

What qualifies as rheumatoid arthritis?

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Received: December 17, 2012 Revised: January 13, 2013

Accepted: January 23, 2013

Published online: March 12, 2013

Key words: Rheumatoid arthritis; Spondyloarthropathy; Ankylosis; Accelerometry; Animal models

Rothschild B. What qualifies as rheumatoid arthritis? *World J Rheumatol* 2013; 3(1): 3-5 Available from: URL: <http://www.wjgnet.com/2220-3214/full/v3/i1/3.htm> DOI: <http://dx.doi.org/10.5499/wjr.v3.i1.3>

Abstract

Expansion of diagnostic criteria for rheumatoid arthritis and deletion of exceptions increases sensitivity, but at the expense of specificity. Two decades later, modification of criteria included the caveat: "absence of an alternative diagnosis that better explains the synovitis." That puts great faith in the diagnostic skills of the evaluating individual and their perspectives of disease. The major confounding factor appears to be spondyloarthropathy, which shares some characteristics with rheumatoid arthritis. Recognition of the latter on the basis of marginally distributed and symmetrical polyarticular erosions, in absence of axial (odontoid disease excepted) involvement requires modification to avoid failure to recognize a different disease, spondyloarthropathy. Skeletal distribution, pure expression of disease in natural animal models and biomechanical studies clearly rule out peripheral joint fusion (at least in the absence of corticosteroid therapy) as a manifestation of rheumatoid arthritis. Further, such studies identify predominant wrist and ankle involvement as characteristic of a different disease, spondyloarthropathy. It is important to separate the two diagnostic groups for epidemiologic study and for clinical diagnosis. They certainly differ in their pathophysiology.

INTRODUCTION

Perhaps the most problematic challenge to clinical diagnosis has been the 1987 revised criteria^[1] for rheumatoid arthritis. It discarded the diagnostic exclusions portion of previous criteria^[2], such that sensitivity may have been increased, but at the expense of specificity. The result has been a tendency^[3-5] to group all individuals with a predominantly non-axial inflammatory arthritis in this rheumatoid arthritis category. The 1987 criteria do not address the nature of erosions, their specific distribution and the issue of joint ankylosis, characteristics which separate the those newly diagnosed (according to the criteria) as having rheumatoid arthritis into two groups. Such a binary approach^[6-9] divides criteria-fulfilling individuals according to location of erosions on or around joints, skeletal distribution of erosions and presence or absence of reactive new bone formation and joint ankylosis. The 2010 criteria^[10] address this question by the inclusion "absence of an alternative diagnosis that better explains the synovitis." These are clinical criteria designed to identify individuals who may have early rheumatoid arthritis. Their sensitivity and specificity seem predominantly determined by the clinician's ability to recognize evidence of alternative diagnoses.

The archeologic record provides unique insight to this question of the more generally applied 1987 criteria's specificity, as two segregated patterns of disease are observed. Rheumatoid arthritis is clearly recognized in 7 populations as the only polyarticular inflammatory disease present^[11]. The erosions are marginal to joint surfaces' ankylosis is absent; metacarpal phalangeal joint involve-

ment is prominent and periarticular osteopenia, invariably present. This contrasts with other archeological sites, in which erosions, while polyarticular, are more usually limited in distribution, are predominantly subchondral in distribution, ankylosis is present, wrist and ankle involvement are prominent and periarticular osteopenia is absent in more than 50%^[6,12-22]. The neologism “osseotropism” was introduced^[23] to characterize the tendency of specific diseases to affect such specific areas of the musculoskeletal system. The characteristics of the second group of individuals were indistinguishable from other individuals in those same populations with spondyloarthropathy diagnosed on the basis of axial disease (sacroiliac joint erosions or fusion, syndesmophytes, or zygapophyseal joint erosion or fusion)^[12,13,16,21,24]. Fusion of joints through the articular surface (ankylosis) is not surprising in a disease that primarily erodes subchondral bone. This exposes trabeculae, allowing growth across the joint, a process quite different than what is observed in true rheumatoid arthritis.

The two groups also have very different smoothness of movement or resistance of the joint surface to transitional movement, as determined by accelerometer studies. That translates joint movement into a quantifiable electric impulse, providing a measure of vibration intensity/power^[25]. Individuals with periarticular osteopenia and symmetrical polyarticular marginal erosions, but no axial disease or peripheral joint fusion (classical rheumatoid arthritis) had low vibration/power, while those with subchondral erosions and/or peripheral joint fusion had high vibration/power. Individuals with spondyloarthropathy, diagnosed on the basis of axial disease, showed the same high vibration/power^[25-27].

While it has been suggested that some dogs and pigs had rheumatoid arthritis^[28-32], the presence of subchondral erosions and joint fusion^[16,21,23,24] are actually more characteristic of spondyloarthropathy^[33,34]. Indeed, evaluation of over 30 000 non-human mammalian skeletons reveals many cases of spondyloarthropathy, but not a single instance of actual rheumatoid arthritis^[6,14,35-39]. There clearly are two distinct groups that fulfill the revised criteria for rheumatoid arthritis.

The archeologic record, biomechanical studies and the presence of only one of the varieties of this so-called “rheumatoid arthritis” in animals all support the contention that the revised criteria have limited value in distinguishing these groups, as Silman^[9] previously suggested. The article by Can *et al*^[40] illustrates this quite well. It describes a high frequency of spondyloarthropathy in patients who fulfill the 1987 criteria for rheumatoid arthritis. While it suggests two coexisting diseases, the more parsimonious interpretation is that the diagnosis of rheumatoid arthritis was incorrect in those patients. Robinson *et al*^[41] suggest a third, unrelated group, but use the narrow comparison with ankylosing spondylitis, rather than the more general spondyloarthropathy categorization. These opinion pieces emphasize the importance of separating at least the two diagnostic groups segregated herein for epidemiologic study and for clinical diagnosis. They certainly

differ in their pathophysiology.

CONCLUSION

Rheumatoid arthritis and spondyloarthropathy are clearly different disorders, distinguished by clinical appearance, radiologic findings, pathophysiology, biomechanical characteristics and representation (or lack thereof) in the zoological record. The significance of biochemical and inflammatory markers is difficult to assess, as rheumatoid arthritis criteria utilized in its classification are insufficiently specific. The tendency to group all individuals with a predominantly non-axial inflammatory arthritis as having rheumatoid has compromised any comparisons, as it also includes many with spondyloarthropathy. The neologism “osseotropism” was presented, to categorize the joint specificity of the two diseases, to facilitate discriminating between them. Utilizing the criteria of joint distribution, presence or absence of subchondral erosions or peripheral joint fusion, analysis of biochemical and inflammatory laboratory markers may provide additional insights at to the vary different pathophysiological processes represented by these phenomena.

REFERENCES

- 1 Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, Healey LA, Kaplan SR, Liang MH, Luthra HS. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; **31**: 315-324 [PMID: 3358796 DOI: 10.1002/art.1780310302]
- 2 1958 REVISION of diagnostic criteria for rheumatoid arthritis. *Arthritis Rheum* 1959; **2**: 16-20 [PMID: 13618213 DOI: 10.1002/1529-0131]
- 3 Hacking P, Allen T, Rogers J. Rheumatoid arthritis in a medieval skeleton. *Int J Osteoarchaeol* 1994; **4**: 251-255 [DOI: 10.1002/oa.1390040310]
- 4 Rogers J, Waldron T, Dieppe P, Watt I. Arthropathies in palaeopathology: The basis of classification according to most probable cause. *J Archaeol Sci* 1987; **14**: 179-193 [DOI: 10.1016/0305-4403(87)90005-7]
- 5 François RJ, Eulderink F, Bywaters EG. Commented glossary for rheumatic spinal diseases, based on pathology. *Ann Rheum Dis* 1995; **54**: 615-625 [PMID: 7677436 DOI: 10.1136/ard.54.8.615]
- 6 Rothschild BM, Martin LD. Skeletal Impact of Disease. Albuquerque: New Mexico Museum of Natural History Press, 2006
- 7 Rothschild BM, Turner KR, DeLuca MA. Symmetrical erosive peripheral polyarthritis in the Late Archaic Period of Alabama. *Science* 1988; **241**: 1498-1501 [PMID: 3047874 DOI: 10.1126/science.3047874]
- 8 Rothschild BM, Woods RJ, Ortel W. Rheumatoid arthritis “in the buff”: erosive arthritis in defleshed bones. *Am J Phys Anthropol* 1990; **82**: 441-449 [PMID: 2399957 DOI: 10.1002/ajpa.1330820406]
- 9 Silman AJ. Problems complicating the genetic epidemiology of rheumatoid arthritis. *J Rheumatol* 1997; **24**: 194-196 [PMID: 9002036]
- 10 Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B, Costenbader KH, Dougados M, Emery P, Ferraccioli G, Hazes JM, Hobbs K, Huizinga TW, Kavanaugh A, Kay J, Kvien TK, Laing T, Mease P, Ménard HA, Moreland LW, Naden RL, Pincus T, Smolen JS, Stanislawski-Biernat E,

- Symmons D, Tak PP, Upchurch KS, Vencovsky J, Wolfe F, Hawker G. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010; **62**: 2569-2581 [PMID: 20872595 DOI: 10.1002/art.27584]
- 11 **Rothschild BM**, Woods RJ, Rothschild C, Sebes JI. Geographic distribution of rheumatoid arthritis in ancient North America: implications for pathogenesis. *Semin Arthritis Rheum* 1992; **22**: 181-187 [PMID: 1295091 DOI: 10.1016/0049-0172(92)90018-9]
- 12 **Rothschild BM**, Woods RJ. Spondyloarthropathy: erosive arthritis in representative defleshed bones. *Am J Phys Anthropol* 1991; **85**: 125-134 [PMID: 1882978 DOI: 10.1002/ajpa.1330850202]
- 13 **Rothschild BM**, Woods RJ, Rothschild C. Erosive arthritis of the spondyloarthropathy variety: Diagnostic criteria based on virgin populations. *Paleopath Bull* 1991; **72**: 6-7
- 14 **Rothschild BM**, Woods RJ. Spondyloarthropathy as an Old World phenomenon. *Semin Arthritis Rheum* 1992; **21**: 306-316 [PMID: 1604326 DOI: 10.1016/0049-0172(92)90024-8]
- 15 **Rothschild BM**, Woods RJ. Character of precolumbian North American spondyloarthropathy. *J Rheumatol* 1992; **19**: 1229-1235 [PMID: 1404158]
- 16 **Rothschild BM**, Woods RJ. Implications of osseous changes for diagnosis of spondyloarthropathy. *J Orthop Rheumatol* 1992; **5**: 155-162
- 17 **Rothschild BM**, Rothschild C. Spondyloarthropathy in northeastern North America [Abstract]. *Arthritis Rheum* 1992; **33**: R44
- 18 **Rothschild BM**, Rothschild C. 19th century spondyloarthropathy independent of socioeconomic status: lack of skeletal collection bias. *J Rheumatol* 1993; **20**: 314-319 [PMID: 8474069]
- 19 **Dutour O**, Panuel M, Rothschild BM. Spondyloarthropathies in early Holocene Saharan population. *J Comp Human Biol* 1994; **45**: S44
- 20 **Rothschild B**. Rheumatoid arthritis in a medieval skeleton: An illogical diagnosis for a case of spondyloarthropathy. *Int J Osteoarchaeol* 1995; **5**: 198-199 [DOI: 10.1002/oa.1390050216]
- 21 **Rothschild BM**. Paleopathology, its character and contribution to understanding and distinguishing among rheumatologic diseases: perspectives on rheumatoid arthritis and spondyloarthropathy. *Clin Exp Rheumatol* 1995; **13**: 657-662 [PMID: 8575149]
- 22 **Rothschild BM**, Arriaza B, Woods RJ, Dutour O. Spondyloarthropathy identified as the etiology of Nubian erosive arthritis. *Am J Phys Anthropol* 1999; **109**: 259-267 [PMID: 10378463]
- 23 **Rothschild BM**. Osseotypes and spondyloarthropathy exposed. *Curr Rheumatol Rev* 2005; **1**: 57-63 [DOI: 10.2174/1573397052954145]
- 24 **Rothschild BM**. What is this disease we call spondyloarthropathy? *Clin Exp Rheumatol* 2003; **21**: 283-285 [PMID: 12846045]
- 25 **Verrall EH**. Development of a Noninvasive Diagnostic Technique to Diagnose Knee Pathologies Using Acceleration Measurements of the Loaded and Unloaded Knee [dissertation]. Akron: University of Akron, 1996
- 26 **Reddy NP**, Rothschild BM, Verrall E, Joshi A. Noninvasive measurement of acceleration at the knee joint in patients with rheumatoid arthritis and spondyloarthropathy of the knee. *Ann Biomed Eng* 2001; **29**: 1106-1111 [PMID: 11853263 DOI: 10.1114/1.1424916]
- 27 **Shah EN**, Reddy NP, Rothschild BM. Fractal analysis of acceleration signals from patients with CPPD, rheumatoid arthritis, and spondyloarthropathy of the finger joint. *Comput Methods Programs Biomed* 2005; **77**: 233-239 [PMID: 15721651]
- 28 **Anderson ST**, Schiller CA. Rheumatoid-like arthritis in a lion tailed macaque. *J Rheumatol* 1991; **18**: 1247-1250 [PMID: 1941834]
- 29 **Bennett D**. Immune-based erosive inflammatory joint disease of the dog: canine rheumatoid arthritis. *J Small Anim Pract* 1987; **28**: 799-819 [DOI: 10.1111/j.1748-5827.1987.tb01346.x]
- 30 **Halliwell RE**, Lavelle RB, Butt KM. Canine rheumatoid arthritis--a review and a case report. *J Small Anim Pract* 1972; **13**: 239-248 [PMID: 4662835 DOI: 10.1111/j.1748-5827.1972.tb06341.x]
- 31 **Pedersen NC**, Castles JJ, Weisner K. Noninfectious canine arthritis: rheumatoid arthritis. *J Am Vet Med Assoc* 1976; **169**: 295-303 [PMID: 986380]
- 32 **Sikes D**. A rheumatoidlike arthritis in swine. *Lab Invest* 1959; **8**: 1406-1415 [PMID: 14446629]
- 33 **Rothschild BM**, Rothschild C, Woods RJ. Inflammatory arthritis in canids: spondyloarthropathy. *J Zoo Wildl Med* 2001; **32**: 58-64 [PMID: 12790395]
- 34 **Nunn CL**, Rothschild B, Gittleman JL. Why are some species more commonly afflicted by arthritis than others? A comparative study of spondyloarthropathy in primates and carnivores. *J Evol Biol* 2007; **20**: 460-470 [PMID: 17305811 DOI: 10.1111/j.1420-9101.2006.01276.x]
- 35 **Weckenmann M**, Klemm HW, Möllenbruck G. [Prognosis of postoperative complications from the chronomedicine viewpoint]. *Langenbecks Arch Chir* 1997; **382**: 284-290 [PMID: 9498197]
- 36 **Rothschild BM**, Wang X, Shoshani J. Spondyloarthropathy in proboscideans. *J Zoo Wildlife Med* 1994; **25**: 360-366
- 37 **Rothschild BM**, Rothschild C. No laughing matter: Spondyloarthropathy and osteoarthritis in Hyaenidae. *J Zoo Wildlife Med* 1994; **25**: 259-263
- 38 **Rothschild BM**, Rothschild C. Post-Paleocene inflammatory arthritis. *J Vert Paleontol* 1996; **16**: 61A
- 39 **Rothschild BM**, Rothschild C. Trans-mammalian pandemic of inflammatory arthritis (Spondyloarthropathy variety): Persistence since the Pleistocene. *Paleontol Soc Publ* 1966; **8**: 330
- 40 **Can G**, Solmaz D, Binicier O, Akar S, Birlik M, Soysal O, Akkoc N, Manisali M, Onen F. High frequency of inflammatory back pain and other features of spondyloarthritis in patients with rheumatoid arthritis. *Rheumatol Int* 2013; Epub ahead of print [PMID: 23129430 DOI: 10.1007/s00296-012-2553-7]
- 41 **Robinson PC**, Wordsworth BP, Reveille JD, Brown MA. Axial spondyloarthritis: a new disease entity, not necessarily early ankylosing spondylitis. *Ann Rheum Dis* 2013; **72**: 162-164 [PMID: 23100608 DOI: 10.1136/annrheumdis-2013-202073]

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