

New drug for MDR tuberculosis

Multidrug-resistant (MDR) *Mycobacterium tuberculosis* (resistant to both isoniazid and rifampicin) causes, worldwide, about 490 000 new cases of tuberculosis and 110 000 deaths each year. New drugs are needed urgently. The new drug, TMC207, is a diarylquinoline that inhibits mycobacterial ATP synthase, a new mechanism for anti-tuberculosis drugs. Preliminary *in vitro*, animal, and human testing has shown it to be a drug of promise for the treatment of MDR tuberculosis. Now the results of the first stage of a phase II trial in South Africa have been reported.

A total of 47 patients with newly diagnosed MDR pulmonary tuberculosis were treated with a standard five-drug (kanamycin, ofloxacin, ethionamide, pyrazinamide, and cycloserine or terizidone) regimen, and randomised to TMC207 or placebo for 8 weeks. The rates of conversion to negative sputum cultures were 48% (TMC207) vs 9% (placebo). The time to conversion was shorter in the TMC207 group (hazard ratio 11.8) and the number of colony-forming units in sputum declined more rapidly. Adverse events were usually mild but nausea occurred in 26% vs 4%.

In the second stage the study will be extended to 24 weeks.

Non-invasive ventilation for weaning off invasive ventilation

Non-invasive ventilation via a facemask may facilitate weaning from invasive ventilation via an endotracheal tube. A systematic review and meta-analysis has provided further evidence.

The review included 12 trials (530 patients) mostly of patients with chronic obstructive pulmonary disease (COPD). Non-invasive weaning from mechanical ventilation was associated with a 45% reduction in mortality, and a 71% reduction in risk of ventilator-associated pneumonia. It also reduced length of stay in ICU by 6 days, length of stay in hospital by 7 days, and duration of ventilation.

Epinephrine and dexamethasone for viral wheeze in infants

There is uncertainty about the value of inhaled bronchodilators and steroids for infants who wheeze. Now a multicentre trial in Canada, published in the *New England Journal of Medicine*, has shown that treatment with oral dexamethasone and inhaled epinephrine (adrenaline) in the emergency department reduced rates of hospital admission.

The trial was carried out at eight centres during December to April in 2004–2007. A total of 800 infants aged 6 weeks–12 months (median 5 months) with a diagnosis of acute bronchiolitis (defined as a first episode of wheezing

associated with signs of an upper respiratory tract infection during the peak respiratory syncytial virus season) were randomised to four treatment groups in the emergency department: epinephrine plus dexamethasone (ED), epinephrine plus placebo (EP), dexamethasone plus placebo (DP), and double placebo (PP). Epinephrine was given as two doses each of 3 ml of 1:1000 solution via a nebuliser. Dexamethasone was given orally in an initial dose of 1.0 mg/kg followed by five doses of 0.6 mg/kg at 24-hour intervals. Rates of hospital admission by day 7 were 17% (ED), 24% (EP), 26% (DP), and 26% (PP). There was a significant 35% risk reduction in the ED group but this result became insignificant after statistical adjustment.

Anti-tuberculosis-drug resistance worldwide

The monitoring of anti-tuberculosis drug resistance worldwide has been undertaken by the Global Project on Anti-Tuberculosis Drug Resistance since 1994. A recent report, published in *The Lancet*, has included data from 83 countries and territories from 2002–2007, including 90 726 patients.

The average prevalence of resistance to any drug in new cases was 11%. In eight countries there was no multidrug resistance (MDR) but the prevalence was 7% at two sites in China and 7–22% in nine countries of the former Soviet Union. The prevalence of MDR tuberculosis in new cases increased between 1994 and 2007 in parts of Russia but it remained constant in Estonia and Latvia and decreased (among all cases) in Hong Kong and the USA. Thirty-seven countries reported data on extensively drug resistant (XDR) tuberculosis. Five countries of the former Soviet Union reported at least 25 cases and XDR tuberculosis occurred in 7–24% of MDR tuberculosis cases. Data from Africa are sparse.

Inhaled steroid for infants after RSV infection – negative study

Respiratory syncytial virus (RSV) commonly causes bronchiolitis in infancy and there may be recurrent wheezing after recovery from the acute phase. Now a study in The Netherlands, published in the *BMJ*, has shown that inhaled steroid does not prevent the recurrent wheezing.

A total of 243 infants (126 boys) with lower respiratory tract RSV infection were randomised to extra-fine hydrofluoroalkane beclomethasone or placebo via a pressurised metered-dose inhaler and a spacer for 3 months. The number of days of wheezing in the following year was similar in the two groups. Among infants who had not needed mechanical ventilation steroid treatment was associated with a significant 32% reduction in days with wheezing.

It was concluded that inhaled steroid should not be generally used for infants with RSV infection.