Has the Time Come to Require Nontuberculous Mycobacteria Reporting?

In 1893, The New York City Board of Health approved a recommendation from Hermann Biggs, New York City’s eminent public health officer, “that all physicians practicing their profession in this city be requested to notify this Board of all cases of pulmonary tuberculosis coming under their care.” [1] What about the reporting of nontuberculous mycobacteria (NTM)?

NTM are ubiquitous environmental microorganisms that can be recovered from soil, fresh water (natural and treated). In the past, there was no evidence of human-to-human or animal-to-human transmission of NTM. However, recent findings investigating outbreaks in patients with cystic fibrosis using thorough conventional epidemiologic and state-of-the-art molecular typing investigations such as whole-genome sequencing have challenged the dogma of non-person-to-person transmission, indicating potential transmission of *Mycobacterium abscessus* subspecies *massiliense* between these patients [2]. Because NTM may be found in both natural and manmade reservoirs, human infections are suspected of being acquired from these environmental sources [3].

The National Notifiable Diseases Surveillance System is complex [4]. It involves reporting of state and locally mandated conditions by health care providers and clinical laboratories to state and local health departments. Health departments, in turn, process this information and use it to track health conditions; control disease through case management, for partner notification, and response to outbreaks; generate reports; and notify the Centers for Disease Control and Prevention of conditions that are designated “notifiable” by the Council of State and Territorial Epidemiologists. While tuberculosis is a national notifiable condition/disease, NTM are not part of this system.

The State Reportable Conditions Assessment is an annual, web-based assessment of reportable conditions [4]. Ongoing since 2007, this joint effort by the Council of State and Territorial Epidemiologists and Centers for Disease Control and Prevention collects publicly available information on what conditions are reportable in states, territories, and other large jurisdictions, and who is required to report them. The State Reportable Conditions Assessment is intended to be a publicly available, national repository of jurisdiction-specific information that can be used by public health officers, researchers, and health care providers. The Council of State and Territorial Epidemiologists is charged with providing a comprehensive and accurate list of reportable conditions by state and territory. With your participation, the Council will achieve a 100% response rate.

The State Reportable Conditions Assessment covers reporting requirements, as defined by regulation or legislation, for conditions defined as reportable by clinicians (i.e., health care providers), laboratories, hospitals, and other reporters in your jurisdiction. State Reportable Conditions Assessment responses should reflect these reporting regulations or rules as closely and accurately as possible. Any conditions that must be reported to the state public health agency should be considered reportable in the State Reportable Conditions Assessment. If a condition is reportable to another department within your state (e.g., Department of Agriculture) but the state health agency receives this information as the result of a data-sharing agreement, then the condition should also be considered reportable. Conditions that are not named on your jurisdiction’s lists but fall under general, catch-all reporting language, such as “all outbreaks,” “disease of public
health importance,” etc., are considered implicitly reportable in the State Reportable Conditions Assessment and should be included in your responses. The State Reportable Conditions Assessment is divided by section based on condition types; one of the 14 sections is *Respiratory Conditions (Infectious)*. The results of the 2016 assessment are still pending.

In our view, there are five good reasons to put a health condition under public health surveillance:

1. Each reported case prompts an immediate public health response (as with measles, syphilis, meningococcal disease, or tuberculosis).
2. Case reporting is done to enable detection of clusters or outbreaks (this might apply to histoplasmosis or hepatitis B or certain cancers or birth defects).
3. Surveillance data are needed to plan public health interventions.
4. Surveillance data are needed to evaluate public health interventions.
5. Real-time surveillance data can help clinicians make better decisions about care of individual sick people.

NTM clearly qualify for surveillance for public health interventions due to their environmental source (especially water).

Recently, websites from every state in the United States, the District of Columbia and New York City were searched for information about notifiable disease reporting requirements for health care providers and laboratories. Preliminary results were presented as a poster at the 2015 American Society for Microbiology Conference [6]. The following eleven states have reporting requirements for nontuberculous mycobacteria:
<table>
<thead>
<tr>
<th>State</th>
<th>Reporting Time for NTM</th>
<th>What is Required to be Reported (websites accessed on 12-11-2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maryland</td>
<td>within one working day</td>
<td>Mycobacterium spp., other than Mycobacterium tuberculosis complex or Mycobacterium leprae</td>
</tr>
<tr>
<td>Mississippi</td>
<td>one week</td>
<td>Nontuberculous mycobacterial disease</td>
</tr>
<tr>
<td>Missouri</td>
<td>within 3 days</td>
<td>Nontuberculosis mycobacteria (NTM)</td>
</tr>
<tr>
<td>Nebraska</td>
<td>within 7 days</td>
<td>Mycobacteria spp. (including M. tuberculosis complex organisms [for genotyping] and all “atypical” species, to include culture, nucleic acid tests, or positive histological evidence indicative of tuberculosis infection or disease)</td>
</tr>
<tr>
<td>Nevada</td>
<td>not specified</td>
<td>Submission of isolates of Mycobacterium spp.</td>
</tr>
<tr>
<td>New Jersey</td>
<td>within 72 hours</td>
<td>Mycobacterium, atypical</td>
</tr>
<tr>
<td>New Mexico</td>
<td>within 24 hours</td>
<td>Tuberculosis or other nontuberculous mycobacterial infections (including Mycobacterium avium complex or leprosy)</td>
</tr>
<tr>
<td>Ohio</td>
<td>close of the next business day</td>
<td>Mycobacterial disease other than tuberculosis (MOTT)</td>
</tr>
<tr>
<td>Oregon</td>
<td>one working day</td>
<td>Nontuberculous mycobacterial infection (nonrespiratory)</td>
</tr>
<tr>
<td>Virginia</td>
<td>immediate</td>
<td>Results of cultures positive for any member of the Mycobacterium tuberculosis complex (i.e., M. tuberculosis, M. bovis, M. africanum) or any other mycobacteria. Results of rapid methodologies, including acid hybridization or nucleic acid amplification, which are indicative of M. tuberculosis complex or any other mycobacteria.</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>within 72 hours</td>
<td>Mycobacterial disease (nontuberculous)</td>
</tr>
</tbody>
</table>

Strollo et al. [7] reported that the state-specific case numbers and costs are critical for quantifying the burden of pulmonary NTM disease in the U.S. Available direct cost estimates of NTM disease medical encounters were applied to NTM disease prevalence estimates derived from Medicare beneficiary data (2003 to 2007). Persons younger than 65 years of age were included as well. In 2010, the authors estimated 86,244 national cases totaling $815 million in costs. Medical encounters among individuals aged 65 years and older ($562 million) were more than two-fold higher than those of persons younger than 65 years of age ($253 million). Projected 2014 estimates resulted in 181,037 national annual cases totaling $1.7 billion.

Research needs for NTM are enormous [8]. First, it will be necessary to develop a robust knowledge of dose-response for NTM disease caused by the major infecting species: M. avium, M. intracellulare, M. chimaera, and M. abscessus. Once that is known, surveillance can identify sources that are of higher and lower risk. Second, as antibiotic therapy for NTM disease requires combinations of antibiotics that carry with it debilitating side effects, efforts must be taken to rigorously test the efficacy of any measures for exposure reduction. Finally, protocols for reduction in numbers of NTM in premise plumbing and instruments will require identification of anti-mycobacterial disinfectants and methods to kill NTM cells in biofilms. NTM in biofilms are more resistant than those in water suspension and can serve to repopulate premise plumbing and instruments after disinfection. Finally, efforts must continue to discover and develop novel anti-NTM antibiotics. These antibiotics may not be hand-me-downs from anti-M. tuberculosis drugs as they are at present. The [njhealth.org/MycobacterialConsultation](njhealth.org/MycobacterialConsultation)
Co-editors: Charles Daley, MD and Max Salfinger, MD, FIDSA, FAAM
NTM are free-living bacteria, not obligate parasites of higher organisms, and thus present a more complex metabolism and structure than that of *M. tuberculosis*.

With the growing number of patients suffering from NTM pulmonary disease, e.g., annual increase of 8% among Medicare beneficiaries [9], and the potential of person-to-person transmission among cystic fibrosis patients [8], it is imperative to include pulmonary NTM disease in the National Notifiable Diseases Surveillance System to elucidate a more accurate account of the disease burden.

References:


Max Salfinger, MD, Mycobacteriology and Pharmacokinetics Laboratory, National Jewish Health; Joseph O. Falkinham, III, PhD, Virginia Tech – College of Science; Richard S. Hopkins, MD, MSPH, former Florida State Epidemiologist & Adjunct Professor of Epidemiology, Colleges of Medicine and of Public Health and Health Professions at the University of Florida; Philip B. Leitman, President of NTM Info & Research (NTMir)

**Centers for Disease Control and Prevention (CDC). Reported Tuberculosis in the United States, 2015. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. Executive Commentary (Reprint):**

**Introduction**

For the first time since 1992, the number of U.S. TB cases reported to the National Tuberculosis (TB) Surveillance System (NTSS) increased over the previous year. In 2015, the 50 United States and the District of Columbia reported 9,557 TB cases to CDC, representing a 1.6% increase from 2014 (Table 1). Twenty-seven states and the District of Columbia
reported increased case counts from 2014 (Table 30), and four states (California, Texas, New York, and Florida) accounted for 50.6% of the national case total (Table 31). Despite this slight increase in case count, the TB incidence rate per 100,000 persons has remained relatively stable at approximately 3.0 since 2013 (Table 1). Seven states and the District of Columbia reported incidence rates above the national average (Table 30). The National Center for Health Statistics reported 493 deaths in 2014 (the most recent year for which mortality data are available) that were attributable to TB, an 11.2% decrease from 2013 (Table 1).

**NTSS Description**

Since 1953, in cooperation with state and local health departments, the United States national tuberculosis program has collected information on each newly reported case of tuberculosis (TB) disease in the United States. In 1985, CDC began collecting individual TB case reports using the Report of Verified Case of Tuberculosis (RVCT). The RVCT was expanded in 1993 in response to the TB epidemic of the late 1980s and early 1990s, and reporting areas began submitting the RVCT electronically via the TB Information Management System (TIMS). CDC has maintained a dynamic TB surveillance case registry since 1993. In 2009, CDC expanded the RVCT again and reporting areas transitioned from TIMS to data collection via the Public Health Information Network/National Electronic Disease Surveillance System.

In addition to the 50 United States and the District of Columbia, CDC accepts TB case reports from four U.S. insular areas (American Samoa, Guam, Puerto Rico, and the U.S. Virgin Islands) and four sovereign nations that have signed compacts of free association with the United States (Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Republic of the Marshall Islands, and Republic of Palau). In this report, these sovereign nations are referred to as “freely associated states.”

Each annual TB surveillance report includes updated case counts for each year in the dynamic surveillance database, starting in 1993 through the newly available data. Reporting areas update past years’ data as needed and accordingly data for past years might not match data published in previous annual reports. This annual summary contains information through 2015.

**Demographics**

Overall since 1993, TB incidence rates have declined in almost all racial and ethnic groups: among American Indian/Alaska Natives, from 14.4 to 6.1 cases/100,000 persons (–57.6%); among Asians, from 42.2 to 18.2 cases/100,000 (–56.9%); among non-Hispanic blacks/African Americans, from 29.1 to 5.0 cases/100,000 (–82.8%); among non-Hispanic whites, from 3.6 to 0.6 cases/100,000 (–83.3%); and among Hispanics/Latinos, the decline has been from 20.4 to 4.8 cases/100,000 (–76.5%). However, since 2013, TB incidence rates have increased among American Indian/Alaska Natives (+12.3%), Native Hawaiian/Other Pacific Islanders (+59.7%), and persons reporting multiple races (+4.8%), although these increases should be interpreted with caution because of the small sizes of the underlying populations. Since 2013, TB incidence rates have continued to gradually decline among non-Hispanic blacks/African Americans (–6.4%), non-Hispanic whites (–12.1%), and Hispanics/Latinos (–4.0%). While the TB incidence rate for Asians also declined from 2013 to 2015 (–1.0%), in 2015 the overall TB incidence rate for Asians remained over three times higher than that for Hispanics/Latinos or blacks/African Americans (Table 2).

Although the incidence rates for both the foreign-born and the U.S.-born populations have declined substantially since 1993, the decline has been less among the foreign-born (–55.6%) than among the U.S.-born (–83.8%) (Table 5). Foreign-born persons are defined as anyone born outside of the United States or U.S. insular areas and freely associated states (with the exception of those born abroad to U.S. parents). This includes naturalized U.S. citizens, permanent residents, visitors, persons with student or work visas, refugees, and persons with undocumented or unknown immigration status. The burden of TB was markedly different between foreign-born and U.S.-born populations at 15.1 and 1.2 cases/100,000 persons, respectively, which is roughly a 13-fold difference (Table 5). The majority of these cases progressed from latent TB infection acquired years in the past.
Foreign-born persons continued to represent the majority of U.S. TB cases (66.4%), roughly the same proportion as in 2014 (Table 5), and in 36 states and the District of Columbia, ≥50% of TB cases occurred among foreign-born persons (Table 34). Asians represented nearly half (47.8%) of the reported foreign-born TB cases in 2015 (Table 19). Hispanics comprised the second largest group of foreign-born TB cases (32.0%, Table 19). In comparison, among U.S.-born persons, blacks/African Americans represented the largest percentage (35.9%) of TB cases, followed by whites at 31.1% (Table 18).

Collecting information on country of birth can help direct TB prevention efforts, both primary prevention efforts around the world, as well as secondary prevention efforts in the United States to screen and treat individuals for latent TB infection. From 2011 through 2015, the top five countries of origin of foreign-born persons with TB were Mexico, the Philippines, India, Vietnam, and China (Table 6). The distribution of TB cases among foreign-born persons by world region of origin is influenced by the size of the total population from those regions living in the United States, as well as the prevalence of TB in those regions.

Of the 6,350 TB cases reported among foreign-born persons in 2015, the majority of cases occurred among persons born in the Americas region (35.7%), and those born in the Western Pacific region (32.6%), which is similar to the distribution of cases by world region of origin in 2014 (Table 20). From 1993 through 2015, the percentage of cases increased among persons born in the Eastern Mediterranean region (2.8% in 1993 to 4.6% in 2015), the Southeast Asia region (5.6% in 1993 to 15.7% in 2015), and the Africa region (2.4% in 1993 to 8.7% in 2015) (Table 20).

In 2015, TB incidence rates continued to decline for persons <5 years old and 15–24 years old; however, the incidence rate for persons 45–64 years old increased slightly from 3.5 to 3.6 cases/100,000 persons. Incidence rates for all other age groups remained similar to 2014. The highest burden of disease continues to be among older adults. In 2015, adults ≥65 years old had an incidence rate of 4.8 cases/100,000, while children 5–14 years old had the lowest rate at 0.5 cases/100,000 (Table 4).

**HIV Coinfection**
The proportion of TB cases with a reported HIV test result who were co-infected with HIV has decreased from 48.2% in 1993 to 5.5% in 2015. In the past 3 years, this proportion has declined from 6.4% in 2013 to 5.5% in 2015 (Table 11).

**TB Treatment Regimens and Drug Resistance**
The proportion of TB patients prescribed the recommended initial treatment regimen including isoniazid, rifampin, pyrazinamide, and ethambutol increased from 40.3% in 1993 to 84.7% in 2015. The proportion of patients who completed therapy within 1 year increased from 63.4% in 1993 to 89.6% in 2013 (the latest year for which complete outcome data are available). The proportion of persons receiving directly observed therapy for at least a portion of the treatment duration also increased from 36.1% in 1993 to 92.1% in 2013 (Table 10).

In 2015, 1.1% of reported TB cases had primary multidrug resistance (MDR), defined as no previous history of TB disease and resistance to at least isoniazid and rifampin (Table 9). This percentage has remained stable, fluctuating between 0.9% and 1.3% since 1996. The proportion of primary MDR TB occurring in foreign-born persons has increased from 25.3% (103 of 407) in 1993 to 86.3% (63 of 73) in 2015, which is similar to the proportion in 2014 (Table 9). In 2015, there was one case reported of extensively drug-resistant (XDR) TB, defined as resistance to isoniazid and rifampin, plus resistance to any fluoroquinolone and at least one of three injectable second-line anti-TB drugs (i.e., amikacin, kanamycin, or capreomycin).

**Genotyping**
TB genotyping is a laboratory-based analysis of the genetic material of the bacteria that cause TB disease. TB genotype clusters are defined as two or more cases with matching genotypes in the same county during a 3-year time period. Cases that are clustered may be the consequence of recent transmission, while unique cases are more likely attributable to reactivation of infection that was acquired in the past. Among genotyped cases during 2013–2015, 21.5% were clustered...
During this period, the percentage of clustered cases among U.S.-born persons with TB was 36.0%, compared to 14.4% among foreign-born persons diagnosed with TB in the United States (Table 22). However, not all clustered cases result from recent transmission.

In 2015, CDC scientists developed and published a new genotype-based method to estimate the proportions of cases attributable to recent transmission in defined populations (e.g., geographic areas). The method, which was validated using epidemiologic data, attempts to identify a “plausible-source case” for each genotyped TB case using a combination of genotyping and spatial, temporal, clinical, and demographic criteria. In 2016, an estimate was published that approximately 14% of genotyped cases during 2011–2014 were attributed to recent transmission. The method also was refined by distinguishing limited versus extensive recent transmission based on the size of plausible transmission clusters. State-level estimates were published.

Conclusions
The overall number of TB cases in the United States increased in 2015 compared with the previous year, after having declined yearly during 1993–2014. The increase in the overall case count in 2015 and leveling of the U.S. incidence rate since 2013 raise concern that current TB control practices might no longer be sufficient to sustain the previously observed rate of decrease in U.S. TB incidence. Statistical modeling has shown that decreasing the prevalence of latent TB infection will also be key to eliminating TB in the United States. Resuming and accelerating progress toward TB elimination will require an intensified, dual approach that includes strengthening existing systems to prevent transmission of infectious TB disease and increasing efforts to detect and treat latent TB infection. CDC continues to work with its partners to achieve the goal of TB elimination in the United States. Current TB control strategies prioritize the early diagnosis, isolation, and treatment of people with infectious TB disease. This approach protects patients’ health, prevents transmission to others, and allows for timely contact investigations to detect and prevent additional cases. These TB control efforts are essential, but by themselves cannot eliminate the disease from the United States. More than 85% of U.S. TB cases are associated with longstanding, untreated latent TB infections, and public sector efforts alone will be insufficient to reach all of those who need to be tested and treated for latent TB. These efforts must also include public health systems and private providers, who are often on the front lines of health care in the communities most affected by TB.

Global TB disease burden and the incidence in the United States are closely related, emphasizing the continued need to strengthen existing support for TB control efforts abroad. This is particularly true as relates to the countries of persons who have lived in countries where TB disease is more common. Foreign-born persons continue to be disproportionately affected by TB; now accounting for 66.4% of total cases. To achieve TB elimination, intensified efforts continue to be needed to address the persistent disparities that exist between U.S.-born and foreign-born persons, as well as among U.S.-born racial and ethnic minorities.

Ongoing surveillance and improved TB control and prevention activities will be essential in light of the increase in TB case count in 2015 and the leveling of U.S. TB incidence rates in recent years. CDC also continues to study available data on TB and latent TB infection trends in the United States to better inform TB prevention and control efforts. Ultimately TB elimination will require a sustained focus on domestic TB control, a strengthened effort to diagnose and treat latent TB infection, and continued support of global TB control initiatives.


Recent Staff Publications


Meetings/Conferences/Lectures

21st Conference of The Union North America Region, February 22-25, 2017, Vancouver, BC, Canada
Website: https://bc.lung.ca/support-services/union-north-america
Email: tbconference@bc.lung.ca

The 54th Annual Denver TB Course, April 5-8, 2017, Molly Blank Conference Center at National Jewish Health Main Campus. For more information and registration: https://www.nationaljewish.org/tbcourse2017

Save these dates for the NTM Lecture Series:
• NTM Lecture Series for Providers, October 19-20, 2017
• NTM Lecture Series for Patients and Families, October 21, 2017
Details about these lectures will be posted at a later date. To add your name to the contact list, please call 800.844.2305 or email: proed@njhealth.org

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