

# THORAX

## Editorials

### Infection with *Mycobacterium kansasii*

The first problem encountered when discussing *Mycobacterium kansasii* is what collective name to give the group of non-tuberculosis causing mycobacteria of which it forms a part. Such terms as "anonymous" or "atypical" should be discarded.<sup>1</sup> My personal preference is for "environmental mycobacteria," as it is the ability of *M kansasii*, *M xenopi*, *M malmoense*, *M avium-intracellulare* complex and other species to exist freely in the environment which is their main distinguishing feature from the obligative parasites *M tuberculosis* (and its Asian and African variants) and *M bovis* which cause tuberculosis. The North American term may eventually become the standard – that is, "mycobacteria other than tuberculosis (MOTT)" – or, more succinctly, "non-tuberculous mycobacteria."

*Mycobacterium kansasii* is one of the environmental mycobacteria widely distributed throughout the world, occurring in soil, house dust and tap water, and it may infect wild or domestic animals as well as humans. Frequency of infection depends on the occurrence of these mycobacteria in the environment. *Mycobacterium kansasii* is the commonest species encountered in Western Europe and parts of the United States.<sup>2,3</sup> It is also the commonest species found in the UK, but in the south east of England infection is predominantly caused by *M xenopi*.<sup>14</sup> Skin testing cannot be relied on to make the diagnosis because of the non-specificity of mycobacterial antigens.<sup>5</sup> Skin testing with multiple types of PPD does not distinguish between infection caused by *M tuberculosis* and *M kansasii*. Sites of infection reported include soft tissue, bone and joints, and the genitourinary system, but pulmonary disease and lymphadenitis are the commonest sites and cause the most important clinical problems.

With the exception of the *M avium-intracellulare* complex, which is closely associated with HIV infection,<sup>6-9</sup> the incidence of disease caused by these organisms does not seem to be changing, so that in countries where the incidence of tuberculosis is falling the frequency of environmental mycobacterial disease, relative to tuberculosis, is rising.

With declining clinical expertise in mycobacterial diseases, infection with environmental mycobacteria such as *M kansasii* is often mislabelled tuberculosis. Although the pathology and presentation, both clinically and radiologically, is indistinguishable from *M tuberculosis*, the metabolism of the bacterium, structure of its cell wall, drug sensitivities, and therefore treatment regimens, differ. The public health implications are different from tuberculosis. Disease caused by *M kansasii* and other environmental mycobacteria is not considered to be transmissible and is therefore not notifiable. No contact tracing is required.

Chronic pulmonary disease caused by *M kansasii* can range from mild, self-limiting, trivial disease to severe

progressive and fatal disease with extensive cavitation. On direct smear *M kansasii* cannot be distinguished from *M tuberculosis*.<sup>10</sup> Only when culture results are available three weeks or more after specimens have been taken will it be possible to distinguish between the bacillus causing tuberculosis and one that does not. In the meantime the patient will probably have been started on antituberculosis chemotherapy comprising isoniazid, rifampicin, and pyrazinamide.

Most strains of *M kansasii* are resistant to isoniazid and pyrazinamide. Valuable time may therefore have been lost treating with only a single effective agent with the theoretical possibility of resulting resistance to rifampicin, although this appears to occur rarely if at all. Fortunately *M kansasii* is almost always sensitive to ethambutol, so the addition of this very useful fourth drug should be considered if infection with an environmental mycobacterium is considered likely.

Whereas drug sensitive tuberculosis almost invariably responds to six months of chemotherapy, diseases caused by the environmental mycobacteria including *M kansasii* have traditionally been treated for one or two years.<sup>11,12</sup> A three drug regimen including a potentially toxic dose of isoniazid of 600 mg/day has been recommended.<sup>13</sup> The Research Committee of the British Thoracic Society<sup>14</sup> has conducted a prospective study of the treatment of *M kansasii* infection in the UK and the results, reported in this issue of *Thorax*, suggest that "short course" chemotherapy in the form of nine months of rifampicin and ethambutol is now possible.

About 50 patients with two or more isolates of *M kansasii*, indicating the presence of clinically significant disease, are currently reported to the Mycobacterium Reference Unit of the PHLS annually. Despite the increase in HIV infection this seems to have altered little in the past decade. It is the *M avium-intracellulare* complex which is implicated as the HIV related opportunist mycobacterium in this country, although *M kansasii* may be increasing in the USA because of HIV infection.<sup>9</sup> To do any form of randomised controlled trial of the chemotherapy of *M kansasii* in the UK would therefore be impractical. Members of the British Thoracic Society and the Mycobacteria Subcommittee of the BTS Research Committee are to be congratulated on providing useful information on chemotherapy from the patients available in a prospective study: 173 over a period of four years.

Two facts which emerge from this study require further explanation. Firstly, there was a 9.7% relapse rate; for *M tuberculosis* this would be regarded as unacceptably high. As the authors point out this is higher than in other studies using longer periods of treatment and sometimes including isoniazid.<sup>2,3</sup> On the other hand, the studies quoted had

shorter periods of follow up. The authors' suggestion that three of the patients in this study who returned with *M kansasii* disease after treatment may have been reinfected rather than having relapsed, because chest radiographic shadowing was at a new site, seems dubious. With the use of DNA fingerprinting it may be possible to substantiate such a claim.<sup>15</sup> Many clinicians might feel that, on the basis of this study with such a high recurrence rate – be it relapse or new infection – a full 12 months of chemotherapy is warranted.

Secondly, 23% of patients died during the study or during the follow up period. For patients with a mean age of 55.5 years this seems high, although a retrospective study by Banks *et al*<sup>10</sup> found a 30% mortality rate. This suggests a high incidence of concomitant serious disease. Unfortunately the authors tell us very little about the causes of death except that most died from respiratory disease, cardiovascular disease, or neoplasia (site or sites not stated). One suspects that most died from smoking related disease but no smoking history of the patients seems to have been available. From my own experience I believe smoking plays an important part in the pathophysiology and slow response to treatment of lung infections caused by environmental mycobacteria in most patients, perhaps by interfering with ciliary motility or macrophage function.<sup>16</sup>

It should also be pointed out that HIV testing was not carried out in the BTS study although there is no reason to suppose that any of the patients might have been infected with HIV. Conclusions as to the treatment of HIV seropositive individuals infected with *M kansasii* where treatment tends to be less successful<sup>17,18</sup> should therefore not be drawn from this study.

It is clear that if the length of time for the treatment of the environmental mycobacteria is to be reduced to six months or less, new drugs will be required. Of the other environmental mycobacteria commonly causing pulmonary or other serious disease, only *M xenopi* is relatively susceptible to first line drugs but reliable data are scarce.<sup>19</sup> For *M malmoense* and the *M avium-intracellulare* complex chemotherapy is unreliable<sup>20,21</sup> and resection should be considered.<sup>22,23</sup>

Multiple drug regimens including rifabutin, the quinolones, and the newer macrolides such as clarithromycin and azithromycin are sometimes effective in the treatment of disseminated *M avium-intracellulare* complex in the HIV positive individual.<sup>24</sup> Chemotherapy of other environmental mycobacterial infections such as *M fortuitum* or *M chelonae* which usually affect the soft tissues is also problematic. Resection may be the only effective treatment. The increase in infection by the *M avium-intracellu-*

*lare* complex due to HIV may be the stimulus to develop the new drugs so urgently needed.

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