

Antibiotic treatment in Reiter's syndrome

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Unfortunately there are virtually no hard data to support a scientific discussion of the place of antibiotic treatment in Reiter's syndrome (RS). Almost inevitably, therefore, such a discussion is susceptible to philosophical analogies, clinical impressions, or emotional beliefs. Nevertheless, it ought to be possible to achieve a consensus on the practical questions of what antibiotic, in what dosage, and for what period of time should be employed, if at all, in the management of cases of the disease. The following points can be made as a basis for a workshop discussion.

(1) All students of RS would probably agree that no antibiotic has a direct effect on the arthritis, and that no discernible change in the arthritis can be attributable to any antibiotic within several weeks of such therapy. This 'fact' does not, however, exclude the use of antibiotics, because one has only to turn to rheumatic fever to appreciate that, while penicillin has no direct effect whatever on the arthritis of rheumatic fever, it has a definite role in the management of cases. It is in this latter type of usage that antibiotic therapy may be rational.

(2) Patients with RS precipitated by intestinal infections such as dysentery or yersinia presumably require a course of antibiotics that would eradicate the responsible pathogen. Preferences might vary between microbiologists, and also might be determined by antibiotic sensitivity testing, but ampicillin or tetracycline would probably be generally acceptable.

(3) Patients with RS that has been unquestionably precipitated by a venerally acquired non-gonococcal urethritis would logically receive a course of tetracycline or erythromycin to eradicate either *Chlamydia* or *Ureaplasmas*. One or other of these organisms would be present in the urethra in 70%–90% of cases. These organisms might or might not be aetiologically related to the arthritis, but their capacity for causing urethritis is now becoming generally accepted. To eradicate them from the genital tract is rational, regardless of the presence of arthritis. Courses of either erythromycin or tetracycline, 500 mg thrice daily for 10 days, with

similar treatment for conjugal partners, would be a minimal programme. The incidence of genital infection with either or both of these organisms in cases of RS is sufficiently high, the difficulties of culturing them so great and, the harmlessness of tetracycline or erythromycin so satisfactory that this antibiotic regimen should be instituted in all cases without the requirement of obtaining positive cultures.

(4) Cases in which antibiotic treatment would be controversial are the following: (a) Cases in which the precipitating cause of the syndrome is not clear and a venereal, enteritic, or colitic origin is not obvious. (b) Cases of recurrence of the syndrome without an obvious precipitating cause. (c) Cases in which the syndrome is incomplete and the urethral component is absent. (d) Cases in which there appears to be a persistent pyuria or low grade urethritis after a course of antibiotics. (e) Cases in which there have been multiple sexual exposures and these are likely to recur.

(5) Most investigators of RS concede that some cases seem to be aetiologically related to 'infection' by agents insensitive to tetracycline. Some investigators consider that this applies to all cases and that the association of *Chlamydia*, *Ureaplasma*, or enteric pathogens is coincidental. There are no hard data to prove either view.

I was recently impressed by two cases of RS in which definite pyuria persisted after nine days of tetracycline 1.5 g/day—a result which was incompatible with a tetracycline-sensitive organism causing the urethritis. Moreover, in 1964 I noted that the persistence of urethritis after tetracycline treatment seemed more common in patients with RS than in those with uncomplicated urethritis.

Recent studies in Seattle have shown that neither *Chlamydia* nor *Ureaplasma* could be isolated in about 20% of cases of non-gonococcal urethritis, which also proved more resistant to minocycline—the most active tetracycline against both organisms. The implication of these observations is that an agent insensitive to tetracycline must be the cause of the urethritis in these 20% of cases of non-gonococcal urethritis. Perhaps RS is a complication of infection

by this agent and has no relationship to coincidental chlamydial or ureaplasma presence in the genital tract.

(6) The recent Seattle study³⁴ of the treatment of uncomplicated non-gonococcal urethritis with sulfisoxazole, which is effective against *Chlamydia*, and aminocyclitols (streptomycin or spectinomycin), which are effective against *Ureaplasma*, have supported the opinion that both these microorganisms cause urethritis. Unfortunately, it has not yet been possible to do a similar study of patients with RS, and the difficulties of doing so seem insuperable.

General discussion

DR. G. W. CSONKA: Dr. David Taylor-Robinson and I inoculated our urethras with a cloned ureaplasma strain. Within three days I had mild dysuria; three days later a definite urethritis, cystitis, and then arthralgia with heel pain that was quite sharp, so much so that I was hobbling around and had to tell

my wife, who knew nothing about the experiment, that I had hurt it while gardening. I then took tetracycline in high doses for two weeks and the symptoms cleared rapidly. The ureaplasma disappeared within 24 hours. Dr. Taylor Robinson ignored the symptoms of urethritis for four weeks without treatment. During that time he got unequivocal angular conjunctivitis as well as marked cystitis and prostatitis. Whereas my symptoms and signs of urogenital infection cleared promptly, presumably because of the early tetracycline treatment, Dr. Taylor-Robinson had evidence of continued urogenital infection after his tetracycline therapy for the next six months. We assumed that was because he had delayed the tetracycline therapy. His urine showed 'prostatic threads' for the full six months observation period and these were studied by electronmicroscopy. Antiureaplasma antibodies were demonstrated in my serum for three weeks and in his serum for six months. Fortunately, neither of us was HLA-B27 positive. We had forgotten to test for this before the experiment.