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TB NOTES

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Notes from the Director

Dear Colleague:

Looking back over 2017, I would like to thank the staff of CDC's Division of Tuberculosis Elimination (DTBE) and our partners in public health for their collective efforts that led to another successful year. The accomplishments and major activities of the year include the following:

In recognition of World TB Day in March, DTBE recognized 13 TB Elimination Champions working to expand latent TB infection testing and treatment in their communities. DTBE released preliminary TB surveillance data for the United States. In November, the full surveillance report was released. There were 9,272 reported TB cases, reflecting continued, albeit slow, progress in combatting TB.

The 2017 National TB Conference in April, sponsored by the National Tuberculosis Controllers Association in collaboration with the Association of Public Health Laboratories, was held in Atlanta, GA. The conference highlighted innovative work in TB prevention, management, and care across the country. It also paved a way forward as TB professionals came together to discuss their challenges and share best practices on how to achieve TB elimination in the United States.

This year DTBE developed creative communication and education tools, including Implementing an Electronic Directly Observed Therapy (eDOT) Program: A Toolkit for Tuberculosis (TB) Programsand a new video, "5 Things to Know About TB." The video highlights the continuing problem of TB in the United States and the importance of addressing latent TB infection though targeted testing and treatment. We also had the privilege of sharing the experiences of four TB survivors through the TB Personal Stories project.

DTBE established the National Tuberculosis Molecular Surveillance Center (NTMSC) at the Michigan Department of Health and Human Services (MDHHS) Bureau of Laboratories. The center will be equipped to perform both conventional genotyping and whole genome sequencing (WGS) for all isolates of *Mycobacterium tuberculosis*.

The Tuberculosis Epidemiologic Studies Consortium (TBESC) developed and is currently testing a new latent TB infection surveillance system – Surveillance for TB Elimination Management System (STEMS). STEMS is a real-time case management and surveillance system for latent TB infection currently used by all TBESC health department sites and the Dr. Bates Outreach Clinic at the Arkansas Department of Health.

Several long-time DTBE staff retired this year. Frances Tyrrell, MPH, MT (ASCP), SM— Laboratory Consultant; Wanda Walton, PhD, MEd— Branch Chief for the Communications, Education, and Behavioral Studies Branch (CEBSB); Glenda Newell— Statistical Assistant/Analytic Steering Committee Coordinator in the Surveillance, Epidemiology, and Outbreak Investigations Branch (SEOIB); Michael Fraser—Public Health Advisor in the Field Services Branch (FSB), and Stefan Goldberg, MD— Senior Medical Officer in the Clinical Research Branch (CRB).

Thank you for everything you do in the fight to end TB.

Philip LoBue, MD, FACP, FCCP

Director

Division of Tuberculosis Elimination

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Communications, Education, and Behavioral Studies Branch Updates

TB Program Managers' Course

The overall purpose of the TB Program Managers' Course is to improve the planning and managerial capabilities of new TB program managers throughout the country. The course is designed for TB controllers, program managers, public health advisors, and nurse consultants with programmatic responsibilities at the state, big city, territory, or regional (within a state) level. Course participants occupy a TB program management position for at least 6 months but no more than 3 years, and are nominated by the DTBE Program Consultant for their area.

The course was held November 6-9, 2017 at the Centers for Disease Control and Prevention's Global Communications Center. The 4-day in-person training was divided into 18 sessions. The course emphasized the practical application of planning, management, and evaluation concepts to the specific issues and concerns of TB programs. Skills essential to TB program management were presented, followed by learning exercises and polling questions that encouraged participants to use knowledge learned.

The Communications, Education, and Behavioral Studies Branch (CEBSB) would like to thank the faculty and participants of the 2017 TB Program Managers' Course for making the course such a success. We appreciate the hard work of the faculty in preparing the materials for their sessions and the participants' enthusiasm during the course. An extra thank you goes out to the participants who traveled long distances from the U.S.-affiliated Pacific Islands.

Submitted by Molly Dowling, MPH, DTBE

New TB Personal Stories

CEBSB is proud to share the personal stories of four TB survivors: Kate, Nauman, Nicole, and Thomas. These new stories are part of our ongoing TB Personal Stories series to help raise awareness about TB in the United States. You can view the video, print, and social media content for each survivor by visiting CDC's TB Personal Stories website.

- Kate became very sick while pregnant with her second child. She was diagnosed with TB and spent more than two months in the hospital. One of her biggest worries during treatment was how the TB medicines would affect her baby. Video
- Nauman's treatment for drug-resistant TB lasted for a year and a half. Side effects from the medications and the length of treatment made completing treatment difficult. Video technology helped make his treatment much more convenient. Video
- Nicole was diagnosed with TB shortly after moving to another state. Being away from friends and family, the nurses from the health department gave her much needed support. Video
- Thomas was not sure what was going to happen when he was diagnosed with TB. He hopes his story will encourage TB patients and health care providers to talk about what to expect during treatment. Video

Many TB patients report feeling isolated and stigmatized throughout their treatment. Hearing from TB survivors who share their experiences can motivate and encourage patients to complete treatment. Using patient stories in online, print, and social media content is a powerful tool to reach clinicians, policy makers, and members of the public less familiar with TB.

DTBE would like to thank Kate, Nauman, Nicole, and Thomas for sharing their TB stories. We would also like to thank the National TB Controllers Association, Stop TB Partnership, and We Are TB for their contributions to this project.

Submitted by John Parmer, PhD, MPH, DTBE

Laboratory Branch Updates

Eighth Anniversary of Molecular Detection of Drug Resistance Implementation

DTBE implemented a clinical laboratory service, Molecular Detection of Drug Resistance (MDDR), for U.S. TB Control Programs in September 2009. The service uses Polymerase Chain Reaction (PCR) to amplify targeted genetic loci followed by DNA sequencing to detect mutations associated with drug resistance. Culture-based drug susceptibility testing (DST) is also performed. The service has evolved from the original test panel performed on isolates of *Mycobacterium tuberculosis*, Sanger sequencing of genetic loci associated with resistance to isoniazid, rifampin, fluoroquinolones, and second-line injectable drugs to include sequencing for detection of resistance to PZA and ethambutol, testing of NAAT-positive sediments from clinical specimens, and incorporation of a pyrosequencing screen for resistance to isoniazid and rifampin.

We tested 215 samples for MDDR in 2010. In 2016, we tested 710 samples (a 324% increase), and in September 2017, we reached the milestone of 4,000 samples tested since the inception of this important clinical service. Turn-around time for MDDR results is calculated quarterly; mean turn-around time has consistently been 2 or 3 calendar days and, in general, more than 90% of results are available within 4 days of sample receipt.

We strive to continually enhance the MDDR service. In the past two years, we have incorporated testing additional loci associated with isoniazid and fluoroquinolone resistance and we are currently evaluating additional loci purported to be associated with PZA resistance. We are also in the process of transitioning the service to a next generation sequencing platform and redefining our testing algorithm for the eventual inclusion of whole-genome sequencing.

We are very proud that the MDDR service has been adopted into the tuberculosis testing algorithm in the United States. Offering this service has brought the DTBE's Laboratory Branch closer to our Public Health Laboratory and Tuberculosis Control Program partners. We appreciate feedback on the service and we are always happy to answer questions. TBLab@cdc.gov

Submitted by Beverly Metchock, DrPH, D(ABMM), DTBE

Clinical Research Branch Updates

The Latest News from the TB Trials Consortium (TBTC)

TBTC 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 December 7, 2017, the study had a total of 1,522 participants, 61% of target enrollment. The AIDS Clinical Trials Group (ACTG) network is collaborating with TBTC, contributing substantially to enrollment. Twenty-two ACTG sites and 9 TBTC sites are open for enrollment. Study 31 is evaluating a novel 4-month regimen for active TB based on the use of daily, high-dose rifapentine.

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") was implemented in sites in Cape Town, South Africa, and in Lima, Peru. Enrollment and

follow-up for the study are complete. The study is currently in the analysis phase. Last month an article on the trial design was published in Trials:

Bouton, T. C., Phillips, P. P., Mitnick, C. D., Peloquin, C. A., Eisenach, K., Patientia, R. F., Diacon, A. H. (2017). An optimized background regimen design to evaluate the contribution of levofloxacin to multidrug-resistant tuberculosis treatment regimens: study protocol for a randomized controlled trial. Trials, 18(1), 563.

The main report from 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 also been recently published in the Annals of Internal Medicine.

Belknap R, Holland D, Feng PJ, Millet JP, Caylà JA, Martinson NA, Wright A, Chen MP, Moro RN, Scott NA, Arevalo B, Miró JM, Villarino ME, Weiner M, Borisov AS; TB Trials Consortium iAdhere Study Team. Self-administered Versus Directly Observed Once-Weekly Isoniazid and Rifapentine Treatment of Latent Tuberculosis Infection: A Randomized Trial. Ann Intern Med. 2017 Nov 7. doi: 10.7326/M17-1150. [Epub ahead of print]. PMID: 29114781.

Submitted by Barbara DeCausey, MPH, MBA, DTBE

Data Management, Statistics, and Evaluation Branch Updates

TB Education and Training Network (TB ETN)/ Program Evaluators Network (PEN) Webinar Summary

On December 7, 2017, the TB Program Evaluators Network (TB PEN) hosted a webinar through the National Prevention Information Network titled "Reporting for TB Infection from Diagnosis to Treatment Completion: Forging the Surveillance System of the Future with Lessons from the Past" and was presented by Andrew Tibbs. Mr. Tibbs is a senior epidemiologist with the Massachusetts Department of Public Health and chairs a latent TB infection surveillance workgroup for the Society for Epidemiology in TB Control (SETC), a subcommittee of the National Tuberculosis Controllers Association (NTCA). Over 225 TB health professionals from around the United States participated in the webinar. After his talk concluded, Mr. Tibbs facilitated a lively question and answer session to address issues and concerns from the audience.

The goal of the webinar was to update participants on recent discussions related to latent TB infection surveillance infrastructure including the implementation of a standardized case definition for latent TB infection. Mr. Tibbs also shared lessons learned from the Massachusetts experience with latent TB infection reporting and surveillance, and discussed the roles of and opportunities for training, education, and evaluation.

The following are highlights from the webinar presentation:

- New approaches and strategies will need to be implemented in order to reach TB elimination in the United States.
- In Massachusetts, latent TB infection has been a reportable condition since the early

2000's. However, latent TB infection is underreported in Massachusetts due to lack of education and training for providers, limited availability of follow up information, and no plan in place to evaluate or utilize data.
- Lessons learned in Massachusetts include being clear with providers and clinics about expectations and utilization of data, keeping a narrow focus for defining at risk individuals, and building partnerships with the community and private providers.
- SETC, a subcommittee of NTCA, developed a workgroup to examine latent TB infection surveillance at the national level. The workgroup currently has representation from 17 states, 2 counties, 1 city, and CDC. The purpose of the workgroup is to consider latent TB infection surveillance and come to a representative consensus on the direction and priority of latent TB infection surveillance activities, and to share the agreed upon position with partners.
- In 2017, the Council for State and Territorial Epidemiologists adopted the SETC surveillance definition for latent TB infection, Establishing a Case Definition for Latent TB Infection (TB Infection).
- Education and training play an integral role in latent TB infection surveillance. Many people need training on topics related to latent TB infection surveillance. There is a gap in training and education for latent TB infection surveillance in many jurisdictions.
- Elimination of TB is possible with effective public health action against latent TB infection. Measuring effectiveness of action will require building evaluation components into latent TB infection surveillance activities (including electronic surveillance systems which can capture information from a variety of sources), tools to measure the surveillance system and interactions with the surveillance system, updates to current systems that will allow us to measure reductions to disease transmission and attribute them to latent TB infection identification and treatment.
- Decreasing latent TB infection is a difficult task that will not be possible without forethought in training, education, and evaluation. However, we can learn from previous experiences and we have the advantage of building latent TB infection programs from the ground up.

TB PEN would like to thank Peri Hopkins, Health Education Specialist with CEBSB in DTBE, and the TB Education and Training Network for their support of this webinar.

To request an archived version of the latent TB infection surveillance webinar please send an e-mail to tbpen@cdc.gov.

Submitted by Rachel Yelk Woodruff, MPH, DTBE

New CDC Publications

October 2017

Reaves EJ, Shah NS, France AM, Morris SB, Kammerer S, Skarbinski J, Bradley H. Latent tuberculous infection testing among HIV-infected persons in clinical care, United States, 2010-2012. Int J Tuberc Lung Dis. 2017 Oct 1;21(10):1118-1126. doi: 10.5588/ijtld.17.0041. PMID: 28911355.

Sigal GB, Segal MR, Mathew A, Jarlsberg L, Wang M, Barbero S, Small N, Haynesworth K,

Davis JL, Weiner M, Whitworth WC, Jacobs J, Schorey J, Lewinsohn DM, Nahid P. Biomarkers of Tuberculosis Severity and Treatment Effect: A Directed Screen of 70 Host Markers in a Randomized Clinical Trial. EBioMedicine. 2017 Oct 24. pii: S2352-3964(17)30417-6. doi: 10.1016/j.ebiom.2017.10.018. [Epub ahead of print] PMID: 29100778.

Tasillo A, Salomon JA, Trikalinos TA, Horsburgh CR Jr, Marks SM, Linas BP. Cost-effectiveness of Testing and Treatment for Latent Tuberculosis Infection in Residents Born Outside the United States With and Without Medical Comorbidities in a Simulation Model. JAMA Intern Med. 2017 Oct 16. doi: 10.1001/jamainternmed.2017.3941. [Epub ahead of print] PMID: 29049814

Willby MJ, Wijkander M, Havumaki J, Johnson K, Werngren J, Hoffner S, Denkinger CM, Posey JE. Detection of Mycobacterium tuberculosis pncA mutations by the NIPRO Genoscholar™·PZA-TB II as compared to conventional sequencing. Antimicrob Agents Chemother. 2017 Oct 30. pii: AAC.01871-17. doi: 10.1128/AAC.01871-17. [Epub ahead of print] PMID: 29084743

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Boyd R, Ford N, Padgen P, Cox H. Time to treatment for rifampicin-resistant tuberculosis: systematic review and meta-analysis. Int J Tuberc Lung Dis. 2017 Nov 1;21(11):1173-1180. doi: 10.5588/ijtld.17.0230. PMID: 29037299.

Mathema B, Andrews JR, Cohen T, Borgdorff MW, Behr M, Glynn JR, Rustomjee R, Silk BJ, Wood R. Drivers of Tuberculosis Transmission. J Infect Dis. 2017 Nov 3;216(suppl_6):S644-S653. doi: 10.1093/infdis/jix354. PMID: 29112745.

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Hall EW, Morris SB, Moore BK, Erasmus L, Odendaal R, Menzies H, van der Walt M, Smith SE. Treatment Outcomes of Children With HIV Infection and Drug-resistant TB in Three Provinces in South Africa, 2005–2008. The Pediatric infectious disease journal. 2017 Dec 1;36(12):e322-7. doi: 10.1097/INF.0000000000001691.

Morris S, Miner M, Rodriguez T, Stancil R, Wiltz-Beckham D, Chorba T. *Notes from the Field*: Tuberculosis Control Activities After Hurricane Harvey — Texas, 2017. MMWR Morb Mortal Wkly Rep 2017;66:1362–1363. DOI**:** /10.15585/mmwr.mm6649a5
Olano-Soler H, Thomas D, Joglar O, et al. Notes from the Field: Use of Asynchronous Video Directly Observed Therapy for Treatment of Tuberculosis and Latent Tuberculosis Infection in a Long-Term–Care Facility — Puerto Rico, 2016–2017. MMWR Morb Mortal Wkly Rep 2017;66:1386–1387. DOI: 10.15585/mmwr.mm6650a5
Thai LH, Nhat LM, Shah N, Lyss S, Ackers M. Sensitivity, completeness and agreement of the

tuberculosis electronic system in Ho Chi Minh City, Viet Nam. Public Health Action. 2017 Dec 21;7(4):294-8. Doi: /10.5588/pha.17.0081.