Paleopathology

Origins of spondyloarthropathy in Perissodactyla

B.M. Rothschild, D.R. Prothero, C. Rothschild

Reprint

Clinical and Experimental Rheumatology 2001; **19**: 628-632.

Origins of spondyloarthropathy in Perissodactyla

B.M. Rothschild[1,2,3], D.R. Prothero[4], C. Rothschild[1]

Bruce M. Rothschild, MD; Donald R. Prothero, PhD; Christine Rothschild, RN.

[1]Arthritis Center of Northeast Ohio, [2]Northeastern Ohio Universities College of Medicine, Youngstown, Ohio, USA; [3]Carnegie Museum of Natural History, Pittsburgh, Pennsylvania; [4]Department of Geology, Occidental College, Los Angeles, California, USA.

Please address correspondence and reprint requests to: Bruce M. Rothschild, MD, Arthritis Center of Northeast Ohio, 5500 Market Street, Youngstown, OH 44512, USA. E-mail: bmr@neoucom.edu

Received on September 5, 2000; accepted in revised form on May 28, 2001.

Clin Exp Rheumatol 2001; 19: 628-632.

Key words: Spondyloarthropathy, reactive arthritis, horse, rhinoceros, animal model of arthritis.

ABSTRACT

Objective

Spondyloarthropathy has clearly been documented as not limited in occurrence to humans. Transmammalian in nature, it is of interest to understand the antiquity, and perhaps the origins, of this disorder in animal groups sufficiently represented in the skeletal record.

Methods

Fossil and recent skeletons of perissodactylae from North America were systematically examined to determine the occurrence and population frequency of spondyloarthropathy.

Results

Spondyloarthropathy was the most common form of arthritis recognized in the extant and fossil records. Common in extinct families such as Brontotheriidae and Chalicotheriidae, a progressive increase in the frequency of spondyloarthropathy was observed through geologic time in Equidae and Rhinocerotidae.

Conclusion

Erosive arthritis of the spondyloarthropathy variety is now documented as not only persisting in Perissodactyla, but as actually increasing significantly in frequency (3-6 fold). Given the unusual evolutionary penetrance of this "disease," the possibility must be considered that its persistence provides evidence for some unknown benefit to the affected host.

Introduction

Assessment of the antiquity and implications of the erosive arthritis spondyloarthropathy has been limited by the available anthropologic record (1). Contrary to arthritis caused by direct bacterial invasion (2,3), the prolonged existence of other forms of erosive arthritis has only recently been recognized (3). As spondyloarthropathy is not limited in occurrence to humans (4-8), an alternative approach was considered. Given the substantial representation of mammals in the fossil record (4-10), it seemed appropriate to investigate an order in which contemporary occurrence has been noted. Notation of the frequent occurrence of erosive arthritis in extant perissodactyls stimulated study of its nature and antiquity.

Materials and methods

Survey was performed of modern and fossil mammal holdings of the Academy of Natural Sciences of Philadelphia, Pennsylvania; American Museum of Natural History, New York City, New York; British Museum of Natural History, London, United Kingdom; Carnegie Museum of Natural History, Pittsburgh, Pennsylvania; Cleveland Museum of Natural History, Ohio; Canadian Museum of Civilization, Hull, Ontario, Canada; Denver Museum of Natural History, Colorado; Field Museum of Natural History, Chicago, Illinois; Florida Museum of Natural History, University of Florida, Gainesville; Institute Royale de Sciences Naturale, Brussels, Belgium; Los Angeles County Museum of Natural History, California; Museum of Comparative Zoology, Cambridge, Massachusetts; Michigan State Museum of Natural History, East Lansing, Michigan; Museum of Vertebrate Zoology, Berkeley, California; Museo Distoria Naturale-Sezione di Zoologia "La Specola" Universita di Firenza; National Museum of Canada, Ottawa, Ontario, Canada; National Museum of Kenya, Nairobi, Kenya; National Museum of Natural History, Washington, D.C.; Royal Ontario Museum, Toronto, Ontario, Canada; Rykshius Museum van Naturlyhe Historie, Leiden, Netherlands; San Diego Museum of Natural History, California; Simon Fraser University, Vancouver, British Columbia, Canada; South Carolina State Museum, Charleston; University of Arizona, Tucson, Arizona; University of Kansas Muse-

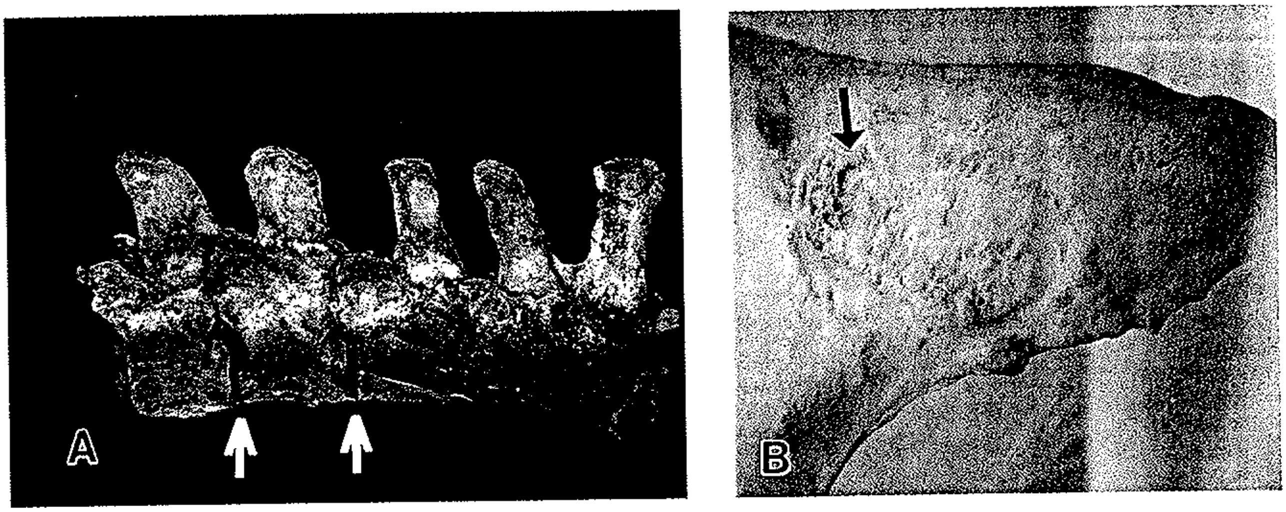

Fig. 1. Spondyloarthropathy in Pleistocene and modern horses. (**A**) Lateral view of fused vertebrae. Full fusion noted on right with early calcification (**arrow**) in anulus fibrosis on left. (**B**) "En face" view of sacroiliac joint. Erosions marked by arrow.

um of Natural History, Lawrence, Kansas; University of Michigan, Ann Arbor; University of Nebraska, Lincoln, Nebraska; University of Pretoria, South Africa; University of Witterswatersrand, Johannesburg, South Africa; and Yale Peabody Museum, New Haven, Connecticut.

The diagnosis of spondyloarthropathy was made on the basis of specific sacroiliac (SI) or zygapophyseal (ZA) joint erosions or fusion or vertebral bridging in the form of syndesmophytes (1-12). The skeletal remains of fossil and recent mammals were subjected to visual examination of all articular regions, to identify all occurrences of articular and peri-articular bony alterations throughout each skeleton, to specify the types of bony alterations at each occurrence, and to map the distribution of occurrences in each skeleton. Lesions were distinguished from artifact as previously described (3). In the event of disagreement as to whether a lesion represented an erosion or artifact, for the purposes of this study it was treated as artifact.

The incomplete nature of preservation of skeletal fossil remains can compromise the assessment of the population frequency of spondyloarthropathy. For this study the sacroiliac joint was therefore considered "sentinel." The ratio of affected to preserved sacroiliac joints was utilized to estimate the population frequency of spondyloarthropathy.

Results

Crater-shaped holes with smooth, rounded edges in the iliac component of or fusion through the sacroiliac joint identified spondyloarthropathy in Perissodactyla (Fig. 1). The presence of syndesmophytes or sacroiliac joint involvement was used as the numerator in determining the frequency of spondyloarthropathy. Given the incomplete state of the fossil record, the presence of sacroiliac joints themselves was utilized as the denominator. Although spondyloarthropathy can also produce erosions in other joints (1-12), isolated occurrence cannot be evaluated epidemiologically, and so will be listed solely for completeness. Characteristic erosive lesions with reactive new bone formation were found as isolated phenomenon in metacarpals of three Miocene Rhinocerotidae (UF 59699, UF 59700 and UF 59702), metapodials (UNSM 1568-46 and UNSM 1869-46) and scapula (UNSM 7196-80) of Teleoceras, and calcanei of Pliocene Rhinocerotidae not identified as to species (UNSM 676-40 and UNSM 3012-49).

Shoulder and knee involvement were

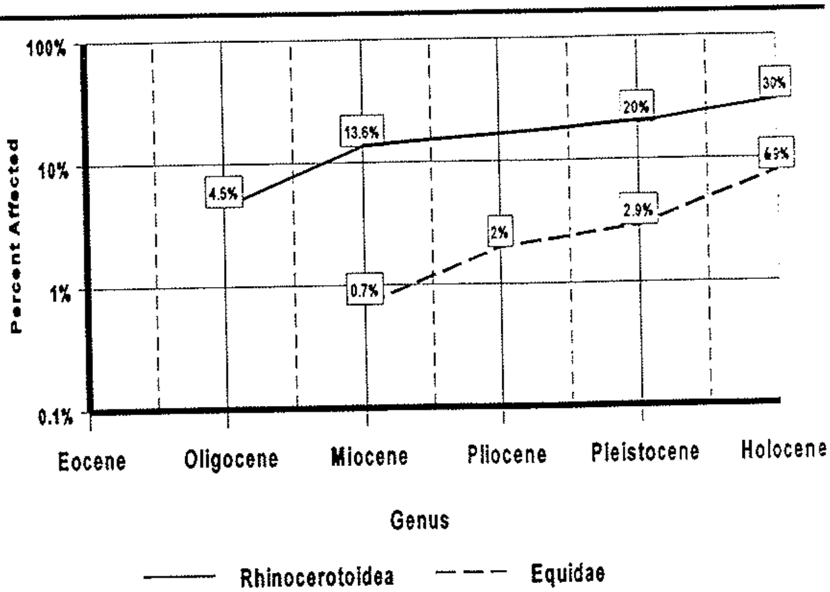

Fig. 2. Phylogenetic distribution of spondyloarthropathy in Perissodactyla by epoch.

Table I. Phylogenetic distribution of spondyloarthropathy in Perissodactyla by epoch.

Genus	Eocene	Oligocene	Miocene	Pliocene	Pleistocene	Holocene
Rhinocerotoidea	7*	1/22*	13/95		1/5	28/87
Amynodontid						
Metamynodon		2				
Hyracodontid						
Forstercooperia	1					
Hyrachyus	6					
Hyracodon		8				
Rhinocerotid		1/12	13/87	1	1/5	28/87
Aceratherium				1		
Aphelops			2/5			
Ceratotherium						7/24
Diceratherium			17			
Dicerorhinus						2/9
Diceros						8/30
Menoceras			25			
Peraceras			1/1			
Rhinoceros						11/24
Subhyracodon		1/11				
Teleoceras			9/39			
Trigonias		1				
Brontotheriidae	3/23	8				
Dolichorhinus	2/4					
Megacerops	1/2					
Helaletidae	2					
Chalicotheriidae		1/14				
Moropus		1/13				
Tylocephalonyx		1				
Tapiridae			1		3	13/65
Tapirus						13/65
Equidae	9	37	1/137	1/49	9/304	13/163
Archaeohippus		2	3			
Cormohipparion				1		
Dinohippus				5		
Equus asinus						3/18
burchelli						1/53
caballus					4/104	2/22
fevus przwalskii				2/13		
grevyi						1/18
hemionus/kiang					1	1/20
neogaeum				1		
pacificus				3		
scotti				1		
simplicidens				1		
zebra				3/19		
Hipparion				4		
Hippidion				2		
Hypohippus			1			
Hyracotherium	8					
Kalobatippus				2		
Merychippus				24		
Mesohippus			19			
Miohippus			1			
Nannippus					1	1
Neohipparion				2		
Orohippus	1					
Parahippus			15			
Plesippus						2
Pliohippus				1/11	19	2
Protohippus				3		

*Fractions indicate number affected compared to number evaluated; freestanding numbers indicate numbers evaluated, as none were affected.

noted in one extant rhinocerotid, Diceros bicornis (NMNH 271189). Reactive bone changes were noted in metapodial III of a Miocene Parahippus leonensis (UF 164393) and in an unnumbered USNM Miocene Peraceras. Fusion of the navicular-ectocuneiform in a Pleistocene horse (LACM 8599) from California is compatible with a diagnosis of spondyloarthropathy.

Spondyloarthropathy was noted in Eocene Perissodactyla (Tables I, II), specifically Brontotheriidae (13%). While insufficient numbers of Brontotheriidae were available to assess its presence in the Oligocene, 7% of Oligocene Chalicotheriidae were affected.

Spondyloarthropathy was not observed in Eocene Rhinocerotidae, although the sample size was small. Such lesions were present in 8.3% of Oligocene Rhinocerotidae, specifically Subhyracodon NMNH 3919 (Tables I, II). Well represented in Miocene rhinocerotidae (13.8%), the Peraceras, Aphelops and Teleoceras were specifically affected. Diceratherium and Menoceras appear to have been spared. While insufficient Pliocene examples were available to assess its frequency, 20% of Pleistocene Rhinocerotidae were affected, contrasted with 32% of recent Rhinocerotidae (Fig. 2).

Spondyloarthropathy was observed in 20% of extant Tapiridae (Tables I, II). Tapiridae are insufficiently represented in the examined fossil record to assess its frequency in the evolutionary history of the group.

The first notation of spondyloarthropathy in the fossil record of the Equidae (Tables I, II) was in the Miocene, in a specimen of Pliohippus (AMNH 71123). That individual represents less than 1% of the Miocene Equidae that were evaluated. Two percent of Pliocene and 3% of Pleistocene Equidae were affected, compared with 8% of the extant genus Equus (Fig. 2).

Eighty-seven percent of the affected individuals had axial joint disease. Sixty-three percent had sacroiliac joint erosions; 13%, sacroiliac joint fusion; 8%, syndesmophytes (anulus fibrosus calcification) (Fig. 1); 5%, zygapophyseal joint disease; and 6%, costovertebral erosions or fusion. Peripheral joint

Table II. Identification of spondyloarthropathy in Perissodactyla.

Family	Individuals with Spondyloarthropathy*
Rhinocerotidae	
Aphelops	AMNH FAM 114805; UF 69944
Ceratotherium	AMNH 51858; BMNH 75-2384; FMNH 29174; FMNH 125413; NMNH 164635; NMNH 164589; NMNH 164592
Diceros	AMNH 24741; AMNH 113776; AMNH 133777; BMNH 1876.2.15.5; IRSNB 9714; NMNH 162933; NMNH 198298; NMNH271189
Peraceras	UNSM 14-22-637
Rhinoceros	
sondaicus	BMNH 1948.12.20.1; NMNH269392
unicornis	AMNH 35759; AMNH 54456; BMNH 1953.8.13.2; BMNH 1961.5.10.1; FMNH 57639; IRSNB 1208; LACM 85986; NMNH 336953; UNSM-ZM13844
Subhyracodon	NMNH 3919
Teleoceras	AMNH 44-1944.1; AMNH 15489; AMNH 8392; AMNH 8415; AMNH 8431; UNSM 2708-87; UNSM 2079-76; UNSM PI2240; UNSM PI2270
Not identified to species -	Love bone bed UF - not catalogued
Brontotheriidae	
Dolichorhinus	AMNH 1843; CM 3147
Megacerops	AMNH1848
Chalicotheriidae	
Moropus	AMNH 1920
Tapiridae	
Tapirus	BMNH 63.7.1.1; BMNH 85.802; BMNH 85.809; LACM88943; NMNH 11883; NMNH 14648; NMNH 15540; NMNH 218726; NMNH 252944; NMNH 261025; NMNH 270353; NMNH 281393; ROM 94410
Equidae	
Equus	LACM 8599; LACM 121054; NMC 45629; UNSM SH-40; UNSM 574-48; UNSM 8053-41; UNSM 10222-39
asinus	BMNH 1960.11.10.4; BMNH 1981.12.9.1; IRSNB 12970
burchelli	CM 17826
caballus	NMNH 15780; NMNH 267482; RMNH 123861; RMNH 145107; RMNH 29797; RMNH 400330
fevus przewalskii	BMNH 1963.1.25.1; NMNH 303321
grevyi	AMNH 82037
hemionus	BMNH 1957.7.18.1
zebra	CMNH 6845; CMNH 30381; IRSNB 3974
Pliohippus	AMNH 71123

* AMNH - American Museum of Natural History, AMNH FAM - American Museum of Natural History, BMNH - British (London) Museum of Natural History, CM - Carnegie Museum of Natural History, CMNH - Cleveland Museum of Natural History, FMNH -Field Museum of Natural History, IRSNB Institute Royale de Sciences Naturale, Brussels, LACM - Los Angeles County Museum, NMC National Museum of Canada, NMNH - National Museum of Natural History (Smithsonian), RMNH - Rykshius Museum van Naturlyhe Historie, ROM - Royal Ontario Museum, UF - University of Florida, UNSB and UNSM - University of Nebraska.

erosions and fusion were distributed to the shoulders, elbows, wrists, forefeet, knees, ankles and hindfeet.

Osteoarthritis was extremely rare in the fossil record. Minimal osteophytes were found in one Miocene Aphelops (UF 69977). Isolated exostoses in Miocene Parahippus leonensis (UF 163928 – tarsal and UF 168370 – mid-III phalanx) and a Pleistocene Sheridan County, Florida horse (UNSB 6747), fractures in an Eocene Palaeosyops (AMNH 129392 – foot) and a Pleistocene horse (UF 136490 – metapodial with secondary infection), a metapodial stress fracture in a Miocene Peraceras (UNSM 8001.82) and scapula and metapodial infection in two Miocene Teleoceras (UNSM 2479-76 and LACM 92016-MP, respectively) and 3rd phalanx in a Pleistocene Dawson horse (NMC 36318 – third phalanx) were noted.

Discussion

Sacroiliac joint erosions and/or fusion and syndesmophytes (Tables I, II, Figure 1) in Brontotheriidae, Chalicotheriidae, Rhinocerotidae (Subhyracodon, Peraceras, Aphelops, Teleoceras and all extant species), Tapiridae, and Equidae are pathognomonic for spondyloarthropathy (1-12). Diagnosis was confidently made, as the limitations of x-ray interpretation (2, 13-15) do not apply to direct visual examination (16). (False positive x-ray interpretations, indicating the presence of sacroiliac joint erosions or fusion, relate to the irregular shape of the human sacroiliac joint). The only phenomenon which may occasionally mimic the sacroiliitis of spondyloarthropathy (on direct visual examination) is infectious sacroiliitis (2, 3). However, infection-related bone lysis and exuberant new bone formation are quite distinctive and thus were easily excluded in this study (2, 3).

Recognition of spondyloarthropathy, on the basis of pathognomonic sacroiliitis extended back to the Eocene in the Perissodactyla (Tables I, II). It was common in extinct families such as Brontotheriidae (13% in the Eocene) and Chalicotheriidae (7% in the Oligocene) and present in 20% of extant Tapiridae. A progressive increase in the frequency of spondyloarthropathy was observed through geologic time. This ranged from 8.3% of Oligocene Rhinocerotidae to 15% in the Miocene, 20% in the Pleistocene and 32% in extant species (Fig. 2). This compares to an increase in frequency in equidae from less than 1% in the Miocene to 2% in the Pliocene, 3% in the Pleistocene, and 8% in extant animals (Fig. 2).

Among the Miocene Rhinocerotidaet Peraceras, Aphelops, and Teleoceras were affected, while Diceratherium and Menoceras appear to have been spared (unaffected). While most of the affected horses were not identified to species, reactive bone changes were noted in metapodial III of Parahippus lemesis (UF164393) and probably represent an example of the peripheral arthritis that often occurs in spondyloarthropathy.

Perhaps the most impressive aspect of Perissodactyl evolution is the size progression. While spondyloarthropathy was common the Perissodactyl giants (Brontotheridae and Chalicotheridae), they left no known descendants. This is not so for horses and rhinos. Early horses were quite small and early rhinos relatively smaller than their modern descendants.

While this might suggest a relationship or at least a direct correlation of body mass with spondyloarthropathy occurrence, examination of the full record of this almost pan-mammalian disease (17) suggests otherwise. The frequency of spondyloarthropathy is actually indistinguishable among monkeys, from the squirrel-sized Callithrix to howler or capuchin monkeys (18). The frequency of spondyloarthropathy in chimpanzees (28%), gorillas (20%) and orangutans (17%) also does not (19-21) support a body mass relationship. The frequency in bears (equivalent in polar and sloth bears) is independent of size/mass (22). The frequency in European bison is actually significantly greater than in the much larger American bison (17). The evolutionary advantage of spondyloarthropathy still remains elusive, though quite impressive. A structural support contribution to mass effect, however, seems unlikely.

Osteoarthritis proved to be a relatively rare problem in Perissodactyla, in agreement with observations of other free ranging mammals (4-9). Exostoses were also rare. The very low frequencies of fractures and infection may reflect a low population occurrence or simply poor survivorship. Animals with fractures or infections may have quickly succumbed and therefore were not available for analysis. Stress fractures appear to be extremely rare in free-ranging Perissodactyla, for they were observed in only one individual – in a Miocene Peraceras.

Conclusion

While spondyloarthropathy is classified as a disease, perhaps (analogous to malaria-protective effects of sickle cell anemia), is its persistence evidence for some unknown host benefit? Rhinocerotidae and Equidae are represented by extant fauna (e.g., Rhinoceros) and are amenable to chrono-epidemiologic analysis of the disease impact. Such analysis may allow greater understanding of the contemporary distribution of the disease. Perhaps further study will allow identification of the nature of that theoretical benefit.

Acknowledgements

We wish to express our appreciation to Drs. Laura Abraczinkas, Jon Alexander, Roy Carlson, Ken Carpenter, Ameolere Coeriomon, Melissa Morales Cogan, George Culver, Ted Daeschler, Mary Dawson, Francis Desmedt, Lize De Wet Bronner, Judith Eger, Marc Frank, Wolfgang Fuchs, Eugene Gaffney, Linda Gordon, John Heyning, Thor Holmes, Dave Janiger, Cheri Jones, James Kitchny, Tom Labedz, Meave Leakey, Bryn Mader, Larry Martin, Timothy Matson, Candace McCaffrey, Bruce McFadden, Chuck Merbs, Nina Mudida, Guy Musser, Marta Pagesi, Darlene Patterson, Bob Purdy, Albert Saunders, Kevin Seymour, Sally Shelton, Bill Stanley, Hans Dieter Sues, Duane Schlitter and Richard Thorington for their assistance in facilitating our examination of the collections they manage and to Charles Kibiy, Ogetto Mwebi, and Ezekiel Savala for assistance in the examination process.

References

1. ROTHSCHILD BM, WOODS RJ: Character of pre-Columbian North American spondyloarthropathy. *J Rheumatol* 1992; 19: 1229-35.
2. RESNICK D, NIWAYAMA G: *Diagnosis of Bone and Joint Disorders*. Philadelphia. Saunders, 1988.
3. ROTHSCHILD BM, MARTIN L: *Paleopathology: Disease in the Fossil Record*. London, CRC Press, 1993.
4. ROTHSCHILD BM, WOODS RJ: Spondyloarthropathy in gorillas. *Semin Arthritis Rheum* 1989; 18: 267-76.
5. ROTHSCHILD BM, WOODS RJ: Spondyloarthropathy as an Old World phenomenon. *Semin Arthritis Rheum* 1992; 21: 306-16.
6. ROTHSCHILD BM, WANG X-M, CIFELLI R: Spondyloarthropathy in ursidae: A sexually transmitted disease? *Natl Geographic Res* 1993; 9: 382-284.
7. ROTHSCHILD BM, WANG X-M, SHOSHANI J: Spondyloarthropathy in proboscideans. *J Zoo Wildlife Med* 1994; 25: 360-6.
8. ROTHSCHILD BM, ROTHSCHILD C: No laughing matter: Spondyloarthropathy in hyaenidae. *J Zoo Wildlife Med* 1994; 25: 259-63.
9. ROTHSCHILD BM, WOODS RJ: Arthritis in New World monkeys: Osteoarthritis, calcium pyrophosphate deposition disease and spondyloarthropathy. *Intl J Primatol* 1993; 14: 61-78.
10. BJORKENGREN AG, SARTORIS DJ, SHERMIS S, RESNICK D: Patterns of paravertebral ossification in the prehistoric sabertoothed cat. *Amer J Roentgenol* 1987; 148: 779-82.
11. MCEWEN C, DITATA D, LINGG D: Ankylosing spondylitis and spondylitis accompanying ulcerative colitis, regional enteritis, psoriasis, and Reiter's disease: A comparative study. *Arthritis Rheum* 1971; 14: 291-318.
12. GOFTON JP, BENNETT PH, SMYTHE HA, DECKER JL: Sacroiliitis and ankylosing spondylitis in North American Indians. *Ann Rheum Dis* 1972; 31: 474-81.
13. DURBACK MA, SCHUMACHER HR, EDELSTEIN G: Abnormalities of the sacroiliac joints (SIJ) in diffuse idiopathic skeletal hyperostosis (DISH): Demonstration by computerized tomography (CT). *Arthritis Rheum* 1988; 31: S102.
14. DIHLMANN W: *Diagnostic Radiology of the Sacroiliac Joints*. Stuttgart, Georg Thiene Verlag, 1980.
15. RESNICK D, NIWAYAMA G, GEORGEN TG: Degenerative disease of the sacroiliac joint. *Invest Radiol* 1975; 10: 608-21.
16. ROTHSCHILD BM, POTEAT GB, WILLIAMS E, CRAWFORD WL: Inflammatory sacroiliac joint pathology: Evaluation of radiologic assessment techniques. *Clin Exp Rheumatol* 1994; 12: 267-74.
17. ROTHSCHILD BM, ROTHSCHILD C: Spondyloarthropathy as a transmammalian phenomenon, reproducible in its manifestations across species lines. *J Paleopath* 2000; 11: 103-4.
18. ROTHSCHILD BM, WOODS RJ: Arthritis in New World monkeys: Osteoarthritis, calcium pyrophosphate deposition disease and spondyloarthropathy. *Intl J Primatol* 1993; 14: 61-78.
19. ROTHSCHILD BM, WOODS RJ: Spondyloarthropathy in gorillas. *Semin Arthritis Rheum* 1989; 18: 267-76.
20. ROTHSCHILD BM, WOODS RJ: Reactive erosive arthritis in chimpanzees. *Amer J Primatol* 1991; 25: 49-56.
21. ROTHSCHILD BM, WOODS RJ: Inflammatory arthritis in Pongo. *J Med Primatol* 1996; 25: 414-8.
22. ROTHSCHILD BM, WANG X-M, CIFELLI R: Spondyloarthropathy in Ursidae: A sexually transmitted disease? *National Geographic Research and Exploration* 1993; 9: 382-284.