Chlamydia-Induced Arthritis: Five Insights and a Possible Cure

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About one in 20 patients with genital chlamydia, the most prevalent sexually transmitted disease in the US, progress to reactive arthritis. This is simple to treat, but devilish to detect and diagnose.

Source: Rheumatology Network

Inflammatory arthritis can follow urogenital infection with *Chlamydia trachomatis*, the most prevalent sexually transmitted bacterial infection in the US. It can also follow infections with a respiratory form of *Chlamydia* which is almost ubiquitous. Clinicians often don’t recognize this, and even when they do, may not know that these forms of arthritis seldom respond to standard antibiotic therapy.¹²

Some strains of chlamydiae home from the origin of infection to the joint, but documenting that arthritic symptoms originate from the infection is a challenge, as we review below. However, recent studies have provided much new information regarding the basic biology and pathobiology of *C. trachomatis*, and an effective therapeutic strategy is emerging.

1. Genital infection with *C. trachomatis* is widespread, and about 5% of patients with a documented genital chlamydial infection develop the arthritis. About half of these proceed to chronic disease.¹² The apparently low incidence is partly a result of missed diagnoses and partly due to other causes, including host genetic background, the mixture of chlamydial strains initiating the genital infection, and other as yet unknown pathogenic factors.³ (see also below)

2. Ocular strains of *C. trachomatis* are implicated in the pathogenesis of Chlamydia-induced arthritis. There are two groups of *C. trachomatis* serovars: the ocular strains causing trachoma and the strains causing genital infections. (A separate biovar causes lymphogranuloma venereum.)¹² If the infecting genital inoculum includes ocular strain organisms in addition to those of one or more genital strains, those ocular organisms rapidly disseminate from the genital tract within monocytes and home to the joint, where they settle in synovial tissue.⁴ There, they can persist for years, generating a Th-1 type immune response in the joint that includes production of interleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), and interferon gamma (IFN-γ).¹²,⁵,⁶

3. Because of the nature of these persistent synovial infections, molecular diagnostic tests (e.g., PCR) are the methods of choice for diagnosis, but there are many challenges to achieving this.¹³,³,⁷ Thus it is difficult to say how many cases of arthritis trace, in fact, to chlamydiae. It is not only possible but probable that the low number of diagnosed cases is due to the lack of standard PCR assays in many clinical microbiologic settings. The assays do exist in a commercial and officially approved form, but they are not in standard use in many clinical microbiology labs. In addition, we showed years ago that using PCR on synovial fluid is ineffective. It is synovial tissue that should be tested. The odds of marrying the availability of the appropriate PCR assay with the availability of synovial tissue samples make it likely that many cases are overlooked.

4. It is not clear which specific chlamydial gene products induce this inflammatory reaction, and is it unclear why ocular strains should be the primary elictor of the arthritis. The chlamydiae that infect synovial tissue exist in a metabolically active state that exhibits an unusual profile of gene expression.¹³ That profile includes down-regulation of some genes and up-regulation of expression from others, particularly heat shock protein-60-encoding genes.⁸

5. *Chlamydia pneumoniae*, a respiratory pathogen, also elicits inflammatory arthritis. Epidemiologic studies indicate that infection with this organism is virtually ubiquitous, but (for reasons yet to be elucidated) 10% or less of such infections lead to diagnosed cases of arthritis.⁹ Interestingly, the characteristic features of *C. pneumoniae*-induced inflammatory arthritis differ somewhat from those of *C. trachomatis*-induced disease. They lack the suite of extra-articular characteristics including keratoderma blenhoragicum, conjunctivitis, and others.¹

Specific rifampicin regimens are the only known ways to resolve *Chlamydia*-induced arthritis. Many studies have shown that standard treatment of genital or pulmonary chlamydial
infections is effective at eliminating the organisms in the genitalia and the lungs, but ineffective as a means of eliminating chlamydiae that persistently infect synovial tissue.\textsuperscript{1-3} Recent studies, however, have indicated that treating Chlamydia-induced arthritis with one of two antibiotic regimens (doxycycline + rifampicin or azithromycin + rifampicin) clears the organism in many patients.\textsuperscript{10} This observation presents the encouraging prospect of a cure for Chlamydia-induced arthritis.\textsuperscript{11} Grant applications are in process for a large multi-center trial to test the efficacy of these regimens against Chlamydia-induced arthritis.

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