Resurgent Tuberculosis: Deadly Disease of Globalization

by Christine Craig

Two epidemiological reports released in the last few months on the extent of extensively drug resistant tuberculosis (XDR-TB) in South Africa, are critical warnings of the global threat of this virtually incurable disease, especially in conjunction with its "companion" ailment, HIV/AIDS.

TB in any form is not some rare, exotic ailment, but an illness whose onset and transmissibility have long been understood. With decent infrastructure and living conditions, TB could have been contained and driven back to almost nil incidence. However, with the last three decades of international decline in economic conditions, affecting concentrations of people in Africa and Asia, and in localized areas in the Americas and Europe, the resurgence of TB, with its deadly mutations, was predictable.[1]

On Sept. 16, 2006, the Department of Health for South Africa issued a horrifying report on the presence of XDR-TB,[2] including the situation in KwaZulu-Natal. Certain patients at the Church of Scotland Hospital in Tugela Ferry were found, in the Fall of 2005, to be infected with a strain of TB not responding to *any* treatment. A survey over the following 12 months, turned up 53 patients, almost all co-infected with HIV, who were suffering from untreatable TB which, in the immune-compromised patients, was quickly fatal. All but one of the 53 died within three weeks of diagnosis. Those 53 victims represented 16 percent of all confirmed cases of XDR-TB globally during 2006.

This bombshell report conjured up images of a catastrophe in the making in the AIDS-wracked areas of South Africa, precipitating a flurry of meetings among international health professionals, and leading to the creation of the World Health Organization (WHO) Global XDR-TB Task Force, which convened in October to address the threat of untreatable TB in the age of HIV.

Pieter Brueghel's "The Triumph of Death" (detail, 1560), shows the toll of the White Plague (what we call today tuberculosis) in Europe.

The Global XDR-TB Task Force found, to its horror (but no great surprise) that, in the renewed war against a strengthening foe, the ammunition was low, and the supply lines were cut. Although warnings had been out since the early 1990s that multi-drug resistant (MDR) TB was a rising threat, as evidenced by the well-documented outbreaks in the United States and in Eastern Europe during the late 1980s, no agencies had really taken it seriously as a global danger at the time.

XDR-TB is now considered endemic in the KwaZulu-Natal province of South Africa. In the January 2007 issue of *PLoS Medicine*, J.A. Singh et al. presented a truly frightening view of the situation. More than 30 new cases are detected each month, with a total of more than 300 cases, and the disease has been reported in 39 hospitals, plus other areas of the province. And that is just the official tally, which most certainly understates the case, as many of the poor never seek medical help.

The authors note: "In recognition of the global threat posed by these factors, on September 9, 2006, WHO urged a response to the outbreak akin to recent global efforts to control severe acute respiratory syndrome (SARS) and the bird flu...."

Europe's White Plague

That the Western world would be so shocked and surprised by this turn of events is remarkable in itself, considering that, just two centuries ago, tuberculosis was so virulent in Europe that many

feared it would destroy Western civilization. The list of artists, philosophers, and scientists who suffered or died from TB is endless, including Friedrich Schiller, Percy Shelley, Bernhard Riemann, John Keats, and Vladimir Vernadsky.

It is estimated that in 1800, the death rate per year from tuberculosis in Western Europe (and in urban North America) was 1 percent. At the peak of the long epidemic, perhaps 25 percent of Western Europeans died of tuberculosis. There was no cure for the disease, nor was the causative agent known at that time.

And yet, over the next two centuries, "consumption" (as it was known) lost its grip on the European continent, slowly and steadily receding, even in the absence of any satisfactory medical treatments for the disease. Those with active disease were still very likely to die, but fewer were getting active disease.

Robert Koch (1843-1910) discovered the tuberculosis bacillus using a novel staining procedure. He then proved it to be the infective agent in tuberculosis using now-classic animal and bacterial culture experiments.

It has been just 125 years since the famed bacteriologist and Göttingen-trained physician Robert Koch identified and characterized the minuscule tuberculosis bacillus in his home laboratory in Berlin, in 1881, proving it to be the source of the disease, and giving hope that the TB leviathan then devouring the European populace, could be brought down by science.

It has been almost 100 years since the discovery of the only vaccine ever developed against tuberculosis—the Bacille Calmette Guèrin (BCG) vaccine, based on a highly attenuated *Mycobacterium bovis* strain—a vaccine found to give some protection to children against the gruesome childhood killers, miliary tuberculosis and tubercular meningitis.

It has been only some 60 years since the development of the first effective antibiotics against tuberculosis: streptomycin and para-amino salicylic acid (PAS), discovered by Selman Waksman and Jorgen Lehmann, respectively, around the end of World War II.

By 1960, a team led by Dr. John Crofton of Edinburgh, had successfully tackled the recalcitrant tuberculosis problem in Scotland with a remarkable protocol using triple-antibiotic therapy in an 18-month-long treatment regimen, which could successfully cure even advanced pulmonary tuberculosis cases caused by drug-resistant strains. And, under the joint control of the British Medical Research Council and the WHO, trials of Crofton's methods had been carried out in Madras, India among the poor—with astounding success.

Policy makers, including scientists, began to believe that TB could be tackled by drug technology alone, even without costly investments in economic development and public health infrastructure!

A mere five years later, tuberculosis had already been dropped from courses at the Harvard School of Public Health, a disease deemed no longer important in the training of future health-care professionals. Science had won, and tuberculosis, long the scourge of Europe and the U.S., receded from the consciousness of the populace (Figure 1).

The world didn't really take notice of tuberculosis again as a global problem until the second half of the 1980s, when the long trend of TB incidence-decrease in developed countries was shattered by a sudden upward tick in notifications, noted most strongly in the United States and in post-Soviet Eastern Europe. The situation was documented in great detail in the United States by outraged public health professionals, especially in New York City, where most of the increase was occurring (Figure 2).[3]

The Nature of the Beast

Tuberculosis is usually caused by *Mycobacterium tuberculosis,* an ingenious and insidious organism: a minuscule bacterium hardly bigger than a virus, surrounded by an impervious waxy coat. In many of its features within the host body it acts similarly to the Human Immunodeficiency Virus (HIV), secreting itself within immune cells called phagocytes, the very cells that would otherwise seek it out and destroy it.

Within the phagocyte, the tubercular bacillus hides in the central vacuole, protected from chemical destruction by its waxy coat. Here it grows and reproduces very slowly, and is spread with the phagocytes throughout the lymphatic system. Most often, the disease affects adults in its pulmonary form. Children are often afflicted with primary infections affecting the lymphatic system or other organs, including a rapidly fatal systemic form called miliary tuberculosis.

During the host's first (primary) infection with TB, a battle with the immune system ensues, and, almost always, the immune system wins, at least in the short term. The infection becomes "latent."