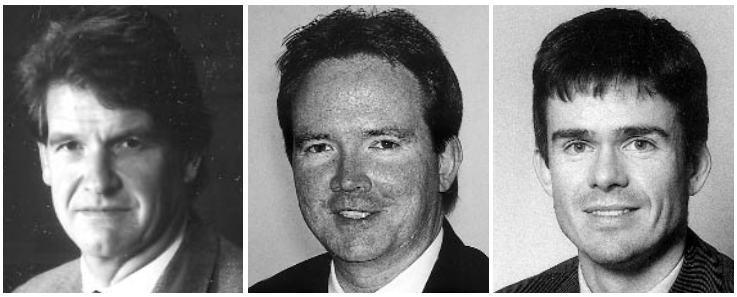
Editorial

Treatment of Rheumatoid Arthritis 2001



In the June and July issues of *The Journal* a number of senior rheumatologists, reviewing the last 15 years of therapy, have undertaken a systematic evaluation of the treatment outcomes of patients with rheumatoid arthritis (RA)[1]. The authors' aim was to develop a consensus report for the treatment of rheumatoid arthritis in the 21st century. This is a very broad remit — how have the authors fared?

For many years rheumatologists were more preoccupied with the toxicity of the available drugs rather than stressing the crippling consequences of the disease. Therefore it is appropriate that the authors begin with the consequences of RA, emphasizing how even mild disease may lead to irreversible damage and how it is easy to underestimate disease induced disability. This is a useful reminder.

The report moves to the concept of disease activity. It is here that the authors are less convincing in their paradigms. They correctly identify synovitis as the key clinical abnormality to be suppressed, but then include the surrogates of the American College of Rheumatology core set, which offsets the purer paradigm of synovitis. Perhaps a division between disease activity and damage would have been a better distinction to make? It is the concept of disease severity that is perhaps the weakest point of this otherwise excellent article. The authors define disease severity as "persistent high levels of disease activity" or "substantial damage" or "rapid acceleration." While the first definition cannot be disagreed with, the others are redundant, as damage is a consequence of persistent disease activity. Certainly, waiting for radiographic damage to be evident might be seen as reverting to old treatment approaches. The old equation of level of inflammation × time = damage probably adequately encompasses both this concept and the three definitions that are produced in this document. The modern aim should be to focus on frequent, accurate assessment of inflammation ensuring adequate suppression.

The goals stated in the report include the admirable aim of eliminating synovitis (which represents a cure), or the lesser one of controlling synovitis. The latter aim may appear straightforward, but in practice it is difficult to define. This difficulty arises because of (1) a lack of knowledge of what levels of inflammation are critical for damage progression, and (2) the inaccuracy of our current measurements of disease activity.

The monitoring of patients is discussed and the ACR improvement criteria are dealt with in this context. It is rightly pointed out that ACR criteria are difficult to manage in a busy routine practice. Additionally, while valuable in clinical trials, they represent percentage change and are therefore dependent on baseline levels of activity; in particular this applies to the swollen and tender joint counts. The latter themselves may even be inaccurate, as suggested by comparison with new imaging techniques such as magnetic resonance imaging and ultrasound[2]. Also, the criteria do not give any indication of absolute levels of inflammation that are important for the damage equation and for assessment of treatment "failure." For example, in severe disease, a reduction of 50% in the components of the ACR criteria may still leave the patient with unacceptably high levels of inflammation. Work from our group demonstrates that the criteria are insensitive to change in early RA, where disease may be mild or in evolution. An analysis of 222 patients from the Yorkshire Early Arthritis Register (YEAR) with early RA treated with sulfasalazine monotherapy demonstrated ACR 50 response in 30% of cases at 6 months. Of the 70% not satisfying ACR 50, up to half this group achieved a disease activity level generally accepted as a satisfactory outcome, 45% had a normal acute phase response, and 5% met ACR remission criteria[3]. If ACR 50 had been used as part of an algorithm to determine additional disease modifying antirheumatic drug (DMARD) therapy, a significant number of patients would have been unnecessarily exposed to additional drugs. Such results suggest a discrepancy between absolute levels of disease activity and the ACR improvement criteria. Simply demonstrating improvement may have

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no bearing on longterm outcome, whereas adequate suppression of disease activity will be reflected in longterm functional and radiographic measures[4,5]. This brings into question the utility of these criteria in evaluating patients with early RA; thus using the criteria as suggested by the authors may not achieve their stated goals.

The section on DMARD therapy is underpinned by the concept published 10 years ago that longterm pain relief was achieved better with DMARD than nonsteroidal antiinflammatory drugs (NSAID), with the cost benefit very much in favor of the former. However, since that time less toxic NSAID have been introduced, which might alter the cost benefit ratio, and it would be appropriate to at least discuss this issue.

In terms of choice of specific DMARD, the authors logically choose methotrexate, which is the overwhelming drug of choice in North America; although they perhaps could have discussed the head-to-head studies of methotrexate as first drug, which have failed to show any significant benefit over sulfasalazine[6,7]. Other studies that have failed to show the benefit of combination therapy, including methotrexate over monotherapy, also need to be discussed[8]. The major benefit of combination DMARD therapy in complex protocols needs to be distinguished from the confounding effects of corticosteroids[9]. The importance of individualizing therapy is correctly highlighted in the guidelines. It is also important to consider the health economic advantages of matching the benefits of adequate disease suppression with the risk of toxicity.

Overall, these guidelines provide an authoritative summary of the modern approach to RA management, with suppression of inflammation as the key concept. Clinical rheumatologists should now focus on accurate assessment of disease activity and consequent targeted treatment protocols.

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