# **RHEUMATOID ARTHRITIS**

Version 2 Final

EBM – Rheumatoid Arthritis 2 Final

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## **Document control**

#### **Version history**

Version	Date	Comments		
2e Draft	28/02/08	Customer comments incorporated		
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### **Changes since last version**

#### 1. Introduction

Rheumatoid arthritis is a chronic autoimmune disease, producing joint damage mediated by cytokines, chemokines, and metalloproteases. It is speculated that rheumatoid arthritis is a relatively new disease because there is a surprising lack of historical evidence for its existence.

#### **Description**

It is a common systemic disease characterised by a chronic inflammatory synovitis which typically affects the peripheral joints but which may affect any synovial joint in the body and periarticular synovial structures (bursae and tendon sheaths). It can manifest as a single episode of painful, stiff joints lasting a few months or as an aggressive, destructive arthritis that progresses rapidly to severe physical disability. Most frequently the patient follows a relapsing and remitting course over many years. [1]

Rheumatoid arthritis is typically a distal, symmetrical, small joint polyarthritis involving the proximal interphalangeal and metacarpo- and metatarsophalangeal joints of the hands and feet, knees and cervical spine. The shoulders, elbows and hips are less frequently involved but can cause considerable morbidity. [2]

The disease is regarded as an autoimmune disease and can have extraarticular manifestations that may involve cardiovascular, respiratory, nervous and lymphatic/haematological systems and the skin, connective tissues, eyes, and mouth.

Equally important to affected individuals is the potential loss of social and financial independence. [3]

The disease also exerts a considerable burden on society in terms of direct (i.e. medical care) and indirect (ability to work) costs. [4]

## 2. Aetiology

#### **Aetiology**

Although rheumatoid arthritis is regarded as an autoimmune disease, details of its pathogenesis remain unclear. It is probably a multifactorial disease which occurs when several risk factors occur simultaneously.

There is considerable evidence for an important genetic component and a substantial portion of this risk seems to lie in the HLA region (HLA-DR4).

Predominant non-genetic factors include a theoretical ubiquitous infective cause or trigger and environmental influences. [5] The onset of rheumatoid arthritis occurs more commonly in winter [2]. Cigarette smoking is also thought to play a role. [6]

Hormonal influences may be significant because use of the oral contraceptive pill postpones or modifies the presentation. Clinical signs and symptoms vary in intensity with the menstrual cycle, often abate during pregnancy and flare in the post partum period.

Interestingly, in middle aged men nonarticular features (fever, weight loss, anaemia, pleural effusions and vasculitic lesions) may dominate the clinical picture. [2]

The main pathology in rheumatoid arthritis is an auto-immune mediated thickening and inflammation of the synovial membrane, which becomes infiltrated with inflammatory cells. The synovial lining layer becomes continuous with vascular tissue, termed pannus, which grows over cartilage and causes erosion of articular cartilage and underlying bone due to its high content of macrophages and osteoclasts. With time this results in degeneration of the cartilage and the joint.

Plasma cells in the subsynovium synthesise large quantities of immunoglobulin much of which is IgG and IgM rheumatoid factor (i.e. immunoglobulin with reactivity to self Ig-G). These autoantibodies form immune complexes that activate complement and this can cause or maintain local inflammation.

Several observations suggest that the inflammation in rheumatoid arthritis is a T-Cell mediated phenomenon.

Rheumatoid nodules develop in about 30% of patients with RA. They are granulomas consisting of a central necrotic area surrounded by palisaded histiocytic macrophages, all enveloped by lymphocytes, plasma cells, and fibroblasts. Nodules and vasculitis can also develop in many visceral organs. [7] Other granuloma formation may be seen on the surface of the pleura, pericardium and endocardial valves.

#### **Prevalence**

Rheumatoid arthritis affects about 1% of the American and Western European population with much lower rates in oriental and black populations. Although virtually non-existant in Nigeria, prevalence among US blacks is around 1%. There is a ratio of 3:1 females to males. It may occur at any age, onset is rare under 20 and over 80 (1) and peaks in the fourth and fifth decade.

The sex difference is most pronounced in those with early onset disease, 6:1 females to males, but is almost equal by age 65 years.

# 3. Characteristics signs and symptoms in articular rheumatoid arthritis

The common symptoms and signs are joint swelling, stiffness and deformity, nodules, vasculitis and malaise.

Onset may be acute with simultaneous inflammation in multiple joints but is more often insidious with progressive joint involvement. Affected joints are tender, swollen and warm and both active and passive movements are limited. This is due to joint effusion and florid synovitis.

Tenderness of affected joints is a very sensitive sign and synovial thickening, eventually of all affected joints, is a most specific sign. Symmetrical involvement of hands (PIP and MCP), feet (MTP), wrists, elbows and ankles is typical but any joint may be affected

Generally patients complain of feeling unwell in themselves and present with loss of function and pronounced stiffness more than pain. Morning stiffness of more than 60 minutes is almost pathognomonic of active rheumatoid arthritis. Stiffness of more than 60 minutes duration may also occur after prolonged inactivity and at night. [7]

Inflammatory tenosynovitis can erode through tendons causing rupture and compression of nerves by synovitis and this can commonly lead to in carpal tunnel syndrome. [8]

Individual joints may be affected as follows:

#### **Cervical spine**

Frequently involved. Atlanto-axial subluxation gives rise to neck pain, neck stiffness, paraesthesiae and sensory changes. Abnormal gait and urinary retention or incontinence occurs if there is spinal cord involvement.

A "Cock robin" posture is due to erosion of vertebral body(ies) in cervical and upper thoracic areas.

#### Hands and wrists

Fixed deformities, particularly flexion contractures, may develop rapidly; ulnar deviation of the fingers with an ulnar slippage of the extensor tendons off the metacarpophalangeal joints is typical, as are swan-neck and boutonnière deformities. Over time the metacarpophalangeal joints sublux. Range of movement and strength may be dramatically reduced.

Carpal tunnel syndrome can result from wrist synovitis pressing on the median nerve.



Ulnar deviation



Boutonniere deformity

#### Feet and ankles

In decreasing frequency there can be involvement of metatarsal phalangeal joints, talonavicular, subtalar, and ankle joints. Lateral deviation of the toes causes hallux valgus. Dorsal subluxation of the metatarsophalangeal joints uncovers the heads of the metatarsals and may cause metatarsalgia, a painful sensation of "walking on marbles". Both medial and lateral arches may collapse, resulting in pes planus and heel valgus, accelerated by rupture of the tendon of tibialis posterior, a frequent association. Metatarsophalangeal joint" [2] involvement can also cause hammer toes.



#### **Shoulders**

Effusions with inflamed rotator cuff tendons give rise to painful abduction arcs and loss of shoulder movements. Rupture of the rotator cuff can occur.

#### **Elbows**

75% of patients with rheumatoid arthritis complain of elbow pain, 20% severely. Joint effusions, progressing to bony destruction may occur. Range of movement and strength decreases, especially in pronation and supination.

#### Hips

Subtle reduction of internal rotation.

In established rheumatoid arthritis, secondary degenerative changes can result in rest pain.

After a variable period of time, rheumatoid arthritis may become inactive and may then be described as "burnt out". At this stage there may be no swelling or redness, but deformed joints, surgical scars and muscle wasting may all be evident.

The degree of nonarticular involvement varies and may precede articular disease.

**Appendix 1** outlines the common extra articular manifestations.

#### Revised criteria for classification of rheumatoid arthritis (1987):

Any four criteria must be present to diagnose rheumatoid arthritis. Criteria 1-4 must have been present for at least six weeks.

- 1. morning stiffness for an hour or more
- 2. arthritis of three or more joint areas
- 3. arthritis of hand joints (wrist, metacarpophalangeal or proximal interphalangeal)
- 4. symmetrical arthritis
- 5. rheumatoid nodules
- 6. serum rheumatoid factor by a method positive in less than 5% of normal control subjects
- 7. radiographic changes (hand x-ray changes typical of rheumatoid arthritis that must include erosions or unequivocal bony decalcification). [9]

#### **Patterns of Onset**

There are several distinct patterns of onset.

#### **Insidious onset**

In 70% of cases, increasing joint involvement develops over weeks or months. This has a relatively poor prognosis. Usually peripheral small joint involvement is followed by proximal joint (knees and hips) involvement.

#### **Palindromic**

In about 20% of patients, persistent joint disease is preceded by self limiting attacks of a few days of synovitis in various joints. About 50% of patient who have these self limiting attacks eventually develop chronic rheumatoid arthritis.

#### **Explosive onset**

10% of cases show precipitate onset with severe symmetrical polyarticular involvement occurring over 24 to 48 hours. Paradoxically they seem to do better in the longer term. [10], [11]

#### Systemic onset

Fever, myalgia, weight loss, anaemia, pleural effusions and vasculitic lesions may be severe sometimes in the absence of marked joint pathology. It is particularly common in middle aged men.

#### Mono and Pauci articular onset

Patients with limited joint involvement, usually young women, who are persistently seronegative for rheumatoid factor; usually pursues a benign course. [2]

#### Polymyalgic onset

Limb girdle muscle symptoms may precede overt arthropathy particularly in the elderly. It may be difficult to differentiate from polymyalgia rheumatica initially. There is an impressive response to steroids initially but less so with progression of synovitis.

#### **Examination**

Soft boggy swelling of synovitis and knee effusions are common. Crepitus is found in early disease of degenerative joints.

Joint counts - tenderness and swelling are measured separately. Swollen joint count is a better measure of inflammation than tender joint count because tenderness may be due to other causes whereas swelling is usually not.

Investigations: A detailed table of investigations and prognostic factors generally undertaken in Rheumatoid Arthritis is given in Appendix 2.

#### **Differential Diagnosis**

Most exclusions are relative since two diseases causing arthritis can coexist.

#### Polymyalgia rheumatica

In the elderly, onset of proximal manifestations may be confused with polymyalgia rheumatica

#### **Osteoarthritis**

Typically, the OA patient stiffens whilst sitting down to lunch whereas a rheumatoid arthritis patient is usually enjoying the best part of their day.

#### Crystal Arthropathies (gout, pseudogout)

Crystal deposition in joints may mimic the swelling and redness of rheumatoid arthritis.

#### **SLE**

Rheumatoid arthritis shares many features with other collagen vascular diseases, particularly SLE. [7]

#### Acute rheumatic fever

Here there is a typical migratory joint involvement pattern.

#### **Sarcoidosis**

Granulomatous reticulosis affecting almost any organ, including the small bones of the hands and feet.

#### **Amyloidosis**

Amyloid accumulation can be found in various organs.

#### Whipples disease

Malabsorption syndrome of which arthritis can be one of the manifestations.

#### Inflammatory bowel disease

Crohn's disease and ulcerative colitis are both frequently associated with inflammatory joint manifestations.

#### Investigations

Until recently, Rheumatoid Factor (RF) was the test of choice. Recently, an assay of anti-CCP (antibody to cyclic citrullinated peptide) has become available and is showing promise of increased sensitivity and specificity (67% and 95% respectively, versus 69 and 85% for RF). Its exact role is yet unclear. [12]

#### 4. Treatment

The goals of treatment are to control synovitis, relieve pain, maintain function, improve quality of life and minimise drug side effects while being cost effective. [13]

Deterioration in joint function and x-ray changes occur most rapidly early in the disease because cartilage had limited capacity for regeneration. Therefore all patients with rheumatoid arthritis should be referred early for specialist opinion.

Management by a multidisciplinary team via hospital is considered best practice today. [14] Treatment plans have to take account of comorbidities, age, expectations and lifestyle. [8]

Evidence is now accumulating that early, more aggressive intervention can improve longer term disease outcome. [15]

#### **Drugs**

Two main drug classes are considered in the treatment of rheumatoid arthritis.

Non-steroidal anti-inflammatory drugs (NSAIDS) and Disease modifying antirheumatic drugs (DMARDS).

NSAIDs – reduce joint pain and swelling but may take up to two weeks to start having an effect. There may be gastrointestinal and renal side effects and they are more toxic than previously appreciated. They do not reduce disability over the long term.

(They are fully discussed in the sections on osteo-arthritis)

DMARDS – are used to relieve pain and swelling, and to improve function. In addition, it is considered that they may reduce disease progression.

The use of these drugs is indicated in all patients who continue to have active disease (stiffness, joint pains and elevated ESR) after three months of NSAID treatment.

A major review of clinical trials of their use was undertaken by Clinical Evidence (June 2005) [13] who reported on their effectiveness (beneficial, likely to be beneficial and inconclusive) in conjunction with first or second line treatment options.

The DMARD methotrexate is widely used as first-line treatment in people with rheumatoid arthritis because of consensus about its effectiveness in practice.

Sulfasalazine and combined treatment with methotrexate and sulfasalazine are as effective as methotrexate in improving pain, joint swelling, and function in people with early rheumatoid arthritis who have not previously received DMARDs.

Antimalarials may improve symptoms and function in DMARD-naïve people, and are reasonably well tolerated, but radiological evidence of erosion is more marked with antimalarials than with sulfasalazine.

There is a variety of DMARDs available for second-line treatment of rheumatoid arthritis. However there is no clear evidence that any one is superior to another.

Methotrexate, sulfasalazine, penicillamine, and leflunomide cause similar improvements in symptoms and function when given to people as second-line DMARD treatment, although methotrexate causes fewer adverse effects.

Methotrexate leads to improvement within six to eight weeks. Other DMARDs take three to six months to produce a beneficial effect. Relapse occurs if the drug is discontinued (11). Some are less toxic than previously thought and are more effective analgesics than NSAIDs over long periods.

A recent introduction has been the class of drug known both as tumour necrosis factor antagonists (TNFAs) and cytokine inhibitors. Etanercept and Infliximab are the two examples currently in use and it is considered that in second line therapy adding either to methotrexate is more effective than using methotrexate alone.[16]

Infliximab allows rapid disease control and reduces rheumatoid arthritis disease activity. It appears to have an acceptable safety profile in trials to date.

Etanercept appears to reduce radiological progression.

Currently both etanercept and infliximab have to be administered by injection. For maintenance, etanercept 25mg. twice weekly and infliximab 200mg (3mg./Kg.) eight weekly. However etanercept appears to be associated with fewer side effects.

Oral gold was less effective than both methotrexate and sulfasalazine in improving measures of disease activity in people with rheumatoid arthritis, although it had less toxicity. Reviews found that oral gold and antimalarial drugs caused comparable improvements in measures of disease activity, but that oral gold was less effective than penicillamine.

Parenteral gold caused similar improvements in measures of disease activity compared with methotrexate, but caused more adverse effects. Parenteral gold is associated with higher levels of toxicity than most of the other commonly used disease-modifying antirheumatic drugs. It also had higher total drop out rates than the other drugs.

Corticosteroid use is controversial. Although corticosteroids reduce the

rate of progression of the disease they are generally avoided because of long term effects. They are indicated for life threatening complications of RA such as vasculitis or pericarditis. Intra-articular steroid injections are used for one or two affected joints. Their current effectiveness as either first or second line therapy is classed as "unknown".

#### **Occupational Therapy**

In everyday practice, the substantial impact of skilled occupational therapy (OT) intervention on quality of life for patients with RA is clear. The OT approach is multifaceted and includes:

Activities of daily living, particularly washing, toileting, dressing, cooking, eating and working. Sometimes the provision of equipment and adaptations is fundamental to the management of RA. [17]

Joint protection including adapting movement patterns, assistive devices, rest regimens, energy conservation techniques, exercise and splinting. Studies in patients with longer disease duration have shown encouraging results. [18]

#### **Physiotherapy**

Thorough physical therapy evaluation should be performed initially, including functional assessment (transfer status, gait analysis, activities of daily living etc.), range of movement of all joints, strength, posture and respiratory status. This gives a baseline for future reference and an accurate and objective basis for treatment goals. [19]

Exercise and physiotherapy are used to maintain or to improve muscle tone in order to prevent or correct deformities and to maintain or increase joint mobility and function.

The aim is to achieve the right balance between exercise and rest. Strong muscles protect joints, but inflamed joints should be rested initially and then gradually worked through a full range of non weight-bearing exercises.

A variety of treatment modalities including heat therapies, cold therapies, electrotherapy (e.g.TENS), mobilisation and massage are used in physical therapy.

#### **Splinting**

Is used:

- To rest actively inflamed joints at night and during flare ups.
- For stabilisation in optimum position for use
- To prevent deformity and contractures

Support splints may preserve adequate function and improve pain but may restrict dexterity.

One study showed splinting produced no change in grip strength and there was no difference in grip strength between various pain levels. [20]



#### Surgery

Pain is the primary indication for surgery. The most common procedures involve hip, knee, shoulder, elbow and hand joint replacements. Other procedures include synovectomies, wrist stabilisation, forefopot arthroplasties and excision of the head of the radius.

Strong willed, strong boned, strong muscled and well informed patients are the best candidates for surgery but post operative restoration of function is difficult to predict and a multidisciplinary approach is needed. Unfortunately most patients do not fit this profile, and a



frailer patient with osteoporosis, either due to the disease mechanism, disuse osteopenia or therapeutic steroid use, is the norm, making surgery technically more difficult and complications more common.

Different types of surgical intervention are appropriate to different stages of the disease process:

Early synovitis: non-operative/splinting

Persistent synovitis: synovectomy of joints, which continue to have active synovitis despite local steroid injections, may prevent erosions

Specific deformation: reconstructive

Severe crippling: salvage

The most successful procedures for rheumatoid arthritis are carpal tunnel release, resection of metatarsal heads, total knee arthroplasty (after which synovitis disappears) and total hip arthroplasty.

Joint replacement surgery has revolutionised the outlook for RA patients because it relieves pain and improves function.

Cemented hip implants have 90% success rate. There is a higher failure rate in rheumatoid arthritis than in osteoarthritis and revision outcome is much poorer. Excision arthroplasty (Girdlestone) as a salvage procedure is still performed in failed primary and revision arthroplasty.

Tendon transfers across the wrist may redirect line of muscle action where a joint deformity is exacerbated by the "bowstringing" effect of tendons crossing that joint, which have come to lie eccentrically due to the initial deformity.

#### **Podiatry and Dietetics**

Appropriate footwear and orthoses are effective with regards to comfort level, and stride speed and length. [21]

Both weight management particularly when weight bearing joints are involved, and interventions to address cachexia where patients do less well and have poorer functional status can be effective. [22]

Analysis of clinical trials of fish oil supplementation in RA concluded that while there was reduction in the number of tender joints and in duration of morning stiffness, no effect was seen on disease activity or progression of RA. [23]

### 5. Prognosis

All studies of RA over ten years or more show severe morbidity [24] and patients with rheumatoid factor appear to have a more severe course. Spontaneous remission in RA usually occurs within the first two years. However 50 - 90% of those affected have progressive disease [24] and even after five years of antirheumatic drug therapy, complete remission is rare. [25]

Almost 50% of patients show joint space narrowing and/or erosion in the first two years, therefore permanent articular damage is often present which is progressive in almost all patients.

About 50% of maximum scores for joints space narrowing and radiographic erosion is seen by five years of disease.

Decline in functional status is seen in most patients with RA over periods longer than a decade. Many patients, however, show an improvement in morning stiffness over this time suggesting "burn out" but this still leaves significant losses in functional capacity.

Clinical markers derived from joint counts, and functional status measures including patient self-report questionnaires, demographic measures and co-morbidity studies appear to be the most effective currently available data to predict mortality in rheumatoid arthritis.

Formal education level is highly predictive of morbidity and mortality in RA, a more formal education correlating with less morbidity and mortality. A hypothesis has been proposed that low formal education is a variable that identifies behavioural risk factors predisposing to the aetiology and poor outcomes of most chronic diseases and is probably related to efficiency in using medical services, problem solving capacity, sense of personal responsibility, capacity to cope with stress, life stress, social isolation, health focus of control and learned helplessness [24].

Many patients with mild disease are not referred and do well. Functional outcome of RA after about six years of disease is fairly good and while functional impairment of different joints had progressed, most patients were still classed as mildly disabled. [26]

In a ten-year follow up study of hospital admissions:

- 25% were considered fit for most activities
- 40% had moderate functional impairment
- 25% were severely disabled
- 10% were wheelchair bound [2]

In the United States, among men 18 – 65 years with arthritis only 56% were working compared with 89% of men with no arthritis. Amongst women with arthritis 31% were working compared with 62% of women with no arthritis [24].

Work disability is seen within ten years of disease onset in at least 50% of patients younger than 65 years who were working at the time of disease onset.

Work disability has been primarily studied for patients under care referral centres and may not represent all patients with rheumatoid arthritis [24].

Poor outcomes in terms of functional disability correlates with female sex and seropositivity.

#### **Life Expectancy**

Rheumatoid arthritis significantly shortens life expectancy. Higher mortality rates are found among patients with persistent joint inflammation, seropositivity, functional loss, and lower levels of education. Overall the disease decreases life expectancy by three to ten years in both men and women. They die of expected causes, e.g. cardiovascular, cerebrovascular or malignant disease, but at a younger age [8].

The most important determinants of prognosis are the severity and persistence of disease activity.

Disease that remains confined to the hands and feet has a good prognosis.

Some features have shown association with a poor outcome and are given in Appendix 3.

Measures indicating functional disability, as well as age and comorbidities, predict five-year mortality more effectively than laboratory data. Measures of inflammatory activity may underestimate long tem outcomes in rheumatoid arthritis.

## 6. Main Disabling Effects

An important feature of the musculoskeletal system is that any impairment alters the biomechanics of contralateral joint structures or those continuous in the kinetic chain. This usually also increases baseline energy expenditure for activity.

Pain, deformity, muscle wasting and flexion contracture may all contribute towards functional impairment.

Extra-articular manifestations may further contribute towards the overall level of functional impairment.

Common measurements of overall severity of disease include grip strength, global severity, joint count, morning stiffness, HAQ-DI scale [Appendix 4], ESR and haemoglobin level.

Signs of synovitis are most useful in the assessment of disease activity. The reduction in the range of movement is a useful indicator of current or potential functional problems. An indication of the activities of daily living likely to be affected beyond certain reductions is given in [Appendix 5]

Most individuals with early rheumatoid arthritis can perform tasks of daily living, although with discomfort or impaired efficiency. This is achieved because people adapt and work within their pain and limited joint movement. When contractures or joint deformity progresses beyond a certain range for a joint the impairment will result in a functional deficit. [27]

Functional disability progresses more rapidly in the first few years than in the latter course of the disease and 50% of patients have considerable difficulty performing their pre-morbid domestic, work and social functions within six years of their first clinic visit.

Pain, which is unpredictable and varies in intensity and duration, is a key feature of RA and night time pain often contributes to sleep disturbance. [28]

Fatigue due to poor sleep and functional impairment may both adversely affect social activity which in turn may adversely affect mood. This may account for depressive symptoms occurring more commonly in those suffering from RA than in the general population.

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# **Appendix 1**

#### Common extra-articular manifestations of Rheumatoid Arthritis

Skin Subcutaneous nodules. Vasculitis. Thinning and

ulceration.

Eyes Episcleritis (<1%). Keratoconjunctivitis sicca (15-25%).

Cardiac Pericarditis and pericardial effusions - 50% of

asymptomatic patients undergoing echocardiography have

evidence of pericarditis [12]

Constrictive pericarditis. Aortitis

Conduction defects Coronary arthritis Myocarditis

Respiratory Crico-arytenoid joint inflammation. Interstitial lung disease

(frequently found at autopsy). Visceral nodules. Pleural effusions. Bronchiolitis obliterans. Pulmonary arteritis.

Neurological Atlanto-occipital subluxation and spinal cord compression.

Carpal tunnel syndrome and entrapment neuropathy. Mononeuritis multiplex. Muscle wasting. Peripheral

neuropathy.

Haematological Anaemia of chronic disease. Thrombocytosis

General Rheumatoid nodules are characteristic and are found in

25-50%. They form subcutaneously in bursae and along tendon sheaths, over pressure points e.g. olecranon, ulna border of forearm. Achilles tendon and ischial spines. Splenomegaly and lymphadenopathy. Sjögrens syndrome. Sicca symptoms – dry mouth. Low grade fever.

Amyloidosis in internal organs.

### **Appendix 2**

Investigations and prognostic factors in Rheumatoid arthritis

Prognostic Indicators Elevated ESR in 90%, plasma viscosity, C-reactive

protein (acute phase indicators – persistently elevated associated with worse prognosis). Creactive protein is better indicator than ESR or

viscosity [27].

FBC Hb 8-10 in 80% normochromic normocytic anaemia

Thrombocytosis may be present Neutropenia and

splenomegaly = Felty's syndrome (2%)

Rheumatoid factors Antibodies to altered gamma globulin are present in

about 70%. Various tests – different sensitivity and specificity. High titres broadly correlate with more severe disease. False positive results occur more

frequently with ages.

Synovial Fluid Cloudy, sterile, reduced viscosity, 3000 – 50,000

WBCs per microlitre Synovial fluid complement is

often less than 30% serum level.

Radiology Early disease -soft tissue swelling only later -

periarticular osteoporosis, joint space narrowing (articular cartilage) and marginal erosions, then joint degeneration and deformity. The rate of deterioration clinically and radiologically is highly variable. X-rays are used to monitor progression.

# **Appendix 3**

#### Features associated with poor outcome in RA

- □ Persistently high acute phase response
- □ High titre of rheumatoid factor
- □ Erosion during the first year
- □ Family history of rheumatoid arthritis
- □ HLA-DR4
- □ Extra-articular disease
- □ Insidious onset
- □ Female sex
- □ Low educational attainment
- □ High level of functional disability
- □ Low socio-economic status
- □ Early age of onset (10)

# **Appendix 4**

# Health Assessment Questionnaire (Modified for British rheumatoid arthritis patients ) [29]

Patient Label		∥D	ate	
We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments at the end of this form. PLEASE TICK ONE RESPONSE WHICH BEST DESCRIBES YOUR USUAL ABILITIES OVER THE PAST WEEK:				
	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	Unable to do
	Score = 0	Score = 1	Score = 2	Score= 3
1. DRESSING AND GROOMING - Are you able to				
Dress yourself, including tying shoelaces and doing buttons?				
Shampoo your hair?				
2. RISING - Are you able to				
Stand up from an armless straight chair?				
Get in and out of bed?				
3. EATING - <i>Are you</i> able to				
Cut your meat?				
Lift a full cup or glass to your mouth?				
Open a new carton of milk (or soap powder)?				
4. WALKING - Are you able to				
Walk outdoors on flat ground?				
Climb up five steps?				

PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE					
ACTIVITIES: Walking stick		Cri	utches		
Devices for dressing e.g. buttonhook, zipper pull, long handled shoe horn		Sp	Crutches Special or built-up chair Wheelchair		
Walking frame		Other (please specify)			
Built-up or special utensils  PLEASE TICK ANY CATEO	ODIES E	OP.	WHICH VOILIE	NIALLY NEEL	NELD EDOM
ANOTHER PERSON:	JORIES F	UK	WHICH 100 03	OUALLI NEEL	D HELP PROM
Dressing and grooming	Rising		Eating	Walking	
	Without ANY difficulty		With SOME difficulty	With MUCH difficulty	Unable to do
	Score = 0	)	Score = 1	Score = 2	Score= 3
5. HYGIENE - Are you able to					
Wash and dry your entire body?					
Take a bath?					
Get on and off the toilet?					
6. REACH - Are you able to					
Reach and get down a 5lb object (e.g. a bag of potatoes) from above your head?					
Bend down to pick up clothing from the floor?					
7. GRIP - Are you able to					
Open car doors?					
Open jars which have been previously opened?					
Turn taps on and off?					
8. ACTIVITIES - Are you able to					
Run errands and shop?					
Get in and out of a car?					
Do chores such as vacuuming, housework or light gardening?					

# PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE ACTIVITIES:

Raised toilet seat	'' ' ' '	Long handled appliances for reach	
Bath seat	Bath rail	Other (please specify)	

# PLEASE TICK ANY CATEGORIES FOR WHICH YOU USUALLY NEED HELP FROM ANOTHER PERSON:

Hygiene	Peach	Gripping and opening things	Errands and
riygierie	Neach	Oripping and opening things	housework

#### **SCORING OF HAQ**

Add the maximum score for each of the 8 sections and divide by 8 to give a score between 0-3.

If aid/device or help is needed the score for that activity automatically = 2 (*unless 3 has already been ticked*.)

Normal function = 0

Most affected function = 3

# **Appendix 5**

Joint	Reduction to	Effect on	
Temporo-mandibular	< 2.5 cms of opening	Biting, eating	
Temporo-mandibular	Fusion	Chewing	
Shoulder	< 90° Abduction	Washing , dressing	
Elbow	< 140° Flexion	Dressing (top buttons)	
Elbow	< 80° Flexion	Carrying a shopping bag	
Elbow	< 40° supination	Use pen or pencil	
Elbow	< 60° pronation	Operating yale type lock	
Hip	< 110° flexion	To rise unaided	
Hip	< 90° flexion	To sit comfortably	
Knee	< 90° flexion	To rise unaided	
Knee	< 45° flexion	Walk or use stairs	
Knee	< Full extension	Walking steadily	
Knee	> 20° fixed flexion deformity	Fatigue on walking	
Ankle	< 20° plantar flexion	Difficulty walking	
	< 10° dorsiflexion	-	