INTRODUCTION

Part 1 of this in-depth review briefly commented on the increasing problem of antibiotic resistant organisms, and specifically discussed methicillin-resistant *Staphylococcus aureus*. Part 2 of this review considers multidrug resistant tuberculosis (MDRTB). The review is based on published information on MDRTB from general and specialist journals. Relevant papers were identified from a Medline literature search of all articles published from January 1994.

EPIDEMIOLOGY OF MULTIDRUG RESISTANT TUBERCULOSIS

*Mycobacterium tuberculosis* continues to be the leading cause of adult death from any single infectious agent worldwide, and annually is responsible for an estimated 3 million deaths. The decline in clinical cases of tuberculosis has reversed in recent years due to several factors including improved case ascertainment, demographic factors, socio-economic trends, neglected tuberculosis control in many countries, and the HIV epidemic. The emergence of multidrug resistant tuberculosis (MDRTB) has re-emphasized the importance of tuberculosis control.1

Drug resistant tuberculosis is defined as a case of tuberculosis excreting bacilli resistant to one or more antituberculous drugs. It may be primary, as a result of transmission of a resistant strain, or acquired, which is the result of the preferential replication of mutants in patients receiving inadequate therapy.

MDRTB is tuberculosis resistant to at least isoniazid and rifampicin, and is already established worldwide. The prevalence appears to be higher in those countries considered by the World Health Organization as having poor control programmes. Several countries such as Russia, the Baltic States, Cote d’Ivoire and the Dominican Republic have been identified as ‘hot zones’ of ongoing transmission.2 In Latvia, 22.1% of all patients presenting for treatment for tuberculosis between 1994 and 1997 had MDRTB.
The overall problem of resistance remains low in the UK. However, the UK drug resistance surveillance system 'MYCOBNET' indicates that the prevalence of MDRTB in initial isolates, that is, first isolates from newly diagnosed patients, rose from 0.6% to 1.7% between 1993 to 1996, with 1.9% prevalence in greater London. In 1997, the annual prevalence was 1.3% (45 cases out of 3579) with greater London having the biggest problem (1.5%) compared to 1.1% outside the greater London area (personal communication Dr F. Drobniewski). It is too early to know whether there is a downward trend, but the situation in London is of particular concern.

PATHOGENESIS

Tuberculosis is spread from person to person almost exclusively by the respiratory route, and gains access to the body by inhalation of infective droplets of less than 5 μm. In the general population, once infected, there is an estimated 10% lifetime risk of progression to disease. By contrast, studies suggest that the lifetime risk of developing disease in HIV-infected individuals is greater than 50%.

There is no evidence to suggest that MDRTB is more infectious than drug-sensitive tuberculosis, but because the available treatment regimens are less effective, those with MDTRB are likely to be infective for longer periods of time. BCG immunization has been shown to offer approximately 70% protection from tuberculosis in UK teenagers, lasting for at least 15 years, and in immunocompetent individuals the protection against MDRTB afforded by BCG vaccination is thought to be no different to that from the drug-sensitive disease.

CLINICAL IMPORTANCE OF MDRTB

The importance of MDRTB clinically is related to its high case-fatality rates in both immunocompromised and immunocompetent patients. Mortality rates as high as 80–90% in HIV-positive patients, and 44% in HIV-negative patients have been reported.

Additionally, MDRTB is a significant threat to tuberculosis control because it is associated with prolonged sputum positivity (and consequently a higher transmission risk), is less likely to be cured, and will require the use of second-line/third-line treatments which are more toxic, more expensive, and less effective than standard drugs. Treatment of MDRTB is complex and time-consuming and should only be carried out by physicians with experience in managing complex resistant cases.

CONTROL OF MDRTB

Outbreaks of MDRTB in the US and Europe have emphasized the importance of control. These outbreaks have occurred mainly in institutional settings such as prisons, residential homes and hospitals, and have mainly, but not exclusively, been in HIV-infected patients.

Important contributory factors in these outbreaks include inadequate infection control measures, especially lapses in respiratory isolation, inadequate ventilation in respiratory isolation rooms, and 'immunocompromise convergence' (i.e. the assembling of immunocompromised HIV-infected patients in institutions such as hospitals).

The Control of Substances Hazardous to Health (COSHH) Regulations 1994 require that those responsible for the management of an individual with an infectious disease, and the infected individual, take reasonable precautions to prevent transmission of the infection to other susceptible individuals. The key elements in tuberculosis control are the prompt recognition, confirmation and treatment of cases, together with the instigation of infection control measures to reduce airborne infection.

Effective control requires a multi-disciplinary approach involving the hospital infection control team, microbiologist, TB physician, consultant in communicable disease control, and occupational health department.

All hospitals should develop and implement a local TB infection control policy or plan based on assessment of risk of MDRTB. Hospitals catering for those with MDRTB should ensure that they have access to appropriate isolation facilities. Expert engineering advice should be obtained concerning the air handling systems within the hospital, and the infection control team should be aware of the airflow characteristics of all isolation rooms.

Patients in whom MDRTB is likely or confirmed, should as a minimum, be admitted to a negative pressure single isolation room until multidrug resistance is excluded or until sputum smears have been negative on three consecutive occasions over 14 days. If suitable facilities are not available, the patient should be transferred to a centre where such facilities, together with treatment expertise, do exist.

While patients are infectious, visitors should be kept to a minimum, and a nursing system should exist whereby the number of healthcare workers exposed is kept as low as possible. Staff or visitors who have not been checked for immunity to tuberculosis, or those with a negative skin test who have not received BCG vaccination, should not visit. Contact with immunocompromised individuals must be avoided.

Personal protective equipment in the form of suitable particulate masks which filter down to particles of 1 μm in diameter (e.g. the Tecnol PFR95) should be worn by all who enter rooms of patients with suspected or confirmed MDRTB, and a respiratory protection programme should be implemented. The masks should also be worn by staff during aerosol generating procedures, such as sputum induction, bronchoscopy, and pentamidine therapy. In addition, these procedures should only be performed in suitably ventilated facilities.
The decision to discontinue strict isolation and infection control procedures should only be made after discussion between the clinician with responsibility for the patient, the hospital infection control team, occupational health and a consultant in communicable diseases.

OCCUPATIONAL HEALTH

The role of occupational health personnel is both to protect the healthcare workers against acquiring tuberculosis occupationally and to ensure the prompt detection of tuberculosis in new and existing staff in order to protect patients and colleagues.

Most studies have shown that the incidence of tuberculosis in healthcare workers, with the exception of pathology and mortuary staff, is no higher than the general population. Yet Meredith et al. showed that healthcare workers (mainly nurses, midwives and doctors) in England and Wales were more likely to have notified tuberculosis than the general population (after demographic and socio-economic factors had been taken into account). This indicates that tuberculosis remains a hazard in the healthcare setting. In their study no cases of MDRTB were notified, but staff transmission of MDRTB has been documented elsewhere. Staff protection begins at pre-employment, and the procedures for MDRTB are generally no different from the procedures for tuberculosis. Staff who have not been checked for immunity to tuberculosis, or those with a negative skin test who have not received BCG vaccination, should not be involved in the care of patients with infective MDRTB, and neither should those who are immunosuppressed.

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Occupational health departments will also be responsible for assessing the need for contact tracing of staff. In general, immunocompetent contacts should be screened and managed, in line with the British Thoracic Society guidelines of 1994. Procedures may involve checking BCG vaccination status, Heaf testing and symptom enquiry. Chemoprophylaxis may need to be considered, and if appropriate, should be supervised by a designated tuberculosis physician. However, there are few studies that evaluate the benefits of contract tracing in staff. In a recent outbreak, 792 staff had possible exposures to MDRTB and were screened, but none were found to have become infected. Tracing and screening was a lengthy process involving several hospital departments over many months.

Finally, occupationally acquired MDRTB is a prescribable disease, and there is a specific requirement for employers to report MDRTB infection in employees under the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995.

REFERENCES