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LYMPHOGRANULOMA INGUINALE (PORADENITIS)*

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MY own experience of climatic bubo or lymphogranuloma inguinale is limited to Indian and European sailors and others of the male sex returning from China, India, West Africa, South America and other tropical countries. It is undoubtedly more common in hot climates and amongst coloured people. The disease as we see it is characterised by subacute or chronic inflammatory changes in the inguinal or inguinal-crural group of glands which frequently break down, suppurate and form sinuses. Periadentitis is marked. There is almost invariably a history of intercourse with coloured women during leave in ports. Constitutional symptoms are common, but by the time the patients are seen at the Hospital for Tropical Diseases the herpetiform primary lesions are not generally evident, and fever, if initially present, has often disappeared. Complications in the male include elephantiasis of the penis, scrotum and lower limbs, and in most instances at least follow radical excision of the glands. Stricture of the rectum is much rarer in males than in females. I have seen one such case in a male from South America ; fistulæ were present, and there was a history of gonorrhœal proctitis and syphilitic infection as well. The Frei test in this case was positive.

The historical aspects of the disease have been very ably reviewed by Stannus¹ in his recent monograph on the subject and call for no reference here, except perhaps to point out that Manson, at the beginning of the present century, stated he had seen many cases of climatic bubo

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in China and believed the virus gained entry *viâ* some lesion on the leg or genitals. The majority of patients seen in this country are imported from the tropics and subtropics, but definite cases where the infection has been acquired in England have been reported by Stannus² and Anwyl-Davies.³ On the Continent the disease has been found in most cities in which it has been looked for, including Berlin, Hamburg, Paris, Stockholm and Bucharest, and in the United States it specially affects the negroid population.

CLINICAL MANIFESTATIONS

Primary Lesion.—The most characteristic form for the primary lesion is a small herpetiform vesicle, circular or oval in shape, which sometimes suppurates. The lesions are sometimes multiple and of small size, varying from a sago grain to a split pea. They are transitory, heal spontaneously, and generally pass unnoticed by the medical attendant as well as by the patient. Common sites for the primary lesion in the male are the coronal sulcus, but they may also occur on the inner surface of the prepuce, on any part of the glans penis or have an intra-urethral distribution. Some authors have described the primary lesion as a papule 3 to 4 mm. in diameter, and a third type of lesion consisting of a small, hard, elastic nodule 5 to 10 mm. in diameter, lying deeper in the tissues of the penis, has been recorded. Inflammation and thickening of the dorsal lymphatic of the penis has been described, but most patients develop adenitis without any specific lymphangitis being observed. Several instances of extra-genital infection amongst surgeons have been reported.

Incubation Period.—From a few days to three weeks may elapse between the infecting coitus and the appearance of the primary lesion (Frei, Hoffmann and Hellerström).

Adenitis.—Enlargement of the glands follows in from one to eight weeks, the earliest symptoms being stiffness and aching in the groins on walking, associated with or followed by the appearance of swelling. At onset, the enlarged gland is slightly tender, movable and unassociated with changes in the overlaying skin; it invariably belongs to the medial group of inguinal

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lymphatic glands. Subsequently the swelling may disappear spontaneously, develop slowly for many months, or suppurate. Typically, the whole group of inguinal glands or inguino-cruro-iliac glands are involved. Periadenitis is a conspicuous feature: the conglomerated mass of glands is hard and fixed and adherent to the overlying skin which develops a purplish colour. Severe pain rarely if ever occurs apart from secondary infection. About one-third of the cases show bilateral involvement, and often the iliac glands are palpably enlarged as well, though they do not break down and suppurate like the inguinal ones. In my experience at least two out of every three cases show enlarged, palpable iliac glands. Rarely, suppuration may occur in the intra-abdominal glands with the formation of a loin abscess. The incidence of suppuration in the inguinal glands is unknown, but not infrequently multiple foci of suppuration occur with the production of fistulæ from which thick, yellowish-white, tenacious pus exudes. Sometimes small abscesses are formed. Once suppuration has occurred it may take from two to twelve months before the condition is healed. General adenopathy and splenic enlargement have been reported. Their incidence must be very rare and in those who have been to the tropics one has to be very careful in ascribing splenomegaly to such a cause.

Constitutional Symptoms.—These vary considerably, but are seldom entirely absent. They include lassitude, prostration, anorexia, nausea, vomiting, loss of weight and fever, which may be associated with rigors and sweats. Fever is by no means invariable: when present, it may be of short duration and disappear in a few days, or it may be much more prolonged so that enterica is simulated. In other cases remission of fever may occur, to be followed after a quiescent interval by relapse due to the extension of the process locally.

Rheumatic and Skin Manifestations.—Articular joint pains, diffuse swelling about the joints and actual arthritis have been described. Erythema nodosum, which has been reported by a number of observers, including Hellerström,⁴ is stated to appear from the sixth to the eighth week after the onset of adenitis. Apart from joint pains, none of these manifestations have been observed amongst sailors in the Hospital for Tropical Diseases so far as I am aware.

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LABORATORY DATA

(1) *Pus*.—The pus obtained from the buboes by aspiration is bacteria-free and contains large numbers of degenerated pus cells, but if it is inoculated into the groin of a series of guinea-pigs, one or more may develop buboes as shown by Findlay.⁵ It is not improbable that the virus has died out in certain specimens of pus, and this may be the reason why some do not make satisfactory antigens. The virus itself passes through the Berkefeld filters, and can be transmitted to both mice and certain species of monkeys by intra-cerebral injection.

(2) *Gland Section*.—On section the glands are found to be matted together and often show a reddish tinge. Focal softening and suppuration is frequently noted, and cavities may be found filled with muco-pus of a greenish or grey colour. Microscopic examination reveals granulomatous tissue composed of fibroblasts, epithelial cells which often present a palisade arrangement, polymorphonuclear leucocytes and occasionally giant cells; the microscopical picture is by no means always atypical.

(3) *Blood Changes*.—These are in no way characteristic. There may be a mild degree of anæmia, but frequently the red cell counts and hæmoglobin percentage are normal. The total leucocyte count varies from 6,000 to 15,000 cells per cubic millimetre, and at different stages in the disease there may be a relative increase in different cell elements.

Frei's Intracutaneous Test.—The skin test devised by Frei⁶ in 1925 has been an important factor in determining the incidence of the disease in the community and recognising its more uncommon clinical manifestations.

Preparation of Antigen.—The antigen may be prepared from pus withdrawn by aspiration from the bubo before fistulæ have formed. The pus must be bacteriologically sterile and free from blood. It is mixed with 5 parts of saline in a sterile tube, stored in jena hard-glass ampoules, and heated to 60° C. for two hours in a water bath, and for one hour at 60° C. on the following day. Subsequently it should be tested for sterility under aerobic and anaerobic conditions. The antigen is stated to remain active for several months, but this is by no means always the case. Antigens have also been prepared by grinding up infected gland tissue with saline. Recently Grace and Suskind⁷

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manufactured an antigen from the brain of mice infected by intracerebral inoculation with the virus, and this is now on the market in America.

Technique of the Test.—After disinfecting by alcohol, the skin of the underside of the forearm is injected with 0.1 c.c. of antigen and a corresponding area on the other side with 0.1 c.c. of normal saline. Normal controls should be similarly inoculated. The result is read after forty-eight hours. A positive reaction is recorded if there is a palpable infiltrated, inflammatory, dome-shaped area, 0.5 mm. in diameter or larger. In the centre of the papule there may be a small area of necrosis and surrounding it an area of erythema. Sometimes vesiculation or pustulation ensues.

Results of the Test.—Failure to obtain positive reactions in known cases should lead to suspicion in regard to the activity of the antigen. Our experience at the Hospital for Tropical Diseases suggests that some specimens of sterile pus obtained under the conditions which Frei describes are non-antigenic, and it appears advisable to test all such specimens by intracerebral inoculation of mice to see if they contain potent virus before they are accepted for use. With a number of antigens strictly prepared according to Frei's directions we have observed negative results. Last year, when in New York, I saw tests performed by Grace and Suskind with their mouse-brain antigen; the results appeared satisfactory. Unfortunately, Strauss and Howard⁸ have recently reported that if normal mouse-brain be stored for more than a month it gives rise to positive reactions in normal people. Should this be confirmed it makes it improbable that the mouse-brain antigen will be of clinical value.

Specificity of the Reaction.—The mass of evidence in the literature definitely supports the view that the test is specific. Careful controls, however, must always be made. From this viewpoint the substitution of sterile pus produced by chemical means and heated at the same time as the bubo pus utilised as antigen would be vastly superior to the usual saline control which is invariably negative. A series of normal people must also be inoculated with each fresh batch of antigen, and this should be retested from time to time as it may deteriorate with keeping.

Significance of the Reaction.—Once a positive reaction has become established, it may remain positive for life;

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in other cases positive reactions become negative after some years. A positive reaction only means that at some time or other the patient has been infected with the virus ; it affords no index to present infection.

TREATMENT

Medical treatment is far from satisfactory, the very multiplicity of remedies being the surest index that no true specific has yet been discovered.

General treatment is important and consists of bed rest, fresh air, a well-balanced nourishing diet adequate in vitamins and the usual tonics. Where there is anæmia with a lowered hæmoglobin value iron is indicated.

In the early stages, especially when the disease is confined to the medial group of inguinal glands, excision may produce most satisfactory results. The temperature soon falls and healing rapidly ensues. If sinuses have developed or the crural glands be extensively involved, operation is contraindicated owing to the danger of elephantiasis of the scrotum or limb supervening. Where pus is present, aspiration under strict asepsis should be performed. Non-specific protein therapy as advocated by Hanschell ⁹ is worthy of trial, a series of intravenous injections of T.A.B. vaccine being given at three- or four-day intervals, commencing with 100 millions, and increasing by 100 millions to 400 millions per cubic millimetre. Antimony compounds, including tartar emetic, stibenyl, fouadin, etc., have their advocates, whilst local X-ray treatment has on occasion appeared useful. The value of vaccine therapy has not yet been assessed.

In long-standing cases fistulæ may need to be opened up and plugged with B.I.P.P. or iodoform gauze.

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