

Rheumatoid Arthritis in Recession



In 1979 the rheumatologist Watson Buchanan and the mathematician Robert Murdoch proposed a bold hypothesis in *The Journal*: that rheumatoid arthritis (RA) would eventually disappear¹. The basis of their hypothesis was that RA appeared to be following the pattern of an infectious illness and, if it continued to do so, it would naturally recede and vanish, probably sometime in the next 100 years. They also argued that as the prevalence of the disease decreased, its severity would similarly decline. In many ways this contradicts the widely-held assumption that medicine and, in particular, medical interventions have turned the tide against the many epidemics of diseases of the 19th and 20th centuries.

Buchanan and Murdoch took as their example the decline in incidence of tuberculosis that occurred long before the introduction of drug therapy, but they could equally have chosen leprosy or scarlet fever. Deaths due to coronary artery disease, usually described as a noncommunicable disease, have also been showing a decline since the 1950s, prior to the introduction of effective therapies. Many hypotheses have been suggested, but one of the most appealing was offered by the late Lewis Thomas. He suggested that the catalyst was the advertising campaigns for aspirin for musculoskeletal symptoms and headaches that arose with the introduction of television in the 1950s².

We consider the evidence that Watson and Murdoch postulated and how the data presented by Sokka and Pincus³ published in this issue support the view that RA may now be a much milder disorder.

Epidemiological studies of RA reflect interesting patterns in prevalence and more recently a declining trend in incidence. Within Europe the disease is differentially distributed across countries, with much lower numbers in countries around the Mediterranean than in Scandinavian populations, a phenomenon that has yet to be fully explained. In North America the highest recorded prevalence has been found in the native Indian population⁴. Within Africa and Asia RA is more common in urban than in rural populations, but even within urban populations the numbers do not approach those seen in North America and Northern Europe⁵. It is not clear if this is due to reporting bias or a true difference.

In a systematic review of the epidemiology of RA, Alamanos and colleagues⁶ identified 9 incidence studies — of these, only 3 provided data on secular trends in RA. All 3 studies were retrospective and based on case record review. In northwestern Greece no significant change in trends was observed between 1987 and 1995⁷. However, in Rochester, MN, USA, a halving of the incidence to 32.7 per 100,000 was seen in 1985 to 1994 compared to the interval extending from 1955 to 1964⁸. The most robust data of secular trends in RA has been obtained from Finland⁹, where the Sickness Insurance Act, which provides free drugs to all patients with chronic diseases, allows trends in disease patterns to be tracked accurately. Using these data, a 15% reduction was seen in 1990 compared to the years 1980 and 1985 in 5 districts of Finland. An extension of this study to 2000¹⁰ showed that compared to 1980 there was a further reduction to a halving in the age and sex-adjusted incidence of RA to 55 per 100,000. Two studies in non-Caucasian populations — the Pima Indians¹¹ and the Japanese¹² — have also shown a decrease in incidence. The peak age of onset appears to be increasing in men but decreasing in women. Paralleling this fall in incidence there has also been a fall in the proportion of patients with rheumatoid factor (RF), a phenomenon first noted in the 1970s and confirmed in male and female Pima Indians¹³, a trend now confirmed by many others.

In keeping with the clinical ruminations of rheumatologists who trained in the 1970s and 1980s, that the severity of rheumatoid disease is decreasing, it is now rare to encounter the more severe phenotypes such as rheumatoid vasculitis or Felty's syndrome. The need for major joint replacements in people with RA also seems to have decreased, although this may arguably have arisen from better treatment rather than milder disease.

The Sokka and Pincus report in this issue provides supportive evidence for the observation that the joint disease in RA at presentation is also less severe. The databases of 1892 consecutive patients with RA seen between 1980 and 2004 in Finland and 478 in Nashville, TN, USA, were scrutinized for their baseline erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and RF. Results were sim-

See ESR, CRP, or RF are normal at presentation in 35%-40% of patients with RA, page 1387

ilar from both sites, but the database was more comprehensive for the Finnish patients. (In Finland, median ESR was 35 in 1980–1984, 31 in 1985–1989, 33 in 1990–1994, 29 in 1995–1999, and 28 in 2000–2004. CRP levels also showed a progressive fall from 21 in 1980–1984 to 11 in 2000–2004. RF was positive in about 60% at both centers.) Reviewed in the article were 84 other cohorts reported in the literature for which mortality outcomes had been reported: here, trends in lower ESR with time were also noted. Although similar findings have been noted by others, this Sokka and Pincus report pulls these findings together. In keeping with these data, Sokka, *et al* previously reported on progression of radiological damage at recruitment and at 5 years in 3 cohorts of patients with RA recruited 1983–85, 1988–89, and 1995–96¹⁴. Patients in the last cohort had the lowest rate of progression. Similar findings have been reported from The Netherlands.

Sokka and Pincus acknowledge that there are more missing data and that disease duration was longer in the Nashville cohort versus that from Finland; no clinical data are presented, and the number of patients with normal results may be an underestimate resulting from spectrum bias. Despite these limitations this article adds to accumulating evidence that the pattern of RA disease is changing.

Despite intense efforts no infectious agent has yet been identified in RA. However, some environmental agents such as tobacco smoking appear to be contributory to development of RA. The absence of RA in Europe prior to the 17th and 18th centuries¹⁵ has led to the suggestion that the disease was imported from the New World, where paleontological evidence has identified a disease with signs like those of RA especially in populations in whom tobacco smoking was common¹⁶. A considerable body of epidemiological evidence now supports the view that smoking is associated with both the onset and severity of RA. In both the USA and the UK, falls in the numbers of smokers have been recorded in both men and women. There are similarities in the changes in RA incidence and smoking prevalence rates, adding weight to the argument linking RA with cigarette smoking. Recently, biological plausibility for the link has also been proposed by Klareskog, *et al*¹⁷.

Evidence supporting the hypothesis that RA is now in recession is compelling. The study by Sokka and Pincus adds to the existing body of evidence that severity of the disease is in decline. Current guidelines advocate the early aggressive treatment of all patients with RA; such recommendations have invariably been derived from selected populations with more severe disease. However, as highlighted in the Sokka and Pincus study, many with early RA will have a much milder disease in whom management strategies have yet to be validated.

NICOLA ALCORN, MB, ChB, MRCP;
MENG MAY CHEE, MB, ChB, MRCP;

ROBERT MURDOCH, BA, BSc, DCompSc;
RAJAN MADHOK, MD, FRCP,
Centre for Rheumatic Diseases
Glasgow Royal Infirmary
Glasgow, United Kingdom

Address correspondence to Dr. Alcorn.
E-mail: Nicola.Alcorn@ggc.scot.nhs.uk

REFERENCES

1. Buchanan WW, Murdoch RM. Hypothesis: that rheumatoid arthritis will disappear. *J Rheumatol* 1979;6:324-9.
2. Thomas L. The fragile species. New York: Robert Stewart/Charles Scribner's Sons; 1992.
3. Sokka T, Pincus H. Erythrocyte sedimentation rate, C-reactive protein or rheumatoid factor are normal at presentation in 35%-40% of patients with rheumatoid arthritis seen between 1980 and 2004: Analyses from Finland and the United States. *J Rheumatol* 2009;36:1387-90.
4. Ferucci ED, Templin DW, Lanier AP. RA in American Indians and Alaskan natives: a review of the literature. *Semin Arthritis Rheum* 2005;34:662-7.
5. Adebajo AO. Rheumatoid arthritis: A twentieth century disease in Africa? *Arthritis Rheum* 1991;34:1158-65.
6. Alamanos Y, Voulgari PC, Drosos AA. Incidence and prevalence of rheumatoid arthritis based on the 1987 American College of Rheumatology criteria: A systemic review. *Semin Arthritis Rheum* 2006;36:182-8.
7. Drosos AA, Alamanos Y, Voulgari PV, et al. Epidemiology of adult rheumatoid arthritis in Northwest Greece 1987-1995. *J Rheumatol* 1997;24:2129-33.
8. Doran MF, Pond GR, Crowson GS, O'Fallon WM, Gabriel SE. Trends in incidence and mortality in rheumatoid arthritis in Rochester, Minnesota, over a forty-year period. *Arthritis Rheum* 2002;46:625-32.
9. Kaipiainen-Seppanen O, Aho K. Incidence of chronic inflammatory joint disease in Finland in 1995. *J Rheumatol* 2000;27:94-100.
10. Savolainen E, Kaipiainen-Seppanen O, Kroger L, Luosajarvi R. Total incidence and distribution of inflammatory joint diseases in a defined population: results from the Kuopio 2000 arthritis survey. *J Rheumatol* 2003;30:2460-68.
11. Jacobsson LT, Janson RL, Knowler WC, et al. Decreasing incidence and prevalence of rheumatoid arthritis in Pima Indians over a twenty-five year period. *Arthritis Rheum* 1994;37:1158-65.
12. Shichikawa K, Inoue K, Hirota S, et al. Changes in the incidence and prevalence of rheumatoid arthritis in Kamitonda, Wakayama, Japan, 1965-1996. *Ann Rheum Dis* 1999;58:751-6.
13. Enzer I, Dunn G, Jacobsson L, Bennett RH, Knowler WC, Silman A. An epidemiological study of trends in prevalence of rheumatoid factor seropositivity in Pima Indians: evidence of a decline due to both secular and birth-cohort influences. *Arthritis Rheum* 2002;46:1729-34.
14. Sokka T, Kautiainen H, Hakkinen A, Hannonen P. Radiographic progression is getting milder in patients with early rheumatoid arthritis. Results of 3 cohorts over 5 years. *J Rheumatol* 2004;31:1073-82.
15. Short CL. The antiquity of rheumatoid arthritis. *Arthritis Rheum* 1984;17:193-205.
16. Rothschild BM, Woods RJ. Symmetrical erosive disease in Archaic Indians: the origin of rheumatoid arthritis in the New World? *Semin Arthritis Rheum* 1990;19:278-84.
17. Klareskog L, Padyukov L, Loretzen J, Alfredsson L. Mechanisms of disease: Genetic susceptibility and environmental triggers in the development of rheumatoid arthritis. *Nat Clin Pract Rheumatol* 2006;2:425-33.

J Rheumatol 2009;36:1353-4; doi:10.3899/jrheum.090571