Volume 13 | Number 4
Winter 2021

TN Department of Health

PUBLIC HEALTH LABORATORY NEWSLETTER

OZ Implementation is Underway

Submitted by: Gwendolyn McKee, MBA, BSMT | PH Laboratory Manager 3, Newborn Screening Mass Spectrometry and Lysosomal Disorders

TDH has begun the implementation of the OZ system for Newborn Screening samples. The OZ system is designed to improve the quality of care and reduce the time of intervention related to Newborn Screening. As of December 8, 2021, fifteen hospitals are using the OZ system to submit electronic laboratory orders for their specimens.

Currently, much of the demographic information is handwritten on the Newborn Screening sample cards when the specimen is collected before being sent to the Public Health Lab via courier or mail. This increases the chance for human error and may impact accurate assessment of the specimen and results. Specimens with missing or inaccurate demographic information are reported as unsatisfactory until the appropriate information is received, and corrections have been made. Missing and inaccurate information related to the date or time of collection and/or transfusion date can impact results and delay reporting results to the provider or birthing facilities, and therefore, hinder patient care.

The OZ system will capture demographic information directly from the patient's medical record and send it electronically to the Public Health Laboratory. Once the specimen is received, the specimen will be matched to the electronic record and eliminate manual keying of the majority of the demographic information at the laboratory. This will improve the timeliness for both the hospitals and the Public Health Lab by decreasing the amount of errors on the specimen card, reducing information searches and eliminating re-keying of data elements at the lab.

In addition, the OZ system also offers a Track Kit component that allows for cross-checking to verify that the specimen has been received at the lab. The kit also provides a shipping manifest and the ability for the facility to ensure every specimen has been received by the Public Health Lab. Hospitals will also be able to use the system to order specimen cards before cards are depleted or expire.

In 2022, it is planned to have most, if not all, of Tennessee's birthing facilities enrolled in the OZ system. The Public Health Laboratory is also working to use the OZ system to develop electronic laboratory reporting to enable the reporting of results back to the birthing facilities using the system by the summer of 2022.

As a result of implementation of this system, we anticipate an improvement in our processes by reducing human error and the timeliness of result reporting, allowing for the improvement of quality care and time to intervention.

Tennessee Emerging Infections Program

Submitted by: Katie Garman | Director, Enteric Disease Surveillance and Outbreak Investigation, CEDEP

The Emerging Infections Program is a population-based network including the Centers for Disease Control and Prevention and state health departments, working with collaborators (academic centers, local health departments, infection control practitioners and other federal agencies) to assess the public health impact of emerging infections and to evaluate methods for their prevention and control.

The Tennessee Emerging Infections Program is a collaborative effort of the Communicable and Environmental Diseases and Emergency Preparedness section of the Tennessee Department of Health, the Vanderbilt University School of Medicine, the Department of Health Policy and the Centers for Disease Control and Prevention.

The core activity of the EIP is active surveillance of laboratory-confirmed cases of reportable pathogens. Laboratory directors and staff, physicians, nurses, infection control practitioners and medical records personnel are key participants in EIP. Components of the EIP in Tennessee investigate foodborne infections (FoodNet), invasive bacterial infections (ABCs), influenza activities and healthcare associated infections. A list of all reportable pathogens by specimen source under enhanced surveillance can be found at: https://www.tn.gov/content/dam/tn/health/program-areas/lab/announcements/EIP_Benchbuddy_%20updated_07_27_2021.pdf.

Spotlight on Safety: Biosafety in Microbiological and Biomedical Laboratories BMBL 6th Edition

Submitted by: Rolinda Eddings, MT(ASCP) | PH Laboratory Consultant 3, Safety Officer and Responsible Official

The BMBL was initially published in 1984 and is a joint publication between the Centers for Disease Control and National Institutes of Health. Each revision has built upon advances in biomedical science and establishes performance-based guidelines. This guidance document is not regulatory, but very important as a reference and standard for best laboratory practices. The 6th edition may be accessed at: https://www.cdc.gov/labs/BMBL.html.

Changes to the BMBL 6th edition include:

- More emphasis on risk assessment. The best practices outlined in the BMBL may or may not fit your laboratory needs/activities or institutional risk tolerance.
- New appendices have been added: Large Scale, Sustainability, Inactivation and **Clinical Laboratories (Appendix N)**
- Declarative Statements
  - Current language: "The laboratory supervisor must enforce the institutional policies that control access to the laboratory"
  - New language: "The laboratory supervisor enforces the institutional policies that control safety in and access to the laboratory"
- Occupational Health
  - Overhauled to emphasize the need for a risk-based approach to providing occupational health support to laboratories
- New overarching introduction notes the applicability of additional resources for agent information
  - Public Health Agency of Canada's Pathogen Safety Data Sheets: https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html
  - Control of Communicable Diseases Manual: https://www.apha.org/ccdm
  - Manual of Clinical Microbiology: https://clinmicronow.org/doi/book/10.1128/9781683670438.MCM
  - ABSA International Risk Group Database: https://my.absa.org/tiki-index.php?page=Riskgroups
- Primary Containment
  - Harmonized with NSF/ANSI 49 Standard with exhaust alarm requirement for canopy connected Class II Type A biosafety cabinets
  - Recommendations provided for laboratories that choose to allow ultraviolet lights in BSCs
- Updated to identify U.S. regulations surrounding disinfectants
  - Clarified relationship between concentration and activity level of disinfectant
- Transportation updated to reflect changes in contacts at regulatory agencies
  - DOT will now require "hands-on" training for certification of shipping infectious substances

For more details regarding changes in the BMBL 6th edition go to: https://absa.org/bmbl/

Announcements

- **Change in Laboratory Results Reporting: Effective December 13, 2021), County and Metropolitan Health Departments can expect qualitative (reactive/non-reactive/indeterminate) and quantitative (viral load) results for Hepatitis C Nucleic Acid Amplification Tests.**
- **Environmental Microbiology Fee Increase: Rates for water bacteriological testing increased 10% effective September 2021.**

Please visit the TDH Laboratory Services Webpage for more information and other announcements: https://www.tn.gov/health/health-program-areas/lab.html

Methylmalonic Acidemia Screening in Tennessee

Submitted by: M. Christine Dorley, PhD, MT(ASCP), Assistant Director | Newborn Screening
on behalf of Jordan McCorkle, Former PH Laboratory Scientist , Newborn Screening

Methylmalonic acidemia is an example of an inborn error of metabolism. MMA is a condition caused by inheriting two broken copies of a specific gene resulting in an autosomal recessive metabolic disorder. MMA is a devastating disorder that occurs in the US at a rate of about 1: 50,000 births and as such, makes it a good candidate for Newborn Screening. [1,2] The disease caused by this genetic mutation presents itself in older infants (one month to one year) with progressive mental and developmental delays, seizures, coma, enlarged liver, kidney failure, respiratory and heart dysfunction, and in severe cases, death. Total deficiency of vitamin B_{12} results in an identical syndrome and highlights the metabolic processes implicated in the mechanisms of MMA.[3]

MMA occurs when an individual is unable to form functional enzymes which are needed to breakdown amino acids (specifically isoleucine, methionine, valine, threonine), with the most severe forms of the disease arising when the *MUT* gene is implicated. The *MUT* gene encodes methylmalonyl-coenzyme A mutase which is responsible for converting methylmalonyl-coenzyme A to succinyl-coenzyme A in the mitochondria and requires vitamin B_{12} (cobalamin) to form a fully functioning enzyme. When this protein can no longer function efficiently, a buildup of methylmalonic acid and related compounds occurs and these can then be targeted for analysis through tandem mass spectrometry. The TDH Public Health Laboratory Newborn Screening section screens for this disorder using the analyte marker C3 (propionylcarnitine) and the ratio of C3/C2.

The Newborn Screening section has validated a second-tier test that specifically targets MMA and related disorders in order to improve positive predictive values and decrease wait times for affected families. Treatment options for this disorder include dietary changes (such as a low protein diet, carnitine and cobalamin supplementation) and kidney or liver transplant. [4] Despite these treatments, continued neurological decline may occur. As recently as 2017 a lipid nanoparticle encapsulated mRNA therapy (the same approach as Pfizer's Covid-19 mRNA vaccine) was tested on mice and showed around 80% reduction in methylmalonic acid in the blood, highlighting the promise of new approaches. [5]

References:

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4366921/
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3210240/
3. https://www.nejm.org/doi/full/10.1056/NEJM197808172990701
4. https://www.sciencedirect.com/science/article/pii/S0022347615000980
5. https://www.sciencedirect.com/science/article/pii/S2211124717317485

Azole Resistance in *Aspergillus fumigatus* and the Link to Agricultural Use

Submitted by: Natasha Lindahl, MT(ASCP)CM | PH Laboratory Manager 2, Special Microbiology

Aspergillus fumigatus and humans have both been indirectly impacted by practices meant to provide food supply security such as the broad use of antifungals in modern agriculture. Since the beginning of agricultural history, farmers have dealt with a number of environmental challenges that reduced crop yields such as droughts, pests and fungal blights. During the growing season of 1973, the highly efficient broad-spectrum azoles were first released for the agricultural use. The azoles were used for 20 years in agriculture prior to their introduction to human medicine in the early 1990's. *Aspergillus fumigatus*, though not directly targeted by the application of fungicides, has become the unintended target to the widespread use of azoles in agriculture.

Aspergillus fumigatus is found in nature as an organism that feeds on dead and decaying organic matter and as an accidental opportunistic pathogen. Globally, it causes 300,000 cases of invasive disease and more than ten million cases of chronic and allergic disease due to the inhalation of spores on an accidental basis. Clinical management of aspergillosis largely relies on the Azole class of antifungals. The first-line antifungals recommended for treatment clinically are Voriconazole and Isavuconazole. Clinical resistance to azoles in *Aspergillus fumigatus* is becoming an increasing problem. Patients can develop resistance during their treatment; however, the emerging resistance has been mainly linked to the use of azoles in agriculture. Resistance mechanisms have developed over time as a slow shift resulting in decreased sensitivity via mutations in target proteins.

The TDH Public Health Laboratory is one of two Antimicrobial Resistance Lab Network regional sites offering testing for azole resistance in *Aspergillus fumigatus*. Following testing, results will be reported to submitting facilities as well as jurisdictional public health departments within two weeks of receipt of the isolates. Testing is available to all states at no cost, including shipping. Clinical, reference and public health

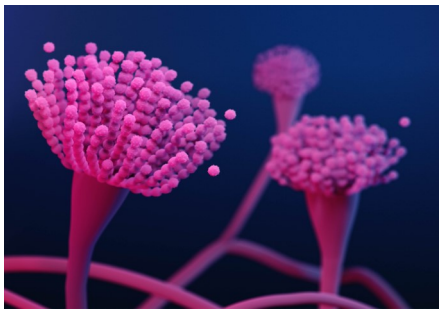

Image: CDC/Stephanie Rossow

laboratories submitting isolates should:

- Submit clonal isolates (selected from a single colony) that have already been identified as *Aspergillus fumigatus* by any CLIA-approved method.
- Ship on Sabouraud Dextrose agar slant.
- Prioritize isolates from invasive infections, as well as isolates that, if tested, show resistance to azoles.

For more information or to discuss the submission guidance and shipping instructions, please contact the AR Lab Network Regional Laboratory at the Tennessee Public Health Laboratory in Nashville: ARLN.health@tn.gov

For more information, please see the CDC AR Lab Network guidance on the CDC's AR Lab Network website: https://www.cdc.gov/drugresistance/laboratories.html

References:

https://www.cdc.gov/drugresistance/laboratories.html

Barber AE, Riedel J, Sae-Ong T, Kang K, Brabetz W, Panagiotou G, Deising HB, Kurzai O. 2020. Effects of agricultural fungicide use on Aspergillus fumigatus abundance, antifungal susceptibility, and population structure. mBio 11:e02213-20. https://doi.org/10.1128/mBio .02213-20.

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Dorley Receives 2021 APHL Everyday Life Saver Award in Newborn Screening

During the Association of Public Health Laboratory's Newborn Screening and Genetic Testing Symposium in October, Newborn Screening Assistant Director Dr. Christine Dorley was awarded the APHL Everyday Life Saver Award in Newborn Screening. The award is given to honor a person working in newborn screening and judged by the Symposium Planning Committee to have made meaningful and significant contributions to their newborn screening program. The intent of this award is to highlight the small but substantial ways the recipient contributes to the morale of their team and/or operations of their program on a daily basis.

Dr. Dorley's contributions to the TN Newborn Screening program have been substantial and far reaching for families across the State of Tennessee. Dr. Dorley's accomplishments include:

- In 2017, led the Tennessee effort to onboard the testing for Lysosomal Storage Disorders.
- Awarded over $1,000,000 in grants for new testing and equipment for the NBS laboratory.
- Helped decrease the unsatisfactory rate to less than 2.7% of TN submissions.
- Achieved a turn-around time of 100% specimens reported by day of life 5 and 99.7% by day of life 7.
- Led an effort (over a holiday weekend) to process four days of specimens from South Carolina NBS as a result of a South Carolina network outage.
- Maintained and coordinated NBS operations during a one year period that experienced network outages and staff shortages from several catastrophes including a bombing, a tornado and winter ice storms.

Dr. Dorley brings a passion everyday for her work in Newborn Screening and uses it to inspire her staff and coworkers. She is admired by her staff and peers and uses that trust to educate and develop the NBS workforce. The citizens of Tennessee are fortunate to have someone as compassionate and competent as Dr. Dorley to oversee the NBS effort and protect babies born in the State. She is truly a life saver.

EMPLOYEE NEWS

Welcome New Employees!

Matthew Lisk
Admin Secretary
Administration

Hailee Clemons
Contract Admin Assistant
Human Resources

Galen Montgomery
Contract Scientist
Molecular Biology

Sheri Haviland
Admin Secretary
Knoxville Regional Lab

Darian Williams
Contract Scientist
Molecular Biology

Karen Beasley Maynard
PH Laboratory Scientist 2
Molecular Biology

Promotions

Victoria Arnish
PH Laboratory Scientist 2
Newborn Screening

Zachary Perry
PH Laboratory Manager 2
ARLN

Patrick Leathers
PH Laboratory Manager 2
Chemistry

Bel Dalton
PH Laboratory Scientist 1
ARLN

Aida Liza Trinidad
PH Laboratory Scientist 2
Newborn Screening

Bill Moore
PH Laboratory Consultant 2
Chemistry

Retirements

Monna Jedd
6 years of Service
PH Laboratory Scientist 2
Special Microbiology

Interested in a Public Health Lab Career?

Visit https://www.tn.gov/health/health-program-areas/lab/lab-services-careers.html for current employment opportunities!

The Mission of Laboratory Services is to provide quality testing services through innovation, collaboration, and education that protects and improves the health of all.

Department of Health, Authorization No. 343472, December 2020. This public document was promulgated at a cost of $0.00 per copy.

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Tennessee Department of Health
Division of Laboratory Services
630 Hart Lane | Nashville, TN, 37243
T: 615-262-6300 | F: 615-262-6393 | https://www.tn.gov/health/health-program-areas/lab.html