



DELAWARE LABORATOR

Summer 2007

EXTENSIVELY DRUG-RESISTANT TB (XDR-TB)

Diane M. Hindman, BS, MT (ASCP) SM, Microbiologist II



Inside this issue:

| | |
|--------------------------------------|---|
| <i>Extensively Drug Resistant TB</i> | 1 |
| <i>DPHL Meetings and Trainings</i> | 2 |
| <i>Why We Analyze Drinking Water</i> | 3 |
| <i>New Employees</i> | 3 |
| <i>DPHL New Equipment</i> | 4 |
| <i>NLTN Meeting</i> | 5 |

Many of us have been reading about the dangers posed by resistant strains of tuberculosis since an American who was initially reported with extensively drug-resistant tuberculosis (XDR-TB) traveled to Europe and back. At the end of May, CDC announced it had taken the rare step of issuing a federal public health isolation order against the Atlanta-area man after he flew to Paris and Montreal, potentially exposing over 100 people.

So, what exactly is extensively drug-resistant TB? Like all TB bacteria, XDR-TB is spread when a person with the infection in their lungs or throat coughs, sneezes, speaks or sings. Depending on the environment, the bacteria can remain airborne for several hours. People inhaling these bacteria can become infected. Though rare in the US, XDR-TB is serious because it leaves patients with less effective treatment options, and they often have worse treatment outcomes.

Since the 1990s, public health programs have become accustomed to dealing with multi-drug resistant tuberculosis (MDR-TB). These strains of *Mycobacterium tuberculosis* are resistant to isoniazid and rifampin, two of the most effective first line antibiotic drugs, but susceptible to other first line and second line drugs. Huge efforts have been made in the United States to promote appropriate treatment of all TB patients in order to prevent the emergence of more resistant strains. Proper management of identified cases

is critical in order to assure infection control.

Unfortunately, TB bacteria have emerged that are resistant to the most powerful medicines available. XDR-TB is resistant to isoniazid and rifampin, and at least three of the six main classes of second-line drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid). When TB bacteria are resistant to the most powerful medicines, only less effective, more toxic and very costly medicines are left for treatment, and in some cases, there are no effective medicines at all. This is why XDR-TB is much more costly and deadly than the usual forms of TB. The case fatality rate for XDR is 30-35 percent. In HIV positive patients, it exceeds 95 percent.

Drug resistance is a man-made problem. XDR-TB strains have been found in over 30 countries including the U.S. In the face of federal cuts to TB funding to most states since 2005, public health programs have less than adequate staff to find and treat all of these cases and their contacts. Across the U.S., this front-line work—labor intensive directly observed therapy is essential to prevent the development and spread of drug resistant strains of TB.

In Delaware, all first time TB isolates from patients are requested to be sent to the Delaware Public Health Lab (DPHL) for susceptibility testing. Any reports of positive cases that come from

Continued, Page 3

Special Points of Interest

DPHL Meetings and Training, March—June 2007

Page 2

New Equipment

Page 4



DPHL MEETINGS AND TRAININGS, MARCH – JUNE 2007

Marion Fowler, Microbiologist II and Tara Lydick, Chemical Preparedness Coordinator

The small state of Delaware was well represented at the March 12-16, 2007 Emergency Response for Chemical Laboratory Conference (ERCLC – formerly known as PHELGM) in Atlanta, GA by Chemical Preparedness Chemists Lynne Dyer and Jaccie Barnes. This conference was a series of highly technical workshops structured as reviews and introductions to current and emerging methods, techniques, and instrumentation for bench chemists.

“We went back to [chemistry] school; learning more about instrumentation and theory in three hours than what we may have had at the University in a semester”. This year’s conference was also open to Environmental Laboratory personnel who are being integrated into chemical terrorism response. Outside of training, this meeting allows many of the differing state chemists to meet in person and exchange troubleshooting techniques, methodology issues and solutions, and highlight their state’s progress and involvement in preparedness activities.

On March 22, 2007, DPHL and the NLTN sponsored the first “Agents of Bioterrorism: Training for the Sentinel Lab”. This wet workshop provided hands on training to many of Delaware’s hospital laboratorians. Due to its success, the wet workshop will be held yearly. The class will be expanded to a full day. The morning session will include lectures, power point presentations and classroom information related to the BT agents, Laboratory Response Network, and safety procedures. The afternoon session will consist of the hands- on wet workshop and will be held in the laboratory. There will be plenty of time to observe the microorganisms, record observations, look at smears and review the unknowns.

Public Health week was the first week in April and Representative Mike Castle visited the DPHL during the second week of April. Representative Castle, Dr. Jaime Rivera, Director of Public Health and Dr. Paul Silverman, Associate Deputy Director spent several hours touring the Lab. Representative Castle was especially interested in learning about laboratory biological and chemical terrorism preparedness and DPHL staff was happy to enlighten him!



Left: Representative Michael Castle visits the DPHL Lab.

Right: Rep. Castle speaks with Jaime Rivera, MD, FAAP, Director of Public Health



Left: Rep. Castle and Dr. Jane Getchell, Lab Director.

Right: Lynne Dyer, Analytical Chemist III discusses Chemical Terrorism Preparedness with Rep. Castle.

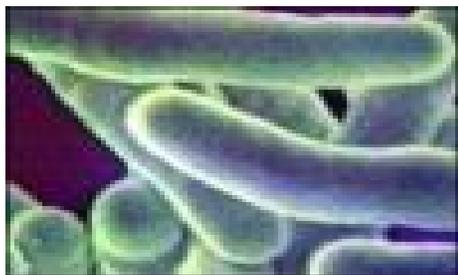


The third week of April was National Medical Laboratory Week. Governor Minner signed a proclamation to honor all laboratory scientists. Dr. Jane Getchell and Rebekah Parsons were at the signing, which included a discussion of the need for certification of clinical laboratory professionals and the declining work force of skilled laboratory scientists.

Tara Lydick, Chemical Preparedness Coordinator, attended the Department of Transportation (DOT) Transportation of Hazardous Materials Certification course in Oklahoma City, Oklahoma April 9-13. This course covered the latest updates to the Code of Federal Regulations 49, Parts 100-185 as well as an overview of the requirements for each mode (air, highway, vessel, and rail) of transportation. This course or an equivalent certification is required for all HazMat employees every two years as defined in the regulations. Revisions to the collection, packaging, shipping, and documentation modules will be made and distributed electronically to all sentinel and Level 3 facilities and HazMat teams. Any changes in contact information should be directed to Liz Moore at liz.moore@state.de.us.

Continued, page 6

Drug Resistant TB, continued from page 1



reference labs are also sent to the Delaware TB Program office at the Thomas Collins Building in Dover, so that we are aware of Delaware cases that may have been tested out of state.

Fortunately, only a single case of MDR-TB has been reported in Delaware, and this occurred in October 1996. Delaware has never had a case of XDR-TB, but remains on the lookout for it. The DPHL procedure for susceptibility testing includes routine broth testing against the first-line drugs of isoniazid, rifampin, ethambutol, PZA and streptomycin. Any occurrence of resistance is confirmed prior to reporting out. Any case of MDR-TB or XDR-TB is automatically referred to CDC for follow up testing to second line drugs in the categories of aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid. CDC has a standard protocol, but testing of specific drugs and MICs may be available on request.

For more information, use the following suggested links:

Laboratory handling: http://www.cdc.gov/tb/xdr/tb/Biosafetyguidance_xdr/tb.htm

General info: <http://www.cdc.gov/tb/faqs>
<http://www.who.int/tb/en>



WHY WE ANALYZE DRINKING WATER

Amir Saad, Ph.D., Analytical Chemist III

Many pollutants (i.e. nitrate, lead and cyanide) are colorless, odorless, and even tasteless and can only be detected by laboratory analysis.



The Delaware Public Health Laboratory, performs analysis for Coliform bacteria and over 140 chemical pollutants in drinking water, including:

- | | |
|----------|----------|
| arsenic | uranium |
| nickel | fluoride |
| cyanide | nitrate |
| hardness | nitrite |
| copper | iron |
| fluoride | cadmium |
| mercury | sodium |
| lead | chromium |

Pesticides (such as Chlordane)
 volatile organic compounds (such as benzene and MTBE)*
 Disinfectants, also known as trihalomethanes (such as chloroform and bromoform)

According to Ed Hallock, Program Administrator, the Delaware Office of Drinking Water, annual testing for bacteria and testing every three years for pollutants (such as nitrate) is recommended for private wells. Bacterial and chemical water analysis test kits cost only \$4 for the citizens of Delaware, and can be purchased with sampling instructions from the following:

Sussex County Health Unit
 Georgetown
 (302) 856-5496

James Williams State Service Center
 Dover
 (302) 744-1220

New Castle County Health Unit
 Wilmington
 (302) 995-8650

*The next Laboratory will feature the newly purchased Gas Chromatography/Mass Spectrometer (GC/MS) and its use for analyzing volatile organic compounds (VOCs).

New Employees at DPHL



The Newborn Screening Laboratory welcomes Shakimma (Kimmie) Turner to their ranks. Kimmie was promoted from the Environmental & Molecular Biology Section of Delaware Public

Health Laboratory. She brings a variety of laboratory skills, enthusiasm and a willingness to work hard. Congratulations Kimmie!

Amanda Bundek joined the Environmental & Molecular Microbiology Laboratory as a microbiologist II. She is also responsible for testing in the Virology Section. As a Virginia Tech graduate with a BS in biochemistry, Amanda has held chemist positions at Dade Behring and at the Medical Examiner's Office. She also participated in research projects at the National Institute of Health. Amanda is enthusiastic about joining DPHL and focusing more on her biological background.



Congratulations Kimmie and a warm welcome to Amanda!!

DPHL NEW EQUIPMENT, MARCH – JUNE 2007

Tara Lydick, Chemical Preparedness Coordinator

In June, the Chemical Preparedness Laboratory installed a new high performance liquid chromatograph tandem mass spectrometer (HPLC/MS/MS or LC/MS/MS). The Applied Biosystems, Inc. API 4000 with an Agilent Technologies, Inc. Series 1200 HPLC allows DPHL to meet its Laboratory Response Network – Chemical (LRN-C) Level 2 laboratory methodology requirements and expand their capabilities.

HPLC/MS/MS or LC/MS/MS



DPHL purchased this instrument through CDC Public Health Emergency Preparedness Cooperative Agreement funding. The instrument includes a 96-microwell plate and standard autosampler, capillary and isocratic pumps for nano and micro flow rates, a diode array detector and software capable of transferring results directly to our Laboratory Information Management System. Because of its size, power, and exhaust requirements, the Chemical Preparedness Laboratory relocated other instruments and equipment to provide a physical space and allow the LC/MS/MS to be integrated into the laboratory uninterrupted power supply, unfortunately slowly displacing one of our analysts. A name will be determined once the instrument's personality is found — hopefully not Greedy!

The instrument will be used for a variety of methods, beginning with the nerve agent metabolites in urine method training in October 2007. Upon successful validation, the Chemical Preparedness staff will attend training to bring on board other methods including ricin and abrin (ricinine and abrinine biomarkers) in urine, nitrogen mustards in urine, adamsite (vomiting agent), riot/tearing agents, and lewisite metabolites. As part of the all-hazards approach and full use directives, the Chemical Preparedness laboratory anticipates utilizing the instrument for other preparedness and routine testing, including development of Environmental Laboratory Response Network, Food Emergency Response Network, EPA water security initiative, and EPA unknown chemical screening methods. Because of the wide range of materials, matrices, and testing algorithms, this instrument can also be used for biomonitoring and biota monitoring studies, should funding become available. The instrument can also serve as a back-up instrument for the Newborn Screening Program.

Unlike a gas chromatograph mass spectrometer (GC/MS), the LC/MS/MS is able to analyze materials in the liquid phase or when soluble in a wide range of solvents. This allows DPHL to analyze materials of a

higher molecular weight range, which may not be volatile enough for analysis through GC/MS. The liquid chromatograph (LC or HPLC) introduction system performs separations based on the type of column and the solvents used as the mobile phase to push and separate the analytes and components of interest. This allows differing matrices and materials to be readily analyzed. The sample is stripped of solvent, ionized, and introduced to the mass spectrometer. Through the use of a series of electrical voltages, the quadrupole induces a field that allows the ions to be separated according to the mass and charge of the analyte. The resulting signal can then be used to determine the concentration and identity of the analyte.

However, analysts must optimize the conditions for the analytes of interest. If too much voltage is applied, the analyte can fragment into smaller well defined patterns. The fragmentation analysis can be useful in differentiating compounds of similar molecular weight or structural isomers. To best utilize the fragmentation analysis, a second quadrupole is needed. This type of instrument is frequently called a “tandem mass spectrometer” because it has more than one quadrupole in sequence or tandem. DPHL's new system is a triple quadrupole with a quadrupole ion filter. With this configuration, the analyst can perform a variety of studies by the use of the second quadrupole as a collision cell. Simply, the ions of interest are selected in the first quadrupole and then collide with a gas in the second quadrupole. The new ions generated then travel into the third quadrupole. Once here, ions of interest can be selected and read for analysis. There are several variations on this technique, including product ion scans, precursor ion scans, and neutral loss scans allowing specialized detection leading to conformational or transitional analysis. Interpretation of the mass spectra generated requires a complex software package and a devoted analyst. Many chemists have devoted their life's work to the understanding of specific mass spectrometry analysis techniques.

With the installation of this instrument, the Chemical Preparedness staff completed brief familiarization training at DPHL. Two chemists traveled to Framingham, MA to attend the Applied Biosystems API 4000 operator's training course in June. Now that staff have returned and worked with the instrument, Applied Biosystems will provide an on-site course in preparedness techniques with the LC/MS/MS for DPHL staff. In October 2007, two chemists will travel to Atlanta, GA to complete the CDC's training on nerve agent metabolites in urine. Upon their return, they will validate the method over the course of the next 90 days. After completing the next scheduled proficiency test, the Chemical Preparedness Laboratory will earn LRN-C Qualified status for this method and be eligible to attend ricinine and Abrinine Biomarker training at the CDC. DPHL is excitedly looking forward to the expansion of capabilities and techniques this new instrument offers. Please do not hesitate to contact the Chemical Preparedness Coordinator with any inquires, questions, or comments regarding the instrument or Chemical Preparedness Program.

**NATIONAL LABORATORY
TRAINING NETWORK
SAN ANTONIO, TEXAS,
APRIL 27—MAY 2, 2007**

Kathy Gray, DPHL State Training Coordinator

Tex-Mex dining, the Spurs fans, the Riverwalk, the Alamo, the Night in Old San Antonio Fiesta, and the National Laboratory Training Conference IV — I had the great fortune to visit San Antonio in April and experience all of the above.

I was there to learn more about the NLTN and its planned reorganization and the benefits the NLTN brings to Delaware Public Health Lab. Almost every state was represented at this national meeting and while I am familiar with the state training coordinators (STC) in my region, I had not met anyone outside of the Northeast region. I am part of a large network of knowledgeable, resourceful, and creative people dedicated to the continuing education of laboratory professionals and the advancement of the profession in public health as a whole.

The theme of the conference was “Preparing the Laboratory Workforce”. Lectures and presentations were given on such topics as shortages in the public health and healthcare fields; the improvement, maintenance and recruitment of staff at all levels; diversity; and the education of the public about public health (and general health related occupations) - who we are, what we do, and how to work together for solutions to the growing need to fill these positions. Some states have produced very creative presentations about biology and health-related fields for kids as young as 10 years old to introduce them to science outside of the classroom. The purpose is to get them interested in a science field in general so they will hopefully pursue a career in that subject.

Competent people are needed to not only fill open positions now, but also to train the upcoming workforce as current public health personnel age and retire. Programs must be developed and staffed at universities. Cooperative agreements must be forged between hospitals, corporate and commercial entities, communities, and governmental agencies to ensure the proper training of this workforce.

Once the workforce is in place, constant improvement via continuing education is needed as technology, sciences, and new issues evolve. Bioterrorism and chemical terrorism require special training for events we hope never happen. We are constantly practicing drills, testing samples, and testing ourselves to be ever-ready for whatever may come to our community – whether it is a pandemic flu, a chemical terrorism event, or an outbreak of gastroenteritis at a community picnic, public health and all its partners must be ready at all times.

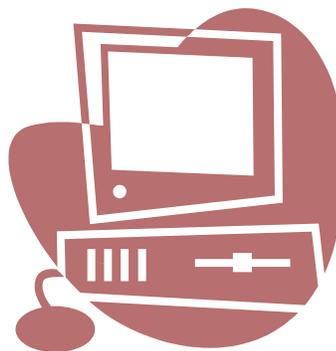
The NLTN is undergoing reorganization in an ongoing effort to bring programs and resources to each state in an economical and

effective manner. With NLTN’s resources, we can remain up-to-date on our methods, technology, information and training. Regional groups are giving way to a more national system. Programs once done regionally will now be available on a national level. I am looking forward to the positive changes this will bring to our lab and to the public health laboratory system in general.

NLTN CALENDAR OF UPCOMING EVENTS
July—September, 2007

| Date | Title | Location |
|------|---|------------------|
| 7/16 | Laboratory Identification of Emerging Pathogenic Molds | Atlanta, GA |
| 7/24 | 2007 Harmonization of Shipping Regulations | Chattanooga, TN |
| 7/25 | 2007 Harmonization of Shipping Regulations | Knoxville, TN |
| 7/25 | Biomonitoring: The Challenges of Human Exposure Assessment | Waltham, MA |
| 7/26 | 2007 Harmonization of Shipping Regulations | Johnson City, TN |
| 8/7 | 2007 Harmonization of Shipping Regulations | Memphis, TN |
| 8/8 | 2007 Harmonization of Shipping Regulations | Jackson, TN |
| 8/15 | Phlebotomy: A Sharper Focus | |
| 8/22 | Identification of Medically Important Filamentous Fungi | Ankeny, IA |
| 9/12 | Identification of Medically Important Filamentous Fungi | St. Paul, MN |
| 9/12 | Serologic Testing for Parasitic Diseases | |
| 9/26 | Fungal Identification in the Clinical Lab: Quality, Cost-Effectiveness and Clinical Relevance | |

For more information on any of the listed events, contact the National Laboratory Training Network at http://www.cdc.gov/nltn/nltn_cal.aspx



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New!!! Biological Preparedness Section; Preparedness Testing Forms and Procedures; Chain of Custody Forms and Procedures; Packaging and Shipping Instructions; View Past Issues of the Laborator.

www.dhss.delaware.gov/dph/lab/labs.html

The Laboratory Preparedness Advisory Committee (LPAC) meeting was held on May 3, 2007 at the Delaware Public Health Laboratory (DPHL). The format included a morning session on bioterrorism and clinical public health issues, lunch and discussions on chemical terrorism and environmental public health issues. The morning session discussed the upcoming College of American Pathologists (CAP) Laboratory Response Network (LRN) survey and the shipping requirements as well as DPHL's involvement in the recent food outbreaks. The afternoon session discussed better integration of suspected chemical exposure responses beyond simply collecting an environmental sample. A preliminary draft of collection protocols and kits was distributed for comment by participants as well as the annual survey for all sentinel, Level 3, and LPAC laboratories: The Instrumentation, Methodology, Matrices, and Protocols Survey targets all laboratories, response groups, and emergency departments involved in any potential exposure or preparedness incident. If you have not received a copy of the survey, please contact Tara Lydick via e-mail, tara.lydick@state.de.us.

Tara Lydick attended the International Association of Fire Chiefs Hazardous Materials Response Conference in Hunt Valley, MD on May 31—June 2, 2007. This international conference provides 80 minute to full-day training and discussion sessions on a variety of response issues, ranging from the basics (decontamination, ICS and NIMS compliance) to new techniques for an ever-changing world. One session dealt with integrating a regional group to better align with national and regional risk assessments and needs. Another topic hotly debated was the use of handheld field screening kits for biological agents. The Department of Homeland Security has endorsed two opposing protocols: one is

an all-hazards triage protocol to rule out other hazards before biological testing at a LRN reference laboratory (such as DPHL), while the other is an ASTM standard for any suspected biological agent which directs responders to collect all visible powder for the LRN Reference Laboratory and use a swab for in-field screening. Any group wishing to be involved in further discussion of Delaware's collection protocols should contact Tara Lydick by e-mail.

It's the end of an era...or at least a year, as Dr. Jane Getchell turned over her president's scepter at the annual meeting of the Association of Public Health Laboratories held in Jacksonville, FL on June 3-5, 2007. Dr. Getchell has been heavily involved in APHL's Infectious Disease Committee as well as working hard as president to ensure that APHL maintains a strong voice representing laboratorians and the vital work they do. This year's meeting also served as the First State Environmental Laboratory Conference, working to bring environmental laboratories involved in the public health arena to participate in APHL and also have a voice for their needs. Posters were displayed throughout the meeting, with vendors in the exhibit hall. The meeting, serving as the annual business meeting, provided three days of roundtable, plenary, and concurrent sessions spanning a wide range of topics. Tara Lydick presented a short overview of the work done as a member of the Environmental Health Committee on the Department of Homeland Security Targeted Capabilities Lists for the Environmental Monitoring and Assessment and the Site Remediation and Assessment working groups. The closing keynote speaker challenged public health professionals to not only consider standard laboratory testing, but to look further at food, environmental, and other responses as a vital interest of the public and their health.

Collaborative efforts to develop surge capacity within Delaware and between neighboring states are in progress. Dela-

ware's Christiana Care Health System and DPHL are working on a memorandum of understanding for surge capacity. Maryland has recently passed a law that allows it to help another state or receive help from another state before a state of emergency is declared. For the Maryland law to be effective, Delaware and other neighboring states must pass a similar law.



DELAWARE DIVISION OF PUBLIC HEALTH LABORATORY

30 Sunnyside Road
Smyrna, DE 19977
(302) 223-1520

Built: 1990

Business Hours: 8 a.m. – 4:30 p.m.

Purpose: The Division of Public Health Laboratory currently offers consultation and laboratory services to state agencies, Delaware Health and Social Services and Division of Public Health programs including:

- HIV surveillance and prevention
- Immunization
- Lead
- Epidemiology
- Newborn Screening
- STD prevention
- TB Elimination
- Drinking water
- Preparedness

Jaime "Gus" Rivera, MD, FAACP
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If you have questions regarding these articles or would like to receive a hard copy of this newsletter, contact the Delaware Public Health Laboratory at 302.223.1520.



"To Protect and Enhance the Health of the People of Delaware"