Philadelphia Department of Public Health

Philadelphia TB Newsletter

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Tuberculosis Control Program
500 S. Broad Street, 2nd Floor
Philadelphia, PA 19146

The Philadelphia TB Newsletter is a quarterly publication that is intended to be a resource for clinicians, infection control personnel, and laboratories who diagnose, treat, and/or report tuberculosis (TB) in Philadelphia. It provides treatment updates and recommendations, reviews local and national TB epidemiology, and presents case studies.

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INSIDE THIS ISSUE

Tuberculosis Genotyping Program

By Dan Dohony, MPH
CDC Senior Public Health Advisor

The Philadelphia TB Program has been approved to participate in the CDC Tuberculosis Genotyping Program. Currently, all TB isolates from the Philadelphia TB Lab are being sent to the Michigan Department of Public Health Lab which has been contracted by the CDC to perform genetic analysis on *M. tuberculosis* complex isolates. As of December 31, 2007, the National Tuberculosis Genotyping Database had received 32, 783 isolates and identified 9,199 specific strains of M. tuberculosis. Of these, 7,500 are unique genotypes with no other national matches. Hospital and commercial labs are encouraged to send TB isolates to the Philadelphia TB Lab for inclusion in the genotyping program.

Genotyping is considered to be a difficult concept for most lay people to understand, but is really quite simple. Genotyping is analyzing the DNA of each TB isolate to determine the genetic constitution or the DNA fingerprint. Each new bacillus from the reproduction of Mycobacteria is therefore a replicate of its parent strain. Diversity among TB isolates is common as Mycobacteria have manifested mutation strains which assist in identifying instances of recent transmission of TB and the chains of transmission that occur among persons with TB.

There are many advantages to genotyping in identifying, tracking, and controlling tuberculosis:

- TB genotyping results, when combined with epidemiologic data, help to distinguish TB patients who are involved in the same chain of recent transmission.
- Results provide help in early detection of outbreaks by confirming linkages between cases when people share a genotype cluster. This allows for earlier treatment.
- TB controllers can track unexpected or unusual transmissions when people who would not normally be connected are both part of a genotypic cluster.
- Identification of false positives due to cross-contamination in labs between patient specimens and control strains.
- It also helps to identify TB patients whose disease is the result of reactivation of a TB infection that was acquired in the

(Continued on page 4)

Ten Killer Facts about TB

- Every 20 seconds, someone in the world dies of TB.
- Two billion people, or about one-third of the world's population, are infected with the bacteria that causes TB.
- About one out of every 10 of those people will develop active TB.-- If left untreated, a person sick with TB in their lungs can infect 10 to 15 people a year.
- TB is the leading infectious killer of people living with HIV/AIDs in the world.
- Some 9.2 million new cases of tuberculosis occurred worldwide in 2006, up nearly 40 percent from 1990, due mostly to population growth.
- India had the highest number of new absolute cases, followed by China, Indonesia, South Africa and Nigeria.
- Just 22 countries account for 80 percent of the worldwide cases of TB. The disease is most prevalent in developing countries.
- Multi drug-resistant TB, a form of TB that does not respond to the usual drugs and must be treated with special drugs, has proliferated in recent years and causes about 130,000 deaths annually.
- An even more extreme form of drug resistant TB, known as XDR-TB, is virtually incurable.

Source: World Health Organization

New Developments in TB Diagnosis and Treatment

By Christina Dogbey, MPH
Tb Epidemiologist

Research on new tuberculosis diagnosis and treatment got a significant boost from the National Institutes of Health this year. In September, Sequella, Inc, a clinical stage biopharmaceutical company received $2.3 million to develop the new tuberculosis antibiotic drug SQ 641. SQ 641 is a promising anti-TB agent with the potential to provide early and prolonged bacterial clearing during the intensive phase of TB treatment (Sequella Inc, 2008).

The compound is active in inhibiting the synthesis of translocase 1 (TL-1), an enzyme required for cell wall synthesis in all bacteria, including Mycobacteria. Currently the drug is in Phase 2 clinical trials.

Sequella Inc. is also continuing research in the areas of TB diagnosis (the TB Patch-a non invasive method for the diagnosis of active TB disease, phase III), drug therapy (SQ 109, phase II) and medication adherence (the Drug Compliance Monitor- a watch-like device that monitors concentrations of medication in the blood, Phase I).

For more information about the grant, its funded research or Sequella, Inc., please visit http://www.nih.gov. or http://www.niaid.nih.gov

Focus on Service: School DOT/ DOPT

By Christina Dogbey, MPH
Tb Epidemiologist

One of the many services that the PDPH TB Control program provides is school directly observed therapy (DOT) and directly observed preventive therapy (DOPT) for our pediatric patients. This method of treating our patients utilizes TB Control's partnership with the Philadelphia School District to provide medication to school-age children through school nurses.

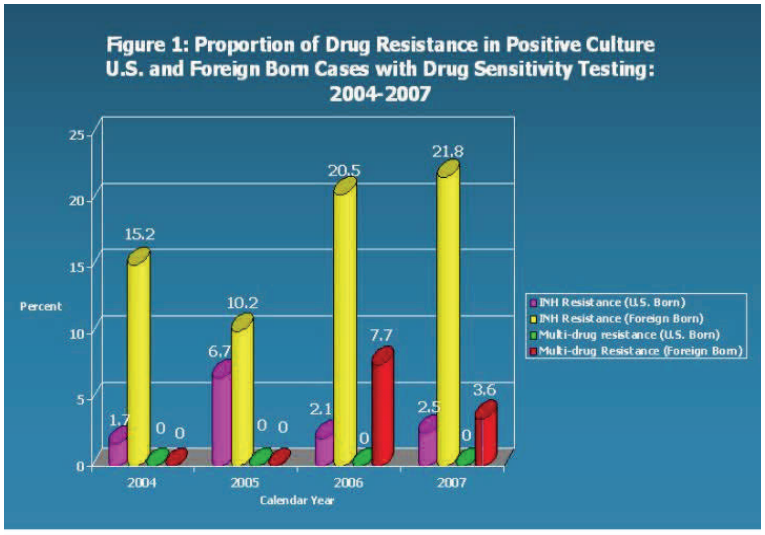
The process begins when our medical staff recommends school DOT (for active TB disease) or DOPT (for latent TB infection) for pediatric cases being managed by TB Control. Both the parent and the nurse of the school the child attends fill out and sign a form that gives consent for the child to be medicated at school. The TB control field worker assigned to that case makes monthly drop-offs of the prescribed medications to the school nurse. The nurse, in turn submits monthly Medication Administration Records (MARs) to TB Control either by fax, or by giving them directly to the field worker at the time of medication delivery. Parents are still required to bring their children to the TB Control Flick Clinic for medical follow up to assure the medications are being tolerated well and are effective.

For more information on this and other services provided by the TB Control Program, visit our website at http://www.phila.gov/health/units/tb/index.html

Emerging Drug Resistance: Clinical Implications for the Treatment of TB and LTBI

By Christina Dogbey, MPH TB Control Epidemiologist
David Schlossberg, MD Medical Director, TB Control Program

For the last 40 years, the mainstay of therapy for LTBI has been treatment with Isoniazid (INH) for a duration of six or nine months. In recent years, regimens using Rifampin (RIF) have been growing in popularity due to shorter therapy course, less toxicity and an increase in INH resistance. The Centers for Disease Control and Prevention has approved a four-month RIF regimen as an alternative therapy for LTBI. The current recommendation for the initial therapy of active tuberculosis (TB) indicates a four-drug therapy regimen that includes Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA) and Ethambutol (EMB). TB cases that demonstrate resistance to recommended agents are likely to require alternative therapy rather than the standard regimen. Knowing the patterns of drug susceptibility and population trends in Philadelphia will help inform clinical decisions about empiric treatment of TB and LTBI, pending susceptibility results.



Graph showing specific rates of resistance in selected groups identified in the Philadelphia Tuberculosis Patient Population : 2004-2007
Source: PDPH TB Control Program

Beginning in 2004 and through the end of 2007, the PDPH TB Control program observed a marked increase in the number of culture positive cases caused by drug resistant strains of M. *tuberculosis*. Over that three-year period, the PDPH TB Control Program counted 394 culture positive cases of TB, of which 376 had antibiotic susceptibility testing performed on their isolates. Seventy-one isolates (18.6%) demonstrated resistance to at least one anti-TB agent, with 36 of those being resistant to at least INH and two being resistant to RIF. Two hundred and sixty four isolates (67%) were tested for susceptibility to PZA with 13 being resistant. Additionally, five isolates (1.3%) were multi-drug resistant tuberculosis (MDR-TB), defined as resistance to INH and RIF.

As the number of immigrants from TB endemic countries to Philadelphia increases, the TB Control program has noted that the burden of drug resistant TB is disproportionately represented in foreign-born patients. Of the seventy-one INH resistant isolates, 31 were from foreign-born patients many of whom were born in countries with a high prevalence of INH resistance. Furthermore, the percentage of all foreign-born INH resistant cases more than doubled from 10% in 2005 to 22% in 2007. One of the two RIF resistant cases was foreign born and all five MDR-TB cases were foreign born. Resistance to PZA was evenly distributed between foreign born (7/131) and U.S. born (6/133) patients.

(Continued on page 4)

Philadelphia Department of Public Health

Tuberculosis Control Program

500 S. Broad Street

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Phone: 215-685-6873 or 215-685-6744

Reporting

All TB cases and suspected cases must be reported to the TB Control Program within 24 hours of identification. To report a case or suspect, call 215-685-6873. Reports can also be faxed to 215-685-6477 or submitted through the Pennsylvania National Electronic Disease Surveillance System (PA-NEDSS). Reporting information is available on the TB Control website at www.phila.gov/health or can be obtained by calling 215-685-6873.

(Continued from page 3)

The prevalence of resistance to Isoniazid, particularly in foreign-born patients, suggests Rifampin should be strongly considered for treatment of LTBI in this population, except for HIV-positive patients (who occasionally have undetected active TB disease and would thereby be treated with Rifampin monotherapy) and patients who are taking medications whose serum levels are critical (e.g. Coumadin, birth control pills) and would be altered by Rifampin. If active TB disease is suspected, the resistance patterns described above and demographics of the patient should be considered in the choice of anti-TB agents for empiric therapy while cultures are pending. The observed resistance to PZA suggests that Pyrazinamide susceptibility should be determined routinely, since PZA susceptibility can no longer be assumed in the Philadelphia population, and PZA resistance requires extension of the basic regimen from 6 months to 9 months. As all of the MDR-TB in Philadelphia occurred in foreign-born patients, an expanded regimen should be considered pending culture results, in selected patients from countries with high rates of resistance.

The empiric treatment of active tuberculosis and latent tuberculosis infection assumes susceptibility to first line anti-tuberculosis agents. When deciding to initiate therapy, pending culture and drug susceptibility results, careful consideration of these resistance trends is warranted to help achieve the goal of TB elimination.

Genotyping

(Continued from page 1)

past, as compared to re-infection based on genotypic similarity of isolates.

- The National Tuberculosis Genotyping Program's method of testing (spoligotyping) is more rapid and less expensive than either REA or RFLP ensuring more timely lab clearing, epidemiologic and outbreak investigations .
- Regular genotyping of isolates aids in monitoring the transmission of *M. tuberculosis*, especially when a highly infectious strain is present.
- Possible correlation of genotypes with multi-drug resistance and tracking the prevalence and types of antibiotic resistance.
- TB genotyping informs public health planning, program evaluation, TB education.

For more information on the TB genotyping program or to arrange to send TB isolates to the TB Lab, please call 215-685-6744.