The place of leprosy in the control–elimination–eradication spectrum

Editor – I would like to expand on Lockwood & Suneetha’s reflections on the leprosy elimination campaign (1), and in particular their statement that “leprosy is perhaps more appropriately classed as a chronic stable disease rather than as an acute infectious disease responsive to elimination strategies”, by using the control–elimination–eradication (CEE) paradigm that has served public health workers and surveillance experts so well in the fight against communicable diseases since the late 19th century (2).

Infectious disease “elimination” commonly refers to reducing the number of cases of disease to a small and routinely manageable number. Thus, prevalence trend is a key yardstick in the CEE paradigm. When leprosy elimination campaigns were put in place in the 1990s, their primary goals were to implement enhanced surveillance activities in order to detect leprosy cases promptly and to treat them immediately with multidrug therapy (3). Between 1985 and 2002, global leprosy prevalence fell by about 95% (1). In May 2001, the World Health Assembly affirmed that “the overall target, set ten years ago, for the global elimination of leprosy as a public health problem has been attained” (4).

“Control” is usually the first approach to cope with the deleterious effects of intractable infectious diseases such as tuberculosis and syphilis. When the prevalence and adverse effects are curtailed, the focus normally shifts from control to elimination. For example, as the prevalence of Chagas disease continues to fall in Central America, the focus has shifted from disease control to disease elimination, through vector control activities and the screening of blood banks (5).

Smallpox is probably the only human disease so far that has reached the “eradication” end of the spectrum (no cases reported since 1979), though dracunculiasis (guinea-worm disease) — which, like leprosy, is a chronic stable disease — and poliomyelitis are also inching very close to being eradicated. For instance, there are currently less than 800 incident cases of polio worldwide, and the formidable infrastructure for polio eradication makes it more likely than ever that the disease will be eradicated during this decade (6). Interestingly, erstwhile polio researchers expressed serious doubts concerning the feasibility of poliomyelitis elimination or eradication about a century ago, when poliovirus microbiology and vaccination were less well understood (7).

It is noteworthy that diseases that have progressed steadily from the control to the eradication ends of the spectrum are invariably those whose microbiology has been well delineated and for which effective control and treatment measures to interrupt transmission are available. The microbiology of leprosy is not yet fully elucidated, and it appears unlikely that multidrug therapy alone would prevent leprosy transmission (1). Given these gaps in current knowledge concerning microbiology and therapy, it is not surprising that the elimination stage appears to be the dead end for efforts to reduce the scourge of leprosy. While it would be counterintuitive to go back to the control stage of the paradigm, given the tremendous progress made in case detection and treatment (especially since the introduction of multidrug therapy in the 1980s), it is also clear that unless we can bridge the gaps in our knowledge of leprosy microbiology and transmission mapping, leprosy elimination is unlikely to progress to leprosy eradication.

Rather than table a World Health Assembly resolution that leprosy has not been eliminated, as reportedly suggested by some evaluators of the Global Alliance for the Elimination of Leprosy (1, 8), it might be more productive to work towards overcoming our knowledge gaps with regard to leprosy microbiology and therapy. Unless extraordinary resources are provided for clinical and epidemiological research, leprosy will remain a disease that is eliminated but is far from eradicated. Such an approach might in fact stimulate interest among a new generation of researchers, and generate research funding from donors that hitherto appear reluctant to support leprosy research.

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Niyi Awofeso1


Invest in breaking the barriers of public–private collaboration for improved tuberculosis care

Editor – Mahendra Nath & Utarini rightly call for an urgent move from feasibility studies of public–private collaboration in tuberculosis (TB) control to studies that analyse success factors as well as the cost and cost-effectiveness of such initiatives (1). WHO is currently coordinating a number of operational research initiatives that focus on these issues.

In the August 2004 issue of the Bulletin, we published a study on success factors for public–private collaboration in TB control (2). That analysis was based on project evaluations of four initiatives in three countries. We

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are continuously updating this analysis based on a rapidly growing body of data from more than 40 ongoing projects in 14 countries. A policy framework and tools to help implementation have been developed based on field experiences and operational research. Information about WHO’s work on private sector involvement in TB control can be found on the web site: http://www.who.int/tb/dots/ppm.

Mahendradhata & Utarini highlight the fact that public–private collaboration for improved TB control takes place in a context of constrained resources and competing interests. Our analysis suggests that government investment is indeed crucial in order to ensure technical capacity-building in the private sector, managerial capacity-building in the public sector, improved supervision and quality control of private providers, and improved surveillance. Public funding is also needed in order to secure a supply of drugs and consumables free of charge to TB patients attending private clinics. While additional investments will be required, cost-effectiveness analysis of two collaborative projects in India has demonstrated that the amounts of such investments would be comparable, on a cost per successfully treated case basis, to those required by the public sector (3). From a societal perspective, a significant added value would be a substantial reduction in the financial burden on patients and, potentially, early detection and reduction in transmission of TB.

From documented experiences, what do we already know about why partnerships work? As expected, the determinants of success are precisely the factors that help to counter some of the well-known barriers to collaboration (4). First, a genuine commitment on the part of the public sector demonstrating that it is indeed interested in working with private providers; second, justifiable additional investments — human and financial — to help build the collaboration and contribute further to TB control; third, a proper situational analysis to develop a locally appropriate task-mix for public and private providers; fourth, orientation and training of both public and private providers to prepare them to work together; and finally, a built-in monitoring and evaluation system to continue to measure the benefits and to improve upon the collaboration (2, 5).

For Mahendradhata & Utarini’s own project, if they intend to apply first what they mentioned first — the strategy of strengthening regulatory structures — then a word of caution is called for. Regulation of private providers is indeed crucial and must be dealt with. To begin with a heavy emphasis on “regulating” providers, however, could turn the project into a non-starter. Experience shows that in public–private partnership building, when to employ a strategy is as important as the strategy itself. This and similar potential stumbling blocks could be avoided if private providers are involved in the process right from the first step of planning an intervention and, more importantly, in a spirit of partnership.

Competing interests: The authors work with the Public–Private Mix for DOTS Initiative in the Stop TB Department at WHO.

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Can clinical algorithms deliver an accurate diagnosis of HIV infection in infancy?

Editor – The Integrated Management of Childhood Illness (IMCI) guidelines established clinical criteria to identify children with suspected HIV infection for HIV testing and specific management. In an article published in the Bulletin, based on a study conducted in South Africa, Horwood et al. report that they have fine-tuned these criteria into a clinical algorithm (1). This algorithm has been incorporated into the 2003 edition of the South African IMCI guidelines to maximize identification of HIV infected children (1, 2). Horwood et al.’s study clinically assessed 690 hospital outpatients, aged 2–59 months, in an HIV prevalence setting of 28.7%. In the absence of screening questions, the clinical algorithm was applied and yielded a sensitivity of 70%, specificity of 80% and a positive predictive value (PPV) of 59%. The validity of the algorithm for the 226 infants (2–11 months), 38% of whom were infected, did not differ from that for the older age categories (1). Validation of the clinical algorithm in different settings was invited (1).

Vertically exposed infants in prevention-of-mother-to-child transmission (PMTCT) programmes in low-resource settings rely on clinical assessments for HIV diagnosis since infants are first tested at 12 months of age using an HIV enzyme-linked immunosorbent assay (ELISA). The HIV prevalence among infants will vary according to the availability of PMTCT services and the mode of infant feeding. We carried out a study to establish an affordable and accurate diagnostic protocol for HIV using a cohort of 301 infants attending a PMTCT clinic at Coronation Women and Children's Hospital, a secondary-level hospital in Johannesburg, South Africa (3). At 12 months of age, the infant’s true HIV-infection status was determined using polymerase chain reaction (PCR) testing according to the Centers for Disease Control and Prevention (CDC) guidelines, in conjunction with clinical assessments (4). In a predominantly exclusively formula-fed population, 26 patients (8.7%) were HIV positive (3). At the visits at 6 weeks and at 3, 7 and 12 months of age, 18 different doctors experienced in local paediatric HIV care and blinded to the HIV test results prospectively diagnosed the infant’s HIV infection status based on clinical findings. Two-thirds of all clinical examinations were performed by paediatricians. The clinical findings were recorded on a structured data collection tool.

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that concentrated on clinical features derived from CDC clinical guidelines (i.e., recurrent infections, weight gain, candidiasis, lymphadenopathy, hepatosplenomegaly) (4). The number of HIV-infected infants who were correctly clinically diagnosed in our study increased with age from 56% at 6 weeks of age to 93% at 12 months of age.

The performance of the IMCI algorithm in our study population was retrospectively assessed by applying our source data to the South African 2003 IMCI clinical algorithm which consists of asking, looking and feeling for eight features of symptomatic HIV without the screening questions (5).

The disturbing finding was that the algorithm would have detected only 17% of HIV-infected infants at 6 weeks of age. Even though the detection rate improved to 50% for infants aged 12 months, this was still much lower than the rate of 70% reported by Horwood et al. (1). Retrospective application of the IMCI algorithm to clinical data collected by highly skilled personnel therefore yielded particularly poor sensitivity in detecting HIV infection throughout infancy.

A long-term prospective study in Rwanda has documented that HIV-infected children in Africa develop early morbidity and mortality (6). In our cohort, all 15 surviving HIV-infected infants available for assessment at 12 months of age were symptomatic and required specific medical interventions, e.g. antifungal treatment for oral thrush. Despite this clinical scenario, eight (53%) of the 12-month-olds would not have been detected by the IMCI algorithm. The high early mortality rate of HIV-infected infants is a further concern, particularly with the increasing availability of antiretroviral therapy. Of the 10 HIV-infected infants who died before their first birthday, 5 (50%) would have remained undiagnosed by the IMCI algorithm. The clinical assessments in our study missed 2 (20%) of these children. Like Horwood et al., we noted that the higher sensitivity of the doctors’ clinical assessments was often attributable to the detection of hepatosplenomegaly, which is not included in the IMCI algorithm (1).

Clinical diagnosis of HIV infection in infancy remains a challenge. Additional prospective assessments of the IMCI clinical algorithm in vertically exposed infants in PMTCT settings with different HIV prevalence are required. It is a cause for concern that in our PMTCT setting the IMCI algorithm used by highly skilled clinical practitioners only identified approximately half of the infants experiencing HIV-related mortality and morbidity at 12 months of age. In an era of expanding antiretroviral scale-up programmes, clinical assessment remains an unacceptably insensitive diagnostic tool for ensuring that HIV-infected infants access care. A more pragmatic approach may be to invest in assessment of affordable, simple methods of testing for early diagnosis of infants rather than relying on clinical skills alone.

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