# TUBERCLE

# The global tuberculosis situation and the new control strategy of the World Health Organization

The World Health Organization Tuberculosis Unit undertook a special study [1] in 1989/90 to determine the nature and magnitude of the global tuberculosis problem by reviewing the official statistics and the available data from both published and unpublished field studies, including the article by Murray *et al.* [2]. The findings of this study are summarized in Table 1.

## Infection

About 1,700 million people, or one third of the world's population are, or have been, infected with *Mycobacterium tuberculosis*. The overall proportion of infected people is similar in the industrialized and developing nations. However, 80% of infected individuals in industrialized countries are aged 50 years or more while 75% of those in developing countries are less than 50 years old. This is the result of differences in the past and current levels of transmission of the infection and in the population structures in these two areas.

## Disease

It is estimated that, in 1990, there were 8 million new cases of tuberculosis in developing and industrialized countries: 7.6 million (95%) in the former and 400,000 (5%) in the latter. The largest numbers were in the WHO's Western Pacific Region (2.6 million), the South-East Asian Region (2.5 million) and the African Region (1.4 million). The highest incidence was in the African Region (272 cases per 100,000).

## Death

It is estimated that tuberculosis caused 2.9 million deaths in 1990, making this disease the largest cause of death from a single pathogen in the world. While the largest number of deaths occurred in the South-East Asian Region (940,000), the Western Pacific Region (890,000) and the African Region (660,000), it is estimated that more than 40,000 deaths still occur annually in the industrialized nations.

## Characteristics of patients

There is a striking difference in 'who suffers from tuberculosis' between developing and industrialized countries due to the differences in the pathogenesis of the disease in these countries. In the industrialized countries, tuberculosis is mainly seen in the elderly and is usually the result of endogenous reactivation of infection contracted in the past. Only a small percentage of all cases are the result of recent infection and these occur mainly in ethnic minorities and migrants. In developing countries the risk of infection remains high and tuberculosis afflicts nearly all age groups. While 1.3 million cases and 450,000 deaths from

**Table 1** The global toll of tuberculosis.

| Region | People infected (millions) | New cases | Deaths |
|---|---|---|---|
| Africa | 171 | 1 400 000 | 660 000 |
| Americas* | 117 | 560 000 | 220 000 |
| Eastern Mediterranean | 52 | 594 000 | 160 000 |
| South-East Asia | 426 | 2 480 000 | 940 000 |
| Western Pacific† | 574 | 2 560 000 | 890 000 |
| Europe and other industrialized countries§ | 382 | 410 000 | 40 000 |
| Total | 1 722 | 8 004 000 | 2 910 000 |

*Excluding USA and Canada.
†Excluding Japan, Australia and New Zealand.
§USA, Japan, Australia and New Zealand.

tuberculosis in developing countries occur in children under the age of 15 years [3], the greatest incidence and mortality is concentrated in the economically most productive age group of the population (15–59 years). More than 80% of the tuberculosis toll in the developing world falls in this age group. Furthermore, it is estimated that tuberculosis accounts for 26% of avoidable deaths.

## Current levels and past trends of infection

Countries can be divided into four groups in terms of the current level and past trends of the annual risk of infection and health resource availability [4] as shown in Table 2. In industrialized countries (group I), tuberculosis has been declining very rapidly as transmission, measured as the annual risk of infection, has diminished. Nevertheless, tuberculosis remains one of the most common notifiable infectious diseases. Furthermore, in many industrialized countries, the declining trend has slowed down and, in some countries (USA and Japan), it has reversed. In some middle-income developing countries (group II), tuberculosis has declined relatively rapidly and has begun to lose its status as a major public health problem. In other middle-income developing countries (group III), the decline is slow and tuberculosis remains a major public health problem. In these countries there is a higher frequency of patients with drug-resistant disease than in other countries, due to a combination of the poor quality of treatment in the national tuberculosis control programmes in the past and the uncontrolled use of anti-tuberculosis drugs in the private sector. In the majority of low-income developing countries (group IV), there has been almost no observable decline and the absolute number of cases is probably increasing due to population growth.

## Current status of control activities

In order to assess the current status of tuberculosis control activities in developing countries, WHO undertook another special study in 1989 [5]. The results of this study can be summarized as follows:

### Monitoring

The majority of countries do not have a built-in mechanism to monitor the outcome of treatment. The WHO investigation has so far identified less than 15 countries with such a built-in monitoring system to produce, on a regular basis, crucial information on the percentage of patients who were cured or who died or absconded. Many countries, however, have partial information on the outcome of treatment based on *ad hoc* surveys in a limited number of treatment centres.

### Cure rates

In many developing countries less than half of the tuberculosis patients who started treatment were cured or completed their course of chemotherapy. However, four countries (Malawi, Mozambique, Nicaragua and Tanzania), which have built in systems to monitor treatment outcomes, achieved cure rates of over 80%. These excellent results were obtained with technical and financial assistance of the International Union Against Tuberculosis and Lung Disease (IUATLD).

### Coverage of tuberculosis services

It is roughly estimated that less than half of the existing tuberculosis patients in developing countries, excluding China, are covered by the treatment services. This proportion varies considerably among the different WHO regions (Table 3). There has been no significant change in the coverage rate of services in any region over the past 15 years.

### The impact of HIV infection

It is estimated that more than 3 million people are dually infected with the tubercle bacillus and HIV in the world, 2.4 million in Sub-Saharan Africa alone. HIV infection is the highest risk factor so far identified which increases the chance of latent infection with tubercle bacilli progressing to active tuberculosis by reducing the protection provided by cell-mediated immunity [6]. Presently, less than 5% of cases of tuberculosis throughout the world are associated with HIV infection but the majority of these cases are

Table 2   The epidemiological pattern of tuberculosis.

| Countries or areas | Annual risk of infection | | Health resource availability |
|---|---|---|---|
| | Current level (%) | Annual decline trend (%) | |
| I Industrialized | 0.1–0.01 | >10 | Excellent |
| II Middle-income in Latin America, West Asia and North Africa | 0.5–1.5 | 5–10 | Good |
| III Middle-income in East and South-East Asia | 1.0–2.5 | <5 | Good |
| IV Sub-Saharan Africa and Indian subcontinent | 1.0–2.5 | 0–3 | Poor |

concentrated in only 10 Sub-Saharan African countries. In these countries, the AIDS epidemic is having a devastating effect on tuberculosis control programmes, with up to 100% increases in reported tuberculosis cases in the last 4–5 years [7]. There are more demands for diagnostic services, anti-tuberculosis drugs, hospital beds and other supplies and services in areas where they are already in short supply. HIV infected persons have a higher frequency of extrapulmonary tuberculosis, which is more difficult to diagnose than pulmonary tuberculosis. Also, as HIV infected persons have, in certain instances, had adverse reactions to drugs, particularly to thiacetazone, patient management is becoming increasingly difficult. As the association between tuberculosis and HIV infection becomes more widely known, the diagnosis of tuberculosis will begin to carry an additional social stigma. It also creates fear among health care workers who become reluctant to work in the programme. A higher mortality rate among HIV-related tuberculosis patients, together with the difficulties described above, may frustrate the workers and decrease the credibility of the programme.

## Objectives and policy of the WHO tuberculosis programme

The objectives of the programme are to reduce:
  i) tuberculosis mortality;
  ii) the prevalence of the disease which is currently estimated at more than 20 million world-wide; and
  iii) the incidence of tuberculosis.

The basis of WHO's control policy (case-finding and treatment with priority being given to sputum smear-positive infectious cases, and BCG vaccination at birth) was formulated more than a quarter of a century ago, with the aim of achieving the above three objects. It was based on a relatively comprehensive understanding of the natural history and epidemiology of the disease, and on the availability of relatively effective and simple intervention techniques. Since then, no major policy changes have occurred, except that it was realised that the epidemiological impact of mass BCG vaccination had been grossly over-

**Table 3** Estimate of tuberculosis service coverage in developing countries: 1988–1989.

| Region | Service coverage (%) |
| --- | --- |
| Africa | 24 |
| Americas* | 42 |
| Eastern Mediterranean | 70 |
| South-East Asia | 44 |
| Western Pacific† | 88 |
| Total | 46 |

*Excluding USA and Canada.
†Excluding China, Australia, Japan and New Zealand.

estimated [9]. Although BCG prevents childhood tuberculosis, particularly the most severe forms (more than 50,000 deaths in children aged 0–4 years can be prevented by increasing BCG coverage from the current 81–90%), its preventative effect on the infectious types of adult tuberculosis is limited. BCG vaccination does not therefore contribute significantly to the reduction of the transmission of infection. Otherwise, from a scientific perspective, this policy is basically sound for achieving the programme objective in countries where the risk of infection remains substantial.

This control policy was, in fact, implemented in the industrialized countries and in some middle-income developing countries, leading to a rapid decrease in the incidence of tuberculosis. For example, after the implementation of modern tuberculosis control, the annual decline rate in Western European countries reached 10–15%, compared with 4–5% as a result of the general improvement in socio-economic conditions (housing, nutrition etc.) and the isolation of tuberculosis patients in sanatoria in the pre-control era [10]. While the incidence in these industrialized countries has reached a very low level, its decline rate has recently slowed down since the majority of cases now originate from the still large pool of persons infected in the past. Thus, it should be realized that these countries have reached a stage in which the once very effective tuberculosis control strategies no longer have the same impact. A new strategy is therefore needed in order to achieve the elimination of tuberculosis in the future. (The working definition of elimination of tuberculosis is the achievement of an incidence of less than one case per million of the population [13]).

On the other hand, the implementation of this policy in the majority of developing countries has not been successful. The main problem in the majority of developing countries is that not 'enough' tuberculosis patients are cured to achieve the objectives of the programme. This is probably due to a combination of the following factors:

1. Technical policies are largely concentrated on 'what should and could be done' in relatively well-developed health service systems or under special research settings, and often lack the component of 'how to do it' under different settings.

2. Some of the intervention technologies, which are effective, simple and affordable in well-developed health service systems, are not necessarily effective, simple and affordable in poorly developed health service systems.

3. Some of the technical policies appear to have been taken as dogma (e.g. tuberculosis patients should not be hospitalized) so that there has been a tendency to discourage result-orientated and local innovative approaches.

## Outline of the new WHO tuberculosis control strategy

Given the current tuberculosis situation in the world, as described above, there is an urgent need to develop control and elimination strategies which include *specific target settings* and the identification of *key activities* and *monitoring indicators* for the following groups of countries:

i) low-income developing countries in which health infrastructures are still poorly developed;

ii) middle-income countries with relatively well-developed health infrastructures;

iii) industrialized countries with a low incidence of tuberculosis and

iv) countries with an AIDS epidemic.

Some important components of the new WHO tuberculosis control strategy, the development of which was based on a series of workshops, case studies etc. over the last 2 years, are as follows:

### Improvement of the cure rate

The prime objective of the control programme is to improve the cure rate of tuberculosis patients under treatment, particularly sputum smear-positive patients. The proposed target rate is 85% in developing countries and 95% in industrialized countries. Experience of tuberculosis control programmes in more than a dozen countries has clearly demonstrated that both the introduction of short-course chemotherapy in place of 'standard' chemotherapy and improved systems for the management of treatment are necessary for the achievement of this 85% cure rate in developing countries which lack exceptionally well-developed or manpower-intensive health services [13]. In addition, operations research has shown that short-course chemotherapy, which at present costs US$ 30–40 per patient, is more cost-effective than 'standard' chemotherapy, which costs US$ 15. This is mainly because short-course

therapy makes it much easier to achieve a high cure rate by securing patient compliance, reducing the number of patients under treatment at a given time and preventing the emergence of drug resistant bacilli, especially when combined tablets (isoniazid/rifampicin) are used [14].

However, as experienced on many occasions, the introduction of short-course chemotherapy does not automatically lead to an 85% cure rate without simultaneous improvement in the management of the treatment system. Key factors for an improved management system include a regular supply of anti-tuberculosis drugs and a rigorous cohort analysis of the outcome of treatment of all sputum smear-positive patients at all treatment centres. The latter will show the health workers how well or badly they are implementing the treatment activities.

### Expansion of tuberculosis services

The second objective, which should not be actively pursued until the first objective has been achieved, is to expand the tuberculosis services by fully utilizing the available health services networks, at least down to district hospital levels, in order to detect more cases, particularly sputum smear-positive cases. It should be realized that the establishment of a microscopy service below district hospital level is not necessarily effective. This is mainly because the prevalence of tuberculosis is usually much lower than that of common infectious diseases, such as diarrhoea and pneumonia, so that less than five smear-positive cases can be expected in a year at a typical health centre in a developing country covering 10 000 inhabitants. In this situation, it is not easy to maintain a high quality of sputum examination by microscopy.

The most effective factor that increases the services coverage rate is a high cure rate of diagnosed cases, which can attract tuberculosis

Table 4   New tuberculosis control strategy targets and expected impact.

| Countries | Target cure rates (%) | Case-finding coverage rates (%) | Expected duration to achieve 50% reduction of tuberculosis incidence | Expected number of annual tuberculosis deaths prevented world-wide |
|---|---|---|---|---|
| Low-income developing countries with poorly developed health services | 85 | 60–65 | 10–12 years | |
| Middle-income developing countries with relatively well-developed health service systems | 85 | 85 | 8 years | 1 200 000 |
| Industrialized countries and low tuberculosis incidence countries | 95 | NA | Not known | |

NA: Due to the lack of a method to estimate the incidence of tuberculosis when the annual rate of infection becomes low, it is impossible to monitor the case-finding coverage rate.

patients from even very remote areas. By achieving a high cure rate in all district hospitals, where tuberculosis is diagnosed by direct microscopical examination, often with the use of chest X-ray for screening, a 65% case-finding coverage rate has been achieved in Tanzania. It would be quite possible to achieve much higher services coverage rates in countries with more developed health service infrastructures. Tentatively proposed target tuberculosis services coverage rates are 60–65% in low income countries with poorly developed transport and communication systems, and 85% in middle-income countries with relatively well developed infrastructures.

## The proposed global target

The proposed global target of WHO's new tuberculosis control strategy is to achieve, by the year 2000, an 85% cure rate of all sputum-positive patients under treatment and 70% case detection. Different targets are set according to the health related resource availability of the various countries. The expected impact of the control strategies is shown in Table 4. Achievement of these targets will have three significant effects. First, it is expected that the annual tuberculosis death rate will be reduced by 40%, from the present level of 2.9 million to 1.7 million. Secondly, the worldwide prevalence of tuberculosis will be reduced by 50% from the current level of more than 20 million by curing vast numbers of chronic/retreatment cases by short-course chemotherapy. The majority of this reduction will occur in countries belonging to WHO's Western Pacific and South-East Asian regions. In some countries in these regions the prevalence of tuberculosis is 3–5 times higher than the incidence. Thirdly, in high and middle incidence countries, the incidence of tuberculosis is expected to be halved in 12 years with an 85% cure rate and a 60–65% case-finding coverage rate, and in 8 years with an 85% cure rate and an 85% case-finding coverage rate.

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