

Not The Lucy, not The One

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The question of the antiquity of rheumatoid arthritis assumes clear agreement on how to make the diagnosis and distinguish it from other forms of arthritis. One could perhaps examine this from the perspective of the lumpers-splitter controversy, wherein most patients today presenting with inflammatory arthritis seem to be classified as rheumatoid (1). That of course resolves at times agonizing questions of differential diagnosis and makes it easier to identify patients for drug studies and gain third party payer 'cooperation.' After all, does it make a difference? Differential diagnosis could simply be considered a tool to categorize patients to facilitate and tailor therapeutic approaches. If there is no significant difference among diseases in their therapeutic responsiveness, is it 'overkill' to segregate them into different categories?

The answer to that last question is a subject unto itself and beyond the scope of this discussion. Identifying the antiquity of disease, however, has major implications that require a different perspective. Lumping diseases with similar, but not identical, manifestations is perhaps one of the greatest challenges to epidemiology. One would not today consider lumping most rashes as manifestations of leprosy, as was common in Biblical and even Medieval Europe and Asia (2). Such lumping precludes epidemiologic study and, indeed today, we have not been successful in making any cogent assessment of the diseases that actually afflicted those individuals. While many of those individuals were confined to so-called 'leper asylums,' findings in associated cemeteries are quite different from those in individuals and populations with modernly diagnosed leprosy, at times when effective treatment was not available (3). The fallacy of diagnostic assumption is further evidenced by the attempt to blame the 'explosion' of syphilis on Pope Clement's closing of those leprosoria in 1510 (4). Assumptions and opinions have long blocked progress on understanding of the diseases afflicting those individuals. The problem has not been any less for rheumatoid arthritis (5-10).

The real issue is not whether diseases can be lumped, but whether doing so precludes our goals/mission. Is our goal simply to identify the earliest occurrence on a given continent or in a given hemisphere or is it to identify the origin and spread of the disease, to provide potential clues to its derivation? While great strides have occurred in treatment of rheumatoid arthritis and we as rheumatologist help many people and contribute significantly to improving the quality of life for many individuals with rheumatoid arthritis, I suspect that few of us are really satisfied. Perhaps we will be able to do more for our patients if we can identify the actual cause of rheumatoid arthritis.

Paleoepidemiology, the study of disease in ancient populations, offers the possibility of tracking down its origins and perhaps provide new investigative directions to identify its cause. Just as data-based medicine has taken a central position in rheumatology decision processes, so too has data-based paleopathology (11) replaced the opinion-based approach (5-7). Opinion-based reports seem to classify most forms of erosive arthritis as rheumatoid, predominantly because of lack of knowledge of the existence of other varieties (e.g. spondyloarthropathy (6,12). Kilgore's (6) study of Nubians is the classic example. Appropriately population based, she found a pauciarticular arthritis [indistinguishable from that reported by Ciranni *et al.* (5)]. Re-examination revealed the classic population characteristics of spondyloarthropathy (13-17). The average number of bone groups (e.g., metacarpals were considered one group; shoulders, a second) affected among Nubians was 6 (6, 17), classic for spondyloarthropathy (13-17), but clearly and statistically less than the 12 found with rheumatoid arthritis (12, 18-21). Kilgore subsequently deleted rheumatoid arthritis as the diagnosis, accepting that the Nubians actually had spondyloarthropathy (Kilgore, personal communication).

What criteria should we use for identification of rheumatoid arthritis in ancient populations? Perhaps the most reasonable approach is to examine those

populations in which the disease was originally and unequivocally diagnosed, people who had lived in the catchment area encompassing the western portion of the Tennessee and Green Rivers (12, 18-20). Recall that the diagnosis of rheumatoid arthritis was confirmed by comparison with modern clinical populations. As the x-ray is the common denominator between clinical and archeologic populations, it was pertinent to note that the character and distribution of erosions was identical in the two groups (12, 18-22). Among the dozens of afflicted individuals from those sites, erosions were symmetrically distributed at joint margins with marked periarticular/perilesional osteopenia, but no new bone formation. The average number of joint groups was 12. Erosions involved the subchondral surface only as extension of marginally distributed erosions, never primarily and joint fusion was notable in its absence.

A very famous cartoon shows an anthropologist entering a cave in South Africa (home of the *Australopithecus* generally known as Lucy). The anthropologist meets Lucy (of Charlie Brown fame) in the cave. The anthropologist exclaims 'Not The Lucy.' Science fiction aficionados will recognize the phrase 'Not The One' from Babylon 5. Ciranni *et al.* (5) have clearly presented a case of inflammatory arthritis from the 16th century. While some may use rheumatoid arthritis as a lumping category, comparison to individuals from the ancient North American catchment area requires the response: 'Not The One,' not the same disease.

The atypical character of the case presented by Ciranni *et al.* (5) presents several challenges to accepting a diagnosis of rheumatoid arthritis. Joint fusion has been documented in the archeologic record as indicative of either spondyloarthropathy or infection (11). It has never been found in populations which clearly had rheumatoid arthritis, except in the modern era - with steroid use and effect (11). Even if one argued that fusion could occasionally be found in rheumatoid arthritis, is it not paradoxical that almost all the alleged European cases (5-10,12), in-

cluding this one, have joint fusion? Spondyloarthropathy presents as a population phenomenon with a spectrum of joint involvement. Five to ten percent of individuals with spondyloarthropathy actually have polyarticular disease, which may even be symmetrical (13-17, 23, 24). Involvement limited to five joint groups (wrists, metacarpal phalangeal and shoulder joints) in Ciranni *et al.*'s (5) 'Braids Lady' is typical of that seen in spondyloarthropathy (13-17, 23, 24) and so substantially less than that seen in rheumatoid arthritis (12, 18-24) that it could at best be considered an outlier - even if there were no evidence of joint fusion. (Ciranni *et al.*'s (5) Figure 3 actually illustrates new bone formation and peri-articular sclerosis, characteristic of spondyloarthropathy (13, 17, 23, 24) and contrary to what is found in rheumatoid arthritis (12, 18-24). Their (5) Figure 5 reveals classic subchondral erosions of spondyloarthropathy (13-17, 23, 24), at variance with what was seen in the catchment area where rheumatoid arthritis took its origin (12, 18-20). Increased subchondral trabeculae in figure 5 is also the opposite of what is found in rheumatoid arthritis (12, 18-24), but classic for spondyloarthropathy (13-17, 23, 24).

What does study of art and imagery contribute to our understanding of rheumatoid origins? Separation of style and substance seems to be the major challenge. Appelboom's (25) 1987 conference on Art, History and Antiquity of Rheumatic Diseases was sentinel in my understanding of the question. While cases of alleged rheumatoid arthritis were presented by physicians, the present art historians had difficulty containing their mirth. The felt it was all style (artistic) and that there was no actual evidence of arthritis! Marcel Kahn has subsequently studied over 10,000 paintings (personal communication, Marcel Kahn, 1990) and has yet to identify rheumatoid arthritis earlier than 1800. The issue is even more complicated, as some hand positions may even be non-specific or arranged. Ulnar deviation is a non-specific phenomenon in mummies. Mays' (26) diagnosis of rheumatoid arthritis on that basis has

long since been falsified (11,12,18). Given the problems of interpreting visual imagery, it is an even more daunting task to attempt interpretation of ancient writings - when even the meanings and usage of words have changed, are controversial or non-specific.

Paleoepidemiology seems the most reliable mechanism for establishing disease origins. Paleopathologic identification of a disease perhaps compatible with the diagnosis of interest is not the same, nor does it often allow the same degree of diagnostic confidence. Diagnosing a disease, on the basis of what would at best be considered an outlier, may fulfill the academic desire to identify the earliest or first possible case. It does not, however, actually document the existence of the disease (11). Progress requires study of patterns. Patterns are reproducible, with rheumatoid arthritis looking no different today than it did 6500 years ago (12,18-20), and still not identifiable outside the North American catchment area until the 18th century (27). What was present in pre 18th century Europe was a different disease from rheumatoid arthritis originally seen in North America; European disease was not The (same) One.

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