SPONDYLOARTHROPATHIES

1. AIMS

To recognise the different syndromes that have an association with the HLA B27 antigen and to develop a management strategy for each one.

2. INTRODUCTION

The spondyloarthropathies are a family of interrelated, but heterogeneous, conditions. There can be a marked overlap between the different conditions. All of these conditions are associated to a greater or lesser extent with the HLA B27 antigen. The diseases included in this group are ankylosing spondylitis, Reiter’s syndrome, reactive arthritis, psoriatic arthritis, and the enteropathic arthritis associated with inflammatory bowel disease.

Disease classified under the spondyloarthropathies

♦ Ankylosing spondylitis (AS)
♦ Reiter’s syndrome / Reactive arthritis
♦ Enteropathic arthritis (Crohn’s disease, ulcerative colitis)
♦ Psoriatic arthritis

2.1 Similarities between the spondyloarthropathies

The arthritis associated with these diseases occurs mainly in the lower limbs and is usually asymmetrical. With time many of these patients develop radiographic evidence of sacroiliitis. It is from this spinal involvement that the term spondyloarthritis arises, “spondyl” implying spinal involvement. Many other features such as oral ulceration and anterior uveitis of the eye can occur in all of these disease and are called overlapping features. Features of rheumatoid arthritis, such as the rheumatoid factor and subcutaneous nodules, are absent. All of them are to varying degrees associated with the HLA B27 antigen. There is a significant familial aggregation.
2.2 Immunopathogenesis of the spondyloarthropathies

2.2.1. The HLA-B27 Antigen

Although the precise etiology is unknown, there is a strong association between this group of diseases and the HLA-B27 antigen. HLA-B27 forms part of the class I antigens of the major histocompatibility complex (MHC) and is expressed on the surface of many cell types. This supports the view that these diseases are due to a genetically determined immune response to environmental factors.

One hypothesis is that an immune response is triggered by an infection in the gastrointestinal or genitourinary tracts. Some Chlamydia, Salmonella and Yersinia antigens can be found in the synovial fluid of patients who had infections with these pathogens. Some peptide fragments from these bacteria possibly bind to the HLA-B27 antigen and are presented to the T-cells, thus triggering an autoimmune response.

An alternative hypothesis suggests an autoimmune reaction to self-antigens, because of mimicry between fragments of the infecting microorganisms and host tissue i.e. antigenic fragments between fragments of bacteria and self-antigens. These infecting organisms may be Gram negative bacteria, such as Klebsiella which have been shown to possess antigens that resemble the HLA-B27 antigen. They may give rise to antibodies that crossreact and bind to HLA-B27 positive cells resulting in disease manifestations.

3. ANKYLOSING SPONDYLITIS.

3.1 Definition

Ankylosing spondylitis is a chronic systemic inflammatory rheumatic disorder that affects mainly the axial skeleton (spine), although peripheral joint involvement is also important. Sacroiliac joint involvement is the hallmark of the disease. The name is
derived from the Greek ankylos meaning ‘bent’, and spondylos meaning ‘spinal vertebra’.

Features:
- Mainly spinal involvement
- Sacroilitis is the hallmark
- Peripheral joints often involved.

3.2 Epidemiology

3.2.1. Prevalence

1-2% of adults carrying the HLA-B27 antigen are likely to develop ankylosing spondylitis. Almost all Caucasians with ankylosing spondylitis are HLA B27 positive.

3.2.2. Racial Distribution

The HLA B27 antigen is found predominantly in Caucasian populations. About 7% of Caucasians carry the antigen, with higher carrier rates in the Scandinavian and Scottish populations and very high rates in certain North American Indian populations. The prevalence is below 1% in American Blacks and Japanese. HLA-B27 is virtually absent among black Africans.

3.3. Pathology

The primary pathologic site in ankylosing spondylitis is the enthesis. This is the site of the insertion of tendons, ligaments or capsule into bone. There is an initial inflammatory erosive process at the site of the enthesis. This is followed by a healing process, during which fibrosis and later new bone formation occur. The new bone stretches into the tendon or ligament and appears on X-ray as a bony spur. At the edge of the vertebral bodies this process occurs in the outer layers of the annulus fibrosis and the new bone is known as a syndesmophyte. With time these syndesmophytes form bone bridges between the vertebral bodies, eventually resulting in the spinal ankylosis characteristic of this disease. The ankylosis pulls the spine into
flexion and severely involved individuals can be so flexed that they cannot look forward.

- The enthesis is the site of insertion tendons, ligaments or capsule onto bone.
- Enthesiopathy is the inflammatory reaction at the site of the enthesis.

### 3.4 Clinical Features

The onset of ankylosing spondylitis is usually in late adolescence or early adulthood and very uncommon after the age of 40 years.

#### 3.4.1 Skeletal manifestations

- **Low back pain and stiffness**

Low back pain of insidious onset is the most common and initial symptom. The pain is dull in character and felt deep in the gluteal region, but later it may localize to the region of the sacroiliac joints or be referred toward the iliac crest, the greater trochanteric region or down the dorsal thigh. Coughing, sneezing and movements that cause a sudden twist of the back can accentuate the pain.

N.B. Insidious onset of bilateral low back pain in a young person must be investigated for possible ankylosing spondylitis.

The pain may be unilateral or intermittent at first, but within a few months becomes persistent and bilateral, and the lower back becomes stiff and painful. The low back stiffness is worse in the morning and may awaken the patient from sleep. The pain and stiffness is eased by exercise or physical activity and worsened by prolonged periods of inactivity.

N.B. The back pain of ankylosing spondylitis is eased by exercise and made worse by rest.
The disease may remain localised to the low back, but in a significant percentage of cases the inflammatory process will spread up the back and later involve the thoracic and cervical spine, with pain and often flexion deformities.

We have no way of predicting which patients will have only localised disease and which will progress to severe disease. Fortunately it is relatively few that progress to severe flexion deformities.

N.B. Once the ankylosis is complete, inflammation subsides and the pain decreases. The patient is then left with a painless but rigidly fused spine in a flexed position.

You must be able to tell inflammatory back pain from simple or mechanical back pain. Inflammatory back pain has an insidious onset and mechanical pain usually has a more acute onset. About 95% of mechanical back pain spontaneously improves within a month, but inflammatory back pain is continual for months or years. Inflammatory backs are stiff in the mornings but improve with exercise. The opposite is true for mechanical back pain.

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♦ **Enthesitis**

Enthesitis can cause pain and tenderness of costosternal junctions, spinous processes, iliac crests, greater trochanters of the femurs, ischial tuberosities, tibial tubercles, or heels (Achilles tendonitis or plantar fasciitis)

♦ **Chest pain**
Thoracic spine involvement includes the costovertebral joints and reduced chest expansion may be noted even early in the disease. Pain at the costosternal and manubriosternal joints is very common, caused by enthesitis of these joints.

- **Extra-axial joints**

  - **Hips and shoulders**
  Pain in the hips and shoulders may be the first symptom in up to 15% of patients. These are the most frequently involved joints other than the spine.

  - **Hip disease**
  Patients with onset of the disease in childhood are prone to hip involvement. If hip involvement has not occurred in the first ten years of the disease, it is very unlikely to occur later. When hip involvement does occur, the destruction usually requires hip replacement.

  - **The knee joint**
  The knee joint may also be affected, frequently presenting with an intermittent effusion and later a constant effusion. This joint may also be destroyed requiring replacement.

  - **Temporomandibular joint**
  Temporomandibular joint involvement occurs in about 10% of patients

### 3.4.2 Extra Skeletal Manifestations

- **Constitutional symptoms**

  Fatigue, loss of weight and low grade fever frequently occur.

- **Eye disease**
Acute anterior uveitis or iridocyclitis occur in 25-30% of patients at some time in the course of the disease. It presents as an acutely painful, red eye and is typically unilateral. The eye is red and painful with photophobia and increased lacrimation. It is easily mistaken for a viral or bacterial infection. Treatment is with corticosteroid eye drops. Posterior synechiae and glaucoma may develop as complications in patients with repeated or severe attacks or where treatment was delayed or not given.

N.B. Do not mistake the immune mediated red eye of uveitis for a bacterial infection.

♦ Enteric mucosal lesions

Mouth ulcers are common. Small enteric mucosal ulcers have also been detected in the terminal ileum and colon by ileocolonoscopy in 30-60% of patients with ankylosing spondylitis. They may be asymptomatic or cause mild abdominal pain.

♦ Cardiovascular disease

Cardiac involvement is a very rare complication of ankylosing spondylitis. It may be clinically silent or cause life threatening complications. Inflammation occurs in the proximal part (first few centimetres) of the aorta (aortitis). This may lead to dilatation of the aorta ring, which in turn leads to dilatation of the aortic valves and aortic incompetence. Aortic incompetence, as well as cardiac conduction defects, occur twice as often in patients with severe peripheral joint disease. The risk increases with an increase in the age of the patient, as well as with a longer duration of the disease.

Cardiac manifestations:
- Proximal aortitis
- Aortic valve

Incompetence
- Conduction abnormalities
Pulmonary disease

Lung involvement is rare and occurs late in the course of the disease, with a slowly progressive fibrosis of the upper lobes of the lungs. Cysts form in this fibrotic tissue and for unknown reasons these patients are prone to infection by the fungus *Aspergillus*.

N.B. Cystic lung lesions in ankylosing spondylitis is often *Aspergillus* infection.

Neurological involvement

Although the spine ankyloses with time, the new bone is of poor quality. This rigid fused spine fractures easily, resulting in a variety of neurological complications. With ankylosis of the cervical spine, a very limited amount of movement may be left in the atlanto-axial joint. This is clinically seen as a very limited ability to nod the head. These patients are at high risk of anterior atlanto-axial subluxation and damage to the spinal cord at this level.

Renal involvement

A mild immunoglobulin A nephropathy has been reported in many patients with ankylosing spondylitis.

The main extra-articular manifestations in order of frequency are:

- Eye disease
- Enteric mucosal lesions
- Cardiovascular disease
- Pulmonary disease
- Neurological involvement
- Renal disease
3.5 Physical Examination

Clinical signs are sometimes minimal in the early stages of the disease and you must specifically look for the following:

♦ Spinal mobility

On inspection loss of the normal lumbar lordosis is seen early in the course of the disease. Also look for limitation of forward flexion, hyperextension and lateral flexion. The Schober test is useful for measuring loss of forward flexion. Spinal rotation may cause pain.

The Schober Test for Lumber Flexion:

Find the L5/S1 spines. Mark the skin with a pen 5cm below this landmark and 10cm above, with the patient to bend forward as far as possible and measure the distance between the two skin marks. With a normal spine the distance will increase by at least 5 cm.

♦ Chest expansion

Mild to moderate reduction of chest expansion is often detectable at an early stage. Less than 5cm expansion between full exhaling and full inhaling in young persons with low back pain, should prompt consideration for the diagnosis of ankylosing spondylitis. Chest expansion should be measured at the level of the fourth intercostal space in males and below the breasts in females.

N.B. Always measure the chest expansion. Less than 5 cm in a young person is abnormal.

♦ Sacroiliac joints
Direct pressure over the sacro-iliac joints may cause pain, but is a very unreliable test. Another test is to compress the two iliac bones of the pelvis together or to force them apart, with the patient lying supine on the examination couch. Obviously when the sacroiliac joints have fused these signs will become negative.

♦ Posture

The normal lumbar lordosis is lost early in the course of the disease. In those with progressive disease a gradually increasing kyphosis of the dorsal spine gives the patient a stooped appearance. If the neck becomes involved, the cervical spine develops a fixed flexion deformity. In advanced disease this can be so severe that the patient cannot lift the head to look forwards. Fortunately this very severe form of the disease is rare.

N.B. Ankylosing spondylitis is a disease of flexion.

3.6 Radiography and Imaging

The earliest, most consistent and characteristic findings are seen in the sacro-iliac joints, with sacroilitis that is usually symmetrical. The radiological appearance consists of blurring of the subchondral bone plate, followed by erosions and sclerosis of the adjacent bone, particularly in the inferior third of the joint. Fibrosis of the joint is followed by interosseous bridging and with time complete obliteration of the joint by ossification.

N.B. With complete ankylosis of the sacroiliac joint, the lines of the joint can still be seen on X-ray and can be mistaken as normal. Look for bony trabeculae running over the joint line.

Bony erosions and osteitis at sites of osseous attachment of tendons and ligaments are seen.
After sacroilitis the most characteristic radiological lesion is the syndesmophyte. This is an enthesitis occurring in the longitudinal ligaments of the vertebrae. Ossification of this ligament is seen as bony spines running upwards and downwards along the lateral side between the vertebral bodies. Ultimately these will form the bony bridges, fusing or ankylosing the vertebral bodies. It is popularly known as the bamboo spine as on X-ray it looks like a piece of bamboo.

3.7 Investigations

An elevated ESR is present in up to 75% of patients with ankylosing spondylitis. Tests for Rheumatoid factor and antinuclear antibodies are negative.

A mild normocytic normochromic anaemia is present in 15% of patients with AS.

The synovial fluid in patients with AS does not show markedly distinctive features when compared to other inflammatory arthropathies.

Testing for the presence of the HLA-B27 antigen can be used as an aid during diagnosis, but it should not be used as a routine or screening test.

N.B. The diagnosis remains a clinical and radiological one.

3.8 Management

Early diagnosis and management is important, as adequate treatment can slow the ankylosing process considerably and reduce or prevent the degree of flexion deformity. Young patients should also be advised as to career choices and an appropriate lifestyle as early as possible.

3.8.1 Objectives of management

The objectives of the treatment is to relieve pain, stiffness and fatigue and to maintain good posture, good physical and good psychosocial functioning. One should also aim to prevent flexion deformities.
3.8.2 Exercise

Exercise is the mainstay of treatment. Treatment must be combined with an intensive educational programme. One must stress to the patient that the long-term success of treatment is dependant on a regular home exercise programme.

In the initial phase or if the pain is very severe, hydrotherapy is particularly helpful. Gentle full range of movement in water, and heated water if at all possible, is very beneficial. As the disease is a disease of flexion, all exercises must encourage extension.

The second part consists of the patient’s own home exercise programme. This must be individualised to the patient’s own choices. Some may prefer a gymnasium programme, while others might prefer a sport that gives full range of movement. Contact sport should be avoided. It is important that the patient enjoys what he has to do, otherwise he will almost certainly not continue in the long term.

N.B. Exercise are critical in the treatment programme.

3.8.3 Medication

♦ Relief of Pain.

Relief of pain should be regarded as the first priority, so as to enable the patient to take part in his exercise programme. As his exercise programme progresses, he should experience less and less pain. The analgesic requirements can then be reduced. Any of the anti-inflammatories can be used, but doses towards the upper therapeutic range are required. The timing of the NSAID consumption is also important. Medication must be timed to give maximum pain relief at the time the patient will be doing his exercises or playing sport.

♦ Second line treatment
Sulfasalazine and methotrexate give symptomatic relief where exercise and NSAID’s were not sufficient, but whether they affect the long term course of the disease is as yet unknown.

♦ **Corticosteroids**

Systemic corticosteroids have little part to play in the treatment of ankylosing spondylitis. Locally injected corticosteroids may be employed in the management of the enthesitis, especially where it impairs an exercise programme.

4. **PSORIATIC ARTHRITIS**

4.1 **Definition**

Psoriatic arthritis is an inflammatory arthritis associated with the skin disease psoriasis. The rheumatoid factor test is negative and subcutaneous nodules are absent.

4.2 **Epidemiology**

The prevalence of inflammatory arthritis in patients with psoriasis is around 10%. The sex ratio is equal, but in the group of patients with symmetrical polyarthritis, females predominate while in those with mainly spinal involvement males predominate.

4.3 **Pathogenesis**

Although the etiology of psoriatic arthritis is unknown, twin studies have shown a genetic predisposition to the disease.

The pathology of the skin and joint lesions in psoriatic arthritis is that of an inflammatory reaction. Lymphocytic infiltrates are found in the synovium, with high levels of pro-inflammatory cytokines in the synovial fluid.
4.4 Clinical Features

Psoriatic arthritis is a systemic inflammatory disease with articular and extra-articular features.

4.4.1 Clinical Subgroups of Psoriatic Arthritis

There are five main patterns of psoriatic arthritis:

1. Arthritis of the distal interphalangeal joint is almost associated with psoriatic changes in the associated nail. This must be differentiated from osteoarthritis and gout, the only other diseases to affect the distal interphalangeal joints.
2. Destructive (mutilans) arthritis: severe destruction of the joints can lead to the near disappearance of the joint with shortening of the involved digits.
3. Symmetric polyarthritis indistinguishable from rheumatoid arthritis.
4. Asymmetric oligoarthritis, with less than four joints involved in an asymmetric fashion.
5. Spondyloarthropathy: Sacroiliitis occurs in up to one third of patients with psoriasis. The sacroiliitis is often unilateral. It can be clinically indistinguishable from ankylosing spondylitis.

Other clinical features of psoriatic arthritis include dactyliitis, tenosynovitis, and enthesitis. Dactyliitis (“sausage digit”) occurs in more than 30 percent of patients and is characterised by a diffuse swelling of the entire digit, along with arthritis of the DIP, proximal, interphalangeal, and metacarpophalangeal joints.

4.4.2 Associated Extra-articular Features

♦ Skin lesions

In 75% of cases psoriasis precedes the arthritis, in 15% of cases the onset of arthritis and skin disease is at the same time, and in 10% arthritis precedes the psoriasis.
Most patients with psoriatic arthritis have the classic psoriasis vulgaris pattern of skin lesions. There is no direct relation between the severity of skin lesions and the degree of joint inflammation in psoriatic arthritis.

Nail lesions, including pitting, ridging, and onycholysis, are the only clinical features of skin psoriasis that are significantly associated with the development of psoriatic arthritis. Nail lesions occur in 90% of patients with arthritis and 40% with skin disease alone.

Typical signs of psoriatic nail involvement include:

1. **Pitting**: More than 20 pits in total are diagnostic
2. **Onycholysis**: This is separation of the nail from the nailbed
3. **Horizontal ridges**

Any two of these features is strongly suggestive of psoriasis.

♦ **Eye Involvement**

Ocular involvement, either conjunctivitis or iritis, occurs in up to 33% of patients.

4.5 **Laboratory Features**

There is no diagnostic laboratory test for psoriatic arthritis. The ESR is elevated in 40 to 60% of the patients.

4.6 **Radiographic Features**

Cartilage loss and erosions radiologically identical to rheumatoid arthritis are seen in the proximal and distal interphalangeal joints. Remember though that in rheumatoid arthritis the distal interphalangeal joints are not involved. The joint involvement may also be asymmetrical, while rheumatoid arthritis is much more symmetrical.
N.B. If you see radiological changes of erosions and joint space narrowing typical of rheumatoid arthritis, but the distal interphalangeal joints are also involved, then rather consider psoriatic arthritis as your diagnosis.

The destructive process can lead to ankylosis of the joint or in some cases to complete destruction (osteolysis) of the joint, the involved digit becoming visibly shorter. If you traction these joints they telescope in and out. Another typical lesion is the central erosion, destroying the center of the joint. This appears on X-ray with one side of the joint hollowed out and the other side no more than a pointed stub. Textbooks call it the “pencil-in-a-cup” lesion.

Enthesitis with inflammation and swelling of the periosteum near the joint, can lead to a swollen digit, giving the entire digit (toe or finger) a swollen shape similar to a sausage, hence the term “sauage digit”.

Characteristic features of psoriatic arthritis include:

- Asymmetrical joint space narrowing of the small joint of the hands.
- Joint margin erosions.
- A tendency to ankylosis of the joint.
- Complete destruction (osteolysis).
- Central destruction of the joint.
- Enthesitis and periostitis.
- Proliferative new bone formation at entheses, particularly around pelvis and calcaneum.

**4.7 Diagnosis**

N.B. It is crucial to perform a careful history and physical examination, looking for hidden psoriatic lesions, particularly in the ears, the hairline, the umbilical area, the anal cleft and the nails.

**4.8 Clinical Course and Outcome**
The course of psoriatic arthritis is usually flares of disease activity interspersed with remissions, with a minority of patients (<5%) developing erosive and deforming arthritis. A younger the age at the onset, female gender, and acute onset of arthritis are more common in patients with severe arthritis.

4.9 Treatment

The treatment of psoriatic arthritis is aimed at controlling the inflammatory process. The skin and joint aspects of the disease need to be treated simultaneously. Initial treatment is nonsteroidal anti-inflammatory drugs (NSAIDs) for joint disease, and topical therapies for the skin. Some patients have a worsening of psoriasis with NSAIDs. In these cases, a drug belonging to a different family of NSAIDs should be used.

In many, if not most cases, anti-inflammatory drugs and skin treatment alone are insufficient and the joints remain painful and swollen. Methotrexate then becomes the disease modifying drug of choice. Gold salts, antimalarials, D-penicillamine, and salazopyrine can also be effective.

5 REITER’S SYNDROME/REACTIVE ARTHRITIS

5.1 Definition of Reactive Arthritis

Reactive arthritis is an acute arthritis that develops soon after or during an infection elsewhere in the body, but in which viable microorganisms are NOT present in the joint. Noninfections components of the infective organism have been found in the synovial fluid and joint tissue in these cases.

5.2 Pathogenesis.

The proposed immunopathogenesis of reactive arthritis is the same as with ankylosing spondylitis. Why some patients will develop ankylosing spondylitis and others Reiter’s syndrome or one of the other related conditions, is as yet unknown.
**REITER’S SYNDROME**

Reiter’s syndrome is considered as one of the manifestations of reactive arthritis. Reiter’s syndrome refers to a triad of arthritis, urethritis and conjunctivitis, although all three need not necessarily be present at the same time.

Reiter’s syndrome is a triad of:
- arthritis
- urethritis
- conjunctivitis

### 5.3 Epidemiology of Reiter’s syndrome

The male to female ratio is 5:1, but the full blown syndrome with all three systems involved occurs 20:1 more in males. It is mainly seen in young adults.

In 60% of patients with Reiter’s syndrome, the HLA-B27 antigen is found to be present. However even after a suitable triggering infection, HLA-B27 positive patients do not always develop reactive arthritis. In HLA-B27 positive patients the disease is more severe, with a greater tendency to become chronic.

### 5.4 Clinical Features

The severity of the disease varies from mild cases that go unnoticed, to a severe disease that destroys joints and causes blindness from uveitis. The symptoms of arthritis typically appear within 1 to 3 weeks after an episode of urethritis or diarrhea. Constitutional symptoms are usually mild and fever, if present, is low grade without accompanying chills.

#### 5.4.1 Joints and Musculoskeletal Symptoms
Joint involvement varies from mild arthralgias to severe disabling polyarthritis. Joint stiffness, myalgia, and low back pain are prominent early symptoms. The back discomfort radiates into the buttocks and thighs. It is made worse by bed rest and inactivity. A monoarthritis or an asymmetrical oligoarthritis are the most common forms, with the weight bearing joints most commonly affected. The wrist may also be an early target.

The inflammation is usually low grade, manifesting more as joint tenderness, stiffness, and restricted range of motion, than as gross swelling. It may vary from day to day and shift from one joint to another.

The distinctive arthropathy of Reiter’s syndrome consists of a local enthesopathy. In the digits, this gives the appearance of a uniformly swollen “sausage” finger or toe.

The presence of a sausage digit is of great diagnostic help, as it is only associated with Reiter’s syndrome and psoriatic arthritis.

N.B. Only Reiter’s syndrome and psoriatic arthritis gives noninfective “sausage shaped” digits (sepsis can also give dactylitis).

The spine is prominently involved in patients with severe, chronic, or recurrent disease. Sacroiliitis develops in 30% of patients overall and is related to the presence of the HLA-B27 antigen. It is very often unilateral, unlike ankylosing spondylitis.

5.4.2 Urogenital Tract

Urethritis is always present but not always a prominent feature of Reiter’s syndrome. As a precipitating event, it precedes the symptoms of Reiter’s syndrome by 1 to 3 weeks. Circinate balanitis, small, shallow and painless ulcers of the glans and urethral meatus of the penis, cystitis and prostatitis, as well as pelvic inflammatory disease in women, are frequently found. Prostatitis is common and has been reported in up to 80% of patients. Urogenital tract inflammation has a tendency to relapse and urethral strictures are a frequent problem in chronic cases.
5.4.3 Mucous Membranes and Skin

♦ Keratoderma blenorrhagica

Keratoderma blenorrhagica is a hyperkeratotic skin lesion that is seen in 15% of patients and occurs most commonly on the soles of the feet. It begins as clear vesicles on erythematous bases and progresses to macules, papules, and nodules. Small lesions are the most common, but in severe cases there can be large lesions covering almost the entire underside of the feet.

Carefully inspect the underside of the feet for these lesions as, being painless, the patient is often unaware of them.

♦ Other conditions

The nails can become thickened and ridged. Keratotic material accumulates under the nail and lifts it from the nail bed. Superficial oral ulcers are an early and transient feature of the disease. Erythema nodosum is a unique feature when Yersinia infections trigger the syndrome.

5.4.4 Eye

Conjunctivitis is an essential part of the triad in diagnosing Reiter’s syndrome. Diagnostic problems arise when the conjunctivitis occurs at times other than with the arthritis or urethritis.

The conjunctivitis is immune based and not of infective origin. Antibiotic therapy will no help.

Immune mediated inflammation of the uvea is common (uveitis). In severe recurrent cases loss of vision in the affected eye can occur. The ocular lesions may be the first manifestation of Reiter’s syndrome and have a strong tendency to recur.
5.4.5 Gastrointestinal Tract

Enteric infections or inflammatory diseases can be the etiologic triggering events. The precipitating episode of diarrhoea is often mild, but may occasionally be bloody and prolonged. Other signs of Reiter’s disease start 1 to 3 weeks later.

5.4.6 Heart

Conduction abnormalities and aortic regurgitation occur in a very small percentage of patients and then only in those with severe and longstanding disease.

5.5 Reiter’s Syndrome and HIV Infection

The most common rheumatic syndrome seen in patients with HIV infections is a syndrome very similar to Reiter’s syndrome.

N.B. Beware of underlying HIV infections in patients presenting with a clinical picture similar to Reiter’s syndrome.

5.6 Course and prognosis

The initial attack may be mild, but is often severe with much joint pain. This initial attack may last from a few weeks to several months. A small number of patients may have only a single, self-limiting episodes of disease, but up to 50% of patients have recurrent bouts of arthritis. During the subsequent 10 to 20 years, chronic arthritis or sacroiliitis develop in 25% of patients.

5.7 Laboratory Evaluation

Determining if the HLA B27 antigen is present is not diagnostic, but would make you much more suspicious that your patient has one of the spondylarthropaties. Remember the majority of people carrying the HLA-B27 antigen in fact never develop any of these diseases.
N.B. The presence of the HLA-B27 antigen is not diagnostic of this group of diseases.

5.7.1 Detection of an Infection

The first group of laboratory tests documents the presence of a specific bacterial infection. Microbiologic and serologic studies form the cornerstone of diagnosis. Every effort should be taken to isolate the causative microorganism from the throat, faeces or urogenital tract. In most cases the results are negative and serology is then needed. Negative serology however does not rule out the diagnosis of reactive arthritis.

A third of patients have clinically inapparent infection by either Chlamydia or one of the enterobacteria. Because chronic antimicrobial therapy is possibly beneficial in Chlamydia-induced Reiter’s syndrome, it is important to look for Chlamydia in every case of Reiter’s syndrome. Whether the cost is justified in a serological and bacteriological search for other infecting agents which can trigger the synovitis e.g. Salmonella, Shigella, Yersinia, Campylobacter, Borrelia, Neisseria and streptococci, is debatable. The immunological damage was probably done 1-3 weeks prior to the symptoms and the infection already cleared. Remember that Salmonella, Borrelia and Neisseria can also cause true septic arthritis.

5.7.2 Demonstration of Inflammation

A moderate neutrophilic leucocytosis, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein, are common during the acute illness. These values slowly return to normal as the disease subsides.

5.7.3 Joint Fluid aspiration

Joint fluid should be aspirated if possible. Gram stain and bacterial culture should be performed to exclude sepsis.
5.8 Radiologic Findings

Sacroiliitis and intervertebral syndesmophytes that may be indistinguishable from ankylosing spondylitis and psoriatic arthritis occur only in the chronic cases. Joint erosions occur late in the course of the disease and then only in patients with severe, chronic disease.

5.9 Differential diagnosis

The most important condition to rule out is septic arthritis. Other conditions that may be confused with Reiter’s disease are gout, RA, AS and psoriatic arthritis. With a careful history, examination and follow up the correct diagnosis can usually be made.

5.10 Treatment

The severity of Reiter’s disease varies from mild arthralgias to a severe arthritis. The therapy has to be adjusted accordingly.

Planter fascitis is very common and can be very crippling. Tenderness is felt all along the plantar fascia, but usually worse at the anteromedial edge of the calcaneous (an enthesopathy). A shoe orthosis designed to support the bony medial foot bridge will take the strain off the ligamentous plantar fascia and will considerably relieve the pain. All shoes must be well cushioned and very comfortable.

   Tip: Anti-pronation shoes for runners are very comfortable and support the foot bridge very well.

Joint symptoms are best treated with nonsteroidal anti-inflammatory drugs (NSAIDs).

When NSAIDs fail to control the arthritis, sulfasalazine may be added. Patients usually show improvement within 2 to 6 months. Systemic corticosteroids are of little help, even at doses of 20 to 40 mg per day. Methotrexate has been shown to be effective.
Because Reiter’s syndrome frequently pursues a relapsing course, with variable intervals of remission, punctuated by periods of acute exacerbation, it is difficult to assess the efficacy of any form of therapy.

Gold salts, antimalarials and penicillamine may be tried if the above therapies are ineffective.

Patients with severe or intractable Reiter’s syndrome represent one of the most challenging problems in clinical rheumatology.

6. ENTEROPATHIC ARTHROPATHIES

A number of bowel diseases, of both the small and large intestine, are associated with arthritis. A pauciarticular (four or less joints involved), asymmetrical pattern and the occurrence of sacroiliitis in the presence of inflammatory bowel disease can occur.

Enteropathic arthropathies include:
- Inflammatory bowel diseases - Crohn’s disease
  - ulcerative colitis
- Infectious enteritis
- Whipple’s disease
- Intestinal bypass surgery
- Coeliac disease

A reactive type of arthritis as already described, but in the absence of other criteria found in ankylosing spondylitis, Reiter’s syndrome or psoriatic arthritis, requires a full investigation of the intestinal tract.

The arthritis is characterized by its pauciarticular and asymmetrical pattern. Monoarthritis is not uncommon. Men and women are equally affected. Large and small joints are involved, predominantly those of the lower limbs. The arthritis is generally migratory and transient, but recurrent. Evolution to chronicity may occur,
together with radiographic erosive lesions. A flare of the gut symptoms often precedes a flare in the peripheral arthritis. Enthesopathies can occur.

- Acute anterior uveitis occurs in 10%. It is associated with HLA-B27 and with axial involvement. Conjunctivitis and episcleritis are the other ocular manifestations.
- Skin lesions occur in 10-25% of patients. Erythema nodosum is the most common, and coincides with exacerbations of the gut inflammation.