Principles of Rheumatoid Arthritis Control

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ABSTRACT. One percent of the UK population suffers from rheumatoid arthritis (RA), with a female to male ratio of 3:1. The disease has a major influence on employment and disability rates. About 15% are classified as having serious illness, which prognostically is equivalent to 3-vessel coronary artery disease. Overall life expectancy for those with RA is reduced on average by 5 years. Financial costs are enormous. Per-patient, each year, direct and indirect costs total about £7000. Costs escalate with disease severity. In a specialist rheumatology clinic, about 12% of new referrals have RA, and these patients account for more than 40% of the followup workload. The approach to management is changing, with emphasis on earlier, more aggressive intervention. This is acknowledged to improve outcome. For the severe disease, management has been revolutionized by the introduction of biologic agents. RA is managed by a multidisciplinary team, and there are active patient support groups. Advances in knowledge about genetic and immunological mechanisms of disease hold promise for further progress. Never was there a greater need for a successful alliance to deliver effective, high quality services involving government, professionals, patients, and their advocates. (J Rheumatol 2003;30 Suppl 67:10–13)

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DISEASE MODIFYING DRUGS
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MORTALITY
MORBIDITY

There is no universally accepted definition for rheumatoid arthritis (RA). The following definition, now 45 years old, remains all-encompassing and clinically relevant: a chronic systemic inflammatory disorder of unknown etiology characterized by the manner in which it involves the joints[1].

It has been suggested that RA is a relatively new disease. Possibly it was described by Thomas Sydenham in 1676, but it was a French medical student, Landré-Beauvais, who in 1800 provided the first undisputed and accepted description of RA. It was first called "rheumatoid" by Garrod in 1859.

Perhaps it is a case of familiarity breeding contempt, but the fact frequently overlooked is that RA is a very serious disease. This is a message that has not been adequately acknowledged, bearing in mind the heavy burden RA causes in terms of both human suffering and financial consequences to health services. In the UK, RA affects about 1% of the population, with a female to male predominance of 3:1. It is the commonest inflammatory polyarthropathy seen, with 0.5 million people affected in England and Wales alone. It can be a multisystem disease in its manifestations, including the frequently overlooked psychological consequences. These result in depression, low self-esteem, and an undermining of morale due to pain and occupational, social, and domestic limitations.

Fifteen percent of those with RA are classified as having serious disease, with progressive, aggressive, and unrelenting disease failing to respond adequately to existing therapies. At 2 years, 25 to 33% are unable to work fulltime, and 40% discontinue employment within 5 years[2]. Within 5 years, major home adaptations are required in about 10%; after 20 years of RA, 25% have had joint replacements[3]. The prognosis for severe cases is equivalent to triple-vessel coronary heart disease or Stage 4 Hodgkin's disease, while life expectancy once the disease is established is reduced on average by 5 years[4].

The financial consequences of RA are enormous[5]. The direct costs per patient per annum in the UK are £3250; of this, 30 to 65% is from hospitalization and 5 to 30% from medication. The indirect costs, which include the costs of care and loss of employment, amount to £3420. Costs rise inexorably as the disease progresses, with 20% of the severest cases incurring 80%[6]. All the above result in a total cost to the UK health service budget of £3.8 to £4.5 billion per year. Globally, the economic consequences are incalculable.

In a typical rheumatology clinic, 12% of new referrals will have RA, whereas followup cases account for 42% of the workload[7]. This ratio of new to followup patients of 1:3.5 is open to criticism from those unfamiliar with the nature and natural history of RA. When rheumatologists take on a patient with RA, they are at the beginning of a long professional relationship unlike that for most other medical specialties.

Mindful of the venue of this international meeting and its aims, it should be noted that Buddha taught that there are 5 things no one can accomplish[8]: (1) to cease growing old, when growing old; (2) to cease being sick; (3) to cease

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dying; (4) to deny extinction when there is extinction; and (5) to deny exhaustion.

Many of these wise teachings stand today, but there is increasing evidence that item 2 no longer applies for RA, in view of increasingly effective treatments available.

PRINCIPLES OF DISEASE CONTROL RELEVANT TO RA

There is a simplistic view that if the cause of RA can be discovered, then a cure will naturally follow. It is true that we know more about RA than about many other musculoskeletal disorders, but we know little about its cause and cure. Nonetheless, this is not a prerequisite for effective disease control. In fact it is possible to effectively manage many diseases whose causes are unknown — diabetes and hypertension are examples that parallel RA. On the other hand, in some diseases we know the causes, but compared to RA, management may be far less satisfactory. Two extreme examples are AIDS and variant Creutzfeldt-Jakob disease.

For RA, effective management rests on 3 principles:

1. to reach an accurate diagnosis
2. to intervene early, since this improves outcome
3. to adopt a multidisciplinary approach

Each of these principles will now be considered independently.

An Accurate Diagnosis

The emphasis must be on *early* diagnosis. This can be difficult, since accepted criteria on which the diagnosis of RA depends must be met[9]; however, these are not always unequivocally in evidence in the early stages, which can undermine the ability to adopt a management plan. Nonetheless, a doctor experienced and skilled in the management of rheumatic diseases can reach an early diagnosis with a high degree of certainty in most patients. The attainment of an accurate diagnosis in an individual, therefore, relies on access to specialist rheumatology services. Services further rely on appropriate health care systems to be in place.

Early Intervention

Increasingly there is a trend for early introduction of disease modifying agents, which have been demonstrated to improve outcome[10]. The aim is to progress through single and combination therapies[11], moving to biologic agents when necessary; not neglecting the role of surgery, prophylactic to protect joints and to correct deformities, as well as replacing joints beyond the reach of conservative treatment. Conventional wisdom was of a treatment pyramid with simple analgesics on the bottom, moving on and up through nonsteroidal antiinflammatory drugs, physical measures, disease modifying agents, corticosteroids, immunosuppressants, and surgery. The ranking of many of these interventions now needs to be changed to a far more aggressive and early interventionist approach, with disease modifying agents approaching the first line of treatment. The overriding aim is to prevent or retard clinical progression and radiological erosive disease.

Multidisciplinary Approach

Patients should have early access to the multidisciplinary team, including for the emotional and psychological aspects of disease. While the rheumatologist might lead such a team, he or she is not necessarily always the most important member at a particular time in the natural history. Sadly, the doctor/patient relationship has been undermined as a result of errors of judgment and misunderstandings on both sides, as well as being subject to external, harmful influences. Rheumatology practice relies on mutual respect, trust, and confidence between patient and doctor. Not only is it essential that the individual with RA be involved in all aspects of decision-making with regard to treatment, but confidence in therapy and in the rheumatologist helps to improve compliance and efficacy. Patients might find considerable comfort in being introduced to UK support groups such as Arthritis Care and the National Rheumatoid Arthritis Society (NRAS). Above all it behoves us to attend to all aspects of the patient's needs, to adopt a holistic approach, and to remember that medicine remains an art based on scientific principles. Scientific enthusiasm laced with compassion, common sense, and the ability to listen and communicate makes the best rheumatologists.

Opportunities

There are increasing opportunities for control of RA. Research is key to improvement; we already enjoy far greater understanding of disease mechanisms in RA. Advances in genetics and immunology have helped to shed light on the pathogenesis of RA and hold great promise, particularly with regard to treatments. It is no longer in the realm of science fiction to postulate gene therapies as realistic prospects. To date, the unravelling of the immunological aspects has translated into the production of biologic agents. Moreover, we have a range of other better and safer therapies with which to monitor beneficial and adverse effects more closely. A new generation of nonsteroidal antiinflammatory drugs, the cyclooxygenase-2 inhibitors, reduces the risk of gastrointestinal adverse effects. Increasingly there is a role for combination disease modifying agents and evidence to support their efficacy[11].

Beyond the test tube, bioengineering holds out great hope for improvement in joint replacement; for example, surface hip replacements are increasingly recognized as more appropriate for a select group, particularly younger patients.

Turning back to the teachings of Buddha, it is clear that he already recognized and documented the importance of innovative thinking combined with careful observation and

objective, rigorous analysis of results. These are listed under Purification of the Mind[12]:

- Develop right ideas
- Base ideas on careful observation
- Understand causes and effects and their significance
- Neglecting the significance of causes and effects results in suffering.

The Bone and Joint Decade provides a further opportunity for disease control in RA by facilitating international cooperation and exchange. Collection of disease-specific data on a cohort of patients receiving treatment could provide greater insight into its effectiveness and wider appreciation of adverse effects. Such an opportunity exists in the UK through the British Society for Rheumatology registry for patients with RA receiving anti-tumor necrosis factor-α therapy. In the UK, individual patient consent is a prerequisite to entering such details. A summary of the data to be collected is given in Table 1.

Shortcomings

The notion that increased access to information for those with RA must always be beneficial needs to be challenged. A surfeit of information can result in misinformation: Most rheumatologists can recall patients who have been terrified or misled by their inability to interpret and place in perspective the information with which they are bombarded, particularly through the Internet. This further illustrates the importance of the close professional relationship between the rheumatology team and the person with RA.

A major shortcoming in RA patient care is the inadequate provision, certainly in the UK, of specialist rheumatology services. While there is no lack of enthusiasm among doctors in specialist training to pursue a career in rheumatology, there is woefully inadequate undergraduate training in rheumatology, even into the postgraduate level. For those wishing to pursue a specialist career, it is necessary to obtain the diploma of membership of one of the Royal Colleges of Physicians (MRCP) in the UK (London, Glasgow, or Edinburgh). As part of the final clinical examination, which tests examination and diagnostic skills, it is sobering to note that only 5 minutes are devoted officially to assessing a candidate's abilities in rheumatology. This compares unfavorably with, for example, cardiovascular and respiratory disorders, on which a candidate is tested for twice as long.

Such reflects the approach of successive governments, which have tended to focus on the more emotive medical conditions. Rheumatic diseases have a depressingly low profile and are not considered "sexy." Rheumatological services are patchy and unevenly distributed throughout the UK. There is the inevitable economic competition to provide for those with RA, many of whom are now living longer; their disease is therefore but one of myriad disorders from which our ageing population suffers.

The cost-effectiveness of interventions has been questioned, which leads to inadequate resources and rationing of care. Such demands for cost-effectiveness provide other, perhaps unreasonable, obstacles to increasing the range of treatments and justifying bids to increase resources. Should there be 2 or more treatments of equal worth, then the cheaper option will by its nature be the more cost-effective; not to use this by choice would be irresponsible. As clinicians, however, we need to make a stronger case for clinical effectiveness. Health economics remains an imprecise science, and we should not forget that "medicine is more than an exercise in health economics: it is part of the fabric of social life, and it enshrines the age-old obligation to heal the sick."

Table 1. BSR registry for RA patients receiving anti-TNF-α therapy.

Baseline	Quarterly
Age	Record of episodes of intercurrent illness
Gender	
Postal code (for social deprivation index)	Surgery
Comorbidity	Infection
Ischemic heart disease	Malignancy
COAD	Hospitalization
Asthma	Drug toxicity
Hypertension	Outcome data
Stroke	
Diabetes	
Medication	Quarterly returns would continue for 3 years after treatment starts, regardless of whether or not it is continued. Thereafter returns will be made on an annual basis
Smoking status	
Alcohol intake	
Baseline outcome data	
HAQ score	
SF12	
DAS	

COAD: chronic obstructive airway disease. SF12: Medical Outcome Study Short Form-12. DAS: Disease Activity Score.

To enhance and make more uniform the control of RA, attempts are being made in the UK to devise measurable and minimum clinical standards that have the full support of the Royal Colleges, General Medical Council, and central government. Such standards might include:

1. Minimum time of access to specialist services following diagnosis of RA
2. Defined standards of monitoring for those taking disease modifying drugs
3. Availability of multidisciplinary services, laboratory and imaging diagnostic facilities, and in-patient beds
4. Optimum number of rheumatologists per defined population
5. Referral rates for major joint replacements.

SUMMARY

The principles of RA control rely to a considerable degree on a successful alliance among governments, other funding agencies such as insurance companies, on patients and their advocates, and on all professionals involved in the care of those with RA. The following (see also Table 2) summarizes those principles: the role of the World Health Organization cannot be overestimated: this is exemplified by the Bone and Joint Decade meeting and by our host the Japan Rheumatism Foundation. The exchange of international ideas and experiences at this and other such meetings will enable us to deliver better care for those with RA and bring about more effective management, particularly in patients with severe disease.

Table 2. Principles of a joint disease control program for rheumatoid arthritis—summary.

Early diagnosis Early intervention	} Access to specialist services
Reduce morbidity/mortality	
Improve quality of life	
Work closely with patient organizations	
Ensure minimum standard of general education	
Multidisciplinary approach	
Encourage multinational research	
Share ideas—Bone and Joint Decade	
Raise “profile” of RA among professions, public, politicians	
Acknowledge but do not accept current limitations and resources	
Encourage international co-operation and uniform standards through WHO	

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