



Management of disease due to *Mycobacterium kansasii*

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In many ways, *Mycobacterium kansasii* is probably the easiest of the nontuberculous mycobacterial (NTM) pathogens to treat effectively. This relative ease in treatment stems from similarities between *M kansasii* and *Mycobacterium tuberculosis*, especially the excellent activity of antituberculosis drugs against *M kansasii*. In fact, there is more data demonstrating the efficacy of antituberculous drugs for treatment of *M kansasii* infections than for any other NTM infection. Unfortunately, management of *M kansasii* infection involves more than just the availability of effective drugs. The similarity to *M tuberculosis* also means that *M kansasii* isolates can be associated with aggressive and destructive lung disease and that improper treatment, either caused by physician error or patient nonadherence, can result in extensive lung destruction and/or the emergence of drug-resistant *M kansasii* isolates. This discussion will emphasize the many weapons in the treatment armamentarium against *M kansasii* disease, but it must be kept in mind that timely diagnosis before the development of extensive disease and effective overall treatment strategies are equally important, ensuring that patients receive the appropriate medications for a sufficiently long period of time.

Pathogenesis and epidemiology

Infection by *M kansasii* probably occurs via an aerosol route. Although it is not known with certainty, tap water is likely a major reservoir for *M kansasii* causing human infection. The organism has been isolated from tap water in the same communities

where patients with *M kansasii* disease have been identified [2,31]. Isolates of the same phage type as those isolated from patients have been recovered from drinking water distribution systems in the Netherlands [3,4], and environmental isolates of the same genotype, determined by pulse field electrophoresis (PFGE) as clinical isolates, have been identified in Paris, France [5]. Isolation of *M kansasii* from tap water can be intermittent, which may explain why some investigators have failed to recover it from that source. No other environmental (water or soil) source of *M kansasii* has been identified. The reasons for this inability to isolate *M kansasii* from environmental sources such as surface water are so far unknown.

Recent genetic studies have shown there is genetic diversity among *M kansasii* isolates recovered throughout the world [5,6]. A frequently used technique is Restriction Fragment Length Polymorphism (RFLP) analysis of chromosomal DNA. The procedure entails Endonuclease' digestion of whole DNA which yields many variably sized fragments that are separated by Pulsed Field Gel Electrophoresis (PFGE). The DNA fragment patterns may be read and compared visually or scanned into a computer base. One recent DNA-based study using PFGE has shown the presence of five taxonomic groups among both environmental and human isolates [5]. One predominant PFGE pattern, however, was found in patients with *M kansasii* disease [5]. Zhang et al recently evaluated 51 clinical isolates of *M kansasii* from the United States by PFGE [6]. Half of the United States isolates had the same PFGE pattern that was the predominant pattern reported by Picardeau [5]. Epidemiologic studies of strain relatedness of *M kansasii* in suspected outbreaks will be difficult, given the close relationship of most clinical *M kansasii* isolates by PFGE.

Lung disease caused by *M kansasii* occurs in geographic clusters. In studies from southeast England

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and in Wales, *M kansasii* disease occurred more frequently than disease caused by *Mycobacterium avium* complex (MAC) [7,8]. Because it is not a public health problem and not reportable, only estimates are available for its relative prevalence. *M kansasii* is generally the second most common cause of NTM lung disease in the United States and occurs most commonly in the southern and central United States in a pattern described as an inverted “T”. The states with the highest incidence of disease include the southern states of Texas, Louisiana, and Florida, and the central states of Illinois, Kansas, and Nebraska. Bittner et al recently reported that *M kansasii* was the most common mycobacterial pathogen isolated at a Veterans Affairs Hospital in Omaha, Nebraska, over a 20-year period between 1971 and 1990 [9]. In this study, the number of *M tuberculosis* isolates declined over a 20-year period, whereas the number of *M kansasii* isolates remained relatively stable over that same time period and resulted in a total number of *M kansasii* isolates that exceeded the number of *M tuberculosis* isolates. In a demographic study of NTM pulmonary disease in Texas, *M kansasii* was second only to MAC as a cause of NTM lung disease. It was also reported that *M kansasii* cases were significantly more likely to come from urban than rural areas, which is consistent with our current understanding of reservoirs of *M kansasii*, as noted above [10]. In geographic areas where HIV infection is common, the prevalence of *M kansasii* disease may be very high. This increase is likely explained by the susceptibility of the host population at risk for *M kansasii* infection rather than factors related to presence of the organisms in the environment or virulence of the organisms [11].

Clinical aspects of *M kansasii* disease

Pulmonary disease is the most frequent clinical manifestation of *M kansasii* infection in immunocompetent patients. Of all NTM, *M kansasii* lung disease most closely parallels the clinical course of *M tuberculosis*. *M kansasii* primarily affects middle-aged white men, but it can affect adult patients of any sex, race, or age. Risk factors for *M kansasii* infection include pneumoconiosis, chronic obstructive lung disease (COPD), previous mycobacterial disease, malignancy, and alcoholism [1,10–14]. The combination of HIV infection and silicosis can result in potent susceptibility to mycobacteria including *M kansasii* [12]. A recent study also found that approximately 40% of immunocompetent patients with *M kansasii* lung disease had no identifiable predisposing condition [11].

Until recently, symptoms of *M kansasii* lung disease were felt to be essentially identical to those of patients with reactivation pulmonary tuberculosis. The chest radiographic changes were also described as very similar to reactivation pulmonary tuberculosis including cavitory infiltrates with an upper lobe predilection (Fig. 1). In some series, approximately 90% of patients with disease caused by *M kansasii* had cavitory infiltrates [10]. Not surprisingly, many patients with *M kansasii* lung disease enter the health care system as tuberculosis suspects. Noncavitory or nodular/bronchiectatic lung disease has been recognized as a major feature of disease caused by MAC and *M abscessus* but has not been recognized as part of the spectrum of *M kansasii* lung disease. It is now apparent, and perhaps not surprising, that patients with *M kansasii* lung disease can also present with noncavitory (nodular/bronchiectatic) infiltrates similar to MAC lung disease [15] (Fig. 2). Though nodular/bronchiectatic disease accounts for 50% of MAC lung disease, it is unknown how often this form of *M kansasii* lung disease occurs. The natural history of cavitory lung disease caused by *M kansasii* in



Fig. 1. A 50-year-old male cigarette smoker with extensive bilateral fibronodular and cavitory infiltrates caused by *Mycobacterium kansasii*.

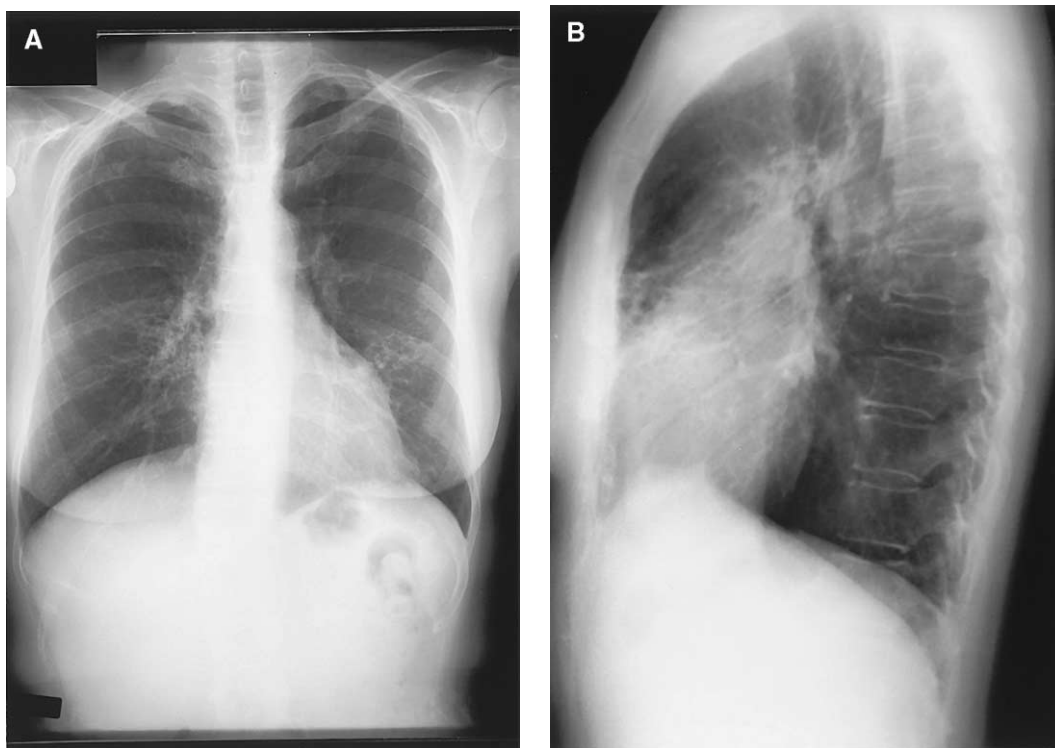


Fig. 2. A 68-year-old cigarette-nonsmoking female with *Mycobacterium kansasii* lung disease. (A) Mid and upper lung reticulonodular densities on posterior-anterior view. (B) Primarily right middle lobe and lingular infiltrates on lateral view.

patients receiving no drug treatment is characterized by persistence of sputum positivity and progression of clinical and radiographic disease, sometimes with extensive lung cavitation and destruction (Fig. 3). Presumably, patients with noncavitary *M kansasii* disease would also experience progressive clinical and radiographic disease if left untreated. Because of the potential for untreated disease to progress, patients with pulmonary disease (cavitary or noncavitary) should receive drug therapy.

M kansasii may produce pulmonary disease in AIDS patients not associated with dissemination [12,13,16,17]. *M kansasii* pulmonary disease in HIV-infected patients generally presents with the same symptoms as immunocompetent patients, although weight loss is more common in AIDS patients. Cavitation on chest radiograph is less common, whereas interstitial infiltrates and hilar adenopathy are more common in AIDS patients with *M kansasii* lung disease than immunocompetent patients. As is seen with tuberculosis, *M kansasii* disease can present over a wide range of CD4 cell counts. Patients with high CD4 counts tend to present with cavitary radiographic abnormalities, whereas

patients with very low CD4 counts are more likely to present with noncavitary radiographic findings, intrathoracic adenopathy, and/or disseminated disease. The majority of patients with disseminated *M kansasii* have far advanced lung disease and profound immunosuppression. Dissemination of *M kansasii* also can occur in non-HIV infected patients who are profoundly immunocompromised, such as patients who have undergone organ transplantation [1,17,18].

Diagnosis of *M kansasii* disease

M kansasii is isolated from respiratory specimens using standard mycobacteriology laboratory techniques. Identification of *M kansasii* isolates usually is accomplished with a highly sensitive and specific commercial DNA probe (Accuprobe; GenProbe, Inc. San Diego, CA) in larger reference and state health laboratories. This method, along with high-performance liquid chromatography (HPLC) analysis of mycolic acid esters, has generally replaced utilization



Fig. 3. A 44-year-old female cigarette smoker with a history of cough for more than 1 year with no radiographic evaluation during that time. This patient's sputum was subsequently strongly acid fast bacilli smear- and culture-positive for *Mycobacterium kansasii*. The chest radiograph shows essentially complete cavitory and infiltrative destruction of the left lung at the time *M kansasii* disease was diagnosed.

of colony morphology and pigmentation for early presumptive identification of *M. kansasii*.

In general, *M. kansasii* lung disease is diagnosed according to the American Thoracic Society (ATS) guidelines in a symptomatic patient with compatible radiographic abnormalities and multiple respiratory specimens that are culture-positive for *M. kansasii* [19]. There has been controversy about the applicability of the ATS NTM diagnostic guidelines for patients with *M. kansasii* respiratory isolates [13]. As noted, these guidelines emphasize the isolation of NTM species from multiple respiratory specimens. The bases for the controversy are essentially twofold. First, in an area with a high incidence of tuberculosis, patients with acid fast bacilli (AFB) smear-positive sputum and an abnormal chest radiograph will likely receive empiric antituberculosis therapy, which is also highly active against *M. kansasii*, making attempts to obtain further (confirmatory) isolates from patients with *M. kansasii* disease less likely to be successful.

Secondly, *M. kansasii* infection has the potential for a rapidly fatal outcome if untreated in an HIV-infected host; therefore, initiation of therapy in HIV-infected patients without confirmatory isolates may be necessary. Recent studies suggest that, in the appropriate clinical setting (especially in the face of cavitory lung disease), a single culture-positive specimen for *M. kansasii* is adequate for making a diagnosis and initiating therapy [12,13]. Though most *M. kansasii* respiratory isolates are clinically significant, it is noteworthy that *M. kansasii* also can be recovered from asymptomatic patients with or without radiographic abnormalities. The patients with radiographic abnormalities will likely show progression of disease; however, the clinical course is less certain for those that do not have radiographic abnormalities [11,13]. The clinical significance therefore, of a single positive sputum culture for *M. kansasii* from an asymptomatic patient with a normal chest radiograph is unknown. If therapy is not initiated for a patient with a respiratory culture positive for *M. kansasii*, it is not only reasonable but also highly desirable to follow that patient closely with serial sputum AFB analysis and chest radiographs. Patients with untreated *M. kansasii* disease can undergo very severe and impressive lung destruction over relatively short periods prior to the diagnosis of *M. kansasii* lung disease (see Fig. 3). Patients with disseminated disease are diagnosed by isolating the organism from otherwise sterile sites such as blood or lymphatic tissue.

M. kansasii in vitro drug susceptibility

Untreated ("wild") strains of *M. kansasii* are inhibited by rifampin, rifabutin, isoniazid, ethambutol, ethionamide, amikacin, streptomycin, clarithromycin, and probably ciprofloxacin at concentrations readily achievable in the serum with usual therapeutic doses [20–23]. *M. kansasii* is also usually susceptible in vitro to sulfamethoxazole, amikacin, the newer quinolones, and clarithromycin [20–23]. Isolates are usually resistant to high concentrations in vitro and therefore achievable levels of pyrazinamide (PZA) and capreomycin. Typical minimal inhibitory concentrations (MICs) for untreated *M. kansasii* strains are outlined in Table 1. These "wild" strains are highly susceptible to rifampin with MICs ≤ 1.0 $\mu\text{g/mL}$ and rifabutin with MICs ≤ 0.5 $\mu\text{g/mL}$. Isolates of *M. kansasii* with high-level (> 8.0 $\mu\text{g/mL}$) resistance to rifampin are usually cross-resistant to rifabutin, whereas isolates with low-level rifampin resistance (MICs 2.0–8.0 $\mu\text{g/mL}$) are rifabutin susceptible with MICs ≤ 0.5 $\mu\text{g/mL}$ [23]. MICs for untreated strains of *M. kansasii* to isoniazid

Table 1
Minimum inhibitory concentrations (MICs) for some drugs in the treatment of *M kansasii* lung disease

Drug	MIC ($\mu\text{g/mL}$)
Rifampin	≤ 1.0
Rifabutin	≤ 0.5
Isoniazid	1–4.0
Ethambutol	≤ 5.0
Clarithromycin	≤ 0.25
Streptomycin	2–8.0
Sulfamethoxazole	≤ 4.0
Ciprofloxacin	0.5–2.0
Gatifloxacin	≤ 0.025
Moxifloxacin	≤ 0.025

generally range for 1.0–04.0 $\mu\text{g/mL}$ [23], which are 10–50 times higher than isoniazid MICs for tuberculosis ($\leq 0.1 \mu\text{g/mL}$). MICs of *M kansasii* for ethambutol are comparable to *M tuberculosis*, with all susceptible MICs $\leq 5.0 \mu\text{g/mL}$. As with ethambutol resistance in tuberculosis, resistant MICs ($>5.0 \mu\text{g/mL}$) are associated with previous ethambutol therapy, resistance to other drugs including rifampin, and treatment failure. Acquired or secondary resistance to rifampin, ethambutol, and isoniazid (defined as significant changes in MICs associated with treatment failure or relapse) has been demonstrated in isolates from treatment failure cases, and resistance to the first two agents is reliably demonstrated by current *Mycobacterium tuberculosis* (MTB) susceptibility test methods (proportion method in agar) [20,22,23].

The concentrations of antituberculous drugs used for routine mycobacteria susceptibility testing, including *M kansasii*, were chosen for their usefulness with *M tuberculosis*. Because *M kansasii* is less susceptible to these drugs in vitro (but still susceptible to achievable blood levels of these drugs), some isolates may be reported resistant to isoniazid at 0.2 or 1.0 $\mu\text{g/mL}$ and to streptomycin at 2.0 $\mu\text{g/mL}$. These isolates are susceptible to slightly higher drug concentrations, so that laboratory reports of resistance to the low concentrations of these two drugs have no clinical or therapeutic significance as long as a rifampin-containing regimen is being used. Thus, when clinically indicated, isoniazid and/or streptomycin should be used against *M kansasii* regardless of the in-vitro susceptibility results. For patients who have previously received isoniazid (INH) or streptomycin, however, performing susceptibility tests to these drugs may be necessary.

The only drug for which resistance in vitro to a defined drug concentration has been regularly associated with treatment failure for *M kansasii* is rifampin. As acquired rifampin resistance may develop during therapy and as the history of prior therapy may not be

known, all initial isolates of *M kansasii* as well as those from patients with known prior therapy should be tested to rifampin by the agar proportion method. Also, testing should be performed when the patient's sputum fails to convert from smear and/or culture positive or when a relapse occurs during therapy. For patients whose isolate is rifampin-resistant, testing to all potentially useful agents, including rifabutin, ethambutol, and clarithromycin, should then be performed.

Treatment of *M kansasii* disease

There have been several retrospective and prospective studies of various treatment regimens for *M kansasii* lung disease that form a reasonable basis for drug therapy recommendations [22,24–26]. The key to successful therapy of *M kansasii* lung disease is inclusion of rifampin in a multidrug regimen. For antimycobacterial drug regimens without rifampin, the sputum conversion rates at 6 months have ranged from 52–81% [22,27]. Relapse rates were approximately 10% even in patients who achieved an initial response. Sputum conversion rates with rifampin-containing regimens at 4 months were 100% in 180 patients from 3 studies [22,24,25]. The incidence of treatment failure in these studies was 1.1% and was invariably associated with the development of rifampin resistance. Long-term relapse rates from these three studies of rifampin-containing regimens also were very low (0.8%).

The current ATS recommendation for treatment of lung disease caused by *M kansasii* is the regimen of isoniazid (300 mg/day), rifampin (600 mg/day), and ethambutol (25 mg/kg/day for the first 2 months, then 15 mg/kg) given daily for 18 months [19] (Table 2). The recommendation for an initial ethambutol dose of 25 mg/kg/day is based on its inclusion in early treatment trials, however, the necessity for this high dose initially has not been rigorously tested. Because most patients with *M kansasii* lung disease are tuberculosis suspects, they are frequently started empirically on four antituberculosis drugs, including INH, rifampin, and ethambutol. This approach has a fortuitous benefit in that patients who prove to have *M kansasii* lung disease will receive adequate therapy from the outset. This treatment approach may be most important in areas with a high incidence of *M kansasii*, such as reported by Bittner et al [9]. Documentation of at least 12 months of negative sputum cultures is felt by many experts to be important for successful therapy. In patients who are unable to tolerate one of these three drugs, clarithromycin appears to be a reasonable alternative based on its low

Table 2

Recommended regimens for treatment of *M kansasii* infection

(1) Pulmonary or disseminated disease in the immunocompetent host or for HIV infected patients not on PIs or NNRTIs or with dosage adjustment of Efavirenz

Rifampin 600 mg/day

Isoniazid 300 mg/day

Ethambutol 25 mg/kg/day for 2 mos, then 15 mg/kg/day
Oral medicines for 18 mos, and 12 mos of sputum culture negativity

For severe disease, consider adding streptomycin 0.5–1.0 gm IM TIW^b for the first 2–4 mos of therapy or clarithromycin 500 mg BID

(2) Pulmonary or disseminated disease in the immunocompetent host that is rifampin-resistant or in patients who are rifampin-intolerant

Clarithromycin 500 mg BID

Isoniazid 900 mg/day (plus pyridoxine 50 mg/day)

Ethambutol 25 mg/kg/day

Sulfamethoxazole 1.0 gm/TID

For severe disease, consider streptomycin 0.5–1.0 gm IM TIW for the first 2–4 mos of therapy

Duration of therapy as above

(3) Pulmonary or Disseminated infection in HIV positive patients not on selected PIs (Indinavir, Nelfinavir, Amprepavir), or NNRTIs (Nevirapine, Efavirenz.)

Clarithromycin 500 mg BID

Rifabutin 150 mg/day

Ethambutol 25 mg/kg/day for 2 mos, then 15 mg/kg/day

Isoniazid 300 mg/day

For severe disease, consider streptomycin 0.5–1.0 gm IM TIW for the first 2–4 mos of therapy

Duration of therapy as above or as appropriate for level of immune function.

^a NNRTIs, nonnucleoside reverse transcriptase inhibitors; PIs, protease inhibitors; TIW, Three times weekly.

^b Substitute rifabutin 150 mg/day for rifampin in patients receiving appropriate PIs or NNRTIs

MICs to *M kansasii* and excellent activity in vivo against other NTMs; however, only limited clinical data is available to support its use (see below).

In spite of the relatively large number of agents available to treat *M kansasii* lung disease, formidable obstacles remain for the successful management of these patients. The major problems are the result of the need for multiple expensive drugs administered over a long period of time without support from state departments of health. Daily rifampin, ethambutol, and isoniazid would cost a patient thousands of dollars for 18 months of therapy. It is also sometimes difficult, for a variety of reasons, for patients to

complete 18 months of therapy. As with pulmonary tuberculosis, patients sometimes stop therapy after taking medications long enough to feel better but well before the disease has been eradicated. Patients with *M kansasii* would clearly benefit from administration of medication by directly observed therapy (DOT), both to improve adherence with therapy that should increase the number of patients who successfully complete a course of therapy and to avoid the emergence of acquired rifampin resistance as a result of medication nonadherence. Unfortunately, in the face of competing monetary demands for tuberculosis control, it is not likely that state departments of health will have sufficient funds to treat *M kansasii* in this manner. Certainly, treating *M kansasii* lung disease would be facilitated, from both cost and adherence perspectives, if there were a short course and/or an intermittent regimen that was reliably effective.

Results of four short-course treatment trials for *M kansasii* lung disease have provided some provocative results but have yet to clearly demonstrate equivalence to the 18-month daily treatment regimens. The first short-course regimen was a study of 40 patients by Ahn et al demonstrating that the addition of intermittent streptomycin 1 gm twice weekly for the first 3 months to the previously recommended three-drug regimen given for 12 months resulted in apparent cure of all but one patient [25].

A second trial sponsored by the British Medical Research Council of daily ethambutol 15 mg/kg and rifampin 450–600 mg given for 9 months was completed in 154 patients [28]. Most patients received multiple drugs for presumed tuberculosis initially, but INH was discontinued in all patients when *M kansasii* was identified as the pathogen. All isolates were susceptible in vitro to rifampin and ethambutol, and all were judged to be resistant in vitro to INH. Sputum conversion was achieved in 99% of patients, but with a relapse rate of 12% with a 5-year follow-up. For the majority of these patients, relapse was attributed to medication noncompliance or severe underlying disease. This study suggests that isoniazid does not contribute greatly to the treatment of *M kansasii*, and that 9 months is not a long enough treatment period for the two-drug regimen utilized in this study.

The third short course study was published by Sauret et al who described 28 patients with *M kansasii* lung disease [29]. Fourteen patients received rifampin 600 mg/day, INH 300 mg/day, and ethambutol 25 mg/kg daily for the first 6 months. The ethambutol was then discontinued with continuation of rifampin and isoniazid to complete a total of 12 months. A second group of 14 patients were treated with the same regimen for 18 months. All patients in both

regimens converted their sputum to negative. After 12–30 months of follow-up, only one patient (7%) in the 12-month treatment group and no patients in the 18-month group had relapsed after completing therapy. The use of high-dose (25 mg/kg/day) ethambutol is not without risk, and may not be readily accepted in the United States.

This study also appears to contradict the findings of the study by Jenkins et al with respect to the importance of INH in the treatment regimen [28]. Almost certainly, rifampin is the critical agent for efficacy, and whereas companion drugs may not enhance efficacy, they are essential to prevent the emergence of resistance to rifampin. Both ethambutol and INH appear to be effective for this latter role.

Griffith et al evaluated a three times weekly (TIW) regimen including clarithromycin, rifampin, and ethambutol in 15 patients with *M kansasii* lung disease [15]. The primary treatment end point was 12 months of sputum AFB culture negativity. Three patients were lost to follow-up (two had converted to AFB culture-negative sputum before dropping out of the study, and one patient is still on therapy). The remaining 11 patients successfully completed therapy with a mean duration of therapy of 12.9 months. All patients who successfully completed therapy remain AFB-culture negative. No patient from this study has relapsed so far.

In patients whose organisms have become resistant to rifampin as a result of previous therapy, a regimen consisting of initial streptomycin or amikacin, high-dose isoniazid (900 mg), high-dose ethambutol (25mg/kg/day), and sulfamethoxazole (1.0 gm three times per day) until culture negative 12–15 months has been used successfully [20,23]. Results with this regimen have included sputum conversion in 18 of 20 patients (90%) after a mean of 11 weeks, with only one relapse (8%) among patients culture-negative at least 12 months on therapy.

Based on in vitro activity against *M kansasii* and the limited clinical data cited above, clarithromycin may be especially useful in retreatment regimens for rifampin-resistant strains, perhaps allowing for omission of the aminoglycoside as a substitute for patients intolerant to one of the first-line drugs and in the treatment regimen for all patients with *M kansasii* infection (pulmonary and/or disseminated) and AIDS. The newer quinolones may also be useful in the treatment of rifampin-resistant *M kansasii* strains, but there are no treatment data currently available. It is quite possible that a regimen including clarithromycin and one of the newer quinolones could be as or more effective than the current rifampin-based regimens.

The introduction of a new classes of antiretroviral drugs including the protease inhibitors (PIs) and non-

nucleoside reverse transcriptase inhibitors (NNRTIs), has complicated the treatment of pulmonary and disseminated *M kansasii* disease in patients with AIDS. Rifamycins (rifampin more than rifabutin) accelerate the metabolism of most available protease inhibitors and NNRTIs through induction of the hepatic P-450 cytochrome enzymes, resulting in subtherapeutic levels of the PIs and NNRTIs. Low levels of these drugs facilitate or enhance rapid mutational resistance in HIV strains to the antiretroviral drugs. This drug interaction is even more important in the treatment of *M kansasii* disease than for the treatment of tuberculosis because of the almost essential role of rifamycins in the treatment of *M kansasii* disease. Currently, it is recommended that Indinavir, Nelfinavir and Amprenavir not be used with Rifampin [32]. It is also recommended that Delaviridine and probably Nevirapine not be used with Rifampin [32]. Efavirenz can be used with Rifampin at 800 mg/day [32]. To complicate the situation even more, PI's inhibit the metabolism of Rifamycins, resulting in increased serum levels of Rifamycins and the potential for drug toxicity (Rifabutin more than Rifampin).

There are several options for treating patients with *M kansasii* disease who are also undergoing therapy for HIV infection [32]. These considerations are similar to those involved of the treatment of HIV infected patients with Tuberculosis [30]. One approach for patients with a low HIV viral load is the use of nucleoside reverse transcriptase Inhibitors (NRTIs) as initial therapy for HIV disease which would allow the use of the standard Rifampin containing regimen for *M kansasii* disease. Efavirenz, with appropriate dosage adjustment can also be added to a multi-drug HIV treatment regimen containing NRTI's and the patient could still receive a Rifampin based treatment regimen for *M kansasii* disease. For patients receiving the PI's Indinavir, Nelfinavir and Amprenavir or the NNRTI's Nevirapine or Efavirenz, Rifabutin could be substituted for Rifampin in the *M kansasii* regimen. The addition of Clarithromycin to the *M kansasii* treatment regimen would also likely improve the efficacy of the regimen, although the risk of Rifabutin-related toxicity would be augmented. It is clear that the treatment of *M kansasii* disease in HIV infected patients can be complicated. Physicians who do not routinely treat HIV infected patients or who are not familiar with the drugs involved should seek expert consultation for the management of these patients.

Treatment monitoring

Serial sputum AFB analysis is the most important element of disease monitoring in *M kansasii* lung disease. The sputum analysis is an indication of patient response to therapy and allows determination of the time that sputum converted to negative on therapy (which will dictate the length of therapy in some patients). Additional routine sputum analysis will indicate relapse of disease in patients who had previously converted sputum to AFB negative. Patients who have relapsed microbiologically while on therapy will need repeat in-vitro susceptibility testing for new *M kansasii* isolates. Certainly, some patients have resolution of cough and sputum production during therapy, making sputum analysis impossible. Every effort should be made, however, to collect sputum for AFB analysis throughout the course of treatment. Too often, patients have sputum collected initially, in order to make the diagnosis with no attempt to monitor therapy with follow-up sputum analysis. Patients who are failing therapy may not be recognized until therapy is discontinued, unless there is careful surveillance for AFB in sputum during therapy.

Periodic chest radiographs are also helpful in this setting. The chest radiograph is likely to improve slowly; therefore, frequent radiographs are not necessary as long as the patient appears to be responding to therapy. Because of the potential for drug-related adverse events, patients initially require at least monthly contact with health care workers. The inclusion of ethambutol at a dose of 25 mg/kg/day in the routine treatment regimen dictates that visual symptoms and simple visual acuity and color vision testing should be checked at least monthly. With decrease in the ethambutol dose to 15 mg/kg/day, visual acuity and red green color discrimination need be assessed only with symptomatic changes in the patient's vision. The necessity for frequent patient contact to evaluate possible drug toxicity also facilitates frequent evaluation of disease symptom status.

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