

## What qualifies as rheumatoid arthritis?

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### 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.

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

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### INTRODUCTION

Perhaps the most problematic challenge to clinical diagnosis has been the 1987 revised criteria<sup>[1]</sup> for rheumatoid arthritis. It discarded the diagnostic exclusions portion of previous criteria<sup>[2]</sup>, such that sensitivity may have been increased, but at the expense of specificity. The result has been a tendency<sup>[3-5]</sup> 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<sup>[6-9]</sup> 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<sup>[10]</sup> 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<sup>[11]</sup>. 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%<sup>[6,12-22]</sup>. The neologism “osseotropism” was introduced<sup>[23]</sup> 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)<sup>[12,13,16,21,24]</sup>. 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<sup>[25]</sup>. 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<sup>[25-27]</sup>.

While it has been suggested that some dogs and pigs had rheumatoid arthritis<sup>[28-32]</sup>, the presence of subchondral erosions and joint fusion<sup>[16,21,23,24]</sup> are actually more characteristic of spondyloarthropathy<sup>[33,34]</sup>. Indeed, evaluation of over 30 000 non-human mammalian skeletons reveals many cases of spondyloarthropathy, but not a single instance of actual rheumatoid arthritis<sup>[6,14,35-39]</sup>. 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<sup>[9]</sup> previously suggested. The article by Can *et al*<sup>[40]</sup> 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*<sup>[41]</sup> 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.

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