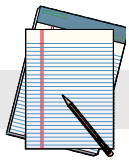

Changing the Strategy for Tuberculosis Control

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Tuberculosis is the major infectious cause of death in the world today, as it has been for at least the past two centuries. It is currently estimated that 3 million persons die annually from this disease. This is a fact despite the great advances in the treatment and prevention of TB that have occurred since the discovery of streptomycin in 1944 and the subsequent development of highly effective antituberculosis antibiotics. Whereas this was the situation worldwide up to the discovery of effective antibiotic therapy, this tragedy persists today mainly in the third world and is clearly related to unavailability of the antibiotics or their misuse.

In Israel as in the rest of the so-called western world (mainly Europe, North America and parts of Africa and South America), the impact of antibiotic therapy lowered both the death rate and the morbidity rate from tuberculosis in the 1950s through the 1970s to such an extent that the word "eradication" appeared in enlightened discussions of the tuberculosis problem. This euphoria turned out to be premature as two major facts were not taken into account: a) the prolonged course of antibiotic therapy that was required to effectively treat tuberculosis was frequently not carried out by patients who quickly felt well and thus saw no need to continue with the treatment, and b) the major population centers of the world – China, India, the Far East, among others – were unable to provide their citizens with adequate antituberculosis therapy.

These two facts have been responsible in great part for the development of strains of *Mycobacterium tuberculosis* that are resistant to one or more of the first-line antibiotics (isoniazid, rifampicin, ethambutal, pyrazinamide and streptomycin). The major threat has been the appearance of strains that are resistant to both isoniazid and rifampicin at least, and these strains are designated "multi-drug resistant." For patients in whom these strains are the cause of the disease, treatment is required for 2 years – often utilizing antibiotics that are generally less effective than the first-line drugs and cause many unpleasant side effects in the treated patients. The success rate of treatment of these cases is at best 75% compared to > 95% in cases caused by *M. tuberculosis* sensitive to the first-line antibiotics. In addition, the cost is many times higher than that of a course of treatment in a patient receiving therapy with the first-line drugs for 6 months.

A major legislative effort is being made in the United States to deal with the lack of resources needed to control tuberculosis in the third world. Representative Sharrod Brown of Ohio has introduced a bill into the U.S. Congress that would invest $100 million in international tuberculosis elimination and control efforts. Such an investment is only a beginning, but its wider impact may be the enlistment of financial support from other western countries. This support is essential to provide the means for the professionals to organize an effective program to deal with the tuberculosis problem in countries with a high prevalence, especially in the third world.

By the early 1990s a reasonable approach was crystalized for the problem of non-compliance with treatment; i.e., the use of directly observed therapy to ensure the completion of the 6 month course of therapy, or even longer in complicated cases. This form of therapy, acronym DOT, proved to be effective, but it imposed additional cost and responsibility on the institutions and people who administered antituberculosis therapy. Even in the U.S., the intention to apply DOT to all patients being treated and all persons with latent infection receiving INH (or other) so-called preventive therapy was not totally successful. And yet the justification for this approach to therapy was clear – patients who were dealt with in this manner recovered at a rate that approached the dream of the early years! Recommendations have recently been made by the Institute of Medicine of the U.S., a highly prestigious organization, for the elimination of tuberculosis as a problem in America. Once again the concept of eradication has appeared.

In Israel as in the rest of the western world, the problem of tuberculosis worsened in the 1990s – but for different groups of people than had been encountered in the U.S. AIDS was a major source of tuberculosis morbidity in the U.S., whereas in Israel that problem was relatively less critical. The main groups

TB = tuberculosis

DOT = directly observed therapy

of Israeli cases were and are to be found in foreign workers who have come from third world countries with very high prevalence rates of active tuberculosis, from new immigrants to Israel especially from Ethiopia and the former Soviet Union, and among the Holocaust survivors whose infection obtained during the epidemic of tuberculosis that occurred in Europe during World War II has only recently become active.

In this issue of the journal, Chemtob et al. [1] present an epidemiological analyis of the results of a survey of patients treated for tuberculosis in Israel in the early 1990s. In that previous study, Dr. Daniel Chemtob (Director of the Ministry of Health's Department of Tuberculosis and AIDS) clearly showed that close to 50% did not complete the course of treatment prescribed for them. This fact emphasized the importance of establishing a country-wide program of tuberculosis treatment within which DOT was an integral part. And so it came to pass.

From 1 April 1997, the date that the current program was activated, all aspects of care of tuberculosis patients including seeking and considering treatment of contacts have been the responsibility of the nine centers established by the Ministry of Health. These centers are located all over Israel and cooperate with the local offices of the Ministry of Health in finding contacts and informing the public about the tuberculosis problem. In addition, all patients with active tuberculosis requiring hospitalization are sent either to Shmuel Harofeh Hospital near Tel Aviv or Rebecca Ziv Hospital in Safed.

The major innovation in treatment, DOT, was included in the therapy of every patient with active tuberculosis treated by the centers since 1 April 1997. The success of DOT was the result of the cooperation of the four health maintenance organizations (sick funds). Many of the patients were given DOT by nurses in the local branches of the HMO to whom the medications were sent monthly by the regional tuberculosis center. Other means – such as home visits by employees of the centers and enlisting colleagues of the patient at his or her worksite, having the patients come directly to the center each day in order to receive their treatment – were used to ensure that DOT was indeed utilized. The choice of tactic for applying DOT is arrived at by the center's doctor and nurse in consultation with the patient. Forms listing each day's treatment are signed by whoever is responsible for providing the DOT and sent to the centers responsible for the patients' care. Personnel of the local offices of the Ministry of Health conduct periodic spot checks on those administering the DOT.

The success of the program in Israel is indicated by the positive outcome of treatment since the program was initiated. Certainly there are difficult patients: drug addicts, alcoholics, homeless, etc., and these patients have tested the ingenuity of the centers in order to achieve the main objective – completion of the prescribed course of treatment. In the pursuit of this end many inducements have been added, such as providing snacks for the patients when they come to the center, attempting to help them with their social problems, etc. Furthermore, an employee of the center frequently makes house calls in order to keep the treatment going, an effort in which the local offices of the Ministry of Health have been very helpful.

The program works. Each day brings new challenges and new problems, but Israel has set up a structure within which these challenges can be dealt with effectively. The future presents the opportunity to improve the program even further and for Israel to be that "Light unto the nations of the world" – especially in dealing with tuberculosis.

HMO = health maintenance organization

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