

Arthritis and Intestinal Disease

IAN HASLOCK, MD, Rheumatologist, South Teesside Group of Hospitals, and
VERNA WRIGHT, MD, FRCP, Professor of Rheumatology, University Department of Medicine and the General Infirmary at Leeds

The course of intestinal disease is frequently complicated by involvement of the musculo-skeletal system. Such involvement may range from a transient arthralgia to a permanent and disabling arthritis. It is important that clinicians treating the primary disease are aware not only that the rheumatic complications exist but also of their prognosis and treatment. This review will, therefore, emphasise the prognostic and therapeutic aspects of the varied rheumatic complaints associated with intestinal disease.

INTESTINAL INFECTIONS

Enteric infections may be complicated by two forms of joint disease. The commoner form is the polyarthritis occurring 5 to 14 days after the initial intestinal symptoms (Berglof, 1963). The incidence in patients with salmonella infections has been estimated as 2.4 per cent (Vartiainen and Hurri, 1964). The pattern of joint involvement may resemble acute rheumatoid polyarthritis, but the disease is self-limiting, lasting for days or, rarely, weeks only. Salicylate therapy may be required for symptomatic relief.

A more serious, but rarer, complication of enteric infection is the development of a septic arthritis. This is more common in children than adults, and usually presents with a monoarthritis showing the classical signs of pain, swelling, redness and reduction in range of movement (David and Black, 1960). The infecting organism may be cultured from the joint. Treatment is by elimination of the infection, which is usually achieved by systemic administration of antibiotics, which penetrate into the joint in adequate concentration (Drutz *et al.*, 1967; Deodhar *et al.*, 1972).

Brucellosis frequently produces articular symptoms, arthralgia occurring during the febrile episodes in 32 per cent of patients (Hardy, 1937). A more severe arthritis has been observed in over 20 per cent of patients, in some cases with radiological changes (Rotes-Querol, 1957), and occasional isolation of brucella from the joints. Although this usually regresses over a period of months, a small number of patients progress to a frank septic arthritis involving the peripheral joints, the spine or the sacro-iliac joints. Treatment may be difficult, and surgical drainage of the affected area may be necessary, especially where there is associated osteomyelitis.

An arthritis following dysentery has been described as similar to that following salmonella infections. It seems likely, however, that this is the post-infective form of Reiter's disease. In an army camp in North America nine such cases followed an outbreak of bacillary dysentery affecting 602 personnel in whom there was no immediate venereal exposure (Noer, 1966). The disease may also follow attacks of amoebic dysentery (Moorhead 1916; Grave *et al.*, 1949; Marche, 1955) and has been observed following seasonal, toxic non-specific diarrhoea among French troops in Algeria (Roumagnac *et al.*, 1958; Masbernard, 1959). The incidence and geographic distribution of these cases generally corresponds with the behaviour of the preceding dysentery (Paronen, 1948) although this is not invariable (Manson-Bahr, 1943). The endemic sporadic form is related to the incidence in the fly population (Marche, 1955), the seasonal incidence of diarrhoea, and lack of hygienic facilities. Newcomers to the area seem more susceptible (Roumagnac *et al.*, 1958). Paronen found the incidence of Reiter's disease to be 0.24 per cent among 150,000 cases of dysentery.

Reiter's disease is usually the post-sexual form in the United Kingdom, but occasional cases may follow dysentery which is the common predisposing factor in continental Europe. It is of interest that Reiter's original description was of the post-dysenteric form of the disease (Reiter, 1916) and the largest reported series in the world is the 344 cases described by Paronen (1948) following an outbreak of Flexner dysentery in the Finnish army. The diagnostic triad in Reiter's disease is urethritis, conjunctivitis and arthritis, although one of the classical triad may be absent in some cases. Many other features are frequent accompaniments of the disease, the most important being oral and genital ulceration, keratoderma blenorrhagia on the palms and soles, and pain under the heels, frequently associated with plantar spurs. The ocular component of the disease may involve the whole uveal tract. The arthritis may be mild and transient or become chronic, painful, and potentially disabling. Radiologically, signs of an erosive arthritis are often associated with florid periosteal new bone formation. Plantar spurs are common. Sacro-iliitis is usually a later feature and the spinal involvement may progress to a final stage indistinguishable from advanced ankylosing spondylitis. Treatment is based on the use of analgesic/anti-inflammatory drugs, usually salicylates or phenylbutazone. Joint effusion is often considerable, and aspiration affords considerable relief. Local hydrocortisone injections may be effective in the treatment of heel pain. Where sacro-iliitis heralds a spondylitic type of disease, the treatment should follow the same course as that of patients with idiopathic ankylosing spondylitis, that is, constant attention to mobility of the spine and chest and a daily regime of home exercises.

Although the precise aetiology of Whipple's disease remains unknown, the finding of bacilliform bodies on electron microscopy and the response to long-term tetracycline therapy suggest an infective cause. Despite the high cure-rate associated with modern therapy, the arthritis of Whipple's disease remains important as it precedes intestinal symptoms in a number of cases, often by many years (Maizel *et al.*, 1970). Whipple's initial description of the disease (Whipple, 1907) was of a physician who presented with an episodic polyarthritis, and this is the pattern of arthritis observed ever since. No consistent radiological changes have been shown in affected joints, although a form of ankylosing spondylitis may occur with appropriate radiological changes in the sacro-iliac joints and spine (Kelly and Weisiger, 1963). Synovial biopsy shows non-specific inflammatory changes and synovial analysis shows typical changes of inflammation with no diagnostic features (Caughey and Bywaters, 1963). The joint manifestations of the disease disappear with the intestinal ones once therapy is established. Their main importance lies in the recognition of the pattern of 'intestinal synovitis' without overt intestinal disease. This is extremely rare in conjunction with ulcerative colitis and Crohn's disease, and should, therefore, provide an early clue to the diagnosis of Whipple's disease.

INTESTINAL INFLAMMATORY DISEASE

The main interest in the association between gastrointestinal and articular disease lies in the musculo-skeletal complications of ulcerative colitis and Crohn's disease. Although the association of articular and intestinal disease has been recognised since the last century (White, 1895), the details of the relationship have not been evaluated until relatively recently.

Two distinct types of joint disease complicate the inflammatory intestinal diseases. The first is called 'intestinal synovitis'. This is an episodic polysynovitis involving large joints more than small, and lower limb more than upper limb joints (Wright and Watkinson, 1965a; Haslock and Wright, 1973). The synovitis almost invariably occurs either simultaneously with the onset of intestinal symptoms or during the course of the intestinal disease. There is a tendency for exacerbations of intestinal and articular symptoms to occur in parallel. The synovitis may occur in association with erythema nodosum. There are three ways in which the synovitis associated with ulcerative colitis differs from that associated with Crohn's disease. Firstly, colitic arthritis is more frequently found in patients with extensive gut involvement, and those showing the major local complications of colitis such as pseudopolypsis, peri-anal suppuration and massive haemorrhage (Wright and Watkinson, 1965a). In contrast, the presence of the major complications of Crohn's disease, particularly fistula formation, do not increase the incidence of

synovitis (Haslock and Wright, 1973). Large intestinal Crohn's disease does, however, increase the risk of synovitis developing (Cornes and Stecher, 1961). The second difference is in the effect of surgery on the intestinal synovitis. Where total procto-colectomy is undertaken in ulcerative colitis, the synovitis regresses and does not return. Although surgery in Crohn's disease may result in regression of the articular symptoms, recurrence or development of joint disease may take place postoperatively. The reason for this difference becomes apparent when the likely aetiology of the synovitis is considered. Intestinal synovitis is considered an apposite name since the synovitis appears to be a complication of active intestinal disease. The rarity of reported cases in which articular symptoms preceded intestinal ones, the tendency for joint and gut symptoms to wax and wane in parallel and the remission following surgery, especially the complete remission after total procto-colectomy in ulcerative colitis, all suggest that some factor in the diseased gut initiates the synovitis. Whether this initiating factor involves toxic absorption or an immunological reaction remains speculative. If this thesis is true, it would be expected that the incidence of synovitis in Crohn's disease, with the larger area of potentially affected gut and the impossibility of radical surgical cure, would be higher than that in ulcerative colitis. This is, in fact, the third difference between the two. Estimates of the incidence of intestinal synovitis in association with the two diseases vary widely. In both ulcerative colitis and Crohn's disease incidences varying from 0 (Feder, 1938; Flood *et al.*, 1956; Kiefer and Ross, 1945) to 22 per cent (Fischel, 1949; Bockus *et al.*, 1956; Kirnser *et al.*, 1957; Hammer *et al.*, 1968) have been reported. The variation frequently reflects the specialty of the investigators, series reported by rheumatologists usually showing a higher incidence of joint disease than those reported by surgeons. However, there are three sets of data in which direct comparisons have been made by closely associated workers of the comparative incidence of intestinal synovitis. These all show a higher incidence of the synovitis in association with Crohn's disease than with ulcerative colitis (Table 1).

TABLE 1. Percentage of patients with intestinal synovitis.

	Ulcerative colitis	Crohn's disease
Cornes and Stecher (1961)	9.5	10.7
Hammer <i>et al.</i> (1968)	12.4	22.2
Haslock <i>et al.</i> (1973)	12.1	20.7

Few pathological clues have been obtained from synovial biopsy or synovial analysis as to the aetiology of intestinal synovitis. Changes in both synovium

and synovial fluid are compatible with a non-specific inflammatory process. A single case has been reported in which the synovial biopsy from a patient with Crohn's disease has shown granuloma formation (Lindstrom *et al.*, 1971).

The treatment of intestinal synovitis should take into account the self-limiting nature of the condition. Control of the intestinal disease usually results in regression of the joint symptoms, while eradication of the intestinal disease effectively prevents recurrence of the synovitis. Analgesic/anti-inflammatory agents may be required, although the presence of active intestinal ulceration may restrict the choice of preparation. Aspiration of affected joints may give considerable relief where a significant effusion has developed, and intra-articular hydrocortisone is useful in controlling acute inflammation.

The second type of arthritis associated with intestinal disease is ankylosing spondylitis. Although several case reports of the association had been published previously, its extent was highlighted by Acheson (1960). He studied the discharge records of the Veterans' Administration Hospitals, and found that 3.0 per cent of patients with Crohn's disease and 2.6 per cent of patients with ulcerative colitis had also been diagnosed as having ankylosing spondylitis. This was about twenty times the frequency with which ankylosing spondylitis was diagnosed in a random sample of medical and surgical patients. Similar conclusions were drawn from a study in Edinburgh (McBride *et al.*, 1963) in which an increased incidence of colitis and Crohn's disease was found in spondylitics attending for radiotherapy, and an increased incidence of ankylosing spondylitis in the patients attending the gastroenterology clinic, when compared with the population. Wright and Watkinson (1965b) found that sacro-iliitis was even more common than clinical ankylosing spondylitis, and this finding has been confirmed in subsequent studies in which the sacro-iliac joints have been X-rayed in the absence of symptoms referable to them (Ansell and Wigley, 1964; Haslock, 1972). Whether this sacro-iliitis is an early stage in the development of full-blown ankylosing spondylitis, a *forme fruste*, or a separate condition will not be known until long-term follow-up of patients with asymptomatic sacro-iliitis has been undertaken. Until then it is safest to advise an appropriate range of home exercises which should be undertaken in anticipation of the possible development of more widespread disease.

Ankylosing spondylitis associated with intestinal disease follows a contrasting course to intestinal synovitis. The onset of the articular symptoms often precedes the intestinal ones (Fig. 1) and the course of the two conditions continues independently (Acheson, 1960; McEwen *et al.*, 1958; Haslock and Wright, 1973). Thus, severity, extent, location and other complications of the intestinal disease do not influence the development of the spondylitis, and surgery has no effect on its progress. Peripheral joint involvement may occur,

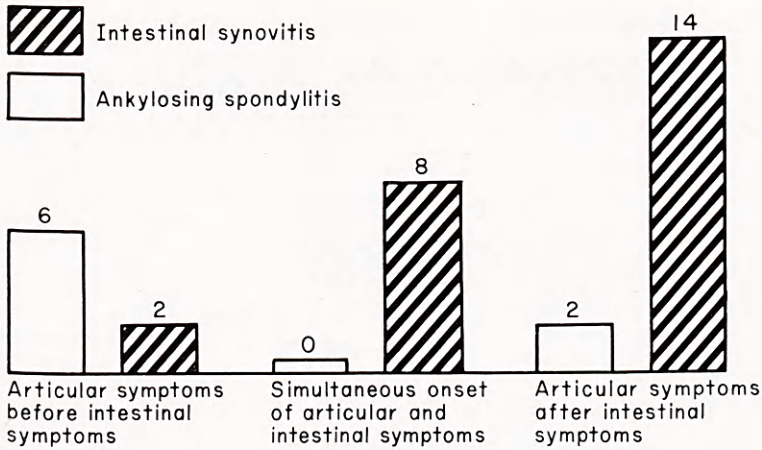


Fig. 1. Time of onset of articular and intestinal manifestations in patients with Crohn's disease (from Haslock, 1972).

but may be distinguished from intestinal synovitis by its more persistent nature and the association of appropriate radiological signs.

The aetiology of the spondylitis has recently been clarified by two family studies undertaken in Leeds (Macrae and Wright, 1973; Haslock, 1973), the probands being found within a 20-mile radius from the city centre. In addition to the 91 patients with ulcerative colitis and 116 with Crohn's disease, 326 first-degree relatives, 109 second-degree relatives and 110 spouses were studied with respect to their musculo-skeletal complaints. Ankylosing spondylitis was diagnosed using the New York CIOMS criteria (Bennett and Burch, 1968), and the patients diagnosed as having definite or probable ankylosing spondylitis by these criteria are shown in Fig. 2. A gradation can be seen, with the incidence of arthritis being directly proportional to the closeness of the blood relationship. This strongly supports the suggestion that ankylosing spondylitis is an hereditary accompaniment of inflammatory bowel disease. This has previously been suggested by consideration of isolated families, particularly the remarkable family reported by Sherlock *et al.* (1963), but had never previously been quantitated using randomly selected probands.

The treatment of ankylosing spondylitis associated with bowel disease is similar to that of idiopathic ankylosing spondylitis. A programme of active exercises should be devised for the patient, who must be persuaded to make them a part of everyday life. The use of analgesic/anti-inflammatory drugs may be restricted by gastrointestinal upset and bleeding. Drugs which frequently cause diarrhoea, such as the fenemates, are best avoided, especially

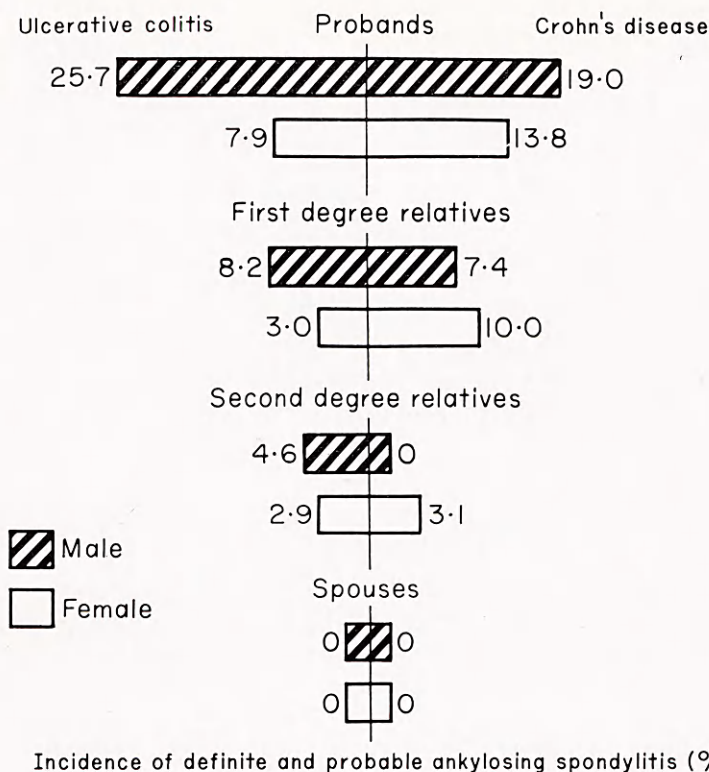


Fig. 2. Association of inflammatory bowel disease and ankylosing spondylitis.

in patients with ileostomies. Care is necessary at the time of acute exacerbation of the intestinal disease or during the period around surgery when the patient may be bed-fast and weak, leading to fixation of the joints in disadvantageous positions. A programme of careful assisted physiotherapy is mandatory at such times.

The patient with bowel and joint disease can only be advised and treated properly when an accurate diagnosis of both diseases is made. This is epitomised by back pain, which may be caused by osteoporosis, particularly when steroid therapy has been used (Haslock, 1972), referred intestinal pain (Hilton, 1860) or the occurrence of incidental rheumatic disorders, which have been recorded in 45 per cent of one series (Wright and Watkinson, 1965a). The temptation to dismiss rheumatic complaints as trivial in face of the severity of the bowel disease occasionally results in such measures as the provision of surgical corsets for patients with undiagnosed backache, which may be disastrous in those with ankylosing spondylitis. This particularly applies to female

patients, who comprise a higher proportion of patients with spondylitis associated with bowel disease than those with idiopathic ankylosing spondylitis. Similarly, patients with ankylosing spondylitis must be considered at risk of developing inflammatory bowel disease. The studies of Jayson and his colleagues (Jayson and Bouchier, 1968; Jayson *et al.*, 1970) have shown that up to 18 per cent of patients with ankylosing spondylitis investigated by sigmoidoscopy, barium meal and rectal biopsy showed unequivocal evidence of ulcerative colitis or Crohn's disease. Several of these patients were asymptomatic.

INTESTINAL SURGERY

The final association between joint disease and the gut is a rarity as yet unreported in this country. The operation of jejunocolic bypass is occasionally used in the treatment of gross obesity. In one series of 31 patients who had undergone this operation, 6 developed postoperatively a polyarthritis, described as 'of rheumatoid type', but without the serological features of rheumatoid arthritis. One patient underwent reconstruction of the bowel, and the arthritis in this patient went into complete remission following the second operation (Shagrin *et al.*, 1971). While it is not anticipated that such patients will be encountered frequently, it is possible that they will provide an experimental model through which the aetiology of intestinal arthritis may be discovered.

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Distractions

Looking up the past, the amateur's eye is drawn to useless ephemera long dissolved in time. Checking certain items in *Vanity Fair* the text seemed of less interest than the advertisements. Here was Laurent Perrier et Cie selling in 1895 the 'most powerful nerve tonic known to science' their Coca-Tonic Champagne. At 3s. 9d. a pint it had the commercial edge on today's tranquillisers. But if music was better for the nerves, what about a Broadwood rosewood grand piano for £20? Or a quiet stay at the Midland Railway Hotel in Liverpool where there was a telephone in every room. Jump a reign to King George V when, in 1911, Madame Tussauds had life-like portrait models of His Majesty and Queen Mary, ably supported by a 'Speaking Likeness of T. W. Burgess, Swimmer of the Channel, modelled direct from life'. At the Gaiety Theatre it was inevitable that Mr George Edwardes was producing a show, but with competition from Sarah Bernhardt who was playing at the Coliseum. The Hippodrome had the 'sensation of the century' with 'Leoncavallo conducting his masterpiece Pagliacci' twice daily, his programme having the curious support of Woodward's sea-lions and seals. Those dear dead days, so very dead and not so dear for many.