NATURAL HISTORY OF ARTHRITIS FOLLOWING VENEREAL URETHRITIS

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The aim of this paper is to present personal clinical observations on the natural history of arthritis associated with genital infection, but it is necessary first to review some of the earlier descriptions of the condition and to discuss its relationship to the gonococcus.

Previous Investigations

Harkness (1950) and McCahey (1933) stressed the important contributions of Brodie (1818, 1836), Fournier (1868), and Launois (1899) in defining the characteristics of this form of arthritis. Many casual references to joint involvement in "gonorrhoea" can be found in the literature of the 19th century and earlier, but these authors first reported cases in sufficient number and detail to construct the predominant patterns of the disease.

Brodie (1818, 1836) reported case histories of six patients with the symptom complex of urethral discharge, arthritis, and inflammation of the eyes:

- (i) In a man aged 45, arthritis and conjunctivitis developed about a week after a urethral discharge. The joints of the feet and knees were first involved and later the right elbow and shoulder were painful but without "any perceptible swelling". The attack lasted 6 to 7 weeks; 6 months later he had "another attack of the same complaint" lasting about 6 weeks, and after 3 months iritis occurred. He subsequently had a second attack of iritis 4 years later.
- (ii) The second patient suffered nine attacks in the course of 20 years. "In three of the attacks purulent ophthalmia was the first symptom; in one of them the first symptom was inflammation of the urethra, although from particular circumstances, he could not believe that he had been exposed to the risk of infection. In four other attacks the affection of the joints took place without any preceding inflammation either of the eye or urethra". Three isolated attacks of "inflammation of the sclerotic coat and iris of one eye" occurred over a subsequent period of 4 years.

- (iii) In this patient "symptoms resembling gonorrhoea were followed by a purulent ophthalmia and inflammation of the synovial membranes;" 5 years later "he had a similar attack", and after a further 2 years "he still laboured under a chronic inflammation of the synovial membranes of the knees and ankles, the consequence of the last attack, by which his lower limbs were completely crippled".
- (iv) The fourth patient complained of "a severe ophthalmia which was followed by inflammation of the urethra, and then the joints became affected".
- (v) This patient "laboured under strictures of the urethra. He had four attacks of the disease in the course of a few years. The inflammation of the urethra was in all of them the first symptom; which was followed by purulent ophthalmia and afterwards by inflammation of the synovial membranes and swelling of nearly all the joints".
- (vi) The report of the sixth case is found in the 4th edition (1836). Two days after a long ride on horseback a slight swelling of the left knee developed in a man aged 23. About 10 days later "a slight purulent discharge took place from the urethra with little or no pain". The knee then became very painful and swollen, but it had "entirely disappeared and he was quite recovered" in 2 weeks. Conjunctivitis accompanying the other symptoms was transient, but "the purulent discharge from the urethra continued for some time afterwards".

It is possible to construct from the above descriptions a fairly definite disease pattern of recurrent episodes of acute urethritis, arthritis, and conjunctivitis. Usually the urethral discharge preceded the other symptoms, and occasionally (Case *ii*, above) some of the attacks occurred without ocular or urethral symptoms. The arthritis affected the knees, ankles, and feet predominantly, but one patient had "swelling of nearly all the joints". The condition was evidently a self-limiting disease, and the only record of permanent joint damage is contained in the words "his lower limbs were completely crippled". A frequent sequel was recurrent iritis.

Fournier (1868), writing from Paris on *rhumatisme blennorrhagique*, brought forward evidence to differentiate between this form of arthritis and rheumatic fever. He gave case reports of 21 male patients, of whom ten had recurrent attacks, up to four in number, and thirteen had involvement of the eyes. The descriptions enable us to add further details to the picture of "gonorrhoeal" arthritis.

Hydrarthrosis of one or both knees was frequent (Cases 2, 6, 11, and 19), and involvement of the toe joints was mentioned specifically in Cases 2, 6, and 11. The classical painful heel (*douleur exactement localisée sous un talon*) was observed in Case 6. Case 18 demonstrated in the second attack a number of characteristic features: pain in a costo-chondral junction, localized bone tenderness over the tibial tubercle and head of the ulna, and tenosynovitis. In Case 7 conjunctivitis was seen with urethritis in 1861 and 1865, but there were no associated symptoms when this patient had urethritis in 1864, and at no time did he have arthritis. The case reports gave little information on the duration of the attacks of arthritis, but in Case 2 the third attack of severe polyarthritis confined the patient to bed for 5 months, and a further 2 or 3 months elapsed before the stiffness had gone. The second attack of arthritis in Case 18 lasted 5 months, and in Cases 14 and 21 the arthritis was reported as continuing for 4 months.

Launois (1899) gave a detailed account of the relapsing course of the disease. A paper on *arthropathies récidivantes* included a clear description of keratoderma blennorrhagica appearing during a severe and prolonged attack of urethritis and arthritis, which towards the end of its course was complicated by iritis. Failure to find the gonococcus suggested that this organism was not responsible for the disease in this patient.

Having first had gonorrhoea at the age of 20, the patient contracted, 10 years later, a recurrence of the "gonorrhoea" associated with arthritis lasting 3 months. At the age of 33, urethritis was again complicated by arthritis, and this attack subsided completely after 5 months, but the arthritis relapsed 6 months later and complete recovery was delayed until the end of a further 7 months.

At the age of 39 a fifth attack of urethritis occurred. As on the previous four occasions arthritis appeared, first affecting the ankles, but spreading in about 2 weeks to the elbows, the left wrist, and the right knee. A severe illness followed, with marked wasting, weakness, anaemia, and an extremely painful polyarthritis. The head was described as being fixed on the shoulders, the spine was tender, and flexion and extension of the body were impossible. It was noted that the temporomandibular joints and finger joints were unaffected, and Launois emphasized that the lower limbs bore the brunt of the attack and that there was severe arthritis in the feet. He described the generalized skin eruption and continued: *le bord interne de chacun des gros orteils est le siège d'une prolifération épidermique énorme, disposée sous forme de stratifications. Ces croûtes cornées, véritable kératoses, . . .* In describing his failure to recover the gonococcus, he wrote: *La pression de l'urètre, méthodiquement pratiquée, permet*

d'obtenir quelque gouttes de muco-pus . . . L'examen bactériologique du pus et de l'urine, pratiqué à plusieurs reprises, n'a jamais permis de constater la présence du gonocoque; par contre le colibacille existe en grand abondance dans l'urine.

In the fifth month of this attack, at the time that iritis developed, improvement in the joint condition occurred and continued over the next 3 months.

Unfortunately Launois did not state the degree of improvement and whether or not the joints returned to normal. A photograph of the patient's knees and feet has been reproduced (Fig. 2a, p. 185, below) to show the characteristic appearances so commonly found in the latter stages of this disease.

During World War I further evidence was brought forward to establish the non-gonococcal origin of some of these cases and for the first time the triad of urethritis, arthritis, and conjunctivitis was separated into the venereal and the post-dysenteric forms.

Waelsh (1916) noted, amongst 44 patients with abacterial urethritis of venereal origin, one with rheumatic pains of the knees and ankles, and one with conjunctivitis. Fiessinger and Leroy (1916) and Reiter (1916) each noted the triad of symptoms following bacillary dysentery. The post-dysenteric syndrome in the incomplete form had, however, been reported earlier, for many authors had noted already the occurrence of arthritis following dysentery, and Markwald (1904) described a patient with both urethritis and conjunctivitis complicating dysenteric infection.

Between 1916 and the publications of Harkness (1949, 1950) little was added to the understanding of either the aetiology or natural history of "venereal arthritis". Many papers were published, but diagnostic criteria were ill-defined and the follow-up of patients was inadequate (Lees, 1932; Myers and Gwynn, 1935).

Keefer and Spink (1937) reported a 5-year study of 140 cases of "gonococcal arthritis"; the gonococcus was isolated from the synovial cavities in only twenty cases, and the exudate from the conjunctivitis occurring in 21 of the 140 patients was sterile. Destruction of the synovial membrane was observed when a joint infected with the gonococcus was examined histologically, and this contrasted with proliferation of the membrane in a sterile joint. Bauer and Coggeshall (1939) defined "proved gonorrhoeal arthritis" on the basis of a history of gonococcal infection, a history of joint disease compatible with gonococcal arthritis, and the isolation of gonococci from the genito-urinary focus or the synovial fluid; in only three of fourteen such patients was the gonococcus isolated from the joints. Bauer and Engelmar (1942) described a case of polyarthritis following "non-specific" urethritis; in the 13th week of the disease the synovial membrane showed hyperaemia and cellular infiltration. Vallee (1946) published the case history of a

patient followed for 19 years, during which he had six attacks of urethritis, arthritis, and conjunctivitis; a "calcification of the lateral spinal ligaments of the lower thoracic region" was observed. Hollander (1946) reported 53 cases of "non-specific" urethritis and arthritis in U.S. Army personnel, and later stated that attacks of the disease lasted from 3-17 months, most commonly about 5 months (Hollander, 1949). A follow-up enquiry was said to have revealed "a chronic arthritic involvement of a type resembling rheumatoid arthritis" in one patient, but no details were given. Hollander quoted two papers describing the development of rheumatoid arthritis after an original attack, but reference to the originals does not support this conclusion; Twiss and Douglas (1946) did not follow their two patients long enough, and Strachstein (1945) did not mention chronic arthritis, but claimed a cure.

Harkness (1949, 1950) was the first to state authoritatively that the usual clinical pattern of joint disease associated with a gonorrhoeal urethral discharge was identical with that following "non-specific" urethritis. In other words, the arthritis following gonorrhoeal urethritis was not a "true gonococcal arthritis" in the majority of cases. Harkness supported this contention with evidence derived from chemotherapy. The gonococcus is extremely sensitive to penicillin, and penicillin resistant gonococci are rarely found, yet penicillin given for gonorrhoeal urethritis did not prevent the development of arthritis, nor did penicillin have any effect on the course of the arthritis when already present.

In discussing the clinical features of the arthritis in his 126 cases of "non-gonorrhoeal" origin, Harkness stressed the salient points, the usual polyarthritic nature with frequent relapses and the predilection for the joints of the lower limbs. In 70 per cent. of his patients there was involvement of the knee, in 55 per cent. of the ankle, and in 25 per cent. of the small joints of the feet. The incidence of involvement of other joints was less than 20 per cent.

Approximately similar figures are quoted for "presumed gonococcal arthritis" by Lees (1932), Myers and Gwynn (1935), Keefer and Spink (1937), and King and others (1946), though the last-mentioned found the feet to be involved more frequently than the ankles. Harkness gave an account of some of the residual joint disturbances that follow recurrent attacks, and mentioned ligamentous laxity of the knees and fingers as a result of prolonged joint swelling. He quoted the history of a patient who had recurrent attacks for 15 years; the knees showed clinical evidence of chronic arthritis, and x ray examination showed subchondral sclerosis, narrowing of the "joint spaces", marked irregularity of the contours of the femoral and tibial condyles, and considerable osteoarthritic osteophyte formation. Radiographs of another patient who had recurrent attacks for 12 years showed extensive new bone formation in the soft tissues over the

medial femoral condyles and similar changes, not so well marked, over the lateral condyles. Harkness found periostitis of the os calcis with subcalcaneal spurs in fourteen cases; seven radiographs illustrated their varied appearance.

Accepting the thesis put forward by Harkness, there would appear to be three possibilities regarding the aetiology of the venereal disease causing urethritis and arthritis with eye and skin complications:

(1) The disease is caused by the gonococcus in a form different from its usual coccal state. In support of this there is some evidence suggesting that the gonococcus may have a filterable phase (Klieneberger-Nobel, 1951; Dienes and Weinberger, 1951).

If this hypothesis were true, the filterable form of the organism would possess different pathological propensities from the coccal form, and would be resistant to antibiotics.

(2) The disease is related to the gonococcus in the same way as rheumatic fever is related to the streptococcus. Such an allergic hypothesis is theoretically quite possible, and would, of course, account for the lack of response to antibiotics. There is, however, no direct evidence to support it.

(3) The disease is an infective process unrelated to gonorrhoea. It may, however, be associated with gonorrhoea in mixed infections. The causative agent may possibly be a virus or a pleuropneumonia-like organism.

The third hypothesis has proved the most attractive to the majority of workers, and Harkness devoted much discussion to the evidence in its favour. Since viruses cannot be cultured, the evidence for a viral aetiology is based on the alleged demonstration of inclusion bodies in urethral, synovial, or conjunctival cells. The significance of the inclusion bodies themselves is, however, still debated.

The field of the pleuropneumonia-like organisms has grown steadily since Klieneberger (1935) and Dienes and Edsall (1937) brought them into prominence. The facts available give no more than circumstantial evidence of a relationship between the organisms and venereal urethritis and arthritis.

Although they occur frequently in inflammatory conditions of the genital tract (Dienes, 1940; Klieneberger-Nobel, 1945; Salaman, 1946; Beveridge and others, 1946; Harkness and Henderson-Begg, 1948; Randall and others, 1950; Melén and Odeblad, 1951), they have also been found in the apparently normal genital tract of both female (Melén and Odeblad, 1952) and male (Melén and Linnros, 1952). There is no proof as yet that pleuropneumonia-like organisms are anything more than com-

mensals (Edward, 1952). The claim of Dienes and others (1948) to have recovered the organisms from the joint cavities in two patients has not yet been confirmed, in spite of enthusiastic efforts by many workers to substantiate it.

A strong argument in favour of the separate-agent hypothesis is the occurrence of the syndrome as a sequel of dysentery, and from the present literature (Gounelle and Marche, 1941; Paronen, 1948; Marche, 1950) this would seem to be identical with the venereal form of the disease. There is no association with the gonococcus, and the suggestion that the infective agent gains entry through the damaged intestinal mucosa is wholly reasonable, though unproved. By analogy, the supposition that the urethra is the portal of entry of the agent in the venereal syndrome is entirely logical.

As already noted, gonococcal infection of the synovial fluid was found in twenty patients by Keefer and Spink (1937), and in three patients by Bauer and Coggeshall (1939). Other published accounts of true gonococcal arthritis refer in the main to isolated cases, although Keefer and Rantz (1939) refer to five patients, Bauer and others (1942) to two, and Spitzer and Steinbrocker (1949) to five patients with the proved disease. Hench and Boland (1946) stated that proved gonococcal arthritis among American soldiers in World War II appeared to be rare. Levy (1950), in a review of 106 British Army patients with arthritis of venereal origin, stated that "in 12 years of V.D. practice not one case showing a purulent arthritis or a completely disorganized joint" had been seen. He concluded, like Harkness, that the cause of the arthritis in gonorrhoea was not due to the gonococcus alone, but was "of the same aetiology as the arthritis occurring in 'non-specific' urethritis".

These two opinions appear to be in conflict with the findings of Keefer and Spink that 26 per cent. of 78 patients showed gonococci within the synovial cavity. However, this work was carried out before the introduction of chemotherapy, which may have caused an actual change in the frequency of true gonococcal arthritis over the last 15 years. It is also possible that the incidence of these two types of arthritis is influenced by geographical and racial features. It was the impression of Fearnley (1953) that true gonococcal arthritis was unusually frequent in Java at the end of World War II, and Levy (1950) noted that in Malays arthritis following gonorrhoea was cured by penicillin, whereas in Europeans penicillin was of little value. Moreover, Levy observed that "non-specific" urethritis often appeared in Europeans in whom gonorrhoea had been treated with penicillin, whereas residual urethritis was rarely if ever observed in Asiatics. This observation led him to favour hypersensitivity to the gonococcus as an aetiological mechanism in "non-specific" urethritis and venereal arthritis.

Hereafter the term "gonococcal arthritis" refers to the arthritis which results from invasion of the

joint by the gonococcus in the form of a pyogenic diplococcus.

The term "venereal arthritis" refers to the condition of the joints arising from some cause other than invasion of the joints by the pyogenic gonococcus. This name does not exclude the possibility that the disease may be due to the gonococcus existing in some other form than its usual coccocal state; nor does it exclude the possibility of hypersensitivity to the gonococcus as the aetiological factor.

If it is held that a hypersensitivity mechanism is the causative agent, there would be an exact analogy with the streptococcus and arthritis. The term "streptococcal arthritis" is, by common consent, confined to the joint disease in which streptococci can be isolated from the joint, whereas the term "rheumatic fever" is used when the precise relationship between the streptococcus and the arthritis is unknown.

Personal Observations

In recent years about 800 new cases of gonorrhoea and a similar number of new cases of "non-specific" urethritis have been treated annually at the White chapel Clinic. In the past 3 years, about twenty patients have been admitted to hospital annually for venereal arthritis. The out-patient records of the Clinic are available since the 1920s, and it has therefore been possible with the help of in-patient notes to follow cases over many years.

To obtain information about the clinical course of arthritis associated with venereal urethritis the records of all patients treated between 1938 and 1947 for "gonococcal arthritis" or "urethritis and arthritis" were studied, together with those of patients seen since 1947 who had had multiple attacks over a period of at least 5 years. Attempts were then made to trace these patients so that they could be examined personally. Since many of the Clinic patients are seamen or itinerant manual labourers, only a small percentage could be traced and examined, and it is thus impossible to deduce from the data presented any statistical facts about the incidence of chronic or recurrent arthritis in patients who have had one attack. In addition to the above material, Dr. Harkness of St. Peter's Hospital, and Dr. McElligott of St. Mary's Hospital, kindly allowed the author to investigate their former patients, two of whom were successfully traced and examined.

All the patients who have been included to illustrate the chronic or recurrent course of "venereal arthritis" were seen and examined by the author.

When there was a history of previous hospital admission the records were obtained in nearly all cases. Many patients were treated during service in the Armed Forces, and without exception the Ministry of Pensions has forwarded details of these attacks of arthritis. It was impossible to obtain information on the initial arthritic attacks of Cases 36 and 33 in 1918 and 1923 respectively, for, although the attacks were prolonged and relatively severe according to the patient's account, no in-patient treatment was given.

Hospital treatment for a manifest urethral discharge associated with an attack of arthritis was given to 21 patients during the years 1950, 1951, and 1952; of these, fourteen were seen by the author. This group will be discussed with reference to two questions:

- (i) The relationship of the gonococcus to "venereal arthritis".
- (ii) The effect of treatment on the course of arthritis.

Lack of acquaintance with the routine procedures of a venereal disease clinic has, in the past, been a source of error. Where a frank urethritis exists, the diagnosis of gonorrhoea or "non-specific" urethritis is relatively easy, and depends solely on reliable bacteriological examination. But identification of the gonococcus necessitates trained laboratory workers, and is not in the province of the general clinician. It is not adequately appreciated that the differentiation of gonococci from Gram-negative cocco-bacilli, occurring frequently in the lower genital tract, may be difficult. Venereal arthritis is often mistaken for some other form of arthritis, since often the patient does not complain of a urethral discharge or give any history of past urethritis, and the condition is not investigated with this in mind. The diagnosis of urethritis cannot be excluded until the patient has been examined in the early morning about 8 to 10 hours after passing urine.

The subject of "chronic prostatitis" will always be disputable. The diagnosis is made after examination of secretion obtained by prostatic massage, and if this fluid shows more than a specified number of leucocytes the label "chronic prostatitis" is applied. The results of such tests vary widely from time to time in the same patient, and an assured diagnosis requires repeated examinations. In some patients the diagnosis will be unequivocal, in others it can be excluded with certainty, but there is a group where the evidence is doubtful, and these patients will be assessed differently by separate observers. In such cases other evidence is needed for a satisfactory diagnosis.

The gonococcal complement-fixation test (G.C.F.T.) has also led to confusion. Briefly, the presence of a positive reaction indicates that the patient has probably been infected by the gonococcus in the past, but it does not indicate at what time the infection occurred. Conversely, a negative G.C.F.T. does not exclude past or present gonococcal infection, as the test may spontaneously become negative after a variable length of time. In fact the test may only be of value when the diagnosis of chronic prostatitis is in doubt; here the added fact of a positive G.C.F.T. is strong supportive evidence that the patient has had a genital infection.

In this study of venereal arthritis there has been no systematic investigation of synovial fluid. From previous experience it seemed unlikely that any new facts would emerge without the use of specialized techniques, as yet not available for routine work. In three cases synovial fluid was obtained and it was sterile in all; pleuropneumonia-like organisms were not cultured on the two occasions that such examinations were performed and the hospital virus laboratory failed to find inclusion bodies in the cells of the synovial fluid of one patient.

Relationship of the Gonococcus to Venereal Arthritis

Case 1.—A man of 57 was admitted to a surgical ward of the London Hospital in 1944 with a diagnosis of cellulitis of the left middle finger, which was described on admission as "red, greatly swollen, hot and tender; pus localized to the back of the proximal phalanx". On the fifth day in hospital pus was aspirated which on culture grew *N. gonorrhoeae*; in spite of local penicillin injections, on the twelfth day an incision had to be performed and 5 ml. of pus evacuated. This proved to be sterile on culture, but Gram-negative intracellular diplococci were seen in the smear. At operation the interphalangeal joint could be moved in all directions and the destruction of the joint was confirmed by x-ray examination. Although this man denied any exposure to risk of venereal disease, the G.C.F.T. was strongly positive, and gonococci were subsequently cultured from prostatic secretions.

No other proved case of suppurative gonococcal arthritis has been found in the records of the London Hospital for the past 15 years.

In the years 1950, 1951, and 1952, 21 patients were admitted for arthritis associated with a manifest urethral discharge; two of these were admitted for second attacks in this 3-year period. In nine of these episodes the urethral discharge yielded gonococci, in twelve the urethritis was diagnosed as "non-specific", and in two penicillin had been given before the patients were seen in the Clinic, where bacteriological examination showed no gonococci.

Fig. 1 illustrates the relationship of the gonococcal urethritis to the development of the arthritis. It also shows the relationship between antibacterial therapy and the onset and duration of the arthritis. It is not easy to fix the end-point of an individual attack of arthritis, for residual stiffness may persist for a variable period. The diagram represents as nearly as possible the time during which the disease would be described as "active"; it does not show the severity of the arthritis, but an attempt has been made to indicate when improvement seemed to begin.

It will be seen that in Cases 3, 4, 5, 6, and 8 penicillin was given before the arthritis developed. In the other three (Cases 2, 7, and 9) the onset of arthritis preceded treatment, but after administration of penicillin, and later of either aureomycin or streptomycin, the arthritis persisted for 3, 12, and 2 months respectively.

The clinical course of the arthritis in these eight patients with gonorrhoea was in no way different from that in the other thirteen patients. Conjunctivitis occurred in both the attacks in Case 6 and in Cases 4 and 9. In Case 7 conjunctivitis and widespread keratoderma blennorrhagica developed and were followed at the end of 11 months in hospital by iritis. Of the patients with "non-specific" urethritis, four had conjunctivitis. In this 3-year period no case of "non-specific" urethritis ran as severe a course as that in Case 7 following gonorrhoea. But in 1948 one patient (Case 23) had a similar severe polyarthritis of 6 months' duration with conjunctivitis and keratoderma blennorrhagica following "non-specific" urethritis.

This evidence supports the view that the common form of venereal arthritis is not true gonococcal arthritis. When this latter condition does occur it is a pyogenic arthritis leading to suppuration and destruction of the joint.

Treatment of Venereal Arthritis.—Chemotherapeutic agents, antibiotics, artificial fever, and more recently ACTH and cortisone have all been used in the treatment of venereal arthritis. Observations on the value of these forms of therapy (Ford, 1953) led to the conclusion that the arthritis is unaffected by antibiotics, but that temporary suppression of the clinical symptoms may be achieved by the administration of ACTH or cortisone; it was remarked that it has yet to be proved that fever therapy is effective. The underlying course of the disease is therefore in no way affected by any treatment at present available.

Fig. 1.—Duration of arthritis in relation to onset and duration of gonococcal urethritis, and treatment with antibiotics.

Course of Individual Attacks of Venereal Arthritis.

As already noted in the writings of Brodie, Fournier, and Launois, the commonest clinical patterns of arthritis involve the knee joints, ankles, and feet. The duration of the attacks is, as a rule, measured in weeks, and the condition usually subsides spontaneously within 3 months. This study confirms the following facts:

(a) Hydrarthrosis of one or both knees is common with or without arthritis in other joints.

(b) Acute or subacute arthritis of the ankle, tarsal, or metatarsal joints, either separately or together, is frequent.

(c) Tenderness under the heel is exceedingly common.

(d) The elbows, wrists, and shoulders may be involved singly or in combination, but rarely symmetrically, except that both wrists may be affected.

(e) One or more metacarpophalangeal and proximal or distal interphalangeal joints of the hands may be involved, although bilateral symmetrical polyarthritis of the finger joints is uncommon.

(f) Tenderness over spinous processes and pain on motion of the spine is quite commonly seen.

Certain clinical features of the arthritis are not frequently seen in other forms of joint disease:

(i) Circumscribed areas of extreme tenderness clearly described by Fournier are found over the periosteum. The skin over these areas is often normal, but may be slightly red and swollen.

Case 12.—There was, on one occasion, localized tenderness over the tibial insertion of the medial ligament of the knee and on another occasion an area of similar tenderness over the medial condyle of the femur.

Case 18.—An area of acute tenderness at one time developed over the right iliac crest near the anterior superior iliac spine.

Case 15.—This patient complained of localized tenderness over the right medial tibial condyle at a time when the knee joint itself was not tender.

Localized tenderness over the malleoli in the absence of definite arthritis of the ankle joints is a common occurrence, as also is tenderness over the posterior attachment of the plantar fascia.

(ii) Localized swelling and tenderness of one part of the peri-articular structures may occur in the absence of generalized swelling of the whole joint. Frequently, and especially in the region of the feet and ankles, one side of the joint is inflamed and the other side normal. In the clinical material reviewed here, definite tenosynovitis was not seen, and this is in distinction to the descriptions of other authors. Possibly this asymmetrical involvement of the peri-articular tissues is regarded as tenosynovitis by these authors, but the term "tenosynovitis" should be restricted to the description of the appearances where the

actual outline of the tendon sheath can be traced and recognized from the area of inflammation.

(iii) Acute arthritis arises in the sternoclavicular, acromioclavicular, and manubriosternal joints, and acute tenderness of costo-chondral junctions may develop. There was involvement of the right acromioclavicular joint early in the course of the disease in Case 7, and months later there was a large effusion into the left sternoclavicular joint, and swelling and tenderness appeared over the manubriosternal articulation. In Case 16 the second right costo-chondral junction was painful and tender during the attack in 1951.

(iv) The distal interphalangeal joints of the fingers are sometimes affected; for example, in Case 7 the distal interphalangeal joint of the left index was the first finger joint involved. The distal and proximal interphalangeal joints of the left index were the only two finger joints affected in Case 15.

In recent years a number of patients have been seen at the London Hospital who have had severe and prolonged attacks of venereal arthritis.

Case 7.—This patient contracted a second attack of gonorrhoea in February, 1952; 10 days later he complained of pain in the right ankle followed in 3 days by pain in the right shoulder and conjunctivitis. He was admitted to the London Hospital with fever, conjunctivitis, shallow ulcerations on the dorsum of the tongue, circinate balanitis, a urethral discharge, and arthritis of the right knee, right ankle, and right acromioclavicular joint. Treatment with penicillin (600,000 units daily for 3 days and 1,000,000 units daily for 2 days) did not affect the fever, urethritis, or conjunctivitis, and the arthritis spread to involve nearly all the joints; initially the knees, ankles, feet, and right acromioclavicular joints were the most severely involved, but later the arthritis was most active in the elbows, wrists, and cervical spine. In the sixth month of the disease acute arthritis of the left sternoclavicular and manubriosternal joints arose, and from the seventh to the ninth months most of the small joints of the hands were swollen and painful. The arthritis gradually subsided from the ninth month onwards, and by the end of the fourteenth month of the disease there was minimal pain and swelling only of the left mid-tarsal joint and the metatarsophalangeal joint of the fourth right toe, although there was some ligamentous laxity of the knees and several finger joints.

During the first 9 months in hospital there was extensive keratoderma blennorrhagica, and in the eleventh month severe iritis in the right eye, which responded slowly to local cortisone therapy.

Case 23.—In this patient two attacks of gonorrhoea in 1940 and 1945 preceded "non-specific" urethritis in 1948 which was followed by swelling of the left knee and conjunctivitis. He was admitted to the London Hospital with fever to 100.5°, acute arthritis of the right elbow,

and left knee and ankle, slight conjunctivitis, severe balanitis, circinate erosions over the soft palate, and a slight urethral discharge. He ran a low-grade fever for 15 weeks and for the first 4 months had widespread keratoderma blennorrhagica. The arthritis involved the left knee, left ankle, right elbow, both wrists, the proximal interphalangeal joints of the index and middle fingers of the left hand, and the right temporomandibular joint, and there was also tenderness over the spines of C7 and T1. The attack subsided only after 6 months, and 4 years later he had had no further attacks or joint pain and was working as a packer.

In three other cases recurrent subacute attacks involved many joints, including one or several joints of the fingers.

Case 11.—Urethritis, during April, 1949, was followed by arthritis of the right ankle, both knees, and the proximal interphalangeal joint of the right middle finger, and the patient was admitted to hospital for 12 weeks. Within 4 days of leaving hospital, however, he attended the Whitechapel Clinic with a non-gonococcal urethral discharge. A week later he was admitted to the London Hospital with effusions in both knees, tender heels, and swelling of the right ankle, third left toe, fifth right toe, and the proximal interphalangeal joint of the right middle finger. He was not free from joint pain for a further 4½ months. In May, 1950, "non-specific" urethritis recurred, and during the next 4 months he was treated in the London Hospital and at the Whitechapel Clinic for arthritis of the same joints as were involved previously. When seen in March, 1952, he had been well for 18 months, although a symptomless swelling of the proximal interphalangeal joint of the right middle finger persisted; x-ray examination showed only soft tissue swelling around the involved joint.

Case 25.—Acute urethritis in 1947 was followed by generalized polyarthritis and keratoderma blennorrhagica affecting the soles of the feet and the scalp; he remained in hospital for 12 weeks. In 1948, he complained of joint pain which required treatment for 3 months, but his first attack of iritis in 1949 was unaccompanied by arthritic symptoms. During the second half of 1951 he was in hospital for almost 6 months with a relapse of arthritis, keratoderma, and iritis, and again there was widespread joint involvement. When seen at the London Hospital in December, 1951, "low-grade" arthritis was persisting in the left elbow, left wrist, metacarpophalangeal joint of the left thumb, and the proximal interphalangeal joints of the right index, middle, and ring fingers. A year later these joints were free from "active" arthritis, and he complained only of a "frozen" left shoulder and severe pes planus, the residua of the initial attack in 1947.

Case 16 (also discussed below in a later section on the development of ankylosing spondylitis) showed typical relapsing polyarthritis. A first attack following gonor-

rhoea and a second attack following "non-specific" urethritis persisted for 8 and 4 months respectively. A third attack started in September, 1951, when a slight non-gonococcal urethral discharge and balanitis preceded arthritis of the left ankle and tenderness of the second right costochondral junction. He was admitted to the London Hospital for 5½ weeks, during which time the arthritis spread to both knees, the right wrist and shoulder, the metatarsophalangeal joint of the second right toe, and the proximal interphalangeal joint of the left ring finger. During the fourth month of the disease, "low-grade" arthritis persisted in these joints and only subsided over the next 6 months. Radiographs of the hands and wrists in January, 1952, showed periostitis of the right radius and ulna and soft tissue swelling of the proximal interphalangeal joint of the left ring finger. A year later, when clinical examination revealed no evidence of "active" arthritis in any peripheral joint, these changes were reduced.

Course of Chronic and Recurrent Arthritis.

The natural history of the disease was observed in 21 patients selected on the following criteria: presence of recurrent or chronic arthritis over a period of 5 years or more, and satisfactory evidence of genital infection. In all except two patients, arthritis and urethral discharge were associated on at least one occasion. In Cases 36 and 39 a diagnosis of genital infection was made on the basis of chronic prostatitis; both denied acute urethritis, though the finding of a positive G.C.F.T. in both made this denial suspect. Many patients who had had one attack of the disease were interviewed, but as there were no subsequent attacks they have been excluded.

Broadly speaking, there are three main clinical syndromes of the disease in its chronic form, although, as far as one can tell, there is no fundamental difference between the groups. These syndromes are:

- (1) Multiple attacks without residual joint damage.
- (2) Residual deformities of the feet.
- (3) Ankylosing spondylitis.

All the patients fell into one of these groups, except two (Cases 38 and 39) which will be considered separately. Since this paper is concerned primarily with arthritis, the problem of recurrent iritis will not be discussed in detail. Iritis, as Brodie first pointed out, is frequently observed with or without joint disease. Six of these 21 patients had relapsing iritis, and two others had the recurrent condition following a single attack of venereal arthritis.

In the present series, eleven patients had painful feet as a sequel to intermittent or chronic arthritis,

and only seven had no residual joint damage. Yet those with no residual lesion may be the larger group, since they are less likely to come to notice in a follow-up enquiry. Ankylosing spondylitis occurred in four patients.

(1) *Multiple Attacks without Residual Joint Damage* (Cases 6, 14, 21, 22, 26, 27, 28, see Appendix).—The early clinical course of the disease in the seven patients in this group showed no particular features which distinguished them from the remainder. There were no differences in treatment, and the arthritis was associated with gonorrhoea in some and with "non-specific" urethritis in others. Conjunctivitis was present at one time or another in four of the seven patients, but none had iritis. The episodes of arthritis usually lasted up to 2 months, although in Case 27 the patient complained of arthritis of the left ankle, followed by pain in the foot for nearly 5 months. One patient (Case 28) had seven episodes between 1945 and 1952, and another (Case 6) had four attacks during 14 years under observation. In Cases 14 and 26, recurrent arthritis was observed during the 1930s, but examination in 1952 revealed no sequelae, and the arthritis was in no way characteristic in distribution. The knees and feet were usually affected, but a more generalized poly-arthritis including a wrist, a thumb, and a finger, occurred in Case 28, and in Cases 21 and 26 finger joints were involved.

(2) *Residual Deformities of the Feet* (Cases 8, 25, 29, 30, 31, 32, 33, 34, 36, 37, 38: see Appendix for 8, 29, 30, 31, 32, 33, 34).—The commonest deformity of the feet was the painful calcaneal spur which was seen in eight of them (Cases 8, 29, 30, 31, 32, 33, 36, 38). The spur arises

from chronic periostitis at the posterior attachment of the plantar fascia and the repeated minor traumata of weight-bearing on the heel probably combine with the "low-grade" infection to maintain the chronic inflammation. A large spur may be palpable on the under surface of the heel, although radiography more readily demonstrates its presence. The spur is typically "fluffy" or "ragged" in x-ray appearance, but sometimes the outline is sharply defined. Figs 3, 4, and 5 (overleaf) show the varied shapes and sizes of the spurs encountered. Those of three patients (Case 8, Fig. 4a; Case 33, Fig. 3d; Case 36, Fig. 3e and f) were "clean-cut" in appearance, and such spurs do not necessarily indicate venereal arthritis. Heavily-built manual labourers and patients with rheumatoid arthritis may show spurs, but these tend to resemble that in Case 8 which is small, rather than those in Cases 33 and 36 which are prominent.

Periostitis of the os calcis may occur over the entire inferior and posterior surfaces of the bone. The extension of the condition over the posterior aspect is due, in all probability, to strain at the attachment of the Achilles tendon. In the radiograph there is irregularity and increased density of these surfaces, shown most clearly in Cases 29, 31 and 32 (Fig. 5c and d; Fig. 3a and b). In Cases 31 and 32 the patients complained of generalized tenderness of the heels. The second patient (Case 32) also had periostitis of the left tibial tubercle which caused a persistent localized swelling with tenderness from 1947 onwards. A radiograph in 1952 showed increased bone density and "fuzziness" of the periosteal outline with irregular calcification in the lower part of the infrapatellar tendon (Fig. 3c). This condition seems analogous to periostitis of the os calcis.

Fig. 2(a).—Outward deviation of toes (from Launois, 1899, by permission of *La Presse Médicale*).
(b).—Case 25, outward deviation of toes.
(c) and (d).—Case 25, pes planus.

Fig. 3(a).—Case 31, periostitis of inferior and posterior surfaces of left os calcis.
 (b).—Case 32, periostitis of inferior and posterior surfaces of left os calcis.
 (c).—Case 32, periostitis of left tibial tubercle and calcification of infrapatellar tendon.
 (d).—Case 33, left calcaneal spur. (e) and (f).—Case 36, calcaneal spurs, both feet.

Pes planus occurred in four patients (Cases 25, 30, 34, 37) and there was almost complete collapse of the longitudinal arches of the feet in two. Fig. 2 (c and d) illustrates the condition in Case 25. In Case 30 the patient had complained of painful feet for 15 years, and radiographs in 1937 had showed "very advanced infective arthritis of the small joints with much bone and cartilage destruction". When x-rayed in 1952, "lipping" of the margins of the tarsal joints and periosteal new bone formation on the posterior aspect of the tibia were prominent (Fig. 4b). The extreme flat foot caused the characteristic gait in both patients and in each walking was painful. Two patients (Cases 34 and 37) had lesser degrees of pes planus.

Conversely, three patients had pes cavus (Cases 8, 29, and 38), but it was impossible to determine the exact cause of this deformity. In each patient there was a fixed dorsiflexion of all the toes at the metatarsophalangeal joints, giving multiple "hammer toe" deformities, but

a similar condition of the toes was also present in Case 30 where flat foot was extreme. The radiograph of the left foot in Case 8 (Fig. 4a) illustrates both the pes cavus and the dorsiflexion contractures of the toes; it was taken in 1948 when the patient was admitted to the Orthopaedic Department of the London Hospital for amputation of all the toes to relieve his disability.

Persistent inflammation of the metatarsophalangeal joints, causing pain in the forepart of the foot on walking and tenderness to pressure over the metatarsal heads, is frequent in chronic and recurrent venereal arthritis. One patient (Case 29) complained of such pain first in 1930, and continuously from 1941 onwards. A lateral deviation of the toes accompanied fixed dorsiflexion of the proximal phalanges, and antero-posterior radiographs of the feet in 1952 (Fig. 5a and b) showed gross disorganization of the metatarsophalangeal joints with subluxation and much new bone formation. Deviation of the toes outwards, analogous to ulnar deviation of the fingers in

Fig. 5(a) and (b).—Case 29, disorganization of metatarsophalangeal joints with subluxation, new bone formation, and lateral deviation of toes, both feet.
 (c) and (d).—Case 29, periostitis of inferior and posterior surfaces of os calcis, both feet.

rheumatoid arthritis, was also observed in Case 25 (Fig. 2b), and Fig. 2a from Launois, 1899) illustrates the same appearance.

The arthritis in these eleven patients followed both gonorrhoea and "non-specific" urethritis, but in Cases 25 and 30 subsequent urethritis (gonococcal and "non-specific" respectively) was unaccompanied by relapse of the arthritis. In Cases 25 and 38, the initial attack involved many joints in both the arms and legs, and in Cases 8 and 31 pain and swelling of a wrist joint accompanied arthritis of the knees, ankles and feet. In Case 25 severe pes planus was associated with a "frozen shoulder", present since the first attack in 1947, and in Cases 36 and 37 ankylosing spondylitis accompanied abnormalities in the feet. One patient (Case 38) had a more widespread chronic arthritis, to be discussed later. Iritis recurred in four of the eleven patients (Cases 25, 36, 29, and 38), of whom the latter two had conjunctivitis during acute attacks of arthritis.

(3) *Ankylosing Spondylitis*.—The fact that four patients (Cases 16, 35, 36, 37) out of the 21 studied, presented the clinical syndrome of ankylosing spondylitis, was unexpected. The significance of this observation is open to question, since in a clinic population of this kind the discovery of four cases over the period of study could be due to chance. Nevertheless, in each case the arthritis started in peripheral joints, and it was only subsequently that the diagnosis of ankylosing spondylitis was made. Moreover, it seems unlikely that the random selection from a general "rheumatism" clinic of 21 patients suffering from chronic or recurrent arthritis of peripheral joints would yield four cases of ankylosing spondylitis.

Case 16.—This patient had three attacks of generalized polyarthritis associated with urethritis. The initial episode, in 1942, followed gonorrhoea, continued for 8 months, and was accompanied by relapsing conjunctivitis, corneal ulceration, and keratoderma on the toes. Later episodes, in 1950 and 1951, followed "non-specific" urethritis; they were less extensive, though in each attack the joints of the upper limbs were involved

together with the knees and feet. Stiffness of the spine was first noted and ankylosing spondylitis diagnosed when the third attack was subsiding; a review of the history, however, revealed earlier spinal symptoms. For several years the patient had complained of intermittent sciatica; for 2 years he had had low back pain; in 1950 his chest expansion was reduced; and earlier in 1951 he was tender over the sacro-iliac joints. The radiograph of these joints (Fig. 6a) was taken in November, 1951.

Case 35.—This patient contracted gonorrhoea in 1938, followed a month later by conjunctivitis, iritis, and polyarthritis. When the arthritis had persisted for 3 months he was referred to the London Hospital for treatment with the Kettering Hypertherm, and 2 months afterwards there was "a complete recovery from arthritis". During the next 11 years he had recurrent iritis of the left eye. In April, 1952, severe polyarthritis necessitated re-admission to the London Hospital. On admission, gross limitation of motion of the spine and reduced chest expansion were observed, yet even on direct questioning the patient would only admit to some pain and stiffness of the neck related to his acute symptoms. The arthritis of the peripheral joints subsided completely after 6 months, but stiffness of the spine remained, although some improvement followed a course of deep x-ray therapy. The radiograph of the sacro-iliac joints (Fig. 6b) was taken in January, 1953.

Case 36, arthritis was not associated with a manifest urethritis. The patient first attended the London Hospital in 1950 and said that in 1918 he had had "rheumatoid arthritis" of the knees and ankles lasting 4 months and accompanied by photophobia. He was treated in other hospitals for iritis in 1934 and 1947, but no further joint symptoms arose until May, 1950, when the left ankle became swollen and painful and the left heel tender. The left lower leg was treated in plaster for 5 months without improvement, and a diagnosis of chronic prostatitis with a positive G.C.F.T. was made in the Whitechapel Clinic. In January, 1951, he still had persistent swelling and pain in the left foot, and was admitted for fever therapy. In February, 1952, when he was

Fig. 6(a).—Case 16, sacro-iliac joints.

(b).—Case 35, sacro-iliac joints.

Fig. 7(a).—Case 37, obliteration of left sacro-iliac joint and “blurring” of margins of symphysis pubis.

readmitted for pain in both feet, slight stiffness of the lumbar spine was observed and a routine radiograph of the sacro-iliac joints showed “blurring” of the joint outlines. During the next 6 months stiffness of the spine progressed and reduced chest expansion and dorsal kyphosis developed. A course of radiotherapy to the spine in June, 1952, was followed by considerable improvement, and in January, 1953, he had a greater range of movement and less pain.

Case 37.—This patient contracted gonorrhoea, followed by pain in one knee, in 1932. In October, 1939, and in May, 1940, he was admitted to hospital for pain in the buttocks, thighs, and low back associated with non-gonococcal urethral discharge; on the second occasion he also had pain and swelling of the left foot. In September, 1940, he “was now developing ankylosing spondylitis” and a spinal support was ordered; 4 months later he was admitted to the London Hospital for pain and swelling of the right ankle and metatarsophalangeal joints of the right foot. In March, 1952, he had complete rigidity of the dorso-lumbar spine and poor costal movement, but the only abnormality in the limbs was moderate bilateral pes planus. Radiographs of the spine (Fig. 7a and b) showed calcification of the lateral spinal ligaments, obliteration of the left sacro-iliac joint, and “blurring” of the margins of the symphysis pubis.

(b).—Case 37, calcification of lateral spinal ligaments.

Two further cases (38 and 39) did not fall into any of the groups described above.

Case 38.—This patient had urethritis, conjunctivitis, and polyarthritis in 1931, and subsequently a chronic relapsing iritis. From the initial attack onwards he complained of variable pain in the ankles, heels, and feet, and in 1947 fluid was removed from the left knee on four occasions. Afterwards “low-grade” arthritis of the left knee and elbow, and of the metacarpophalangeal joint of the right index finger, was followed by slight limitation of movement of the left shoulder and localized tenderness over the right acromioclavicular joint. In April, 1952, moderate pes cavus of both feet with tenderness of the heels and dorsiflexion contractures of the toes accompanied the chronic arthritis of the other joints. Radiographs of the left knee (Fig. 8a and b) showed thinning of the “joint space” and marked osteo-arthritic osteophyte formation; a radiograph of the right hand (Fig. 8c) showed

Fig. 8(a) and (b).—Case 38, marked osteo-arthritis of left knee, lateral and posterior views.

(c).—Case 38, erosion of proximal articular surface of second right proximal phalanx, and cystic area in ulnar styloid.

an erosion in the proximal articular surface of the second proximal phalanx and cyst formation in the ulnar styloid. Thus this patient had not only the deformities of the feet common in venereal arthritis, but also chronic arthritis in a number of other joints. He did not, however, have arthritis of the wrists not of the fingers except for the single metacarpophalangeal joint, and there were no subcutaneous nodules.

Case 39.—This patient was admitted to the London Hospital in 1942 with arthritis of the knees; evidence of chronic prostatitis and a positive G.C.F.T. were found. He was re-admitted in 1944 complaining of pain in the right hip, but no objective signs of arthritis were observed and no comment was passed on his other joints. In 1952 and 1953 he had chronic arthritis of both elbows, both wrists, and several metacarpophalangeal and proximal

interphalangeal joints in both hands, accompanied by subcutaneous nodules below the left elbow. He therefore showed the typical features of rheumatoid arthritis, but his case history was deficient in several important respects. The arthritis started while he was in prison and he was unduly reticent about the mode of onset, the records of his wartime admissions gave inadequate information about the duration and distribution of the arthritis, and there was no record of acute urethritis. It is thus difficult to relate the rheumatoid arthritis to the genital infection, and the two conditions may have been coincidental.

Discussion

In recent years many writers have suggested that rheumatoid arthritis follows venereal infection. Hench and his collaborators, who have frequently

propounded this view, make the following statements:

It is not sufficiently understood that rheumatoid arthritis can be precipitated by a gonorrhoeal infection . . . also a mild, intermittent or quiescent rheumatoid arthritis can be aggravated by acute genital gonorrhoea (1946).

It would appear that "post-gonorrhoeal rheumatoid arthritis" is now more common than gonorrhoeal arthritis (1948).

It is a main argument of this paper that a distinct form of arthritis exists which is related to venereal urethritis, and that a careful study of these cases shows a clear-cut distinction from the natural history of classical rheumatoid arthritis. The predilection for the joints of the lower limbs, the periods of remission with acute or subacute self-limited relapses, the frequency of associated conjunctivitis and iritis, the residual deformities in the feet in the absence of permanent joint damage in the hands or elsewhere, and the development of spondylitis, are all characteristic of this disease, but are not features of rheumatoid arthritis.

The evidence for regarding non-specific infective arthritis as identical with rheumatoid arthritis rests on two claims:

- (i) if the patient is followed for a sufficient length of time, the typical features of rheumatoid arthritis will develop;
- (ii) pathological studies fail to reveal a histological difference.

However, many of the patients described above have been observed for more than 10 years, and in none did typical rheumatoid arthritis develop (the reasons for excluding Case 39 from this group have been given). No histological studies were made, but the pathological evidence may be interpreted incorrectly, for similar macroscopical and microscopical appearances do not necessarily indicate common causation; this has been clearly shown by the study of the morbid anatomy of the terminal stages of chronic Bright's disease. It is not possible to infer that venereal infection is the only, or even a common cause of non-specific infective arthritis; nevertheless, the recognition of venereal arthritis as an entity is important, because it is the only member of the group of chronic "proliferative" arthritides where the infectivity of the aetiological agent, the portal of entry, and the method of transmission are known.

Many venereologists believe that genital infection is a frequent cause of ankylosing spondylitis, and it is claimed (King, 1953) that careful examination of patients with ankylosing spondylitis will usually reveal evidence of chronic prostatitis. Forestier

(1939), reviewing 153 patients with ankylosing spondylitis, stated:

In 60 per cent. of the cases a history of past genito-urinary infection is reported, . . . one-third of our patients had had some gonococcal infection some time previously.

An early diagnosis of ankylosing spondylitis is made when radiographic "blurring" of the sacroiliac joints accompanies low back pain, and it is only later that the "poker back" and "bamboo spine" develop. In the spine the disease usually runs a predictable course, but the frequency of associated arthritis in the peripheral joints has been repeatedly debated. The classical view, held in England (Buckley, 1948), is that the disease is usually confined to the spine, but that progressive ankylosis of the hips and shoulders may occur in the late stages; involvement of peripheral joints is considered exceptional. This is in conflict with American opinion (Boland, 1949), which regards peripheral arthritis as common and, although the absence of rheumatoid nodules and the classical "rheumatoid hand" is admitted, refers to the condition as "rheumatoid spondylitis".

The four patients described here in whom the spine was affected did not conform to the pattern of classical ankylosing spondylitis where progressive spinal stiffness is always the predominant symptom; on the contrary, in each patient there was an initial polyarthritis or arthritis of the ankles and feet, and it was only subsequently that spinal stiffness arose. It is possible that the divergent views on the frequency of peripheral arthritis in ankylosing spondylitis may reflect the existence of two syndromes of unrelated aetiology; it may be that cases in which both the spine and peripheral joints are affected result from venereal infection, whereas the "classical" cases are caused by some other agent. This was suggested by Buckley (1943):

If the hands or feet are affected before or simultaneously with the spine, the diagnosis is not ankylosing spondylitis, but infective arthritis, possibly of gonorrhoeal origin, affecting the spine.

He quoted the work of Batson (1940), who showed the presence of venous anastomoses between the prostatic venous plexus and the vertebral veins, and suggested that this was a possible route of spread of the aetiological agent from the infective focus in the prostate to the spine. Venereal infection is not, however, the only cause of spinal and peripheral arthritis, for Marche (1950) observed sacro-iliac arthritis as a prelude to ankylosing spondylitis in the post-dysenteric syndrome.

In this paper the term "venereal arthritis" has been used to describe arthritis following venereal

urethritis when the gonococcus cannot be isolated from the joints and the disease does not run the course of a suppurative arthritis. The term "gonococcal arthritis" has been restricted to the condition where gonococcal invasion of the synovial tissues has been proved. It has been conceded that the arthritis following dysentery may be similar in clinical features and natural history to venereal arthritis, but the mode of infection is so different that the alternative title of "post-dysenteric arthritis" has been used. The name "infective arthritis" has been avoided, as it seems too indefinite, and the more informative "infective arthritis of venereal origin" is also avoided as being too long. The condition has frequently been called "Reiter's disease" or "Reiter's syndrome", but these are unsatisfactory names for the following reasons:

- (i) Reiter's paper made a negligible if not misleading contribution to the subject since he described one case following dysentery, and attributed the arthritis to a spirochaete;
- (ii) there is confusion when ocular manifestations are absent, as indeed they usually are.

Hollander (1946) suggested the term "infectious uro-arthritis", but this implies infection of the urinary tract rather than of the genital organs. Correct nomenclature will have to await the discovery of the cause of the disease.

This paper has been concerned with arthritis and venereal infection in men and no observations have been made on women. It was thought that no conclusions of value could be obtained from a study of women:

- (i) gonorrhoea in women is frequently overlooked, because the symptoms are so mild;
- (ii) "non-specific" venereal infection in women is difficult to diagnose with certainty;
- (iii) in recent years the association of arthritis with venereal infection in women is uncommon; in the past 18 months only two cases have been seen at the Whitechapel Clinic, and in the last 5 years only four patients have been admitted to the London Hospital;
- (iv) both the pattern of joint disease following venereal infection and the triad of urethritis, arthritis, and conjunctivitis are rarely seen in women.

Summary

The usual form of arthritis following gonorrhoea is identical with that following "non-specific" urethritis. It is an entity with a recognizable distribution and clinical course.

The natural history of the disease is characterized by self-limiting attacks of about 1 to 12 months'

duration, but recurrent or chronic arthritis may lead to residual deformities of the feet and occasionally to ankylosing spondylitis. Permanent joint damage elsewhere is unusual and rheumatoid arthritis is not a sequel.

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Histoire naturelle de l'arthrite consécutive à une uréthrite vénérienne

RÉSUMÉ

La forme habituelle de l'arthrite consécutive à une blennorrhagie est identique à celle consécutive à une uréthrite non spécifique. C'est une entité reconnaissable par sa distribution et par son évolution clinique.

L'histoire naturelle de la maladie se caractérise par des attaques d'envergure limitée et d'une durée de 1 à 12 mois. Une arthrite récurrente ou chronique peut mener

à la déformation résiduelle des pieds et quelquefois à la spondylite ankylosante. Des lésions permanentes des autres articulations sont rares et n'entraînent pas l'arthrite rhumatismale.

Historia natural de la artritis consecutiva a una uretritis venérea

SUMARIO

La forma habitual de la artritis consecutiva a una blenorragia y la consecutiva a una uretritis banal es idéntica y se reconoce por su distribución y por su evolución clínica.

La historia natural de la enfermedad se caracteriza por ataques que se limitan espontáneamente y que duran de 1 a 12 meses. Una artritis recurrente o crónica puede llevar a la deformación residual de los pies y, a veces, a la espondilitis anquilosante. Lesiones permanentes de otras articulaciones son raras y no conducen a la artritis reumatoide.

APPENDIX

Very short reports are given below of the seven patients (Cases 6, 14, 21, 22, 26, 27, 28) who had recurrent attacks without residual joint lesions. More detailed reports are given of seven (Cases 8, 29, 30, 31, 32, 33, 34) of the eleven patients who had residual deformities of the feet. The other four patients (Cases 25, 36, 37, 38) in this group are described in detail above (pp. 184, 189, 190).

RECURRENT ATTACKS WITHOUT RESIDUAL JOINT LESIONS

Case 6.—Arthralgia associated with a positive G.C.F.T. in 1938 and 1939; recurrent attacks of gonorrhoea, conjunctivitis, and arthritis in 1946, 1950, and 1951; no abnormalities found on examination in 1952.

Case 14.—Gonorrhoea on six occasions between 1931 and 1946; arthritis in 1933 and in 1935, the latter attack being associated with conjunctivitis; pains in hips, thighs, and feet in 1937 and 1940; "non-specific" urethritis accompanied by arthritis in 1950; no arthritis in any joint in 1952.

Case 21.—"Non-specific" urethritis in 1931, 1937, and 1939; polyarthritis following "non-specific" urethritis in 1945; mild urethritis without arthritis in 1946; relapse of "non-specific" urethritis, followed by arthritis in 1950; transient pain and swelling of right knee in May, 1952, but no abnormalities on examination in October, 1952.

Case 22.—Arthritis of both knees, following "non-specific" urethritis in 1941 and 1952; all joints normal in 1953.

Case 26.—Gonorrhoea in 1931; non-gonococcal urethritis and arthritis in 1933; further arthritis with painful heel in 1936; relapse of arthritis in knees and feet in 1938, but uncomplicated gonorrhoea in 1940; healthy and without arthritis in 1952.

Case 27.—Urethritis, conjunctivitis, and arthritis in

1943; "acute lumbago" followed by arthritis of left ankle and a painful right heel in 1950; no evidence of joint disease in 1952.

Case 28.—Urethritis in 1935; recurrent attacks of "non-specific" urethritis, conjunctivitis, and arthritis in 1945, 1946, 1947, 1948, 1949, and 1952; healthy and no arthritis in November, 1952.

RESIDUAL DEFORMITIES OF THE FEET

Case 8.—1935, pain and swelling in both knees and ankles, lasting about 7 weeks; treated in bed at home in Ireland by private doctor. Pain was not migratory, unassociated with conjunctivitis or urethritis; he recalled the word "synovitis" being used.

1942, while in Army in Middle East, admitted to hospital for 12 days with diarrhoea of 2 days' duration with up to seven liquid stools a day, no blood or mucus. Diarrhoea had cleared in about a week, but on the 9th day after admission pain and swelling of left knee developed, and persisted up till his discharge 4 days later. Medical opinion at this time stated:

"It seems doubtful if so mild an attack of diarrhoea can really be considered the cause of the arthritis."

October, 1945, while still in Army, pain and swelling of right wrist arose; he was admitted 2 weeks later to Black Notley Hospital.

Examination.—Febrile to 101° F.; redness, swelling, and tenderness of right wrist, right 3rd and 4th toes and left 2nd toe. Prostate enlarged, irregularly hardened, and excessively tender, expressed excretion showing pus.

Investigations.—White blood count 12,200, 63 per cent. P.; E.S.R. 63 mm./hr.; G.C.F.T. positive, prostatic smear "Numerous pus cells, moderate number of intracellular and extracellular Gram-negative diplococci, morphologically indistinguishable from gonococci, moderate secondary infection"; synovial fluid sterile.

Treated with sulphamerazine and penicillin without improvement, fever persisted for 6 weeks, and arthritis spread to involve left knee. He was discharged after 16 weeks in hospital.

1948, admitted to Orthopaedic Department of London Hospital for amputation of all toes of both feet at M.T.P.J. on account of multiple hammer-toe deformities.

X-rays.—Feet, pes cavus with small calcaneal spurs and dorsiflexion contractures of toes (Fig. 4a).

March, 1952, 1 week after exposure to infection, attended Whitechapel Clinic for gonorrhoea; given 300,000 units of penicillin, but 9 days later complained of pain and swelling of left knee and dorsum of left foot. Admitted to London Lock Hospital for 1 week and treated with 1 mega unit penicillin daily for 6 days. Transferred to London Hospital with fever to 101° F., circinate balanitis, and arthritis of left knee and left mid-tarsal joint.

Investigations.—E.S.R. 95, 110, and 112 mm./hr (Westergren); blood uric acid 1.6 and 2.5 mg. per cent.

X rays.—Small, sharply-defined left calcaneal spur, no bony abnormality in left ankle, minimal osteo-arthritic changes in left knee and slight sclerosis and irregularity in outlines of sacro-iliac joints (of questionable significance).

Treated with ACTH 120-40 mg. daily for 14 days, with temporary remission in fever and arthritis, followed by mild relapse on stopping treatment. Discharged after 8 weeks in hospital, but did not attend for follow-up.

Case 29.—1924, admitted to London Hospital for one month complaining of rheumatism of right knee and M.T.P.J. of right foot. At this time it was recorded that he had had gonorrhoea in 1907 and 1917, and gonococcal rheumatism 18 years before. He stated that he had then been admitted to the Seamen's Hospital, Greenwich, but it was impossible to trace the records. During this London Hospital admission he ran a low-grade fever up to 99.4° F., and was treated with aspirin by mouth and local hot fomentations, and methyl salicylate to the right knee.

September, 1930, pain in soles of feet, heels, toe joints, left knee, left hip, and right shoulder. At Whitechapel Clinic a hallux valgus deformity of left big toe was observed with tenderness along Achilles tendon. G.C.F.T. was negative; prostatic smear showed pus and secondary organisms, and grew staphylococci on culture. Diathermy treatment to both feet. He was observed for 6 months, and on one occasion complained of pain in right temporomandibular joint.

February, 1934, returned to Whitechapel Clinic complaining of tenderness under both heels of 10 weeks' duration.

Examination.—Prostatic smears showed pus, and repeated vesical cultures grew staphylococci, one out of nine vesical cultures was reported as growing gonococci.

1935, began intermittent dilatations for urethral stricture, continued from then onwards.

1941, complained of some pain in M.T.P.J. of right foot and thereafter had variable intermittent pain in both feet.

October, 1951, after one of his periodic dilatations, complained of dysuria followed by reddening of left eye, and pain and swelling of left knee. Went to bed for some weeks and also complained of pain in shoulders and right knee.

January, 1952, seen in the Department of Physical Medicine for marked swelling, tenderness, and redness of left knee and tenderness over ischial tuberosities.

Investigations.—White blood count 9,400 (P. 66 per cent.); E.S.R. 40 (Wintrobe uncorrected); G.C.F.T. negative.

April, 1952, seen for follow-up and found to be attending Westminster Hospital for iritis of left eye.

Examination.—Slight pain in left shoulder on raising arm fully above head, and slight stiffness of neck both probably compatible with age; slight pain on movement of left knee with about 5° loss of full extension; pes cavus deformity of both feet with decreased movements of mid-tarsal joints; bilateral hallux valgus and quite marked dorsiflexion deformities of all toes at M.T.P.J.

X rays.—Marked new bone formation along posterior and inferior surfaces of calcanei with large calcaneal spurs; gross disorganization of all M.T.P.J. of both feet, with partial subluxation, partial obliteration of joint outlines, and considerable new bone formation in region of joints (Fig. 5a-d).

Case 30.—1933, gonorrhoea while in the Navy.

February, 1935, pain in soles of feet treated at a Naval Hospital and diagnosed as flat foot and metatarsalgia.

May, 1935, urethritis followed 14 days after an exposure to infection, admitted to Naval Hospital, Plymouth, for 10 weeks, complaining of painful swollen feet. Smear from urethral discharge showed "morphological intra- and extra-cellular gonococci".

X rays.—"No evidence of arthritis of the joints of the feet, but the inferior part of the tuberosity of each os calcis is arthritic."

A fever up to 101.4° F. accompanied arthritis in feet and one month later right big toe became swollen and tender.

April, 1937, admitted to Naval Hospital, Chatham, with arthritis of both ankles, preceded by a urethral discharge for 1 week. On admission, urethral smear showed gonococci; 2 days after admission M.T.P.J. of left great toe swollen and painful, and later arthritis involved both knees. During the 3rd, 4th, and 5th months of this admission he complained of variable symptoms related to feet, right ankle, and cervical spine.

X rays.—In the 6th month "right knee—nil abnormal seen; both feet—very advanced infective arthritis of the small joints, much bone and cartilage destruction".

Discharged after 6½ months in October, 1937, as medically unfit for further service: "except for the small joints of both feet, this case is now clear of arthritis, invalidated as no further change is expected in the condition of the feet".

1937-1947, complained of variable pain and stiffness in both feet.

1947, "non-specific" urethritis developed 2 weeks after an exposure to infection and one week later left ankle and right mid-tarsal joints were swollen and painful. Admitted to St. Charles's Hospital for about 5 weeks and treated with irrigations and fever. Following his discharge from hospital he was treated in the Department of Physical Medicine for pain in the feet and ankles.

August, 1948, complained of urethral discharge, seen in the Whitechapel Clinic 4 days later, no gonococci found; G.C.F.T. negative; only other complaint, slight backache.

March, 1952, seen for follow-up; no further episodes of urethral discharge nor of arthritis; but he had continued to have painful feet.

Examination.—Both feet showed slight valgus and eversion deformity with marked loss of longitudinal arches and stiffness and loss of motion at mid-tarsal joints with slight tenderness to pressure; marked hammer-toe deformity of four smaller toes from a fixed dorsiflexion of proximal phalanx to an angle of about 40-50°; ankylosis of I.P.J. of great toes.

X rays.—Feet, marked bilateral plantar spurs; considerable lipping around edges of small joints of feet; some periosteal new bone formation around medial surface of medial malleolus, and considerable disorganization of joints at base of toes with dorsiflexion deformity (Fig. 4b).

Sacro-iliac joints, a slight "blurring" and irregularity of the joint margins, of doubtful significance.

Case 31.—1936, "gonorrhoea" treated at Lambeth Hospital.

November, 1946, gonococcal urethritis following exposure to infection, treated at Whitechapel Clinic with 150,000 units penicillin. After 2 days he complained of pain and swelling of right wrist and right knee. He was given another 300,000 units of penicillin and admitted to St. Charles's Hospital.

Examination.—Arthritis of left elbow, right shoulder, right wrist, and both knees; treated with penicillin, radiant heat, "Aolan", and T.A.B. Discharged himself against advice after 18 days.

February, 1947, still walking with a cane on account of pain and swelling of right knee.

March, 1950, attended Bethnal Green Hospital complaining of pain in ankles and toes; both ankle joints observed to be slightly swollen.

April, 1952, seen for follow-up, complained of intermittent pain in feet, ankles, and heels.

Examination.—Generalized tenderness over ligaments of feet, over insertions of Achilles tendons and heels; generalized swelling of both feet.

X rays.—Sacro-iliac joints, right knee and right hand showed no significant changes; x rays of left ankle and foot showed marked roughening of

posterior and inferior aspects of left os calcis with moderate-sized plantar spur (Fig. 3a).

Case 32.—March, 1947, admitted to St. Andrew's Hospital for 10 weeks with arthritis of right knee and left ankle, and a tender swelling over left tibial tubercle. G.C.F.T. positive. Treated with penicillin and prostatic massage. Transferred to St. Charles's Hospital for 3 weeks.

Investigations.—E.S.R. 53 and 55 mm./hr; G.C.F.T. positive; scanty Gram-positive cocci in urethral smear.

Treated with penicillin and "Aolan" injections.

August, 1947, attended Whitechapel Clinic with balanitis and paraphimosis; continued treatment and observation during next 2½ years for recurrent balanitis and chronic prostatitis. Variable complaints of pain in left heel, left ankle, and both knees for following 9 months.

April, 1948, re-admitted to St. Charles's Hospital with persistently painful and swollen left heel; treated with penicillin.

February, 1949, re-attended Whitechapel Clinic for secondary syphilis.

December, 1951, treated in Whitechapel Clinic for gonorrhoea and given streptomycin.

February, 1952, pain in left heel more marked and E.S.R. 21 mm./hr.

March, 1952, generalized moderately tender swelling of left heel and swelling of left tibial tubercle; hallux valgus and hammer toe deformities of left foot said to have been present since an injury 27 years before; blood uric acid 2.7 mg. per cent.

X rays.—Increased density of os calcis with irregular periosteal outline and plantar spur; increased density of left tibial tubercle with irregularity in periosteal outline and calcification in infrapatellar tendon (Fig. 3b and c).

November, 1952, still complaining of painful, tender left heel.

Case 33.—1923, urethral discharge and pain in many joints with swelling of feet; in bed at home for many weeks, walked with a stick for several months and off work for 2 years. Treated as out-patient with urethral irrigations and prostatic diathermy at a hospital in Jersey, but the urethritis persisted for about 3 months. No further urethral or articular symptoms.

1950, attended Metropolitan Hospital for 6 months for pain and swelling of right big toe and pain in both heels.

February, 1952, pain in right tibial tubercle, followed by pain and tenderness over inner aspect of right knee, and swelling and tenderness at base of toes of both feet. Referred to Whitechapel Clinic where circinate balanitis and a scanty mucoid non-gonococcal urethral discharge were observed.

Investigations.—E.S.R. 20 and 23 mm./hr (Westergren); blood uric acid 2 and 3.3 mg. per cent; G.C.F.T. negative.

X rays.—Slight irregularity of contour of left sacro-iliac joint of doubtful significance; bilateral calcaneal spurs of moderate size with sharply-defined outlines (Fig. 3d).

April, 1952, admitted to London Hospital for 3 weeks, but no treatment given as arthritis of M.T.P.J. of both feet was subsiding spontaneously.

January, 1953, re-admitted to London Hospital for recurrence of arthritis of M.T.P.J. of both feet. Treated with "Pyrifer" on three occasions without improvement, and later with long-acting ACTH gel (20-40 mg. daily) with partial suppression of symptoms. Discharged after 8 weeks to continue ACTH gel injections on alternate days as an out-patient. Further blood uric acid reported as 2.9 mg. per cent.; no urethral symptoms during this attack of arthritis.

Case 34.—1922 and 1940, attacks of gonorrhoea.

November, 1944, gonorrhoea treated at St. Mary's Hospital with sulphadiazine; 12 days later pain in right ankle and left knee; after 2 weeks admitted to St. Charles's Hospital.

Examination.—Acute arthritis of right ankle; low grade fever 99-100°; E.S.R. 27, 41, and 24 mm./hr; G.C.F.T. positive.

Received "Aolan" injections on two occasions; discharged after 10 weeks.

November, 1948, treated at St. Mary's Hospital for slight "non-specific" urethritis and given sulphadiazine and penicillin.

July, 1949, pain in right foot persisting for 2 months; treated at St. Mary's Hospital, and admitted for 3 weeks in August. Given streptomycin and penicillin. E.S.R. varied between 47 and 76 mm./hr. Symptoms subsided in the 3rd month.

March, 1950, attended London Lock Hospital for 6 months complaining of persistent variable pain in feet and heels; on one occasion "puffiness and tenderness of right ankle below internal malleolus" was observed, and later 2nd and 3rd M.T.P.J. and attachment of Achilles tendon were tender.

November, 1952, follow-up; no further attacks of definite arthritis, but intermittent pain in 2nd right toe and generalized vague "rheumatism".

Examination.—Marked bilateral flat foot and some swelling of 2nd right toe at D.I.P.J.

X rays.—Both ankles and feet within normal limits except for disorganization of P.I.P.J. of the 2nd right toe.