WHO's role in tuberculosis research

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Further development of new technologies to detect TB in the lungs (as shown on the right) is badly needed.

Although significant advances in the fight against tuberculosis (TB) may be made by proper application of existing diagnostic and treatment technologies, considerably more progress might be possible if new tools were available. The most commonly used diagnostic tests - sputum smear microscopy, culture of mycobacteria for identification and tests for TB drug sensitivity, tuberculin skin testing, and chest radiography - are decades old and suffer from various drawbacks.

Smear microscopy, while identifying the most infectious cases of pulmonary tuberculosis, is not sensitive to low levels of disease and requires well-maintained equipment and well-trained laboratory workers. Culturing and drug susceptibility testing call for even more expertise, require up to two months to give results, and cost still more. Tuberculin skin testing is primarily used in surveys to estimate the risk of infection, but it is not sufficiently accurate to be useful as a diagnostic test for active disease. Chest radiography is expensive and generally available only in hospitals and specialized diagnostic centres. Furthermore, there is evidence that over-reliance on radiography leads to over-diagnosis of tuberculosis and unnecessary expenditure on drugs and on staff time. It may also not be able to detect the early stages of disease. Thus, new, simple and rapid tests would significantly improve tuberculosis diagnosis.

Modern short-course therapy for tuberculosis works very well but requires patients to take medication regularly for at least six months to be cured. Not surprisingly, patients all too often stop taking their medicine prematurely. Furthermore, in some countries drug-resistant TB appears to be on the increase. Tuberculosis drugs may also be used to treat persons infected by the tubercle bacilli before they develop the active disease. This preventive chemotherapy may be useful in limiting the increase in tuberculosis due to HIV infection, but again it involves taking medication for relatively long periods and its cost-effectiveness remains to be determined. It is clear that new drugs are needed to shorten current therapy, to improve preventive therapy, and to treat persons with drug-resistant TB.

Finally, although BCG vaccination has been widely applied, it has had little apparent epidemiological impact on tuberculosis incidence. Because BCG does prevent serious and often fatal forms of tuberculosis in young children, its use in newborn children is still vital. However, research is badly needed to develop new, effective vaccines against tuberculosis. Especially beneficial would be a vaccine which is capable of protecting already infected persons from developing the active disease.

WHO's involvement

For these reasons, WHO's Tuberculosis Programme is actively promoting the development and assessment of new tools for the diagnosis, treatment and prevention of tuberculosis. Clearly, tuberculosis research will be most economically and easily conducted in countries where the disease is most prevalent. This is especially true for clinical therapy trials, which involve comparison of a new drug or a new drug regimen with standard treatment, and require substantial numbers of patients to be followed for relatively long periods of time. Although there
are existing infrastructures to support these types of trials in developed countries, it would be difficult for investigators in those countries to recruit the required number of patients and follow them for the required period.

Given the scarcity of resources available for TB research, it is imperative that the global research effort be properly coordinated, avoiding unnecessary duplication and helping to ensure that funding is being applied to the studies of greatest importance. WHO’s Tuberculosis Programme has taken on this coordinating role, with an emphasis on studies which may yield results in three to five years and which are of special relevance to developing countries hardest hit by tuberculosis. Chosen as the most important research areas are:

- Laboratory and clinical studies of both existing and promising new anti-TB drugs and drug regimens, new methods of drug delivery and new ways of stimulating the body’s immune system to improve treatment;
- The development and assessment of new, rapid diagnostic tests for active tuberculosis and TB infection;
- Epidemiological studies using new techniques (such as DNA “fingerprinting”) to improve TB control, and studies to define better the groups and individuals at increased risk of tuberculosis;
- Studies on the interaction of tuberculosis and HIV infections that would have direct and immediate application to national tuberculosis programmes.

**Funding prospects**

In the past it proved difficult to attract funding for research studies. Fortunately, with the successful initiation of the research programme, the prospects for increased funding are good. The most critical need for research and development studies is the availability of a laboratory capable of isolating and identifying *Mycobacterium tuberculosis*, and of reliably performing drug susceptibility studies. Development of research and laboratory infrastructure will be an important component of future activities.

The research component of WHO’s Tuberculosis Programme works closely with WHO’s Global Programme on AIDS in the management of the TB-related portion of HIV research. Support has been provided to monitor HIV-associated tuberculosis trends in Uganda and the United Republic of Tanzania, and to determine the infectiousness of HIV-associated tuberculosis in the Dominican Republic. The research in Africa has demonstrated the tremendous impact of HIV on the tuberculosis problem. Studies to evaluate the efficacy and toxicity of short-course chemotherapy in HIV-infected TB patients are under way in Haiti (in adults) and the Dominican Republic (in children). Another paediatric study in Zambia has shown that fatal skin reactions occur frequently in children treated with the anti-tuberculosis agent thiacetazone, and has led to a change in WHO recommendations on TB therapy for persons who are also at risk of HIV infection. A unique study in Uganda to evaluate the operational feasibility of isoniazid preventive chemotherapy for HIV-infected persons is critical to the process of assessing new public health policies which could emphasize the role of TB prevention for high-risk populations in the developing world.

In the area of diagnostic studies, close cooperation is maintained with the tuberculosis component of the WHO/UNDP Programme for Vaccine Development, and support has been provided for assessment of new tests such as PCR (polymerase chain reaction) for TB diagnosis. In the field of drug development, WHO-supported studies have shown the potential of the new quinoline derivative, sparfloxacin, for tuberculosis treatment, and the great activity of a new rifamycin antibiotic, rifapentine, for tuberculosis preventive therapy. A comprehensive, global drug development plan has been proposed, specifying the role of WHO in this activity, and emphasizing the coordination of clinical therapy trials through a network of collaborating centres.

Clearly there are tremendous challenges to be met in tuberculosis research, and WHO believes that, with the help of the global research community, it will make an important contribution to the advance against this old disease.

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