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Engaging North Korea on Mutual Interests in Tuberculosis Control

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As this paper goes to press, relations on the Korean Peninsula are at their tensest level in more than 20 years. Since 2006, when the Democratic People's Republic of Korea (DPRK) announced that it had restarted its nuclear facilities, the government has challenged international nonproliferation treaties on several occasions. Domestic plans for transfer of leadership to Kim Jong-un bring new complexities to government relations with the outside world. Following military incidents in 2010 along the long-disputed Northern Limit Line in the Yellow Sea, China, which is North Korea's most important ally, the United States, South Korea, and other governments have been working intensively behind the scenes to keep tensions in check.

The DPRK is a foreign policy conundrum. While the regime's nuclear ambitions remain at the forefront of international security concerns,[1] the world is painfully aware that this isolated and enigmatic country of 24 million people is also plagued by crippling energy, food, and medical shortages.[2] Since the famines of the 1990s, rates of tuberculosis (TB), a disease that exploits malnutrition and other conditions that compromise natural immunity, have risen dramatically and are now among the highest in the world outside of sub-Saharan Africa, including more than triple the rates in China and South Korea.[3] From 1995 to 2003, the U.S. government provided more than a billion dollars in food, energy, and medical assistance to North Korea.[4] Absent an impact of humanitarian efforts on broader diplomatic opportunities, international humanitarian contributions have fallen off dramatically in recent years even as the North Korean economy continues to struggle. In the decade since the breakdown of the Agreed Framework, it is increasingly apparent that policies tying economic aid to nuclear disarmament are not working.[5]

In this paper, we describe our experience working with the civilian DPRK Ministry of Public Health (MoPH) to develop the country's first modern TB laboratory.[6] Begun in 2008, this unique collaboration of U.S.-based voluntary interests, including a major medical institution, a humanitarian nongovernmental organization (NGO), and a nonprofit sponsor, has achieved a critical public health objective during a period otherwise marked by profound deterioration of relations with the United States and its allies in East Asia. Because coordinated global efforts are needed to control TB in the antibiotic era, we argue such engagements can encourage broader assimilation within the international health community.

We first provide background on the modern history of TB epidemics, the new challenges to global health security posed by the emergence of drug-resistant strains, and how these epidemics can interact with major geopolitical events. We hypothesize that the TB situation in North Korea today bears ominous parallels with conditions accompanying the end of the Cold War in Europe and that Northeast Asia faces a similar set of challenges as it contemplates opportunities for assimilation. We then describe the process of implementing the laboratory project and our objectives for sustaining this effort. We conclude by discussing implications of these efforts for North Korea and global health security interests.

Tuberculosis and Health

M. tuberculosis, the cause of human tuberculosis, is an airborne pathogen that chronically infects more than one-third of the world's population, causing more than nine million cases of active TB and nearly three million deaths each year.[7] Classically associated with conditions of poverty, malnutrition, aging, and medical conditions that suppress the immune system, 80 percent of cases occur in the developing world. Because of

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its intimate association with general health, particularly in adults of reproductive age, the World Bank and the World Health Organization (WHO) have characterized TB control as one of the most cost-effective investments developing countries can make.[8]

A pathogen of humans for more than 50,000 years,[9] *M. tuberculosis* has developed strategies for interacting with the human life span. The natural history is characterized by three principal stages: exposure, latent infection, and active disease with transmission to new hosts.[10] Of those exposed to an infectious TB case, about 30 percent are thought to develop the state of latent infection, during which the host remains healthy, but TB bacilli may survive for decades within clusters of immune cells. Latent infections constitute the pathogen's population reservoir. Although the normal human immune system is substantially equipped to control a latent infection, in 10 percent of these infections, the latent state is terminated by a breakdown in immune defenses brought on by malnutrition, illness, or aging, and the individual develops the active, contagious form of the disease. Without treatment, about 50 percent of active cases will die, and each infectious case at this stage will disseminate the TB bacillus to 10 to 20 other persons.[11] In this way, *M. tuberculosis* is able to infect successive human generations. In the pre-antibiotic era, TB epidemics could rage for centuries, devastating isolated populations weakened by hunger and acute infections.[12]

Although antibiotics have greatly improved the treatment outcome for TB, current therapy still requires the combined use of at least four different antibiotics administered in an uninterrupted manner for at least six months.[13] Because TB capitalizes on any condition that jeopardizes the individual's general health, attention to the patient's nutritional status and underlying medical conditions is also required. The use of fewer drugs, interruption of drug therapy, inadequate nutrition or intervening illness can result in poor clinical outcome (including death) and the dissemination of TB to other persons. For these reasons, control of TB requires primary-care approaches and rational drug management strategies, including sustainable, stable, public health structures.

Drug-Resistant Tuberculosis

The discovery of curative drugs in the middle of the 20th century, including their application to massive global public health campaigns, came at a critical time in the political realignment of the postwar world and the emergence of modern global markets. These developments have fundamentally altered the course of TB epidemics, particularly in the West. For example, rates of TB in the United States today are 3.6 per 100,000 population (compared with a global average of 137 per 100,000 in 2009[14]) compared with 53 per 100,000 in 1953 when the first anti-TB drugs were introduced.[15]

By the late 20th century, however—within the short span of one human generation—two developments began to threaten these gains. The first, during the 1980s, was the emergence of AIDS, a disease that attacks the same immune cells required to control a latent TB infection. The AIDS epidemic has had a profound impact on TB trends, particularly in Africa where up to 30 percent of new TB cases may be due to HIV co-infection.[16] The second development was the emergence of multidrug-resistant strains of TB (MDR TB), first reported in the early 1990s.[17]

MDR TB—defined as resistance to at least isoniazid and rifampicin, the two most powerful front-line TB drugs—now accounts for nearly a half million cases of TB annually, including an estimated 150,000 deaths in 2008.[18] Treatment of MDR TB requires up to two years of complex drug management with regimens that often have toxic side effects and are 50–200 times more costly than drugs needed to treat persons with TB caused by drug-sensitive strains.[19] Although survival rates are improving, they are only marginally better than those of the pre-drug era. Cases of extensively drug resistant TB (XDR TB), defined by resistance to the major first- and second-line TB drugs and largely incurable, have now been reported in 58 countries with the laboratory capacity to test for it, and it may account for up to 10 percent of MDR TB cases globally.[20] These trends raise the specter of an era in which current drugs are no longer effective.

Resistance to TB drugs arises from spontaneous mutations in the TB genome under drug selection pressure and is thus a man-made phenomenon. These mutations develop rapidly in the setting of monotherapy (use of only one drug for treatment) and will amplify quickly to affect remaining drugs in the armamentarium.[21] For this reason, compared with new TB patients, risk of MDR TB is about 5.5 times greater in patients who have received inadequate therapy in the past.[22] Because MDR TB may develop over months or years, inadequately treated persons who continue to be infectious can spread drug-resistant strains to persons in their communities.[23] If inadequately treated persons migrate across frontiers, drug-resistant strains can be spread to other populations.

In absolute numbers, about 50 percent of MDR TB cases occur in China and India although the highest proportions of TB cases with MDR (9 percent of the world's cases) reside in eastern Europe and Central Asia.[24] As many as 50 percent of cases in countries of the former Soviet Union are resistant to at least one TB drug.[25] In parts of the Russian Federation and the countries of Kazakhstan, Tajikistan, Uzbekistan, and the Republic of Moldova, 25 percent of new TB patients and more than 50 percent of previously treated patients suffer from multidrug-resistant disease.[26] The age of these victims peaks in young adulthood, suggesting a relatively recent introduction.[27] Multidrug-resistant strains may have been amplified by prolonged drug shortages that occurred during the period of economic destabilization accompanying the collapse of the Soviet bloc in the 1980s.[28] With the end of the Cold War in Europe, drug-resistant strains from this epicenter have now been tracked by molecular fingerprinting methods to North America, Europe, the Middle East, and even to South Africa.[29]

The magnitude and dissemination of the MDR epidemic in eastern Europe and Central Asia caught the world off guard and caused a reevaluation of global strategies for TB control. Laboratories with capacity to test for drug resistance were not available in most high-burden countries,[30] and it was quickly recognized that the cost of treating MDR and XDR far exceeds public health budgets of developing countries.[31] Since 2000, massive resources have been organized through such mechanisms as the STOP TB Partnership (www.stoptb.org) to manage MDR and XDR TB and control its spread. These programs include the Green Light Committee, which finances second-line drug procurement and MDR treatment[32] and the Global Laboratory Initiative designed to set quality assurance standards for drug susceptibility testing and accelerate access to modern TB diagnostics.[33] With additional support from programs like the President's Emergency Plan for AIDS Relief (PEPFAR), the Obama Global Health Initiative, UNITAID, and the Foundation for Innovative Diagnostics (FIND), 27 high-burden MDR TB countries—15 of which were states of the former Soviet bloc—have been targeted for aggressive scale-up operations.[34]

The Soviet experience shows that drug-resistant strains of TB, generated in one region as a consequence of failed public health programs, can disseminate to spawn outbreaks of drug-resistant disease both regionally and remotely. This experience also reminds us that MDR epidemics leave costly legacies for which the world community is ultimately responsible. *We contend that political and economic conditions coinciding with the emergence of new drug-resistant strains in the former Soviet Union still persist in Northeast Asia.*

Tuberculosis in North Korea

Health system

TB care in North Korea was heavily influenced by the Soviet model of centralized administration and sanatorium care. During the 1960s and 1970s when Soviet bloc subsidies were plentiful, North Korea implemented a universal health care program (Article 72 of the Constitution), and the "No. 3 (TB) Prevention Department" of the MoPH built a multitiered residential treatment system for TB with its own pharmaceutical industry. The No. 3 (TB) Prevention Department includes 10 provincial TB hospitals as well as approximately 225 remotely located 60–70 bed TB "rest homes" in each of the country's counties and municipal districts.[35]

Since the loss of Soviet aid in the 1990s,[36] the TB pharmaceutical industry has virtually disappeared; much of the public health infrastructure, including physical plant and medical equipment, has not been updated in decades. Chronic energy and supply shortages plague operations at every level. Today the country relies almost entirely on a dwindling supply of donors for basic medical supplies, including TB drugs and diagnostics. The DPRK is not eligible for basic health sector development funds, such as through the World Bank, International Monetary Fund, or the Asia Development Bank.

Epidemiologic Trends

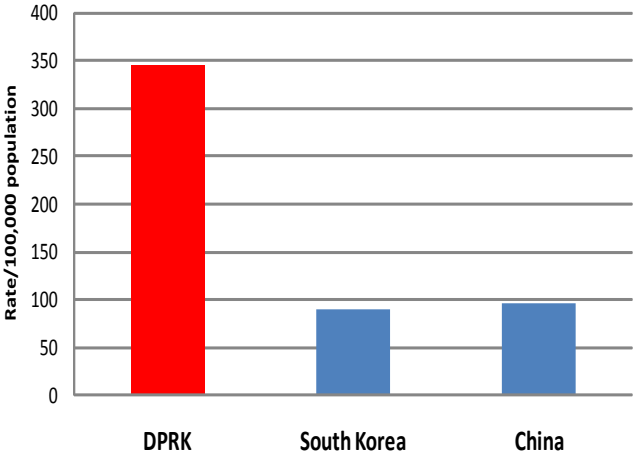
In 1998, WHO established a country office in Pyongyang.[37] This program, which is supported by continuing cooperative planning agreements between the WHO and the government, provides one source of documentation of health trends inside the DPRK. These and other planning documents make it clear that the famines of the mid-1990s had a profound impact on the general health status of the population, including rates of infant and maternal mortality, hepatitis, malaria, and TB.[38] From 1996 to 1999, rates of mortality due to TB tripled to more than 100 per 100,000 population, rivaling some of the worst rates in the developing world.[39] A UNICEF-funded nutrition survey carried out in 2004 among 4,800 households in 160 *dong* and *ri* jurisdictions by the DPRK Institute of Children Nutrition estimated that 23 percent of children were undernourished and that 37 percent of children were of stunted height.[40] A new United Nations census released in 2010 estimates that life expectancy has declined by 3.4 years (to 69.3 years) since 1993, while infant and maternal mortality rates have risen 36 percent and 46 percent, respectively, in the same period.[41]

TB caseload estimates provided to WHO by the MoPH for 1994, the period just before the great famines, show a TB incidence rate of about 38 per 100,000 population.[42] Although these figures pre-date the development of standardized reporting systems, such rates would be in a range reported by middle-income countries today. In 2001, MoPH adopted the WHO-sponsored Directly Observed Short Course Therapy (DOTS) program for TB control, including its treatment standards and reporting formats.[43] In 2006, three years after this program was implemented nationwide, an incidence rate of 178 per 100,000 was reported.[44] In 2009, following a small community infection survey,[45] WHO doubled its estimates to 345 per 100,000 population.[46] For 2010, North Korea is expected to require drugs for nearly 100,000 TB patients, translating to a case rate more than 370 per 100,000 population.[47] Compared with the 22 historically designated high-burden countries,[48] TB incidence in North Korea ranks number seven or number eight in the world, being one of the highest outside of sub-Saharan Africa and 3.7 times the rates in China (98 per 100,000) and South Korea (90 per 100,000) in 2009 (***Figure 1***).[49] Age-specific case trends and an annual risk of TB infection estimated at 3.2 percent suggest the epidemic is still expanding,[50] plausibly fanned by continuing food shortages and acute infections such as measles that are known to suppress the immune system.[51]

TB Assistance to North Korea

As a low-income country (less than $1,000 annual income per capita) with a TB incidence rate in excess of 100 per 100,000, the DPRK meets high-priority conditions for assistance through the world STOP TB partnership of funds. From 2001 through 2007, the country received basic TB drugs and diagnostic supplies through the WHO-sponsored Global Drug Facility (GDF). However, the adequacy and sustainability of this assistance, often supplemented by NGO donations,[52] have been complicated by the country's diplomatic isolation. In 2003 and 2006, for

Figure 1: **Incidence of Tuberculosis in Three Northeast Asian Countries, 2009**



Source: World Health Organization, Global TB Report, 2010

example, the country lost bids to qualify for longer-term TB assistance through the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund). Following the nuclear test in 2006, a $400,000 grant to WHO for expansion of TB programs in the DPRK from the Canadian International Development Agency (CIDA) was withdrawn.[53] In 2010, following two exceptional years of bridge funding through GDF and WHO regional budgets, the Global Fund reached an agreement with the DPRK that is expected to continue first-line TB medicines for at least another two years. Because the DPRK is subject to the Global Fund's "additional safeguards" policies, the award will be administered by UNICEF and is contingent on the government's acceptance of new in-country monitoring programs.[54]

As a result of this problematic funding history, critical capacity needs of the DPRK national TB program have been postponed even as the country's epidemic has continued to expand. The precise magnitude of this epidemic is uncertain, however, because published epidemiologic data may differ from statistics heard by NGOs on the ground, and Web resources often present differing estimates. In addition to basic energy and nutritional needs not covered by standard TB program assistance, one of the most critical of the postponed agendas has been development of resources to diagnose and treat drug resistance. Until initiation of the U.S.-DPRK Tuberculosis Project, the DPRK national TB program was one of the few operating in a country with a TB burden as high as 345 per 100,000 population that lacked funding for development of at least one facility for diagnosis of TB by culture and drug susceptibility testing. In the absence of such facilities, the contribution of drug resistance to this epidemic, including the types of drugs needed to treat patients who fail to respond to standard therapy, cannot be determined. Although the DPRK is not a candidate for the global MDR scale-up effort targeted to high-burden countries, rates of drug resistance are likely to be significant, a prediction based on retreatment rates reported to WHO as well as regional trends.[55]

Regional Implications

The DPRK's TB epidemic has important implications for Northeast Asia, including provinces of northeast China, Mongolia, and neighboring oblasts of the Russian Federation. Rates of drug resistance in Northeast Asia are some of the highest in the world outside of the Russian Federation, with which the area shares extensive borders. In 2008, the China Center for Disease Control reported that rates of drug resistance in the northeastern provinces of Inner Mongolia Autonomous Region, Liaoning, and Heilongjiang exceeded 7 percent among new cases of TB and ranged from 24 percent to 37 percent among previously treated cases.[56] A small nationwide survey carried out in Mongolia during 1999 found rates of isoniazid mono-resistance to be as high as 30 percent, although rates of multidrug resistance may be lower than in neighboring areas owing to the relatively late introduction of rifampicin in that country.[57]

High background rates of MDR TB, especially among previously treated patients in this region, may be due to shared historical circumstances. Public health systems in this part of the world are still recovering economically from the breakup of the communist bloc. Older, sanatorium-style systems of TB care are common, and much of the laboratory infrastructure requires upgrading.[58] Although one-fourth of the world's MDR TB cases are thought to occur in China alone,[59] there is only one certified supranational TB reference laboratory (located in Hong Kong) serving the entirety of continental East Asia. South Korea's supranational TB reference laboratory, a designated training center in the international reference and research system, is inaccessible to North Korea. In short, because of the constraints of Cold War relations, this region is poorly prepared to respond to a collapse of TB care on or within its borders. For this reason, the response to the DPRK TB epidemic must also be looked at in the context of supporting an important health security agenda for an epidemiologically vulnerable region of the world.

In summary, the TB epidemic in the DPRK has evolved ominously since the breakup of the Soviet Union and the famines of the 1990s. In contrast with the Soviet experience, and in part in response to it, the global health community is far better organized today to ensure that no country, regardless of its political system, goes without basic TB drugs. At the same time, because of continuing diplomatic isolation, the country remains "off the radar" for internationally funded MDR scale-up programs. This should be seen as an urgent regional priority.

The U.S.-DPRK Tuberculosis Project

Goals

The goals of the U.S.-DPRK Tuberculosis Project are to develop sustainable professional and academic collaborations with the North Korean Ministry of Public Health focused on mutual interests in TB control and to facilitate networking with other TB programs in the region and internationally.

History

The concept for this project arose indirectly from unofficial discussions attending the so-called track 2 arm of the six-party talks. In February of 2007, during the fifth round of the six-party talks, the DPRK agreed to phase out the Yongbyon nuclear plant in exchange for economic assistance and eventual normalization of relations.[60] Working with this framework, Stanford professor of political science, John Lewis, solicited School of Medicine colleagues to assess the prospects of engagement focused on mutual interests in TB control. Following these discussions, Lewis obtained approvals for a delegation of DPRK public health officials to meet with TB specialists at Stanford. In January 2008, with sponsorship from the Freeman-Spogli Institute's Center for International Security and Cooperation (CISAC) and Walter H. Shorenstein Asia-Pacific Research Center (APARC), four DPRK MoPH officials and one protocol officer spent a week in northern California, touring TB facilities in the San Francisco Bay Area (***Figure 2***). The Bay Area TB Consortium (Stanford/BATC), an affiliation of TB physicians, microbiologists, and epidemiologists drawn from the area's medical schools and public health departments, was organized by Stanford School of Medicine to host the delegation along with ex officio representatives from the Korea Society, Eli Lilly Foundation, the U.S. Centers for Disease Control and Prevention (CDC), and WHO.

Figure 2: **MoPH Delegation at Stanford University, 12 January 2008**

During these discussions, MoPH representatives, led by the director general of the No. 2 and No. 3 (TB and Hepatitis) Departments, requested assistance to complete a modern TB reference laboratory at the campus of the No. 3 (TB) Prevention Hospital in the capital city of Pyongyang. Although WHO and MoPH had devised a site plan and equipment inventory for this project in 2006, the initiative had since stalled for lack of funds.[61]

Implementation

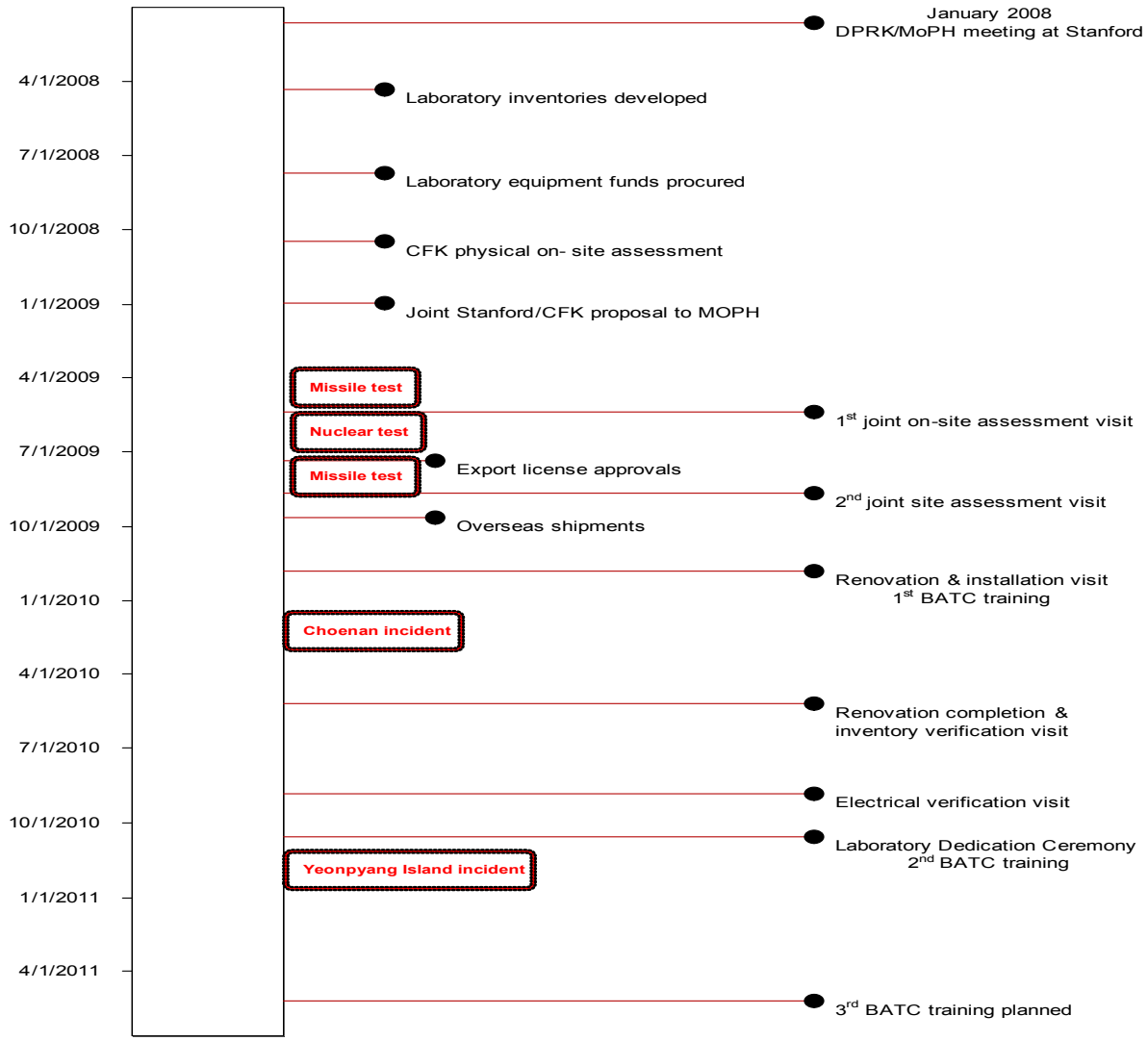
From this seminal meeting at Stanford, the U.S.-DPRK Tuberculosis Project evolved into the partnership of the Stanford Bay Area TB Consortium, the Nuclear Threat Initiative/Global Health and Security Initiative (NTI/Global Health and Security Initiative), and Christian Friends of Korea. Together, our organizations have contributed a combined total of more than $500,000 to develop the DPRK's first modern TB laboratory. Since October 2008, representatives of this partnership have completed a total of nine in-country visits, including two extended visits involving large rotating work teams. Despite significant diplomatic reversals coinciding with our schedule, momentum was not affected, and U.S. teams experienced extraordinary cooperation from MoPH and other government officials. Implementation of the project progressed through four principal stages, including organizational development, site assessments, installations, and technical training (***Figure 3***).

Organizational development (March 2008–December 2008). Shortly after the meeting at Stanford, organizers obtained the proposed TB laboratory inventory from WHO representatives in Pyongyang and, with assistance of Dr. Gail Cassell of the Eli Lilly Foundation, successfully applied to the NTI/Global Health and Security Initiative of the Nuclear Threat Initiative for $230,000 to carry out site assessments and purchase the recommended equipment and supplies. During this phase, Stanford organizers also initiated contacts with the U.S.-DPRK NGO community and established ongoing working relations with world health officials in Pyongyang, New Delhi, and Geneva to ensure that laboratory donations conformed to international standards and plans for the DPRK. In October 2008, Christian Friends of Korea (CFK), a U.S. NGO with more than 15 years of experience provisioning and renovating TB facilities in North and South Hwanghae provinces, was able to visit the proposed laboratory site during one of its regular in-country technical missions. CFK developed a physical infrastructure report, identifying an additional $300,000 in necessary infrastructure renovations, including plumbing and electrification, needed to support the proposed Stanford and NTI equipment donations.

On the basis of these assessments, in December 2008, Stanford and CFK approached the DPRK's mission to the United Nations in New York to propose a joint undertaking. Under this plan, CFK agreed to organize logistics and in-country visits, secure necessary U.S. export licenses, and complete physical renovations in cooperation with MoPH and local hospital staff. Stanford/BATC agreed to carry out training and technology assessments, complete procurement of the TB laboratory inventory in collaboration with its funding sponsor, and organize in-country expert training workshops. Thus, the project built upon a previously established foundation in U.S.-DPRK NGO relations and evolved to combine a strong mix of U.S.-based scientific, humanitarian, and health policy expertise in TB control.

On-site assessments (April 2009–September 2009). Following MoPH acceptance of this proposal, joint Stanford/CFK site assessment teams visited the laboratory site in May and August

Figure 3: **U.S.-DPRK Tuberculosis Project Implementation Schedule**



of 2009 (***Figure 4***) to develop work plans and procurement specifications in consultation with MoPH and WHO representatives. Technical expertise on the assessment teams included a construction engineer, a biomedical engineer, and a clinical laboratory consultant from CFK and, on behalf of the Stanford/BATC, a supervising scientist from a TB public health laboratory in California and a TB epidemiologist from Stanford School of Medicine. Three coordinators from the MoPH's Department of External Affairs were assigned to facilitate in-country delegations during the first on-site assessment visit, and they have remained invaluable partners of the project ever since.

Based on these site assessments, license applications for renovation materials and laboratory supplies were developed by Stanford, NTI/Global Health and Security Initiative, and CFK and were submitted by CFK to the Bureau of Industry and Security of the U.S. Department of Commerce in the early summer of 2009. Following the issuance of export licenses in July 2009, procurements were completed and overseas containers were packed and shipped during September 2009. Some materials were purchased in China and shipped overland in late October and early November 2009.

Delivery and installation (November 2009–October 2010). From 29 October to 24 November 2009, a 22-member revolving delegation, including CFK and Stanford/BATC work teams and a representative from the NTI/Global Health and Security Initiative, received approval from the DPRK government to spend nearly a month working at the laboratory site in Pyongyang. Scores of MoPH personnel (including lab staff, doctors, nursing students, and volunteers) worked side by side with skilled CFK volunteer construction teams to remodel rooms, install electrical and plumbing systems that included a new water tank, and build workbench spaces (***Figure 5***). A CFK bioengineer together with five Stanford/BATC laboratory trainers and 14 MoPH laboratory physicians installed and tested several pieces of equipment. Freezing temperatures and lack of central power at that stage of the project caused most of the work during this visit to be performed using backup diesel generator power donated by the project. Two additional visits in May and August of 2010 were required to complete the renovations and verify inventory.

Figure 4: **Site Planning Visit, May 2009**

During the summer of 2010, CFK raised $49,000 in additional funds and oversaw the installation of a four-kilometer dedicated high voltage cable connecting the laboratory to the municipal power supply.

Figure 5: **CFK and MoPH Work Crews Threading New Electrical Lines, November 2009**

Training and technical assistance programs (November 2009–present). The Stanford/BATC team includes public health laboratory specialists from the state of California's TB laboratory system, the director of the Stanford Hospitals Clinical Microbiology Laboratory, and infectious disease faculty from the Stanford School of Medicine. Individual members of this group have extensive experience in international health, including service on WHO working committees and on advisory panels of country-based infectious disease control programs. During initial site assessments, this team assisted MoPH in conducting training self-assessments and developing training curricula. Because culture and drug-resistance testing using conventional systems can require more than three months to yield results, the Stanford/BATC team also recommended training in more rapid detection systems recently approved by WHO for resource-limited settings.[62] Since November 2009, a total of nine BATC laboratory trainers have conducted two five-day training workshops in collaboration with MoPH physicians and laboratory technicians (***Figure 6***). These sessions have covered basic safety procedures, inventory maintenance, and culture and drug susceptibility testing using rapid as well as conventional testing systems. The team also works closely with CFK's biomedical engineer and a clinical laboratory professor from Andrews University. Additional workshops and training exchanges are planned for 2011.

Figure 6: **National Tuberculosis Reference Laboratory, Joint Bay Area TB Consortium-MoPH Training Workshop, October 2010**

Future of the Project

On 18 October 2010, the DPRK's first TB laboratory designed to perform reference-level quality assurance, culture, and drug-susceptibility testing was formally opened in a ceremony hosted by the vice minister of the Ministry of Public Health. In addition to representatives from Stanford/BATC and CFK, officials from the WHO Pyongyang office, UNICEF (the new Global Fund agent for the DPRK), and staff from the No. 3 (TB) hospital campus were in attendance. Located within the No. 3 (TB) Prevention Hospital, the new facility of more than 2,500 square feet features 13 rooms modeled and equipped to international laboratory standards and a dedicated power supply to run incubators and other essential equipment on a 24-hour basis. The laboratory has a staff of 14 administrators, physicians, and technicians. Along with the director general of the No. 3 (TB) Prevention Department, three of these physicians have been with the project since the meeting at Stanford in 2008.

Role of the laboratory in tuberculosis control. The new laboratory addresses a critical outstanding priority of the DPRK Country Strategic Plan with WHO, and it positions the MoPH to begin qualifying for new drugs to treat MDR TB. To prepare for its role in national TB control, the new reference laboratory must undergo international inspections and participate in field trials designed to assure the reliability and quality of laboratory results. Ultimately, the plan is to develop capacity to test several thousand cases of suspected MDR TB per year. The laboratory is also expected to develop capacity to provide surveillance for the national TB control program, determine prevalence of drug resistance in North Korea,[63] and guide treatment in patients suspected of having drug resistance.[64] By offering modern, reference-level diagnostic and clinical consultation services, the laboratory can also serve as a national resource or "center of TB excellence" for physicians, laboratorians, and medical and laboratory trainees throughout the country. This resource can also help integrate TB care provided by other ministries into the MoPH DOTS program.

We believe these goals are feasible over the next two to three years, particularly if MoPH is able to build academic collaborations with scientific teams such as the BATC and develop affiliations with international laboratory and medical organizations. The high literacy rate in the DPRK and the competencies observed by the BATC training team also suggest that MoPH possesses the human capital needed to realize these goals. The project is currently raising funds to develop reciprocal educational exchanges that will strengthen qualifications for international accreditation and create opportunities for collaborative research on MDR TB with academic institutions in the region as well as abroad.

Factors contributing to success. The momentum of this project has depended on several interrelated factors. First, the project addresses a public health priority (TB control) that is recognized at the highest levels of the DPRK government. The expertise assembled through the Bay Area TB Consortium and efforts to involve world health authorities in planning are important as MoPH moves toward qualifications for broader international support. Second, NTI/Global Health and Security's prior work building cooperation across disputed borders and recognition of the need for cooperative disease surveillance[65] led to critical funding support for laboratory donations. Having this funding secured at an early stage of planning helped greatly to spur the organizational partnerships needed to implement the project. Third, humanitarian aid to TB programs in the DPRK has a unique history. Of the U.S. NGOs operating in North Korea, CFK is one of only two sanctioned to have a direct relationship with the MoPH. The preexistence of this highly valued relationship, including CFK's reputation for trust building, follow-through, and sincere humanitarian focus, was a critical factor in gaining acceptance from government officials on both sides of the Pacific. Fourth, academic institutions must be prepared to anticipate significant infrastructure needs in the DPRK that are precedent to building productive program collaborations. Thus, partnering with CFK also brought important experience and capacity to address critical renovation and electrical power needs associated with TB programs in the DPRK. Finally, the continuity of personnel on both sides enabled an atmosphere of mutual trust, understanding, patience, creativity, and focused persistence to flourish.

Many challenges along the way—such as delivery delays, freezing temperatures, retrofitting problems that could not be resolved within the expected schedule, sickness on the work teams, and the need to improvise training conditions in the early stages—could have derailed the initiative. These were overcome cheerfully and in good faith and have contributed to strengthening ties between the U.S. and DPRK teams. At the same time, the next stage of this project—to develop specific educational exchange and research opportunities with Stanford/BATC and other TB laboratory programs—is critical to establishing the sustainability of our efforts and the potential for this unique U.S.-DPRK cooperation to have a meaningful impact on TB trends in the DPRK.

Implications

The modern history of TB epidemics, including emergence of HIV and MDR TB in the second half of the 20th century, has taught us that professional and economic isolation are dangerous co-conspirators. Control of TB in the antibiotic era requires coordinated international approaches to upgrade laboratory infrastructure, manage global drug supplies, and support research for new diagnostics, drugs, and vaccines. Academic collaborations with the DPRK focused on TB research and control offer important, ideologically neutral opportunities for assimilation within the international health and related scientific research community. Through the World STOP TB partnership, the American-Thoracic Society, the U.S. CDC, and the International Union against Tuberculosis and Lung Disease, the international TB professional community has developed an extensive global network of training, consultancy, and quality assessment resources. Providing opportunities for North Korean public health officials to link to this dynamic pedagogic community should be a priority.

The establishment of a reference-level national TB laboratory in the DPRK also begins to address an important "blind spot" in TB control for Northeast Asia. The laboratory can serve as a basis to foster new professional relations applied to regional disease surveillance, infrastructure development, innovative professional practices, and other technical assistance exchanges. Regional partnerships, such as the Middle East Consortium on Infectious Disease Surveillance and the Mekong Basin Disease Surveillance Network, show that such engagements are possible despite the lack of diplomatic relations among member countries.[66] Another region of the world that would benefit from cross-border planning for TB control encompasses the Eurasian arc from Afghanistan to Pakistan, India, and the southern republics of the former Soviet Union. For political reasons similar to those affecting Northeast Asia, countries in this cluster report to different WHO regional headquarters.

In contrast with the situation 25 years ago, the world is in a far better position today to recognize the risks of MDR TB epidemics where food and TB drug shortages persist. Although substantial resources are now available to respond to MDR TB hot spots, the TB epidemic in North Korea illustrates that these mechanisms still do not work well in non-treaty areas—where, nonetheless, they may be most needed. First, in regions isolated by conflict, epidemiologic trends are often difficult to track or the documentation simply does not exist. Second, high-level political agreements needed to engage in regional planning and to implement critical assistance programs may not be possible. Third, food, immunization, and energy shortages, typically not embraced as TB program assistance, are part of weakened public health systems and need to be integrated into international TB response systems. Finally, policy, humanitarian, and medical communities need to work creatively together to structure the opportunities that lead to constructive, sustained engagement in areas isolated by conflict. For these reasons, private initiatives such as ours remain vital to extend the frontiers of global TB control efforts.

Our project worked within an existing bureaucratic structure that is unique to the history of TB assistance for the DPRK. For these efforts to translate into broader engagement opportunities for U.S. academic institutions, additional education is needed. At the present time, the primary point of access for university engagement is through the Korean-American Private Exchange Society (KAPES), a self-described nonprofit North Korean entity established in 2005 and charged with managing U.S.-based humanitarian and academic relationships. This structure faces limitations in introducing the extraordinary range of intellectual resources that U.S. universities can bring to academic collaborations with North Korean scientists. Recent efforts like the U.S.-DPRK Scientific Exchange Consortium[67] are important not only to educate North Korea about the organization of higher education and research in the United States but also to promote a coordinated approach to academic engagement on the U.S. side.

Summary and Conclusions

Historically, health assistance has been relegated to the role of humanitarian effort and has occupied a subordinate role in foreign policy. With globalization and the emergence of shared threats such as HIV, MDR TB, avian influenza, and bioterrorism, health and security policy are increasingly connected.[68] As one of the last outposts of Cold War politics,[69] the 60-year-old Korean conflict challenges us to recognize this connection. While media coverage of North Korea remains dominated by conventional security concerns, U.S. citizens, including more than two million ethnic Koreans, are increasingly aware of the economic rigors faced by the North Korean people.[70]

As some observers are suggesting,[71] economic sanctions intended to induce the DPRK to abandon its nuclear weapons programs may be untenable from both security and humanitarian perspectives. In this view, by greatly discouraging foreign private sector participation, economic sanctions have had the unintended effect of exacerbating a public health crisis in the DPRK. Tuberculosis trends, a barometer that touches every aspect of human health, illustrate the deadly externalities of this approach. Our experience shows that constructive health engagements with the DPRK are possible despite diplomatic reversals at the state-to-state level. A review of sanctions policies with the aim of facilitating broader public health engagements, like the U.S.-DPRK Tuberculosis Project, is urgently needed for humanitarian reasons. In the longer term, expanded public health exchanges may also contribute to the reduction of tensions on the Korean Peninsula and a positive evolution of relations with the DPRK.

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