The management of rheumatoid arthritis has been transformed in recent years. No longer is this disease necessarily chronic and progressive, resulting in joint deformity, functional impairment, and severe disability—and this is because we are using traditional treatments more aggressively and have access to new and often very effective ones. We have a financial price to pay for this progress, but key to successful management are careful assessment of disease activity, use of new imaging techniques and immunological tests, and early use of powerful drugs. If there is one introductory message it is treat early, and treat hard, which means early referral for specialist management.

Rheumatoid arthritis does not respect age boundaries; it occurs in all age groups, from childhood to ripe old-age, although its peak prevalence is at 35–65 years. For years we have tried to identify the cause, but although we now understand far more about the immunological cascade that results in joint inflammation, we are still unclear about the triggers. Something sets off the B-lymphocytes and T-lymphocytes, which between them produce markers of trouble (such as autoantibodies) and inflammatory chemicals (cytokines, including tumour necrosis factor and interleukins).

As in other inflammatory joint diseases, the triggers may be bacterial or viral. We know, for example: that food-poisoning organisms such as Campylobacter spp and Salmonella spp can provoke a reactive arthritis; that Streptococcus spp can result in vasculitis with arthritis (Henoch-Schönlein purpura) or rheumatic fever; and that viruses such as Coxsackie, can also provoke an arthritis. There is some evidence for mycoplasma as a trigger for polymyalgia. We have failed, however, to identify any definitive trigger for rheumatoid arthritis; perhaps it is a reaction to a common gene sequence that occurs in several organisms, but in particular the explosive onset of this disease that one sees in older people keeps the issue of an infective trigger alive.

Features of disease

The characteristics of rheumatoid arthritis hardly need repeating; joint swelling and tenderness, a symmetrical distribution; puffiness of the hands and wrists (figure 1) with inability to make a fist, girdle pain, and morning stiffness. Fatigue and a flu-like feeling are usual; patients feel awful. In elderly patients who already have limited mobility, this added burden can tip them into complete dependence; they may be unable to get out of bed, unable to manage stairs, or even get to the toilet. Early
With a positive test but no clinical evidence of arthritis. The cyclic citrullinated peptide antibody test is useful in these situations. It is highly specific and the antibody can appear even before the arthritis does, so a positive test confirms rheumatoid arthritis. However, we also see patients with a negative rheumatoid factor test who have inflammatory joint disease. If we measured any of the other rheumatoid factors (i.e., IgG, IgA) we might find evidence of disease, but these tests remain in the realms of research. The importance of these results is for prognosis and treatment response, and in fact, the management of inflammatory joint disease, whether seropositive or not, is nowadays universally aggressive.

In the same way as we have sought a trigger for rheumatoid arthritis, we have tried to identify which patients will do badly. As a general rule: seropositive disease is worse in that joint damage is more likely; arthritis with insidious onset is worse than explosive onset; and older patients seem to do better, although this may be because we do not see them for such a long period. We also know that rheumatoid arthritis predisposes patients to heart disease, probably associated with the high levels of C-reactive protein, and now we have ample evidence that the life-shortening effect of rheumatoid arthritis is as strong as diabetes. Yet we do not have a Quality and Outcomes Framework for rheumatoid arthritis.

**Box 1: Diagnosis**

<table>
<thead>
<tr>
<th>Tests for disease</th>
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<tbody>
<tr>
<td>Full blood count</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>C-reactive protein</td>
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<tr>
<td>Rheumatoid factor</td>
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<tr>
<td>Autoantibodies</td>
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<tr>
<td>Anti-CCP antibody (if available)</td>
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<table>
<thead>
<tr>
<th>Tests for damage</th>
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<tbody>
<tr>
<td>Small joint ultrasound</td>
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<tr>
<td>MRI</td>
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**Starting treatment**

Recent scares about non-steroidal anti-inflammatory drugs (NSAIDs) and methotrexate have caused much concern among doctors and patients alike, and there is certainly some evidence of consumer resistance to these treatments. Steroids have always been problematic. It is thus important, when discussing the risks of treatment, to also discuss the risks of no treatment.

I find that discussing “what I would do if I developed rheumatoid arthritis” is reassuring for patients. I also use an analogy that this disease is a disease of the white blood cells similar in some ways to lymphoma, and one would not delay treating that disease.

For an older person I would prescribe steroids as a quick fix. This treatment can be sold as a test; if it works, the problem is definitely inflammatory—even more so if, after a test withdrawal of 2 weeks, all the symptoms return. I use 5–15 mg of enteric-coated prednisolone daily. This treatment covers the time in which test results are awaited.

If the clinical diagnosis is clear, then I prescribe disease-modifying antirheumatic drugs straight away, with methotrexate as first choice (box 2). Patients are given a full explanation of benefits and risks, with an information leaflet and the number of our telephone helpline. They are also directed to the department’s website. I am particularly keen to begin treatment swiftly in high-risk patients. In those of potentially lower risk (such as, perhaps, the seronegative group) one might compromise with an ultrasound or MRI scan.
and force the issue of treatment if damage is apparent. Waiting for X-ray evidence of erosions is, to my mind, no longer acceptable; the aim is prevention of joint damage, not arresting it once it has started.

However the appearances of rheumatoid arthritis on MRI have not as yet been codified, and one may see suspicious changes that do not fit with the clinical pattern. We must also bear in mind the problems of interpreting older trials that included both new and longstanding patients; the rates of progression or erosions are different in the two groups, but huge numbers of trials have failed to separate these disparate groups in analysis.

Recent research suggests that starting with a combination regimen may be more effective than starting with a single disease modifying drug. Thus, the COBRA regimen uses methotrexate, sulfasalazine, and high-dose tapered steroids. We are still unsure whether such an intensive regimen works better than escalated methotrexate; in COBRA the dose of methotrexate was 7.5 mg weekly, while many rheumatologists nowadays will, like me, start at 10 mg and escalate to 20 mg after 4–8 weeks if no response is seen. We await further trials on the relative efficacy of more intense step-up approaches (such as adding hydroxychloroquine or sulfasalazine), but at present that is my preferred strategy. It is often possible to tail-off steroids altogether—the risk of osteoporosis, on top of that associated with age, must be borne in mind, but the risk may be offset by the benefits of restored mobility and exercise tolerance. Methotrexate is cheap—at around £75 per patient per year—and adding sulfasalazine or hydroxychloroquine does not increase the cost much.

### Box 2: Treatments

#### Disease-modifying antirheumatic drugs
- Methotrexate*
- Sulfasalazine*
- Hydroxychloroquine*
- Leflunomide
- Azathioprine†
- Penicillamine†
- Ciclosporin†

#### Steroids
Orally, intramuscularly, or by intra-articular injection

#### Biologicals
- **TNF-α blockers**
  - Infliximab intravenous administration every 2 months
  - Etanercept subcutaneous self-injection once or twice a week
  - Adalimumab (self-injection weekly/fortnightly)
- **B-cell depletion**
  - Rituximab relatively ineffective in seronegative disease
- **T-cell depletion**
  - Abatacept licensed but not approved by NICE
- **IL-6 blockade**
  - Tocilizumab EU approval decision awaited§

*These are used as triple therapy with or without steroids
†Used less frequently
§This product was given a positive opinion by the EMEA in November 2008*

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**Figure 3:** Cervical subluxation in rheumatoid arthritis

A) This patient’s head is fixed in this position, which led to difficulties eating
B) This patient has longstanding rheumatoid arthritis and chronic obstructive pulmonary disease. Surgery in this case would be highly risky (note the step at C4/5). The patient was advised to wear a supportive collar when travelling.
by the 28-joint Disease Activity Score and must have failed two standard disease modifying drugs, one of which must be methotrexate. Rituximab is cheaper than the others at around £6000–7000 yearly, as opposed to £9000–10,000, but it is a second-line agent and doesn’t seem to work well in seronegative patients. Another compound, abatacept, a T-cell blocker, is available, but is not approved by NICE. A further option is tocilizumab, which blocks interleukin-6, and is under regulatory review by the EMEA.

Some evidence supports the notion that if we relaxed the entry criteria, and thus used these biological agents earlier, we might get better results, but further large-scale research is required. Certainly, the effects of biologicals can be absolutely magical, but we need to monitor for long-term side-effects, which is undertaken by the British Society for Rheumatology’s Biologics Register. We now have 10-year data, at best, for etanercept.

**Additional therapies**

Treatment with biologicals has no age barriers, although risks exist, such as reactivation of latent tuberculosis, and increased overall risk of serious infection. We recommend influenza vaccination for all patients with rheumatoid arthritis, that some patients should probably also have the polyvalent pneumococcal vaccine (Pneumovax), and that patients on immunocompromising drugs should not be given live vaccines.

We should not be afraid of steroids. I recall one patient referred from another department, under whose care a succession of disease modifying drugs had been tried without much benefit. “The only time I feel really well”, she said, “is when they change my drugs and put me on steroids to cover the changeover”. I added a small dose of prednisolone daily and she was fine for years. Likewise, intra-articular injections of steroids may produce substantial relief (and sometimes a spill-over systemic effect) and they reduce joint damage by removing local inflammation. With knees, these injections may, by preventing large effusions, reduce instability and secondary mechanical damage.

Intramuscular steroids may be effective occasionally, but if repeated the effect becomes lessened and shorter, and trying to control flare-ups with large and then tapering doses of oral steroids significantly increases the risk of side-effects. In older patients, skin thinning can be seriously problematic and lead to long-term leg ulcers (figure 2).

Be wary of flares. A sudden reactivation of a joint in a patient with dormant disease might be due to something else; infection, perhaps, or an insufficiency fracture (figure 3).

It is interesting that NSAIDs appear so far down my list of therapies. The risks of these drugs are often overplayed; it is not reasonable to frighten a patient whose arthritis is well-controlled by NSAIDs with the spectre of serious risk of sudden cardiac death, for example. However, the older the patient, the higher the risk of gastrointestinal bleeding. Ordinary analgesics such as paracetamol, combinations (co-codamol, co-dydramol), or tramadol are safer and, in conjunction with disease modifying drugs, may be all that is necessary. Alongside the use of powerful drugs is the important matter of supporting patients. Physiotherapeutic interventions, including hydrotherapy, may be very helpful. Hand specialists, who are often occupational therapists, can assist with...
teaching strengthening exercises and providing splints. Podiatry and appliance services may mitigate the risks of foot ulcers and ankle dysfunction (figures 4 and 5). A specialist nurse can provide adjunctive input with psychological support, management of flare-ups, and monitoring. Lastly, local patients’ groups such as those sponsored by the National Rheumatoid Arthritis Society12 play a vital part in education and self-help. These services may be particularly helpful for older patients whose own support networks may be fragile.

Surgery can be a very important part of management—joint replacement, tendon sheath surgery, excision arthroplasty (eg, in feet) may transform life. No patient is too young or old for surgery, but enthusiasm must be tempered in the face of concomitant disease. Diabetes, hypertension and respiratory problems are all more common in the older person and increase surgical risk. Elbow surgery remains problematic, but in recent years the success of knee surgery has overtaken that of hips, and shoulder replacement is now an effective treatment for severe damage. Patients with neck pain should always have lateral X-rays of the neck in flexion and extension; subluxation may compromise the spinal cord and result in paraplegia. If nodules are problematic they may be removed, but can recur and care needs to be taken in areas where skin healing may be poor (figure 6).

The continuing support of experts, whatever their discipline, is essential and is, for me, a powerful disincentive to discharge patients from rheumatology clinics; one can cut down follow-up by increasing the time intervals between appointments, but anything less may be seen as abandonment. Of course a stable patient in remission can be released—as long as any necessary monitoring arrangements such as regular blood tests for those on methotrexate are firmly in place, and they are offered the opportunity to make immediate contact in the event of a problem. Can we predict which patients will need to see us urgently? No, not entirely, although in older patients an explosive onset may rapidly remit, and indeed one may wonder, once the patient is settled on methotrexate, whether the remission is despite or because of the drug. But again, if the patient was me, I would always treat early and hard. In my experience the risks of this strategy considerably outweigh the risks of undertreating too late.

I have no conflict of interest.

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