Tuberculosis in women and children

Globally, 700,000 women die from tuberculosis every year; this disease kills more women than do all causes of maternal mortality combined. Case-fatality rates seem to be higher in women than in men, and women are more often diagnosed with extrapulmonary tuberculosis. This sex difference might indicate under-reporting, because access barriers are higher for women because of sociocultural disempowerment, stigma, different patterns of health-care use, or lack of financial resources; however, poorly elucidated biological factors could account for some of the sex differences.

In tuberculosis-endemic areas, such as sub-Saharan Africa and India, the greatest burden of tuberculosis in women is during the childbearing years (15–49 years); this burden has been greatly exacerbated because of epidemiological changes induced by the global HIV/AIDS epidemic. Women account for up to 70% of HIV-infected adults in sub-Saharan Africa, which has shifted the male-to-female case-notification ratio such that more female than male cases of tuberculosis are now detected in countries where the HIV prevalence exceeds 1%. Tuberculosis in pregnancy has been associated with increased risk of low birthweight, prematurity, intrauterine growth retardation, and fetal death. Maternal tuberculosis is also an important risk factor for tuberculosis and mortality in infants, particularly in babies born to HIV-infected women. Targeted strategies to prevent, diagnose, and treat tuberculosis in HIV-infected pregnant women should promote both maternal and child health. Operations research with robust cost-effectiveness analysis is urgently needed to guide the nature and prioritisation of interventions in resource-restricted settings—eg, to assess the value of finding active tuberculosis cases and screening for latent tuberculosis infection, with provision of preventive treatment in HIV-infected women accessing antenatal care.

Children younger than 15 years contribute 15–20% of the global tuberculosis disease burden, with incidence rates about half those reported in adults, although accurate quantification is difficult because of poor case-ascertainment and restricted data for surveillance. Tuberculosis in children indicates continued transmission in settings with poor epidemic control, but is likely to be grossly underdiagnosed and under-reported in these areas. A common misperception is that children rarely develop serious forms of tuberculosis. Autopsy studies from sub-Saharan Africa showed that tuberculosis is a major cause of mortality in children younger than 5 years, in children both infected and not infected with HIV. Mycobacterium tuberculosis is also one of the most frequently identifiable causes of disease in children with community-acquired pneumonia that does not respond to first-line antibiotics. Full appreciation of the diversity of disease and the range of co-infecting pathogens associated with tuberculosis in children is slowly emerging with improved access to advanced diagnostic facilities.

The diagnosis and control of childhood tuberculosis is fundamentally different from that in adult tuberculosis, although immunocompromised individuals have a similar disease risk and profile. New diagnostic methods that accurately differentiate latent tuberculosis infection from incipient or active disease are urgently needed, especially for diagnosis in young children and immune compromised adults. Because of the high risk of disease progression, children with documented tuberculosis...
exposure or infection represent an opportunity for targeted disease prevention. This targeted prevention is rarely implemented in tuberculosis-endemic areas, mainly due to concerns about feasibility and drug resistance. However, simple, symptom-based screening approaches can be used in even the most resource-restricted settings, while use of isoniazid monotherapy offers excellent protection to asymptomatic child contacts with minimum risk of creating drug resistance. Family-centred tuberculosis control provides a means for active case-finding and the provision of preventive treatment to high-risk contacts.

Despite the escalating drug-resistant tuberculosis epidemic, the identification of new antituberculosis drugs is crucial. However, children are often excluded from drug trials because of a lack of financial incentives and difficulties in the measurement of microbiological outcomes. These are not insurmountable barriers, because extrapolation of efficacy data for adults seems reasonable, and paediatric formulations can be made available to poor countries through initiatives such as the Global Drug Facility. However, the need for child-friendly formulations and unique age-related pharmacokinetic and toxicity profiles require specific safety and dose-ranging studies in children. These studies should be done as early in the drug-development pathway as possible, as soon as initial adult safety and efficacy studies have been completed and preferably before drugs are licensed for use in adults.

Women and children have unique susceptibilities and might encounter substantial barriers to access appropriate care. Subgroups that require particular consideration include HIV-infected pregnant women, socially or culturally marginalised individuals, and very young or immunocompromised children. Young children are particularly susceptible, and every effort should be made to prevent exposure to tuberculosis and to provide preventive treatment should exposure occur. Apart from improvement of tuberculosis control, innovative strategies to advance tuberculosis prevention and treatment in women and children would contribute to the attainment of Millennium Development Goals 4 and 5 by reduction of the mortality rate in young children and women of reproductive age, particularly in tuberculosis-endemic areas.

*Ben J Marais, Amita Gupta, Jeffrey R Starke, Asma El Sony
Department of Paediatrics and Child Health, Faculty of Health Sciences, Stellenbosch University, Tygerberg 7505, South Africa (BJM); Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, MD, USA (AG); Infectious diseases Section, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA (JRS); and Epidemiological Laboratory (Epi-Lab), Khartoum, Sudan (AES)

bjmarais@sun.ac.za

AES is past-president of the International Union against Tuberculosis and Lung Disease (IUATLD). BJM, AG, and JRS declare that they have no conflicts of interest.