

Principles of tuberculosis control in low income countries

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It is often hard for us to realize the extent and severity of the effects which tuberculosis has had in our society. In Canada, in the 1920s, one out of every 150 young women in their 20s died every year of tuberculosis. In each village there was a death every year to remind the community of the seriousness of the disease. Since then, tuberculosis has declined to such an extent that many of our governments no longer consider it a priority and many of our medical colleagues believe that the disease has disappeared from the community. The effects of this misperception are very serious, indeed. At the present time in Canada, the most common cause of death from tuberculosis is the failure of the medical practitioner to diagnose (and therefore to treat) the disease.¹ A similar situation holds in other industrialized countries in which this problem has been examined.^{2,3,4}

The successes achieved by the organized fight against tuberculosis are one of the "miracles" of the health revolution. The development of the strategy for the fight against tuberculosis has a long history. The international efforts were first organized in Berlin almost one hundred years ago and were the precursors of the International Union Against Tuberculosis and Lung Disease (IUATLD) and the recent breakthrough in the fight against tuberculosis in low income countries. The history of the tuberculosis campaign is strongly related to the IUATLD throughout its course.

The highest rates ever recorded in communities were in countries which are now industrialized. Tuberculosis killed one of every 150 persons in the general population in cities such as London, Stockholm, New York, Hamburg, Taipei and Tokyo. This level was reached in the late 18th century in Scandinavia and Britain, the early 19th century in continental Europe, and the eastern United States, and in the late 19th century in Asia. Presently, the level of the tuberculosis problem is more than one hundred times lower. The rate of decline prior to the use of chemotherapy, was approximately 4%, after its introduction, the rate of decline increased to around 10% but has recently slowed or stopped.⁵ Tuberculosis becomes more and more a disease of subgroups in the population⁶ who either have been previously infected (for example, immigrants^{7,8,9} in those whose immunity is reduced (AIDS, silicosis, or diabetes patients) or among whom transmission of tuberculosis continues at a high rate (for example, in urban slums).

The record of tuberculosis in low income countries has not been as positive as in industrialized countries. Much of the difficulty has been related to the inability to achieve satisfactory treatment results in patients with active tuberculosis.¹⁰ This difficulty has recently been overcome by an approach to Tuberculosis Services developed by the IUATLD in collaboration with the Health Authorities of some low income countries and with donor partners.¹¹ Within these programmes, more

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than 70,000 cases of tuberculosis are diagnosed and treated per year (greater than one out of every ten new cases in sub-Saharan Africa), the majority (more than 75%) are documented to be cured, and the cost of the programmes is such that these programmes have been judged by the World Bank Health Sectors Priority Review to be among the most cost-effective of any health intervention in low income countries (the donor contribution is equivalent to approximately US\$ 30 per case).

Since the demonstration of this type of programme, at least 29 other low income countries have secured donor partners for their National Tuberculosis Programmes and are implementing similar plans to those developed by the IUATLD (and now adopted by the World Health Organization in its new Global Programme).

The introduction of infection with the human immuno deficiency virus (HIV) has led to a rise in the notification rate of tuberculosis in a number of countries, particularly in sub-Saharan Africa. This has led some people to feel that the situation is hopeless for containing the tuberculosis problem in such countries.¹² Such pessimism is unwarranted. Within the IUATLD-assisted programmes, it has been possible to continue the high rate of documented cure as was the case prior to the advent of HIV, although a slightly higher proportion of the patients die while on treatment.

A. THE PHILOSOPHICAL BASIS FOR A TUBERCULOSIS CONTROL PROGRAMME

1. Rationale for a programme

Although tuberculosis is a very serious disease, it is, nevertheless, curable and preventable and the elimination of this disease must remain the goal of the fight against tuberculosis. Elimination is possible because:¹³

- the source for the spread of infection is always a person who has symptoms and can be relatively easily identified;

- the spread of infection can be stopped if the infectious cases are recognized early and successfully treated;
- the transmission cycle of tuberculosis is inefficient so that any amount of appropriate intervention will reduce the problem;
- the tools necessary to achieve this are already available.

2. The basis of tuberculosis treatment

The treatment of tuberculosis, as with most other bacterial diseases, has its basis in chemotherapy. The agents effective against tuberculosis have been available and utilized for just about a half a century and their use has revolutionized the field of tuberculosis. The role of chemotherapy in the management of tuberculosis is illustrated by what it has been able to accomplish since its introduction.

a. Prevention of death

At the height of the epidemic of tuberculosis, every community experienced death from the disease.¹⁴ Every second patient who developed "open" tuberculosis could be expected to die of their disease.¹⁵ With the discovery of para-amino salicylic acid and then of streptomycin, the case-fatality ratio fell immediately to nearer one in ten, although the prolonged survival of patients without cure actually increased the prevalence of infectious tuberculosis in the community.¹⁶ Unfortunately, many of those whose lives were saved either remained, or became again, bacteriologically positive and were not permanently cured of their disease.

b. Prevention of relapse: Duration of chemotherapy

The inability of chemotherapy to achieve permanent cure led investigators to conclude that chemotherapy was only an "adjunct" to older forms of treatment such as pneumothorax and thoracoplasty and that life-long chemotherapy would be necessary. Systematic investigations of the effects of chemotherapy subsequently revealed a dual component to the action of chemotherapy: the initial, rapid reduction in the large population of bacteria

within the body followed by the "sterilizing" action of prolonged treatment. Thus, it could be shown, that utilizing the initial compounds introduced for the treatment of tuberculosis for a sufficient period of time allowed the virtual assurance of permanent cure. The introduction of rifampicin-containing regimens into general use in the late 1960s greatly reduced the duration of chemotherapy required to obtain a high degree of success in preventing relapse.

c Prevention of resistance: Multidrug chemotherapy

A second problem faced at the outset of the introduction of chemotherapy was the rapid development of drug resistance when only a single agent was used for treatment. This was shown to be due to the selection of naturally occurring resistant strains of bacilli which are rare but present in all large populations of mycobacteria (in patients with extensive disease). Sir John Crofton, who pioneered the concept of "multidrug chemotherapy" in the middle 1950s¹⁷ showed that, with the application of multidrug chemotherapy, the large number of chronic and usually resistant cases could be cured and the large "prevalence backlog" removed.

3. Objectives in treatment of tuberculosis

Clearly, the introduction of chemotherapy has greatly facilitated the humanitarian aims of preventing death and reducing suffering due to tuberculosis. However, these aims could be achieved in the private sector without an organized "programme."

As tuberculosis is a contagious disease, there are also public health aims to be achieved in the application of chemotherapy. The ultimate aim must be the eventual elimination of tuberculosis from society. The rationale for this is the inefficiency of tuberculosis transmission,¹⁸ contagious cases (those with acid-fast bacilli directly visible on microscopic examination of their sputum) are always symptomatic, thus easily detected and placed on treatment; the efficiency of chemotherapy ensures that virtually all of them are rapidly rendered non-contagious.

The effects of chemotherapy have been evaluated.¹⁹ When no chemotherapy is given (for example, prior to the advent of chemotherapy¹⁵), approximately 50% of patients die within 5 years, 25% "cure themselves" (their immunity is strong enough to overcome the bacteria and cause them to become inactive), leaving about 25% with continuing disease, capable of infecting other persons. With chemotherapy given within an organized programme which is functioning well, very few patients die (8% die during treatment, only one-third of whom die of tuberculosis), most (84%) can be documented to complete their treatment and become bacteriologically negative, 2% remain bacteriologically positive and 6% are unaccounted for (abscond from treatment or move to another area). When chemotherapy is given without support and direction of a strong programme, the results are often very poor.¹⁹ A review of results of the National Programmes in Korea and Taiwan in the 1960s,²⁰ and of the Programme in Tanzania prior to the technical assistance given by the IUATLD, indicates that, whereas the fatality rate is markedly reduced to only 10%, the proportion of patients documented as cured does not rise to the same degree, with only 60% cured, leaving a large proportion (30%) who either remain positive or are unaccounted for. Many cases in the latter group take enough treatment to begin to feel better and then discontinue it, returning for a bit more when the symptoms return. The prevalence surveys in Korea and China²¹ identified more than one-half of all cases discovered as having been previously treated but having failed to be cured, remaining infectious in the community and further promoting the transmission of tuberculosis. The significance of these cases is only appreciated when it is realized that approximately three quarters of them harbour resistant bacilli, and the infection which they cause is with these bacilli. It is clear that the inadequate treatment of tuberculosis is

worse, from an epidemiological point of view, than no treatment at all.

The IUATLD model for National Tuberculosis Programmes in low-income countries has demonstrated a remarkable success¹¹ with a high degree of cost-efficiency.²² The requirements to achieve such results include political commitment on the part of the government, diagnosis and follow-up based on the results of bacteriological examination with a system of quality assurance, consistent supply of medications and materials, proper recording and reporting of cases and careful control of the use of rifampicin through directly-observed therapy, combination tablets and a balance of regimens for new and retreatment cases.

B. ORGANIZATION OF THE TUBERCULOSIS PROGRAMME

1. Establishment of objectives

To achieve the elimination of tuberculosis, the fight against tuberculosis must be organized into a formal programme with standardized case management. Such a programme must be: country-wide, permanent, adapted to the local situation and integrated into the general health services. Standardized case management is the only form of primary prevention of tuberculosis.

2. The "management package"

The attainment of the public health aims of treatment is possible by the application of a "management package" emphasizing the efficient detection of contagious (smear positive) cases from among symptomatic patients presenting themselves to the health service, with rapid and persistent implementation of chemotherapy which quickly renders them non-contagious.

a. Establishing an adequate "cure ratio" of contagious cases

In spite of this relatively straightforward management system, the ability to maintain a high degree of efficiency is not easy. In a surprising number of circumstances, poor results have been documented: many low-

income countries have historically failed to achieve good results¹⁰ and the programmes in large urban centres of industrialized countries have been notorious in their failure.²³

The achievement of cure in a high proportion of cases is almost wholly dependent on achieving a low rate of defaulting from treatment: fatality rates can be quickly reduced and the proportion of cases who fail to be cured by modern treatment regimens is very low. One of the most important means of ensuring good adherence with treatment is the provision of consistent, pleasant, free care at a high level of competence such that patients trust in the service because of the good results it achieves. It is a stupid patient who would seek help in a service which is disorganized, unpleasant and is known to give poor results because of inconsistent supply of medications, inappropriate hours of service and inadequate or impolite staff.

b. Preventing infection

Can this approach prevent infection with tuberculosis? Evidence from tuberculin surveys in a number of settings have shown that the widescale and efficient application of chemotherapy has been accompanied by the establishment of infection-free cohorts of the population. Thus, the case-management strategy appears to have been effective in preventing further infection in the major part of the population.

3. Implementation of interventions

A significant proportion of the results of the campaign against tuberculosis are the results of the programme itself rather than, simply, of the tools (such as chemotherapy) which are their component parts. This point can be seen when comparing the overall results, under operational circumstances, of treatment programmes. The programme must have a clearly defined structure with lines of responsibility, recognized leadership and a system of information and supply which functions regularly. To achieve this, specific persons must be assigned to take responsibility and then be trained and regularly supervised to carry it out. The most important

part of the training is the use of standardized forms to record what is done routinely which are then reviewed and discussed during regular supervision visits. A programme should never be introduced country-wide at a single point in time; it should always proceed from the most promising points of implementation, using these points as training foci for further expansion. The programme must, however, be then steadily expanded to bring the services to the patients and to prevent them from travelling to the services, in which case they will be unable to follow their treatment regularly because it is situated too far away from their habitation.

4. Maintaining the "package"

In order to achieve the elimination of tuberculous infection in the community, it is necessary, after stopping its transmission (which, as we have seen, is possible with the efficient application of chemotherapy) to then maintain this "case management package" for a whole generation while the remaining heavily-infected sector of the population ages and dies out. This, however, requires a great deal of political commitment because, as the number of cases declines, the cost per case rises, other priorities emerge and the political will to maintain the services for years after the awareness of the problem has declined is notoriously limited. The consequences of not maintaining vigilance are evident from the example of the United States of America.²⁴

5. Ensuring efficiency: Evaluation

The level and distribution of tuberculosis in the community constantly changes. In order to efficiently target services, it is essential to monitor the distribution of the disease and the measures used to deal with it.

a. Monitoring the results of interventions

The target of the tuberculosis programme is to find and cure a high proportion of all the infectious (smear positive) cases in the community. The evaluation of the results of treatment of the smear positive cases is essential to ensure that the target is being met. Standardized methods and definitions have

been developed to carry this out. It is clear that poor treatment of tuberculosis cases can actually aggravate the situation of tuberculosis in the community. For this reason, it is essential to monitor the results of treatment of the infectious cases.

b. The distribution and determinants of tuberculosis

The most reasonable means by which to monitor the distribution of tuberculosis in the community is by means of mandatory notification of all bacteriologically proven cases. This relatively efficiently identifies the high risk groups which appear and targets the services in their direction. In addition to monitoring the distribution of the cases, it is important to monitor the coincidence of tuberculosis and the human immunodeficiency virus (HIV). For this purpose, regular assessment of the prevalence of HIV in a representative sample of the cases of tuberculosis is of value. In addition, it is worthwhile to monitor the occurrence of resistance to medications in the tuberculosis patients. For these activities, standardized protocols have been developed.

C. Elimination: what is needed?

1. Challenges to be faced in case-management-based prevention

Prevention based upon a case-management strategy utilizing chemotherapy has at least two important limitations. The first is that, with improper use of medications, resistance to the agents used for the chemotherapy will develop. The advantage with mycobacterial diseases has always been the prolonged cycle of the micro-organisms in the population. For example, with tuberculosis, it requires some 5 years of misuse of medications to create a sufficient reservoir of acquired drug resistance to be an important component of transmission; the new infection resulting from this transmission ordinarily takes about 10 years to begin to appear as new forms of contagious tuberculosis (the early forms following infection are often non-contagious forms,²⁵ thus taking almost 2 decades before its appearance as a recognized problem in the community (virtually exactly the period of time

taken by the so-called "superbug" strains of isoniazid-rifampicin resistant tuberculosis to gain attention). The beginnings of this cycle are evident from an example in Djibouti²⁶ and the prolonged period required after the introduction of two new chemotherapeutic agents to overcome its effects have been illustrated in Korea²⁷ and Algeria.²⁸

The second problem with the case-management strategy is the necessity of maintenance of political commitment to see the problem through to completion after the initial successes. The fact that tuberculosis becomes increasingly a problem of disadvantaged subsets of the population²⁹ magnifies this difficulty. As the political will to continue the fight wanes, there is a need to develop a "constituency" in the private sector to lobby for the needs of tuberculosis. Such a non-governmental organization may even, on occasion, need to provide the care which the government may refuse to do.

2. Opportunities of which to take advantage

In spite of the potential problems which we are facing in tuberculosis control, opportunities exist at present for the control of tuberculosis. First, tuberculosis has a rather slow epidemic cycle under normal circumstances. The development of drug resistance even with well managed programmes has not yet overshadowed the capability of reducing tuberculosis to very low levels in those countries which have rigorously applied the principles of tuberculosis control: the reduction in tuberculosis has been faster than the emergence of drug resistance.

Second, the tools required to control tuberculosis are available, remarkably cheap and efficient to apply, if applied in a standardized fashion. This is well demonstrated in the poorest countries in the world. The application of the same tools in an unstandardized manner has produced the opposite results - a disaster.

Third, we have a window of opportunity; HIV infection has not yet spread widely in many countries where tuberculosis is very

common (especially some countries of Asia) enabling us, if we act quickly, to gain an advantage before it emerges.

d. Effecting change: the need for global solidarity

It must be kept in mind that tuberculosis will not be eliminated anywhere until it is eliminated everywhere and that the fight against tuberculosis must be international and collaborative. It must be a priority for every government to provide the means to implement a National Tuberculosis Programme. Every low income country, where tuberculosis is common, must indicate that tuberculosis is a national priority. Without this indication, collaborative links are impossible.

It must be a high priority for every industrialized country to participate in the global campaign against tuberculosis. The World Bank has clearly shown that, of any participation in the health sector of low income countries, assistance to National Tuberculosis Programmes fashioned after the model of the IUATLD- assisted Programmes is the best investment. Among the governments of the so-called "Group of Seven Most Industrialized Countries", only Japan and France have contributed to these programmes in any substantial manner. Moreover if, for example, Germany were to contribute *per capita* a similar amount as Norway or Switzerland, there would be enough money to provide assistance to all countries of Africa who do not presently have donor partners and the total amount of money required would be much less than the cost of a single military aircraft.

In addition to support for low income countries, it is also necessary to pay attention to the situation in industrialized countries. Failure to do so can very easily lead to a situation like that in Harlem, New York in the USA. The most important priority is the proper education of health care workers to ensure that they understand tuberculosis and especially the fact that it has not yet disappeared from the community. The delay or failure of diagnosis, leading to avoidable morbidity and mortality,

can only be prevented by proper education of health care personnel. Part of the strategy to ensure this level of expertise in the community is to ensure that there is a "central team", as in low income countries, who give their full-time to the supervision, coordination, and training to other health care personnel concerning tuberculosis and who ensure that the information concerning tuberculosis and its trend in the community is accurate and up to date. The second necessity in industrialized countries is to continually refocus attention on the high risk groups in the community who increasingly contribute the highest proportion of cases and, among these groups, to provide specialized services for the care and prevention of tuberculosis. Finally, the role of preventive chemotherapy must not be neglected.

CONCLUSION

Tuberculosis can be eliminated from our society. We must never lose sight of this fact. However, there is an urgency to apply the methods we have in hand in a rigorously standardized manner before HIV has spread throughout the world and before the poor management associated with unstandardized practice creates extensive amounts of drug resistance. Failure to act now will pass a legacy of shame to succeeding generations.

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