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TB NOTES

TB Notes 4, 2016 August 30, 2016

Notes from the Director

Dear Colleague:

The month of August has been full of exciting updates from DTBE staff. Earlier this month, the Centers for Disease Control and Prevention (CDC)/Division of Tuberculosis Elimination (DTBE), along with the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA), were pleased to announce the release of the 2016 Treatment of Drug-Susceptible Tuberculosis (TB) Guidelines. I'd like to issue a special thank you to the panel of subject matter experts who contributed in the development of the guidelines, including lead author Dr. Payam Nahid, professor of medicine at the University of California, San Francisco School of Medicine, and DTBE's own Dr. Andrew Vernon. The guidelines panel members conducted extensive literature reviews, held numerous discussions with colleagues, and worked diligently to author the new treatment guidelines. Their hard work will help ensure that clinicians have the best data to inform treatment practices. You can read more about the guidelines in this issue of *TB Notes*.

Through the Association of Public Health Laboratories (APHL), DTBE staff in the Laboratory Branch are working with colleagues across the TB community to prevent the spread of TB. The APHL TB Subcommittee has authored key research that addresses some of the most important issues in TB diagnosis and drug-susceptibility testing. The latest updates on the TB Subcommittee are detailed in this newsletter.

Philip LoBue, MD, FACP, FCCP
Director,
Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Highlights from State and Local Programs

Coach-Supported Experiential Learning Facilitates the Onboarding of TB Nurses

During a time of decreasing funding, e-Learning has taken the TB community by storm. Those in the TB training community understand the value of technology to provide training to many people in dispersed locations for less money and less time away from jobs. Although there are many benefits to this type of training, we also recognize the value lost from interactions, networking, and relationship-building that are available during live trainings.

The Southeastern National Tuberculosis Center (SNTC) in Gainesville, Florida offers online experiential, case-based Nurse Case Management (NCM) training that is reinforced by a subject matter expert to "coach" the learner along the way. Through a Learning Experience Manager (LEM) platform (unlike a Learning Management System or LMS), the learner is guided through realistic scenarios as he or she learns the many aspects of caring for the patients. The learning interactions include questions, videos, role plays, and other activities used to teach specific nurse case management processes. Topics include taking an initial patient report, identifying the infectious period, determining the need for a contact investigation, discharge planning, and providing directly observed therapy (DOT).

Throughout the course, the learner receives pearls of wisdom from TB experts and is exposed to many NCM resources gathered from around the U.S., bringing years of knowledge and experience to the learner. All the while, the coach supports the learner by answering questions, prompting further exploration of topics, and providing guidance. The pair interacts through the LEM, which houses the course content and provides structure and a framework for activities.

The course is challenging, and it provides a fresh, engaged perspective to adult learning. Benefits of this experiential learning opportunity for NCM learners and their TB programs include the following:

- Any healthcare provider can be trained at their local site without the need to travel. A computer with internet access is required.
- The coaches are knowledgeable TB nurses with many years of experience in providing onboarding for new TB nurses.
- As part of the learning experience, learners identify resources and NCM processes used within their geographic area of practice, while building a customized electronic notebook of resources to immediately start using in their own program. The course is naturally tailored to each learner's unique environment, enabling a healthcare worker from any state, region, county, or city to benefit.
- This training experience is free to learners.
- The nurse participants learn at their own pace.
- While proceeding through the content, learners receive encouragement by earning badges and interacting with their coach.
- A certificate of completion is provided.
- Nursing continuing education credit is provided.

Contact SNTC for information on course registration.

Submitted by Karen Simpson, MSHSE, Southeastern National Tuberculosis Center

TB Education and Training Network (TB ETN) Updates

TB Education and Training Network Conference

The Tuberculosis Education and Training Network (TB ETN) and the TB Program Evaluation Network (TB PEN), will hold a joint conference in Atlanta, Georgia on September 20-22, 2016. The conference will be held at the Centers for Disease Control and Prevention, Global Communications Center.

During the conference, TB ETN and TB PEN will explore TB education, training, and evaluation. Conference activities will include skills-based workshops, informational presentations, and networking opportunities. Visit the conference website for more information.

Submitted by Peri Hopkins, MPH, DTBE

Office of the Director Updates

DTBE Congratulates Rear Admiral Kenneth G. Castro

Rear Admiral Kenneth G. Castro, MD was recently presented with the 2016 CDC/ATSDR Charles C. Shepard Lifetime Scientific Achievement Award. This award recognizes individuals with a body of work that has contributed to public health. Nominees were judged on their work's scientific merit, its effect on public health and the mission of CDC/ATSDR, and on the leadership and recognition by peers. The award was presented to Dr. Castro on June 8, 2016.

Submitted by Carla Winston, PhD, DTBE

TB Trials Consortium (TBTC) Updates

The Latest News from the TB Trials Consortium

TB Trials Consortium Study 31 (also known as ACTG A5349; "Rifapentine-containing treatment shortening regimens for pulmonary tuberculosis: A randomized, open-label, controlled phase 3 clinical trial") continues to enroll. As of August 24, 2016, the study had a total of 231 participants. Since May, multiple sites of the collaborating AIDS Clinical Trials Group (ACTG) network as well as TBTC sites have become active, reflected by the significant increase in the pace of enrolling.

TBTC Study 32 ("Prospective, Randomized, Blinded Phase 2 Pharmacokinetic/Pharmacodynamic Study of the Efficacy and Tolerability of Levofloxacin in Combination with Optimized Background Regimen (OBR) for the treatment of MDR-TB; Opti-Q") has enrolled steadily at sites in Cape Town, South Africa and in Lima, Peru. It has reached over half of its goal to enroll 62 evaluable patients. This study is a collaboration with Boston University and the National Institute of Allergy and Infectious Diseases.

TBTC Study 33 ("An evaluation of adherence to LTBI treatment with 12 doses of once weekly rifapentine and isoniazid given as self-administered versus directly-observed therapy: iAdhere") has been presented in several venues, including IUATLD's 2014 World Lung Health Conference, ATS 2015, and CROI 2015. The final study report is entering clearance at CDC and should appear in the literature in late 2016.

As of August 24, 2016, TBTC Study 36A has enrolled 216 patients, over 85% of its projected target of 250 persons being treated for active TB disease for the CTB2 (Consortium for TB Biomarkers) specimen bank.

TBTC members and staff are progressing in the planning for TBTC Study 37, which will compare the 3HP regimen for LTBI treatment to a 6-week daily rifapentine-based regimen.

On October 5-7, 2016, TBTC will hold its 38th semiannual meeting in Atlanta. Those interested to attend should contact Ms. Barbara DeCausey via email or phone at 404-639-5330.

Submitted by Barbara DeCausey, MPH, MBA, DTBE

Clinical Research Branch Updates

Treatment of Drug-Susceptible TB Guidelines Recently Released

Earlier this month, the American Thoracic Society (ATS), Centers for Disease Control and Prevention, and the Infectious Diseases Society of America (IDSA) published updated clinical practice guidelines for the treatment of drug-susceptible TB disease. The guidelines were published in Clinical Infectious Diseases. These guidelines update previous ATS/CDC/IDSA guidelines published in 2003. They provide recommendations on the clinical and public health management of active TB disease in settings in which mycobacterial cultures, drug susceptibility tests, and radiographic studies are routinely available.

For all recommendations, literature reviews were performed, followed by expert discussion according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology. Given the public health implications of prompt diagnosis and effective management of TB disease, empiric multidrug treatment should be initiated in almost all situations in which active TB disease is suspected. Clinicians and public health practitioners should see the full-text online version of the document, which provides detailed discussion of the management of drug-susceptible TB disease and recommendations for practice.

Submitted by Andrew Vernon, MD, DTBE

Data Management, Statistics, and Evaluation Branch Updates

Dr. Andrew Hill wins award

Dr. Andrew Hill received the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) award for Excellence in Quantitative Sciences for his work leading the

analysis of data collected as part of the TB component of the 2011-2012 National Health and Nutrition Examination Survey (NHANES). Dr. Hill overcame significant challenges uncovered during the preliminary analysis of the data to develop a sound approach to the interpretation of results. The final published manuscript provides the best estimate of latent tuberculosis infection (LTBI) in the United States.

NHANES is a series of cross sectional surveys designed to assess the health and nutritional status of adults and children in the United States. The survey examines a nationally representative sample of approximately 5,000 persons each year. In 2011-2012, NHANES participants six years of age and older received two tests for TB infection, the Tuberculin Skin Test (TST) and the Quantiferon Gold In-Tube (QFT-GIT) blood test. Additionally, participants were asked questions regarding prior tuberculosis (TB) tests, prior treatment for latent TB infection or TB disease, and prior exposure to TB.

This analysis accomplished by Dr. Hill in 2015 has provided a robust, rigorous, and defensible means of estimating current levels of LTBI in the United States. By making the necessary adjustments so that successive NHANES survey cycles of 1999-2000 and 2011-2012 were directly comparable, the analysis has allowed TB public health professionals to get their first glimpse of TB infection trends over the past 12 years. These methods will be adopted in all future analyses of NHANES data undertaken by CDC Division of Tuberculosis (DTBE) personnel.

Furthermore, these results are now being used to inform crucial epidemiologic parameter inputs into several TB transmission and cost-effectiveness models being developed by DTBE in conjunction with external academic partners as part of the NCHHSTP Economic and Epidemic Modeling Cooperative Agreement (NEEMA). The results of these models will strongly influence national TB control policy in the future.

Submitted by David Wilson, MEd, DTBE

Article on Economic Benefits of Prevented TB Cases

The July 2016 edition of the International Journal of Tuberculosis and Lung Disease (IJTLD) featured an article entitled "Estimating Tuberculosis Cases and their Economic Costs Averted in the United States over the Past Two Decades." The article was written by DTBE authors, and it estimates the number and societal benefits of TB cases averted though TB control. Authors used three different scenarios with varying assumptions to estimate the number of cases averted and corresponding benefits. According to the article, an estimated 145,000–319,000 TB cases were prevented in the United States during 1995–2014. The estimated societal benefits of prevented TB cases ranged from $6.7 billion to $14.5 billion (including deaths). The article was accompanied by an editorial by Drs. Jason Stout and Kristen Dicks, entitled "Calculating the economic benefits of what didn't happen."

Submitted by Suzanne Marks, MPH, MA, DTBE and Leeanna Allen, MPH, DTBE

Laboratory Branch Updates

Association of Public Health Laboratories TB Subcommittee

The Association of Public Health Laboratories (APHL) has a very active committee structure with the Tuberculosis (TB) Subcommittee serving under the broader Infectious Disease Committee. The TB Subcommittee works to aid those who work each day on the front lines to identify and prevent the spread of TB. The composition of the committee is intended to provide representation for differences in TB burden and regional patient populations served as well as partner agencies. Members of the subcommittee represent both low volume and high volume state public health laboratories, as well as the Northeast, Southeast, Midwest, Southwest, and Western Regions. The subcommittee also has representation from Public Health Ontario, Canada, the National TB Controllers Association (NTCA), and the Laboratory Branch in the Division of Tuberculosis Elimination (DTBE) at CDC.

Over the past 12 months, the TB Subcommittee has contributed to several key documents of note. These documents have included a collaboration with the NTCA to help produce the *Consensus statement on the use of Cepheid Xpert MTB/RIF assay in making decisions to discontinue airborne infection isolation in healthcare settings.* Two white papers focused on issues in *Mycobacterium Tuberculosis* complex (MTBC) Drug Susceptibility Testing (DST) were also produced by the subcommittee. The white papers covering both ethambutol (EMB)and pyrazinamide (PZA) each cover the current guidelines, recommendations, and research findings associated with each drug.

While these documents represent a fraction of the work conducted by the TB Subcommittee, they are perhaps the most impactful, with high demand for each. The EMB and PZA white papers help to strike at issues that have long been an area of concern for many of those who work in TB. Work has also begun in earnest on two new TB DST white papers focused on fluoroquinolones (FLQ) and rifampin (RIF). The hope is that this collection will serve as a concise resource on current information available for TB DST. The TB Subcommittee is committed to assisting those who work on a daily basis to combat TB, both in and out of the laboratory, across a wide variety of regions and roles.

Submitted by Paul Zell, MPH Association of Public Health Laboratories (APHL) and Anne Gaynor, PhD, APHL

Surveillance Epidemiology and Outbreak Investigations Branch Updates

Highlights from the 7th Annual Tuberculosis Epidemiologic Studies Consortium Meeting

The Tuberculosis Epidemiologic Studies Consortium (TBESC) is a CDC-funded group of state and local health departments and universities that focus on research to improve diagnosis, treatment, and treatment completion for latent TB infection (LTBI).

The 10 consortium members are –

- California Department of Public Health
- Maryland Department of Health and Mental Hygiene
- Hawaii Department of Health
- Maricopa County (Arizona) Department of Public Health
- Public Health Seattle-King County
- Denver Health and Hospital Authority

- Duke University, North Carolina
- Emory University, Atlanta
- University of Florida Board of Trustees
- University of North Texas Health Science Center

On June 29-30, 2016, approximately 90 people attended the Consortium's 7th annual meeting at the CDC Roybal campus in Atlanta. Highlights from the meeting include the following:

- Richard Brostrom from Hawaii presented on the utility of adding diabetes testing to LTBI screening;
- Bob Horsburgh presented preliminary data on the cost-effectiveness of screening and treatment of LTBI in foreign-born persons;
- Project coordinators, Katya Salcedo, Yoseph Sorri, and Kristian Atchley, shared their experiences and lessons learned about recruitment and follow-ups of study participants;
- Consortium members were updated on the next phase of TBESC, which will focus on barriers to identification and successful treatment of persons at high risk for LTBI. Members also were given a demonstration of the CDC-designed LTBI case management and surveillance tool, Surveillance for TB Elimination Management System (STEMS). Three sites presented their experiences using STEMS;
- Jason Stout described the use of latent class analysis methods to predict LTBI prevalence in high risk populations in the United States and assess the sensitivity, specificity, and positive predictive value of the 3 currently available tests for LTBI;
- 
Christine Ho, CDC TBESC project officer, updated TBESC members on study progress. Of 19,000 participants enrolled to date who had all three LTBI test results available, 16.4% were positive on all three (tuberculin skin test [TST], QuantiFERON Gold, and TSPOT); 56.8% were negative on all three; 18% were positive by TST alone (the other two were negative); 2.14% were positive by QFT alone; 0.73% were positive by TSPOT alone; and 6% were positive on two tests and negative on one.
- Members received updates on progress in development and implementation of new guidelines for LTBI screening and treatment from the U.S. Preventive Services Task Force, the National TB Controllers Association, and the American Thoracic Society/Infectious Diseases Society of America/CDC working group (Phil LoBue, CDC; Bob Belknap, Denver Health and Hospitals Authority; Carol Dukes Hamilton, Family Health International [FHI 360]); and
- Other topics included immunology of LTBI (Philana Lin, Pittsburgh Children's Medical

Center), evaluation of a new QuantiFERON LTBI test in healthcare workers (Niaz Banaei, Stanford University), and a progress report on the national LTBI surveillance system (Adam Langer, CDC).

Submitted by Dolly Katz, PhD, DTBE and Thara Venkatappa, PhD, DTBE

New CDC Publications

July 2016

Castro KG, **Marks SM**, **Chen MP**, **Hill AN**, **Becerra JE**, **Miramontes R**, **Winston CA**, **Navin TR**, **Pratt RH**, **Young KH**, **LoBue PA**. Estimating tuberculosis cases and their economic costs averted in the United States over the past two decades. Int J Tuberc Lung Dis 2016;20:926–33.

Grinsdale JA, Islam S, Tran OC, **Ho CS**, Kawamura LM, Higashi JM. Interferon-gamma release assays and pediatric public health tuberculosis screening: the San Francisco program experience 2005 to 2008. J Pediatric Infect Dis Soc 2016;5:122–30.

Luetkemeyer AF, Firnhaber C, Kendall MA, Wu,X, **Mazurek GH**, Benator DA, Arduino R, Fernandez M, Guy E, Johnson P, **Metchock B**, Sattler F, Telzak E, Wang YF, Weiner M, Swindells S, Sanne IM, Havlir DV, Grinsztejn B, Alland D. Evaluation of Xpert MTB/RIF versus AFB smear and culture to identify pulmonary tuberculosis in patients with suspected tuberculosis from low and higher prevalence settings. Clin Infect Dis2016;62:1081–8.

Scott C, Cavanaugh JS, **Pratt R**, **Silk BJ**, **LoBue P**, Moonan PK. Human tuberculosis caused by *Mycobacterium bovis* in the United States, 2006–2013. Clin Infect Dis 2016;pii:ciw371. Epub ahead of print.

Yakrus MA, **Driscoll J**, McAlister A, **Sikes D**, **Hartline D**, **Metchock B**, **Starks AM**. Molecular and growth-based drug susceptibility testing of *Mycobacterium tuberculosis* complex for ethambutol resistance in the United States. Tuberc Res Treat 2016. Epub ahead of print.

Yelk Woodruff RS, **Pratt RH**, **Armstrong LR**. The US National Tuberculosis Surveillance System: a descriptive assessment of the completeness and consistency of data reported from 2008 to 2012. JMIR Public Health Surveill 2015;1:e15.

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Jereb JA. Interpreting false positive tuberculosis tests in occupational screening: the fault of the test, the testing schedule, or both? Ann Am Thorac Soc 2016;13:1189–90.

Khan A. National tuberculosis prevention and control program evaluation in the United States of America: from concept to practice. Austin Tuberc Res Treat 2016;1:1–5.

Nahid, P., et al. (2016). Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of

Drug-Susceptible Tuberculosis. Clin Infect Dis. doi: 10.1093/cid/ciw376

Willby MJ, Green KD, Gajadeera CS, Hou C, Tsodikov OV, **Posey JE**, Garneau-Tsodikova S. Potent inhibitors of acetyltransferase Eis overcome kanamycin resistance in *Mycobacterium tuberculosis*. ACS Chem Biol 2016;11:1639–46.