

Chapter 2

History of the Attempts to Find the Cause of RA

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Introduction

There has been a continuous debate about the origin and early detection of rheumatoid arthritis. The strongest evidence suggesting recent onset is the absence of the disease in Egyptian mummies. Other rheumatological diseases such as

osteoarthritis, ankylosing spondylitis, gout and chondrocalcinosis are well represented in Egyptian bone specimens and this appeared to be convincing evidence to Professor Watson Buchanan from Glasgow that rheumatoid arthritis was a disease of recent onset which appeared in the last two centuries (Buchanan and Kean 2001).

The presence of erosions in specimens from palaeolithic, antique and medieval cemeteries has been hotly disputed as being due to chemical conditions in the soil and not representing evidence of rheumatoid arthritis.

Another suggestion has been that increased milk consumption occurred during the nineteenth and twentieth centuries, and this has been somehow involved in the onset of rheumatoid arthritis. A similar suggestion has been proposed that type I diabetes correlates well with increased consumption of milk in many countries.

There are two names that dominate the debate about the origin and definition of rheumatoid arthritis. One is that of Landré-Beauvais from Paris and the other one is that of Alfred Baring Garrod from London. They provide a convenient framework to divide the investigations into the origin of rheumatoid arthritis.

The phase before Landré-Beauvais consists of various descriptions which could or could not be called cases of rheumatoid arthritis, involving Roman, Byzantine and Mexican sources.

There has also been an exhaustive investigations of paintings, especially from Dutch and Flemish masters asking whether spindling of fingers was an accurate and realistic portrayal of the sitter or a stylistic exaggeration of post-Renaissance Mannerism (Dequeker 1977).

After Landré-Beauvais, there is an inter-regnum or a period of some 60 years where clinical descriptions appear to resemble modern descriptions of rheumatoid arthritis.

Finally with Alfred Baring Garrod who coined the word 'rheumatoid arthritis', we reach modern times and the search for the cause of this disease.

Rheumatoid Arthritis in Antiquity, India and Byzantium

Examination of burial sites provides a useful way of assessing the distribution of arthritic lesions in a population. The pattern of arthritis in Roman Britain was investigated by examining the skeletons of 416 adults from the Roman cemetery at Poundbury Camp near Dorchester in Dorset (Thould and Thould 1983).

When the Romans invaded Britain in A.D. 43, they soon subjugated the southern Celtic kingdoms. The legion Augusta II, under the command of the future emperor Vespasian, defeated the Celtic Durotriges in a fierce battle at Maiden Castle in Dorset. Around A.D. 70, Durnovaria, which is nowadays known as Dorchester, was built with a forum, public baths, shops, running water and fine houses. Over the next four centuries, the dead were buried in the large Roman cemetery at Poundbury outside the walls. The majority of the inhabitants were Celts being descendants of the Belgae who emigrated to Britain around 100 B.C. They were farmers, artisans and led a physically hard life with a life expectancy of about 40 years. In the 416 skeletons examined, there was a high prevalence of osteoarthritis with particularly severe changes in the vertebral column.

Inflammatory joint disease was seen in two examples. The first was a man with severe inflammatory and exuberant new bone formation affecting the two metacarpo-phalangeal joints and two proximal inter-phalangeal joints in the hands. Radiographic examination showed erosions in the carpus.

The other example was in a woman where inflammatory changes were seen affecting one knee joint, both wrist joints and the right elbow joint. There was fusion of the bones of one foot, including the first and fifth tarsal metatarsal joints. The radiographs of the hands showed erosions of the carpus and metacarpals. The appearances in both of these subjects were compatible with a diagnosis of rheumatoid arthritis.

The finding of two skeletons showing rheumatoid arthritis in a Roman-Celtic population would tend to suggest that it is not a disease of recent onset. The Thoulds argue that 'if we assume the prevalence was about 0.5%, rather than the current British population of 1–2% overall, we would expect to find two examples in a collection 416 skeletons, which was indeed what we found. We contend therefore that rheumatoid arthritis is as old as historical man'.

The oldest proposed written account of a disease that could be called 'rheumatoid arthritis' is generally ascribed to Scribonius Largus who was a military physician and accompanied Julius Caesar on some of his campaigns. Scribonius Largus wrote about a polyarthritis occurring mainly in elderly women. A Roman woman was considered elder between the ages of 35 and 45 years because the general life expectancy was around 40 years.

There is also evidence of the presence of a chronic symmetric polyarthritis in the 'Karakam Samhita', a medical text from India written between 500 B.C. and 100 A.D. The patients had subcutaneous nodules, contractures and sometimes atrophy of the limbs.

A Byzantine emperor, Monomachus Constantine IX (A.D. 980–1055), seems to have been the first illustrious sufferer from rheumatoid arthritis (Caughey 1974). A description of his disease is given by Michael Psellus in his book 'Chronographia' where he describes the emperor suffering recurrent polyarthritis, deformities of the hands and subsequent disability. Professor Watson Buchanan comments 'with delight to us Scottish Presbyterians that according to Psellus, the emperor was naturally inclined to sexual indulgence but could find no satisfaction in cheap harlotry'.

Rheumatoid Arthritis in Mexico

In an examination of the skeletal remains kept at the National Museum of Anthropology of Mexico, 21 cases of erosive arthritis have been studied; 8 skeletons of the Pre-classical era (Tlatilco 1400–600 B.C.), 5 of the Classic era

(Teotihuacan 200 B.C. to 600 A.D.) and 8 from the Post-classic era (A.D. 800–1500). Erosions were found on the articular surfaces, the edges of the articular surfaces and at the capsular insertions of carpal, metacarpo-phalangeal, tarsal and metatarso-phalangeal joints. These appearances were similar to those seen in patients with rheumatoid arthritis (Aceves-Avila et al. 2001).

In 1578, Alonso Lopez de Hinojosos, working in the Hospital Real de San José de los Naturales, in Mexico City, described two different types of gout, one classical gout with tophi as hard nodules and a second type which was a chronic condition of the same joints and disabled the patients by severe contractures and muscular atrophy (Aceves-Avila et al. 2002).

Thomas Sydenham (1624–1689) also distinguished gout from another chronic arthritis resembling rheumatoid arthritis but had been preceded in this description by Lopez de Hinojosos by some 100 years. One of Sydenham's patients also had swan-neck deformities of the fingers.

Evidence from Paintings

In the 'Temptation of Saint Anthony' now in the Escorial Palace near Madrid, a beggar is shown with hand and wrist deformities which resemble those found in patients with rheumatoid arthritis whilst no such deformities can be seen in the other portrayed individuals.

The 'Birth of Venus', now in the Uffizi Gallery in Florence, was painted in 1486 by Sandro Botticelli (1445–1510) and shows characteristic swellings of the proximal inter-phalangeal joints of the right hand suggestive of rheumatoid arthritis. The model for the painting was a married noblewoman Simonetta Vespucci, it is said almost his muse, and Botticelli asked to be buried near her, in the Chiesa di Ognissanti in Florence after his death.

The man in the painting of 'The Donators' by Jan Gossaert also known as Mabuse (1478–1532) has polyarthritis of the

fingers of his left hand with flexion deformities of the second, fourth and fifth fingers, suggestive of rheumatoid arthritis.

In the 'Painter's family' by Jacobo Jordaen (1593–1678), the hands of the serving maid show symmetrical inflammation of the metacarpo-phalangeal joints which are not seen in three other individuals in the painting.

In several paintings by Peter Paul Rubens (1577–1640), hand deformities characteristic of rheumatoid arthritis are clearly depicted.

The painter Siebrandus Sixtius (1538–1631) produced two portraits in which the hands reveal swelling of metacarpo-phalangeal and proximal inter-phalangeal joints, with ulnar deviations and flexion contractures of the fingers (Dequeker 1992).

Landré-Beauvais at the Salpêtrière in Paris

The first unequivocal description of rheumatoid arthritis was made by Augustin Jacob Landré-Beauvais (1772–1840) in Paris. He was born in Orléans and studied under Pierre Joseph Desault and Marie François Xavier Bichat in Paris. From 1772, he pursued his medical education under Jean Louis Petit in Lyon.

In 1796, he obtained an internship at the Salpêtrière, even then a famous hospital where he assisted Philippe Pinel. In 1799, he was appointed professor of clinical medicine at the Salpêtrière which is located on the rive gauche next to the Jardin des Plantes. After the restoration, he also held a chair of medicine at the Paris Polytechnic School. He was removed in 1830 from this post at the insistence of King Louis-Philippe of France.

He proposed and defended his Medical Thesis at the École de Médecine which is situated on the Boulevard Saint Germain in the Latin Quarter on the 16th Thermidor of the year VIII (3rd August 1800).

The ponderous and provocative title of his thesis was 'Doit-on admettre une nouvelle espèce de goutte sous la

dénomination de goutte asthénique primitive?'. The rough translation would be 'Should we accept a new type of gout, under the name of primary debilitating gout?'

Landré-Beauvais described a new syndrome on the basis of nine long-term female residents of the Salpêtrière. He clearly points out the new disease can be distinguished from classical gout. He says the condition occurs mostly in women, with characteristic capsular swelling, limitation of motion of the joints in the hands and fingers and may spread to other joints. Over time, there is the development of bony ankylosis with disorganisation of many joints (Snorrason 1952).

He was emphatic in his view that this was a new clinical condition or syndrome although he was not clear whether it was linked to gout. This new nosological concept was considered by the late Professor Eric Bywaters from the Post-graduate Medical School at the Hammersmith Hospital, a doyen of British rheumatology as the 'first sighting of the disease' (Bywaters 1988).

Alfred Baring Garrod at University College and King's College Hospitals in London

Alfred Baring Garrod was born in Ipswich. He was initially apprenticed at Ipswich Hospital but later moved to University College Hospital in London.

In 1859, he coined the name of 'rheumatoid arthritis' and clearly distinguished it from gout.

In 1863, he became Professor of Materia Medica and Therapeutics at King's College Hospital.

He had an extensive private practice and lived on premises at 63 Harley street, in London.

There is a street in the balneal town of Aix-les-Bains named after him.

In 1890, he was knighted and appointed 'Physician Extraordinary' to Queen Victoria (Fig. 2.1).



FIGURE 2.1 Photograph of Sir Alfred Baring Garrod who coined the term 'rheumatoid arthritis' (With kind permission from the Wellcome Library, London)

Bacteriological Theory

Following the microbial discoveries of Louis Pasteur and Robert Koch, the possibility of infection by microbes crept into the virgin field of rheumatology.

One of the first to recognize the possibility of germs as the cause of the disease was Thomas Maclagen who in 1876 introduced salicin for the treatment of rheumatic fever.

In 1901, William Hunter in London inaugurated the idea of ‘focal sepsis’ which was a bonanza for dentists, otorhinolaryngologists and even general surgeons who began to strip rheumatoid arthritis patients of their teeth, adenoids, tonsils, appendices, gall bladders and even their colons. In the United States, this was exploited on a large scale by Frank Billings in Chicago and by Ed Rosenow at the Mayo Clinic.

Virology Versus Bacteriology

A variety of viral agents have been suggested as causing direct infections of joints and thereby causing rheumatoid arthritis: Epstein–Barr virus, human parvovirus B19 and rubella.

Epstein–Barr virus would appear to be a likely candidate; however, there are some problems with this hypothesis. Epstein–Barr virus establishes persistent infection in 90% of individuals within the first years of life.

Rheumatoid arthritis is a disease predominantly of middle-aged females whilst Epstein–Barr virus exposure occurs in children aged less than 5 years. It is the wrong time-frame.

Clinical and animal studies have suggested a role for parvovirus B19 to be involved, but this could not be confirmed by other workers.

A similar lack of evidence applies to rubella, mumps and measles viruses which are diseases of concern mainly to paediatric physicians.

Other bacterial suggestions have been mycobacteria or mycoplasmas but again with no permanent convincing evidence (Rashid and Ebringer 2007).

Conclusions

Although sightings of clinical conditions resembling rheumatoid arthritis have been made throughout history, it is possible that the low life expectancy of 40 years may have precluded the florid and numerous cases of the condition we find in modern times. Increased life expectancy produced by knowledge of

microbes, adequate sewage disposal, general hygiene, good nutrition, general use of antibiotics and better scientific theories of disease has resulted in a different medical scene compared to the one seen by medical practitioners of old.

The revolutionary definition of new syndromes or diseases as described by Landré-Beauvais and Garrod has produced a recognition of clinical phenomena which may have been around for a long time but was not present in extant medical textbooks and therefore was not condoned by the medical establishments. It is to their credit that they recognised novel forms of disease in their patients.

In view of numerous probable sightings throughout history, it is unlikely that rheumatoid arthritis could be considered as a disease originating in the last 200 years. If a urinary microbe is involved, then the 'theory of recent onset of rheumatoid arthritis' may require some revision.

References

- Aceves-Avila FJ, Medina F, Fraga A. The antiquity of rheumatoid arthritis: a reappraisal. *J Rheumatol.* 2001;28:751–7.
- Aceves-Avila FJ, Delgadillo-Ruano MA, Ramos-Remus C, Gomez-Vargas A. The “Hospital Real de San Josef de Los Naturales” and the rheumatic conditions found in New Spain during the sixteenth century. *Reumatismo.* 2002;54:62–6.
- Buchanan WW, Kean WE. Rheumatoid arthritis: beyond the lymphocyte. *J Rheumatol.* 2001;28:691–2.
- Bywaters E. Historical aspects of the aetiology of rheumatoid arthritis. *Br J Rheumatol.* 1988;27 Suppl 2:110–5.
- Caughy DE. The arthritis of Constantine IX. *Ann Rheum Dis.* 1974;33:77–80.
- Dequeker J. Arthritis in Flemish paintings. *Br Med J.* 1977;1:1203–5.
- Dequeker J. Siebrandus Sixtius: evidence of rheumatoid arthritis of the robust reaction type in a seventeenth century priest. *Ann Rheum Dis.* 1992;51:561–2.
- Rashid T, Ebringer A. Rheumatoid arthritis is linked to *Proteus* – the evidence. *Clin Rheumatol.* 2007;26:1036–43.
- Snorrason E. Landré-Beauvais and his “Goutte Asthénique Primitive.” *ACTA Med SCAND.* 1952; 142, Suppl. 266:115–8.
- Thould AK, Thould BT. Arthritis in Roman Britain. *Br Med J.* 1983; 287:1909–11.