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Propionibacterial versus mycobacterial infection as the cause of sarcoidosis: what do past and current treatment trials tell us?

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For over a decade, there has been compelling evidence that propionibacterial and mycobacterial infections are associated with some cases of sarcoidosis. However, this insight has not been associated with a shift in treatment for sarcoidosis. Corticosteroids remain the cornerstone of treatment of symptomatic disease. Novel immunosuppressive therapies have been developed for treating advanced sarcoidosis. The use of anti-tumor necrosis factor (anti-TNF) therapy is associated with significant clinical improvement in the majority of refractory cases. However, it is not clear that immunosuppressives change the natural course of the disease. Patients treated with immunosuppressive therapy are more likely to have chronic disease. Patients receiving anti-TNF who have treatment withdrawn within the first year of therapy have a reported relapse rate of 50-90%. Therefore, treatments directed toward the putative microbial agent(s) for sarcoidosis is attractive. We have investigated two treatment regimens. The tetracyclines (minocycline and doxycycline) have been used with limited success in case series and anecdotal reports. Recently, a combination of levofloxacin, ethambutol, azithromycin, and rifabutin (or rifampin) (CLEAR) has been reported as effective in cutaneous and pulmonary sarcoidosis. For cutaneous sarcoidosis, CLEAR regimen was superior to the placebo control arm. While CLEAR was designed to treat mycobacterial infection, several of the antibiotics in the CLEAR regimen will be effective against propionibacterial infection. In addition, several of the antibiotics have anti-inflammatory activity. There is a large, multi-center trial of CLEAR for pulmonary sarcoidosis being led by Dr. Wonder Drake. That trial is designed to investigate the potential value of CLEAR, as well as its potential mechanism of action.