

The changing dimensions of rheumatoid arthritis and its treatment

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Unlike degenerative processes, rheumatoid arthritis begins within the synovium, the lining of diarthrodial (moveable) joints. The initial reaction appears to be a cellular immune response directed against an unknown antigen or antigens in a genetically predisposed host. The activation of helper T-lymphocytes leads to release of inflammatory cytokines by these cells, and attraction of macrophages into the synovium and of polymorphonuclear leukocytes into the synovial fluid. The synovial lining cells proliferate in numbers and state of activation. The proliferative "pannus" behaves as a locally invasive malignancy, burrowing into and destroying articular cartilage and subchondral bone.

For many years physicians have known that prolonged administration of glucocorticoids in high doses produce diabetes mellitus, cataracts, fragile skin, osteoporosis and hypertension in patients, and that the standard non-steroidal anti-inflammatory drugs initiate duodenal ulcers and bleeding. Disease-modifying agents such as gold salts were used with good results, but with their own side-effects. In the late 1970s numerous groups demonstrated that methotrexate, used in low doses each week, was very useful and minimally toxic for rheumatoid arthritis. This drug, in a sense, "turned the corner" for therapy in rheumatoid arthritis.

Since then there have been two further advances: the production and successful use of targeted therapy against inflammatory cytokines, and the discovery that the prevalence of rheumatoid arthritis is lower than the "1% of the population" previously thought. We now know that the incidence of rheumatoid arthritis is decreasing. For example, its incidence in Rochester, Minnesota, declined by 50% between 1950 and 1974 (1), and in the same group the age- and sex-adjusted incidence per 100 000 population fell from 62 in the decade of 1955–64 to 33 in that of 1985–94 (2). Throughout these decades there have

been cyclical patterns, suggesting the influence of environmental factors. In addition, seropositivity for rheumatoid factor is decreasing; the highest likelihood of seropositivity was in those born at the turn of the 20th century. Along with the decline in incidence, and a shift towards an older age at onset of rheumatoid arthritis, these data suggest a birth-cohort effect, very likely from something infectious (3).

Rheumatologists are getting better at predicting the course of the condition as well as diagnosing it more accurately. A valuable prediction model for persistent erosive rheumatoid arthritis has been developed in Europe. It consists of seven variables according to which the physician can put a patient at the time of diagnosis into one of three probable outcome cohorts: self-limiting arthritis; persistent but non-erosive arthritis; and persistent erosive arthritis (4). The variables are: symptom duration at first visit; morning stiffness for more than one hour; arthritis in three or more joints; bilateral metatarsophalangeal joint compression pain; rheumatoid factor positivity; anti-citrullinated peptide antibody positivity; and radiographic erosions.

These variables are very similar to those that comprise the American College of Rheumatology Criteria for Classification of Rheumatoid Arthritis. The corresponding weighting system gives the prognostic capacity (4). The unusual addition to the other factors is the anti-citrullinated peptide antibody. A high percentage of patients with rheumatoid arthritis have substantial titres of antibody to peptides containing citrulline, and citrullinated peptides are found in rheumatoid synovium. As of 2003 it has equal weight with rheumatoid factor for predicting destructive disease.

Despite the improved predictions for course, current data suggest that when good physician care is available, medical care costs for rheumatoid arthritis exceed US\$ 6000 a year per

patient (5). Recent trends suggest that this will go down, however.

In addition to drugs, effective chronic disease management includes patients taking a strong interest in and responsibility for their care. The use of allied health personnel to work in small groups with patients who exchange information, complaints, tips on activities of daily living, and sensible exercise, can save visits to physicians as well as to emergency facilities. Part and parcel of better care for rheumatoid patients must be improved education for future physicians. The Bone and Joint Decade International Steering Committee is working hard to increase the quality and quantity of curricula in musculoskeletal medicine in medical schools.

As rheumatologists, orthopaedists and general practitioners, we must capitalize on clinical science to develop better therapy, and use cost-effective techniques of physician and allied health personnel to manage patients in all countries of the world. ■

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