In 1979 the rheumatologist Watson Buchanan and the mathematician Robert Murdoch proposed a bold hypothesis in The Journal: that rheumatoid arthritis (RA) would eventually disappear. 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 1950s.

We consider the evidence that Watson and Murdoch postulated and how the data presented by Sokka and Pincus 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 population. 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 Europe. 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 colleagues 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 1995. 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 1964. The most robust data of secular trends in RA has been obtained from Finland, 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 2000 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 Indians and the Japanese — 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, a phenomenon first noted in the 1970s and confirmed in male and female Pima Indians, 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-
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 1995–96. 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 centuries 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 common. 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 Klarskog, et al.

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.

References


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