**October 30, 2007**
**Senate Health, Education, Labor and Pensions Committee Hearing**
**Protecting the U.S. from Drug Resistant Tuberculosis: Reinvesting in Control and New Tools Research**

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**On behalf of the National Tuberculosis Controller's Association, Stop TB USA & the American Thoracic Society**

**Introduction**

My name is Randall Reves, MD and I am Director of the Denver Metro Tuberculosis Control Program and Associate Professor at the University of Colorado Health Sciences Center Department of Preventative Medicine and Biometrics. I am representing the National Tuberculosis Controller's Association (NTCA), the national association representing state tuberculosis control programs, the Stop TB USA Coalition (formerly the National Coalition for the Elimination of Tuberculosis), the U.S. partner of the global Stop TB Partnership, and the American Thoracic Society (ATS), a medical professional society that was founded over 100 hundred years ago to foster the prevention, detection, treatment and cure of tuberculosis. The NTCA/Stop TB USA/ATS would like to thank Chairman Kennedy, Sen. Brown and Ranking Member Enzi for holding this important hearing and for their leadership on global and domestic tuberculosis control. Tuberculosis is an important global and domestic public health threat that deserves the attention of Congress. I hope the hearing today will encourage the Senate to act favorably on legislation that will provide increased authority, resources and coordination for TB control efforts among key federal agencies.

There are three points I want to make. First, tuberculosis is a problem in the United States. Second, we have tools today to combat the spread of TB. Third, we will never defeat TB until we develop a new generation of diagnostic tools, a new generation of TB drugs and an effective vaccine.

**The Scope of the TB Problem**

What is tuberculosis? Tuberculosis is an airborne infection caused by a bacterium, *Mycobacterium tuberculosis*. It primarily affects the lungs but can also affect other parts of the body, such as the brain, kidneys or spine. Tuberculosis is spread through coughs, sneezes, speech and close proximity to someone with active tuberculosis. People with active tuberculosis are most likely to spread it to other people they spend a lot of time with, such as family members or coworkers. It cannot be spread by touch or sharing utensils used by an infected person. The statistics for TB are alarming. TB is the second leading infectious disease killer in the world, taking at least 1.6 million lives per year.[i]

Until the Andrew Speaker case emerged earlier this year, many Americans thought TB was a disease of the past. The number of persons with newly diagnosed TB in the U.S. appears to be leveling off at just under 14,000 new cases and over 600 deaths each year. Although the number of TB cases in the U.S. continues to fall, the slowing of the decline rate, from 6.6 percent per year in the period 1993-2002 to 3.1 percent per year in the period 2003-2006, is of concern because of the history of TB in the U.S.[ii] In the 1970s and early 1980s, the nation let is guard down and began significantly reducing the TB control infrastructure. Consequently, the trend towards elimination was reversed and the nation experienced an unprecedented resurgence of TB with a 20% increase in cases reported between 1985 and 1992.

That's the medical explanation and statistical background on TB in the U.S. But what do we mean when we say TB is a domestic problem? It means that people in the U.S. are getting TB, including the drug resistant strains featured in the Andrew Speaker case

earlier this year. It means even in the U.S., where the TB incidence is much lower than the developing world, we are still vulnerable to outbreaks of multi-drug resistant (MDR) TB. As the Andrew Speaker story made clear, it only takes one infectious individual in close proximity to other people - in this case an intercontinental flight - to cause a public health alarm.

While the Andrew Speaker story is alarming, the truly alarming news is that TB is mutating. Poor control of TB has lead to the development of drug resistant strains of TB. There are even strains of extremely drug resistant TB that are resistant to 4 or more of the drugs commonly used to treat TB. Without immediate attention to this problem, we may soon see strains of TB that are infectious, lethal and essentially impossible to cure.

While the Andrew Speaker case got media attention, Mr. Speaker is far from the typical case of TB found in the U.S. Let me share with you a more typical example of a TB case found in the U.S. A couple of years ago, I treated a young man with tuberculosis from Egypt. The man mostly likely became infected with TB while living in a refugee camp. Despite completing and passing the mandatory TB screening program prior to enter the U.S., he was hospitalized for pulmonary symptoms shortly after arriving in the U.S. Based on his symptoms and case history, he was presumed to have TB and was put on antibiotic treatment. He responded well to treatment. A few weeks after treatment was initiated and he was discharged from the hospital, test results came back indicating the man had drug resistant TB with resistance to isoniazid, rifampin and streptomycin – the three first line drugs used to treat TB. He survived because initial treatment was included drugs with MDR-TB activity.

The patient remained free of TB after completing 2 years of daily treatment with health care workers delivering and observing ingestion of each dose. Public health workers also did standard contact follow up and identified other members of his family that had MDR-TB. They also were located and treated successfully. This man is now a productive member of our society holding a job and supporting a family.

This case illustrates many of the strengths and weaknesses of the current tools used to detect, treat and cure TB. And let me tell you the Denver is one of the best run TB programs in the U.S. We are experts in both the medical and public health aspects of TB. Any potential flaws in how a case is handled in Denver are going to be magnified in programs with less expertise.

Refugee camps are well recognized as being hot beds for developing drug resistant strains of TB. However, applying standard public health practices for TB in refugee camps could significantly reduce this problem. Identifying cases under a microscope, screening for HIV and providing the standard course of anti-TB drugs can be done cheaply and with a minimum financial investment. Instead, the lack of TB control measures in Egypt meant that my patient and several of his family members developed MDR-TB, significantly increasing the cost of treating the disease and posing significantly higher health risks for everyone they came in contact with.

How this man passed the initial screening test prior to entering the U.S., I don't know, but I would suspect the reason, in part, is due to the lack of fast, cheap tests capable of effectively screening for TB.

While my patient from Egypt responded well to the initial treatment, it was weeks after he was discharged from the hospital that we found out he had MDR-TB. While we were able keep track of Mr. X and alter his treatment according, and provide follow up for two years to ensure he completed his treatment. What if during that two week time frame, he got "lost" and could not be followed up with? Then a super-germ would be circulating throughout the community potentially infecting others. Diagnostic tests that can detect TB in hours or days – not weeks – are needed to accurate detect TB and its level of drug susceptibility.

What if, due to cuts in public health funding, we did not have the staff to follow up with my patient's contacts? Then we would have failed to identify his family members who also had MDR-TB, again putting the community at risk.

**The Need for Better Diagnostics and Drugs**

Why did it take two years to successfully treat his TB? While we should be pleased that the Denver public health system was able visit him daily for two years to ensure he completed his antibiotic treatment, think of the staff time and organizational effort involved in a two year treatment plan. Drugs with shorter treatment times and novel antibiotics to treat TB are desperately needed.

When the first highly successful treatment for TB with INH-streptomycin-PAS was introduced in the 1950s, we failed to ensure that all patients completed the 2-year course of treatment, allowing the bacteria to become resistant. Most experts at the time believed that drug-resistance was harmless since many patients improved clinically despite persistence of positive sputum cultures. The "mutant" bacteria were believed incapable of being transmitted to others. That theory held for 20 years until 1977 when I, as a new CDC trainee stationed in Mississippi, pursued the investigation of a high school outbreak of INH-streptomycin-PAS resistant TB in Alcorn County. These bacteria had spread to 150 students and faculty resulting in five active TB cases. The source was a smoldering community outbreak with a total of 22 active TB cases that began when the public health system failed to ensure treatment for patients diagnosed up to 12 years earlier.

We moved on to the next wonder drug and cured most of the drug-resistant TB cases in Alcorn County using the new wonder drug, rifampin, in combination with ethambutol. At least two patients lapsed from treatment and the bacilli added rifampin resistance to their existing repertoire of drug resistance genes, killing one previously healthy young woman. This shot across the bow by an organism, later named MDR-TB, was largely ignored for the next two decades as we allowed local, state and national tuberculosis control capacity to deteriorate to the point that successful completion of the new 6-month TB treatment in many areas became the exception, rather than the rule.

The end result was extensive, deadly outbreaks of TB in New York City, Miami and other cities in the 1980s and 1990s and MDR strains resistant to more than 6 drugs were found to be readily transmitted. Patients with HIV/AIDS in New York City died within weeks, usually before the drug resistance was detected. We had no new TB drugs to use but learned by experience, not by research, that new fluoroquinolone antibiotics could be used successfully in combination treatment lasting 18-24 months. For patients with MDR-TB this meant going back to treatments we abandoned two decades ago, including lung surgery. We learned to stop complaining about patients who were not compliant, and became committed to ensuring curative treatment. Many programs adopted the approach touted decades earlier by John Sbabaro in Denver, insisting that a health care provider Directly Observe the ingestion of each dose of Treatment (DOT).

There is no scientific reason that we should not have a TB diagnosis confirmed or excluded within days. This can be done in selected places in the US now, but nearly half of all persons with culture-positive TB across the globe cannot get a diagnosis because of reliance on the sputum AFB smear, a 100 year-old test. Most patients with MDR-TB and XDR-TB will die after treatment failure without a culture and/or drug susceptibility test ever being done. There are promising diagnostic tools that will need evaluation in field studies before successful implementation.

In 1993, AIDS was a chronic progressive infectious disease for which treatment only delayed the inevitable progress to death. Because of our national investment in clinical research, HIV infection can now be diagnosed within weeks of onset, and AIDS can now be successfully treated with one triple-drug pill taken daily. These new tools for HIV are also being implemented, with governmental funding, around the globe. We have largely ignored TB research and needs, and millions are now paying for it.

**Domestic TB Control Challenges**

The fiscal year (FY) 2007 funding level of $137.4 million for the Centers for Disease Control and Prevention's Division of Tuberculosis Elimination actually represents a 27% decrease over the past decade when adjusted for inflation. To effectively address TB in the U.S. and appropriately develop both domestic and global preparedness and outbreak response capacity for drug resistant TB, additional resources are urgently required.

In order to prevent the spread of drug resistant TB in the U.S. and to put the nation back on the path to eliminating the disease in the U.S., domestic TB control capacity, and treatment, and prevention systems must be strengthened to ensure diagnosis, and treatment. The following are some additional specific steps that must be taken:

- Improve strategies to identify and treat latent TB infection and reach at-risk populations.
- Intensify TB control activities among persons who regularly cross the U.S.-Mexico border.
- Intensify efforts to prevent, detect, and treat TB among foreign-born persons in the United States.
- Expand U.S. provide leadership and intensify technical assistance activities to address the global TB crisis.

**Conclusion**

The slowing of the decline in the overall national TB rate and the inability to effectively address persistent disparities in TB rates between U.S.-born and foreign-born persons and between minority populations threatens progress toward the goal of eliminating TB in the United States.

The good news is that today, appropriately applying our existing tools can prevent the further development of drug resistant strains of TB. We have successful – but labor intensive - public health strategies to prevent the spread of TB. We even know how to make TB control programs work in the most resource-poor nations in the world. What is needed is the authority and resources to get the job done.

The American Thoracic Society is pleased to support the legislation - the Comprehensive TB Elimination Act - sponsored by Senator Sherrod Brown of Ohio, Senator Kay Bailey Hutchison of Texas, and Senator Edward Kennedy of Massachusetts. This legislation responds to both the real and immediate public health threat that TB poses today as well as looking to the future to ensure that the Centers for Disease Control and state and local public health departments and all health care providers are ready for the future.

It responds to today's needs by expanding the resources and authority of the CDC to more effectively apply today's diagnostic and treatment tools to identify and effectively treat TB in the U.S. The legislation also gives CDC expanded authority to conduct research to develop more effective diagnostic and treatment tools particularly a new generation of anti-TB drugs - to ensure that our public health system is prepared to effectively respond to a mutating TB germ.

I thank the committee for this opportunity to testify on this important subject.

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[i] Tuberculosis, World Health Organization (WHO) Factsheet No. 104, March 2006.

[ii] CDC. *Reported Tuberculosis in the United States, 2006*. Atlanta, GA: U.S. Department of Health and Human Services, CDC, September 2007.