**Rheumatoid arthritis 1: background, symptoms and ensuring prompt diagnosis and treatment**

Rheumatoid arthritis is a debilitating condition that can cause long term disability. Early diagnosis is essential for prompt treatment to help prevent joint erosion with alternating periods of high disease activity and remission. RA can initially present in a similar way to other conditions such as polymyalgia rheumatica, other inflammatory joint diseases and even malignancy. Symptoms may come and go, and, consequently, a definitive diagnosis may take months to be confirmed.

RA is a symmetrical inflammatory arthritis that primarily affects the synovial joints such as hands and feet, shoulders, wrists, knees and ankles (Arthritis Research Campaign, 2002). Its cause is unknown, although it is established that the immune system is triggered and becomes overactive, producing antibodies that work against the body (auto antibodies). At this point, the body no longer recognises its own synovium, which lines tendons and synovial joints, and this then becomes a target for inflammation (synovitis). Persistent synovitis can lead to joint damage and, ultimately, deformity and disability.

The progression of RA and its inflammatory process can affect all systems of the body. For this reason it is associated with complications and comorbidities such as cardiovascular disease, anaemia, osteoporosis and depression. The likelihood of developing RA increases with age; peak onset is thought to be when an individual is their 40s and 50s. RA is two to four times more common in women than men and causes approximately one third of people to stop work within two years of onset (National Institute for Health and Clinical Excellence, 2009).

**Who is affected?**
RA does not distinguish between age, race or social class and, contrary to popular opinion, it is found in all climates. Inflammatory arthritis also affects children, with one in 10,000 diagnosed with juvenile idiopathic arthritis.

**Learning Objectives**
- Know the signs of inflammation.
- Understand and be able to recognise the symptoms of rheumatoid arthritis.

**Introduction**
Rheumatoid arthritis is a painful autoimmune condition characterised by joint inflammation. The last decade has seen a dramatic change in early diagnosis, treatment and management of this long term condition, meaning a brighter outlook for those who are living with it. This two part unit examines the diagnosis, treatment and management of RA.

**Musculoskeletal Health**
The Department of Health (2007) defined long term conditions as those that cannot, at present, be cured but can be controlled by medication and other therapies. Musculoskeletal disorders account for a high proportion of long term conditions. Many are managed within the specialism of rheumatology, an area of medicine that has been conducting research into treatment and management.

The term “rheumatic diseases” accounts for over 200 conditions that affect the joints, bones, muscles and soft tissue of the musculoskeletal system (Hill and Ryan, 2000). “Arthritis” is a commonly accepted, yet non-specific term, in which 200 variations have been characterised. Musculoskeletal conditions constitute the largest single cause of disability in the developed world (Hill, 2006).

**Rheumatoid Arthritis**
Perhaps the most common form of inflammatory arthritis is RA. It affects an estimated 580,000 people in England, with 26,000 new cases diagnosed each year (National Audit Office, 2009). This autoimmune condition is characterised by joint inflammation, causing pain, swelling, heat and stiffness. It is a systemic disease that also causes fatigue, weight loss, flu-like symptoms and anaemia. The condition is also unpredictable in nature, fluctuating with alternating periods of high disease activity and remission. RA can initially present in a similar way to other conditions such as polymyalgia rheumatica, other inflammatory joint diseases and even malignancy. Symptoms may come and go, and, consequently, a definitive diagnosis may take months to be confirmed.

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arthritis every year (ARC, 2003). Although RA affects women more than men, in very older people it is more common in men than women (Hill and Ryan, 2000). Siblings of people who have RA have an increased risk of developing it themselves, yet it is not considered a hereditary disease. Fewer than 100 new cases of inflammatory joint disease are diagnosed in the UK per 100,000 each year; 24 of these are RA (Luqmami et al, 2006).

Lifestyle factors are not a direct cause but are sometimes associated with the condition. There is evidence to suggest a link between RA and smoking (Mattey et al, 2002), while moderate alcohol consumption and a high intake of vitamin C are thought to reduce the risk of developing it (ARC, 2002).

DETECTING SIGNS AND SYMPTOMS
The progression of RA is usually slow; rapid onset is thought to occur only in around 20% of cases. Inflammation, tenderness and mild stiffness – usually with symmetrical distribution – can be early symptoms, as can fatigue and weight loss. Some people delay reporting symptoms to their GP until they have become severe; for this reason, patients will often report irritability, anxiety and depression due to increasing pain and the limitation of mobility and daily activities.

PATHOLOGICAL FEATURES
Inflammation of the synovial membrane surrounding the joint capsules and tendon sheaths is called synovitis. The synovial membrane is the inner membrane of tissue that lines a joint and secretes synovial fluid. The main function of this fluid is to lubricate the joint. Fig 1 shows a healthy joint and one that has been affected by arthritis.

It has been suggested that pathological changes caused by synovitis occur in three stages (Hill and Ryan, 2000):
- Cellular stage: joints become warm, swollen and tender, causing stiffness and restricted movement;
- Inflammatory stage: granulocytes accumulate in the synovial fluid before their destruction during the inflammatory process causes the release of lysosomal enzyme (Hill and Ryan, 2000);
- Destructive stage: primarily affects the hyaline cartilage as vascular granulation tissue or ‘pannus’ starts to erode the cartilage around the joint.

It is typical for synovitis to initially affect the small joints of the hands and feet although any synovial joint can be affected.

DIAGNOSIS
Diagnosis can be difficult, as RA can present in several ways, some of which can be similar to other conditions. It is diagnosed by clinical history, physical examination and investigations such as blood tests, X-rays and/or ultrasound.

In an attempt to classify the condition and provide consistency in diagnosis, the American Rheumatism Association reached consensus on diagnostic criteria (Arnett et al, 1988). It identified seven main diagnostic criteria (Box 1) and agreed that four of those seven should be present to reach a diagnosis of RA.

Diagnosis in practice
Although the seven diagnostic criteria have been useful in providing strict inclusion criteria for clinical trials, they have proved less helpful as a tool for diagnosis in clinical practice, due to their rigid constraints. Many people who are diagnosed with RA do not present in such a typical way, but clinicians’ experience and knowledge enables a diagnosis to be made.

Luqmami et al (2006) suggested that the validity of guidelines for RA can be tested by using a composite index of disease assessments, disease activity score (a 28 joint count, testing for tenderness and swelling), drug toxicity, disability and joint damage. NICE (2009) recommended that people with suspected persistent synovitis should be referred for specialist opinion and diagnosis should be based on clinical findings. It also recommended urgent referral for patients when:
- The small joints of the hands or feet are affected;
- More than one joint is affected;
- There is a delay of three months or longer between the onset of symptoms and the seeking of medical advice.
Blood Tests

As no single blood test can provide a diagnosis of RA, a range of tests are taken to provide an overview of the patient’s health and wellbeing. However, recognised patterns in blood results indicate an acute inflammatory response. Key blood tests help to identify the presence of inflammation and assist in diagnosis, along with clinical examination and patient history.

A number of key blood tests are used to aid diagnosis of RA and monitor blood levels for disease activity while patients are being actively treated with drug therapy. These are:

- Full blood count to ascertain haemoglobin, platelet and white blood cell levels: many people with persistent inflammation develop anaemia. This is often referred to as anaemia of chronic disease or normochromic, normocytic anaemia;
- Liver function and biochemistry tests: these are performed as a baseline to ascertain whether the major organs are able to metabolise and excrete drugs effectively. Certain liver enzymes are temporarily elevated in the presence of inflammation (predominantly alkaline phosphatase and gammaglutamyltransferase and others) with drug toxicity, such as alanine transaminase and aspartate transaminase). However, as abnormally elevated liver enzymes may be indicative of other conditions or due to drug toxicity, such as alanine transaminase and aspartate transaminase. Therefore, provide an indication of autoimmune illness;
- CRP is a non-specific marker of acute inflammation as it reacts much faster than an ESR. A normal CRP range is from 0-8mg/L. A CRP result of >100mg/l indicates infection is present; whereas a CRP of >200 indicates joint damage. It is a relatively new test and therefore not performed as a standard investigation in all centres. A negative result does not exclude the condition. Anti CCP antibodies have not been found at a significant frequency in other diseases to date, and are more specific than RF for detecting RA.

References

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Other Diagnostic Tests

X-rays

Although new drug therapy in RA aims to prevent joint damage, erosions may still be detected on diagnosis. In the past, X-rays have been useful measures for monitoring joint deterioration where bony erosions clearly appear like punctured holes.

Ultrasound

The use of ultrasound scanning is becoming standard practice in assessing and measuring the degree of synovitis in joints and soft tissues. It can also ascertain early erosions and tendon rupture (Kane et al, 2004).

Disease Progression

GPs and community nurses are becoming more experienced in recognising early symptoms of RA. Ideally, prompt referral to a rheumatologist normally takes place within three months of symptoms being reported, enabling early diagnosis and initiation of treatment. Escalation and monitoring of appropriate medication is paramount to patient safety, while aiming to prevent complications.

Over the last decade, advances in pharmacological treatments have been shown to slow down joint destruction and ultimately disability, such as disease modifying and biological drugs. This provides a more optimistic outlook for people with RA.

Part 2 of this unit, to be published in next week’s issue, examines the impact of RA and treatment options.