
**RHEUMATOID ARTHRITIS AND OSTEOPOROSIS**

In this edition there are two papers reporting accelerated bone loss and increased skeletal metabolism, together with two letters reporting fractures, occurring in rheumatoid arthritis (RA). In serial studies Reid *et al.* [1] have found increased rates of bone loss at around 3-4% per year, while Gevers *et al.* [2] have found elevated serum osteocalcin levels, a noncollagenous matrix protein which is produced by osteoblasts, reflecting increased bone formation and hence skeletal metabolism. While these studies appear to be in good agreement, previous reports have indicated that in RA skeletal metabolism may be normal [3], increased [4] or suppressed [5]; that serum calcium may be elevated [6] or low [7] and that osteocalcin may be normal [3] or low [8]. A histomorphometric study of rib biopsies showed that bone formation was reduced, but resorption rates were increased [9]. These results provide conflicting data. There is no adequate explanation for this although the time after onset of disease that is chosen for study may be relevant. For example, following immobilization rapid bone loss occurs but the skeleton eventually becomes quiescent [10].

Thus, while there is little doubt that patients with RA lose bone at an accelerated rate [1, 11], have lower bone mass [12-14] and are at increased risk of fracture [14-16], why the bone loss should occur at all is not well established. Periarticular osteoporosis, which may be due to a local increase in vascularity, paracrine factors, direct erosion by pannus and immobility of affected joints, is a characteristic feature of RA but the concept of a generalized alteration in skeletal metabolism specifically related to the disease is controversial. The problem is that there are so many potential factors which may contribute to bone loss—the patient's age, sex, menopausal status [17], duration of arthritis [18], coexistent disease, immobility, calcium malabsorption [19], drugs, nutrition, vitamin D status [14], etc. Osteoporosis is essentially a disease of elderly women, and women with RA who are postmenopausal will be at greatest risk. Steroid therapy can cause accelerated bone loss, although patients may have a variable skeletal response to this drug [18]. Of the other factors, immobility is likely to be the most important.

Rheumatoid arthritis is a multisystem disease and it is clearly possible that there is skeletal involvement. However, this issue cannot be resolved on the basis of the data that are currently available. With the newer techniques of dual photon absorptiometry and computerized tomography, it is possible to measure bone mineral at sites of clinical relevance such as the spine and femur [20]. It is now recognized that different rates of bone loss may occur at various sites throughout the skeleton, e.g. in postmenopausal osteoporosis there is predominantly spinal bone loss [21] while in anorexia nervosa there is greater bone loss in the femoral neck than in the spine, which has greater loss than the distal radius [22]. Sodium fluoride and low-dose parathyroid hormone, which have

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been evaluated in the treatment of osteoporosis, increase trabecular bone volume but apparently at the expense of cortical bone [23]. To obtain further information in RA, up-to-date methodology should be used to study patients with early disease at a time when they are fully mobile. Nevertheless, in a study of early disease (mean duration 14 months), reduced total body potassium—an index of skeletal muscle mass—was found [3] and it may not be possible to eliminate the influence of mobility completely. Ideally, patients should be premenopausal to avoid the accelerated bone loss which occurs following withdrawal of the protective effect of oestrogen on the skeleton.

Why accelerated bone loss should occur is of academic interest. It does occur and patients sustain fractures, which is of practical relevance. In a population who may already be elderly and infirm, housebound and taking an inadequate diet, a fracture may be a catastrophic event. Currently, it is not possible to increase bone mass predictably in patients with established osteoporosis and it would therefore appear likely that advances in therapy will need to be related to prophylaxis. This may partially come about by educating the population at large. Such an approach seems possible since alteration in diet appears to have been effective in reducing coronary artery disease in the United States [24]. In preventing osteoporosis it is clearly desirable that peak adult bone mass should be attained, and it is probable that regular exercise and an adequate calcium intake are important to the growing skeleton [25]. Adults should also ensure an adequate calcium intake, although the benefit here is much more controversial [26]. In patients with RA the importance of mobility should be emphasized and an adequate diet ensured. However, in considering the prevention of bone loss, most therapies will only have a trivial effect when compared with oestrogen [27, 28]. The possibility of routine oestrogen therapy in women with RA at the time of the menopause should be considered. Low-dose oestrogen therapy is safe and, even if there is a small incidence of side-effects, this is surely an acceptable price to pay when one considers that fracture of the femur is now the leading cause of accidental death amongst the elderly [29].

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REFERENCES
15. Taylor RT, Huskisson EC, Whitehouse GH, Dudley Hart F. Spontaneous fractures of

**EDITORIAL NOTICE**

In order to accommodate an increasing demand for publication in the British Journal of Rheumatology, the Editorial Board has decided to increase the space available to contributors. As you can see in the current edition this has been initially achieved by introducing two columns and a slightly reduced type size. In 1987 and thereafter, the journal will be published on six occasions each year. This policy will substantially reduce the waiting period between acceptance and publication of original work.
New in rheumatoid arthritis

ETODOLAC CAPSULES

Clinical efficacy with patient acceptability

ABBREVIATED PRESCRIBING INFORMATION
Presentation: Lodine capsules contain 200mg etodolac. Basic NHS price 60 x 200mg capsules (£16.80). Uses: Acute or long-term in rheumatoid arthritis. Dosage and Administration: Oral: 200mg twice daily, some patients may require 600mg daily. Safety of doses in excess of 600mg per day not established. Elderly – no change in initial dosage required. Paediatric dosage not established. Contra-indications, Warnings, etc: Contra-indications Hypersensitivity, active peptic ulceration or a history of peptic ulcer disease, patients who experience asthma, rhinitis or urticaria during therapy with aspirin or other non-steroidal anti-inflammatory drugs. Pregnancy: During lactation: Precautions: Although non-steroidal anti-inflammatory drugs do not have the same direct effects on platelets as does aspirin, all drugs which inhibit the biosynthesis of prostaglandins may interfere, to some extent, with platelet function. Patients receiving Lodine who may be adversely affected by such actions should be carefully observed. There has been no evidence of significant changes in renal or hepatic function with the use of Lodine in man. However, impairment of renal or hepatic functions due to other causes may alter drug metabolism; patients receiving long term therapy especially the elderly, should be observed for potential side-effects and their drug doses adjusted as needed, or the drug discontinued. Drug interactions: Highly protein-bound drugs, e.g. anticoagulants. Side Effects: Reported side-effects include nausea, epigastric pain, diarrhoea, indigestion, heartburn, flatulence, abdominal pain, constipation, headaches, dizziness, dryness, tinnitus, rash and fatigue.

Product Licence Number 607/74. For full prescribing information please refer to data sheet. Date of preparation: November 1985.

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Lodine is a Trade Mark.