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ANKYLOSING SPONDYLITIS: YESTERDAY AND TODAY

by

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ANKYLOSING SPONDYLITIS is one of the diseases at the forefront of medical interest at the present time. This renewed interest is largely due to the exciting discovery that approximately ninety-five per cent of individuals with ankylosing spondylitis possess a human leucocyte associated antigen (HLA antigen) shown as HLA-B27.[1,2] We considered that a critical evaluation of the literature of spinal lesions both in prehistoric and modern animals together with the palaeopathological evidence for the existence of spondylitis in ancient man would be of interest to the modern-day study of the disease.

The existence of disease of the spine causing ankylosis has been described in two crocodiles, one from Egypt and the other from Cuba, dating from the Miocene and Pliocene periods respectively.[3,4] Ruffer[3] stated that "the changes due to spondylitis in human dorsal vertebrae show a great resemblance between the lesions of this disease in man and those seen in our crocodile." From examining the illustrations of the crocodile's vertebrae in Ruffer's paper[3] it is clearly evident that there is spinal fusion, but unfortunately only a few vertebrae are illustrated and no radiographs are provided. Numerous other prehistoric animals have been described with spinal lesions similar to human ankylosing spondylitis.[4,5,6] These animals consisted of many different species, which are now extinct such as the dinosaurs[4,5,6] *Diplodocus* and *Polacanthus foxi*, the cave bear *Ursus spelaeus*,[3] and the sabre-toothed tiger *Smilodon californicus*.[4] However, whether these lesions are developmental or pathological, and if pathological

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1 D. A. Brewerton, M. Caffrey, F. D. Hart, D.C.O. James, A. Nicholls, and R. D. Sturrock, 'Ankylosing spondylitis and HLA-B27', *Lancet*, 1973, **i**: 904-907.

2 L. Schlosstein, P. I. Terasaki, R. Bluestone, and C. M. Pearson, 'High association of an HLA antigen W27 with ankylosing spondylitis', *New Engl. J. Med.*, 1973, **288**: 704-706.

3 Marc A. Ruffer, *Studies in the palaeopathology of Egypt*, Chicago, University of Chicago Press, 1921, pp. 184-193.

4 Roy L. Moodie, *Palaeopathology. An introduction to the study of ancient evidence of disease*, Chicago and Urbana, University of Illinois Press, 1973, pp. 128, 410.

5 B. S. Blumberg and L. Sokoloff, 'Coalescence of caudal vertebrae in the giant dinosaur *Diplodocus*', *Arthritis Rheum.*, 1961, **4**: 592-601.

6 P. A. Zorab, 'The historical and prehistorical background of ankylosing spondylitis', *Proc. R. Soc. Med.*, 1961, **54**: 415-420.

whether they bear any relationship to human ankylosing spondylitis is impossible to judge. Zorab[6] when discussing the vertebral lesions of the dinosaur in the Natural History Museum in London cites the opinion of Dr. W. E. Swinton that "it may also have been a normal development, comparable to fusion of the sacral vertebrae in man occurring to provide increased strength of the spine beneath the armour."

Spinal ankylosis in domestic animals and primates which was observed in mummified remains of these animals in Ancient Egypt[4] is similar to that seen in modern animals.[7,8] Spinal ankylosis in domestic animals has been variously called spondylosis, spondylosis deformans, ankylosing spondylosis, and ankylosing spondylitis.[8] In many domestic animals including dogs, cats, sheep, bulls, cows, pigs, and horses the incidence of osteophytic out-growths increases with the age of the animal and is thought to be secondary to degenerative changes in the annulus fibrosus of the intervertebral disc. Thus it is not surprising that similar lesions were present in the mummies of the sacred animals of ancient Egypt. There seems little doubt, however, that a disease indistinguishable pathologically and radiologically from human ankylosing spondylitis can arise spontaneously in the old rhesus monkey *Macaca mulatta.*[7] It should be noted that sacroiliac ankylosis was not present in the monkey with the highly suggestive vertebral changes but was present in old monkeys with no spinal changes.[7]

It is of interest that a cell surface antigen which may be recognized by human HLA-B27 antisera has been found in two per cent of another primate, the chimpanzee.[9] Whether the inheritance of the same or similar cell surface antigen confers the same susceptibility to sacro-iliac and spinal ankylosis in primates as it does in man is unknown, but might provide a fruitful area of research.

EXISTENCE IN MAN

There are two problems facing a reviewer of the historical evidence of ankylosing spondylitis in ancient times. The first is that many of the specimens are incomplete and not all have been X-rayed. The second, and perhaps the most difficult problem, is that of terminology. Ankylosing spondylitis has many eponyms:[10] Bechterew's disease; Marie-Strumpell's disease; Morbus Bechterew-Marie-Strumpell; pelvospondylitis ossificans; rheumatoid ossifying pelvispondylitis; rheumatoid spondylitis; bamboo spine; poker back; spondylitis ankylopoetica; spondylitis deformans; atrophic spondylitis; spondylarthritis ankylopoetica; ankylosing spondyloarthritis; atrophic ligamentous spondylitis; ossifying ligamentous spondylitis; rhizomelic spondylosis; spondylitis rhizomelique. Moreover, many of the earlier workers, such as Ruffer[11] use

[7] L. Sokoloff, K. C. Snell, and H. C. Stewart, 'Spinal ankylosis in old rhesus monkeys', *Clin. Orthop.*, 1968, **61:** 285-293.

[8] K. V. F. Jubb and P. C. Kennedy, 'Degenerative diseases of joints (arthropathy)', in *Pathology of domestic animals*, 2nd ed., New York, Academic Press, 1970, pp. 68-77.

[9] F. H. Bach and J. J. van Rood, 'The major histocompatibility complex – genetics and biology', *New Engl. J. Med.*, 1976, **295:** 806-813.

[10] V. Wright and J. M. H. Moll, *Seronegative polyarthritis*, Amsterdam, North Holland Publishing Co., 1976, pp. 81-84.

[11] M. A. Ruffer and A. Rietti, 'On osseus lesions in Ancient Egyptians', *J. Path. Bact.*, 1912, **16:** 439-465.

Virchow's term "spondylitis deformans" to describe changes which are obviously degenerative in nature. These early workers claimed an extraordinarily high prevalence of "spondylitis deformans", which was interpreted as ankylosing spondylitis, in Egyptian, Roman, and Coptic times.[11,12] It is apparent on reviewing the photographs provided[11] of the specimens that many had ankylosing hyperostosis, a disease which occurs in old age with bony ankylosis of the spine, without sacro-iliac fusion.[13, 14] Indeed, Figure 33 of Ruffer and Rietti[11] illustrates this point where the lesion is clearly osteophytic and is described as "spondylitis deformans". In the same paper, however, there are illustrations (Figures 1-5 and 58-61) which show massive bony fusion of vertebrae consistent with ankylosing spondylitis.

More definite radiological evidence of the existence of ankylosing spondylitis in Egyptian times has recently been reported. [15, 16] Two skeletons, found by Petrie[17] at Hou and dated to about 1500 B.C., show equivocal radiological spinal changes of ankylosing spondylitis. The third, from Naqada, shows syndesmophyte formation and calcification of the interspinous ligament, although the comment of "squaring" of the vertebral bodies cannot be made from the antero-posterior radiograph illustrated.

The diagnosis of ankylosing spondylitis is heavily dependent upon the presence of radiograph sacroiliitis.[18] Ruffer[19] stated "the majority of skeletons with spondylitis deformans had sacro-iliac articular surfaces unworn by friction and with no traces of eburnation." However, he did find two examples of sacro-iliac disease. The first was an elderly female with a large ulcer over the sacrum with a sinus extending from the pudendal labium to the buttock. This ulcer was probably a pressure sore and responsible for the sacro-iliac changes. The second showed ankylosis of the iliac bones and Ruffer describes "the anterior sacro-iliac ligament was completely ossified as far as the lower border of the first sacral vertebra, and posteriorly the bones were united by two strong bridges of osseus tissue separated by a small interval. The articulation appeared to be normal. . . . The process, therefore had attached the sacro-iliac ligament and all the tendons at their points of attachment with the ischium and pubis." It is therefore possible that Ruffer is describing the changes of ankylosing spondylitis including the enthesopathy[20] which frequently occurs.

Despite the lack of radiological evidence of sacro-iliitis we feel that there is sufficient evidence that ankylosing spondylitis existed in Ancient Egypt, but would support

[12] G. Elliott Smith and F. Wood Jones, 'Report on human remains', *The archaeological survey of Nubia 1907-1908.* Cairo, National Printing Department, 1910, vol. 2, pp. 273-277.

[13] J. Forestier and J. Rotes-Querol, 'La hiperostosis anguilesante vertebral senil', *Medna clin.*, 1950, **15:** 84-89.

[14] J.Harris, A. R. Carter, E. N. Glick, and G. O. Storey, 'Ankylosing hyperostosis. 1. Clinical and radiological features', *Ann. rheum. Dis.*, 1974, **33:** 210-215.

[15] J. B. Bourke, 'Review of palaeopathology of arthritic diseases', in D. Brothwell and A. T. Sandison (editors), *Diseases of antiquity*, Springfield, Ill., Thomas, 1967, pp. 357-360.

[16] J. B. Bourke, 'The palaeopathology of the vertebral column in Ancient Egypt and Nubia, *Med. Hist.*, 1971, **15:** 363-375.

[17] W. M. Flinders Petrie, *Diaspolis Parva (The cemeteries of Abadiyeh and Hu)*, London, Special Extra Publication of the Egypt Exploration Fund, 1901.

[18] J. P. Gofton, in P. H. Bennett and P. H. N. Wood (editors), *Population studies of the rheumatic diseases*, Amsterdam, Excerpta Medica Foundation, 1968, pp. 314, 456.

[19] M. A. Ruffer, 'Arthritis deformans and spondylitis in Ancient Egypt', *J. Path. Bact.*, 1918, **22:** 152-196.

[20] J. Ball, 'Enthesopathy of rheumatoid and ankylosing spondylitis', *Ann. rheum. Dis.*, 1971, **30:** 213-223.

Bourke's conclusion: "It is certain that ankylosing spondylitis as we now recognise it was an uncommon disease in ancient Egypt."[15]

Suggestive descriptions of ankylosing spondylitis were made by Hippocrates[10] and the fifth-century neurologist Caelius Aurelianus.[21] Hippocrates referred to the fact that "vertebrae of the spine and neck may be affected with the pain, and it extends to the os sacrum." Aurelianus described a condition where "the patient is seized by pain in the nates, moves slowly, and can only bend or stand erect with difficulty." A possible reference is also made by St. Luke (Chapter 13 verses 10-13) of a woman "bent over and could not straighten up at all."

Perhaps the first family study of ankylosing spondylitis was that of the famous Florentine family, the Medicis, whose remains were studied by Costa and Weber[22] and subsequently reported by Pizon[23] when their bodies were removed from the Medici chapel in 1945. Four generations of male members of this family – Cosimo il Vecchio, his son Piero il Gottoso, his grandson Lorenzo il Magnifico, and his great-grandson Guiliano Duco de Nemours, were examined and two almost certainly suffered from the disease.

Cosimo il Vecchio (1389-1464) was the first of the Medicis to achieve clear pre-eminence in Florence and to establish the powerful influence they were to assert on the Italian Renaissance. He began to suffer at the age of forty-three with pain in the feet which spread to his hands and knees eight year later and thereafter troubled him with many acute attacks of pain in all his joints until he was "tout casse". He died at the age of seventy-six and his son Piero remarked that his father had difficulty with micturition and suffered recurrent attacks of fever in the month prior to his death. Costa describes Cosimo's skeleton as showing signs of ossification of the vertebral ligaments with bony bridging between the vertebral bodies and complete fusion of the interapophyseal joints of the dorsal vertebrae. There were degenerative changes in the left hip joint and the right ankle joint was fused. The whole skeleton was osteoporotic and it is recorded by Costa as demonstrating many of the features of ankylosing spondylitis.

Cosimo's son, Piero il Gottoso (Peter the Gouty, 1416-1469) is reported to have had an attack of fever at the age of twenty-six and to have developed arthritis in his feet at the age of forty. The arthritis in his feet became worse and he often complained of febrile attacks and an itching skin. He died at the early age of fifty-three – "fort navre de gouttes" ("wounded by gout") with uraemic attacks and loss of speech. Examination of the skeleton revealed ankylosis of the sacro-iliac joints with lumbar and dorsal syndesmophyte formation. The left knee was ankylosed in flexion and the feet were fused in equino-varus with fusion of the tarsus and carpus.

Lorenzo il Magnifico (1449-1492) is reputed to have had a chronic arthritis, but this did not prevent him from holding power in Florence from 1469 until his death in 1492. His skeleton showed a curved left humerus with osteophytic formation in the diaphysis and the greater tuberosity, but no changes of spondylitis.

[21] C. C. Mettler, *History of medicine*, Philadelphia, Blakistow, 1947, pp. 813-814.

[22] A. Costa and G. Weber, 'Le alterazioni morbose del sistema scleritico in Cosimo dei Medici il vecchio, in Piero il gottoso, in Lorenzo il magnifico, in Guiliano duca di Nemours', *Archo De Vecchi*, 1955, **23:** 1-69.

[23] P. Pizon, 'La pathologie osteo-articulaire de quatre Medicio', *Presse méd.*, 1956, **64:** 1483-1484.

Guiliano (1479-1516), who became Duco de Nemours, was said to have been afflicted with fevers from the age of nine onwards and is supposed to have suffered with arthritis for thirty-three years. He died at the age of thirty-seven in a grossly debilitated condition possibly due to tuberculosis. Examination of the skeleton revealed that the terminal interphalangeal joint of the left index finger was missing and the four metacarpals and two phalanges of the left hand showed total ankylosis of the metacarpophalangeal joints with thinning of the bony cortex.

It would seem, therefore, that both Cosimo and his son Piero may well have had some form of spondylitis with peripheral joint involvement which could have been produced by ankylosing spondylitis or by Reiter's syndrome (complicated perhaps by gout in Piero's case). The significance of the skeletal abnormalities in the case of Lorenzo and Guiliano is less certain but could have been produced by psoriatic arthritis, rheumatoid arthritis, or even syphilis. However, it is known that first degree relatives of patients suffering from ankylosing spondylitis have an increased prevalence of Reiter's syndrome, psoriatic arthritis, and colitic arthritis,[24] and this could account for the propensity of Cosimo's descendants to develop rheumatic disorders.

Probably the first clear pathological description of the disease was by the Irish physician Bernard Connor (1666-1698) who in his M.D. thesis of 1691 to the University of Rheims, entitled "Une Dissertation Physique sur la Continuité de Plusiers Os, à l'Occasion d'une Fabrique Suprenante d'une Tronc de Squelette Humain, où les Vertébres, les Côtes, l'Os Sacrum, et les Os des Iles, qui Naturellement sont Distinct et Séparés, ne font qu'un Seul Os Continu et Inséparable", and subsequently expanded and translated into English,[25] described an individual whose vertebral bodies were "so straightly and intimately joined, their ligaments perfectly bony, and their articulations so effaced, that they really made but one uniform continuous bone." The figure Connor made of this skeleton shows bony ankylosis of the vertebral column and also of one knee joint, and together with his pathological description almost certainly represents a case of ankylosing spondylitis.

A similar case was reported in the form of a letter from Robert, Lord Bishop of Cork, to the Right Honourable John, Earl of Egmont, F.R.S.[26] Although this case has been claimed to display features of myositis ossificans,[27] the descriptions and figures make no reference to the other congenital abnormalities which occur in this condition.

William Hunter (1718-1783) bequeathed his musuem to his Alma Mater, the University of Glasgow. In the Pathological Department of the Royal Infirmary there is an interesting collection of Hunter's specimens of bone and joint disease. Among the specimens are two whose spines show ossification of the anterior and supra-spinous ligaments with bony ankylosis consistent with ankylosing spondylitis (6.103, 6.105).

[24] V. Wright and J. M. H. Moll, 'Ankylosing spondylitis', *Br. J. Hosp. Med.*, 1973, **9:** 331-341.

[25] Bernard Connor, 'An extract of a letter from Bernard Connor, M.D. to Sir Charles Walgrave', *Phil. Trans. R. Soc. Lond.*, 1695-1697, **19:** 21.

[26] Robert, Lord Bishop of Corke, 'A letter from the right Reverend Father in God, Robert Lord Bishop of Corke, to the Right Honourable John, Earl of Egmont, F.R.S., concerning an extraordinary skeleton, and of a man who gave such to a child', ibid., 1740-1741, **41:** 810-814.

[27] D. O'Connell, 'Ankylosing spondylitis. The literature up to the close of the nineteenth century', *Ann. rheum. Dis.*, 1956, **15:** 119-123.

Unfortunately, one specimen (6,101), labelled in the guidebook "Ankylosis of Entire Vertebral Column, Costovertebral and First Costo-sternal Articulations, and Sacro-iliac Synchondroses, Arthritis Ossificans(?)" is missing. However, the description given by Teacher,[28] although long, is worthwhile stating in full as it is without doubt that of ankylosing spondylitis:

> The vertebrae from the atlas to the last lumbar are ankylosed into a single piece – partly by extensive bony outgrowths from the edges of the bodies similar to those in the preceding specimen, partly by ossification of various ligaments, and ankylosis of a few of the articular processes. There is a decided increase of the normal curve of the lower cervical and upper dorsal regions of the spine; the other curves are about normal. The anterior common ligaments are extensively ossified. These along with the out-growths from the edges of the bodies enclose the inter-vertebral discs in a ring of bone, preventing their condition being made out except in a few cases where the ring is incomplete. At these points the space is seen to be empty, narrowed a little perhaps, but showing no trace of ossification across it. From behind, the posterior common ligament for a great part of its extent and the transverse ligament of the atlas can be seen to be ossified. The odontoid process of the axis is ankylosed to the anterior arch of the atlas. In the dorsal region the ligamentum subflava and interspinous ligaments, and the capsular and other ligaments of the ribs, are all ossified. The cavities of one or two of the costo-vertebral joints, which having been broken or cut, show in section that they are not all obliterated by bone; the ossification which has produced the ankylosis is in the ligamentous structures around them; these joints are consequently thickened. The first two ribs are firmly ankylosed to the sternum by similar thick masses of bone surrounding the joints. Part of the cartilages of the eighth, ninth and tenth ribs are preserved; they are sheathed with bone, and also show some ossifications in their interior. The sterno-clavicular joints are very much deformed by osseous growths around them; the right also shows eburnation of part of its articular surface, such as is seen in arthritis deformans. The intersternal joint is cased with bone growing around its edges; its articular surface has remains of cartilage on it, and there has been no attempt at ossification across it. The sacrum is not ankylosed to the lumbar vertebrae, but there are considerable osseous outgrowths from the edges of its upper surface. The coccyx is ankylosed to it. Both sacro-iliac synchondroses have been sawn off, and the right one forms the next specimen; it was particularly firmly ankylosed to the sacrum. The left was less firmly ankylosed; it is not now in the collection. The greater part of the changes in this and the succeeding specimen are clearly not those of arthritis deformans, but rather of the rare disease described as arthritis ossificans or universal bony ankylosis. Unfortunately, the history of the specimen is unknown.

The right half of the pelvis of this specimen is still in the musum (6.102) and shows a firmly ankylosed sacro-iliac joint and "osseus outgrowths in the position of the attachments of muscles around the crest of the ilium, on the anterior inferior spine, and above the acetabulum where the rectus femoris arises, along the tuberosity of the ischium, iliopectineal line, and on the front of the body of the pubis. . . . The hip appears not to have ankylosed. There is no eburnation or scoring of the articular surfaces, as in arthritis deformans." Five other specimens of the pelvis also show sacro-iliac fusion.

Adequate clinical descriptions of the disease were not made until the following century, apart from a vague reference by Thomas Sydenham (1624-1689) to "rheumatic lumbago". O'Connell[27] cites Lyons[29] as being the first to give a clinical description of the disease, and although the description of the spinal and articular lesions are compatible, features such as the skin being "blistered" and the urine forming a "white earthy sediment" raise the possibility of Reiter's syndrome or psoriatic arthritis.

In his book *Pathological and surgical observations on diseases of the joints'* Sir

[28] John H. Teacher, *Catalogue of the anatomical and pathological preparations of Dr. William Hunter*, Glasgow, University of Glasgow, 1900.

[29] P. M. Lyons. 'Remarkable case of rapid ossification of the fibro-cartilaginous tissues or pure general ankylosis', *Lancet*, 1831, **i**: 27-29.

Benjamin Brodie[30] was the first to describe iritis as a complication of ankylosing spondylitis, and Copeman[31] considered he was the first to associate the pathological changes with the clinical features of the disease.

In the latter quarter of the nineteenth century the disease came to the general attention of the medical profession, particularly from the observations of Fagge,[32] Davies-Colley,[33] Bechterew,[34] Strumpell,[35] Marie,[36] and Leri.[37] It is generally agreed[24, 27] that of these authors Marie deserves to have his name linked eponymously with the disease.

During this century following the Second World War there was a rapid burgeoning of interest in the rheumatic diseases especially after 1948 when cortisone was introduced,[38] the L.E. cell phenomenon was described,[39] and the concept of "collagen" diseases was proposed.[40] In addition during the war and during conscription of young males for the Armed Forces after the war, physicians on both sides of the Atlantic became aware of the relatively high prevalence of ankylosing spondylitis.[41, 42] However, in the United States predominantly the consensus of opinion was that ankylosing spondylitis was a variant of rheumatoid arthritis,[42-54] on

[30] Benjamin Collins Brodie, 'Diseases simulating caries of the spine', in *Diseases of the joints*, 5th ed., London, Longmans, 1850, Case LXXIII.

[31] W. S. C. Copeman, *Textbook of the rheumatic diseases*, 3rd ed., Edinburgh, Churchill Livingstone, 1964, pp. 256-275.

[32] C. H. Fagge, 'A case of simple synostosis of the ribs to the vertebrae, and of the arches and articular processes of the vertebrae themselves and also of one hip joint', *Trans. path. Soc. Lond.*, 1877, **28:** 201.

[33] N.Davies-Colley, 'Synostosis of vertebrae', ibid., 1885, **36:** 359-363.

[34] V. M. Bechterew, 'Steifigheit der wirbelsaule und ihre verkrumnung als besondere erkrankungsform,' *Neurol. Zentbl.*, 1893, **12:** 426.

[35] A. Strumpell, 'Bemerkung über die chronische ankylosirende entzungdung der wirbelsaule und der huftgelenke', *Dl. 2. Nerv. Heilk*, 1897, **11:** 338-342.

[36] P. Marie, 'Sur la spondylose rhizomelique', *Revue Méd.*, 1898, **18:** 285-315.

[37] A. Leri, 'La spondylose rhizomelique', ibid., 1899, **19:** 597.

[38] P. S. Hench, E. C. Kendall, C. H. Slocumb, and H. F. Polley. 'Effect of hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotrophic hormone on rheumatoid arthritis; preliminary report', *Proc. Staff Meet. Mayo Clin.*, 1949, **24:** 277-297.

[39] M. M. Hargraves, H. Richmond, and R. Morton, 'Presentation of 2 bone marrow elements the "tart" cell and the "L.E." cell', ibid., 1948, **23:** 25-28.

[40] P. Klemperer, A. D. Pollack, and G. Baehr, 'Diffuse collagen disease; acute disseminated lupus erythematosus and diffuse scleroderma', *J. Amer. med. Ass.*, 1942, **119:** 331-332.

[41] F. D. Hart, K. C. Robinson, F. M. Allchin, and N. F. Maclagan, 'Ankylosing spondylitis', *Quart. J. Med.*, 1949, **18:** 217-234.

[42] E. W. Boland and A. J. Present, 'Rheumatoid spondylitis', *J. Amer. med. Ass.*, 1945, **117:** 843-849.

[43] A. Oppenheimer, 'Diseases of apophyseal articulations', *J. Bone Jt Surg.*, 1938, **20:** 285-313.

[44] C. J. Smyth, R. H. Freyberg, and I. Lampe, 'Roentgen therapy for rheumatoid arthritis of the spine', *J. Amer. med. Ass.*, 1941, **117:** 826-831.

[45] P. S. Hench, W. Bauer, E.W. Boland, M. H. Dawson, R. H. Freyberg, W. P. Holbrook, J. A. Kay, L. M. Leckie, and C. McEwen, 'Rheumatism and arthritis. Review of the American and English literature for 1940', *Ann. intern. Med.*, 1941, **15:** 1002-1108.

[46] H. F. Polley and C. H. Slocumb, 'Rheumatoid spondylitis; a study of 1035 cases', ibid., 1947, **26:** 240-249.

[47] W. A. Law, 'Surgery in the treatment of rheumatoid arthritis and ankylosing spondylitis', *Proc. R. Soc. Med.*, 1948, **41:** 251-260.

[48] W. Lennon and I. S. Chalmers, 'Ankylosing spondylitis', *Lancet*, 1948, **i:** 12-15.

[49] A. H. Crenshaw and J. F. Hamilton, 'Rheumatoid spondylitis', *Sth. med. J.*, 1952, **45:** 1055-1061.

[50] B. Blumberg and C. Ragan, 'The natural history of rheumatoid spondylitis', *Medicine, Baltimore*, 1956, **35:** 1-31.

[51] H. K. Gibson, 'Ankylosing spondylitis. Aetiology and pathology', *J. Fac. Radiol.*, 1957, **8:** 193-200.

the grounds of similar synovial pathology in peripheral joints, occurrence of peripheral joint disease and raised erythrocyte sedimentation rate. European[55-68] opinion, on the other hand argued for the distinction of ankylosing spondylitis on the grounds of absence of subcutaneous nodules, predominantly males affected, earlier age of onset, lack of response to chrysotherapy, and more favourable prognosis. The discovery of rheumatoid factor by Waaler[69] and Rose *et al.*,[70] and its widespread clinical application,[71] confirmed the European opinion that the two diseases are separate entities.

The growing awareness of the value of epidemiological studies of the rheumatic diseases necessitated clinical, radiological, and serological criteria being established for the different diseases, including ankylosing spondylitis. An initial meeting was held at the National Institutes of Health, Bethesda, Maryland, U.S.A., followed by a second symposium in Rome, in 1960 sponsored by the World Health Organisation through the Council for International Organisations of Medical Science where diagnostic criteria for ankylosing spondylitis were established. These criteria did not prove

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[52] J. J. Calabro, 'A therapeutic approach to rheumatoid spondylitis', *Gen. Practnr., Lond.*, 1960, **22:** 88-95.

[53] W. Graham, 'Is rheumatoid spondylitis a separate entity?', *Arthritis Rheum.*, 1960, **8:** 88-90.

[54] L. D. Baker, 'Marie-Strumpell arthritis and undiagnosed low back pain', *Neb. St. med. J.*, 1948, **33:** 331-337.

[55] W. C. Kuzell, 'Ankylosing spondylarthritis (Marie-Strumpell-Bechterew disease)', *Stanford med. Bull.*, 1948, **6:** 324-333.

[56] R. Mowbray, A. L. Latner, J. Howard, and J. H. Middlemiss, 'Ankylosing spondylitis – radiological, clinical and biochemical investigations in a series of cases', *Quart. J. Med.*, 1949, **18:** 187-201.

[57] A. J. Williams, 'Rheumatoid (Marie-Strumpell) spondylitis', *Calif. Med.*, 1949, **70:** 257-261.

[58] L. J. A. Parr, P. White, and E. Shipton, 'Some observations on 100 cases of ankylosing spondylitis', *Med. J. Aust.*, 1951, **1:** 240-249.

[59] H. F. Turney, 'Ankylosing spondylitis', *Proc. R. Soc. Med.*, 1952, **45:** 57-62.

[60] W. S. C. Copeman and R. M. Mason, 'The medical treatment of chronic backache', *Med. Press*, 1952, 228-292.

[61] L. D. Baker, 'Diagnosis and care of Marie-Strumpell arthritis', *Postgrad. Med.*, 1954, **15:** 428-436.

[62] R. M. Stecher and A. H. Hersh, 'Familial occurrence of ankylosing spondylitis', *Br. J. phys. Med. ind. Hyg.*, 1955, **18:** 176-183.

[63] F. D. Hart and N. F. Maclagan, 'Ankylosing spondylitis. A review of 184 cases', *Ann. rheum. Dis.*, 1955, **14:** 77-83.

[64] H. J. Burrows and J. W. Stewart, 'Discussion on ankylosing spondylitis', *Proc. R. Soc. Med.*, 1957, **50:** 427-432.

[65] V. Forbech, 'Do the mutual features dominate the separating features in rheumatoid arthritis and rheumatoid spondylitis?', *Acta med. scand.*, 1958, **341:** 43-46.

[66] J. Forestier, 'Diagnostic entre la polyarthrite chronique evolutive (rheumatoid arthritis) et la spondylarthritie ankylosante', ibid., 1958, **341:** 33-42.

[67] V. A. McKusick, 'Genetic factors in diseases of connective tissue – a survey of the present state of knowledge', *Amer. J. Med.*, 1959, **26:** 283-302.

[68] J. J. de Blecourt, A. Polman, and T. de Blecourt-Meindersma, 'Hereditary factors in rheumatoid arthritis and ankylosing spondylitis', *Ann. rheum. Dis.*, 1961, **20:** 215-220.

[69] E. Waaler, 'On the occurrence of a factor in human serum activating specific agglutination of sheep blood corpuscles', *Acta path. microbiol. Scand.*, 1940, **17:** 172-188.

[70] H. M. Rose, C. Ragan, E. Pearce and M. O. Lipman, 'Differential agglutination of normal and sensitized sheep erythrocytes by sera of patients with rheumatoid arthritis', *Proc. Soc. exp. Biol. Med.*, 1948, **68:** 1-6.

[71] H. Bartfield, 'Incidence and significance of seropositive tests for rheumatoid factor in non rheumatoid diseases', *Ann. intern. Med.*, 1960, **52:** 1059-1066.

entirely satisfactory and accordingly they were amended at a third symposium in New York City in 1966.[72] These "New York" criteria, we believe, should not only be used in clinical rheumatology practice and in epidemiological surveys, but be applied as far as possible by the palaeopathologist and medical historian.

The discovery of the close association between the histocompatibility antigen, HLA-B27, and ankylosing spondylitis[73] has resulted in a veritable explosion of interest in the disease. The finding that 95 per cent of patients with ankylosing spondylitis have HLA-B27 in contrast to rheumatoid arthritis where the frequency of this antigen is not increased (eight per cent) further supports the contention that they are different disease processes. In fact when the two diseases do infrequently co-exist both rheumatoid factor and HLA-B27 may be demonstrated serologically[74, 75] and the onset of the two diseases in the individual can be recognized.[76]

The fact that histocompatibility antigens are inherited co-dominantly adds support to the historical evidence that the disease is of great antiquity. Recent studies indicate that the prevalence of ankylosing spondylitis is proportional to the frequency of HLA-B27 in the particular population studied.[77] We wonder whether the high prevalence of sacro-iliac arthritis found in the Bodega Head Californians of about 500 B.C.[78] may have been due to ankylosing spondylitis, as their probable descendants, the North American Indians, have a high frequency of HLA-B27[79] and a consequent high prevalence of sacro-iliitis and ankylosing spondylitis.[80]

We have no evidence that individuals carrying the antigen HLA-B27, both with and without ankylosing spondylitis, are any less fertile. In addition, there is no evidence that either the disease or the presence of HLA-B27 would be disadvantageous in terms of natural selection.[81] Indeed, we may cite the remarkable Medici family in support of this. The onset of the disease as seen today is mostly in the third and fourth decades, and may not have seriously influenced an individual's ability to survive, particularly when life expectancy was much less than today.[82] It may be that the inheritance of this antigen may have conferred a selective advantage, as antigen frequencies in populations have been claimed to have been modified by malarial infection, perhaps by differential selection.[83] Thus we cannot agree with the claims made by other authors

[72] Gofton, op. cit., note 18 above.

[73] Brewerton *et al.*, op. cit., note 1 above. Schlosstein *et al.*, op.cit., note 2 above.

[74] G. H. Fallett, M. Mason, H. Burry, A. Mowat, I. Boussina, and J. C. Gerster, 'Coexistence of rheumatoid arthritis and ankylosing spondylitis – report of 10 cases', *J. Rheumatol.*, 1977, suppl. 3, 70-77.

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[77] J. A. Sachs and D. A. Brewerton, 'HLA, ankylosing spondylitis and rheumatoid arthritis', *Br. med. Bull.*, 1978, **34**: 275-278.

[78] J. G. Roney, 'Palaeopathology of a Californian archaeological site', *Bull. Hist. Med.*, 1959, **33**: 97-109.

[79] J. P. Gofton, A. Chalmers, G. E. Price, and C. E. Reeve, 'HL-A27 and ankylosing spondylitis in B.C. Indians', *J. Rheumatol.*, 1975, **2**: 314-318.

[80] J. P. Gofton, P. H. Bennett, H. A. Smythe, and J. L. Decker, 'Sacro-ilitis and ankylosing spondylitis in North American Indians', *Ann. rheum. Dis.*, 1972, **31**: 474-481.

[81] E. P. Radford, R. Doll, and P. G. Smith, 'Mortality among patients with ankylosing spondylitis not given X-ray therapy', *New Engl. J. Med.*, 1977, **297**: 572-576.

[82] Calvin Wells, *Bones, bodies and disease*, London, Thames & Hudson, 1964, pp. 176-179.

[83] A. Piazza, M. C. Belvedere, D. Bernoco, C. Conighi, L. Contu, E. S. Curtoni, P. L. Mattiuz, W. Mayr,

that "ankylosing spondylitis was probably biologically disadvantageous before the advent of effective treatment"[84] since the historical and palaeopathological evidence suggests that the disease is of great antiquity and has not disappeared as a result of natural selection.

There is, therefore, good evidence that ankylosing spondylitis in man has been present in many populations from ancient times and the strong link between the presence of the disease and the possession of HLA-B27 would lend support to this view provided that HLA antigen frequencies in populations have remained fairly constant down the centuries. The position in animals is less clear and the spondylitic-like lesions observed in primates warrant further investigation. Lamartine commented that "History teaches everything, even the future"[85] and this statement is very appropriate to a study of ankylosing spondylitis since much is still to be learned from a re-evaluation of the palaeopathology of this interesting condition.

SUMMARY

The literature of spinal lesions resembling human ankylosing spondylitis in prehistoric and modern animals is critically reviewed. Spinal fusion in prehistoric animals is probably a normal development similar to the fusion of the sacrum in man. In domestic animals many of the instances of ankylosing spondylitis are due to osteophytic outgrowths, although the disease clearly exists in primates. It is unknown whether there is an association with the major histocompatibility antigen, HLA-B27, in these animals.

Despite the lack of radiological evidence of sacroiliitis it seems certain that the disease existed in Ancient Egypt. The famous Florentine family of the Medicis was probably the first family studied with ankylosing spondylitis. The association of the disease with HLA-B27 probably explains why the disease in man is of such antiquity, since there is no evidence that the presence of HLA-B27 is disadvantageous in natural selection.

P. Richiardi, G. Scudeller, and R. Ceppellini, 'HL-A variation in four Sardinian villages under differential selective pressure by malaria', in J. Dausset and J. Colombani (editors), *Histocompatibility testing*, Copenhagen, Munksgaard, 1972, pp. 73-84.

[84] J. S. Percy and A. S. Russell, 'Prevalence of ankylosing spondylitis and its association with HL-A27', *J. Rheumatol.*, 1975, **2**: 351-354.

[85] Alphonse de Lamartine, speech at Macon, France, 1847.