Corticosteroids in rheumatoid arthritis

SIR, The article in the *Annals* by Byron and Kirwan¹ raises the exciting hypothesis that corticosteroids may have a role to play in modifying the disease process in rheumatoid arthritis (RA) and may prevent the development of erosions. Recent data on total bone mass measured by total body calcium (TBCa) in RA may give tentative support to such a hypothesis. Despite an initial lower total bone mass in steroid treated patients with RA, longitudinal assessment of TBCa failed to show any further loss of calcium over an 18 month period, while patients with RA receiving only non-steroidal anti-inflammatory drugs had a mean reduction of TBCa of 3.4% per annum, a figure not reduced in patients responding clinically to suppressive antirheumatic drugs.²

On the basis of this study and the work referenced by Byron and Kirwan a trial of low dose corticosteroids would seem justified. Potential adverse effects, however, must temper our enthusiasm. While my colleagues and I have found little evidence of osteoporosis as assessed by TBCa in patients with RA receiving 5 mg or less of prednisolone/day,³ this is not accepted by all.⁴ Substantial reductions in total bone mass have been shown in patients receiving 4–10 mg of prednisolone/day,^{5,6} a range encompassing the proposed daily dose (7.5 mg/day). Our data show that a mean daily dose of 7.9 mg/day is associated with a mean reduction of over 20% in TBCa.³

The data on total bone mass therefore suggest the need for some caution when considering the proposed multicentre trial. Bone mass assessment in vivo would be difficult in view of the lack of uniformity of methods available in each locality, though metacarpal indices⁷ could be obtained by using non-screen x ray film for routine hand radiographs. Perhaps of more use would be the inclusion in any proposed protocol of biochemical assessments of bone turnover, as both increased bone resorption and decreased bone formation may occur with corticosteroid therapy.⁸ The assessments for consideration might include urinary hydroxyproline/creatinine ratio and urinary calcium/creatinine ratio to assess bone resorption, and serum alkaline phosphatase and serum osteocalcin to assess bone formation. Such an approach to the assessment of bone turnover has recently been used effectively in the assessment of treatment of postmenopausal osteoporosis.⁹

A study of the possible beneficial effects of early corticosteroid therapy seems justified and the use of the multicentre format could allow quick answers. The opportunity to examine the effects of such low dose therapy on bone metabolism should not be missed.

Rheumatology Department,
City Hospital,
Urquhart Road,
Aberdeen AB1 2NJ.

DAVID M REID

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Acetylator phenotypes and rheumatoid arthritis

SIR, I read with great interest the paper in the *Annals* on the acetylator phenotypes and rheumatoid arthritis.¹ The authors found a preponderance of fast acetylators among patients with rheumatoid arthritis severe enough to require second line drugs, and in one of their studies slow acetylators appeared to have milder disease. We, too, found a predominance of slow acetylators among patients with rheumatoid arthritis, but fast acetylators among those who had the most severe disease.² An unfortunate misprint made it appear as if the fast acetylators had less severe disease, but I can take this opportunity to correct this misprint and to offer our previous paper as further suggestive evidence for this concept. The hypothesis remains that either acetylation or some related metabolic process may rapidly metabolise the drugs given for the treatment of rheumatoid arthritis, such as anti-inflammatory or disease modifying drugs, so that the disease has a chance to worsen under the same dosage regimen that works in slow acetylators. Such a conclusion would imply that the severity of rheumatoid arthritis and its response to treatment also are influenced by genetic factors.

Ciba-Geigy Corporation,
Summit,
New Jersey 07901,
USA

GEORGE E EHRlich

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