REITER'S DISEASE IN CHILDHOOD*

BY

IVOR S. MOSS

Guy's Hospital, London

Reiter's disease has rarely been observed in children. The first case to be reported was that of a boy aged 16 years (Junghanns, 1918). The initial symptom was a severe furuncle of the upper lip; 5 days later non-gonococcal urethritis appeared, followed by arthritis of a knee and metatarsal joints. Conjunctivitis, iritis and keratitis occurred after a further 4 days.

The next published account was that by Rajam and Rangiah (1941) who recorded the case of a boy aged 4 years who had urethritis, conjunctivitis, polyarthritis, and keratoderma blennorrhagica.

Koster and Jansen (1946) gave an account of a family in which three boys were affected. The eldest was 15 years old and developed diarrhoea followed by dysuria, bilateral conjunctivitis, and painful swelling of the left big toe and the left ankle joint. No pathogenic organisms were found on smear and culture from the inflamed conjunctiva. The dysuria disappeared after one week but joint involvement persisted for several weeks. Two brothers, one aged 3 and the other 11 years, had similar attacks. Blood tests in the three brothers showed agglutination of Shigella flexneri but the titres were not recorded.

Zewi (1947) recorded ten cases. One was that of a 4-year-old boy who had had diarrhoea for one day, followed by arthritis of the right elbow, both knees, and a metacarlo-phalangeal joint. Urethritis appeared, with purulent discharge and balano-posthitis. The syndrome was completed by the development of conjunctivitis and keratitis. The illness was severe and lasted over 2 months, with fever and a high erythrocyte sedimentation rate (E.S.R.). Zewi also described typical cases in two boys aged 14 and 17 years and in two girls aged 15 and 16 years. The other five patients were young adults. All but one of the ten patients had diarrhoea. Urethritis was present in all the male patients but was not severe. The females had dysuria and frequency of micturition. Blood agglutination tests for dysentery were not recorded.

Florman and Goldstein (1948) gave an account of a boy with Reiter's disease, who had severe diarrhoea lasting 5 days, and then dysuria, urethral discharge, and increased frequency of micturition. Bilateral conjunctivitis and swelling of the right knee appeared after 2 days. The joint was aspirated and greenish-yellow pus was obtained. The inflammation of the right conjunctiva became worse 2 weeks after the onset of the illness and keratitis developed in that eye. After 2 months the arthritis had gone but the keratitis had left a small corneal opacity. Only non-pathogenic bacteria were cultured from the conjunctiva and the joint fluid. Inoculation into rabbit cornea, mouse peritoneum, and mouse brain did not reveal evidence of virus infection. The only positive test was the agglutination of Sh. flexneri VII at high titre. In the first week, the titre was 1 : 1,280 and by the second week it had fallen to 1 : 40.

Gault and Gault (1948) described a girl aged 7 years, with a severe generalized rash of keratoderma blennorrhagica. It was thought that urethritis was cloaked by severe discharge from the lesions in the perineum, buttocks, and inner and outer aspects of the thighs. There was no mention of diarrhoea, arthritis, or conjunctivitis. This was presumably a case of the condition described by Reiter with only partial expression of the syndrome.

Paronen (1948) recorded a series of 334 cases of "Reiter's syndrome" associated with an epidemic ofFlexner dysentery on the Karelian isthmus in Finland. 322 patients (96·4 per cent.) had a history of Flexner dysentery, and only twelve (3·6 per cent.) gave no history of diarrhoea. A boy aged 2 years and 8 months had a typical attack of Reiter's disease; he had had dysentery at the same time as the rest of his

* Received for publication April 8, 1963.
Reiter's Disease in Childhood

family, with bloody diarrhoea and fever for 2 days, bilateral conjunctivitis appeared 10 days later, and urethritis, with swellings of both ankle joints, both knees, and the right elbow, followed after a further 2 days. Blood tests showed agglutination to 1 : 80 for Flexner A + D + Wx. He had recovered fully 4 months later. Paronen recorded three other cases of Reiter's syndrome in boys between the ages of 12 and 15 (exact ages not recorded). He noted that, although at least 150,000 people had dysentery during the epidemic, only 0-2 per cent. of cases were complicated by arthritis. In a series of 460 patients suffering from non-specific urethritis, Morton and Read (1957) reported that fourteen (3 per cent.) developed Reiter's disease. In similar series Grimble (1960) reported an incidence of 3 per cent. in 293 cases and Csonka (1958) an incidence of 0-8 per cent. in 182 cases.

Henckel (1954) reported three cases of Reiter's disease in girls, aged 9 years and 1 month, 2 years and 9 months, and 2 years and 10 months respectively. Diarrhoea preceded the complete syndrome of conjunctivitis, arthritis, and urinary symptoms.

Corner (1950) gave an account of Reiter's disease in a 9-year-old boy. The first symptom was increased frequency of micturition with urinary discomfort. The dysuria ceased after a few days, swelling of the right hip joint occurred and was followed by swelling of both knees and the right ankle. The patient recovered completely after 5 months. Although there was no history of dysentery, blood tests showed agglutination to 1 : 480 for Flexner V during the illness, and became negative on improvement of the syndrome. The E.S.R. was raised to 110 mm./1st hr early in the illness, and fell to normal as recovery ensued.

Cantarutti (1954) reported the first case in Italy of Reiter's disease in childhood. This occurred in a boy aged 10 years; diarrhoea was severe and persisted for 3 days before balanitis, urethritis, and bilateral conjunctivitis appeared, and 2 weeks later polyarthritis, iritis, and keratoderma blennorrhagica confirmed the diagnosis. Ulceration of the mouth, tongue, and palate appeared after a few days. Investigations for pleuropneumonia-like organisms and virus inclusion bodies, and blood agglutination tests were negative. The Wassermann reaction was positive, although there was no evidence of congenital syphilis. The mother's Wassermann reaction was positive and the father's was negative.

Neimann, Pierson, and Ginsbourger (1959) gave an account of Reiter's syndrome in a boy aged 1 year and 9 months. He had diarrhoea for 7 days followed by bilateral conjunctivitis and urethral discharge; 5 days after the onset of urethral discharge he developed swelling of the left shoulder joint and of the right elbow. Blood tests showed agglutination to 1 : 1600 for Gaertner's bacillus (Sach. enteritidis). There was a good response to chloramphenicol and streptomycin, but the arthritis persisted and the left knee and left hand became involved. The arthritis eventually subsided in 3 months after treatment with phenylbutazone.

Jacobs (1961) recorded a case of Reiter's disease in a boy aged 9 years. Abdominal pain and moderate diarrhoea lasted for 2 days and was followed by pain on micturition. There was no actual urethral discharge but the mucosa was reddened. On the third day, he developed bilateral conjunctivitis and swelling of the right knee. The E.S.R. was 56 mm./1st hr; 6 weeks later all symptoms had subsided and the E.S.R. was normal. Blood agglutination tests and virus cultures were negative.

Case Report

A boy aged 10 years was admitted to Guy's Hospital on August 28, 1962, complaining of pain and swelling in the left knee and the right ankle, sore eyes, and urethral discharge. There was no history of significant illness in the past. He was of normal intelligence and led a normal school life. He had been to Spain for a holiday in the latter part of May, 1962.

On July 25, 1962, he had felt ill and bilateral subconjunctival haemorrhages had appeared; 2 days later he had developed diarrhoea, abdominal pain, vomiting, and severe headache. On the following day, a herpetic sore had appeared on the upper lip. The diarrhoea and vomiting had subsided by August 2, but the herpetic sore was still present at the time of admission and an ulcer had appeared inside the mouth.

On August 7, he had developed dysuria with urethral discharge, severe bilateral conjunctivitis and a temperature of 100°F. At this stage he was treated with neomycin eye ointment and an oral sulphamamide preparation. Two days later he had become considerably worse, and chloramphenicol eye ointment was substituted for the neomycin. Conjunctival smears and cultures did not reveal pathogens. The diagnosis of Reiter's disease was then considered.

On August 11, the temperature had risen to 102°F and the right ankle became painful and swollen. The diarrhoea had recurred. A small blood clot was passed in the urine and the urethral discharge persisted. The urine was sterile on culture but contained numerous polymorphonuclear leucocytes. The E.S.R. was 38 mm./1st hr, and the blood was otherwise normal. Agglutination reactions to Salmonella typhi, Salmonella paratyphi A and B, Brucella abortus, and B. melitensis were negative. The gonococcal complement-fixation test (G.C.F.T.), Wassermann reaction, and Kahn test were negative. By August 15, the conjunctivitis had improved but a severe haemorrhagic stomatitis had appeared. Culture from the mouth gave a moderate growth of Strep. viridans, sensitive to...
erythromycin, and treatment was given with that antibiotic.

On August 20, the conjunctivitis had become markedly worse and treatment had been changed to prednisolone and neomycin eye ointment. At the same time, he had developed pain and swelling in both knees, more severe in the left than in the right; 2 days later, the swellings were more pronounced and severe muscular contractions occurred in both knees. Posterior slabs were applied and eased the pains satisfactorily. Over the next week he gradually improved. The urinary symptoms subsided and the eyes no longer caused discomfort, but the joint swellings persisted.

At the time of admission on August 28, he appeared alert and free from discomfort. There was mild conjunctivitis but no iritis or keratitis. There was moderate gingivitis, and a macular eruption on the palate and the buccal mucous membrane. The liver and spleen were not enlarged. The urethral meatus was infected but there was no discharge. There was no enlargement of lymph nodes. There was effusion and stiffness of the left knee and the right ankle. The early morning urine was clear and, on rectal examination, the prostate was normal. The Waaler-Rose test was negative. Radiological examination of the chest, thoracic and lumbar spine, pelvis, sacroiliac joints, and knees showed no abnormality.

By September 9, there was slight residual swelling of the joints involved, but no pain and no limitation of movement. The eyes, mouth, and genitalia were now normal. Blood agglutination tests for *Shigella flexneri* and *Sh. sonnei* were negative. The E.S.R. remained high at 72 mm./1st hr. He was discharged from hospital on September 15.

**Discussion**

The review of the literature shows a total of 24 recorded cases of Reiter’s disease in children including the case here reported (Table). Urethral discharge or other urinary symptoms were present in 22 cases. In general, urinary symptoms were mild. Conjunctivitis was present in 23 cases. Full details have not been recorded in some cases; nevertheless it is clear that eye complications with iritis and keratitis occurred frequently and were more severe than in adults. Arthritis occurred in 23 cases, and required 3 to 4 months before recovery was full.

Diarrhoea was a prominent feature of Reiter’s disease in children. When it occurred, it usually appeared initially preceding other symptoms by a few days or even several weeks. Twenty of the cases began in this way. Blood tests showed agglutination to a significant titre for *Sh. flexneri* in nine cases. In one of these cases there was a positive agglutination test in the absence of diarrhoea (Corner, 1950). In another case (Neimann and others, 1959), there was a positive agglutination test to Gaertner’s bacillus, a feature not previously recorded in Reiter’s disease.

Although the series reported by Paronen (1948) has been of great value, it has led to an undue emphasis on dysentery as a feature of Reiter’s disease in adults. Paronen states that, in his opinion, “Reiter’s syndrome” occurs only after dysenteric infections. Although *Sh. flexneri* has been found more frequently than other bacteria, other forms of dysenteric organisms may yet be identified. It is not known if particular strains of bacteria are more liable to produce the syndrome. It appears that the disease may be due to venereal infection or to dysentery. The unqualified term Reiter’s disease is now used for the condition following non-specific genital infection, and the similar syndrome occurring with bacillary dysentery, is best termed the dysenteric form of Reiter’s disease.

Sharp (1961) studied the frequency of clinical findings in a collection of 586 cases of Reiter’s disease, and compared the genital and dysenteric syndromes. It was found that the incidence and severity of joint involvement and urethral discharge were approximately equal in both groups. Iritis and

**Table**

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<th>Author</th>
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<th>Genito- Urinary Symptoms</th>
<th>Eye Involvement</th>
<th>Joint Involvement</th>
<th>Keratodermia Blennorrhagica</th>
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Total Cases 24 24 23 23 3 20 10
REITER'S DISEASE IN CHILDHOOD

Conjunctivitis were more severe and more frequent in the dysenteric form, but balanitis and keratoderma blennorrhagica were more frequent in the genital form.

PPLO (mycoplasma) have frequently been cultured from cases of non-specific urethritis and occasionally from cases of Reiter's disease, but the significance of these organisms is not understood.

Virus studies have given negative results.

Clinical findings suggest an infective origin, either venereal or dysenteric. This is supported by the finding that children apparently have the dysenteric form of the disease. It has been pointed out (Pearson, Waksman, and Sharp, 1961) that Reiter's disease is very similar to an experimental disease produced in rats by inoculation with mycobacterial antigens. The lesions produced were arthritis, iritis, urethral discharge, and chronic skin conditions similar to keratoderma blennorrhagica. Diarrhoea appeared early in the disease. The syndrome produced was more severe and occurred more frequently in males than in females, just as does Reiter's disease. The arthritis was sub-acute and affected the ankles, wrists, and other peripheral joints. In mild cases healing was complete; in severe cases fibrous or bony ankylosis resulted. The spine and tail were generally involved, sometimes producing a form of ankylosing spondylitis. There is similarity between the experimental lesions and those of several human diseases, including Reiter's disease, the syndromes of Behçet and Stevens-Johnson, ulcerative colitis, ankylosing spondylitis, and sarcoidosis. Fuller understanding of the experimental disease may lead to more knowledge of the rheumatic group of diseases as a whole. Perhaps Reiter's disease may result from a reaction to antigens, produced in non-specific urethritis and in dysentery, which enters the body via the genitourinary tract or the intestinal mucosa.

Auto-immune processes may play a part in the aetiology of Reiter's disease, in view of the high incidence of significantly raised antibodies in the blood to prostate, but not colon, extract in Reiter's disease. A similar result occurs in ankylosing spondylitis and iritis (Grimble, 1963).

Summary

The literature of Reiter's disease in childhood is reviewed and a case reported. Aetiological factors are discussed.

My thanks are due to Dr P. R. Evans, Director of Child Health, Guy's Hospital, for permission to see and report his patient.

REFERENCES


Le syndrome de Reiter chez l'enfant

RÉSUMÉ

L'auteur passe en revue la littérature de la maladie de Reiter chez l'enfant, décrit un nouveau cas, et discute l'étiologie de ce syndrome.
Reiter's Disease in Childhood

Ivor S. Moss

Br J Vener Dis 1964 40: 166-169
doi: 10.1136/sti.40.3.166

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