pennsylvania DEPARTMENT OF HEALTH

Pennsylvania Epi Notes

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The Rise of Multidrug-Resistant Tuberculosis

Background

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. Most cases of tuberculosis affect the lungs, but it can affect any organ in the body. The disease is spread person-to-person by respiratory droplet. Evidence of endemic human infection dates back about 10,000 years,[1] and today it remains one of the most deadly infectious diseases in the world.[2] Without treatment, 20 to 70 percent of those with the disease will die. In 2010, it was estimated that nine million people worldwide had active TB and 1.5 million people died from the disease.[3]

The development of effective drugs to treat the disease in the 1940s was a significant medical advance in TB treatment. In 2009, the World Health Organization (WHO) reported that 87 percent of those with infectious TB worldwide were cured with anti-TB drugs. The total number of cases and case rates have been decreasing worldwide due to successful treatment of the disease.[3] In the United States, 11,182 cases of TB were reported to the Centers for Disease Control and Prevention (CDC) in 2010 for a rate of 3.6 cases per 100,000 persons.[2] This was the lowest reported incidence since 1953, when CDC began counting tuberculosis cases.

Multidrug-Resistant Tuberculosis

It's a bit of a paradox that the antibiotics responsible for curing so many patients have led to a new problem in the treatment of TB: drug resistance. Multidrug-resistant TB has emerged as a serious public health problem in the last 25 years and threatens to turn back the clock on control of the disease. Susceptible TB can become drug-resistant if treated inadequately, which is generally a result of interrupted drug supply, severe side effects or toxicity of the drugs, a chaotic lifestyle, or a lack of resources resulting in an inappropriate drug regimen.[4] Drug-resistant TB takes a variety of forms as shown in Figure 1. Multidrug-resistant tuberculosis (MDR TB) is defined as disease that is resistant to both of the two most effective anti-tuberculosis drugs, isoniazid and rifampin. Most cases of MDR TB occur among persons who have been previously, albeit inadequately, treated for TB. However, MDR TB is infectious, and persons who have never had TB can be infected with drug-resistant strains.[4]

The number of MDR TB cases in the U.S. is small. According to CDC, only 1.3 percent of TB cases in 2010 were multidrug-resistant. In 2010, Pennsylvania tallied three cases of MDR TB out of 238 confirmed TB cases; in 2011, there were four MDR TB cases out of 260 confirmed TB cases.

Up to the early 1990s, the majority of MDR TB cases in the U.S. were among persons born in the U.S. That trend shifted in the late 1990s; now more than 80 percent of MDR TB cases are among persons born outside of the U.S.[5] In Pennsylvania in 2011, about 62 percent of confirmed TB cases were among persons born outside of the U.S. (Figure 2).

Figure 1. Drug-resistant TB cases, Pennsylvania 2011 (N=34)

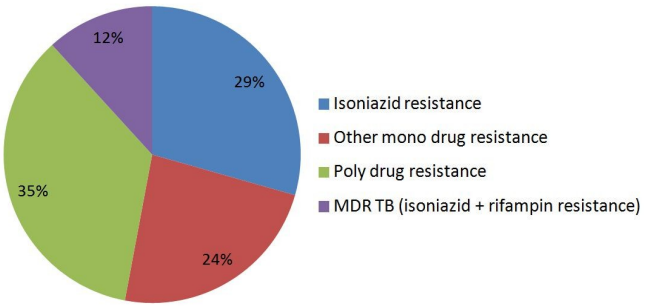
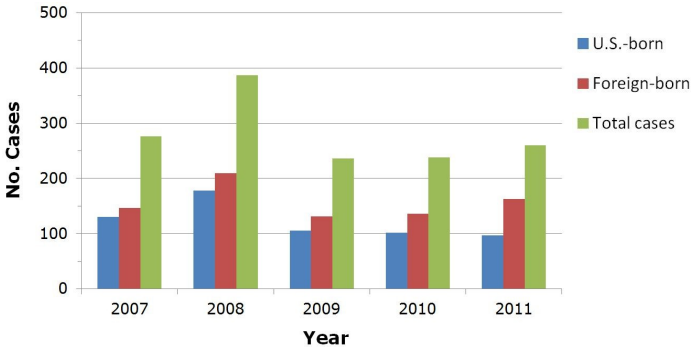


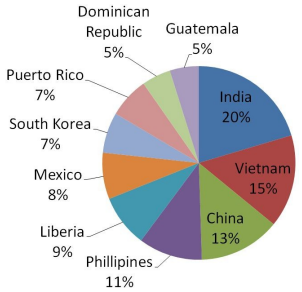
Figure 2. U.S.-born vs Foreign-born TB cases, Pennsylvania 2007-2011



(MDR TB continued)

In 2011 in Pennsylvania, more than half of the TB cases born outside of the U.S. came from India, China, Vietnam or the Philippines (Figure 3). These four countries are considered high MDR TB burden countries based on WHO classification.[3]

Figure 3. Top countries of origin of TB cases, Pennsylvania 2011



XDR TB

Extensively-resistant TB (XDR TB) has been making the news recently. This form of drug-resistant TB is defined as MDR TB with additional drug resistance to two other effective anti-tuberculosis drugs, a fluoroquinolone and a second-line injectable drug. According to the CDC, there were five XDR TB cases in 2008, none in 2009 and one in 2010.[5] The single XDR TB case in 2010 occurred in a Pennsylvania resident.

Cost of MDR TB

The cost of treating MDR TB, or any type of drug-resistant TB, is significantly higher than the treatment of susceptible TB in three key areas: (1) the cost of drugs to treat the disease, (2) patient-related follow-up activities, and (3) contact investigation-related activities. The drugs to treat MDR TB cases are substantially more expensive than the drugs for susceptible TB cases. As the table below shows, the drugs for MDR TB cost as much as 200 times the drugs to treat susceptible TB.

	Susceptible TB	MDR TB
Length of treatment	6-9 mos	18-24 mos
Monthly cost	$120/mo (first two months) $30/mo (remaining months)	$1,000-$3,000
Total cost	$360-$450	$18,000-$72,000

In 2011, Pennsylvania had 260 TB cases, of which four were MDR TB cases. The cost of treating one MDR TB case was almost as much as the cost of treating all of the susceptible TB cases.

Patients with MDR TB require more diagnostic testing and screening to monitor for drug toxicity. In addition, they may suffer from more severe side effects and have more complications from the treatment compared to drug-susceptible TB.[4]

Besides the increased cost and length of treatment, contact investigations and the treatment of those who may have become infected with MDR TB require additional resources and consultation with TB experts.

Policy

The Pennsylvania TB Control Program uses a multi-pronged approach to prevent the development of MDR TB and to discover all drug-resistant cases to ensure appropriate treatment.

- The standard of care requires the use of four anti-tuberculosis drugs for initial treatment to prevent the development of MDR TB.
- Treatment of latent TB infection is started only after TB disease is ruled out.
- The Pennsylvania TB program strives to do anti-TB drug susceptibility testing on all TB cultures in order for appropriate treatment to be prescribed as early as possible in drug-resistant cases.
- Directly Observed Therapy (DOT) is also a standard of care. Healthcare staff observe patients taking all doses of medication to ensure adequate treatment of the disease.
- The PA TB Program provides follow-up on immigrants and refugees entering the state with permanent resident status who are identified overseas as having increased risk for developing active TB.

Even though MDR TB comprises a small percent of the total TB cases in Pennsylvania, maintaining strong policies and funding for TB prevention and treatment are needed to control and reduce the occurrence of MDR TB.

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Pertussis in the Amish Community

Figure 1. Amish buggy in Lancaster County, Pennsylvania *

* Photo courtesy of Pennsylvania Dutch Convention & Visitors Bureau

Background on Amish in Lancaster County, Pennsylvania

The Amish trace their origins back to the early Mennonite and Anabaptist Community and the European reformation movement of the early 1500s. In the late 1600s, a schism occurred in the Mennonite church led by Jacob Amman, and his followers were subsequently called Amish. Key beliefs of the Anabaptist faith were deemed heretical by the Catholic and Protestant Churches and resulted in persecution and death.

The Amish, in search of religious freedom, first settled in Lancaster County in the early 1700s, when William Penn opened the lands of Pennsylvania during his "holy experiment."[1] While Amish are now found throughout Pennsylvania and other states, one of the largest communities is located in Lancaster County.

Amish beliefs on Technology and Immunizations

Key tenants of the Amish belief system are simplicity, humility and community. It is for this reason that the Amish have limited the way modern technology impacts their everyday life. This includes limits placed upon the use of automobiles (while they do hire drivers, ownership is prohibited), the use of simple dress (which encourages a focus on the community versus the individual), and the shunning of electricity and telephones.

While the Amish have no official church view against immunizations, many families choose not to vaccinate. Opposition to vaccination is often based on limited understanding of the benefits, distrust over the safety of the vaccines and religious objections. However, some Amish parents report that vaccinations are simply not a priority given the other demands of daily life.[3] The result is that Amish children are grossly under-vaccinated. A study conducted in 1986 found that only 16 to 26 percent of Amish children had received vaccines against childhood diseases.[2] In 2000, a Pennsylvania Department of Health (PA DOH) survey examined childhood vaccination rates for *Haemophilus influenzae* type b (Hib) in two Pennsylvania Amish communities. Survey results showed vaccination rates of 7 and 28 percent in the two Amish communities, compared to 95 percent among the non-Amish control group.[3] The survey also found that 73 percent of Amish parents would vaccinate their children if it could be done locally.[3]

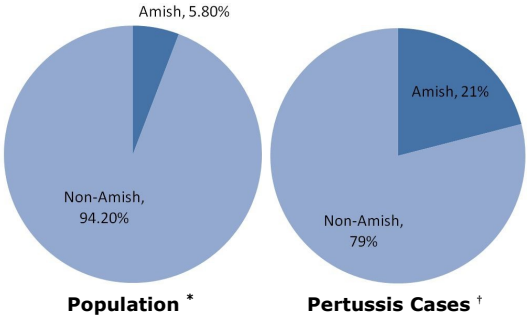
Pennsylvania Department of Health Outreach to the Amish

Between December 1999 and February 2000, eight cases of invasive *Haemophilus influenzae* type b, a vaccine preventable disease, were reported in Pennsylvania. Six of the cases were in unvaccinated Amish children, one of whom died.[3] As a result of this outbreak, a previously eliminated community health nursing position was reinstated at the Lancaster County State Health Center. With increased staffing, the state health center was able to provide outreach education and immunizations to the Amish and Mennonite community in Lancaster County. The state health center now serves 250 to 300 Amish or Mennonite children per year. Though this article highlights outreach efforts in Lancaster County, there are similar efforts in other areas of Pennsylvania with Amish communities.

The Amish and Pertussis

Over the past few years, outreach staff from the PA DOH Southeast District became aware of undiagnosed pertussis circulating in the Amish community. Pennsylvania disease surveillance data also showed that 21 percent of reported pertussis cases in Lancaster County were among Amish persons, yet the Amish accounted for only about 5.8 percent of the county's population (Figure 2). In early 2012, in an effort to control pertussis in the Amish community, a Tdap (combined tetanus, diphtheria and acellular pertussis vaccine) outreach campaign was initiated to target non-immunized Amish adults, suspected as being reservoirs and transmitters of pertussis. Adults had not previously been targeted in immunization outreach campaigns.

Figure 2. Comparison of Lancaster County population and pertussis cases in Amish and non-Amish



* Lancaster County population from U.S. Census (2009), Amish population from Raber's 2011 Almanac
† Pertussis data from PA-NEDSS, 2010-2011

(Pertussis in Amish continued)

Mud Sale Clinics

PA DOH Southeast District staff sought to implement targeted Tdap campaigns at mud sales, or fire sales, in Lancaster County. Mud sales are annual spring events in Lancaster County in which Amish communities partner with local volunteer fire departments to raise money. These sales involve large indoor and outdoor auctions and sell a variety of goods, including baked goods, quilts, livestock, farm equipment, and household goods and supplies (Figure 3). Mud sales are unique events where great numbers of Amish and non-Amish mingle and congregate and are a good opportunity to promote vaccination to the Amish population.

Figure 3. Mud sales *

* Photos courtesy of Pennsylvania Dutch Convention & Visitors Bureau

The PA DOH Southeast District engaged local fire departments in Lancaster County to provide educational materials on immunizations and to inquire about offering vaccine clinics at mud sales. Two fire departments, West Earl Fire Company and Gap Fire Company, agreed to host clinics. In March 2012, clinics were offered at the two mud sales, and a total of 48 Tdap vaccinations were provided. In addition, several referrals were made for home visits. A school catch-up clinic was established at a home where 27 children were vaccinated and Tdap was administered to all mothers. Finally, the groundwork was established to participate in additional mud sales in 2013.

Additional Outreach Efforts

The PA DOH Southeast District staff partnered with Lancaster General Hospital to provide immunization education at Amish households. In May and June 2012, outreach events occurred at two households. A total of 40 persons attended and Tdap was administered to those interested. Additional household referrals were also made.

In the summer of 2012, Southeast District staff partnered with Lancaster General Hospital's Child Protect Program to offer Tdap to all adults accompanying children to the Vaccines for Children clinic.

Since 2007, the Department of Health has been offering Tdap vaccine to birthing hospitals for post-partum mothers in order to stop the spread of pertussis infection to newborns. In Lancaster County, Lancaster General Hospital and Ephrata Community Hospital have been participating and have provided over 9,000 doses of vaccine to new mothers.

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Case Reviews of Three Suspected Pox Cases, April-May 2012

Acute Myeloid Leukemia with Sweet's Syndrome Mistaken for Multiple Infectious Etiologies

On Monday, April 30, 2012, the Pennsylvania Department of Health (PA DOH) Northwest District Office was notified by a local hospital infection control nurse of a patient that was admitted through the emergency department (ED) with suspicion of cowpox. Cowpox was apparently suspected based on comparison of patient lesions with internet pictures as opposed to risk factors for infection (a laboratory-acquired case of cowpox had just been reported in national media). The patient, an adult female, was self-described as homeless with a history of diabetes and intravenous drug abuse. A few days prior to her presentation at the ED, the patient experienced acute onset of chills and myalgias with a raised, erythematic, non-pruritic rash appearing on her hands, legs and face the following day. At the time of the initial examination in the ED, the patient had a fever of 103 degrees Fahrenheit and some of the lesions were umbilicated, while others had a dark eschar-like appearance in the center. Photophobia was also reported. Lesion swabs and fluids were collected and submitted to the PA DOH Bureau of Laboratories (BOL) to rule out orthopox, non-variola orthopox and varicella; additionally, photos of the rash lesions were provided to PA DOH and CDC staff (Figure 1). The patient was promptly transferred to a nearby facility for consultation with an infectious disease (ID) physician. The ID physicians at the facility initially diagnosed the patient with chickenpox (varicella).

Figure 1. Sweet's Syndrome lesions on patient's leg *

* Photo courtesy of treating hospital

The following day, PA DOH BOL reported all lesion swabs were negative for varicella, orthopox and non-variola orthopox; specimens were forwarded to CDC's poxvirus laboratory for additional testing. CDC's rickettsial zoonoses branch was also consulted regarding the possibility of rickettsialpox due to the patient's clinical progression and history of sleeping outdoors (rickettsialpox is transmitted via bites from mites that parasitize rodents). Multiple bacterial and viral etiologies tested at the hospital were negative. Poxviruses were officially ruled out by CDC's poxvirus laboratory on May 2. Specimens were then forwarded to CDC's rickettsial zoonoses branch for additional testing; results later came back as negative. However, on May 4, abnormal cells were noted in a peripheral blood smear resulting in a high index of suspicion of acute myeloid leukemia (AML), which was corroborated by flow cytometry. Following hematologic and dermatologic consult, the diagnosis for the patient was advanced AML with Sweet's Syndrome. The latter is a febrile rash illness sometimes associated with malignancies and often mistaken for an infectious etiology.

Orf

On Monday, April 30, 2012, the PA DOH Southwest District Office was notified by a local hospital emergency department of a probable case of orf. Orf is a common disease worldwide in goats and sheep. It is caused by a virus (parapoxvirus), which causes blisters on the lips and muzzles of animals' mouths, hence the alternative names "sore mouth" and "scabby mouth." Orf is especially common in young animals and may cause them to have difficulty nursing or feeding.

Humans can become infected with orf via direct contact with an infected animal or by touching contaminated equipment such as a harness. Specific activities that may put people at risk include bottle feeding or shearing infected animals. In humans, orf manifests as ulcerative skin lesions, most often on the fingers and hands, and may be painful. Lesions form three to seven days after exposure and can take up to two months to resolve.

The patient came to the hospital for treatment of two painful blisters on the left hand (Figure 1). The individual reported bottle feeding sheep prior to the formation of blisters. Because the patient's exposure history and clinical presentation were consistent with orf, and because obtaining a clinical specimen for testing would have required opening a lesion and risking a secondary infection, no testing was done. Lab testing to diagnose the infection is available at the Centers for Disease Control and Prevention. There is no treatment for the virus and it is rarely transmitted person-to-person. Infection can be prevented by wearing gloves when working with infected animals or by washing hands thoroughly after animal contact.

Figure 1. Orf lesions on patient's hand *

* Photo courtesy of treating hospital

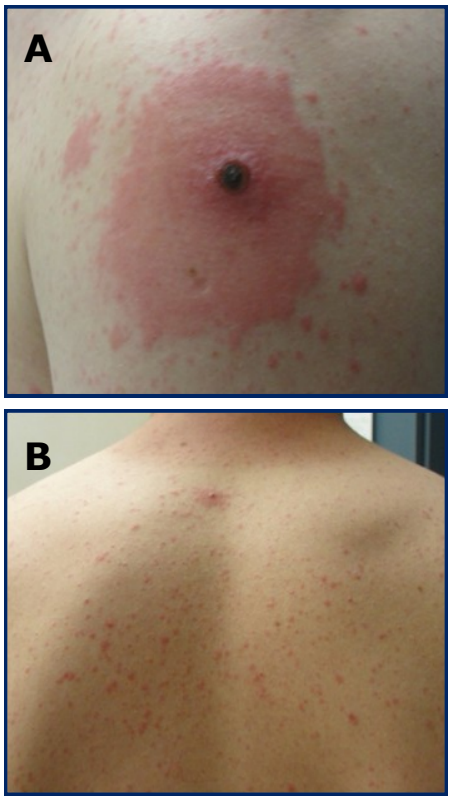
(Case Reviews continued)

Reaction to Smallpox Vaccination

During the run-up to the Iraq War, in December 2002 the Department of Defense (DoD) announced plans to immunize designated service personnel against smallpox, a policy that continues today.[1, 2] In 2008, the DoD transitioned from the use of the vaccine Dryvax to the new-generation ACAM2000™, a live vaccinia virus vaccine manufactured with cell culture technology. ACAM2000™ is administered through the percutaneous route (scarification),[3] and its safety profile is similar to that of Dryvax. Pre-vaccination screening is performed for contraindications to smallpox vaccine, and information on post-vaccination site care is provided to vaccinees.[4]

On May 8, 2012, a central Pennsylvania community hospital emergency department contacted the Pennsylvania Department of Health to report a possible reaction to smallpox vaccine. The 19-year-old patient had been vaccinated on April 27 as part of a pre-deployment medical work-up. On May 6 (nine days post-vaccination), the vaccinee noted having a fever; one day later, the patient noticed a "black spot" at the vaccination site, as well as a red rash with small blisters around the vaccination site and on the trunk, face, palms, soles and legs (Figure 1). At the time of the ED visit, the vaccinee was afebrile but was exhibiting left axillary lymphadenopathy along with the skin lesions. Initial differential diagnosis, based upon observations by the attending physician and guidance from the PA DOH, included mild erythema multiforme and generalized vaccinia. Erythema multiforme is a hypersensitivity reaction, which in its mild form requires only symptomatic therapy; the more severe form, Stevens-Johnson Syndrome, can require hospitalization and intensive treatment. Generalized vaccinia is usually a self-limited and benign complication in primary vaccinees, but can be more severe in certain individuals. It is due to systemic dissemination of the virus from the vaccination site.[5] The patient's medical condition did not warrant admission for care, and the patient was discharged to home from the ED. The patient was temporarily staying with one family member who reportedly had eczema, which is a contraindication to this vaccine. Education, including signs of reaction progression, infection control measures and social distancing, was provided to the patient upon discharge.

Figure 1. Non-viral pustulosis lesions on patient's (A) left deltoid and (B) back *



* Photos courtesy of treating hospital

Clinical information and photographs were forwarded to the Vaccine Healthcare Centers Network (VHCN) through the Centers for Disease Control and Prevention. The VHCN is a Department of Defense organization that supports military immunization programs by carrying out research and providing education and clinical consultation.[6] Following review of the information provided, medical staff from the VHCN felt the reaction was consistent with non-viral pustulosis (NVP). Typically seen in primary vaccinees, NVP has been described within the military immunization program since 2003 and was further identified in literature in 2006. NVP lesions typically erupt one to two weeks after vaccination and consist of follicular and perifollicular papules and pustules that are surrounded by a small, discrete area of reddened edema. The self-limited condition usually requires only symptomatic relief. Further, when lesions have been sampled for virological testing (histology, culture and polymerase chain reaction), they have been negative for vaccinia.[7] Subsequent follow-up with the patient was provided by the VHCN. No secondary cases associated with this patient were identified.

In recent years, PA DOH has investigated three other instances of smallpox adverse reactions in military personnel or their contacts. Because these cases can be medically complicated to manage and require contact investigations, public health should always be notified for appropriate prevention and control measures.

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Cases of select notifiable diseases in Pennsylvania (as of 8/24/2012)*

Disease	Total cases reported for previous 5 years				
	2012 †	2011	2010	2009	2008
Chlamydia	34,400	52,884	47,518	43,068	42,233
Gonorrhea	9,759	13,770	12,883	10,138	11,071
Campylobacter	1,060	1,762	1,624	1,542	1,554
Pertussis (whooping cough)	1,028	547	763	468	368
Salmonella	897	1,844	1,809	1,701	1,721
Giardia	360	792	786	837	873
Varicella (chicken pox)	176	337	373	461	853
Legionella	164	502	324	383	408
Cryptosporidiosis	159	457	485	465	326
Shigella	76	121	634	1,201	248

* Confirmed cases only
† Case counts for 2012 are provisional and subject to change. Counts for earlier years are for complete years.

Disease Reporting

Health care practitioners, health care facilities and clinical laboratories are required to report certain diseases to the Pennsylvania Department of Health. In addition to the diseases on the list, all disease outbreaks and/or unusual occurrences of disease are reportable within the commonwealth. In most cases, reporting must be done electronically via Pennsylvania's version of the National Electronic Disease Surveillance System (PA-NEDSS). To request a PA-NEDSS account, healthcare providers may email PA-NEDSS@pa.gov; please include your contact information and the name and address of the facility for which you will be reporting.

Employment Opportunities

The State Civil Service Commission is currently accepting applications for the following Pennsylvania Department of Health positions:

- Epidemiologist
- Epidemiology Program Specialist
- Epidemiology Research Associate
- Public Health Physician

To apply, click on the links above or visit the Pennsylvania State Civil Service Commission website and click on Job Seekers.

Complete a civil service application for employment for each test announcement for which you are interested. The commission will send you the results of your examination or rating. If you meet the minimum requirements and pass the test, your name will be placed on the list of eligible candidates (eligible list) for that job title according to your score. Positions in the merit system are filled from this pool of eligible candidates. When a job vacancy occurs, the hiring agency requests an eligible list from which to interview for that job title. If you are ranked high enough on the eligible list, you will be contacted for a job interview.

Pennsylvania Epi Notes

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