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Preface

Three infectious diseases – HIV, tuberculosis (TB), and malaria – will kill some six million people during the course of this year. These are three very different diseases. The first is caused by a virus, usually sexually transmitted; the second is caused by an airborne bacillus; the third is caused by a mosquito-borne parasite. Three different classes of organism and three different modes of transmission, but there are at least four features common to these pathogens:

1. all afflict predominantly the poor;
2. none can be reliably prevented by a vaccine;
3. all are treatable with antibiotics;
4. each may become resistant to existing drugs.

These sets of disparities and similarities are the reasons that Partners In Health and its sister organizations are engaged in responding to epidemic disease in Peru, in Haiti, and within the prisons of Russia. It is also for these reasons that together with our sister organizations we have written this Handbook.

PIH's mission is the remediation of inequalities of access to effective therapy, and there is no question that the "neglected diseases of poverty" constitute a growing threat for hundreds of millions, while others are shielded from risk.

The scientific, medical, and public health communities contain large numbers of experts seeking to respond to each of these infectious killers. But there exist, within current agendas for research and action, a series of what can only be considered neglected problems. They are the neglected aspects of neglected diseases.

Neglected Problems within Tuberculosis Control

This Handbook is a how-to guide for those seeking to treat multidrug-resistant tuberculosis within poor communities because MDR TB is itself an underattended problem within international public health. Tuberculosis experts point to a large body of evidence suggesting that the disease itself has been neglected by science and medicine. The list usually refers first to drug and vaccine development (there has been no new class of drug in decades and the most effective vaccine, first administered in 1921, is of very limited efficacy); to poor-quality diagnostics (the same insensitive methods now used to diagnose TB in poor communities were developed over a century ago); and to low levels of funding for basic science and for implementation of effective TB control in those places in which the disease takes its greatest toll. The most effective means of managing drug-susceptible TB, DOTS, is available to only a quarter of those afflicted because sufficient resources have not been invested in TB control.

On such matters, most experts concur. But new and promising developments may be discerned in each of the arenas. Within the "TB community," there is wide agreement regarding the need for better vaccines and new drugs, and a companion volume to this one (The Global Plan to Stop Tuberculosis) calls upon governments and international bodies to fill the funding gap apparent to all those seeking to control TB. DOTS expansion remains the top priority of TB control, and there are many other new challenges, including those posed by HIV-associated TB.

But what about MDR TB treatment in poor communities? Ten years ago, when we first detected the presence of this disease in Haiti, we learned that second-line drugs, though long off-patent, were ridiculously expensive. We also learned that policy makers discouraged cash-strapped national TB control programs from taking on MDR TB treatment, since the major problem, globally, was failure to implement DOTS. Claims that DOTS alone would stop MDR TB abounded and MDR TB therapy was deemed impracticable, even irresponsible, in poor communities such as those served by PIH. The logic was economic. The crude form of the argument went like this: it cost pennies a day for short-course chemotherapy, whereas it could cost $250,000 to treat a case of MDR TB. But do we really know how much it cost to treat MDR TB? Do we know how much it costs to not treat the disease?

TB policy is developed and implemented across steep grades of social inequality. In the same year that the World Bank reported that a full course of DOTS in China costs less than $50, a paper published in *The International Journal of Tuberculosis and Lung Disease* revealed that it costs over $60,000 to treat a single case of pan-susceptible TB in the city of Chicago.

How might people of good will develop MDR TB policies in the context of such inequalities? PIH was able to implement its own policies in Haiti, where there were few cases of MDR TB in large part because rifampin had not yet been used widely in that country. The great majority of Haitian patients responded to DOTS; treatment failure due to drug resistance was rare and we quietly treated the small number of patients with confirmed MDR TB with the second-line drugs to which their infecting strains were susceptible.

But things changed dramatically for PIH in 1995, when PIH's sister organization in Peru, Socios En Salud, began to document treatment failures in northern Lima. Unlike most places in which drug-resistant TB emerges, Lima was a city in which an excellent DOTS program had already been established. Brisk debate arose: some suggested that because DOTS and MDR TB were incompatible, there could be no cases of MDR TB in Peru. But this was, alas, incorrect: the patients referred to us, who had failed DOTS therapy, did indeed have laboratory-confirmed MDR TB. Within a few years, we were able to detect several hundred cases of culture-positive MDR TB in a large and crowded city. There are now thousands of prevalent cases in Peru.

A Blueprint for Responding to MDR TB

What was to be done for these patients, who suffered and, often, died, all the while transmitting their disease to others? Where was the blueprint for responding to the novel problem of MDR TB in "resource-poor settings," the latest euphemism for poor communities? We sought for and found no blueprint. Indeed, MDR TB therapy was dismissed as "not cost-effective" by many specialists, even though it was soon clear that the pathogen was being transmitted to most susceptibles within households, some of which had already lost most of their breadwinners to MDR TB.

Although we did not find a blueprint, we did find, in northern Lima, abundant local resources. Committed nurses and community health workers echoed the views of the families affected by MDR TB: something must be done.

While a vast international debate unfolded in the pages of our medical journals, these valiant health workers implemented the world's first "DOTS-Plus" program. Following the key planks of the DOTS strategy, Socios En Salud worked in concert with local health authorities to deliver directly observed therapy of MDR TB with the second-line drugs necessary to treat this disease. It was a painful process, because the team had to fight not only the ravages of a difficult-to-treat and stigmatized disease, but also a constant undertow of censorious opinion from above. Treatment of MDR TB was not possible in a slum, it was argued. This expensive and difficult project was doomed to fail, according to many.

But DOTS-Plus did not fail. Even those most critical of this effort acknowledged that cure rates exceeded 80% among patients with longstanding, extensive disease due to highly-resistant strains of *Mycobacterium tuberculosis*.

If the first steps were to learn by doing, the next steps were to train others to replicate DOTS-Plus in other communities affected by MDR TB. In order to do so, however, PIH needed allies in international health and policy circles. Another companion volume, the first in this series, sought to document The Global Impact of Drug-Resistant Tuberculosis. Following a 1998 meeting hosted by Harvard Medical School and the American Academy of Arts and Sciences, the World Health Organization established a working group on DOTS-Plus. One of the first projects of the working group, and of the many institutions participating in the group, was to work to decrease prices and increase control of the second-line antituberculous drugs required to treat MDR TB. By the summer of 2000, it was possible to show that prices of most of these drugs had decreased by more than 90%. At this writing, there are dozens of DOTS-Plus programs in Europe, Asia, and Latin America.

None of this would have been possible without the highly professional and courageous community health workers and nurses of Socios En Salud. None of this would have been possible without the patients and their families, who together endured long and arduous treatment in order, as the Peruvians put it, to "say yes to life." This Handbook shows, in great detail, what was done to implement and evaluate DOTS-Plus in northern Lima and beyond. Thanks to generous funding from the Bill & Melinda Gates Foundation, the "northern Lima experiment" is now being scaled up throughout Peru.

CHIPS: Responding to Complex Health Problems among the Poor

Are there other lessons to be drawn from the experience described in this Handbook? Along the way, all involved learned a great deal about responding effectively to complex health problems in poor settings. We hope that our readers will forgive the clumsy acronym, “CHIPS,” but the three diseases mentioned above – HIV, malaria, and tuberculosis – are not only the major infectious killers in much of the world, they also become increasingly complex as time goes by. The emergence of multidrug-resistant strains of each of these pathogens has already been well documented. For this reason alone, the lessons learned in the slums of northern Lima may prove relevant far beyond the borders of Peru.

What are the most important of these lessons? The first lesson is that patient-focused approaches to public health problems are possible and necessary. Although good aggregate outcomes tell part of the story of DOTS-Plus, they don't tell all. Responding effectively to human suffering is always a complex process, in this instance ranging from responding promptly to side effects to offering group counseling to patients and their families, several of which had been decimated by tuberculosis.

The second lesson is that community health workers have a central role to play in the "CHIPS" strategy. Indeed, local workers are the heart of many good TB control programs, and not primarily because reliance on their labor, instead of the labor of physicians, decreases costs. Rather, community health workers live in the same communities as their patients; they share a deep knowledge of the conditions faced by families challenged by both poverty and epidemic disease. Furthermore, community-based therapy of MDR TB decreases the nosocomial and institutional transmission of drug-resistant strains of *M. tuberculosis*, which has been reported from across the globe.

A third lesson concerns rational drug procurement. As long as effective therapies are available to the privileged, "CHIPS" must necessarily include equity strategies designed to remediate inequalities of access. Responding to each of the diseases mentioned above will involve novel forms of drug procurement. Some have noted the "CHIPS paradox," which seeks to decrease drug prices while

increasing the prudent use of antibiotics. As long as people are sick with HIV, MDR TB, and drug-resistant malaria, there will be a constant demand for therapy. Such demand could once be ignored by policy makers. In the global era, however, it is increasingly difficult to silence the voices of the destitute sick. We attempt to do so at our peril.

The fourth lesson the experience in Peru taught us is a great deal about the importance of building both local and global alliances. With strong support from the communities served, the Socios En Salud team was able to initiate a project under difficult circumstances. With support from funders and from the international institutions charged with developing blueprints for novel threats to health and well being, Partners In Health was able to push for new standards of care for those sick with MDR TB. We thought and acted both locally and globally.

Each of these lessons is applicable to AIDS, to drug-resistant malaria, and to many other diseases requiring complex, multidrug regimens for control or cure.

Expected and Unexpected Lessons

The architects of DOTS-Plus in Lima expected, of course, to cure patients. We expected side effects and a difficult time acquiring expensive drugs for which there was, paradoxically, little market demand but great need. We expected to reduce the suffering of the patients served. We were not surprised on these scores. But there were other, unexpected lessons. First, setting policy goals low – "MDR TB cannot be treated effectively in poor countries" – has an untoward impact, and not only on the patients who are written off in this manner. Such policies also diminish the morale of the doctors and nurses who recognize the disease but who are powerless to treat it. A similar process is at work wherever HIV care is needed, but termed "cost-ineffective."

All of us face a future in which tens of millions of deaths from infectious diseases will play a role. Some of these deaths could be prevented through simple vaccination; others could be averted by treatment of active disease. But we must change "could" to "can." Overcoming social paralysis and mobilizing new resources remain the chief challenges for a future in which these diseases will be controlled.

But many people, we have learned, are neither paralyzed nor sedated by claims that these diseases are the natural lot of the poor. From Russia to Haiti to Kazakhstan to the Philippines, we have met wonderful and committed health-care providers who have already aligned themselves with the destitute sick. We hope this Handbook will serve as a blueprint for groups struggling not with paralysis but rather with the very real technical and logistic challenges of responding to complex health problems among the poor. The most complex of these – and AIDS, MDR TB, and drug-resistant malaria are nothing if not complex – will pose serious challenges for even the most committed and experienced groups. Partners In Health and its sister organizations offer up this Handbook in the spirit of pragmatic solidarity with the poor and those who struggle on their behalf.

Paul Farmer, M.D., Ph.D.
Cange, Haiti
April, 2002

[1] Wurtz, White 1999.
[2] Gupta, Kim, Espinal, et al. 2001.