In this edition of Adult Infectious Disease Notes, we outline some of the recent developments in our understanding of Mycobacterium avium complex (MAC) infection in patients with the acquired immune deficiency syndrome (AIDS).

**Incidence:** MAC is the AIDS-defining event in fewer than 5% of AIDS cases (Federal Centre for AIDS and Centers for Disease Control data), but has been reported in 53% of autopsies. Recently, a prospective study of 1006 AIDS patients has demonstrated that the incidence of MAC bacteremia is about 20% per year following an AIDS diagnosis and reaches 50% at 30 months. Most patients with MAC infection have CD4 lymphocyte counts below 50 x 10^6/L.

**The organism:** MAC refers to the 28 serotypes of M avium and M intracellulare. Some taxonomists also classify M scrofulaceum as a member of MAC. However, nearly all MAC isolates from AIDS patients are M avium, in contrast to pulmonary MAC infection, which is more evenly split between M avium and M intracellulare. Furthermore, the majority of M avium strains from AIDS patients has a similar restriction fragment length polymorphism pattern. Finally, macrophages from AIDS patients are significantly more susceptible to in vitro infection with M avium than with M intracellulare.

**How does MAC infection occur?** MAC organisms are widely distributed in the environment, especially in water sources, and in a variety of birds and mammals. Both the gastrointestinal tract and respiratory tract are recognized portals of entry for MAC in AIDS patients; however, the gastrointestinal tract appears to be the more common of the two routes of entry. It is not unusual for MAC bacteremia to occur without documented prior gastrointestinal or respiratory tract colonization, likely because such colonization may be transient.

**Impact of MAC infection in AIDS patients:** It has long been recognized that MAC infection may cause fever, night sweats, weight loss and anemia. Although the role of MAC infection in AIDS mortality was previously questioned, it is now clear that MAC infection is an independent risk factor for mortality in AIDS patients, even after adjusting for CD4 lymphocyte count. The mean survival of AIDS patients with MAC infection who are treated with antimycobacterial therapy is approximately double that of untreated patients.

**Diagnosis:** The most rapid diagnostic technique is the use of acid-fast stains of appropriate body tissues and secretions, with subsequent confirmation by culture. The preferred culture technique is radiometric (BACTEC)
with rapid speciation by DNA probing. The radiometric technique permits direct inoculation of media with the patient’s blood at the bedside. The recently released Roche Septi-Check AFB also appears to an excellent culture technique, but its use for culturing blood is not well documented. In the absence of a radiometric system, blood may be treated using the Dupont isolator (lysis-centrifugation) system or collected into sodium polyanetholesulfonate, lysed with sodium deoxycholate and suspended in bovine serum albumin prior to inoculation in mycobacterial media. Bone marrow culture is more sensitive than blood culture and should be considered when blood cultures are negative and MAC infection is strongly suspected. Furthermore, acid-fast smears of bone marrow may be positive and thus provide a rapid diagnosis, whereas acid-fast smears of blood are invariably negative and are not indicated.

**Prevention:** Recently, two identically designed prospective randomized double-blind clinical trials conducted in adult AIDS patients, with mean CD4 lymphocyte counts of approximately 60 x 10^6/L at enrollment, have demonstrated that rifabutin, given orally in a dosage of 300 mg daily, reduces the risk of MAC bacteremia by a factor of about 2.5. Treatment: MAC isolates are characteristically resistant to most standard antituberculous drugs. However, the outcome of treatment of pulmonary MAC infection in non-AIDS patients has been demonstrated to correlate with the number of drugs used which are active against the infecting strain in vitro. Preliminary evidence suggests that the same holds true in AIDS-associated MAC infection. A number of newer drugs including clarithromycin, azithromycin, rifabutin and fluoroquinolones, as well as the traditional antileprosy drug clofazimine, have greater in vitro activity against MAC than traditional antituberculous drugs. Favourable results with combinations of these agents (usually with ethambutol) have been reported in several uncontrolled series. Of these agents, clarithromycin appears to be the most promising, based on a pilot study of clarithromycin monotherapy. However, clarithromycin monotherapy has been associated with a substantial rate of acquired antibiotic resistance, as would be expected to occur when any slow growing mycobacterial infection is treated with a single agent.

Although the optimal treatment for MAC infection is far from clear, it is evident that combination treatment is required. The ‘ideal’ combination is not currently established, but significant advances can be expected in the next two years as the results of several current multicentre controlled comparative trials become known.

### References


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