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Reiter's disease in three boys

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Iveson, J. M. I., Nanda, B. S., Hancock, J. A. H., Pownall, P. J., and Wright, V. (1975). *Annals of the Rheumatic Diseases*, **34**, 364–368. **Reiter's disease in three boys.** Three cases of Reiter's disease occurring in boys under the age of 16 are reported. One of these presented with a *Salmonella enteritidis* diarrhoea. This conforms to the 'dysenteric' form of Reiter's disease usually seen in Europe and rarely reported in England. Another presented with a monarticular arthritis of the knee, and the third has developed a chronic relapsing erosive arthritis as a result of sexually acquired Reiter's disease—an occurrence not previously reported in this age group.

We draw attention to the frequency of diarrhoea in these children and the sex incidence of 1 female to 4–5 males, which agrees more with Reiter's disease of dysenteric origin than that acquired venereally.

Reiter's disease is usually seen in young men and its occurrence in women and children is rare. Lockie and Hunder (1971), in an excellent review of the literature, found only 20 adequately detailed cases of childhood Reiter's occurring under the age of 16, to which they added one of their own. They found a higher incidence (75%) of diarrhoea in the childhood cases than is usually found in adults—approximately one-third to one-half of all patients (Weinberger, 1962). Diarrhoea preceded the other symptoms or developed early in the course of the disease, but only 2 cases had stool cultures positive for an intestinal pathogen: *Shigella flexneri* being isolated from one and *Salmonella enteritidis* from another.

Of the childhood cases so far reported only 4 have been from England (Corner, 1950; Jacobs, 1961; Gough, 1962; Moss, 1964) and 6 from the United States (Florman and Goldstein, 1948; Margileth, 1962; Herman, 1966; Davies, Haverty, and Boatwright, 1969; Lockie and Hunder, 1971). The last report in England was 10 years ago (Moss, 1964), so that it seemed timely to report our experience.

Three cases of Reiter's disease occurred in boys aged 13, 14, and 15 years, one of whom presented with a *Salm. enteritidis* diarrhoea and another with monarticular arthritis affecting the right knee. The third case illustrates the more chronic relapsing venereal syndrome, resulting from sexual intercourse—a possibility that is generally overlooked in this age group, and has not previously been reported.

Case reports

CASE 1

An obese prepubertal 15-year-old boy was admitted to hospital in December 1971, with a 3-day history of headache, malaise, abdominal pain, profuse diarrhoea, and fever. Clinical diagnosis of infectious gastroenteritis was confirmed by isolation of *Salm. enteritidis* from several successive stools. Treatment with intravenous fluids and codeine phosphate resulted in rapid symptomatic improvement. Examination revealed no abnormalities other than obesity, but he lacked secondary sexual characteristics. On the 8th day of illness he developed a marked bilateral conjunctivitis followed by diffuse painful swellings over the dorsa of both feet, and a transiently painful left elbow. By the following day there was a scanty urethral discharge, and massage in the prostate region produced a small quantity of creamy fluid. This contained a large number of leucocytes, a few epithelial cells, and occasional Gram-positive cocci, but culture yielded only *Staphylococcus albus G.* ESR, which on admission had been 45 mm in 1st hour (Westergren), rose slightly to 56 mm in 1st hour, with these new developments.

Treatment with tetracycline and phenylbutazone was initiated with satisfactory symptomatic relief, but 4 days later he developed transient activity in both wrists and left sacroiliac joint. Intermittent activity persisted until the end of January 1972 and variable degrees of arthralgia affected these sites until April 1972, when ESR had fallen to 19 mm in 1st hour. Since this time he has been symptom free.

The Widal reaction showed a typhi 'O' titre of 1/500 and a paratyphus B 'O' titre of 1/400, 23 days after an initially negative reaction. A third Widal 10 days later showed only a residual titre of 1/125 to the paratyphus B antigen. This result seemed fully consistent with a recent *Salm. enteritidis* infection.

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The following investigations were normal: haemoglobin and white cell count, urine cultures for *Salmonella* and viruses, liver function tests, urea and electrolytes, Wassermann and gonococcal complement fixation test, latex test for rheumatoid factor, antinuclear factor, LE cell test × 3, throat and eye swabs, *x*-rays of chest, wrists, knees, ankles, sacroiliac joints, and lumbar spine.

CASE 2

A pubescent 13-year-old boy presented to the orthopaedic department in February 1973, with a limp and pain in the right knee of 2 days' duration; additionally there was pain in the back and the left side of the chest at the level of the inferior angle of the scapula. Two weeks previously he had had a 3-day attack of diarrhoea followed by a sore throat, itching and redness of, and discharge from, both eyes. Mild dysuria without urethral discharge developed later, lasting for 2 days. There was no history of sexual intercourse and the boy's demeanour and attitude to questioning gave a strong impression of truthfulness. The right knee was swollen, painful, and warm, containing a large effusion, and all movements were painful and restricted. No other joint was affected but the area around the inferior angle of the left scapula was moderately tender. There were no abnormalities in the other major systems but a tachycardia of 110/min was recorded with a fever of 38·4°C. The urine contained a large number of pus cells which were sterile on culture. ESR was 72 mm in 1st hour (Westergren) and white cell count in the blood $18{\cdot}0 \times 10^9$/l (18000 mm^3).

This acute febrile monarticular arthritis in a child led to investigation for acute osteomyelitis. An arthrotomy was performed after aspirating 75 ml of apparently purulent fluid. Exploratory bore holes drilled into the femoral metaphysis failed to locate pus. The knee aspirate contained many leucocytes but there was no growth on culture. Postoperatively he continued to complain of chest wall pain but repeated clinical and radiological examinations were normal. The knee was splinted and treatment with ampicillin and cloxacillin was given orally. Fifteen days after the knee had become swollen arthritis developed in the left ankle and the temperature which had recently been settling again became raised. The spread of the joint disease led to reconsideration of the history and the diagnosis of Reiter's disease. At this point resolution of the joint symptoms began spontaneously and satisfactory pain relief was achieved with phenylbutazone 100 mg b.d. The synovial swelling of the knee and the fever gradually declined over the next few weeks, being completely resolved after 4 months. Eight months later he was well and had developed no further symptoms. Other investigations performed were normal: haemoglobin, antistreptolysin O titre, sheep cell agglutination test, blood, urine, and stool cultures, Wassermann and VDRL, *x*-rays of knee and ankle, urea and electrolytes. Human leucocyte antigen (HL-A) W27 was not detected, but HL-A2, HL-A3, and HL-A7 were present.

CASE 3

A sexually mature 14-year-old schoolboy was admitted to another hospital in January 1972, with a 16-day history of pain and swelling of the third and fourth toes of the right foot, and transiently inflamed conjunctivae. Four days later the left big toe had also become swollen, tender, and red. These digits improved, but 5 days later the right knee became swollen, painful, and stiff, and weight bearing on this leg became impossible. He denied dysuria, frequency, or haematuria. On the day before admission he developed pain in the left thumb with swelling, but except for some anorexia, his general health was good. He was the youngest of 6 children and his only previous illness had been an episode of abdominal pain in 1971, for which no cause was found.

Examination revealed only a small postpubertal schoolboy with a fever of 37·5°C and a circular ulcer, 6 mm in diameter, in the centre of his palate. The fauces were normal and no lymphadenopathy was detected. Urine was normal. The right knee was warm, swollen, contained fluid, and was tender. Circumference was 2 cm greater than the left, with only 30° of flexion. The third toe of the right foot, the left first toe, and left thumb were also swollen and tender.

Laboratory investigations showed Hb 13 g/dl, WBC $9{\cdot}5 \times 10^9$/l (9500/mm^3) (neutrophils 76%), ESR 46 mm in the 1st hour (Westergren), C reactive protein negative, DAT negative, Wassermann negative. Urine contained 66 pus cells/mm^3 the day after admission and 30 pus cells/mm^3 2 weeks later. Virus studies, Brucella antibodies, LE cells, *x*-rays of chest, hands, and feet, ECG, and throat swabs were normal.

Joint signs subsided after admission on bed rest and solprin, 900 mg q.d.s. Penicillin V and ampicillin, initiated before admission, were continued. The fluctuating fever also gradually settled and although minor symptoms continued until May, it was possible to discharge him in early February taking only ibuprofen 200 mg t.d.s.

Over the next year he had transient recurrences of joint swelling affecting the previously involved sites and lasting only a day or two.

In June 1973, the left hallux once again became swollen, to be followed by the other previously affected sites. Eight days later he developed marked bilateral conjunctivitis with a purulent green discharge from the eyes, and the next day right sacroiliac pain. Examination by an ophthalmologist confirmed the presence of conjunctivitis without evidence of anterior uveitis. He initially denied any urinary symptoms but later admitted to dysuria and to having had sexual intercourse before the original episode of the illness. However, the only detectable urinary abnormality on this occasion was the presence of 31 pus cells/mm^3. He was febrile (38°C) and there were several mucosal ulcers on his palate. The metatarsophalangeal and interphalangeal joints of the left first and the right third and fourth toes were warm, swollen, and tender with limited movement. Hb was 16·4 g/dl, WBC $10{\cdot}6 \times 10^9$/l (10600/mm^3), ESR 35 mm, and the sheep cell agglutination test was negative. *X*-rays of the feet showed a reduced joint space of the interphalangeal joint of the left hallux, with a possible erosion. There were erosions at the base of the fourth and fifth right proximal phalanges and in the head of the right fifth metatarsal in association with juxta-articular osteoporosis.

He was treated with tetracycline and phenylbutazone 100 mg b.d. and again improved, but his feet have been a source of considerable pain and his schooling has been intermittently interrupted as a consequence. Recently he has obtained relief of joint pain with indomethacin, but has developed a left anterior uveitis and is currently receiving local therapy with steroids. His blood has been

found to contain the following human leucocyte antigens (HL-A): 2, 3, W27, and W15.

Discussion

It is recognized that Reiter's disease may present either as a predominantly diarrhoeal (or dysenteric) form during which urogenital manifestations occur but may not be prominent, or as a predominantly venereal form which may be accompanied by nonspecific diarrhoea (Hancock, 1964). The distinction is probably artificial but useful for descriptive purposes. The venereal form follows recent sexual contact and is the only type seen in this country, but the dysenteric form is associated with a variety of intestinal pathogens and nonspecific diarrhoeal illnesses, and is seen in Asia, Eastern Europe, and Northern Africa. In France, Germany, and Scandinavia it may follow either form of inflammation.

It was the dysenteric form which was first described by Reiter (1916) and Feissinger and Leroy (1916), and for some years thereafter was the only accepted form of the disease. It is most commonly associated with an epidemic of *Shigella* dysentery (Paronen, 1948; Noer, 1966; Davies, and others, 1969), but has also been seen with amoebic dysentery or seasonal nonspecific diarrhoea. The dysenteric form has not been reported after cholera or staphylococcal intestinal infections (Hahn and Masi, 1969) and has been reported only once after a salmonella infection (Neimann, Pierson, and Ginsbourger, 1959). Sporadic cases may also occur (Davies and others, 1969) but are less frequent than the epidemic variety. The type of *Shigella* dysentery implicated has varied, the commonest being *Sh. flexneri*, but both *Shigella sonnei* and *Shigella dysenteriae* have also been reported (Young and McEwen, 1947).

In England and Wales some 23000 isolations of *Sh. sonnei* occur annually (*British Medical Journal*, 1972) and approximately 180 isolations of *Sh. flexneri* in any period from January to May (*British Medical Journal*, 1970). These figures undoubtedly underestimate the true incidence of these infections, so that it is surprising that no cases of Reiter's disease following these infections have been reported in England recently. This situation is apparently not new—Jonathan Hutchinson, writing in 1880, also noted the infrequency of 'postdysenteric rheumatism' in this country. In contrast, Paronen (1948) reported that Reiter's disease occurred in 0·24% of 150000 cases of *Sh. flexneri* dysentery during a Finnish epidemic, and Noer (1966) saw 9 cases after 602 episodes of proven bacillary dysentery in U.S. sailors during a visit to a port in a locale known to be endemic for Shigellosis.

The difference between post-Salmonellal Reiter's syndrome and 'post-Salmonellal arthritis', of which there have been several reports (Berglöf, 1963; Vartiainen and Hurri, 1964; Warren, 1970) is probably only a semantic one. The described cases have much in common with postdysenteric Reiter's. The arthritis starts one or two weeks after the onset of fever and diarrhoea resulting from infection with *Salmonella typhimurium* or *Salm. enteritidis*. The pattern of joint involvement is similar, the knee and ankle being most frequently affected, and with joint symptoms lasting for up to 6 months. However, the reported sex incidence is equal and conjunctivitis has only been reported in 3 cases, one of whom had ankylosing spondylitis and associated iritis. Unfortunately no information is given regarding genitourinary inflammation in any of the cases. One case occurred in a 9-year-old boy with *Salm. typhimurium* diarrhoea (Berglöf, 1963) and another in a 2-year-old girl with *Salm. enteritidis* infection (Warren, 1970). The incidence of this type of arthritis has been given as 1·9–2·4% for all *Salmonella* infections (Vartiainen and Hurri, 1964) and 2·4–2·5% for *Salm. typhimurium* alone. A suppurative *Salmonella* arthritis also occurs (David and Black, 1960), but this differs from the post-Salmonellal arthritis in the presence of organisms within the joint and in other clinical features of a septic arthritis in a young person.

The diarrhoeal form is the common presentation in those cases of Reiter's disease seen in childhood (Moss, 1964; Lockie and Hunder, 1971; Margileth, 1962). If we add our cases to those reviewed by Lockie and Hunder (1971), there are now 24 well-documented cases of Reiter's disease occurring in children under the age of 16. Of these, 17 have had diarrhoea at some time during the course of the disease and most have presented with it. Of the 13 cases now reported from Great Britain and North America, diarrhoea has occurred at some time during the illness in 9, and has been the presenting feature in 6. Of these 6, one had a stool culture positive for *Sh. flexneri*, and the other for *Salm. enteritidis*. Shigella agglutinins have been found in the blood in several cases.

These findings support the view that diarrhoea is a prominent feature of childhood Reiter's disease, but do not indicate whether it is a precipitating factor, an antecedent infection which allows the entrance of other organisms, or an early symptom of the illness (Weinberger, Ropes, Kulka, and Bauer, 1962). Certainly it is not suggested that the intestinal pathogen is a direct aetiological agent of Reiter's disease in either children or adults. On the other hand, it is possible that the higher incidence of diarrhoea in children may be due to nonspecific 'parenteral diarrhoea' which may occur in infants and children with infection outside the gastrointestinal tract (Ellis and Mitchell, 1968). Possible causative organisms considered recently have been the mycoplasmas and micro-organisms of the genus *Chlamydia*.

Of the 13 cases of juvenile Reiter's now reported from Great Britain and North America, all have been

male, and as far as is possible to detect from the reports, ten were either prepubertal or, as in our Case 2, pubescent; only Gough's (1962) second case and one of our cases have been sexually mature. The subjects have ranged in age from 3 years 2 months to 15 years, with a mean of 9·6 years.

It is interesting that the male predominance so frequently noted in adult series is also found among children. The only reports of childhood Reiter's occurring in girls have come from Europe (Zewi, 1947; Henckel, 1954). This gives a ratio of 1 girl to 4–5 boys, and is similar to that found in Paronen's adult 'dysenteric' cases, of whom 10% were women; but is higher than that of Oates and Csonka (1959) who found a ratio of approximately 1 female to 50 male patients seen in venereal diseases clinics. This seems to indicate that the childhood cases have more in common with the adult dysenteric form than the venereal form.

In none of the previously reported cases had sexual intercourse been recorded as a precipitant of the Reiter's disease in the so-called 'childhood' group, and in most there is no reference to the state of sexual maturity. Our third case highlights the fact that boys under 16 may be sexually mature and active. Consequently typical venereal Reiter's disease may be found in these young people.

A persistently monarticular arthritis has been seen in adult cases of both venereal and dysenteric types (Postma, 1937; King, Williams, Nicol and Loudon, 1946; Paronen, 1948; Harkness, 1950; Guck and Wolf, 1952; Csonka, 1958) and also in childhood cases (Florman and Goldstein, 1948; Jacobs, 1961; Davies and others, 1969). Probably the most common causes of monarticular arthritis in children are trauma (including osteochondritis), Still's disease, and tuberculosis (Bywaters and Ansell, 1965). Occasionally septic arthritis may occur, and it therefore is understandable that the initial investigations of our second case and of that reported by Florman and Goldstein (1948) were undertaken to exclude the possibility of intra-articular or para-articular infection. In both cases purulent but sterile fluid was aspirated from the affected joint and antibiotic therapy started before definitive diagnosis could be made. It is, of course, mandatory in all cases of monarticular arthritis in both adults and children to exclude, by aspiration and culture of joint fluid, the possibility of septic arthritis. The left ankle subsequently became involved, though never to the extent of the right knee.

The mild joint symptoms of our first case are more typical of childhood Reiter's syndrome. The joint disease may vary from mild to severe (Lockie and Hunder, 1971), but recurrence is rarely reported, possibly because follow-up has not usually been prolonged in most cases. Only one of our cases has relapsed (Case 3) and, as with Gough's (1962) case of a 15-year-old boy who denied sexual exposure, bony erosions have developed. Joints of the lower limb have been affected in all the childhood cases, especially the knee and metatarsophalangeal joints. This distribution, and the asymmetry which is also seen, are also features of adult cases. The back and arm pain in Case 2 has been considered a prominent feature of Reiter's, especially in the early stages of an attack (Hancock, 1964). Often fleeting and difficult to localize, the pains are probably of tendinous and myofascial origin. Although pleurisy occurred in 5% of Paronen's cases in adults, there was no evidence of it here.

All our cases had bilateral conjunctivitis of moderate severity but in none were the genitourinary symptoms prominent, there being no clinical urethritis in one and only mild dysuria without urethral discharge in the other two. Prostatitis was shown to be present in the first case when a purulent discharge was produced by prostatic massage, and urethritis in the second by the demonstration of proteinuria and a sterile pyuria. As with the dysenteric form of adult Reiter's the genitourinary symptoms in children are not prominent and the urethral discharge is normally described as scant (Lockie and Hunder, 1971), though it may occur (Moss, 1964; Herman, 1966; Davies and others, 1969). The main indication of urethritis in children has been dysuria or frequency.

Mucocutaneous lesions are infrequent in children, although keratoderma blennorrhagica (Cantarutti, 1954; Gough, 1962) and circinate balanitis (Florman and Goldstein, 1948; Cantarutti, 1954; Jacobs, 1961) have been recorded. The oral ulcers that were seen in Case 3 are therefore unusual, but are not an uncommon finding in adult cases.

Although the increase in promiscuity in young people* has not apparently led to a corresponding increase in juvenile cases of Reiter's disease from sexually acquired infection, there will be the occasional case of this disorder and misdiagnosis is likely if the possibility is not considered. No cases of Reiter's disease were recorded in E. M. Sills' (1973) recent review of the final diagnosis of 150 consecutive referrals of children for arthritis, but 40 (28%) were found to have disorders other than juvenile rheumatoid arthritis. In 6 (4%) the diagnosis remained undefined. It is among the latter group that most cases are probably found.

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*Unsubstantiated statements are avoided as far as possible in this journal, but the authors' opinion here does not appear to detract from the clinical value of this report. *Editor.*

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