

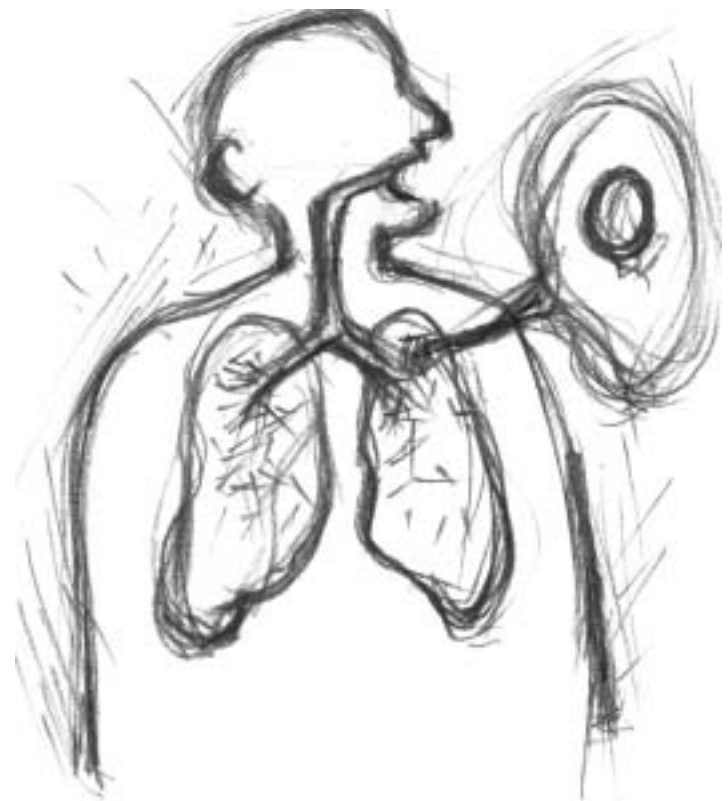
Tuberculosis: An Overlooked Global Threat

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“**W**e live in an age when unnecessary things are our only necessities,” wrote Oscar Wilde in *The Picture of Dorian Gray*. A more accurate statement for today would be that we live in a place where unnecessary things are our only necessities. While

Wilde’s words correctly describe most residents in developed nations, the situation in developing nations is quite different. The tuberculosis crisis is a prime example of this dissimilarity. Tuberculosis has nearly been forgotten in the developed world, but it remains a household problem in poor countries. Although a cure for tuberculosis is readily available, the international community has been slow to respond. This indifference has allowed the disease to take shape into something that threatens even the nations that ignore its existence.

A common misconception in the First World is that diseases such as tuberculosis, polio, and malaria have nearly or completely vanished from the planet. Unfortunately, this is not the case. The primary difference between disease control in developed and developing nations is the lack of funding for prevention and treatment of diseases in Third World countries. Tuberculosis, an airborne infectious disease, is the number one cause of death among adults in the world.¹ The irony of the situation is that it is one of the few diseases that has a cure, and yet one of the most widespread and worsening crises of the time. Many public health officials have even argued that this lack of medical care in poor nations is a human rights issue that must be addressed at once.



Unfortunately, although excellent solutions, such as direct-observed treatment, short-course (DOTS) exist, the overall lack of international effort and interest has led to severe complications that now threaten not only developing nations but the entire world. Multidrug-resistant tuberculosis (MDR-TB) is the most dangerous and complex of these cases. These evolved strains of tuberculosis are making simple first-line drug treatment ineffective in many areas. In the words of Dr. Paul Farmer, a leading infectious disease physician and expert in the field of tuberculosis treatment, "The rapid rise of multidrug-resistant tuberculosis is a public health catastrophe of the first order."²

Multidrug-resistant tuberculosis has made the situation more difficult, but by no means impossible to fight. New strategies to combat MDR-TB, such as DOTS-plus, have been demonstrated to be effective in model programs. The Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global ATM) is an innovative idea to bring aid to poor countries. The Global Tuberculosis Drug Facility allows better access to antituberculosis drugs in countries currently hard-hit by the disease.³ Yet this is not enough to fight such a crisis. As long as the international interest in tuberculosis remains weak, there is no hope in finding an end to the crisis before the disease spreads beyond control.

Tuberculosis Basics

Dr. Farmer wrote, "Looking toward the next millennium it is difficult to be optimistic," in regards to the growing tuberculosis crisis.⁴ And he is right: The World Health Organization (WHO) estimates that 8.4 million people were newly infected with tuberculosis in 1999.⁵ Even more startling is the estimate that one-third of the world's population is currently infected with the disease.⁶ Of course, this one-third is not uniformly distributed among the populations of the world. Tuberculosis is considered a disease of the poor, most prominent in overcrowded resource-poor settings. One report cites that 90 percent of all tuberculosis infection cases are in the developing world.⁷

The cold shoulder given to this disease by most industrialized nations is not surprising. The reaction of these countries to the tuberculosis

pandemic is parallel to their reactions in similar situations. The HIV/AIDS pandemic in Africa, severe malnutrition, and the lack of treatment for other curable infectious diseases are all examples of chronic emergencies in the Third World that are essentially overlooked by developed nations. Resource-poor countries clearly do not have the resources to fight such problems on their own. The global tuberculosis epidemic is not of concern to nations that have, in essence, already dealt with their own national tuberculosis crises. This way of thinking prevails in developed nations even though the WHO declared tuberculosis a global health emergency in 1993.⁸ This negligence has been criticized by many. Farmer wrote, "The appalling global burden of tuberculosis at the turn of the millennium, despite the availability of effective control measures, is a blot on the conscience of mankind."⁹

Tuberculosis drugs, although having slightly improved over time, are very difficult to consume because of their harsh side effects. Short-course chemotherapy was a new form of treatment developed in the late 1960s as an alternative to the initial antituberculosis drugs on the market,¹⁰ but it still has very unpleasant side effects. To avoid these side effects, patients sometimes take the drug course until their health seems to improve, and then stop. But in resource-poor countries, ease is not as much an issue as price.¹¹ Unfortunately, not only does the victim remain infected if treatment is stopped before completion, but he is also very likely to acquire a strain of tuberculosis that is resistant to that drug and can be passed along to others. Dr. Farmer described a situation in Peru where a mother, unable to afford full treatment after becoming infected, developed multidrug-resistant tuberculosis and passed it on to her son. Farmer wrote, "Corina was unable to complete her treatment. As her husband recalls it, they could afford to buy only two of the four drugs prescribed."¹² Both Corina and her son died without receiving a full, correct treatment regimen.

Even in the developed world, treatment was hampered by the lack of patient compliance in taking the necessary medications. To prevent this massive problem of drug resistance, direct-observed treatment (DOT) was standardized by

the WHO in 1991.¹³

According to the WHO, "DOTS is [the most effective strategy] available for controlling the TB epidemic today."⁶ As the name suggests, DOTS is a treatment program in which every tuberculosis patient is observed daily by a health worker to guarantee that medication is taken at the proper times. This greatly reduces the development of drug resistance. The health workers are usually locals and do not need to be trained in medicine, thereby lowering the cost of the program. In areas where DOTS is in effect, tuberculosis cure rates are as high as 95 percent.¹¹ The overall average cure rate from DOTS in 1997 was estimated to be 80 percent, an extremely high success rate.¹⁴ The DOTS protocol requires the following five components:

- Government commitment
- Case detection (by sputum smear microscopy)
- Standardized treatment for six to eight months, DOT for at least the first two months
- Constant supply of all antituberculosis drugs
- Standardized recording and reporting system¹⁴

Through these tenets, DOTS allows resource-poor settings to have nearly the same tuberculosis treatment benefits as countries of the developed world. In fact, treatment is the main reason for the basic disappearance of tuberculosis from the developed world. The DOTS approach to tuberculosis treatment tries to provide DOTS patients with the same opportunities for consistent treatment.

Unfortunately, even with the extremely powerful DOTS strategy, the tuberculosis crisis has continued to worsen over time. Two very important reasons for this have been discussed in numerous publications. The first is that DOTS has not been implemented throughout the world. According to WHO statistics, in principle, 45 percent of the world's population had access to DOTS in 1999.⁵ This number includes developed nations where DOTS is available but not needed because of low tuberculosis rates. A more informative statistic from the WHO is that, in 1999, DOTS treated only 23 percent of infected tuberculosis patients.⁷ The lackluster implementation of the successful DOTS program is a very unfortunate consequence of the inaction of

countries that can afford to help but, at best, choose to act in a very limited capacity. This failure of effective action has now come back to haunt the entire world. The second reason the crisis is worsening is that drug-resistant forms of tuberculosis are now spreading. Where DOTS has not been implemented, there is no standard to guarantee tuberculosis patients are taking the full course of treatment. In resource-poor countries where patients buy only as many drugs as they can afford, acquired drug-resistance has skyrocketed. These strains of drug-resistance can then be passed to others in close contact with the infected person. The same problem occurs in places with little DOTS implementation as a result of mismanagement, such as not having a constant drug supply, doctors prescribing incorrect drugs, and patients not being observed to ensure they take their doses.

Multidrug-resistant tuberculosis is defined as a strain that is resistant to at least isoniazid and rifampicin, the most powerful antituberculosis drugs available (DOTS-plus page, others).¹⁵ MDR-TB is a completely man-made problem resulting from ineffective control of tuberculosis treatment.⁹ In 1997, the WHO published a survey in coordination with the International Union Against Tuberculosis and Lung Disease (IUATLD) on MDR-TB that was an eye-opening report for the world. It detailed the presence of drug-resistant tuberculosis in all 35 countries it surveyed.⁹ The most recent and disturbing survey from 2000 showed the presence of MDR-TB in all 100 countries surveyed.¹⁶ Not only is MDR-TB more expensive to treat because second-line drugs are needed, but in its most extreme case, it threatens resistance to all antituberculosis drugs that have been developed. The world's carelessness in eradicating the disease may have placed tuberculosis parallel to an era before antibiotics. MDR-TB has now become a significant cause of global concern. According to the WHO, "Given the increasing trend toward globalization, transnational migration, and tourism, all countries are potential targets for outbreaks of MDR-TB."¹⁵

The Global Impact of Drug-Resistant Tuberculosis, a report commissioned by the Open Society Institute and Harvard Medical School, says that MDR-TB is a manifestation of the global neglect

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for tuberculosis control.¹⁷ Even more direct are the human rights arguments that suggest fighting tuberculosis is a global responsibility. A report about tuberculosis and human rights, published by the WHO, says, "Vulnerable and marginalized populations bear an undue proportion of health problems. Overt or implicit discrimination violates one of the fundamental principles of human rights."¹⁸ The report argues that all people have the right to certain fundamentals, including basic health care. Access to tuberculosis drugs is essential, especially since these drugs are readily available. Therefore, tuberculosis treatment has become as much a human rights issue as government crimes against a population, for instance.

Possible Solutions

Whether through naivete, carelessness, or blatant disregard, tuberculosis has not received the public attention a disease of its magnitude would have if it were a disease of the developed world. MDR-TB is a major problem that caught much of the international community unawares. Even though MDR-TB has not been able to bring tuberculosis directly into the public eye, the panic it has caused has started to mobilize an international community of concern that was previously deemed unnecessary. New strategies have been developed, drug prices are being questioned and lowered, and funding is being made available. While this is an improvement, the international community still lacks the passion needed to eradicate this disease.

The most promising solution to MDR-TB is based on the already effective DOTS program. The new treatment program, called DOTS-plus, includes the five tenets of DOTS. In addition, DOTS-plus takes into account the need for individual treatment regimens using second-line drugs depending on each patient's particular strain of drug-resistant tuberculosis. The necessity for a new strategy became evident when cure rates in high-MDR-TB regions were analyzed. Low-prevalence-MDR-TB areas have had DOTS success rates up to 95 percent, as previously mentioned. Areas with high-MDR-TB prevalence, on the other hand, have a range of 6 percent to 59 percent for cure rates through DOTS, showing a tremendous 40 to 60 percent drop.¹⁹ Another

study showed that 93 percent of people who failed the DOTS treatment had some form of drug-resistant tuberculosis¹³ (new white plague). The amplifier effect is an additional problem facing many MDR-TB patients being treated only with DOTS. As first-line drugs are continued, the patients may develop resistance to other agents as well as those of their original MDR-TB strain.¹⁰

Leading tuberculosis experts have been quick to emphasize, however, that DOTS is still the main program of treatment. In areas of strong DOTS programs for regular tuberculosis, MDR-TB should not be able to develop. Therefore, a dual program is needed. DOTS-plus must be implemented where MDR-TB is present. At the same time, DOTS programs must be expanded and reinforced to reach all areas of the globe. Another emphasis is that DOTS-plus must be implemented only where DOTS is already a strong program to prevent further drug resistance resulting from inadequate infrastructure.¹⁵ Otherwise, strains of tuberculosis resistant to second- and third-line drugs may develop as freely as MDR-TB has over the last several years. The world will face a calamity in which a curable disease has been transformed into an incurable disease simply due to disorganization.

DOTS and DOTS-plus have established international standards for tuberculosis treatment. Standards alone, however, will not solve the tuberculosis problem. Massive amounts of resources must be mobilized to make the treatment programs successful. A joint international effort has led to the development of several initiatives that will hopefully provide the necessary resources to lessen this crisis. The Global TB Drug Facility (GDF), run through the Stop TB Partnership, is a mechanism intended to bring a constant supply of high-quality but inexpensive first-line tuberculosis drugs to developing nations.³ The GDF also plans rapid DOTS expansion into areas that currently lack the treatment program. Governments and nongovernment organizations (NGOs) apply to the GDF for inexpensive first-line drugs. Approval from the GDF for these drugs means the country has a strong infrastructure present for tuberculosis drug delivery. Thus, the GDF is a way for DOTS programs to successfully maintain a constant supply

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of drugs at a lower price.³

To address the problem of MDR-TB, a Working Group on DOTS-plus for MDR-TB (The Working Group) was established. The Working Group assesses the global MDR-TB crisis and has established the Green Light Committee to ensure proper use of drugs at a lower cost. The Green Light Committee, which includes members of the WHO, Medecins Sans Frontieres (MSF), Harvard Medical School, and the Centers for Disease Control (CDC), among others, will give the “green light” after assessing a certain area’s situation and whether or not it has the infrastructure necessary for proper drug delivery.²⁰ Thus, it has established pilot programs that can serve as models for the future if shown to be successful. Under the organization of the United Nations, the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global ATM), hopes to aid programs that fight the three diseases that are its focus through contributions from governments and organizations. Unfortunately, the Global ATM has so far had a lukewarm response from governments, including the United States. The Global Fund, asking for approximately \$10 billion per year, has only received a fraction of that amount thus far. Once again, this evidences the lack of international commitment.

Fortunately, the work of the WHO, MSF, and Harvard Medical School in lowering drug prices has paid off. Their persistence in negotiations with pharmaceutical companies created a milestone in tuberculosis treatment history in July 2001.²⁰ Through an MSF proposal of bulk purchasing, the tuberculosis drug prices have been dropped by 48 percent to 97 percent for five second-line drugs. This will allow MSF to purchase a full-treatment course for nearly \$3,000, which

normally costs \$15,000. Some countries may see as large as a 94 percent cut in drug prices.²⁰

On the other hand, a question often asked is why no current tuberculosis research is being conducted in pharmaceutical companies, especially considering the disease is the number one infectious killer of adults in the world. A WHO study analyzed the pharmaceutical response to tuberculosis research and found some startling results. The main reason stated in the report was lack of commercial return.¹¹ For such a high investment, tuberculosis drugs do not offer pharmaceutical companies the profit they desire in return. One interviewee in the survey said, “Tuberculosis is life threatening, but it has no commercial lure.”¹¹ No significant drug development has taken place in 25 years.¹¹ However, many public health officials argue that drug development is essential, especially given the current situation. If MDR-TB continues to spread, it is very likely a strain will develop that is resistant to all current tuberculosis drugs. Without continuing drug research, there will be no potential cure against such an evolved disease.

In conclusion, to say the tuberculosis pandemic is an unfortunate crisis right now is a great understatement. The disease has been allowed to evolve into something more dangerous and deadly. Unless the international community responds quickly to this threat, tuberculosis is bound to become a beast beyond all reckoning. Although strategies and solutions have been found, much more must be done to implement them to their full capacity. A partial implementation may do more damage than good. Essential to the success of tuberculosis eradication is massive funding and drug research. Without these, the world will be devastated by the disease. ■

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