Resurgent Tuberculosis: Deadlier Than Ever

by Christine Craig

Two epidemiological reports released in the last six months on the extent of XDR-TB—extensively drug resistant tuberculosis—in South Africa, are critical warnings of the global threat of this virtually incurable disease, and also of its "companion" ailments, in particular HIV/AIDS. Moreover, 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, Asia, and in localized areas in the Americas, the resurgence of TB, and its deadly mutations, were predictable.

This TB situation is exactly what Lyndon LaRouche warned about in 1974, when he commissioned a research effort called the "Biological Holocaust Taskforce," to project what the likely results would be in the physical economy, if the anti-infrastructure, anti-development economic programs proposed at that time, called "post-industrialism"/free trade, were carried through. In 1986, an *EIR* Special Report was issued, "An Emergency War Plan To Fight AIDS and Other Pandemics," stressing the need to reverse the downgrading of living and working conditions, and to build up medical and public health infrastructure. Instead, the population became even more impoverished, and infrastructure ratios—water, housing, and medical care—declined. Today, intervention is needed on an emergency basis.

On Sept. 16, 2006, the Department of Health for South Africa issued a horrifying report on the presence of XDR-TB,[1] including the situation in KwaZulu-Natal (KZN). 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% 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.

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. Though 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 over 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

1. Revised definition for XDR-TB: Resistance to at least the first-line drugs rifampicin and isoniazid (MDR-TB definition), plus resistance to the second-line drug fluoroquinolone, plus resistance to at least one of the second-line injectable drugs, such as kanamycin, amikacin, and capreomycin.

First-line drugs available for treatment: isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin.

Second-line drugs available: kanamycin/amikacin, fluoroquinolones, cycloserine, ethionamide, capreomycin, para-amino salicylic acid.

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

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%. At the peak of the long epidemic, perhaps 25% 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' (what TB was called) 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.

It has been just 125 years since the famed bacteriologist and Göttingen-trained physician Robert Koch identified and characterized the miniscule 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 Guérin (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 Wacksman 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 (BMRC) 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 healthcare 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**).[2]

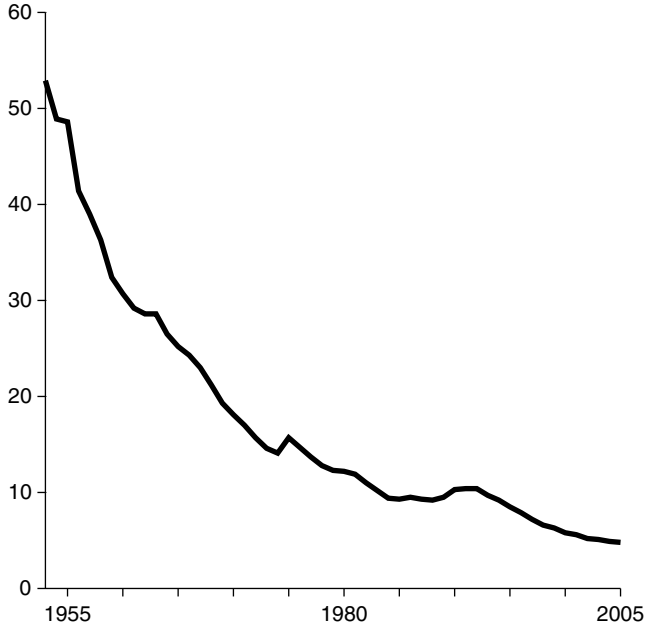
The Nature of the Beast

Tuberculosis is usually caused by *Mycobacterium tuberculosis,* an ingenious and insidious organism: a miniscule bacterium hardly bigger than a virus, surrounded by an

2. For a recent look at the New York City situation as it affected public health, see "Impact of NYC's 1975 Fiscal Crisis on TB, HIV, and Homicide," *EIR,* Aug. 25, 2006. Banker Felix Rohatyn was the author of Big MAC. The article in the March 2006 issue of the *American Journal of Public Health* is, "The Impact of New York City's 1975 Fiscal Crisis on the Tuberculosis, HIV, and Homicide Syndemic."

FIGURE 1

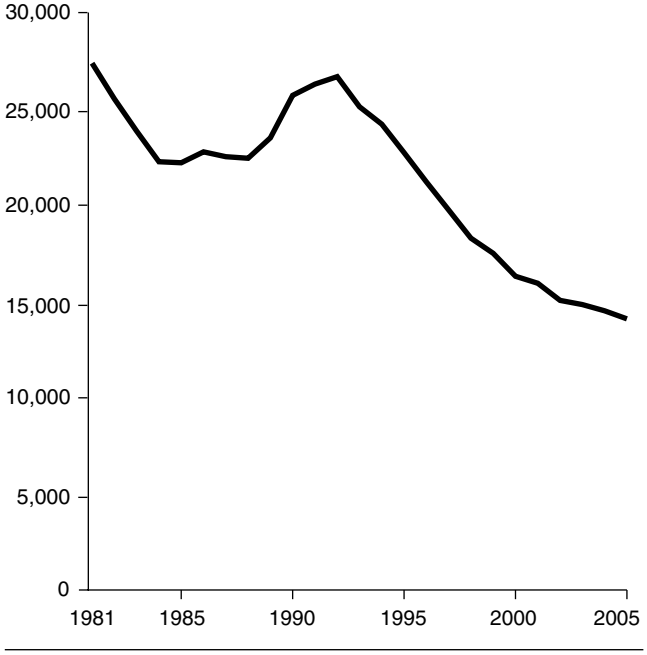
Tuberculosis Rate per 100,000 Population, United States



Source: CDC.

FIGURE 2

Number of Tuberculosis Cases, United States



Source: CDC.

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." Only 5% of primary infections go on to become active diseases within five years, while the lifetime risk of active infection developing is 10% *on average.* Unlike some other disease-causing organisms, however, the immune system's reaction to the TB germ does not confer a lasting immunity on its host. A primary infection which has gone latent does not preclude a reinfection with another TB organism at a later date.

The latent infection is a time-bomb within the host. Under adverse conditions leading to a weakening of the immune system, a latent infection can and does break out into active disease. Undernourishment, stress, injury, coinfection with other diseases, age, drug or alchohol abuse, lung silicosis—any of these bodily insults can tip the scales in favor of the TB bacterium, leading to a potentially fatal and highly infectious illness. Each active infection (which can persist for years if untreated, especially in the pulmonary form) provides many opportunities to spread the disease. One active TB case under conditions of overcrowding and poor ventilation, can infect whole families, school classes, military platoons, homeless shelters, prison cell blocks, and hospital wards.

Such active pulmonary disease must be detected by microscopic examination of sputum samples, followed by drug sensitivity testing of cultures, a procedure which, at present, can take many weeks.

It has been estimated that perhaps one-third of humans on the planet have been infected with TB. That's over 2 billion human souls carrying little time-bombs around in their bodies ready to explode into action when the scales tip in the balance of power. It is this complex and long-lasting interaction between host, invader, and physical and social environment, that determines the imprint of tuberculosis on any human society. In fact, the burden of tuberculosis within any human social group could be considered a rough measure of the social health of that grouping.

The Problem of Microbial Resistance

"It is a sad reflection on society's incompetence that, more than 30 years after the methods for cure and prevention were evolved and before the advent of the HIV epidemic, there were already more patients with active TB in the world than there had been in the 1950's."

—Dr. John Crofton, in the forward to his 1994 medical monograph, Clinical Tuberculosis.

We are presented with a paradox: On the one hand, even before the advent of antibiotic treatments or vaccination for TB, the disease was steadily declining in previously devastated areas of the world. On the other hand, decades after the advent of effective treatment strategies for tuberculosis, there are alarms sounding that TB might be getting out of control. There are several reasons for this, some more complex than others. On the surface, the easy answer is microbial resistance, a phenomenon as old as antibiotics themselves.

Briefly, resistance to antibiotics and similar agents comes about analogously to the way humans become biologically resistant to diseases. Just as tuberculosis or bubonic plague will kill off susceptible individuals, leaving a population more resistant to the diseases, so do antibiotics. Just as some of these resistance factors in humans are inheritable, and passed on to offspring, so too with microbes within the body. When we attack a disease by administering antibiotics, the very susceptible microbes are soon dead, leaving an altered population of microbes less affected. These are the microbes now reproducing. With continued treatment, most of these can also be killed, leaving the immune system to mop up the stragglers. If, however, treatment is removed early, a large population of more resistant microbes remains in the body. These can be spread to others who, if treated with the same antibiotic, might not be cured. And so the cycle goes.

Microbes have many ways to accumulate resistance factors, including mutations and horizontal gene transfer among various organisms. The almost inevitable end result is: Antibiotics become less effective over time, and must be replaced. Resistance to penicillin is a familiar example.

The problem is much worse with tuberculosis, because TB is much harder to kill within the body. One drug alone is ineffective in most cases, as was found early on with streptomycin, one of the early "miracle drugs" for tuberculosis. Streptomycin would knock the disease down, but it would come back, and was then untreatable with streptomycin. Clinicians found out the hard way that it took three different drugs, administered religiously over 18 months, to cure tuberculosis. This regimen, developed in the late 1950s in Scotland, became the foundation for early WH0 tuberculosis control. The rationale for using three drugs was: Organisms resistant to one or two of the drugs would still be killed by the third. Furthermore, one drug worked better early in the infection, whereas another worked best later on. This approach was highly effective in treating individual patients, and was successful in certain areas on a population level. Hence, the complaint by Dr. Crofton, quoted above, one of the developers of triple-antibiotic therapy. Why was tuberculosis still such a big problem in the world, given a highly effective therapy capable of curing almost all tuberculosis? The short answer is inappropriate treatment, which hides a host of sins.

Drug resistance in tuberculosis strains is basically caused by poor implementation of TB control programs by countries. This can include poor drug supplies or quality, poor record-keeping, inadequate treatment regimens, and non-compliance by patients. It can also include poor infection-control protocols in hospitals, and lack of laboratory testing facilities capable of identifying resistant strains in a timely manner. The problem boils down, in other words, to lack of an effective health-care infrastructure.

The gold standard of treatment, developed by 1960, included triple-antibiotic therapy for 18 months. Later research led to fine-tuning the therapy to intermittent regimens for six months. Directly observed treatment was an important part of that strategy, to insure compliance by patients. Treatment would be done on an outpatient basis, because poor families could not be without breadwinners for such long periods. Hospitalization was impractical. In several test programs in Asia and Africa, it was shown by the BMRC tuberculosis group that, with proper drugs and well-designed, well-implemented programs, managed rigorously by outside agencies such as themselves, even poor countries could control TB.

Within a decade, however, WHO was not only slashing its own TB program budget and programs, but was trimming away at the treatment methodologies which it had helped develop. It was found much cheaper to give just one drug, isoniazid, for a shorter period. This worked for many people with relatively uncomplicated tuberculosis, but its frequent failure led to widespread isoniazid resistance. Meanwhile, Britain's premier BMRC tuberculosis unit itself was shut down by 1986, a victim of Margaret Thatcher's cost-cutting measures.

The developed world basically turned away from the poor countries, leaving them to their own devices, with the inevitable results: Tuberculosis programs became a shambles. During that era of indifference, ironically enough, the heavy-hitter in the tuberculosis comeback quietly joined the fray in Africa. Human Immunodeficiency Virus began, largely unnoticed, to spread throughout sub-Saharan Africa, and rising tuberculosis cases mirrored its rise.

TB: Into Africa

Tuberculosis has exacted a stiff toll in South Africa over the last 125 years. Before the advent of European settlers, and later, Asian workers, the population groups appeared to have had little experience with TB. Then came the discovery of diamonds in Kimberley, and later, gold on the Witwatersrand. To work the mines required cheap labor. Young African men

WHO/P. Virot

A tuberculosis patient in Delhi, India, undergoing a World Health Organization-approved treatment.

were recruited from not only South Africa, but from populations even up into the Tropical zone. These disparate groups were brought together into a few, very concentrated locations run by European managers and foremen, packed like sardines into dorm compounds, where they lived for months with deficient diets, deficient wages, and exhausting labor, with little exposure to the Sun, under dangerously primitive mining conditions. They had no families with them. After a few months they presented with scurvy, syphilis, and tuberculosis, whereupon the mine managers mandated that all sick "natives" should be sent back whence they had come, to die or heal. This constant stream of migrations to and from the mines efficiently spread all the diseases incubated in the mining environment to all the home villages of the laborers, infecting wives, families, neighbors, etc. Such policies remained in place until a few decades ago. The endless flow of recruited black Africans were in effect used up like coal, stoking the engines of the mines—a primitive accumulation of human resources—the very circumstances upon which tuberculosis thrives.

Tuberculosis, having been seeded throughout the entire region of the continent, the far-flung populations began that dance so well known to 18th-Century Europeans: The disease ebbed and flowed with the circumstances of the people, advancing with famine and war; receding with peace and plenty; but always reseeded with returning migrants from the mine or manufacturing that built up around the mining industry.

TB in the Era of HIV

If the WHO had not mothballed most of its TB program throughout a good part of the 1970s and 1980s, including its surveillance programs in the various regions, it would have noticed the ominous increase in TB incidence in certain areas of Africa, and probably caught on earlier to the new disease that was behind its increase: HIV. By the time WHO began to pay attention, HIV had gained a strong foothold in sub-Saharan Africa, which has now become a stranglehold. Because TB had earlier been spread widely throughout sub-Saharan Africa as the result of colonial labor policies, there was a large reservoir of latent infection ready to smolder into active disease when HIV invaded the body's immune system. In fact, over 40% of HIV positive patients in the region die, not of AIDS, but of tuberculosis (**Figure 3**).

An example of the synergy between HIV and tuberculosis can be seen in TB incidence in the South African gold mines. According to mine statistics, TB incidence in the mines was stable at about 1% per year up until 1990, whereupon incidence rates began to rise in conjunction with numbers of HIV-positive workers. It has now reached over 4%—a fourfold increase in just over a decade.

When you add to the mix the poverty, economic underdevelopment, and lack of health-care infrastructure in the high-HIV-burden countries of Africa, it is not hard to imagine, that attempts to treat the tuberculosis in HIV-positive patients (a much more complicated task than simple pulmonary tuberculosis) under these conditions would lead to the development of resistant strains which could be easily spread in primitive hospital settings. The existence of supplies of second-line tuberculosis drugs in areas of South Africa has led to their use to treat tuberculosis resistant to first-line drugs. Failure to cure with these drugs has led inevitably to the XDR-TB upsurge among the HIV-positive populace.

Spread of Drug-Resistant TB in Russian Prisons

One of the other main locales for re-emerging tuberculosis has been the Russian Federation. With the post-1991 fragmentation of the U.S.S.R., and the dismantling of the Soviet system in favor of Mandevillian looting of the public coffers by private corporations, the huge public-health system was looted and dismantled as well. What medical treatment capability remained was put on a pay-to-play footing at the same time that the populace, long used to guaranteed employment of some sort, was left with rising unemployment and falling wages, and dismal prospects for the future.[3]

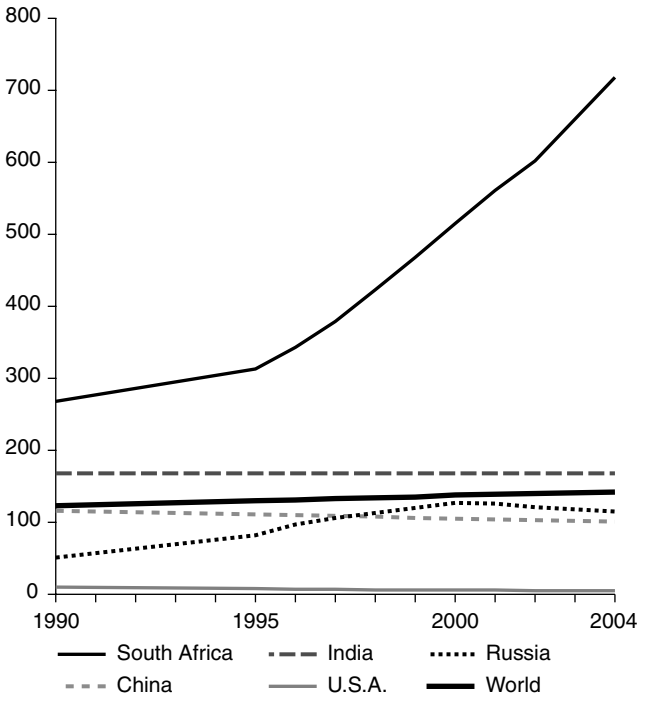
Much of the increase in tuberculosis in Russia since the fall of the Soviet Union, can be attributed to the very efficient

3. For a perspective on the post-Soviet economic policies behind the Eastern European resurgence of TB, read Sergei Glazyev, *Genocide: Russia and the New World Order,* EIR News Service, 1999.

FIGURE 3

Incidence Rates of Tuberculosis in Selected Countries

(1990-2004, per 100,000 population)



Source: WHO.

spreading mechanism provided by the Russian penal system. Russia has the highest rate of incarcerations in the world (the U.S. is second), with 630 prisoners per 100,000 population—over 1 million prisoners total—one-tenth of whom are infected with TB, according to a 2002 study by the Swiss Tropical Institute, titled, "Sentenced to Die? Tuberculosis Control in Prisons with a Focus on the Republics of the former Soviet Union." In the prison system it is estimated that TB rates are 40-50 times that experienced in the civilian population. And at least 20% of prison TB cases are MDR-TB—two to four times the civilian rates. Fully 80% of detainees are estimated to harbor latent TB, and perhaps 80% of prison deaths can be attributed to the disease.

Russian prisons are incredibly underfunded and overcrowded, with poor food quality, poor ventilation, and primitive health services. Most of the incarcerated are young males, and many of these young people become infected while awaiting trial, even before being convicted of a crime. They are unlikely to be eligible for treatment until and unless they are convicted. These unfortunates are warehoused in incredibly cramped pre-trial detention centers, often for many months.

Each year some 300,000 prisoners are released into the general population, and perhaps 30,000 have active tuberculosis. Over 6,000 have MDR-TB. These people will take their diseases back to their towns and families, seeding the countryside with forms of tuberculosis unresponsive to most of the drugs available or affordable within the Russian Federation.

According to a 1999 report produced by the Harvard Medical School, "The Global Impact of Drug-Resistant Tuberculosis," the breeding of multi-drug-resistant strains by the prison system is due to both the high burden of primary and reactivated TB in the prisons, plus poor and incomplete treatment of the infected prisoners, including those released uncured into the general population. The result is many thousands of cases of TB which remain sputum smear positive and infectious long after initiation of therapy with first-line drugs. Only highly supervised and expensive second-line drugs would cure these cases, and those aren't generally available, especially for the poor and unemployed.

Meanwhile, waiting in the wings is the specter of HIV, spreading quickly among the growing population of intravenous drug-users, and beginning to spread to the general population through sexual contacts. The rate of increase of HIV in the Russian Federation is one of the highest in the world, though the percentage of people affected is still small. If HIV moves significantly into the prison system, the deadly synergy of HIV plus TB will be catastrophic, both in terms of mortality, and in production of drug-resistant TB strains.

To get an idea of the power of that synergy, one need only look back on the New York City MDR-TB epidemic, which was spawned in the prison system. It took over $1 billion and several years to stamp out the small epidemic of a few thousand cases in one major city—the wages of the sins of deliberately taking down the health-care system in the city, and dismantling social services in general, in the name of fiscal austerity. In March 2006, a thorough, historical epidemiological study was published by the *American Journal of Public Health,* done by New York City disease experts, of the dramatic increase in death rates from TB and other afflictions (AIDS, hepatitis, syphilis, and drug abuse, from 1979 to 1993), as a direct result of the 1975 austerity initiated by what was called Big MAC (Municipal Assistance Corporation), when hospitals and public health were drastically reduced.

Given the state of the present Russian economy, with the major loss of the public-health sector already accomplished, whence would come the enormous resources necessary to quell a major MDR-TB flare-up in the Russian prison system radiating out to the country at large? And how far beyond the borders of the Russian Federation would the epidemic radiate?

Prospects for the Future

For HIV-positive people exposed to XDR-TB, the future is grim: death within weeks, millions at risk. There are no new drugs ready to roll out, no vaccines we can fly in to

save the day. The last new class of drugs with useful antitubercular activity was discovered decades ago. The only vaccine is almost 100 years old. However, many HIV patients can be successfully cured of the garden-variety of tuberculosis, with rigorous techniques using the best treatment regimens. The obvious answer is, don't create XDR-TB. Bad treatment is worse than no treatment at all, when it comes to development of resistance. The next, and even more obvious answer is, if XDR-TB has the potential to kill millions, perhaps some governments need to step in and encourage drug-research and vaccine companies to develop the new classes of tuberculosis drugs and vaccines necessary to keep ahead of the resistance phenomenon. If the amount of dollars being thrown at bird flu drugs and vaccines were earmarked for tuberculosis drugs and vaccines, useful products could well emerge.

These, as well as the elusive AIDS vaccine, would give the world time to do what really needs to be done. The Great White Plague of Europe was largely reversed, not by drugs and treatments, but by the development of public health as part of the economic and scientific development of Europe. Its reversal went hand-in-hand with learning the science of managing large industrial cities so as to make them fit for human beings to thrive. The TB epidemic in Africa, Asia, and other countries with high HIV burdens is not yet nearly as bad as that in Europe and North America in 1800, but it is moving in that direction. Every year a larger percentage of previously rural people move into expanding slums in the cities of the developing world. These slums are lacking in the basic needs of the new urban underclass, making it the ideal breeding ground for HIV, tuberculosis, and the water-borne diseases which kill so many of the very young.[4]

What must be done to keep the epidemic from expanding, is, not just throw a perpetually evolving group of drugs at billions of the poor and starving people, who are crowded into growing slums throughout the developing and undeveloped world. That is a stop-gap measure. And the paradox is, given the well-known natural history of the tuberculosis disease, developing the capability to carry out the arduous and long-term effective drug and vaccine interventions required in the high-burden TB/HIV countries, would require developing sophisticated health, manufacturing, and education infrastructure within those countries, even should such drugs become available in the near future.

The long-term solution to the problem of tuberculosis lies in economic development: clean cities with room to breathe; clean water; modern sewage treatment plants; productive economies running on nuclear energy technologies; plenty of nutritious food from productive farms; and a modern public health system in every nation. Tuberculosis could not long thrive under those conditions.

---

4. UN-Habitat report for 2006, *The State of the World's Cities, 2006/7.*