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## Etiological agents in patients with sarcoidosis

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All etiologic agents of sarcoidosis induce systemic noncaseating epithelioid cell granulomas and the heterogeneous clinical features of the disease: variable lesion sites, spontaneous regression, chronicity (persistence), and progression into fibrotic lesions. When an etiologic agent is deeply involved in a sarcoid-granuloma, the lesion typically exhibits Th1 immunological features (cytokine profiles and oligoclonal T cell expansion consistent with antigen-driven processes).

The hallmark epithelioid cell granuloma observed sarcoidosis appears in other infectious diseases such as tuberculosis and leprosy, as well as in non-infectious diseases such as chronic beryllium disease. The Kveim test has a specific diagnostic value in screening for sarcoidosis. The test has also shown that active etiological agents or related active substances may be present in homogenate from spleen or lymph nodes obtained from sarcoidosis patients. BALF cells from sarcoidosis patients are also known to manifest a Kveim-like reaction. These data suggest that active, etiological substance can be found systemically in the bodies of sarcoidosis patients. In more recent studies, bacterial DNA was undetectable in Kveim reagents obtained from sarcoidosis patients or control patients. The Kveim-active material may be a cell-bound proteinous material such as lymphokine induced by unknown etiological antigens.

In this review I examine the significance of sarcoid granulomas in comparison with *Mycobacterium tuberculosis*, *Mycobacterium leprae*, and *Propionibacterium acnes*. I focus most closely on the significance of intracellular latent infection and agents that may satisfy the above-mentioned criteria for a systemic granulomatous disease, keeping in mind that multiple etiologic antigens may cause sarcoidosis in genetically susceptible individuals.