assistance in getting research into policy and practice. Education (particularly of students), audit, guidelines, incentives, and sanctions have all been successful levers for change.

Health-sector reform is painful, but Russia is beginning to face up to the epidemic. Support is growing among Russians for more effective approaches to tuberculosis control. International agencies can encourage and cajole, but massive resources for research and development, technical support, and urgently needed drugs are essential.

MERLIN and the Tomsk experience have shown that DOTS alone may not be entirely appropriate for Russia. The presence of a high rate of initial resistance, and the potential for HIV infection mean that there is no time to lose. A specifically Russian approach, based on DOTS, local epidemiology, and health sector reform is urgently needed.

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Sex, gender, and tuberculosis

Vinod K Diwan, Anna Thorson

Tuberculosis kills more than 1 million women per year, and it is estimated that 646 million women and girls are already infected with tuberculosis.[1] In women aged 15–44 years in developing countries tuberculosis is the third most common cause of morbidity and mortality combined, and tuberculosis kills more women than any other infectious disease including malaria and AIDS.[2]

Case-notification rates from countries with a high prevalence of tuberculosis suggest that tuberculosis may be less frequent among females. Globally, the ratio of female to male tuberculosis cases notified is 1/1·5–2·1. 70% more smear-positive male than female tuberculosis patients are diagnosed every year and notified to the WHO. It is unclear why more males than females are diagnosed with tuberculosis. The conclusion of a recent research workshop on gender and tuberculosis was that a combination of biological and social factors is responsible for these differences and that knowledge as well as research within this field is insufficient.[3] Epidemiological information shows that there are differences between men and women in prevalence of infection, rate of progression from infection to disease, incidence of clinical disease, and mortality due to tuberculosis.[4] The HIV epidemic, which affects females and males differently, has further complicated the tuberculosis situation. In sub-Saharan Africa the seroprevalence of HIV is higher in female tuberculosis patients than in male, whereas in Asia HIV prevalence among tuberculosis cases is still higher in males.

Prevalence studies based on tuberculin testing done in different settings show similar patterns with male prevalence exceeding female after 16 years of age. Differences between males and females have also been shown in the development and outcome of active disease, with female cases having a higher progression from infection to disease and a higher case-fatality rate.[4] Although the tuberculin-testing prevalence studies indicate that more males than females are infected with tuberculosis, an alternative explanations for these findings is that there are differences in the immune response to tuberculin. This hypothesis is supported by a study from Japan showing that more male than female tuberculosis cases had a positive tuberculin reaction.[5] Moreover, in a study of senior schoolchildren in Kuwait, boys had a delayed-type hypersensitivity reaction to more mycobacterial sensitins than girls as well as larger scars after BCG revaccination.[6] Differences between females and males in immune response could thus be part of an explanation of differences in symptoms, signs, forms, and outcome of tuberculosis. The immune response to tuberculosis may also be closely related to differences between females and males in type and concentration of non-sex-steroid and sex-steroid hormones secreted.[3] Animal studies suggest that pregnancy induces Th2 activity, which would be detrimental to the course of tuberculosis; however, it has not been possible to relate these findings to clinical or epidemiological characteristics of human tuberculosis. The studies that have been done on pregnancy in relation to tuberculosis in women show conflicting results.[3] It is also noteworthy that despite inconclusive findings on the effects of pregnancy, it is one of the few fields where sex differences in tuberculosis have been explored, thus supporting the traditional view of women as merely vectors for childbearing and caring. Obviously sex-specific biological characteristics in tuberculosis patients have been a neglected area for research, and now need urgently to be acknowledged and explored.

Tuberculosis is a global health emergency and a symptom of global poverty as can be seen by the unequal distribution of both factors in the world. It is important to note that 70% of the world's poor are female and that these women face the greatest obstacles to seeking health

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care and getting successful tuberculosis treatment. Both males and females are infected, progress to disease, and die due to tuberculosis. Whereas males and females share many beliefs and attitudes to tuberculosis, there are considerable differences with regard to stigma and its social consequences.[3] Not only the individuals but also the whole family may suffer from social stigma and its negative consequences, which are harsher for the female family members. Stigma may lead to delays for both sexes in seeking care, but more so for females if the physical, geographical, and economic access to health care is limited. The social structure of many societies in developing countries today relies on women having a double or triple workload—ie, taking care of the family and home, doing agricultural work, and perhaps also doing waged work. The impact of tuberculosis in women is thus severe not only on their families but also on the development of society through loss of workforce, ruined families, and orphaned children.

The WHO is forcefully promoting the brand-name strategy of directly observed therapy short-course (DOTS). "Supervised swallowing" or directly observed therapy (DOT), where health workers or trained volunteers watch the patient take his or her treatment, is one of the five elements of the DOTS strategy. The DOT element means that the patient has to visit the health worker or vice versa. Both these alternatives may impact differently on women and men and may be difficult for women—who have little extra time and poor economic resources—to comply with. This alienating and authoritarian approach may further undermine the status of women and their chances of receiving tuberculosis treatment. DOT may be less effective for women as suggested by a recent randomised controlled trial of DOT versus self-supervised tuberculosis treatment.[7]

Tuberculosis control is a gender issue that has been neglected by the tuberculosis-control programmes. "Gender" refers not only to the physiological differences between sexes but also to the variety of behaviours, expectations, and roles that exist within a social, economic, and cultural context. A gender-based approach to tuberculosis control will assist in understanding not only the biological and cultural differences between the sexes but also the structural violence leading to poverty, grossly inadequate health care resources, and increased risk of tuberculosis and death.[3]

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Children and tuberculosis: protecting the next generation?

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Attitudes to childhood tuberculosis are determined by whether one is a clinician or a health administrator attempting to control tuberculosis. In developed communities tuberculosis occurs mainly in older adults; in developing communities tuberculosis occurs at all ages, albeit with differing manifestations. In developing communities a high disease incidence is encountered in young children. A large proportion of the population is aged less than 15 years and as many as 40% of tuberculosis notifications may be children;[1] tuberculosis may be responsible for 10% or more of childhood hospital admissions and 10% or more of hospital deaths.[2] Furthermore, with an annual risk of infection of 2–3%, close to 40% of the population may be infected by age 15 years.

The figure illustrates schematically the age-related population pyramids in the process of infection (B) and disease development (C). The figure also shows, by way of contrast, the shape of the broad-based population pyramid in a hypothetical developing community (A). The high incidence of disease among the relatively small population of infected infants is noteworthy as is the rapid rise in incidence among teenagers. While those concerned with tuberculosis control will focus upon patients with cavitating disease who are spreading infection, the clinician will be concerned with the varying manifestations of disease occurring from infancy through to adolescence.

Against this background and with HIV-seroprevalence rates among the sexually active population approaching 30% in much of sub-Saharan Africa, what opportunities exist for protecting the next generation against the ravages of tuberculosis?

First, it is unlikely that a new vaccine or new antituberculosis agents will become available in the foreseeable future. In the absence of any better vaccine BCG vaccination of newborn babies should continue and may offer protection against disseminated disease. Even in developing communities a significant proportion of adult-type disease may arise from lymphohaematogenous dissemination to the lung apices, and later endogenous reactivation rather than recent infection.[3] Adolescent BCG vaccination may therefore theoretically help prevent adult-type pulmonary tuberculosis in the older adolescent. If this

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