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Challenges in assessing transmission of *Mycobacterium tuberculosis* in long-term-care facilities

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In 2012, the Centers for Disease Control and Prevention (CDC) reported 3.2 cases of tuberculosis (TB) per 100,000 persons in the United States.[1] Although TB incidence has declined during the past several decades, the 2010 goal of < 1 case per 1,000,000 persons—as established in the national strategic plan for TB elimination—has yet to be achieved.[2] Although persons aged ≥ 65 years accounted for only 14% of the population in 2012, this group represented 22% of reported cases of TB.[3,4] An analysis of 1993–2008 cases reported in the United States showed that the rate of TB among elderly adults was as much as 30% higher than among younger adults.[5] Even more striking are the disproportionate rates documented among those living in long-term-care facilities (LTCFs). Previous reports have estimated that adults aged ≥ 65 years residing in LTCFs may have between 4 and 50 times the risk of developing TB disease than elderly persons living in the community.[5–7]

As of April 2014, approximately 3.2 million workers were employed in LTCFs.[8] The size of this occupational group will grow significantly in the coming years if LTCF resident populations increase as expected. Past estimates suggest the TB case rates are 3 times higher among LTCF workers compared with those working in any other job.[9] Therefore, prevention and control of TB in LTCFs are essential to protect both the residents and employees in these settings. The goal of this article is to summarize findings of an LTCF TB outbreak

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investigation to highlight the unique challenges posed by *Mycobacterium tuberculosis* transmission in these settings.

CASE STUDY

During 2011–2012, the Alaska Department of Health and Social Services, the Anchorage Department of Health and Human Services, CDC's National Institute for Occupational Safety and Health (NIOSH), and CDC's Division of Tuberculosis Elimination investigated suspected *M tuberculosis* transmission at a 190-bed LTCF in Alaska. In April 2011, the investigation was initiated when the facility's annual employee TB screening program identified an aberration in the number of tuberculin skin test (TST) conversions. In contrast to no TST conversions in previous annual screenings, 8 of 230 evaluated employees had documented TST conversions (defined as ≥ 10 mm increase). In this LTCF, employees without a history of TB disease or latent TB infection (LTBI) were screened with a TST upon hire and then every April. Similarly, residents without a history of TB disease or LTBI were screened via TST within 72 hours of admission and then annually during the month of their admission anniversary. Residents and employees with a history of TB disease or LTBI undergo a baseline chest radiograph and annual TB symptom screening via questionnaire.

Subsequent screening of residents from April–November 2011 used an interferon-gamma release assay (IGRA) and identified newly positive IGRA test results, defined as ≥ 0.35 IU/mL, among 8 of 17 residents (47%) of a single secure unit for dementia special care.

Using a risk-stratified approach to preselect those at highest risk of infection, thorough screening of 216 of 350 (62%) current and former employees and 85 of 155 (55%) current and former residents was undertaken via varying combinations of symptom review; TST or IGRA; chest imaging; and sputum collection through expectoration, induction, or bronchoscopy as needed. Deciding between TST or IGRA was based on which test had been used previously for each person evaluated.[10]

Ultimately, 12 residents and 11 employees were found to have new LTBI, and 1 resident was found to have pulmonary TB disease. This resident had a history of pulmonary TB disease in the remote past and resided in the secure dementia special care unit. The resident had a comprehensive negative prior workup for TB between April and November 2011, including chest radiographs, bronchoscopy with bronchoalveolar lavage for acid-fast bacilli (AFB) smear and culture, and stool polymerase chain reaction test for TB. From a pulmonary specimen collected in May 2012, the resident was found to have both a positive AFB sputum smear result and a positive AFB culture result for *M tuberculosis*, which were interpreted as probable reactivation of TB. All 11 employees and 8 of 12 residents with newly diagnosed LTBI were epidemiologically linked to this resident with TB disease, who reportedly did not move outside of this unit during the time at the LTCF. However, no clear epidemiologic link to the other 4 residents, who resided outside of the secure dementia special care unit, was found.

We cross-checked the limited paper visitor and volunteer logs available against the state TB disease database, without any matches. Evaluation of the ventilation system did not find an

airflow pattern that could explain how the other 4 residents could have been infected from the resident with TB disease. One of these LTCF residents with significant weight loss, productive cough, and TST conversion died from respiratory failure during August 2012 while our investigation was still ongoing. Because no postmortem examination was performed, we were unable to determine whether this individual had TB disease and was the source of exposure to the other 3 residents. The 1 resident with documented TB disease received appropriate therapy promptly upon diagnosis, and all those with LTBI were offered treatment. Improvements to administrative controls such as training of employees and improved screening procedures were implemented at the LTCF. No further evidence of ongoing transmission has been noted as of July 2014.[11]

SITUATIONAL ANALYSIS

Throughout the course of the investigation, many diagnostic, staffing, and treatment difficulties were encountered. LTCFs present a unique set of challenges for TB prevention and control, and diagnosing TB among elderly persons can be complicated. Therefore, understanding issues encountered in outbreak investigations aids in refining areas for continued clinical and public health research and informing updated guidelines and policies to protect residents and employees.

Diagnostic challenges

Recognizing signs and symptoms—Administrative controls, starting with early detection of contagious TB, are the cornerstone of preventing transmission in health care settings.[12] However, TB has long been recognized as an imitator of multiple other diseases, making diagnosis challenging even under ideal conditions.[13] Further, aging reduces the ability to mount a cell-mediated immune response, making atypical presentations of TB due to dissemination of TB disease or localization to other organs more common.[6,14] In elderly persons, classic presenting features of pulmonary TB disease such as weight loss, cough, hemoptysis, and night sweats may be either absent or attributable to alternative diagnoses.[6,14,15] Conditions such as dementia and strokes can be associated with dysphagia, increasing the possibility of chronic cough from recurrent aspiration.[16] Elderly persons are also more prone to weight loss because of poor nutrition and increased metabolic demand from chronic diseases.[17] Obtaining reliable information from symptom screening can be especially challenging given the prevalence of cognitive impairments.[18]

TB disease in elderly persons may have an insidious onset with persistently decreased ability to perform activities of daily living, new onset or worsening of preexisting cognitive impairment, and increasing fatigue and dyspnea.[15] Given the broad differential diagnosis necessary for chronic signs and symptoms such as these, TB diagnosis is delayed in some instances, increasing patient morbidity and mortality and allowing more time for transmission, especially in congregate settings.[5,6]

Diagnostic testing—CDC recommendations for TB screening of residents and employees of LTCFs are based on initial and ongoing facility-specific risk assessments.[12] Medium-risk LTCFs, such as the 1 in this investigation before the outbreak, are defined as settings where patients with TB are expected to be encountered. In these settings, initial

screening via a 2-step TST or a single IGRA should be used for baseline LTBI evaluation. Thereafter, CDC recommends annual screening with a single TST or IGRA unless there is documentation of a prior positive TST or IGRA result. In individuals with a baseline positive test result for LTBI, or completion of LTBI or TB disease therapy, a single chest radiograph should be performed to exclude TB disease with routine symptom screening thereafter.[12]

The limitations of TST have been well described. Exposure to nontuberculous mycobacteria can cause a false-positive TST result.[6,12,19,20] False-negative TST results are more common in aging populations due to impaired immunity leading to the possibility of unrecognized TB infection.[5,21] Additionally, TST findings are only valid if the tests are performed and interpreted properly. Therefore, TB should remain in the differential diagnosis in elderly patients residing in LTCFs with clinical signs and symptoms of TB, even for those with a negative TST result.[6]

IGRAs can be performed at a single patient encounter; however, IGRAs have their own limitations. IGRA is generally more expensive than TST, requires proper blood collection and transport, and must be processed promptly.[10] Recent reports have documented variable results with serial IGRA testing, making interpretation challenging.[22] False-positive IGRA conversions have been noted among health care workers in areas or settings with a low prevalence of TB.[22] Additionally, scant data exist on IGRA use in elderly populations.[6,23,24] Finally, use of TSTs and IGRAs in combination can lead to diagnostic dilemmas from discordant results.[10] We encountered both discordance between serial IGRA tests and discordance between IGRA and TST results during our investigation.[11]

A chest radiograph is recommended for persons with signs or symptoms of TB disease or with a positive test result for LTBI and should be performed before initiation of therapy for LTBI to rule out TB disease. Upper-lobe infiltrates, often with evidence of cavities, are the classic TB findings on chest radiograph.[12] The most easily interpretable chest radiograph includes 2 upright views: posterior-anterior and lateral. Proper technique dictates use of the correct exposure, appropriate body positioning, and patient-held maximally inspired breath.[25]

Obtaining adequate radiographs in the LTCF population is challenging. Curvature of the spine and cognitive impairment can make proper positioning and capturing of images at full inspiration difficult.[7] Additionally, most LTCFs are not equipped to perform 2-view, upright chest radiographs within their facilities, but rather are limited to lower quality, portable, single-view, anterior-posterior images. Ideally, LTCF residents with suspected TB disease should be transported to a facility equipped for full diagnostic imaging.

Although chest radiograph remains essential in the clinical evaluation of TB disease, factors unique to elderly populations may limit its value in this population. Classic chest radiograph findings, such as cavities, are less common in this group.[6,14,15] Additionally, underlying parenchymal or pleural abnormalities such as recurrent pneumonias, lung cancer, emphysema, or silicosis can mimic findings of TB or even obscure certain portions of the lung fields, further complicating diagnosis.[5,6,16]

Pulmonary TB disease can be confirmed by isolation of *M tuberculosis* from a culture of sputum. Nucleic acid amplification tests, which can aid in more rapid diagnosis of TB disease, were not available and therefore not used in the initial stages of this investigation.[26] Sputum is preferably obtained as a self-produced, expectorated specimen.[12] Difficulties encountered in gathering expectorated sputum specimens because of cognitive deficits and weak cough limit the utility of this collection method in LTCF populations.[6,7] More than half of residents involved in our investigation, including several with TST conversions, could not produce adequate sputum samples for analysis, complicating our ability to detect TB disease in these individuals.[11]

For patients who are unable to produce an adequate sputum specimen, expectoration can be induced by inhalation of an aerosol of warm, hypertonic saline. This should be done by trained providers in a small, well-ventilated sputum induction booth or in an airborne infection isolation (AII) room.[6,12] In facilities that do not have sputum induction booths or AII rooms, CDC recommends performing sputum collection outside of a building, away from other persons, windows, and ventilation intakes. Further, employees conducting sputum induction should wear NIOSH-approved filtering facepiece respirators or respirators that afford a higher level of protection.[12] Although the facility in our investigation had well-trained respiratory therapists able to collect induced sputum samples outside the building, many LTCFs lack the personnel and recommended resources needed to perform this procedure.

In the event that an adequate sputum specimen cannot be obtained to effectively rule out pulmonary TB disease, bronchoscopy may be considered as an alternative means of obtaining respiratory samples. However, bronchoscopy increases the risk of transmission to health care personnel, cannot routinely be performed within most LTCFs, has risk of complications, is costly, and requires consent from the patient or power of attorney/guardian.[6,12,27,28]

Several studies have shown that TB diagnosis is often made only at autopsy.[19,29,30] Even if diagnosis is after death, contact tracing to find persons who were exposed is essential for reducing morbidity and the risk of second-generation transmission. Autopsy rates have declined to <10% of deaths overall and to <1% of deaths among LTCF residents.[9,31,32] During our investigation, difficulty obtaining autopsies may have limited our efforts to discover the source of the outbreak.[11]

Organization-related challenges

Staffing—Issues in investigating the transmission of *M tuberculosis* in LTCFs are not limited to diagnostic dilemmas. Multiple administrative challenges could be barriers to case finding, including staffing limitations. As health care costs continue to rise, employees and facilities in the industry must increasingly do more with fewer resources. For physicians and other providers, this can mean seeing more patients in less time.[33] In addition, high LTCF employee turnover leads to greater numbers of recently hired, less-experienced, or part-time health care providers. Therefore, routine training and educating staff on TB infection control procedures; recognition of new, subtle, or atypical TB symptoms among residents; and maintaining good communication and continuity of care between providers can be difficult.

Locating former employees during outbreak investigations can also be complicated because contact information is not always available, and this challenged us in our investigation.[9,11]

Volunteers and visitors to LTCFs can also acquire or transmit TB.[9,12] In LTCFs, volunteer and visitor logs may be poorly maintained, further complicating outbreak investigation activities.[9] In our investigation, handwritten names on volunteer and visitor records were often illegible, and logs were only saved for 3 months, preventing thorough evaluation of this group.[11]

Treatment challenges

Because many LTCFs are not equipped to manage residents with TB disease, these individuals are commonly referred to inpatient facilities for initiation of therapy.[12] Treating LTBI and TB disease in elderly populations presents a unique set of challenges related to duration of treatment, drug–drug interactions, and drug toxicities. At the time of our investigation, isoniazid for 9 months was the preferred treatment of LTBI in all age groups.[6,12,34,35] The facility in our investigation used 4 months of rifampin for LTBI treatment in its resident population because of its improved side effect profile.[34,35]

In cases of suspected TB disease, use of standard 4-drug therapy, including isoniazid, rifampin, pyrazinamide, and ethambutol, is recommended while awaiting susceptibility testing.[6,12,36] Before discontinuation of AII precautions and transfer back to the LTCF, individuals being treated for TB disease should complete a minimum of 2 weeks of an appropriate regimen, show signs of clinical improvement, and demonstrate 3 consecutive negative sputum AFB smears.[12,36]

In the past, some have argued for empiric TB disease treatment in elderly persons who have suspected TB because of the diagnostic difficulties encountered in this population.[19,37] When treating known TB disease in patients who take multiple other medications and with elevated numbers of comorbidities, risks of drug–drug interactions and toxicities are concerning.[6,19] The majority of safety trials for use of these agents were conducted in healthy persons younger than age 35 years.[6] Isoniazid intolerance and toxicity increase with age, and isoniazid may increase, whereas rifampin may decrease serum levels of common medications used by elderly persons.[6,36,38] The adverse effect profiles for ethambutol and pyrazinamide also require close follow-up and monitoring.[6,37,38] Although recent studies have shown positive results with a shorter, less-toxic regimen, these studies have not adequately evaluated the safety and efficacy of these newer regimens among elderly individuals.[39,40]

CHALLENGES WITH ENGINEERING CONTROLS AND RESPIRATORY PROTECTION

Because many LTCFs do not expect to encounter patients with TB disease, few have AII rooms available.[6,14] CDC recommends that LTCFs without such resources transfer residents with suspected TB disease to an alternative setting that is equipped for proper isolation and evaluation of suspected TB cases.[12] If immediate transfer is not possible, the patient should be placed in a private room and given a surgical mask pending transfer.[6,12] Employees

should use fit-tested NIOSH-approved filtering facepiece respirators or those with a higher level of protection when entering the room or providing care to patients with suspected or confirmed infectious TB.[6,12] Respiratory protection programs should follow the Occupational Safety and Health Administration Respiratory Protection Standard. This includes development of a written respiratory protection program, medical clearance of employees to wear respirators, fit testing, and training.[41]

Attempts to educate cognitively impaired elderly patients on cough etiquette are unlikely to be successful, and keeping a surgical mask on a disoriented person can be challenging and also distressing for the patient. Isolating such patients may also be problematic due to the risk of more rapid dementia progression or facilitation of delirium.[15,42,43]

CONCLUSIONS

TB in LTCF populations poses several diagnostic, administrative, and treatment challenges that deserve attention and present many important new areas for future research. Continued strengthening of TB surveillance programs is essential. As a part of these efforts, health care providers in LTCFs should consider TB in their differential diagnosis when evaluating ill residents even when IGRA or TST results are negative.

Further studies of IGRA characteristics among elderly populations and reevaluation of the positive predictive value for this assay are needed. Generally, assessment of LTBI conversions should be based on repeated use of a single test (ie, IGRA or TST) rather than use of both the IGRA and the TST in combination.[10] Additionally, continued attempts to not only develop but also use new technologies for improved and more rapid assessment of those with suspected TB are essential.[5,26]

Administrative challenges demonstrate that improvements in surveillance, diagnosis, and treatment are needed. High employee turnover rates emphasize the importance of proper documentation of baseline TB status as well as good contact information for departing personnel. Staff training programs should include materials tailored to all education levels and clinical roles, and be offered during work hours.[12,14] Close monitoring of those performing TSTs or collecting blood for IGRA testing for quality assurance purposes will help maintain a high level of accuracy of test results.[12] Enforcement of visitor and volunteer registration, possibly with computer-based logs to eliminate legibility issues, and longer retention of these records will aid in contact investigations in LTCFs. In addition, a culture of safety that encourages staff participation, immediate reporting of symptoms suspicious for TB among residents, and constant suggestions for improvements must be fostered to empower employees in LTCFs.

Although the number of new TB cases identified in the United States has declined since the resurgence in the early 1990s, Alaska has reported TB rates higher than the national average for the past decade.[44] Areas for improving prevention and control efforts remain, particularly among subpopulations at higher risk for TB. Lessons learned from outbreak investigations such as ours provide valuable insights into the control of TB in high-risk

congregate populations, a step important to ongoing progress toward TB elimination goals in the United States.

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