Rheumatoid Arthritis: An Example of Ecological Succession?

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Abstract. The history of one of the most common of modern-day diseases, rheumatoid arthritis, is reviewed. The disease probably existed prior to 1800 when it was first clearly described, but appears to have become much more common after this time. During the past two decades both the incidence and severity may have been declining. Vasculitis appears today certainly to be less common. The reason for this decline is considered in comparison with the decline in other infectious and non-infectious diseases. A hypothesis is put forward to explain the decline in terms of the botanical concept of ecological succession.

Résumé. L'histoire de l'une des maladies les plus communes chez l'homme, l'arthrite rhumatomale, est exposée dans le présent article. La maladie a probablement existé avant 1800, date à laquelle elle a été décrite pour la première fois, mais elle semble être devenue beaucoup plus commune à partir de cette époque. Au cours des deux dernières décennies, l'incidence et la gravité de la maladie ont peut-être diminué. La vascularité est certainement aujourd'hui moins commune. La raison de ce déclin est examinée en faisant une comparaison avec le déclin d'autres maladies infectieuses et non-infectieuses. Une hypothèse est mise en avant pour expliquer ce déclin dans les termes du concept botanique de succession écologique.

We believe that there is a case for studying disease over a span of time. In the present discussion we adopt this approach with respect to rheumatoid arthritis, one of the most enigmatic of modern-day illnesses. In so doing, we attempt to show that the disease was relatively rare before 1800, and that its severity has begun to decline. An infectious cause is most likely, and the behavior consistent with ecological succession in the botanical world.

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HISTORICAL EVIDENCE OF THE DISEASE

Ancient Skeletons

Several works have suggested that rheumatoid arthritis, if it is not a new disease, then certainly is one that was rare before 1800, when it was first clearly described. Supporting this view is the surprisingly little evidence of the disease in ancient skeletal remains. This is in contrast to clear examples of osteoarthritis, ankylosing spondylitis, diffuse idiopathic hyperostosis, gout, possible psoriatic arthritis, and even a case of ochronosis. In many reports the joint changes are either atypical or there is insufficient detail to make a diagnosis of rheumatoid arthritis. The mummy described by May in 1897 is frequently cited as a typical example of rheumatoid arthritis, but we agree with Short that the radiological changes are consistent with generalized osteoarthritis. Possible examples, however, of rheumatoid arthritis are one found in 400 Saxon and Romano-British skeletons by Rogers et al., and one of two cases found among 416 skeletal remains in a Roman cemetery in England by the two Thoulds. The concept that rheumatoid arthritis may be a New World disease is supported by two recent studies of skeletal remains in Ohio Woodland Indians about 900 to 1,200 years old and in a group of skeletons 3,000 to 5,000 years old in North West Alabama which have demonstrated changes suggestive of a symmetrical erosive polyarthritis. The authors comment that the nature of the severe erosive lesion seen in rheumatoid arthritis is such that they will not be identifiable after some time in the soil, becoming indistinguishable from artefactual damage. Therefore burial methods and soil type may have an important influence on skeletal preservation, and could be one reason for the lack of evidence in some countries of rheumatoid arthritis.

Early Medical Literature

Short carefully reviewed ancient Roman and Greek medical writings, and concluded that Scribonius Largus, Julius Caesar’s Chief Medical Officer, described a polyarthritis which occurred chiefly in elderly women. In addition, Aretaeus (A.D. 81-A.D. 138?) described a polyarthritis which could have been polyarticular gout, because the disease was characterized by long quiescent intervals between acute attacks “kindled up by any slight cause.” Soranus of Ephesus (A.D. 98-A.D. 138) in his treatise On Chronic Disease described polyarthritis which was more common in middle-aged men, causing the joints to “become twisted, with the toes and fingers either turned sideways, or bent over backwards, or rest immovable upon their neighbors.” However, as Short explained, the description includes an acute attack of gout with discharging tophi. Of course, the differentiation between chronic
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tophaceous gouty arthritis and rheumatoid arthritis has always been difficult, even in the present era.\textsuperscript{15} Sturrock et al.\textsuperscript{16} reviewed the early Indian medical writings in \textit{The Caraka Samhita} of the first century A.D., and concluded that the description of deforming polyarthritis was consistent with a diagnosis of rheumatoid arthritis.

Neither Short\textsuperscript{17} nor ourselves have been able to discover any medical writings with descriptions of rheumatoid arthritis until the seventeenth century, when Thomas Sydenham (1624-89) gave a fairly reasonable account.\textsuperscript{18} Possible descriptions were given by Musgrave,\textsuperscript{19} Oliver,\textsuperscript{20} Sauvages,\textsuperscript{21} and Heberden\textsuperscript{22} in the following century. Following the clear description by Landré-Beauvais (1774-1840) in Paris in 1800, a number of French and English physicians described\textsuperscript{23} and illustrated\textsuperscript{24} the classical features of the disease as we know it today.\textsuperscript{25} Rheumatoid arthritis was only named in 1859 by the "Father of Rheumatology," Sir Alfred Baring Garrod (1819-1907).\textsuperscript{26} Juvenile rheumatoid arthritis was also described in the latter part of the last century\textsuperscript{27} including the classical paper by Sir George Frederick Still.\textsuperscript{28}

\textit{Historical Persons}

The best example of a prominent individual having the disease is probably that of the Emperor Monamachus Constantine IX (ca. 980-1055), whose biographer, Michael Psellus, gives a description of a severe crippling polyarthritis beginning in late life and leading eventually to the Emperor becoming bed-ridden.\textsuperscript{29} Copeman\textsuperscript{30} alleges that Mary Queen of Scots (1542-87) suffered from rheumatoid arthritis, but her height and description of "gracile limbs" is more suggestive of an arthritis associated with hypermobility as a result of possible Marfan's syndrome.\textsuperscript{31} It has been suggested that Mme de Sevigne's rheumatic condition,\textsuperscript{32} and the arthritis of Louis XVII,\textsuperscript{33} were due to rheumatoid arthritis. It is particularly interesting that Christopher Columbus (1451-1506) was reported as suffering from rheumatoid arthritis. It developed while he was on his third crossing of the Atlantic in 1498, and was associated with ocular inflammation.\textsuperscript{34} He eventually developed chronic arthritis and was crippled. Whether it was rheumatoid arthritis or Reiter's syndrome is unclear, but may be relevant in view of the recent reports of rheumatoid arthritis-like changes in New World skeletons.\textsuperscript{35}

\textit{Literature and Fine Arts}

There is no reference to polyarthritis in literary sources such as the Bible,\textsuperscript{36} the works of Shakespeare,\textsuperscript{37} or Robert Burns.\textsuperscript{38}

Concerning the fine arts, Talbot in 1981 declared that he had not been aware of rheumatoid arthritis in any painting.\textsuperscript{39} Dequecker\textsuperscript{40}
reviewed a large number of Flemish paintings between 1400 and 1700, and found only five which showed possible rheumatoid arthritis of the hands, although one showed classical temporal arthritis. The most convincing was the joint changes in the fingers of the serving maid in Jacob Jordaens' (1593-1678) The Printers Family, which now hangs in the Prada Museum in Madrid, Spain. Appelboom et al., have suggested that Peter Paul Rubens (1577-1640) may have suffered from rheumatoid arthritis, but the diagnosis could also be gout. Sandro Botticelli (1444-1510) was claimed by Alarcon-Segovia et al. to have depicted rheumatoid arthritis of the hand in Portrait of a Youth, although they did not consider The Birth of Venus to show the disease, as suggested by Dequecker. We tend to agree with Leden, that neither of these paintings shows unequivocal evidence of the diseases. A painting done by William Hoare in 1742, now in the Royal National Hospital for Rheumatic Diseases, Bath, England, shows a patient with typical rheumatoid arthritis, but this has been disputed by Bywaters. Pedersen and Permin made the fascinating suggestion that the famous painters who apparently had had rheumatoid arthritis—Rubens, Renoir, and Dufy—and progressive systemic sclerosis—Klee—developed these diseases as a result of pigments used in the paints. However, the only common ingredient of the paints was turpentine! A Precolumbian figurine has been claimed to show juvenile rheumatoid arthritis.

Pathological Specimens

Although the United Kingdom and Western Europe have a number of excellent pathology museums, we have only examined two, which date from the eighteenth century: John Hunter's in the Royal College of Surgeons London, England, and his brother William Hunter's in the University Department of Pathology, Royal Infirmary, Glasgow, Scotland. Both have several interesting specimens of bone and joint pathology, especially the one in Glasgow. A wide variety of pathology is present, including a classical case of osteitis fibrosa cystica, but there are no examples of rheumatoid arthritis.

RHEUMATOID ARTHRITIS IN MODERN TIMES

From the foregoing it would appear, especially from the paleopathological evidence of the Thoulds and Caughey's description of Constantine IX, that rheumatoid arthritis probably existed before 1800, but perhaps was relatively rare. It is, of course, possible that the disease was diagnosed incorrectly, especially as gouty arthritis. It has to be remembered that even the celebrated Sir William Osler (1849-1919) was confused about rheumatoid arthritis and its distinc-
tation from osteoarthritis as late as 1909, when the last edition of his famous textbook *The Principles and Practice of Medicine* was published with him as the sole author. The relative absence of rheumatoid arthritis could be due to the limited life expectancy of earlier times: as late as 1900 the average age of death in the United States was only 50 years. The prevalence of rheumatoid arthritis is highest in the fifth and subsequent decades of life, which may partly explain the relative absence of the disease in communities with a low life expectancy, although racial predisposition may also be relevant.

Many clinical rheumatologists are of the opinion that rheumatoid arthritis is becoming less common and less severe, with less vasculitis. However, Scott and Spencer on reviewing the literature found no evidence of a decline in incidence. No comparable data are available of long-term studies, such as the one conducted by Duthie et al. in Edinburgh, to determine accurately whether the pattern of disease is changing. Nevertheless, the studies of Silman et al. do suggest that both the incidence and the severity of the disease is less, at least as judged by the prevalence of subcutaneous nodules. In a recent poll of Australasian rheumatologists more than half believe there had been a decline in vasculitis.

The year 1948 was the *annis mirabilis* of rheumatology with the discovery of corticosteroids. Following this there was a spate of publications on various aspects of rheumatoid arthritis, including the clinical and pathological delineation of vasculitis. This was attributed by some to the use of corticosteroids, which is possible, since these drugs block the uptake of immune complexes by the reticuloendothelial system, so favoring deposition in peripheral vessels. The dose of corticosteroids at that time was much higher than current usage and was frequently rapidly changed; both these factors could predispose to the development of vasculitis. Certainly individual units in the early 60s, and even as late as the early 1970s had no difficulty in publishing sizeable series of cases with neuropathy due to vasculitis. In the early 70s in this unit, 43 of 704 patients with rheumatoid arthritis (6.1%) were identified as having vasculitis. In the past three years in the same unit only 2.7 percent of patients had vasculitis. The apparent decline in severity could be due to early institution of so-called disease-modifying drugs, but there is scant evidence that these drugs make any significant impact over the lifetime of the disease.

**DECLINE OF OTHER DISEASES**

If rheumatoid arthritis is less severe than it was two or more decades ago then its decline would not be unusual, since many other diseases, especially those caused by infection, also have behaved in a like manner. Leprosy was common in Europe in the Middle Ages, with Robert
the Bruce, King of Scots, being among the many victims.\textsuperscript{73} It gradually declined, being replaced by tuberculosis;\textsuperscript{74} this in turn steadily declined even in centres of urban poverty and squalor,\textsuperscript{75} such as the city of Glasgow, Scotland,\textsuperscript{76} with antituberculous chemotherapy contributing at most a 50 percent improvement.\textsuperscript{77} Other mycobacteria now appear to be taking the place of the tubercle bacillus.\textsuperscript{78} The history of syphilis is bizarre, being apparently severe when it first occurred in Europe in the fifteenth century, and now much more benign.\textsuperscript{79} The factors responsible for the alternate rise and fall of bubonic plague have long remained a mystery:\textsuperscript{80} likewise, staphylococcal sepsis,\textsuperscript{81} scarlet fever,\textsuperscript{82} and encephalitic lethargica.\textsuperscript{83} In 1906, Brownlee\textsuperscript{84} opined on the basis of statistical studies that:

An epidemic is an organic phenomenon, the course of which seems to depend on the acquisition by an organism of a high grade of infectivity at the point where the epidemic starts, this infectivity being lost from that period till the end of the epidemic at a rate approaching the terms of a geometrical progression.

We might add, in accordance with Creighton\textsuperscript{85} and Greenwood,\textsuperscript{86} that the time frame of such an epidemic may be over several centuries.

However, other diseases not apparently due to infection also show this unexplained rise and fall, the most puzzling being the decline of ischaemic heart disease,\textsuperscript{87} and tooth decay in unfluoridated areas.\textsuperscript{88} The former may, however, be partly explained by changes in diet, especially in the use of margarine instead of butter, and reduction in smoking.

AETIOLOGY OF RHEUMATOID ARTHRITIS

Do these considerations have any bearing on the aetiology of the disease? Bywaters\textsuperscript{89} has recently reviewed the bewildering list of possible aetiological factors considered over the years. A variety of infectious agents have been contemplated including such likely contenders as the Epstein-Barr virus,\textsuperscript{90} mycoplasma,\textsuperscript{91} diphtheroids,\textsuperscript{92} Streptococcus agalactiae,\textsuperscript{93} and Clostridium perfringens.\textsuperscript{94} Transmission of the disease to baboons has, however, proven unsuccessful.\textsuperscript{95} If the disease is of infective origin, then its course since the beginning of the last century and recent possible decline are entirely consistent with an infective aetiology.

One has, therefore, to speculate about factors that led to its development. Hoyle\textsuperscript{86} has suggested that viruses may be created in outer space and carried to earth by meteorites. Halley's comet circled the earth in the late eighteenth century, perhaps spraying the earth with a more virulent strain of a virus, such as the Epstein-Barr virus.
Another factor may involve nutrition. In Europe, at least, the famines of previous centuries were to a large extent eliminated, and crop rotation and land drainage ensured better nutrition to a greater number of the population. Nutrition profoundly influences autoimmune disease in animals, and a more nutritious diet, especially in terms of protein content, could conceivably modify the immune response to allow the development of chronic arthritis. In pigs, a protein-rich diet can lead to a rheumatoid-like arthritis. Saturated fatty acids might also predispose by favoring production of prostaglandins of the 2 series and leukotriene B4, both of which are inflammatory, because unsaturated fatty acids, such as fish oils, which lead to the less inflammatory prostaglandins of the 3 series and leukotriene B5, produce symptomatic relief in rheumatoid patients. Total fasting causes improvement, either by reducing production of chemical mediators of inflammation such as leukotriene B4, changing the bowel flora, gut permeability, or affecting cellular immunity. Some researchers have found an increased permeability of the gut in patients with rheumatoid arthritis using differential sugar absorption, whereas others have not. Intestinal permeability was abnormal when patients were treated with non-steroidal anti-inflammatory drugs. Indium-labelled autologous leukocyte scans have been positive in the ileo-caecal region, although no evidence of inflammation has been found on endoscopy. Could it be that aspirin, introduced in 1899, is an environmental factor leading to the apparent increase in incidence of rheumatoid arthritis, by causing gastrointestinal erosions, so allowing access of gut bacteria and food allergens to pass more readily into the blood stream? On the other hand, Sepkowitz has argued that the decline in use of aspirin in children because of Reye's syndrome may account for the recent increase in rheumatic fever.

Although a genetic factor has been identified in rheumatoid arthritis in twin studies, and an association with HLADR has been demonstrated, the latter does not appear to segregate the disease in kindred studies. Thus, unlike ankylosing spondylitis, the genetic component in rheumatoid arthritis is relatively weak, perhaps explaining why ankylosing spondylitis is present in palaeopathological specimens while rheumatoid arthritis is relatively rare. This is not to suggest that only inherited diseases are to be found in ancient skeletons, for there are many examples of non-inherited diseases, such as osteomyelitis and leprosy. However, a disease with a strong genetic background, such as ankylosing spondylitis, would continue to affect people throughout history, where as a disease with a relatively weak genetic base, such as rheumatoid arthritis, might be expected to wax and wane.

Thus, environmental factors appear more important in seeking clues for the aetiology of rheumatoid arthritis. Allergens in foods, especially
dairy products, appear to be important in certain patients;\textsuperscript{116} however, exclusion diets have not shown particularly dramatic effects.\textsuperscript{117} Coombs and Oldham\textsuperscript{118} have reported early rheumatoid-like joint lesions in rabbits fed cows’ milk.

Arthritis is a well-recognized complication of certain diseases where the integrity of the intestinal mucosal barrier has been breached. These include ulcerative colitis, Crohn’s disease, and following intestinal by-pass surgery for morbid obesity;\textsuperscript{119} and rheumatoid arthritis has been noted to improve with treatment of co-existing gluten sensitive enteropathy.\textsuperscript{120} Thus, it is conceivable that changes in diet may have been responsible for the “outbreak” of rheumatoid arthritis, which appears to have occurred since the turn of the nineteenth century.

ECOLOGICAL SUCCESSION

Ecological succession is a gradual process whereby ecological communities undergo change brought about by a change in one of the species within it. A new species may become established in the community which may replace one or several of the original species\textsuperscript{121} until a new stable state is reached.\textsuperscript{122} Thus, an alteration in one species can eventually modify the whole system. The community controls the nature of the change although the rate and its limits are controlled by the environment. A slow continuous change in one species can produce a discontinuous change in the ecological cycle. For example, a slow change in the degree of virulence in an organism can cause disappearance of the infection.

These systems are well recognized in botany and zoology,\textsuperscript{123} but we believe they are also applicable to human diseases. Humans may be considered to be the physical environment, and the organisms then are the community undergoing development. This concept may be relevant to infectious diseases, where incidence changes without extrinsic alteration; for example, rheumatic fever, plague, scarlet fever, and tuberculosis. Further examples might include changes in the virulence of smallpox\textsuperscript{124} and the recent resurgence of rheumatic fever thought to be due to the reappearance of a group A streptococcus with enhanced rheumatogenic potential.\textsuperscript{125} Mechanisms for these changes are most likely to be due to changes within the organism, because the time over which they occur would be too short for genetic change in humans. Thus, changes in bacteria might modify their virulence. They could be produced by other organisms in the environment, changes in the flora of the gastrointestinal tract or lungs.

Therefore, it may be suggested that the most probable reason for rheumatoid arthritis not being recognized in Europe until the 1800s and the recent decline in its severity is that it is part of the normal
cyclical changes that occur in infections. This could also be affecting the putative infectious agent for rheumatoid disease. Examining the natural history of other diseases makes the changes occurring in rheumatoid arthritis appear to be less unusual. Moreover, it serves to demonstrate the information that can be obtained by looking beyond the lymphocyte.

ADDENDUM

Since the acceptance of this paper an interesting review of individuals afflicted with rheumatoid arthritis by Dr. T. Appleboom, division of Rheumatology, Erasmus University Hospital, University of Brussels, Belgium, has come to the authors' attention. The review is entitled "The Past: A Gallery of Arthritis," and is published in Clinical Rheumatology, 8 (1989): 442-52.

NOTES


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