive reaction was obtained. The patient gave a vague history of a penile ulcer in 1910. On Nov. 28, 1940, he began a course of mapharside and bismuth consisting of alternating bi-weekly doses of 0.04 g. and 0.06 g. of mapharside, and bismuth 0.2 g. bi-weekly. Five injections were given, and on the day following the last he was admitted to hospital in deepening coma. The pupils were small and equal, but responded to light. His knee- and ankle-jerks were present and equal, and the plantar response was flexor. His respirations were stertorous and he was doubly incontinent. There was no paralysis of the limbs, and the attitude of the hands and feet was at times strongly suggestive of tetany. Lumbar puncture showed that the fluid was under slight pressure. Fifteen c.cm. was removed, and 1 c.cm. of adrenaline was given four-hourly. Subsequent examination showed the cerebrospinal fluid to be normal. The temperature, which was 100.4° F. on admission, rose within a few hours to 104.2° F., and the man died.

At necropsy the brain was extremely congested on the surface. The cut surface showed very marked congestion of the small blood vessels in the white matter of both hemispheres. Microscopical examination revealed minute haemorrhages surrounding the small vessels. The only other positive finding was a pronounced fatty change in the liver.

Case II

A woman aged 22 attended the clinic with a gummatous ulceration of the hard and soft palates and ulceration of the left tonsil. Her father had a history of syphilis, and she was considered to be a case of congenital tertiary syphilis. She was 27 weeks pregnant. Her Wassermann reaction was strongly positive. Treatment began on March 10, 1942, with N.A.B. 0.3 g. and Bi 0.2 g. The patient returned on March 17 and was given N.A.B. 0.45 g. and Bi 0.2 g. On March 19 she complained of some headache and dizziness. She relapsed into coma and was admitted to hospital with athetoid movements of the left hand. On lumbar puncture the cerebrospinal fluid was under slight pressure. About 10 to 15 c.cm. was removed, and adrenaline 1 c.cm. was given. A slight increase in protein was found in the fluid. In a few hours the temperature had risen to 109° F., and the patient died.

Examination of the brain showed haemorrhages arranged in a symmetrical fashion in the medulla, both hemispheres, and the corpus callosum. The haemorrhages were punctiform and grouped together, occasionally coalescing to form a larger haemorrhage. They were particularly numerous in the white matter surrounding the basal ganglia, but were also present in the basal ganglia themselves.

Case III

A 24-year-old multipara was admitted to hospital on Jan. 29, 1941. It was her third pregnancy, the previous two having been stillbirths. She showed no clinical signs of either acquired or congenital syphilis. The Wassermann reaction and the Meinicke test were both strongly positive. She was then 32 weeks pregnant.

Treatment was given as follows. Jan. 30: N.A.B. 0.15 g., chlorostab 0.16 g. Feb. 3: N.A.B. 0.3 g. Feb. 6: N.A.B. 0.3 g., chlorostab 0.16 g.

Subsequent Course of Events.—Feb. 7: Patient complained of headache and nausea, vomiting once or twice. Feb. 8: The vomiting restarted and increased in severity. Eventually she became irrational and delirious. On examination there was no evidence of oedema or of renal tenderness. Her blood pressure was 155/90. A catheter specimen of urine showed no albumin, but sugar a trace and acetone ++. On auscultation the foetal heart was heard. A provisional diagnosis of toxæmia of pregnancy was made. An intravenous saline drip was set up and morphine given. Feb. 9: The patient was now comatose. There was spasticity of the arms, pupils were unequal, and the right plantar reflex gave an extensor response. Nothing abnormal was observed in the fundi. A lumbar puncture was done for diagnostic purposes. The cerebrospinal fluid was clear and not under pressure. There was no blood present. Treatment was given to reduce the cerebral oedema—viz., 50 c.cm. of 50% glucose intravenously and a solution of mag. sulph. 50% P.R. In the evening of Feb. 9 the patient died, the temperature rising to 104.4° F. before death.

Post-mortem Report.—Brain: There were punctate haemorrhages in the centrum ovale and in the roofs of the lateral ventricles. Microscopical examination showed multiple haemorrhages into the white matter. These usually had an obvious perivascular distribution.