An approach to rheumatoid arthritis

— S W Brighton

Dr S W Brighton, MB ChB, M Med
Dept of Physical Medicine
Faculty of Medicine
University of Pretoria
Pretoria 0001

Curriculum vitae

Dr S W Brighton studied at the University of Pretoria and received the MBChB in 1963. After some years in hospitals in Durban and London (UK) and then general practice in Pretoria, he joined the staff of the Department of Physical Medicine, University of Pretoria 1975 - 1979, obtained the M Med-degree, and since 1980 has been attached to the Department of Rheumatology (UP). In 1979 Dr Brighton was elected Fellow of the Faculty of Physical Medicine of the College of Medicine of SA. He has published in many medical journals, in RSA and abroad, and is actively involved in research work at the University of Pretoria.

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Summary

In a very practical way the author gives criteria for diagnosing rheumatoid arthritis, its epidemiology, pathology, clinical aspects and therapy

Criteria for diagnosis

Rheumatoid arthritis is a systemic disease of connective tissue which in particular attacks the synovial joints. It is a chronic polyarticular disease which usually attacks the joints in a symmetrical fashion.

There is unfortunately no single sign, symptom or test that is diagnostic of rheumatoid arthritis. The diagnosis of rheumatoid arthritis is based on a combination of signs and symptoms. The American Rheumatism and Arthritis Association have identified eleven criteria known as the ARA criteria for diagnosing the disease, namely:

1. Morning stiffness present for more than 6 weeks
2. Pain on moving the joint, or tenderness in at least one joint for at least 6 weeks
3. Soft tissue swelling of at least one joint for at least 6 weeks
4. Soft tissue swelling in at least one other joint occurring within 3 months of the first
5. Symmetrical joint involvement except the distal interphalangeal joints
6. Subcutaneous nodules
7. Radiological changes typical of rheumatoid arthritis
8. Positive rheumatoid factor
9. Weak mucin clot formation in synovial fluid aspirated from a joint.
10. Histological changes in the synovium considered typical of rheumatoid arthritis
11. Typical histological changes in subcutaneous nodules.

Depending on the number of criteria present the patient may be classified as:

a) Classical rheumatoid arthritis (7 or more criteria)
b) Definite rheumatoid arthritis (5–7 criteria)
c) Probable rheumatoid arthritis (3–4 criteria)
d) Possible rheumatoid arthritis (2 criteria).

Any obvious other diseases must also be excluded. Although cumbersome, these criteria can be of considerable help. A patient with criteria for only probable or possible rheumatoid arthritis must be reassessed regularly as it is with this group of

patients where differential diagnosis can be difficult. A number of other conditions can mimic rheumatoid arthritis.

Epidemiology

The disease has a world-wide distribution but is somewhat more prevalent in developed populations. Women are affected about three times more commonly than men. There is also a slight family tendency to the disease.

Pathology

The inflammatory process starts in the synovial membrane with hyperplasia. This hyperplastic synovium fills the joint space causing the capsule to bulge, and adheres to, and destroys the joint cartilage. Small bony erosions occur at the edge of the cartilage which slowly enlarge and can with time destroy the bony surface of the joint. This combination of bony destruction and stretching of the capsule and other soft tissues of the joint leads to the typical joint deformities of rheumatoid arthritis.

Clinical aspects

Rheumatoid arthritis usually starts slowly, involving at first only a limited number of joints. With time more and more joints become symptomatic, and are usually symmetrically involved. Joint involvement is usually preceded by some constitutional symptoms e.g. tiredness and malaise. Stiffness of the joints is very prominent, particularly in the mornings[2].

Any joint may be involved but the most common are the wrist joints, metacarpophalangeal joints, proximal interphalangeal joints, metatarsophalangeal joints, and the knees. The other joints are less frequently involved and the distal interphalangeal joints hardly ever.

The spindle-shaped swelling of the fingers caused by synovitis of the proximal interphalangeal joints remains one of the best-known signs of the disease. Destruction of the metacarpo-phalangeal joints leads to ulnar deviation of the fingers. Other finger deformities seen but not exclusive to rheumatoid arthritis, is the Swan neck deformity, and the Boutonniere deformity of the proximal interphalangeal joints (Fig 1). The flexor and extensor tendons of the hand are also liable to injury and potential rupture by rheumatoid involvement. Tendons rubbing over the roughened edges of damaged bone, and in particular the carpal bones, are at particular risk.

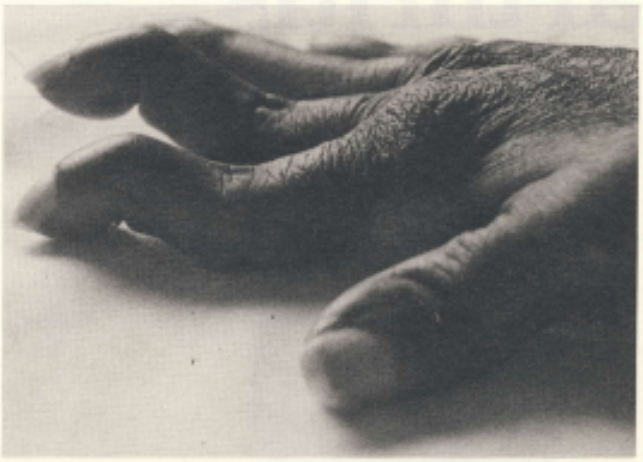

Fig 1 (a): Swan neck deformity

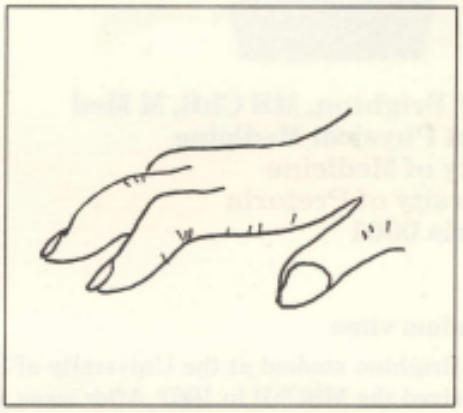

Fig 1 (b): Boutonniere deformity

Foot involvement is common with destruction of the metatarsophalangeal joints, leading to dorsal dislocation of the toes. This exposes the metatarsal heads which become very painful on walking. Pronation of the ankle caused by both mechanical damage to the joint as well as attrition and stretching of the supporting ligaments, e.g. tibialis anterior, is a common cause of painful feet.

Knee involvement is common and as the knee is a weight-bearing joint, severe functional problems may arise. Hip involvement also has severe functional implications.

Rheumatoid involvement of the cervical spine is usually only seen in those patients with severe disease or those that have had prolonged steroid therapy. The most important lesion is softening or rupture of the odontoid ligament. This allows the atlas to prolapse forward on the axis. This may then compromise the cervical spinal cord and can lead to a spastic paralysis or even death from respiratory arrest. To diagnose this a lateral radiograph with the neck in flexion should be taken.

Non-articular manifestations

1. **Nodules**
Subcutaneous nodules develop in 20% of patients. The nodules are hard and vary in size from a few millimetres to 30 mm, in size. They are most commonly found over pressure points e.g. the elbows, but may be encountered anywhere including tendons, sclera, lungs, or the myocardium.

2. **Skin**
Palmar erythema, skin atrophy and vasculitis may all be seen in rheumatoid arthritis.

3. **The eye**
The most common lesion seen is the Sicca syndrome. This is due to reduced tear formation from inflammatory changes to the lacrymal glands resulting in dry eyes, and in more advanced cases dry mouth and vagina. Inflammatory changes may also involve the sclera which on rare occasions may lead to perforation of the eye ball.

4. **The lung**
Up to 20% of patients develop a pleural effusion which has a high protein and low sugar content. Fibrosing alveolitis may occur in patients with long-standing disease. Rheumatoid nodules may occur in the lung and must be differentiated from other causes of a nodule in the lung. Rheumatoid patients who have worked underground in the mining industry may develop massive lung nodules known as the Caplan syndrome.

5. **Hematological**
A normochromic, normocytic anaemia is frequently seen, with the degree of anaemia tending to parallel the degree of activity of the disease. A microcytic anaemia may also be seen and then the possibility of blood loss, and in particular from gastric erosions or ulceration, must be considered.

6. **The kidney**
With the large volume of anti-inflammatory and analgesic drugs consumed by rheumatoid patients, kidney damage may occur but is nevertheless seldom seen at clinically significant levels.

Laboratory investigations[3]

1. **Erythrocyte sedimentation rate.**
During active disease the sedimentation rate is accelerated and may be used as a rough guide to disease activity.

2. **C-reactive protein**
This is an acute phase protein, and like the sedimentation rate, roughly parallels the disease activity.

3. **Rheumatoid factor**
This is never diagnostic of rheumatoid arthritis but if present is of prognostic importance. Two tests are available: the latex fixation test which is a screening test, and the sheep cell agglutination test, which is more accurate. Patients who are positive for this test have a worse prognosis than those who remain negative.

4. **Synovial fluid analysis**
Aspiration of a joint can give valuable information. The fluid from a rheumatoid joint has a low viscosity as opposed to a normal joint, and if a drop of the fluid is added to a tube of dilute acetic acid, a weak mucin clot forms in contrast to normal joint fluid which will form a solid clot in acetic acid.

Radiology

- The earliest radiological signs in rheumatoid arthritis is osteoporosis seen on either side of the joint, called juxta-articular osteoporosis.
- The second change is loss of articular cartilage seen on X ray as loss of joint space.
- The development of bony erosions at the margin of the joint.
- Finally, the deformities and subluxations resulting from the joint damage.

Treatment[4]

The following may be considered:

1. Medical
2. Physical
3. Surgical

1. MEDICAL TREATMENT[5]

Medical treatment of rheumatoid arthritis consists in the initial use of various anti-inflammatory drugs. These may be supplemented under certain conditions with the so-called second line, or slow-acting drugs. Occasionally steroids may have to be used and on rare occasions other drugs such as immuno-suppressives would also have to be considered.

a) **Anti-inflammatory therapy**

(i) Salicylates
The salicylates were for many years considered the basic therapy for rheumatoid arthritis. In adequate dosage they are very effective. Unfortunately the side effects of high-dosage salicylate have made them unacceptable to many patients. Their advantages are cheapness combined with effectivity, but at the expense of considerable gastric intolerance with a high incidence of gastric ulceration. Tinnitus is also a significant problem. A total daily dosage of 4 to 5 gm is required to obtain adequate anti-inflammatory effect.

(ii) The non-steroidal anti-inflammatory drugs
This group, which consists of a large number of drugs, has to a large degree replaced the use of aspirin. They are classified into numerous groups according to chemical structure, but this is of little or no help in deciding on which drug to use. It is far better for the practitioner to get to know about 6

anti-inflammatories, and know them well rather than to always try another one out. Patients tend to have a marked individual response to anti-inflammatories, and one patient may do well on one particular drug while another one will not respond at all. If no response has been obtained within 2 weeks there is little reason to continue with that particular drug.

b) **Second-line or slow-acting drugs**

The important members of this group are the gold salts, D-penicillamine, chloroquine, and salazopyrine.

(i) Gold salts

The two gold preparations available in South Africa are the injectable sodium thiomalate and the oral preparation auranofin. I have personally found that the injectable salt is probably superior to the oral form in severe rheumatoid disease, while the oral form can be very effective in milder cases with less side effects. The important decision is when to use gold, or for that matter any of the second-line drugs. Gold should be considered early in the course of the disease, before extensive bone destruction has taken place. Further, it should only be used in active disease, and where the diagnosis is certain, for example where the patient meets the American Rheumatism and Arthritis Association criteria for classical or definite rheumatoid arthritis. Very early erosions, a high sedimentation rate, positive rheumatoid factor or extra articular involvement would all mitigate for the use of the drug.

Gold salts should be considered early in the course of the disease, before extensive bone destruction has taken place

Numerous side effects of gold have been documented; the most important are bone marrow depression, kidney damage, and skin rash. At each visit it is mandatory to do a full blood-count, urine analysis and an examination of the skin and mucous membranes for a rash or painless ulceration. At the first signs of a leucopaenia or more than a trace of protein in the urine gold treatment should be stopped. Mouth ulcers or a persistent rash should be viewed with suspicion.

The injectible gold salt sodium thiomalate available in South Africa is first given as a test dose of 5 mg. If no untoward allergic reactions occur, a further dose of 10 mg is given and a week later 20 mg. Thereafter 50 mg a week is given by deep intramuscular injection until a total dose of 500 mg has been attained. Thereafer the injections are given at 2-weekly intervals until a total of 750 mg is reached. The injections are then spaced at 3-weekly intervals. After a total dose of 1000 mg monthly maintenance injections may be continued. Seventy percent (70%) of patients will clinically respond to this therapy, but thirty percent (30%) will have side effects necessitating the withdrawal of the drug.

Oral gold is given in dosages of 3 mg three times a day. Side effects, while milder than the injectable gold salts, still require careful monitoring with monthly blood-counts and urine analysis.

Clinical response to any of the gold preparations is slow, taking up to 6 weeks for any response and often considerably longer.

Patients tend to have a marked individual response to anti-inflammatory drugs

(ii) D-penicillamine

D-penicillamine has proved to be a very effective drug, about as effective as gold injections. It is given orally but is expensive. Side effects are about the same as gold except that kidney involvement is much more common. Monthly blood counts and urine analysis is again mandatory. Dosage is at first 150 mg daily. This may be increased by 150 mg increments at 2 monthly intervals up to a maximum dosage of 750 mg. Clinical response may take several months.

(iii) Chloroquine

The antimalarial chloroquine has proved effective in many cases of rheumatoid arthritis. It is not quite as effective as injectible gold but is of considerable value in milder cases and in the elderly rheumatoid patient. Side effects include nausea, but the most feared is retinal involvement. At currently recommended dosages this is unlikely, but 6-monthly examinations by an opthalmologist are necessary. Dosage is 200 mg of chloroquine sulphate or 250 mg of chloroquine phosphate daily.

(iv) Salazopyrine

This drug has recently been introduced in the therapy of rheumatoid arthritis and has proved to be effective. The dosage is 500 mg twice daily, being slowly increased to 500 mg four times a day. The drug is a sulphonamide and all the side effects of this group must be considered.

c) **Steroids**

Systemic steroids have proved to be very effective but the long-term side effects make for caution in the decision to introduce them. Once they have been used it is very difficult to stop the treatment. Steroids should only be considered when all other conventional therapy has failed, or when serious

extra-articular disease is present. In some cases where the second-line drugs have brought partial relief, but the quality of life is still very poor, steroids may be considered. Dosage must be kept as low as possible. The aim should be to reduce symptoms to a tolerable level; trying to totally abolish pain will probably require an unacceptably high dosage.

d) **Immuno-suppression**

On rare occasions the patient fails to respond to any of the above treatments and in these cases immuno-suppression may be considered.

2. PHYSICAL AND OTHER TREATMENTS

1. **Patient advice and information**

It is of the utmost importance that the patient be thoroughly informed as to the nature of his disease, as well as to the probable long-term outcome. It is difficult to forecast the ultimate outcome of the patient's disease but some rough guidelines do exist. If the patient has not developed obvious joint erosions within one year of the onset of the disease, the sedimentation rate has remained no higher than 25 mm per hour and the patient remains seronegative for rheumatoid factor, an optimistic approach can be taken with reasonable certainty. Early onset of joint erosions, very high sedimentation rate, rheumatoid factor positive and the presence of extra-articular disease such as subcutaneous nodules, carries a much more ominous prognosis.

In the presence of poor prognostic signs it remains the duty of the physician in charge of the case to intervene and advise the patient regarding long-term implications of the disease on employment. It is the aim of therapy to maintain the patient's independence at home and at work. The work situation must be carefully considered. Work of a physical nature would obviously not be suitable to a person with joint damage. Where a poor outcome may reasonably be expected, the patient should be tactfully encouraged to try and improve his qualifications, so that more sedentary work may be undertaken. Attempts to improve qualifications or change of work, should be undertaken at an early stage and not be delayed until faced with loss of present employment.

Salicylates are cheap and effective, but at the expense of severe gastric intolerance with a high incidence of gastric ulceration

2. **Rest and exercise**

An acute flare of rheumatoid arthritis is best treated with a short period of bed rest. Ideally hydro-therapy in a heated pool is then introduced. Even a home pool may be used in the warm summer months. If pool therapy is not available, gentle daily exercises taking the joints through their full range of movement should be prescribed.

The ambulant patient should be carefully instructed on the necessity for both daily exercise and rest periods. Working patients should be encouraged to use their lunch break to rest as much as possible. Most employers have a staff rest room, and patients should make every endeavour to lie down for at least half an hour. Their afternoon productivity will increase as a result of this rest.

Many aids and splints are available and the judicious use of these can be of great benefit to the patient. An occupational therapist can advise on which aid would best serve the patient, but if at all possible the patient should visit a centre where the full range of aids are on display. The Johannesburg centre is well worth a visit. (Independent Living Centre, Happiness House, Loveday Street, Braamfontein.)

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Please address all correspondence to:

The Editor
SA Family Practice
PO Box 40447
ARCADIA
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