

19.8 Reactive arthritis 4464

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ESSENTIALS Reactive arthritis a subset of post-infectious arthritis, and causative organisms are usually localized to the gastrointestinal or genitourinary tracts. Following infection, organisms or their components find their way to joints, where they provoke inflammatory immune responses. Whether the responses cross-react with self antigens is unclear; arthritis may be maintained by persistent infection. The disease commonly has specific extra-articular features not seen in other forms of post-infectious arthritis, and is genetically and pathologically a form of spondyloarthritis. Clinical presentation—an acute oligoarthritis of weight-bearing joints is a common finding in secondary care, whereas community cases show mild polyarthritis. In addition to synovitis, enthesopathy is common, and extra-articular features include conjunctivitis, keratoderma, balanitis, and mouth ulcers. Urethritis can be reactive and does not necessarily indicate genitourinary infection. Diagnosis—this depends on a careful history to determine whether there has been preceding infection, followed by examination for synovitis, enthesopathy, and extra-articular features. Definitive proof requires demonstration of recent infection by a triggering organism, using stool culture, urine and genital swabs, nucleic acid amplification techniques, and serology. In some cases, when the nature of the triggering infection cannot be established, patients may be classified as having undifferentiated arthritis. Management—treatment is with symptomatic measures—nonsteroidal anti-inflammatory drugs, intra-articular steroids, and physiotherapy suffice in most cases. Severe, relapsing, or persistent disease may require methotrexate or sulfasalazine, and occasionally biologic drugs such as tumour necrosis factor inhibitors. Little evidence supports prolonged treatment with antibiotics, although chlamydial infection requires conventional short-term treatment. Introduction and historical perspective The term ‘reactive arthritis’ was introduced in 1969 by Aho in Finland, where the combination of a high prevalence of HLA B27 and gastrointestinal yersinia infection afforded opportunities for studying the disease. He defined the condition as ‘an arthritis which develops soon after or during an infection elsewhere in

the body, but in which the microorganisms cannot be recovered from the joint'. However, the condition was first recognized in the eighteenth and nineteenth centuries as an arthritis that followed dysentery or venereal disease, and there were descriptions by Hans Reiter and other contemporaries of the disease among troops affected by dysentery in the trenches of the First World War. The term 'Reiter's disease' has been used extensively since that time, but should now be abandoned for several reasons: Reiter was not the first to describe the disease; he erroneously attributed it to spirochaetal infection; and the triad that makes up Reiter's disease—arthritis, conjunctivitis, and urethritis/ cervicitis—is not a clinically meaningful subgroup within reactive arthritis. The incorrect assumption that a patient with Reiter's triad has sexually acquired reactive arthritis is particularly unhelpful. Definition The term 'reactive arthritis' is sometimes used rather loosely to cover any form of arthritis that follows infection, and then includes post-viral arthritides, rheumatic fever, Lyme disease, and other forms of arthritis that do not generally share clinical features. This usage is not appropriate, and the term 'post-infectious arthritis' is much preferred, with this all-embracing term subdivided into different clinical syndromes, one of which is reactive arthritis (Box 19.8.1). Defined in this way, reactive arthritis is seen as one of the seronegative spondyloarthritides (ankylosing spondylitis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, undifferentiated spondyloarthritis), sharing clinical and immunogenetic features with those diseases. More recently, the Assessment of Spondylarthritis Society (ASAS) has reclassified reactive arthritis as a peripheral spondylarthritis. Other post-infectious arthropathies lack these common features. In the absence of agreed and validated diagnostic or classification criteria for reactive arthritis, Box 19.8.2 presents a useful working classification of those patients who could reasonably be considered to have reactive arthritis. This takes as its starting point the classical pattern of arthritis and typical extra-articular features (Box 19.8.3) that are commonly seen after infection by five organisms—salmonella, yersinia, campylobacter, shigella, and Chlamydia trachomatis. The same clinical syndrome (i.e. arthritis and extra-articular signs) is also seen, but more rarely, following various other infections, especially of the gastrointestinal tract (e.g. by Clostridium difficile); but genitourinary infection with ureaplasma and respiratory infection with Chlamydia pneumoniae can probably also act as triggers of reactive arthritis. The other large group of patients is those who have asymmetric oligoarthritis without extra-articular features, but with definite laboratory evidence of preceding infection by one of the five major reactive arthritis-associated bacteria. Laboratory diagnosis of infection is given priority over symptoms as a classification criterion because infection may be clinically silent. Chlamydia is notorious for this, particularly in women, while in yersinia infection arthritis is inversely correlated with the severity of gastrointestinal symptoms. Positively identifying the triggering infection often poses practical problems. Patients in whom arthritis develops (with or without extra-articular signs) after symptomatic episodes of gastrointestinal or genitourinary infection are therefore usually regarded as having reactive arthritis, even when no triggering organism can be identified, although the diagnosis is inevitably less secure in these cases. Improvement in methods for diagnosing preceding infection should decrease the size of this group, and may show reactive arthritis to be the commonest cause of acute inflammatory oligo- or monoarthritis in young adults. Epidemiology Community studies in Scandinavia, where HLA B27 is present in around 12% of the population (compared with 6–7% elsewhere in Europe), have

19.8 Reactive arthritis 4465

Box 19.8.1 Post-infectious arthritis

- Post-viral arthritis (e.g. parvovirus)
- Post-streptococcal arthritis — Rheumatic fever — Arthritis alone
- Post-neisseria arthritis
- Lyme disease
- Whipple's disease
- Reactive arthritis

19.8 Reactive arthritis 4465 features with those diseases. More recently, the Assessment of Spondylarthritis Society (ASAS) has reclassified reactive arthritis as a peripheral spondylarthritis. Other post-infectious arthropathies lack these common features. In the absence of agreed and validated diagnostic or classification criteria for reactive arthritis, Box 19.8.2 presents a useful working classification of those patients who could reasonably be considered to have reactive arthritis. This takes as its starting point the classical pattern of arthritis and typical extra-articular features (Box 19.8.3) that are commonly seen after infection by five organisms—salmonella, yersinia, campylobacter, shigella, and Chlamydia trachomatis. The same clinical syndrome (i.e. arthritis and extra-articular signs) is also seen, but more rarely, following various other infections, especially of the gastrointestinal tract (e.g. by Clostridium difficile); but genitourinary infection with ureaplasma and respiratory infection with Chlamydia pneumoniae can probably also act as triggers of reactive arthritis. The other large group of patients is those who have asymmetric oligoarthritis without extra-articular features, but with definite laboratory evidence of preceding infection by one of the five major reactive arthritis-associated bacteria. Laboratory diagnosis of infection is given priority over symptoms as a classification criterion because infection may be clinically silent. Chlamydia is notorious for this, particularly in women, while in yersinia infection arthritis is inversely correlated with the severity of gastrointestinal symptoms. Positively identifying the triggering infection often poses practical problems. Patients in whom arthritis develops (with or without extra-articular signs) after symptomatic episodes of gastrointestinal or genitourinary infection are therefore usually regarded as having reactive arthritis, even when no triggering organism can be identified, although the diagnosis is inevitably less secure in these cases. Improvement in methods for diagnosing preceding infection should decrease the size of this group, and may show reactive arthritis to be the commonest cause of acute inflammatory oligo- or monoarthritis in young adults. Epidemiology Community studies in Scandinavia, where HLA B27 is present in around 12% of the population (compared with 6–7% elsewhere in Europe), have

suggested an incidence of 40 to 50 cases/million for each of the endemic organisms (chlamydia, campylobacter). The lower figure of 1.3/million for shigella probably represents a similar incidence to other organisms, as almost all cases were acquired by travellers. Incidence has also been studied in single outbreaks of food poisoning, in which the proportion of infected patients developing arthritis can be accurately assessed. However, in such studies the proportion who develop reactive arthritis varies widely (0–21%). By contrast, careful population studies of campylobacter infection have shown a high incidence (7–16%) of musculoskeletal symptoms not severe enough to require secondary care. The influence of HLA B27 on incidence is important: 60 to 80% of patients with reactive arthritis presenting to rheumatology clinics are positive for HLA B27, whereas among those with mild disease the figure drops to 30% or lower. HLA B27 seems to be associated mainly with the severity and persistence of arthritis, rather than its incidence.

Pathogenesis There is considerable evidence that organisms reach the joints following infection of the gut or genitourinary tract. They may arrive intact, when they can be detected using the polymerase chain reaction (PCR), or as antigenic material (proteins, lipopolysaccharide) that can be demonstrated in synovial macrophages and polymorphs using organism-specific antibodies. This process can continue for months or even years, suggesting that some of the infections (e.g. yersinia), persist such that antigens/organisms continue to reach the joint. Elevated and persistent titres of IgA antibody to these organisms in reactive arthritis compared with uncomplicated infection also favour the idea of persistence. A clear distinction between septic and post-infectious arthritis is no longer possible, as viable organisms can be detected in the joint in various forms of post-infectious arthritis, including Lyme disease and reactive arthritis. However, an important distinction is that in post-infectious arthritis the organisms in synovium or synovial fluid are noncultivable (although viable), and antibiotics generally do not influence the course of disease (see next). Within the joint, cellular immune responses to the bacteria responsible for triggering reactive arthritis are readily detected, particularly responses by CD4⁺ helper T lymphocytes, but also CD8⁺ T cells. Interestingly, although the association with HLA B27 is often taken to imply that CD8⁺ T cells are the principal effector cells in the disease, HIV-positive patients with reactive arthritis present during

Box 19.8.2 Working definition of reactive arthritis

Classical clinical features

- Asymmetric oligoarthritis, lower limbs predominate
- Enthesitis
- Extra-articular signs (Box 19.8.3)

— Classical clinical features and proven infection by salmonella, campylobacter, yersinia, shigella, or Chlamydia trachomatis (whether symptomatic or not)

— Classical clinical features and proven infection by other organisms (e.g. Clostridium difficile, Mycobacterium bovis BCG)

— Any acute inflammatory arthritis (including monoarthritis) and proven infection by reactive arthritis-associated bacteria

— Classical clinical features and preceding diarrhoea or urethritis/cervicitis, infection not proven

Box 19.8.3 Extra-articular features and their occurrence in other forms of spondyloarthritis

- Eyes — Conjunctivitis — Uveitis (ankylosing spondylitis and inflammatory bowel disease)
- Skin and mucous membranes — Oral ulceration — Circinate balanitis — Keratoderma blennorrhagica (psoriasis) — Nail dystrophy (psoriasis) — Erythema nodosum (inflammatory bowel disease)
- Cardiac — Aortitis (ankylosing spondylitis) — Conduction defects (ankylosing spondylitis)

section 19 Rheumatological disorders 4466 stage I infection, when numbers of CD4⁺ T cells are less depressed. By contrast, arthritis can be relatively quiescent in full-blown AIDS. Both CD4⁺ and CD8⁺ lymphocytes produce proinflammatory cytokines such as interferon- γ and interleukin 17 that can drive joint inflammation by secondary effects on synoviocytes. Increased numbers of CD4⁺ IL-17⁺ T cells have been detected in reactive arthritis synovial fluid as compared to paired

peripheral blood. How does HLA B27 influence the course of reactive arthritis— particularly its severity and persistence? It has been proposed that infection generates a B27-restricted response by CD8+ T cells to a bacterial peptide that cross-reacts with a component of the joint (i.e. infection triggers autoimmunity by ‘molecular mimicry’). However, no such autoimmune response has yet been demonstrated. Alternatively, HLA B27 may adversely affect the efficiency with which the immune system clears the triggering organism. In this case disease would not require autoimmunity but be primarily driven by persistent bacterial antigens. Lastly, HLA B27 might affect the immune response to the triggering organism qualitatively (e.g. by allowing hyper-responsiveness to particular antigens, or biasing the immune response in favour of the production of proinflammatory cytokines such as IL-17 and IL-22).

Clinical features

Preceding illness A history of urethritis (dysuria or discharge) and diarrhoea must be sought specifically, as patients do not automatically link these occurrences with their arthritis. The interval between infection and arthritis is variable but not usually more than 3 weeks. By the time a rheumatologist is consulted, many weeks may have passed and the triggering illness forgotten, particularly if symptoms were mild. Note that urethritis may be triggered by gastrointestinal infection: minimally symptomatic gastrointestinal infection and prominent urethritis may cause diagnostic confusion if this possibility is forgotten.

Arthritis The classical clinical picture in reactive arthritis is an asymmetric oligoarthritis (generally fewer than six joints), predominantly affecting the lower limbs (Box 19.8.4). However, any joint can be affected, and some patients have monoarthritis only. Affected joints are often hot and markedly swollen, with septic arthritis and crystal-induced arthritis being the most likely differential diagnoses. Dactylitis, similar to that seen in psoriatic arthritis, also occurs. Many patients describe low back or buttock pain, suggesting involvement of the sacroiliac joint. Arthritis is usually at its worst early in the course of the disease, but new sites can be affected after several months and relapses are not uncommon, even in those in whom disease eventually settles completely. The presence of enthesitis (inflammation of ligamentous and tendinous insertions) in addition to arthritis is helpful diagnostically, with plantar fasciitis and involvement of the Achilles tendon insertion the commonest sites. The features described here are commonly seen in secondary care, but the milder cases detected in community surveys commonly have polyarthritis, whereas some have only inflammatory back pain or an enthesopathy such as reactive tendonitis.

Extra-articular features In acute severe disease patients have constitutional symptoms of malaise, fatigue, and fever. More useful diagnostically are the specific extra-articular signs listed in Box 19.8.3 and illustrated in Figs. 19.8.1, 19.8.2 and 19.8.3. The fact that these extra-articular features are common to other forms of spondyloarthritis greatly strengthens the case for including reactive arthritis in this disease family, and for defining reactive arthritis as a distinct post-infectious syndrome. Extra-articular features are more common in those with severe joint involvement. Conjunctivitis is often transient and no longer present by the time the patient presents. More persistent eye inflammation or painful eyes should raise the question of an acute anterior uveitis rather than a simple conjunctivitis and prompt full ophthalmological assessment. Circinate balanitis is usually asymptomatic and needs to be specifically sought in uncircumcized males. Oral ulceration is usually asymptomatic. Keratoderma blennorrhagica is histologically identical to psoriasis; it is most commonly seen on the soles of the feet, but can also involve the hands or trunk, and psoriaform nail changes are also seen. Erythema nodosum is associated with yersinia infection, but is otherwise uncommon in reactive arthritis. Aortitis and cardiac conduction disorders are rare.

Box 19.8.4 Pattern of joint involvement in reactive arthritis

- Oligo- or monoarthritis — Asymmetric — Predominantly lower limbs
- Coexisting enthesitis or reactive enthesopathy alone
- Sacroiliac joint involvement
- Inflammatory back pain
- Polyarthritis (mild)

Fig. 19.8.1 Ulceration of the tongue in reactive arthritis. Courtesy of Dr CJ Eastwood.

19.8 Reactive arthritis 4467 Differential diagnosis The differential diagnosis of reactive arthritis is summarized in Box 19.8.5. The principal concerns in acute disease are septic arthritis, crystal arthropathies, and other forms of post-infectious arthritis such as Lyme disease, post-streptococcal arthritis, or gonococcal arthritis. In chronic disease it may be difficult to distinguish reactive arthritis from other forms of spondyloarthritis, especially in those with inflammatory bowel disease, and many patients in whom no infectious trigger can be implicated can be classified as having an undifferentiated spondyloarthritis. Laboratory features General The principal aims of investigation are to exclude important differential diagnoses and to identify the triggering organism. Abnormalities in the early stages, when arthritis is most active, are those of a pronounced acute inflammatory response—raised ESR and C-reactive protein, the latter often very marked (>100 mg/litre). Serum uric acid should be checked. Rheumatoid factor and antinuclear antibodies are absent. Positive antineutrophil cytoplasmic antibodies have been described, but the antibodies are not directed against proteinase-3 or myeloperoxidase and the test is not diagnostically useful. Septic arthritis and crystal arthropathies are best excluded by aspiration of synovial fluid followed by culture and microscopy. Findings in synovial fluid are characteristic of an inflammatory arthritis, with elevated white cell counts, which are predominantly neutrophils. Blood, stool, and urine culture should be performed and genital swabs taken if appropriate. Throat swab and antibodies to streptococcal antigens may point to post-streptococcal arthritis, which does not share extra-articular features with reactive arthritis. In endemic areas, Lyme disease should be considered and antibodies to *Borrelia burgdorferi* measured. A chest radiograph may reveal hilar lymphadenopathy, suggesting the diagnosis of sarcoidosis, although *Yersinia* can cause both reactive arthritis and a sarcoid-like illness. Microbiological Stool should be cultured for pathogens associated with reactive arthritis, although cultures are often negative after gastrointestinal symptoms have settled—despite the recent evidence that persistent infection contributes to pathogenesis. Chlamydia infection must be sought in sexually active patients with new partners, particularly when there is no history of gastroenteritis. Formal referral to a department of genitourinary medicine is often helpful. Patients are not infrequently infected with both chlamydia and gonococcus. This can cause confusion, but gonococcal arthritis differs from reactive arthritis with its characteristic rash and absence of classical extra-articular features. Chlamydia can be amplified from urethral or cervical swabs, or from first-catch urine. Nucleic acid amplification techniques using amplification of *C. trachomatis* DNA or RNA

Fig. 19.8.2 Circinate balanitis in reactive arthritis. Courtesy of Dr CJ Eastwood. Fig. 19.8.3 Keratoderma blennorrhagica in reactive arthritis. Courtesy of Dr CJ Eastwood.

Box 19.8.5 Differential diagnosis of reactive arthritis • Septic arthritis • Post-infectious arthritis — Lyme disease — Post-streptococcal or neisseria infection — Viral arthritis • Crystal arthropathies • Other forms of spondyloarthritis • Behçet's • Sarcoidosis • Trauma, sports injury

section 19 Rheumatological disorders 4468 sequences are very sensitive and specific and are the preferred diagnostic method. Spondyloarthritis in the context of HIV infection also needs to be considered, although this is rare in developed countries. By contrast, many cases of reactive arthritis, often related to dysentery, have recently emerged among the HIV-infected population in sub-Saharan Africa, where the disease was previously unknown. HIV testing should be considered, particularly in patients with unusually severe disease and relevant risk factors. Immunological When the triggering organism cannot be demonstrated directly, infection can be inferred on the

basis of immune responses. However, this evidence needs to be interpreted cautiously, as in many cases the findings simply imply immunological memory for the organism in question and do not demonstrate a clear relationship between infection and arthritis. Specific IgM antibodies may indicate recent infection, whereas IgG may reflect remote infection unless titres are increasing. However, when patients present several months into their illness, IgM may no longer be evident and IgG titres stable. In these circumstances high and persistent IgA titres to organisms such as salmonella and yersinia may be useful. Serological diagnosis of chlamydia infection is particularly difficult because of high community levels of infection with *Chlamydia pneumoniae*, an organism that shares several highly conserved antigens with *Chlamydia trachomatis*. Overall, serology is used less commonly for these infections. Lastly, cellular immune responses to triggering organisms can be demonstrated, particularly in the synovial fluid. Again, these demonstrate only T-cell memory for the organism and do not demonstrate causality; patients with, for example, rheumatoid arthritis and incidental salmonella infection will have salmonella-specific T cells in their synovial fluid. Such tests are currently used in research rather than diagnostically. Radiological investigations are not diagnostically helpful in the acute stages of disease, with soft tissue swelling and occasionally periarticular osteopaenia at affected joints being the only abnormalities. MRI using STIR sequences, or less commonly radionuclide scintigraphy, can demonstrate acute sacroiliitis and may show the full extent of acute synovitis and enthesitis, but is not usually required for clinical management. Radiological changes are confined to the few patients with persistent disease (>1 year duration), with the principal features being erosion of affected joints, including the sacroiliac, and new bone formation manifested as periostitis of metatarsal and metacarpal bones and 'enthesophytes', such as plantar spurs. In the spine paravertebral ossification can be seen in the lumbar region: this is asymmetric and differs from the classical changes of ankylosing spondylitis. Erosive changes are also seen at sites of enthesitis such as the calcaneum. Treatment Evidence-based therapies for reactive arthritis are lacking, and consensus opinion is the current guide. The management of reactive arthritis can be divided into two stages: (a) acute reactive arthritis, and (b) refractory (chronic) reactive arthritis, usually defined as disease of greater than six months duration. In the acute phase, affected joints should be rested until they improve substantially. This often needs emphasizing to young, active patients involved in sports, and alternative forms of exercise should be considered. Physiotherapy and advice on exercise is helpful, with quadriceps function needing particular attention in view of the frequent involvement of the knees. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the first line of treatment unless contraindicated, and an adequate trial should be 2 weeks in duration. More than one NSAID could be tried, and patients need to be counselled about side-effects. Synovial effusions should be aspirated and, when septic arthritis has been excluded, will respond well to injection with long-acting corticosteroids. Systemic corticosteroids can be used if multiple joints are affected. If chlamydia infection is established or thought likely, patients require conventional treatment with short-term antibiotics, but there is little evidence that this has any effect on the progress of reactive arthritis. Enteric infections do not require antibiotics in their own right, and the arthritis does not respond to antibiotics (see next). Uveitis requires formal ophthalmological assessment and treatment with local steroids. There are two major unresolved treatment issues in chronic reactive arthritis. Firstly, the place of disease-modifying drugs: sulfasalazine and methotrexate are useful in other forms of spondyloarthritis and on this basis have been used in reactive arthritis, but without controlled trials confined to this condition (because the disease is often self-limiting, controlled trials of second-line agents are difficult to perform). There is one trial where sulfasalazine was used in a 36-week randomized trial in patients not responding adequately to

NSAIDs, but the primary outcome measure was not met although there was a trend towards benefit. The use of TNF inhibitors is not supported by trial data although there are case series. The second issue is whether long-term antibiotics confer any benefit. In a controlled trial in 1991, a subset of patients with evidence of chlamydia infection benefited from prolonged lymecycline, but subsequent trials using ciprofloxacin and azithromycin have been negative. It may be that organisms in the joint, being in an uncultivable state, are also not susceptible to antibiotics, most of which affect bacterial cell division. A trial in 2010 suggested that a combination of rifampicin and doxycycline or azithromycin may be useful in chronic chlamydia-induced reactive arthritis, resulting in affecting joints becoming PCR-negative for chlamydia nucleic acids, but this has not yet been confirmed. Psychological and quality of life issues Reactive arthritis commonly affects young fit adults who have not previously experienced any form of prolonged illness or disability. The danger is that the rheumatologist, all too used to the relatively gloomy prognosis of rheumatoid arthritis, may treat reactive arthritis, where there is a high likelihood of complete resolution of disease, too lightly. Patients need to be given a realistic prognosis (i.e. that symptoms may well persist at some level for 6–12 months, although in the latter stages these are usually very mild compared with those experienced in the first 4–8 weeks). Exacerbations during this time are not uncommon and do not imply that the disease will not eventually resolve. The chances of the patient developing chronic

19.8 Reactive arthritis 4469 arthritis are less than 10%. Patients benefit from continuing psychological and clinical support throughout the course of their illness, with rapid access to joint aspiration and intra-articular steroid injection when there is recurrent joint swelling. Areas of uncertainty Current uncertainties concern classification criteria and management strategies. Both may be resolved by developing more secure diagnostic techniques for identifying the triggering infection. Improved treatment is likely to come from either (1) additional evidence about the importance of persistent infection and how to eliminate it, or (2) discovery of the immune responses responsible for maintaining joint inflammation, whether these are directed against a bacterial antigen or an autoantigen. If a target antigen can be identified, specific immunomodulation strategies would become relevant. Reactive arthritis differs from other forms of inflammatory arthritis in having a clearly defined onset and being triggered by known infectious agents. Genetic influences that result in a minority of infected individuals developing arthritis are being investigated. These include HLA B27, but it is likely that other genes are also involved. Genome-wide association studies in ankylosing spondylitis have identified several genes which influence susceptibility to disease, and many of these are concerned with the production of, and response to, the cytokine IL-23 and the generation of IL-17-producing cells. Since increased numbers of IL-17+ CD4+ T cells have been noted in reactive arthritis synovial fluid, it seems likely that many of the genes which have been implicated in ankylosing spondylitis susceptibility play a similar role in reactive arthritis. FURTHER READING General review Schmitt SK (2017). Reactive arthritis. *Infect Dis Clin North Am*, 31, 265–77. Reviews of pathogenesis Gaston JSH (2000). Immunological basis of chlamydia induced reactive arthritis. *Sex Transm Infect*, 76, 156–61. Sieper J, Braun J (1995). Pathogenesis of spondylarthropathies: persistent bacterial antigen, autoimmunity, or both? *Arthritis Rheum*, 38, 1547–54. Incidence following enteric infection Fendler C, et al. (2001). Frequency of triggering bacteria in patients with reactive arthritis and undifferentiated oligoarthritis and the relative importance of the tests used for diagnosis. *Ann Rheum Dis*, 60, 337–43. Gaston JSH (2005). Shigella induced reactive arthritis. *Ann Rheum Dis*, 64, 517–8. Hannu T, et al. (2002). Campylobacter-triggered reactive arthritis: a population-based study. *Rheumatology (Oxford)* 41, 312–8. Hannu T, et al. (2005). Reactive arthritis attributable to

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Revision #1

Created 2026-01-22 16:40:48 UTC by Omar Ayman

Updated 2026-01-22 16:40:48 UTC by Omar Ayman