Where are we in the Global Fight against TB?

An Update from Dr. T. Jacob John

Tuberculosis (TB) was described a global emergency in 1994 (World Health Organization 1994) but its control strategy has not improved since then. Globally, the estimated number of incident cases of TB increased from 9.24 to 9.27 million between 1990 and 2007, of which 86% are in Asia and Africa (WHO 2009). Three factors are involved in the TB burden: population growth tends to increase, but secular trend and control efforts tend to reduce the number of incident cases. Their sum total has been estimated to be a meagre <1% annual decline of cases. The estimated incidence (per 100 000) was 142 in 2004 and 139 in 2007 (World Health Organization 2009). At this rate, the Millennium Development Goal (MDG) to reduce by half TB prevalence and death by 2015 (compared to 1990 levels) will be missed by a disappointingly huge margin. Poverty is both determinant and consequence of TB. Hence the MDG of poverty reduction also depends on TB control. The annual loss due to TB morbidity in India alone has been estimated at US $ 3 billion (Government of India 2009). A radical re-think and paradigm shift are essential for TB control, especially in high prevalence countries.

There are several reasons why TB has not been controlled by current efforts. Control has to be defined in such a manner that its trajectory can be monitored over time; currently no such monitoring is included in the TB control program in many countries (John 2000). Ideally any infectious disease control requires primary prevention (reduction of the incidence of infection). An additional approach is secondary prevention—in the case of TB, reduction of frequency of latent infection progressing to pulmonary TB. The natural history of TB begins in individuals with primary infection. Pulmonary TB is the infectious form of disease with shedding of mycobacteria into the environment, leading to fresh infections. Much reliance was once placed on BCG vaccination of infants for primary and secondary prevention. However, a large vaccine trial in India showed that BCG did not provide either benefit (Tuberculosis Research Centre 1999). Thus the current control program relies solely on rapid microbiological cure of pulmonary TB so as to reduce the intensity and duration of mycobacterial shedding. These cannot be quantified to monitor control trajectory. There is hardly another epidemiological model of infection-control solely by treatment of end-stage disease.

The current guidelines of 70% case detection and 85% cure rates of pulmonary TB for control were based on mathematical modelling and not epidemiological evidence (Dye et al. 1998). While the cure rate can be monitored among detected cases (the denominator), the case detection rate cannot be monitored since the population-prevalence would be unknown except where case-notification or active search is practiced (Gonzales-Ochoa et al. 2009; Grange et al. 2009; Kritzinger et al. 2009). Even if truly 70% were detected through sputum-smear testing and 85% cured within a few weeks, would that reliably control primary infection rate in susceptible children? In high prevalence communities it will not, as shown in South Africa and in India (John 2008; Kritzinger et al. 2009).
There is often an interval during which a person with pulmonary TB is not symptomatic but sheds mycobacteria into the environment. In highly endemic situations, much of the infection in contacts occurs before diagnosis and start of chemotherapy (Kamat et al. 1996). Microbiological cure takes a few more weeks. Meanwhile, more new infections would have inevitably taken place. In high prevalence communities, children may be exposed to more than one infectious individual. The probability of infection increases with repetitiveness of exposure (in household, neighborhood, school, etc.) and cumulative time of exposure (the function of age). Where prevalence is high, virtually every child is exposed; the likelihood of infection increases as infants grow through childhood to adolescence, as in south India and South Africa (John et al. 1971; Kritzinger et al. 2009). The experience from South Africa shows very high annual risk (rate) of tuberculosis infection (ARTI) despite very high rates of case-finding and cure (Kritzinger et al. 2009). In India, the ARTI has not declined over decades (John 2008). Thus, the present risk-reduction approach for TB control is not on sound epidemiological basis.

From the healthcare viewpoint, all persons with TB deserve diagnosis and treatment. The 70% goal of detection of pulmonary TB is only for public health purpose of TB control. Where disease prevalence is high, the detection rate must also be high, as near 100% as possible — for effective public health and for equitable healthcare. Therefore, in addition to the present method of passive detection through cough clinics, some form of active search must be designed locally for improved case-detection (Murray & Salomon 1998; Gonzales-Ochoa et al. 2009). A relatively simple approach is to capture in the TB control system all patients diagnosed with pulmonary TB in the healthcare system, in both public sector and private. Moreover, every child diagnosed with primary TB must trigger a search for adults with active TB in the household and neighbourhood (John 2008). Similarly, when an adult is detected with TB, all children in contact ought to be screened for infection. These steps will succeed only if there is close coordination between the two systems of TB control and healthcare (John 2008; Gonzales-Ochoa et al. 2009). Unfortunately in many countries TB control and healthcare work in isolated compartments without interaction. An added advantage of such coordination is access to existing microbiology diagnostic laboratories for culture and sensitivity testing so as to expedite case detection and diagnosis of drug resistance — currently resistance is diagnosed only after clinical treatment failure. Where laboratories do not exist, access should be designed locally — if necessary by creating new laboratory facilities at district or provincial level (Gonzales-Ochoa et al. 2009). For countries like India where financial resource is not the major constraint, one sputum culture (in addition to two smears for microscopy) will markedly increase case detection, further improving the control efforts, as practiced in Cuba (Gonzales-Ochoa et al. 2009).

The basic criterion of control — or the expected outcome of control efforts — is declining incidence of infection (ARTI); hence it has to be monitored in all communities over time (John 2000, 2008). Case detection efficiency and cure rate are measures of ‘inputs’, whereas decreasing ARTI is the ‘output’ or
‘outcome’. If tuberculin skin testing (TST) is applied on children, for example at one selected age, such as at 5 years, either in community or healthcare setting, on all children or selected samples, on an annual basis, we can set and monitor a trajectory required for control. We propose, arbitrarily but conservatively and realistically, that annual 5% reduction of ARTI be set as an achievable goal for local TB control. This approach has the added advantage of detecting infected children early in life for giving ‘preventive treatment’, as a means of secondary prevention.

In conclusion, we believe that the TB control programme deserves a transformational change – a paradigm shift in addition to an incremental change of the current strategy for improved case detection as described above. The paradigm shift requires two elements: incidence monitoring and multiple interventions. Everyone must participate in TB control; basic lessons on transmission route, cough etiquette, spitting behavior etc. must become common knowledge through imaginative health education both in schools and in the community. Hospitals have the additional responsibility to ensure infection control in crowded outpatient clinics and wards. The broadened interventions will include local application of epidemiology intelligence, inputs and outcome monitoring, close local level coordination between TB control and healthcare systems, regular but judicious application of microbiology for diagnosis and drug sensitivity monitoring and community education for desired behaviour modification. If ARTI does not decline 5% annually after the necessary lag period following the institution of the new paradigm approach, local epidemiological ‘research’ must be conducted to know why.

The spread of TB in many low income countries has been made worse by the HIV epidemic and the emergence of multi-drug-resistant (MDR) and extensively drug resistant (XDR) TB. We must, for the sake of future generations, and before MDR and XDR TB becomes commonplace, achieve and sustain TB control. A paradigm shift is extremely urgent.

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