



Testimony
Before the Committee on Homeland
Security
United States House of Representatives

**Recent Case of Extensively Drug Resistant TB:
CDC's Public Health Response**

Statement of

Julie L. Gerberding, MD, MPH

Director, Centers for Disease Control and Prevention

U.S. Department of Health and Human Services



For Release on Delivery at 10:00 a.m.
June 6, 2007

Good morning, I am Dr. Julie Gerberding, Director of the Centers for Disease Control and Prevention within the Department of Health and Human Services (HHS). Chairman Thompson, Ranking Member King, and other distinguished Members of the Committee, it is my pleasure to be here to discuss with you HHS/CDC's ongoing investigation of a U.S. traveler recently diagnosed with extensively drug resistant tuberculosis.

Before I begin to describe the specifics of this investigation, I wanted to briefly provide some background information on tuberculosis (TB) and the drug-resistance of TB.

Definition:

Tuberculosis is an airborne infectious disease that is spread from person to person, usually through coughing, sneezing, speaking, or singing. In the late 19th and early 20th centuries, until the introduction of streptomycin in the 1940's, TB was one of the leading causes of death in the United States. Currently, the World Health Organization (WHO) reports that one in three people in the world are infected with dormant or latent TB. TB is a slow growing bacterium that often takes weeks to culture. Only when the bacteria become active do people become ill with TB. Bacteria become active as a result of anything that reduces the person's immunity, such as HIV, advancing age, or some medical conditions. TB bacteria can also become active in individuals that are not immunocompromised. Currently, TB that is not resistant to drugs can be treated with a six to nine month course of "first-line drugs" (the most effective), including isoniazid and rifampin; this treatment cures over 95 percent of patients. However, since people in many resource-poor countries lack access to appropriate treatment, nearly nine million people in the world develop TB disease each year and about 1.6 million die.

TB that is resistant to at least isoniazid and rifampin is called multidrug-resistant (MDR) TB. MDR TB requires treatment for 18-24 months with "second-line drugs" that are much less effective, often poorly tolerated by the patient, and far more costly. The cure rate is 70-80 percent under optimal conditions, but is usually closer to 50 percent. Many countries with a high TB burden find it impossible to treat MDR TB patients because of the cost of second-line drugs, and the more sophisticated laboratory services to diagnose resistance to drugs, and more intensive programmatic support required to administer the drugs. Extensively drug-resistant TB (XDR TB) is a subset of MDR TB caused by strains of bacteria that are resistant to the most effective first- and second-line drugs. Reported mortality rates among persons with XDR TB are extremely high. Among non-immunocompromised persons, reports indicate that less than 30 percent of patients can be cured, and more than half of those with XDR TB die within five years of diagnosis. Among immunocompromised persons, illness is more severe, and mortality rates are even higher and death occurs within a shorter time.

The risk of transmitting any type of TB can depend on several factors, including the extent of disease in the patient with TB, the duration of exposure, and ventilation. Both regular TB and drug-resistant TB bacilli become aerosolized when a person with TB disease of the lungs or throat coughs, sneezes, speaks, or sings. These bacilli can float in the air for several hours, depending on the environment. Persons who breathe air containing these TB bacilli are at risk for becoming infected.

Scope of the Problem:

In response to anecdotal reports from physicians who were finding cases of TB that were unresponsive to the first-line and second-line TB drugs, in 2005 HHS/CDC and WHO jointly conducted a survey, with support from the U.S. Agency for International Development, which examined about 18,000 patient specimens tested during 2000 to 2004 by Supranational Reference Laboratories. Researchers examined the drug-resistant isolates, and found that 10 percent of the MDR TB isolates actually met the definition for XDR TB. XDR TB was identified in 17 countries from all regions of the world, most frequently in the former Soviet Union and other Asian countries. However because many countries do not routinely test all isolates for resistance to second line drugs, the precise global incidence of XDR TB remains uncertain. Because of the ease with which drug resistance can occur (due to the use of second-line drugs in suboptimal conditions, changes in program focus away from TB case management, interruptions in drug availability because of supply management/resource availability/patient drug noncompliance, high HIV prevalence), XDR TB could be much more widespread than this survey shows. The ability of the disease to develop resistance to treatments and to travel easily across borders makes worldwide TB control efforts critical.

TB and the Threat to the United States:

Between 1993 and 2006 in the United States, there were 49 cases of XDR TB reported to HHS/CDC. By comparison, 13,767 TB cases (a rate of 4.6 cases per 100,000 persons) were reported in the United States in 2006 (the most recent year of aggregate annual reporting). The 2006 TB rate was the lowest recorded since national reporting began in 1953. While the total number of MDR and XDR TB cases is relatively small, their impact on U.S. TB control programs can be significant in terms of human capital and financial resources. One patient with MDR or XDR TB requires a minimum of 18-24 months of treatment. Recently collected data show that in-patient costs alone can average \$500,000 per case.

XDR TB continues to be widely distributed geographically abroad and is cause for public health concern in the United States, though the overall domestic risk of XDR TB currently appears to be relatively low. However, due to the ease with which TB can spread, and given its significant health consequences, XDR TB will continue to pose a serious risk to the U.S., as long as it exists anywhere.

TB Prevention and Control: Public Health Partnerships in Action

Generally, TB is a condition that is detected and treated by medical care practitioners. As with other infectious diseases, state, local, and territorial health departments serve important functions to support and augment the medical care system. These "front line" public health agencies are in direct contact with medical care providers and patients, providing important TB control services such as laboratory support, surveillance, contact tracing, and patient counseling. These agencies also generally possess legal authority to isolate or quarantine patients in those rare instances where traditional doctor-patient relationships or other means have failed to protect the community.

At the Federal level, HHS/CDC serves several critical roles in controlling TB. First, HHS/CDC provides leadership and scientific support for TB control efforts, both

nationally and internationally, including our global efforts to eliminate TB and stem the emergence of XDR TB as a health threat. Secondly, HHS/CDC provides approximately \$100 million annually in support to State, local, and territorial health departments for TB control efforts. Third, State and local public health departments routinely test samples of respiratory secretions from patients in order to diagnose tuberculosis and for some state laboratories, including Georgia, HHS/CDC routinely conducts second line drug susceptibility testing. HHS/CDC receives isolates from approximately 20 state laboratories each year as part of those laboratories' regular referral process. Each year HHS/CDC conducts drug susceptibility tests for approximately 1,000 samples. Fourth, HHS/CDC has the capacity to assist state or local authorities with its scientific resources. HHS/CDC may also use its federal legal authorities to prevent the introduction, transmission, and spread of communicable diseases from foreign countries into the United States or between U.S. states. As I will describe, HHS/CDC's involvement in the recent case spanned all of these roles.

The Current XDR TB Investigation: Locate, Isolate, Transport, Investigate

The following narrative is based on information assembled and reviewed in time for this testimony. The ongoing HHS/CDC investigation involves a U.S. citizen with potentially infectious XDR TB who traveled to and from Europe on commercial flights. In late March, the patient was diagnosed with TB by his doctor. Once diagnosed, Fulton County Health Officials became involved in managing the potential public health risk to others.

On May 10th, the Fulton County Health Department became aware that the patient's TB strain was resistant to the first-line of antibiotic treatments. This same day, the county health department met with the patient and his family to inform them of the diagnosis of MDR TB. Our understanding, from conversations with the county health officials, is that they orally advised the patient to forego his planned travel abroad. On the evening of May 10th, the Georgia Health Department emailed HHS/CDC's Atlanta Quarantine Station and reported that they were aware of an MDR TB patient (patient was not identified) that may intend to travel in three weeks. HHS/CDC exchanged emails with the Georgia Health Department with options to prevent travel including written notification under local authority. In the days following this meeting, Fulton County Health Officials attempted to serve the patient with written notice advising that the patient not travel, but the patient could not be located at either his residence or business.

It should be noted that normally when a patient has tuberculosis, he or she voluntarily complies with recommended treatment and recommendations to ensure that they don't put themselves in situations where they could potentially expose others to a serious health threat. Public health practitioners have a high success record using voluntary means of information and advice. In fact, the vast majority of TB patients comply with treatment recommendations, including remaining in isolation units in hospitals or in isolation at home until infectiousness has resolved without the need to invoke state or local legal authorities. It is extremely rare that Federal quarantine or isolation authority is required to manage domestic TB cases.

On May 18th after the patient left the United States, HHS/CDC's Division of Global Migration and Quarantine was notified that the patient traveled internationally against medical advice and his whereabouts were unknown. At this point, HHS/CDC's public health mission focused on locating the patient, isolating him, ensuring safe transportation and contact tracing. Between May 18th through the 22nd, HHS/CDC worked with Fulton County health department, Georgia State Department of Health, commercial airlines and the patient's family to locate him. In addition, on May 22nd, HHS/CDC laboratories determined that the patient had the rarer and deadlier subtype of XDR TB.

On May 22nd, HHS/CDC quarantine officials requested that the Customs and Border Protection (CBP) Atlanta office arrange to have the patient detained upon re-entry to the US. On both May 22nd and 23rd, HHS/CDC spoke with the patient in Rome, Italy and informed him of his XDR TB diagnosis; explained the severity of the disease; instructed him to terminate all travel and to cease use of commercial air carriers; and initiated conversations about the need for isolation, treatment, and travel alternatives. Despite assurances from the patient that he would not travel, it was discovered, on May 24th, that the patient had checked out of his hotel.

With the patient's exact location and intention to travel unknown, HHS/CDC contacted the Transportation Security Administration (TSA) on May 24th and requested them to exercise their authority to prevent the patient from boarding a commercial aircraft and thereby mitigating the risk of transmitting the disease on another long-distance commercial flight destined for the U.S. On May 25th, HHS/CDC learned from CBP that the patient had traveled via commercial airliner from the Czech Republic to Canada and subsequently reentered the U.S. the previous evening. HHS/CDC then notified the Public Health Agency of Canada and requested they initiate efforts to get the passenger manifest of the patient's inbound flight to North America. HHS/CDC called WHO in Geneva on May 24th and the HHS Secretary's Operations Center, the designated Focal Point for the United States under the revised International Health Regulations (2005), officially notified the WHO Secretariat of the case on May 25, even though the Regulations do not come into force for the United States until July 17, 2007.

On May 25th, after repeated prior attempts, HHS/CDC officials made contact with the patient on his cell phone and directed him to report immediately to the Bellevue Hospital in New York City where he would be served a quarantine order for isolation and be evaluated. He followed this direction, and at Bellevue was served a Federal order of provisional isolation and medical examination authorizing medical evaluation and respiratory isolation for 72 hours for extensively-drug resistant tuberculosis (XDR TB). The patient was later safely transported to Grady Hospital in Atlanta, Georgia via HHS/CDC aircraft and was issued a Federal order that mandated continued isolation on arrival in Atlanta, GA. As part of this process, the patient was advised that he could request an administrative hearing to review the order but he did not request such a hearing. On May 31st, he was safely transported by private airplane to National Jewish Medical Center in Denver, Colorado accompanied by his wife and a CDC quarantine officer. On June 2nd, HHS/CDC rescinded the Federal quarantine order for isolation

because Denver health officials assumed public health responsibility for this patient. The patient is currently under the quarantine authority of Denver County.

HHS/CDC is currently investigating the source of the patient's XDR TB. HHS/CDC is conducting an epidemiological investigation to look back at the patient's activities prior to his diagnosis in hopes of learning the source of the exposure. The patient has a history of travel to numerous locations outside of the United States. Sequences of DNA from the patient's TB strain do not match any currently on file in HHS/CDC's TB fingerprinting library. HHS/CDC is making efforts to compare it with TB fingerprinting libraries in other countries.

HHS/CDC Recommendations for Passengers:

Though the risk of transmission to the other passengers on the flights the patient took is low, it is not zero. In accordance with the WHO TB and Airline Travel Guidelines, and to ensure appropriate follow-up and care for persons who may have been exposed to XDR TB, HHS/CDC has recommended that passengers aboard the two transatlantic flights longer than 8 hours in duration who were seated in the same row as the patient, those seated in the two rows ahead and the two rows behind, and cabin crew members working in the same cabin should be evaluated for TB infection. This includes initial evaluation and testing with re-evaluation 8-10 weeks later. Because undiagnosed, latent TB exists in the general population, it is reasonable to expect that some of the passengers will test positive because of a previous exposure to TB, and not because of exposure on the flight in question. While we believe that passengers seated outside the immediate vicinity of the patient are at extremely low risk of contracting XDR TB, given the serious consequences and limited treatment options of XDR TB, we are notifying all U.S. residents and citizens on these flights and encouraging these individuals to seek TB testing and evaluation.

HHS/CDC is taking the lead in contact tracing of the U.S. citizens on these flights and is coordinating with other countries for the contact tracing of their citizens. As of June 5th, HHS/CDC has had direct contact with 245 of the approximately 276 US citizens and residents on Air France 385. Of the 26 high priority passengers, seated in the same row, two rows in front or two rows behind the patient, HHS/CDC has spoken directly with 24 of these individuals.

Isolation and Quarantine, An HHS-DHS Partnership:

To contain the spread of a contagious illness, public health authorities rely on many strategies. Two of these strategies are isolation and quarantine. Both aim to control exposure to infected or potentially infected persons, and both may be undertaken voluntarily or compelled by public health authorities. The two strategies differ in that isolation generally applies to persons who are known or suspected to have a communicable disease, and quarantine generally applies to those who have been exposed to a communicable disease but who may or may not become ill. Isolation is a standard procedure used in hospitals today for patients with tuberculosis (TB), and in most cases isolation is voluntary; however, many levels of government (Federal, state, and local) have basic authority to compel isolation of infected people to protect the public. State and local governments have primary responsibility for isolation and

quarantine within their borders and conduct these activities in accordance with their respective laws and policies.

The Department of Health and Human Services has authority under section 361 of the Public Health Service Act to prevent the introduction, transmission, and spread of communicable diseases from foreign countries into the United States and between states. HHS/CDC, through its Division of Global Migration and Quarantine, is authorized to detain, medically examine, or conditionally release persons suspected of carrying certain specified communicable diseases. The communicable diseases for which Federal isolation and quarantine are authorized are established by Presidential order and currently include infectious TB, cholera, diphtheria, plague, smallpox, yellow fever, viral hemorrhagic fevers, severe acute respiratory syndrome (SARS), and influenza with pandemic potential.

HHS/CDC relies primarily upon DHS for the enforcement of isolation and quarantine orders at the borders, but may also rely on other federal law enforcement agencies and state and local law enforcement. By statute, our DHS partners at the borders -- Customs and Border Protection (CBP) and Coast Guard officers -- aid in the enforcement of rules and regulations relating to quarantine and isolation. Violation of Federal regulations regarding quarantine and isolation constitute a criminal misdemeanor, punishable by fine and/or imprisonment. Federal public health authority includes the authority to release persons from quarantine or isolation on the condition that they comply with medical monitoring and surveillance.

HHS/CDC maintains a close partnership with DHS and its agencies. DHS and HHS signed a memorandum of understanding (MOU) in 2005 that establishes specific cooperation mechanisms as part of a broad framework for cooperation to enhance the Nation's preparedness against the introduction, transmission, and spread of quarantinable and serious communicable diseases from foreign countries into the States, territories, and possessions of the United States. DHS has charged the Homeland Security Institute with facilitating the implementation of the MOU and HHS/CDC's Division of Global Migration and Quarantine is collaborating in this effort. Concurrently, HHS/CDC has conducted table top exercises at ports of entry in cooperation with DHS' component agencies and state and local partners to develop and refine communicable disease response plans.

The partnership between CBP and HHS/CDC is particularly vital, as CBP officers act as HHS/CDC's "eyes and ears" on the ground. In addition to assisting with the enforcement of Federal quarantine and isolation, HHS/CDC helps to train CBP officers to identify and respond to travelers, animals, and cargo that may pose an infectious disease threat. CBP also assists quarantine officials with the distribution of health risk communication materials for the traveling public, such as notices that alert travelers of possible exposure to communicable disease threats abroad and offer guidance on steps they can take to protect themselves.

Next Steps, What More Can Be Done:
With the support of Congress and the President, and in accordance with the

recommendations of the Institute of Medicine (IOM), HHS/CDC is investing in building a Quarantine and Migration Health System that meets the needs of the 21st Century. HHS/CDC is enhancing the numbers and competencies of staff, training, physical space, and utilization of technology to meet the Quarantine System's evolving, expanding role. This has included the creation of additional quarantine stations at airports and other major ports of entry into the United States. HHS/CDC has expanded this critical public health infrastructure to 20 stations and is focusing on fully staffing these stations.

By continuing to expand the capacity of the U.S. Quarantine and Migration Health System through science, partnership, and preparedness, HHS/CDC will be better equipped to play an active role in worldwide biosurveillance, to coordinate nationwide response to global microbial threats of public health significance and to protect the U.S. public from communicable disease threats. The President has requested an additional \$10 million dollars in FY 2008 to support the further enhancement and expansion of the Quarantine and Migration Health System.

In addition, HHS/CDC has been working to update interstate and foreign quarantine regulations [42 CFR Parts 70 & 71] to codify procedures that more completely reflect the 21st century implementation of disease containment measures such as isolation and quarantine, and that strengthen the nation's public health security at ports of entry. On November 30, 2005, HHS/CDC published a notice of proposed rulemaking (NPRM) to update the interstate and foreign quarantine regulations [42 CFR Parts 70 & 71]. Once adopted, these changes will represent the first significant changes to these regulations in 25 years.

Key provisions proposed include: more explicit due process protections for written orders and an administrative review hearing; expanded reporting of ill passengers on board air carriers; and requirements that will facilitate the timely transmittal of passenger and crew contact information to HHS/CDC to ensure quick notification of exposure to communicable disease threats. These procedures are expected to expedite and improve HHS/CDC operations by allowing immediate medical follow-up of potentially infected passengers and their contacts. HHS/CDC received over 500 pages of comments from approximately 50 organizations and individuals regarding the proposed rule. HHS/CDC is currently addressing issues raised during the public comment periods, including working with DHS to most efficiently share contact information, and developing a draft final rule.

To control TB, HHS/CDC and its partners must continue to apply fundamental principles including: (1) State and local TB programs must be adequately prepared to identify and treat TB patients so that further drug resistant cases can be prevented; (2) TB training and consultation must be widely available so that private health care providers recognize and promptly report tuberculosis to the public health system; (3) State and local public health laboratories must be able to efficiently perform and interpret drug susceptibility and genotyping results in TB specimens; and (4) CDC and local health authorities must work collaboratively to ensure that isolation and quarantine authorities are properly and timely exercised in appropriate cases.

The prospects for development of new TB drugs also are promising and those efforts must continue. There are at least 4 new anti-TB compounds entering human trials while others are in advanced preclinical testing. These new compounds represent new drug classes that may offer promise for treating resistant cases.

Conclusion:

We have begun a careful review of our protocols and capabilities. First and foremost, we are reminded that infectious diseases are not a thing of the past, and that we need to continually adapt our prevention and response capabilities in an era of increasing threat and globalization. We are reminded that almost all infectious disease cases are effectively handled within our existing systems of care by patients, clinicians and local public health authorities, and that it is important to continue to reinforce and augment these existing roles and relationships. Our public health protection network assisted us in responding to this event in a more timely and coordinated manner. Public health officials continue a long tradition of working together on every level to identify, contain and mitigate the spread of communicable diseases in US communities and abroad.

The case also reminds us that there are a number of existing channels that we can leverage more effectively in the future. Through the Global Health Security Action Group -- a group of senior policy officials, top scientists, and media experts from the ministries of health of G-7 nations, Mexico, the World Health Organization and the European Commission -- we can quickly convene relevant public health officials via phone and video conferences to convey information on cases like this to our key allies in a more timely and effective way.

In an age of global air travel, infectious diseases can, and do, cross geographic borders every day. People can be infected with a disease and have few visible indications, people can vary in terms of how infectious they are, it is often not possible to rapidly test and confirm whether a person has an infectious disease, and people's health status can change quickly and unpredictably. We will never be in a position where we can guarantee that infectious people will not cross borders, but we will work to ensure that the measures available are as effective as possible. And so too this case reinforces the need to advance our efforts to modernize our Quarantine and Migration Health System and update Federal quarantine regulations; improve our information technology and communications capabilities; and define and exercise our capabilities and relationships with international, Federal, state, and local partners so that we are prepared to deal with situations that pose a threat to public health. We believe the lessons learned from this case will improve HHS/CDC's ability to protect the nation's health in our ever-changing global environment.