

# Rheumatoid Arthritis: Beyond the Lymphocyte



“Some will allow no diseases to be new, others think that many old ones are ceased, and that such which are esteemed new, will have but their time: however, the mercy of God hath scattered the great heap of disease, and not loaded any one country with all: some may be new in one country which have been old in another: new discoveries of the earth discover new diseases: for besides the common swarm, those are endemial and local infirmities proper unto certain regions, which in the whole earth make no small number: and if Asia, Africa, and America should bring in their list, Pandora’s box would swell, and there must be a strange Pathology.”

— Sir Thomas Browne (1605–1682)

This comment by Sir Thomas Browne in *A Letter to a Friend*<sup>1</sup> is particularly germane to the article by Aceves-Avila and colleagues in this issue of *The Journal* on whether rheumatoid arthritis (RA) may have been rare in the Old World, and spread there in the 19th century from America<sup>2</sup>.

## THE OLD WORLD

The strongest evidence that RA did not exist or if it did in very mild form outside the Americas is the absence of the disease in Egyptian mummies. This is in contrast to other rheumatic diseases, including osteoarthritis, ankylosing spondylitis, gout, chondrocalcinosis, and ochronosis<sup>3</sup>. Of course, absence of evidence does not necessarily equate with evidence of absence. The Thoulds found erosions of the carpals and heads of the metacarpals in a Romano-British skeleton, which showed no evidence of ankylosing spondylitis<sup>4</sup>, and Aceves-Avila, *et al* cite 3 other cases of erosive arthropathy from the 7th to 9th centuries and one from the 15th century found by French workers. It is perhaps worth noting the difficulty in interpreting ancient skeletal remains, which includes among other things the nature of the soil, since burial in chalk results in thinning

and perhaps erosions of bone<sup>5</sup>. We agree with Aceves-Avila, *et al* that a multidisciplinary team comprising paleopathologists, archeologists, radiologists, and rheumatologists is necessary for the proper assessment of ancient skeletal remains — an approach first advocated by Dieppe and his colleagues<sup>6</sup>.

Another source of evidence of a disease is in medical museums. We have had the opportunity of reviewing 18th century bone and joint collections of the 2 Hunter brothers, William (1718–1783) in Glasgow University, and John (1728–1793) in the Royal College of Surgeons of England in London. Despite a wealth of bone and joint pathology, including the first case of osteitis fibrosa cystica<sup>7</sup>, we were unable to identify a single case of RA. There has been a sad neglect of medical museums in recent years: one can only wonder what might be in other old collections, such as that of Carl Rokitansky (1804–1878) in the Allgemeines Krankenhaus in Vienna.

From the review by Aceves-Avila and colleagues of references to possible RA in medical literature it appears that a number of authors refer to a polyarthritis particularly affecting females that may lead to deformities. None of these descriptions, in our opinion, give a classical description of the disease as we know it today, including that of Landré-Beauvais (1774–1840) in his MD thesis submitted to the University of Paris in 1800<sup>8</sup>. In the 19th century, however, a number of English and French physicians described<sup>9</sup> and illustrated<sup>10</sup> the classical features of the disease. The disease was only named by Sir Alfred Baring Garrod (1819–1907) in 1859<sup>11</sup>. Juvenile RA was also described in the latter part of the 19th century, including the classical paper by Sir George Frederick Still (1868–1941)<sup>12</sup>.

Similarly, there is no reference to polyarthritis in nonmedical literary sources such as the Bible or the works of Shakespeare (1564–1616)<sup>13</sup> or Robert Burns (1759–1796), despite the fact the latter suffered from “flying gout” during the last 2 years of his life<sup>14</sup>.

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See The antiquity of rheumatoid arthritis, page 751.

Of the historical persons who may have suffered from the disease, Aceves-Avila and colleagues consider the Emperor Monomachus Constantine IX (circa 980–1055) to be the most probable. The emperor developed a severe crippling polyarthritis at the age of 63 that eventually caused him to be bedridden. However, his famous biographer, Marcus Constantine Psellus (1018–circa 1078), records (to our delight as Scottish Presbyterians!) that the emperor was “naturally inclined to sexual indulgence but could find no satisfaction in cheap harlotry”<sup>15</sup>. Recurrent attacks of severe reactive arthritis (Reiter’s disease) can lead to severe crippling joint deformities. The arthritis of Christopher Columbus (1451–1506) could equally have been due to Reiter’s disease, since on his third crossing of the Atlantic he suffered severe ocular inflammation. The latter, however, could have been due to scleritis associated with RA. The arthritis Mary Queen of Scots (1542–1587) suffered during her captivity was considered by the late W.S.C. Copeman to be RA, but was more likely a result of hypermobility due to Marfan’s syndrome. Other notable persons who may have suffered from the disease include Mme de Sévigné and King Louis XVII of France (1785–1795).

Concerning the fine arts, Talbott in 1981 declared that he had not been aware of RA in any painting<sup>16</sup>. In the review by Aceves-Avila, *et al* of paintings that may have depicted RA the most convincing is that of the hands of the maid in *The Painter’s Family* by Jacob Jordaens (1593–1678) and the hand and wrist of the beggar in *The Temptation of St. Anthony* by an unknown artist of the mid 15th to early 16th century Flemish-Dutch School<sup>3</sup>.

From the foregoing it would appear that RA probably existed in the Old World before 1800, but was perhaps relatively rare or relatively mild, or diagnosed incorrectly as gout. Even as late as 1909 Sir William Osler (1849–1919) was confused about RA and its distinction from osteoarthritis in the last edition of his famous textbook, *The Principles and Practice of Medicine*, with him as sole author<sup>17</sup>. The relative absence of the disease could also have been due to the limited life expectancy of earlier times: the life expectancy in the United States was only 47 as late as 1900.

## THE NEW WORLD

Professors Bruce M. Rothschild and colleagues found evidence of an erosive arthropathy consistent in distribution and radiological appearances with RA in Archaic Amerindians, and hypothesized that the disease originated in the New World and achieved worldwide distribution when European settlers came in contact with Indian tribes affected by the disease<sup>18–20</sup>. However, it is surprising that no severe case of RA was found in the ossuaries examined by Rothschild and colleagues. Aceves-Avila, *et al* draw attention to a 16th century Spanish publication in Mexico by Alonso López de Hinojosos, who referred to a joint disease

that might have been RA. López de Hinojosos had emigrated from Spain, but it is uncertain whether he was familiar with this condition there or whether he was describing it in settlers from Spain or in Amerindians. RA is common and frequently severe in some groups of American Indians today<sup>21</sup>, but not associated with HLA-DR4, as in Caucasians<sup>22</sup>.

Aceves-Avila and colleagues opine against Rothschild’s hypothesis that RA is a New World disease, believing that it existed in Pre-Columbian Europe. They rightly point out that RA may not be a single disease and that there are many factors that might influence disease expression, including nutrition, socioeconomic status, host immune function, hormones, and genetics. Intestinal permeability is abnormal in patients with RA treated with nonsteroidal antiinflammatory drugs. Could it be that aspirin is another environmental factor leading to intestinal erosions allowing gut bacteria and/or food allergens to pass more readily into the bloodstream? It is intriguing that the severe so-called “malignant” RA with vasculitis and scleritis coincided with high dose aspirin therapy.

If nothing else the study of the history of disease demonstrates that information can be obtained by looking beyond the lymphocyte.

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