The EpiLink

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Tuberculosis Overview

World TB Day

World Tuberculosis (TB) Day held on March 24, 2007, is recognized as a day to increase awareness of tuberculosis as a global health threat. TB can be cured; however, without adequate resources to prevent and control the disease, millions will continue to become infected or develop disease.

History of World TB Day

In the late 19th century, TB killed 1 out of every 7 people living in the United States and Europe. On March 24, 1882, Dr. Robert Koch announced the discovery of the TB bacillus. At the time, his discovery was the most important step taken towards the control and elimination of this deadly disease.

In 1982, a century after Dr. Koch's announcement, the first World TB Day was sponsored by the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD). The event was intended to educate the public about the devastating health and economic consequences of TB, its effect on developing countries, and its continued tragic impact on global health.

Where We Are Now

TB remains a threat to the health and well being of people around the world. Among infectious diseases, TB remains the second leading killer of adults in the world, with more than 2 million TB-related deaths each year. Until TB is controlled, World TB Day will not be a celebration. But it is a valuable opportunity to educate the public about the devastation TB can spread and how it can be stopped.

Tuberculosis in Texas

Each year, there are more than 25,000 Texans identified with latent tuberculosis infection, over 1,500 diagnosed with TB disease, and approximately 1,500 persons are evaluated as suspected TB. Most have minimal or no health insurance and, therefore, rely on the public

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health system for TB services. With over 1,500 cases per year since year 2000, Texas has consistently ranked within the top 5 of all states in TB morbidity. The greatest numbers of cases of TB are found in Texas counties with urban environments or proximity to the border with Mexico.

Over the last decade, a higher proportion of TB cases are being identified that require intense treatment because of an increasing frequency of complex medical and social conditions. Patients are being diagnosed later in the course of their disease, requiring a longer treatment time with more expensive medications. More patients are identified as migrants or foreign-born, diabetic, homeless, infected with human immunodeficiency virus (HIV), with drug resistance, and with substance abuse issues. These conditions complicate the treatment of TB and usually require a longer period for treatment. It is important to note that in 2005, Texas ranked fourth among the states in numbers of cases resistant to isonaizid and is tied with Minnesota at sixth place for numbers of cases of multidrug-resistant TB.

Tuberculosis Prevention and Control Activities in the State

Tuberculosis prevention and control activities are provided by local health departments (LHD) and Texas Department of State Health Services (DSHS) Health Service Region offices located in jurisdictions without a city or county governed LHD. Local health departments are not required to provide TB services; therefore, DSHS must serve as the safety net for those jurisdictions where no services are provided. DSHS provides medication at no cost for TB patients to promote treatment compliance and reduce the development of drug resistant tuberculosis. DSHS also performs diagnostic TB laboratory services at no cost to LHD. Additionally, DSHS provides funding to health service regions and LHD to support tuberculosis prevention and control activities across the state. Funding is used to provide some core TB services including surveillance, case management, contact investigation, and contracted services (such as radiology, directly observed therapy, and physician services). The need exceeds available resources.

Table 1. Statistical Information on Tuberculosis (TB) in Texas by Health Service Regions (HSR)

	TB Cases					TB Rates†				
HSR	**2002**	**2003**	**2004**	**2005**	**2006**	**2002**	**2003**	**2004**	**2005**	**2006**
1	25	28	27	23	21	3.2	3.5	3.4	2.8	2.6
2/3	416	441	429	415	441	6.5	6.8	6.5	6.2	6.7
4/5N	65	55	48	73	63	4.6	3.9	3.4	5.1	4.3
6/5S	498	531	566	477	491	9.2	9.7	10.2	8.2	8.3
7	115	109	118	88	80	4.8	4.5	4.8	3.4	3.1
8	104	102	149	117	164	4.7	4.6	6.6	5.0	7.0
9/10	81	96	82	80	91	6.5	7.6	6.5	6.3	6.9
11	228	218	243	239	218	12.6	11.8	12.8	12.2	10.8
State Total	1,550	1,594	1,683	1,535	1,585	7.2	7.3	7.6	6.7	6.8

†Rates are expressed as cases per 100,000 population.

Source: Tuberculosis Information Management System 2006 Data.

The state also provides inpatient services for persons who require court ordered management through admission to the Texas Center for Infectious Disease (TCID), located in San Antonio. Patients with resistant or complicated TB disease may also be admitted voluntarily to TCID and the University of Texas Health Center at Tyler.

TB Medical Facts

(Adapted from the CDC Fact Sheet "Tuberculosis: General Information")

What Is Tuberculosis (TB)?

TB is a disease caused by bacteria that are spread from person to person through the air. It affects the lungs, but it can also affect other parts of the body, such as the brain, the kidneys, or the spine. A person with TB can die if they do not get treatment.

What Are the Symptoms of TB?

The general symptoms of TB disease include feelings of sickness or weakness, weight loss, fever, and night sweats. The symptoms of TB disease of the lungs also include coughing, chest pain, and the coughing up of blood. Symptoms of TB disease in other parts of the body depend on the area affected.

How is TB Spread?

TB bacteria are put into the air when a person with TB disease of the lungs or throat coughs, sneezes, speaks, or sings. These bacteria can stay in the air for several hours, depending on the environment. Persons who breathe in the air containing these TB bacteria can become infected; this is called latent TB infection.

What Is the Difference Between Latent TB Infection and TB Disease?

People with latent TB infection have TB bacteria in their bodies, but they are not sick because the germs are not active. These people do not have symptoms of TB disease and they cannot spread the bacteria to others. However, they may develop TB disease in the future. They are often prescribed treatment to prevent them from developing TB disease.

People with TB disease are sick from TB bacteria that are active, meaning that they are multiplying and destroying tissue in their body. They usually have symptoms of TB disease. People with TB disease of the lungs or throat are capable of spreading bacteria to others. They are prescribed drugs that can cure TB disease.

What Should I Do If I Have Spent Time with Someone with Latent TB Infection?

A person with latent TB infection cannot bacteria to other people. You do not need to be tested if you have spent time with someone with latent TB infection. However, if

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you have spent time with someone with TB disease or someone with symptoms of TB, you should be tested.

What Should I Do if I Have Been Exposed to Someone with TB Disease?

People with TB disease are most likely to spread the bacteria to people they spend time with every day, such as family members or coworkers. If you have been around someone who has TB disease, you should go to your doctor or your local health department for tests.

How Do You Get Tested for TB?

There are two tests that can be used to help detect TB infection. The Mantoux tuberculin skin test is performed by injecting a small amount of fluid (called tuberculin) into the skin in the lower part of the arm. A person given the tuberculin skin test must return within 48 to 72 hours to have a trained health care worker look for a reaction on the arm. A second test is the QuantiFERON®-TB Gold test. The QuantiFERON®-TB Gold test is a blood test that measures how the patient's immune system reacts to the germs that cause TB. The newer QuantiFERON®-TB Gold test has very limited availability in Texas. In northeastern Texas, only the UT Heath Center at Tyler is currently using this test for TB screening of its employees who are at risk for exposure to TB disease.

What Does a Positive Tuberculin Skin Test or QuantiFERON®-TB Gold Test Mean?

A positive tuberculin skin test or QuantiFERON®-TB Gold test only tells that a person has been infected with TB bacteria. It does not tell whether or not the person has progressed to TB disease. Other tests, such as a chest x-ray and a sample of sputum, are needed to see whether the person has TB disease.

What is Bacille Calmette-Guérin (BCG)?

BCG is a vaccine for TB disease. BCG is used in many countries, but it is not generally recommended in the United States. BCG vaccination does not completely prevent people from getting TB. It may also cause a false positive tuberculin skin test. However, persons who have been vaccinated with BCG can be given a tuberculin skin test or QuantiFERON®-TB Gold test.

Why Is Latent TB Infection Treated?

If you have latent TB infection but not TB disease, your doctor may want you to take a drug to kill the TB bacteria and prevent you from developing TB disease. The decision about taking treatment for latent infection will be based on your chances of developing TB disease. Some people are more likely than others to develop TB

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disease once they have TB infection. This includes people with HIV infection, people who were recently exposed to someone with TB disease, and people with certain medical conditions.

How is TB Disease Treated?

Taking several drugs for 6 to 12 months can cure TB disease. It is very important that people who have TB disease finish the medicine, and take the drugs exactly as prescribed. If they stop taking the drugs too soon, they can become sick again; if they do not take the drugs correctly, the bacteria that are still alive may become resistant to those drugs. TB that is resistant to drugs is harder and more expensive to treat. In some situations, staff of the local health department meet regularly with patients who have TB to watch them take their medications. This is called directly observed therapy (DOT). DOT helps the patient complete treatment in the least amount of time.

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Trends in Tuberculosis Incidence—United States, 2006

In 2006, a total of 13,767 tuberculosis (TB) cases (4.6 per 100,000 population) were reported in the United States, representing a 3.2% decline from the 2005 rate. This report summarizes provisional 2006 TB incidence data from the National TB Surveillance System and describes trends since 1993. The TB rate in 2006 was the lowest recorded since national reporting began in 1953, but the rate of decline has slowed since 2000. The average annual percentage decline in the TB incidence rate decreased from 7.3% per year during 1993—2000 (95% confidence interval [CI] = 6.9%—7.8%) to 3.8% during 2000—2006 (CI = 3.1%—4.5%). Foreign-born persons and racial/ethnic minority populations continue to be affected disproportionately by TB in the United States. In 2006, the TB rate among foreign-born persons in the United States was 9.5 times that of U.S.-born persons.* The TB rates among blacks, Asians, and Hispanics† were 8.4, 21.2, and 7.6 times higher than rates among whites, respectively. The slowing of the decline in the overall national TB rate and the inability to effectively address persistent disparities in TB rates between U.S.-born and foreign-born persons and between whites and racial/ethnic minority populations threaten progress toward the goal of eliminating TB in the United States. In 1989, CDC and the Advisory Committee for the Elimination of Tuberculosis issued a strategic plan for the elimination of TB, setting an interim target case rate of 3.5 per 100,000 population by 2000 and ultimately the elimination of TB (i.e., <1 case per 1 million population) in the United States by 2010[1].

TB is a nationally notifiable disease. Health departments in the 50 states and District of Columbia (DC) electronically report to CDC any TB cases that meet the CDC and Council of State and Territorial Epidemiologists case definition.§ Reports include the patient's race, ethnicity (i.e., Hispanic or non-Hispanic), treatment information, and drug-susceptibility test results if available. For this analysis, CDC calculated national and state TB rates[2] and rates for foreign-born and U.S.-born persons[3] and racial/ethnic populations[4] by using current U.S. census population estimates for the years 1993 through 2006.

In 2006, TB incidence rates in the 51 reporting areas ranged from 0.8 (Wyoming) to 12.6 (DC) cases per 100,000 population (median: 3.4 cases). Thirty states had lower rates in 2006 than 2005; 20 states and DC had higher rates (Table 1). In 2006, for the second consecutive year and the second time since national reporting began, approximately half of states (26 of 50) had TB rates of ≤3.5 per 100,000 (Figure 1); however, 11 of those 26 states had higher rates of TB in 2006 than in 2005. Seven states (California, Florida, Georgia, Illinois, New Jersey, New York, and Texas) reported more than 500 cases each for 2006; combined, these seven states accounted for 60% (8,259) of all TB cases.

Among U.S.-born persons, the number and rate of TB cases continued to decline in 2006. The U.S.-born TB rate was 2.3 per 100,000 population (5,924 or 43.3% of all cases with known origin of birth), representing a 7.0% decline in rate since 2005 and a 68.6% decline since 1993 (Figure 2).

Among foreign-born persons, the number of TB cases increased in 2006,

but the rate decreased. The foreign-born TB rate in 2006 was 21.9 per 100,000 population, representing a 0.5% decline in rate since 2006 and a 35.8% decline since 1993. As the rate of decline in TB cases among foreign-born persons lagged behind the decline in TB cases among U.S.-born persons, the foreign-born to U.S.-born rate ratio increased 7.0%, from 8.9 in 2005 to 9.5 in 2006. In 2006, approximately half (55.6%) of TB cases among foreign-born persons were reported in persons from five countries: Mexico (1,912), the Philippines (856), Vietnam (630), India (540), and China (376).

In 2006, for the third consecutive year, more TB cases were reported among Hispanics than any other racial/ethnic population. Among persons with TB whose country of birth was known, 95.6% (3,126 of 3,269) of Asians, 74.7% (3,024 of 4,050) of Hispanics, 29.9% (1,110 of 3,712) of blacks, and 17.8% (427 of 2,404) of whites were foreign born. From 2005 to 2006, TB rates declined for all racial/ethnic minorities except American Indians/ Alaska Natives and Native Hawaiians or Other Pacific Islanders[¶] (Table 2).

Human immunodeficiency virus (HIV) contributes to the TB pandemic because immune suppression increases the likelihood of rapid progression from TB infection to TB disease. From 2005 to 2006, among TB cases with HIV status reported,** the percentage of TB cases with HIV infection decreased 4.4% (from 13.0% to 12.4%), but the percentage of TB cases with unknown HIV status increased 10.3% (from 28.7% to 31.7%).[††] The decline in the percentage of TB cases with HIV infection might reflect incomplete reporting of HIV test results attributed to a lack of HIV testing or HIV reporting.

A total of 124 cases of multidrug-resistant TB (MDR TB)[§§] were reported in 2005, the most recent year for which complete drug-susceptibility data are available.[¶¶] The proportion of MDR-TB cases remained constant at 1.2% from 2004 (129 of 10,846 TB cases) to 2005 (124 of 10,662). In 2005, MDR TB continued to disproportionately affect foreign-born persons, who accounted for 101 (81.5%) of 124 MDR-TB cases. The recommended length of drug therapy for most types of TB is 6—9 months. In 2003, the latest year for which treatment data are complete, 82.7% of patients for whom ≤1 year of treatment was indicated completed therapy within 1 year, below the *Healthy People 2010* target of 90% (objective 14-12).

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Editorial Note:

Since the resurgence of TB in the United States during 1985—1992, the annual TB rate has decreased steadily. However, the rate of decrease has slowed. Furthermore, the proportion of TB cases among foreign-born persons has increased each year since 1993. If the global TB pandemic remains unmitigated, eliminating TB in the United States will be increasingly difficult because most foreign-born persons in the United States who progress from latent TB infection to TB disease initially became infected with TB abroad.

To address the higher rate of TB among foreign-born persons in the United States and the increasing proportion of cases they represent, CDC is considering several strategies (e.g., revising overseas medical screening of applicants for U.S. immigration). These strategies should decrease importation of TB into the United States and

improve immigrant and refugee health. CDC also is continuing to work with international partners, including the Stop TB Partnership (http://www.stoptb.org), to strengthen TB control in countries with high TB incidence.

To address the disproportionately high rate of TB in the United States among Asians and Hispanics, CDC is working with international health organizations to help reduce TB in affected countries. To help address the disproportionately high rate of TB among blacks in the United States, in May 2006, the CDC and Research Triangle Institute International convened the Stop TB in the African-American Community Summit to focus attention on the problem of TB in the black community (http://www.cdc.gov/nchstp/tb/tbinafricanamericans).

In 2005 and 2006, reported HIV status (i.e., positive or negative test result) was not available for nearly one third of TB cases reported in the United States. HIV is the most important known risk factor for progression from latent TB infection to TB disease[5]. Patients with TB and HIV are five times more likely to die during anti-TB treatment than patients not infected with HIV, underscoring the importance of early diagnosis and treatment for TB/HIV coinfection[6]. In 2006, CDC issued new guidelines recommending that all patients initiating treatment for TB be screened routinely for HIV infection[7]. CDC also is working to increase awareness of TB/HIV coinfection domestically among health-care providers through educational resources and training courses developed by CDC's TB Regional Training and Medical Consultation Centers in collaboration with the Health Resources and Services Administration.

The need for new anti-TB drugs was emphasized in 2006 by identification of a cluster of extensively drug-resistant TB cases among HIV-infected persons in a rural area of KwaZulu-Natal, South Africa[8]. Progress has been made on several new drugs in the past year. Six agents in five different drug classes are being tested in humans (TMC-207, OPC 67683, SQ109, PA824, moxifloxacin, and gatifloxacin). In collaboration with the Global Alliance for TB Drug Development, CDC's TB Trials Consortium (TBTC) has completed two preliminary trials with moxifloxacin. These trials will help lay the groundwork for a trial of a treatment-shortening regimen for TB. TBTC also is nearing completion of a trial of a 3-month rifapentine-based treatment for latent TB infection.

Despite these targeted measures to control TB, the slowing of the decline in the TB rate indicates a need for improved case management and contact investigation, intensified outreach and testing of populations at high risk, better treatments and diagnostic tools, improved understanding of TB transmission, and continued collaborative measures with other nations to reduce TB globally. These measures are required to fully implement the Institute of Medicine's recommendations for eliminating TB in the United States[9].

Acknowledgments

The findings in this report are based, in part, on data contributed by state and local TB-control officials.

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† For this report, persons identified as white, black, Asian, American Indian/Alaska Native, Native Hawaiian or Other Pacific Islander, or of multiple race are all classified as non-Hispanic. Persons identified as Hispanic might be of any race.

§ Full case definition is available at http://www.cdc.gov/epo/dphsi/casedef/tuberculosis_current.htm. To be considered a confirmed case, cases must meet the clinical case definition or be laboratory confirmed. Cases are not counted twice within any consecutive 12-month period. However, cases in which the patient had previously verified disease are reported again if the patient was discharged from treatment. Cases also are reported again if the patient was lost to supervision for >12 months and disease can be verified again.

¶ Reporting of official CDC TB statistics for race/ethnicity changed beginning in 2003. A "Native Hawaiian or Other Pacific Islander" category was added to the race/ethnicity reporting options, and multiple races also could be reported for a given patient.

** For this report, California was excluded from the analysis of HIV among TB cases because it reports its HIV data separately from its TB data and 1 year behind all other states. HIV data reported by California only includes the number of patients with TB that are HIV positive. The number of patients testing negative, refusing testing, or not offered testing is not reported. Therefore, determining the percentage of patients with a known HIV status for California is not possible because patients are classified as HIV positive or unknown.

†† For this report, the "known HIV status" category is based on the number of cases with reported "positive" or "negative" status. The "unknown HIV status" category is based on "indeterminate," "refused," "not offered," "test performed but status unknown," "unknown," and "data missing" categories. In 2006, HIV status was classified as "data missing" for 0.9% of TB cases (101 of 10,986 TB cases, excluding California). All HIV estimates were based on provisional data.

§§ Defined as a case of TB in a person with a *Mycobacterium tuberculosis* isolate resistant to at least isoniazid and rifampicin.

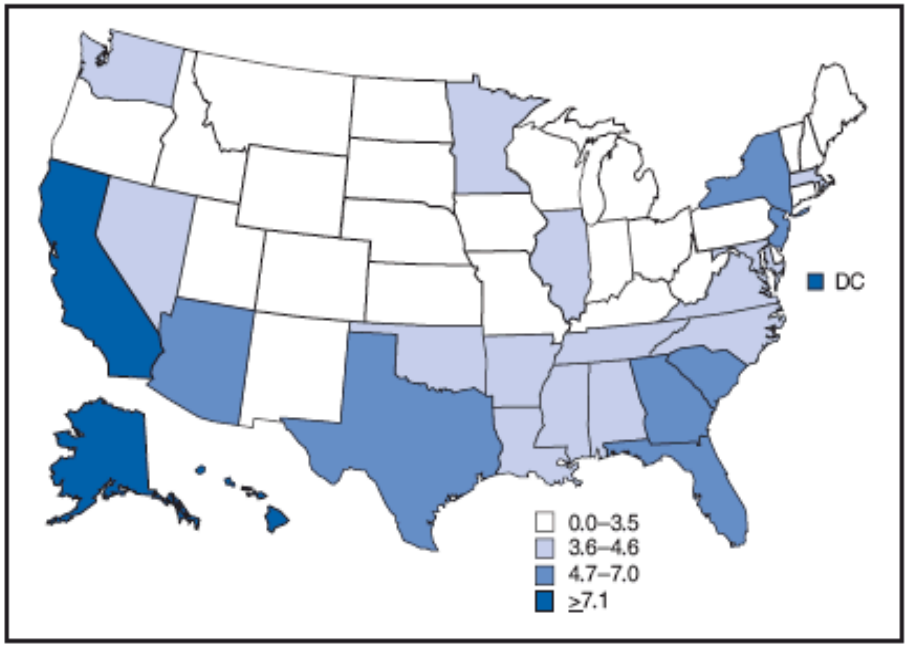
¶¶ Drug-susceptibility testing for isoniazid and rifampicin was performed for 98.3% (11,132 of 11,325) and 97.4% (10,662 of 10,946) of culture-confirmed cases of *M. tuberculosis* in 2004 and 2005, respectively.

TABLE 1. Number and rate* of tuberculosis cases and percentage change, by state/area — United States, 2005 and 2006†

State/Area	2005		2006		% change 2005–2006		Population	
	No.	Rate	No.	Rate	No.	Rate	2005	2006
Alabama	216	4.7	196	4.3	-9.3%	-10.3%	4,548,327	4,599,030
Alaska	59	8.9	70	10.4	18.6%	17.4%	663,253	670,053
Arizona	281	4.7	311	5.0	10.7%	6.8%	5,953,007	6,166,318
Arkansas	115	4.1	102	3.6	-11.3%	-12.4%	2,775,708	2,810,872
California	2,903	8.0	2,781	7.6	-4.2%	-5.0%	36,154,147	36,457,549
Colorado	101	2.2	124	2.6	22.8%	20.4%	4,663,295	4,753,377
Connecticut	95	2.7	89	2.5	-6.3%	-6.4%	3,500,701	3,504,809
Delaware	27	3.2	29	3.4	7.4%	5.9%	841,741	853,476
District of Columbia	55	9.4	73	12.6	32.7%	32.8%	582,049	581,530
Florida	1,093	6.2	1,038	5.7	-5.0%	-6.7%	17,768,191	18,089,888
Georgia	508	5.6	504	5.4	-0.8%	-3.2%	9,132,553	9,363,941
Hawaii	112	8.8	115	8.9	2.7%	1.7%	1,273,278	1,285,498
Idaho	23	1.6	20	1.4	-13.0%	-15.2%	1,429,367	1,466,465
Illinois	590	4.6	569	4.4	-3.6%	-4.1%	12,765,427	12,831,970
Indiana	146	2.3	124	2.0	-15.1%	-15.7%	6,266,019	6,313,520
Iowa	55	1.9	40	1.3	-27.3%	-27.7%	2,965,524	2,982,085
Kansas	60	2.2	81	2.9	35.0%	34.2%	2,748,172	2,764,075
Kentucky	124	3.0	84	2.0	-32.3%	-32.8%	4,172,608	4,206,074
Louisiana	257	5.7	199	4.6	-22.6%	-18.6%	4,507,331	4,287,768
Maine	17	1.3	16	1.2	-5.9%	-6.1%	1,318,220	1,321,574
Maryland	283	5.1	253	4.5	-10.6%	-11.0%	5,589,599	5,615,727
Massachusetts	265	4.1	259	4.0	-2.3%	-2.3%	6,433,367	6,437,193
Michigan	246	2.4	221	2.2	-10.2%	-10.1%	10,100,833	10,095,643
Minnesota	199	3.9	217	4.2	9.0%	8.2%	5,126,739	5,167,101
Mississippi	103	3.5	116	4.0	12.6%	12.5%	2,908,496	2,910,540
Missouri	108	1.9	104	1.8	-3.7%	-4.4%	5,797,703	5,842,713
Montana	10	1.1	13	1.4	30.0%	28.6%	934,737	944,632
Nebraska	35	2.0	25	1.4	-28.6%	-29.0%	1,758,163	1,768,331
Nevada	112	4.6	99	4.0	-11.6%	-14.6%	2,412,301	2,495,529
New Hampshire	4	0.3	17	1.3	325.0%	322.4%	1,306,819	1,314,895
New Jersey	482	5.5	508	5.8	5.4%	5.1%	8,703,150	8,724,560
New Mexico	39	2.0	48	2.5	23.1%	21.3%	1,925,985	1,954,599
New York	1,284	6.6	1,274	6.6	-0.8%	-0.7%	19,315,721	19,306,183
North Carolina	329	3.8	374	4.2	13.7%	11.3%	8,672,459	8,856,505
North Dakota	6	0.9	9	1.4	50.0%	49.7%	634,605	635,867
Ohio	260	2.3	239	2.1	-8.1%	-8.1%	11,470,685	11,478,006
Oklahoma	144	4.1	144	4.0	0.0%	-1.0%	3,543,442	3,579,212
Oregon	103	2.8	81	2.2	-21.4%	-22.7%	3,638,871	3,700,758
Pennsylvania	326	2.6	338	2.7	3.7%	3.4%	12,405,348	12,440,621
Rhode Island	47	4.4	26	2.4	-44.7%	-44.4%	1,073,579	1,067,610
South Carolina	261	6.1	222	5.1	-14.9%	-16.4%	4,246,933	4,321,249
South Dakota	16	2.1	14	1.8	-12.5%	-13.3%	774,883	781,919
Tennessee	299	5.0	279	4.6	-6.7%	-8.0%	5,955,745	6,038,803
Texas	1,535	6.7	1,585	6.7	3.3%	0.7%	22,928,508	23,507,783
Utah	29	1.2	34	1.3	17.2%	14.5%	2,490,334	2,550,063
Vermont	8	1.3	9	1.4	12.5%	12.2%	622,387	623,908
Virginia	355	4.7	331	4.3	-6.8%	-7.7%	7,564,327	7,642,884
Washington	254	4.0	262	4.1	3.1%	1.5%	6,291,899	6,395,798
West Virginia	28	1.5	22	1.2	-21.4%	-21.6%	1,814,083	1,818,470
Wisconsin	78	1.4	75	1.3	-3.8%	-4.3%	5,527,644	5,556,506
Wyoming	0	0.0	4	0.8	—	—	508,798	515,004
U.S. total	**14,085**	**4.8**	**13,767**	**4.6**	**-2.3%**	**-3.2%**	**296,507,061**	**299,398,484**

* Per 100,000 population.
† Data for 2006 are provisional.

FIGURE 1. Rate* of tuberculosis cases, by state — United States, 2006†



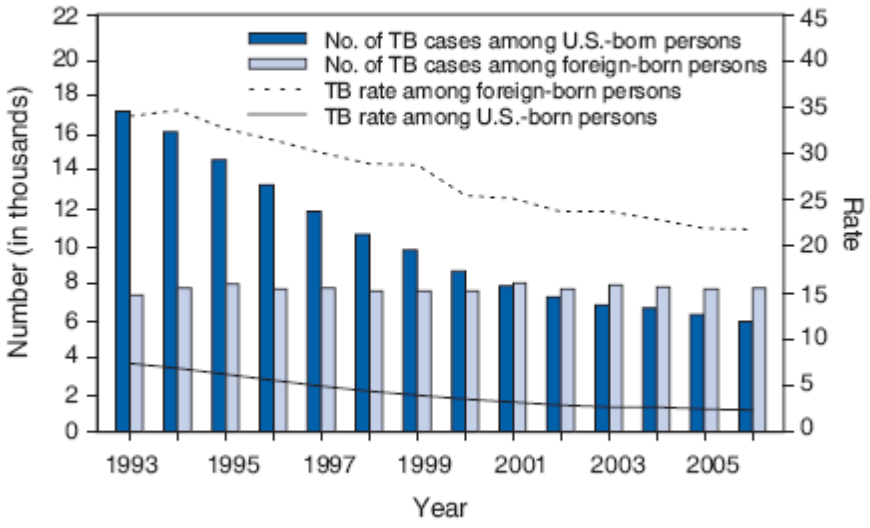
*Per 100,000 population.
†Data are provisional.

TABLE 2. Number and rate* of tuberculosis cases and percentage change, by race/ethnicity† — United States, 2005 and 2006§

Race/Ethnicity	2005		2006		% change 2005–2006		Population	
	No.	Rate	No.	Rate	No.	Rate	2005	2006
Hispanic	4,047	9.5	4,050	9.2	0.1%	-3.0%	42,687,224	44,046,771
Black	3,955	10.9	3,712	10.1	-6.1%	-7.1%	36,324,593	36,693,014
Asian	3,209	25.8	3,269	25.6	1.9%	-1.0%	12,420,514	12,779,154
White	2,579	1.3	2,404	1.2	-6.8%	-7.0%	198,366,437	198,819,462
American Indian/Alaska Native	152	6.8	164	7.3	7.9%	6.6%	2,232,922	2,259,052
Native Hawaiian or Other Pacific Islander	53	13.1	62	15.1	17.0%	15.0%	405,019	411,932
Multiple race	46	1.2	38	0.9	-17.4%	-19.8%	3,973,695	4,093,276
Unknown	44	—	68	—	—	—	—	—
Total¶	**14,085**	**4.8**	**13,767**	**4.6**	**-2.3%**	**-3.2%**	**—**	**—**

*Per 100,000 population.
†Persons identified as white, black, Asian, and of other or unknown races are all non-Hispanic. Persons identified as Hispanic might be of any race.
§Data for 2006 are provisional.
¶Total rates were calculated by dividing the total number of reported cases by the total U.S. Census population, then multiplying by 100,000.

FIGURE 2. Number and rate* of tuberculosis (TB) cases among U.S.- and foreign-born persons, by year reported — United States, 1993–2006†



*Per 100,000 population.
†Data for 2006 are provisional.

Worldwide Emergence of Extensively Drug-resistant Tuberculosis

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Abstract

Mycobacterium tuberculosis *strains that are resistant to an increasing number of second-line drugs used to treat multidrug-resistant tuberculosis (MDR TB) are becoming a threat to public health worldwide. We surveyed the Network of Supranational Reference Laboratories for* M. tuberculosis *isolates that were resistant to second-line anti-TB drugs during 2000–2004. We defined extensively drug-resistant TB (XDR TB) as MDR TB with further resistance to ≥3 of the 6 classes of second-line drugs. Of 23 eligible laboratories, 14 (61%) contributed data on 17,690 isolates, which reflected drug susceptibility results from 48 countries. Of 3,520 (19.9%) MDR TB isolates, 347 (9.9%) met criteria for XDR TB. Further investigation of population-based trends and expanded efforts to prevent drug resistance and effectively treat patients with MDR TB are crucial for protection of public health and control of TB.*

Multidrug-resistant tuberculosis (MDR TB) has been documented in nearly 90 countries and regions worldwide;[1] 424,203 cases of MDR TB were estimated to have occurred in 2004, which is 4.3% of all new and previously treated TB cases.[2] Treatment for MDR TB patients requires use of second-line drugs for ≥24 months. These drugs are more costly, toxic, and less effective than first-line drugs used for routine treatment of TB [3–6]. As with other diseases, resistance to TB drugs results primarily from nonadherence by patients, incorrect drug prescribing by providers, poor quality drugs, or erratic supply of drugs.[7]

To facilitate treatment of MDR TB in resource-limited countries, where most TB cases occur, [1-2] the World Health Organization (WHO) and its partners developed the Green Light Committee, which helps ensure proper use of second-line drugs, to prevent further drug resistance.[8] Nonetheless, the Green Light Committee encountered numerous anecdotal reports of MDR TB cases with resistance to most second-line drugs. Once a strain has developed resistance to second-line drugs, these new TB strains are even more difficult to treat with existing drugs. Untreated or inadequately treated patients are at increased risk of spreading their disease in the community, which could lead to outbreaks in vulnerable populations and widespread emergence of a lethal, costly epidemic of drug-resistant TB, reminiscent of the MDR TB outbreaks in the early 1990s.[9-13] Therefore, to determine whether these anecdotal reports were isolated events, early evidence of an emerging epidemic, or the occurrence of virtually untreatable forms of drug-resistant TB that had not been described previously in different parts of the world, we characterized and quantified the frequency of second-line–drug resistance in several geographic regions.

We sought to determine the extent to which highly resistant M. tuberculosis *strains have been identified by the international laboratories that participate in the Network of Supranational Reference Laboratories (SRLs). The SRL Network consists of 25 highly proficient TB laboratories on 6 continents. These laboratories collaborate with national reference laboratories to strengthen culture and drug-susceptibility testing capacity and to provide quality control for the WHO/International Union Against Tuberculosis and Lung Diseases Global Project on Anti-TB Drug Resistance.[14]*

Methods

Participants

From November 2004 through November 2005, we surveyed the global SRL Network. All SRL directors were invited to participate during the 2004 annual SRL directors meeting, by individual mailings, and by personal phone calls. Drug-susceptibility testing results were

requested for *M. tuberculosis* isolates that had been tested for resistance to first-line drugs and second-line drugs during 2000–2004. Two SRLs were not eligible because they did not test for second-line drugs or tested for <3 classes of second-line drugs. The 14 SRLs that provided data for this study support 112 TB laboratories in 80 countries worldwide (Figure 1). SRLs serve as international reference laboratories to a wide geographic area, performing drug-susceptibility testing that may not be available in a country (e.g., for second-line drugs) and providing quality assurance for first-line–drug testing. Most SRLs also serve as the national reference laboratory for the country in which they are located; they receive varying proportions of isolates from their own and other countries for surveillance, clinical diagnosis, and quality assurance. First-line–drug susceptibility testing is performed on all isolates; second-line–drug susceptibility testing is usually limited to isolates from patients known or suspected to have drug-resistant TB. Of the 14 participating SRLs, not all tested for all 6 classes of second-line drugs, and 4 did not submit data for the entire survey period.

In contrast, the SRL in the Republic of Korea serves as the national reference laboratory and routinely performs an extended diagnostic panel of drug-susceptibility testing on isolates from culture-positive TB patients referred from health centers, hospitals, and clinics in the Republic of Korea. This SRL tests all isolates for 6 classes of second-line drugs; thus, data from the Republic of Korea reflect most culture-positive cases and provide a close approximation to a population estimate of prevalence. Because of the large number of isolates received and because sampling for these isolates is systematically different from that at the other SRLs (testing of all TB patients in the Republic of Korea vs testing of patients more likely to have drug-resistant TB in other SRLs), resistance patterns for the Republic of Korea were analyzed separately from those for the other SRLs.

Laboratory Methods

Among participating SRLs, different but internationally accepted methods were used to test for second-line drug resistance (details available upon request). Validation of drug-susceptibility testing results for second-line drugs was not performed as part of this survey, but as part of their role as global reference laboratories, all SRLs participate in international proficiency testing for first-line drugs. Quality assurance procedures for second-line–drug susceptibility testing have not been developed; as a proxy for quality assurance, we examined the accuracy of second-line–drug susceptibility testing among isolates susceptible to the 4 main first-line drugs (isoniazid [INH], rifampin [RIF], ethambutol, and streptomycin). On the basis of known mechanisms of drug resistance, finding an isolate that is susceptible to all first-line drugs and resistant to second-line drugs is unlikely.[7]

Procedures and Definitions

A standardized reporting form requested anonymous data for all isolates tested for resistance to ≥3 second-line drug classes during 2000–2004. Data were abstracted from the records, electronic or paper, depending on laboratory practices for data management. Results were submitted for 1 isolate per patient. Because SRLs rarely receive multiple isolates from the same patient, reporting of the same patient more than once was unlikely (B. Metchock and G.H. Bai, pers. comm.). No specimens were collected for this study; we used only data from records of isolates that had already been tested. Limited clinical information about the patient was available with each isolate. Consistent data were available for country of origin and date of drug-susceptibility testing. Data about age and TB treatment history were available for <10% of patients, so analysis was not considered reliable for these variables.

To best compare data for the study samples with data from the Global Drug Resistance Survey and other population-based drug-resistance surveillance, we analyzed first-line–drug resistance patterns according to standard methods used in anti-TB–drug

resistance surveys.[1] These patterns included any drug resistance, monoresistance (resistance to only the 1 specified drug), polyresistance (resistance to ≥2 first-line drugs, but which drugs not specified), and multidrug resistance (resistance to at least INH and RIF, with or without other drugs).

We defined 6 classes of second-line drugs as follows: aminoglycosides other than streptomycin (e.g., kanamycin and amikacin), cyclic polypeptides (e.g., capreomycin), fluoroquinolones (e.g., ofloxacin, ciprofloxacin, levofloxacin, and moxifloxacin), thioamides (e.g., prothionamide and ethionamide), serine analogs (e.g., cycloserine and terizidone), and salicylic acid derivatives (e.g., para-aminosalicyclic acid).

For this survey we created a consensus definition that incorporates second-line–drug susceptibility results and is based on international guidelines for management of drug-resistant TB (*15*). The mainstay of an MDR TB treatment regimen consists of 1 injectible drug (e.g., aminoglycoside or cyclic polypeptide) and a fluoroquinolone; additional drugs from the remaining classes are added until the total reaches 4–6 drugs to which the organism is susceptible. If the infecting organism is resistant to ≥3 second-line drug classes, designing a treatment regimen with sufficient drugs that are known to be effective against TB is difficult. Thus, we defined extensively drug-resistant TB (XDR TB) isolates as those meeting the criteria established for MDR TB plus resistance to ≥3 of the 6 classes of second-line drugs.

Second-line–drug resistance patterns were analyzed by geographic region from which the isolate was submitted to the SRL. Regions were grouped into epidemiologically meaningful categories on the basis of prevalence of TB and MDR TB.[1,16] This retrospective survey was evaluated and approved as public health surveillance by the US Centers for Disease Control and Prevention (CDC).

Results

We received data for 18,462 patients from 14 (61%) of 23 eligible SRLs. We excluded those patients tested before 2000 (n=223), tested after 2004 (n = 14), or tested for resistance to <3 classes of second-line drugs (n = 535). Our final study sample consisted of 17,690 patients whose isolates were tested for resistance to ≥3 second-line drugs during 2000–2004 (Figure 2). Of these, 11,939 (67.5%) patients were from the Republic of Korea and 5,751 (32.5%) were from the remaining SRLs.

First-line–Drug Susceptibility

Among isolates from patients from the 13 SRLs other than the Republic of Korea, 3,765 (65.5%) were resistant to ≥1 first-line TB drug (Table 1). Of these, 3,305 (58.5%) were resistant to at least INH and 2,345 (41.5%) were resistant to at least RIF.

Among isolates from the Republic of Korea patients, 2,508 (21%) had resistance to any drug; most (n = 2,196; 18.4%) were resistant to INH.

Single-drug resistance was found for isolates from 884 (15.4%) patients from the 13 SRLs; 456 (8.1%) of these were resistant to INH and 99 (1.8%) to RIF. Among isolates from patients from the Republic of Korea, 952 (8%) displayed single-drug resistance, 666 (5.6%) to INH and 148 (1.2%) to RIF.

Polyresistance other than MDR TB was seen for isolates from 651 (11.5%) patients from the 13 SRLs and 258 (2.2%) from the Republic of Korea SRL. Not all SRLs routinely tested for resistance to pyrazinamide.

Multidrug resistance (i.e., MDR TB) was present in isolates from 2,222 (39.4%) patients from the 13 SRLs and 1,298 (10.9%) from the Republic of Korea.

Resistance to all first-line drugs tested (i.e., MDR TB with additional resistance to ethambutol and streptomycin) was found in isolates from 1,017 (18.6%) patients from the 13 SRLs and 233 (2%) from the Republic of Korea SRL.

Second-line–Drug Susceptibility

Among patients from the 13 SRLs, resistance to aminoglycosides was detected in 489 (8.7%) isolates and to fluoroquinolones in 298 (5.3%) (Table 2). Among isolates from Republic of Korea patients, resistance was most commonly

seen to fluoroquinolones (n = 524, 4.4%) and thioamides (n = 259, 2.2%).

From all SRLs, isolates that were resistant to at least INH and RIF (i.e., MDR TB; n = 3,520) and tested for susceptibility to ≥3 second-line drugs were combined for analysis of second-line–drug resistance patterns. Resistance to ≥1 class of second-line drug was present in 1,542 (43.8%) MDR TB patients (Table 3). The most commonly observed patterns were resistance to aminoglycosides (n = 630, 18.3%), fluoroquinolones (n = 673, 19.3%), and thioamides (n = 605, 19.3%).

MDR TB patients whose isolates had further resistance to ≥3 classes of second-line drugs were classified as XDR TB (Table 3). A total of 347 (9.9%) MDR TB patients met criteria for XDR TB. According to the revised Global XDR TB Task Force definition (www.who.int/mediacentre/news/notes/2006/np29/en/index.html), 234 (6.6%) isolates met criteria for XDR TB. Among XDR TB patients, combination drug-resistance patterns included 90 (3.4%) with resistance to aminoglycosides, capreomycin and fluoroquinolones; 102 (3.4%) with resistance to aminoglycosides, fluoroquinolones, and thioamides; and 94 (3.8%) with resistance to fluoroquinolones, thioamides, and para-aminosalicyclic acid. Nearly half (n = 167, 48.1%) of all XDR TB isolates were resistant to all 4 first-line drugs, bringing the total to ≥7 drugs to which the isolate was resistant.

The proportion of XDR TB patients by region is shown in Table 4. Among the group of industrialized nations, 53 (6.5%) MDR TB patients met criteria for XDR TB. Among patients from Russia and Eastern Europe, 55 (13.6%) MDR TB patients met criteria for XDR TB. Among patients from the Republic of Korea, 200 (15.4%) MDR TB patients, who accounted for 1.7% of all *M. tuberculosis* isolates tested, met criteria for XDR TB.

In evaluating the accuracy of second-line–drug susceptibility testing, we found that 7 (0.1%) of 11,426 patients fully susceptible to all first-line drugs were resistant to 2 second-line drugs, and 109 (1%) were resistant to 1 second-line drug. Most of these patients were resistant to fluoroquinolones.

Discussion

This study represents the first assessment of the widespread occurrence of *M. tuberculosis* with such extensive drug resistance as to be nearly untreatable with currently available drugs, according to international guidelines. We provide data on second-line–drug resistance for the largest sample of patients to date, including >5,000 patients from 47 countries, apart from the Republic of Korea. The definition of XDR TB in this survey is based on WHO guidelines for the programmatic management of drug-resistant TB; the guidelines recommend treatment with ≥4 drugs known to be effective.[15] Therefore, with ≤3 remaining classes of second-line drugs to which the infecting organism is susceptible, treatment of these patients cannot meet international standards. XDR TB has been detected in all regions of the world. XDR TB strains in this study also have high rates of resistance to pyrazinamide and ethambutol, thereby severely limiting the treatment options available.

Analysis of combination second-line–drug resistance patterns is critical for clinicians and policymakers who design treatment regimens for these patients. Although limited data exist in the literature about second-line–drug resistance patterns among MDR TB patients, data from patients undergoing retreatment for TB in Hong Kong showed that 30 (17%) MDR TB isolates were resistant to ≥3 second-line drugs,[17] thereby meeting criteria for XDR TB. A drug-resistance survey of 447 culture-positive new patients and patients undergoing retreatment in Abkhazia, Republic of Georgia, found that of 63 MDR TB patients, 2 (3%) had additional resistance to 3 second-line drug classes, consistent with XDR TB.[18] More recently, clusters of XDR TB have been reported in South Africa and Iran[19,20] and have been associated with HIV infection and rapid and high death rates.

The emergence of new strains of TB that are resistant to second-line drugs, especially

in settings where TB control programs have become unable to adequately monitor treatment regimens for MDR TB, is cause for concern. After the resurgence of TB in industrialized countries during the 1980s and increased awareness of this global problem, implementation of strong TB control programs based on the principles of the global directly observed treatment strategy, short course (DOTS) improved treatment outcomes and reduced TB and MDR TB incidence in several countries. This framework for DOTS, promulgated by WHO, and the pilot MDR TB management projects (DOTS-Plus projects) became the basis for programmatic management of MDR TB, which has demonstrated feasibility and effectiveness in low- and middle-income countries.[5,15] However, second-line drugs are available worldwide outside of well-organized TB-control programs (WHO, unpublished data).

Improper treatment of drug-resistant TB, such as using too few drugs, relying on poor quality second-line drugs, and failing to ensure adherence to treatment, will likely lead to increases in XDR TB. Strengthening basic TB programs and infection control measures is crucial for preventing the selective pressure and environments in which resistant strains are transmitted from person to person. Additionally, MDR TB programs that rely on quality-assured and internationally recommended treatment regimens according to WHO guidelines must be scaled up and strengthened to stem further second-line–drug resistance and spread of XDR TB. The Green Light Committee provides a global mechanism to help affected countries achieve these steps. A commentary published in 2000 predicted that "failure to institute [the] entire DOTS-Plus package is likely to destroy the last tools available to combat [TB], and may ultimately result in the victory of the tubercle bacillus over mankind").[21] XDR TB is an indirect indicator of program failure to adequately diagnose, prevent, and treat MDR TB.

Documenting the emergence of XDR TB requires a laboratory-based diagnosis that relies on first- and second-line–drug susceptibility testing. A limitation to accurate detection of XDR TB is that existing tests for resistance to second-line drugs are not yet standardized and are less reproducible than tests for resistance to INH and RIF. Lack of international recommendations for use, as well as lack of standardization and the historical unavailability of MDR TB treatment in the public sector, has limited use of second-line–drug susceptibility testing on a wider scale. As access to treatment with second-line drugs increases, standardized methods, improved diagnostics, and quality assurance for second-line–drug susceptibility testing are urgently needed to enable reliable testing and design of appropriate treatment regimens. Although internationally accepted methods were used by all laboratories, the precise methods and drug concentrations used varied among participating SRLs.[22] Because these SRLs represent some of the most highly performing laboratories on 6 continents, results of drug-susceptibility testing are credible within the context of stated limitations. Initial studies that standardized different methods for second-line–drug susceptibility testing have been completed,[23-26] but more are needed.

Our study has other limitations. The numbers reported for XDR TB probably represent an underestimate of the true number of cases because not all SRLs and not all national reference laboratories test for all 6 classes of second-line drugs. In the absence of test results for all 6 classes of second-line drugs, we speculate, on the basis of a patient's TB treatment history and known patterns of drug cross-resistance, that many other unidentified patients are likely to have had and died from XDR TB. For example, an MDR TB isolate that is also resistant to an aminoglycoside and a fluoroquinolone but that has not been tested for the other second-line drug classes is very likely to be resistant to an additional second-line drug class for the following reasons: INH and ethionamide have a 15%–20% rate of cross-resistance;[27] kanamycin and capreomycin cross-resistance is common, ranging from 20%–60% (CDC, unpub. data);[28,29] and in this study, isolates

that were resistant to all 4 first-line drugs as well as an aminoglycoside and a fluoroquinolone were 70%–80% likely to be resistant to at least 1 additional class of second-line drug.

Another limitation is that data from most SRLs were drawn from a convenience sample of isolates and reflect referral bias. Thus, these data can not be considered representative of a patient population or region, and actual denominators are difficult to determine. For this reason, although estimates of prevalence are possible, they cannot be generalized to the local or regional population. However, our study is the first to report XDR TB patients in multiple geographic regions; future systematic surveys are needed to determine the true extent of this disease. Data from the Republic of Korea reflect a more comprehensive policy for drug-susceptibility testing and provide an estimate of the population prevalence in this setting. However, the 10.9% rate of MDR TB for the Republic of Korea is higher than rates reported from other national drug resistance surveys and may reflect other unknown referral biases.[1]

Lastly, we had limited clinical information about each patient because information submitted to each SRL varied and was not reliably available for inclusion in the analysis. Data about TB treatment history, patient age and sex, or HIV status are not routinely collected by all laboratories. Genotyping data were not available to confirm whether XDR TB isolates are related to W variant of the Beijing strain, a highly drug-resistant strain of *M. tuberculosis* responsible for large nosocomial outbreaks in New York in the early 1990s.[30]

Despite these limitations, our survey provides the first documentation of the emergence of XDR TB as a serious worldwide public health threat. XDR TB was identified on 6 continents and is significantly associated with worse treatment outcomes than MDR TB.[31,32] The emergence of XDR TB, coupled with the increased use of second-line drugs, suggests that urgent measures are needed to improve rational use of quality-assured second-line drugs. In addition, population-based surveillance for second-line–drug susceptibility testing is needed to better describe the magnitude of XDR TB worldwide, track trends, and plan a public health response. Indeed, the convergence of XDR TB with the HIV epidemic may undermine gains in HIV prevention and treatment programs and requires urgent interventions. These interventions include ensuring adherence to recommended international standards of care aimed at promptly and reliably diagnosing TB, ensuring adherence to recommended treatment regimens with demonstrated efficacy, implementing infection control precautions where patients congregate, and improving laboratories' capacity to accurately and rapidly detect drug-resistant *M. tuberculosis* isolates so that patients can receive effective treatment.[33] Other unmet needs include further development of international standards for second-line–drug susceptibility testing, new anti-TB drug regimens, and better diagnostic tests for TB and MDR TB. Such measures are crucial if future generations are to be protected from potentially untreatable TB.

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Figure 1. Shading indicates 48 countries that submitted at least 1 isolate to participating Supranational Reference Laboratories, 2000–2004.

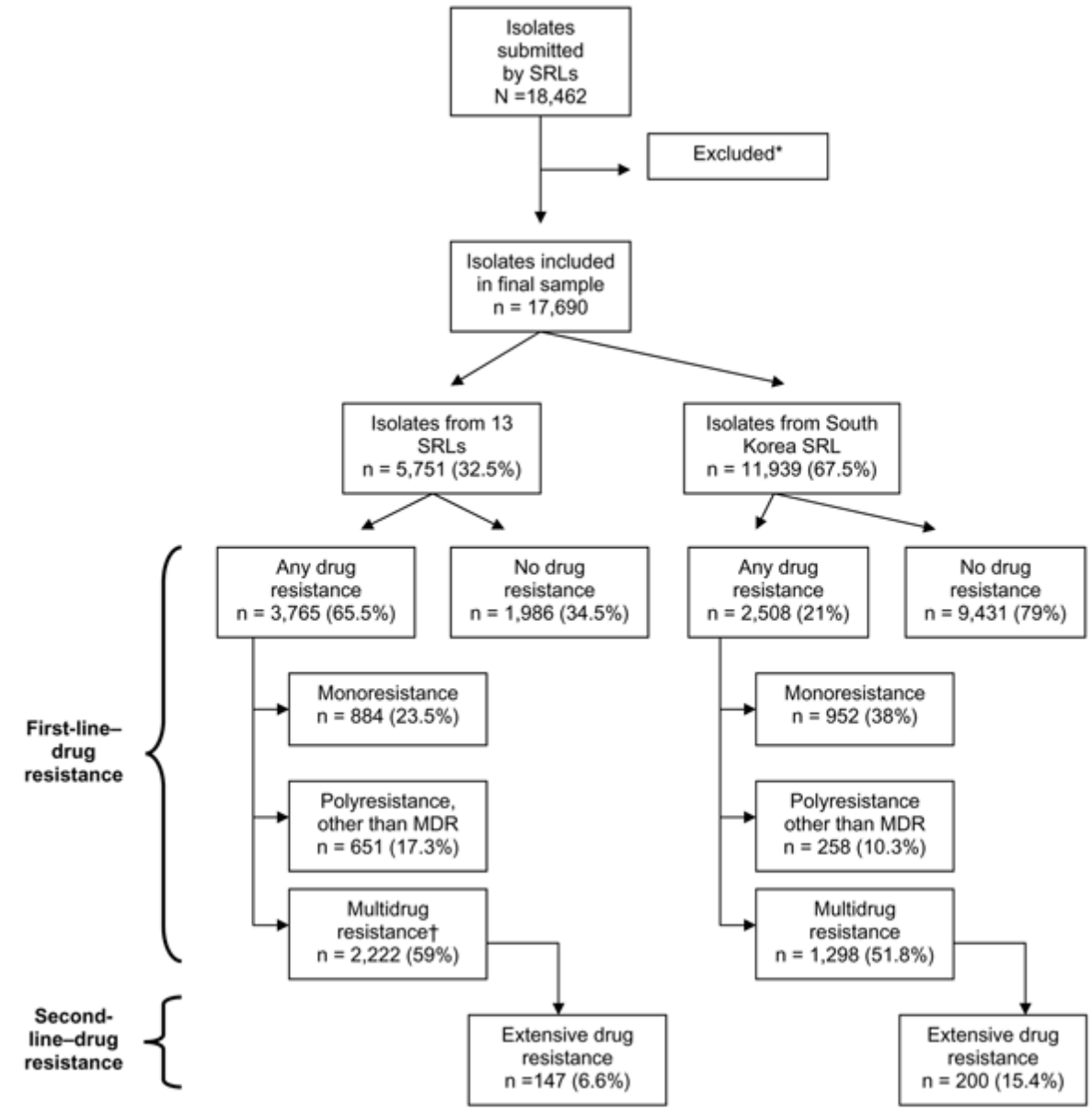

Figure 2. Selection of study sample and summary of drug-resistance patterns of isolates. SRL, Supranational Reference Laboratory. *Tested before 2000 or after 2004 (n = 247) or tested for resistance to <3 classes of second-line drugs (n = 535). †Data for ethambutol resistance missing for 5 isolates.

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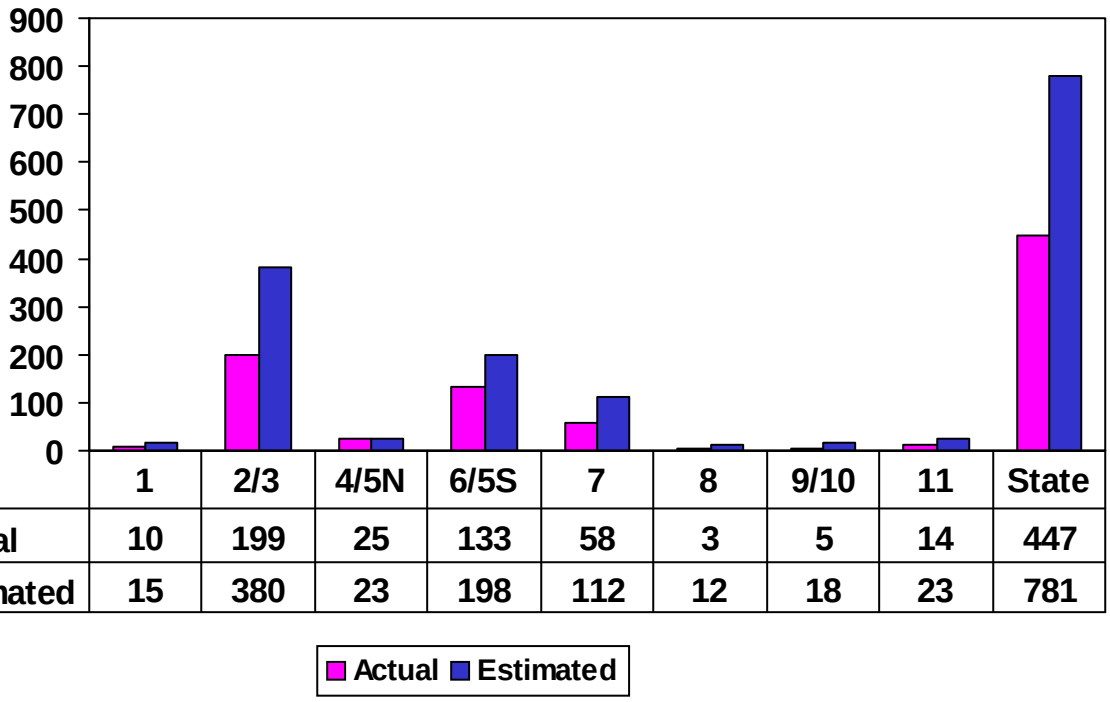
Estimated[†] Number of Babies Born to HBsAg-positive Women vs. Actual (Reported) Number of Babies Born to HBsAg-positive Women by Health Service Region, 2005



	1	2/3	4/5N	6/5S	7	8	9/10	11	State
Actual	10	199	25	133	58	3	5	14	447
Estimated	15	380	23	198	112	12	18	23	781

Source: Department of State Health Services Infectious Disease Intervention and Control Branch Unit Perinatal Hepatitis B Prevention Program 2005 database

[†]Estimates are based on population prevalence rates from the NHANES III (National Health and Nutrition Examination Survey).

A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States

Summary

Hepatitis B vaccination is the most effective measure to prevent hepatitis B virus (HBV) infection and its consequences, including cirrhosis of the liver, liver cancer, liver failure, and death. In adults, ongoing HBV transmission occurs primarily among unvaccinated persons with behavioral risks for HBV transmission (e.g., heterosexuals with multiple sex partners, injection-drug users [IDUs], and men who have sex with men [MSM]) and among household contacts and sex partners of persons with chronic HBV infection.

This report, the second of a two-part statement from the Advisory Committee on Immunization Practices (ACIP), provides updated recommendations to increase hepatitis B vaccination of adults at risk for HBV infection. The first part of the ACIP statement, which provided recommendations for immunization of infants, children, and adolescents, was published previously (CDC. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices [ACIP]. Part 1: immunization of infants, children, and adolescents. MMWR 2005;54[No. RR-16]:1—33).

In settings in which a high proportion of adults have risks for HBV infection (e.g., sexually transmitted disease/human immunodeficiency virus testing and treatment facilities, drug-abuse treatment and prevention settings, health-care settings targeting services to IDUs, health-care settings targeting services to MSM, and correctional facilities), ACIP recommends universal hepatitis B vaccination for all unvaccinated adults. In other primary care and specialty medical settings in which adults at risk for HBV infection receive care, health-care providers should inform all patients about the health benefits of vaccination, including risks for HBV infection and persons for whom vaccination is recommended, and vaccinate adults who report risks for HBV infection and any adults requesting protection from HBV infection. To promote vaccination in all settings, health-care providers should implement standing orders to identify adults recommended for hepatitis B vaccination and administer vaccination as part of routine clinical services, not require acknowledgment of an HBV infection risk factor for adults to receive vaccine, and use available reimbursement mechanisms to remove financial barriers to hepatitis B vaccination.

Centers for Disease Control and Prevention.A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: Immunization of Adul**t.** MMWR 2006;55(RR-16):1-35. Full text is avaialble at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a1.htm.

BOX 1. Immunization strategy to eliminate transmission of hepatitis B virus (HBV) in the United States

- Universal vaccination of infants beginning at birth
- Prevention of perinatal HBV infection through
  - — routine screening of all pregnant women for hepatitis B surface antigen (HBsAg), and
  - — immunoprophylaxis of infants born to HBsAg-positive women or to women with unknown HBsAg status
- Routine vaccination of previously unvaccinated children and adolescents
- Vaccination of previously unvaccinated adults at risk for HBV infection

BOX 2. Geographic regions* with intermediate† and high§ hepatitis B virus endemicity

Africa: all countries
East Asia: all countries
Eastern Europe and Northern Asia: all countries except Hungary
South Asia: all countries except Sri Lanka
Southeast Asia: all countries
Australia and the South Pacific: all countries and territories except Australia and New Zealand
Middle East: all countries except Cyprus
Western Europe: Greece, Malta, Portugal, and Spain and indigenous populations of Greenland
North America: Alaska Natives and indigenous populations of Northern Canada
Central America: Belize, Guatemala, Honduras, and Panama
South America: Argentina, Bolivia, Brazil, Ecuador, Guyana, Suriname, Venezuela, and the Amazonian areas of Colombia and Peru
Caribbean: Antigua and Barbuda, Dominica, Dominican Republic, Grenada, Haiti, Jamaica, Puerto Rico, St. Kitts and Nevis, St. Lucia, St. Vincent and Grenadines, Trinidad and Tobago, and Turcs and Caicos

* A complete list of countries in each region is available at http://www.cdc.gov/travel/destinat.htm.
† Hepatitis B surface antigen (HBsAg) prevalence of 2%–7%.
§ HBsAg prevalence of ≥8%.

BOX 3. Components of a successful adult hepatitis B vaccination program

- Institutional commitment to the program
- Trained and knowledgeable staff who promote the program
- Patients who are informed about hepatitis B and the health benefits of hepatitis B vaccination
- Integrated delivery of vaccination and other services
- Protocols and standing orders
- Protected patient confidentiality
- Infrastructure that ensures vaccine administration is accessible, convenient, and flexible for patients
- Funding for vaccine

BOX 4. Adults recommended to receive hepatitis B vaccination

Persons at risk for infection by sexual exposure

- Sex partners of hepatitis B surface antigen (HBsAg)-positive persons
- Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., persons with more than one sex partner during the previous 6 months)
- Persons seeking evaluation or treatment for a sexually transmitted disease
- Men who have sex with men

Persons at risk for infection by percutaneous or mucosal exposure to blood

- Current or recent injection-drug users
- Household contacts of HBsAg-positive persons
- Residents and staff of facilities for developmentally disabled persons
- Health-care and public safety workers with reasonably anticipated risk for exposure to blood or blood-contaminated body fluids
- Persons with end-stage renal disease, including predialysis, hemodialysis, peritoneal dialysis, and home dialysis patients

Others

- International travelers to regions with high or intermediate levels (HBsAg prevalence of ≥2%) of endemic HBV infection (Figure 4, Box 2)
- Persons with chronic liver disease
- Persons with HIV infection
- All other persons seeking protection from HBV infection

BOX 5. Hepatitis B vaccine schedules for adults (aged ≥20 years)*

0, 1, and 6 months
0, 1, and 4 months
0, 2, and 4 months
0, 1, 2, and 12 months†

* All schedules are applicable to single-antigen hepatitis B vaccines; Twinrix® (combined hepatitis A and hepatitis B vaccine) may be administered at 0, 1, and 6 months.

† A 4-dose schedule of Engerix-B® is licensed for all age groups.

BOX 6. Implementation strategies for adult hepatitis B vaccination

Settings in which a high proportion of persons have risk factors for hepatitis B virus (HBV) infection

- Implement standing orders to administer hepatitis B vaccine as part of routine services to all adults who have not completed vaccination.*

Primary care and specialty medical settings

- Implement standing orders to identify adults recommended for hepatitis B vaccination and administer vaccination as part of routine services.
  - — Provide information to all adults regarding the health benefits of hepatitis B vaccination, including risk factors for HBV infection and persons for whom vaccination is recommended.
  - — Help adults assess their need for vaccination by obtaining a history that emphasizes risks for sexual transmission and percutaneous or mucosal exposure to blood.
  - — Administer hepatitis B vaccine to all adults who report risks for HBV infection.*
  - — Provide hepatitis B vaccine to all adults seeking protection from HBV infection. Acknowledgment of a specific risk factor for HBV infection is not a requirement for vaccination.

Occupational health programs

- Identify staff whose work-related activities involve exposure to blood or other potentially infectious body fluids.
- Provide education to encourage vaccination.
- Implement active follow-up, with reminders to track vaccine-series completion among persons receiving vaccination.
- Provide appropriate postvaccination testing 1–2 months after vaccine-series completion.

* In populations that have expected high rates of previous HBV infection, prevaccination testing might reduce costs by avoiding vaccination of persons who are already immune (see Appendix A, Prevaccination Serologic Testing for Susceptibility).

BOX 7. Settings in which hepatitis B vaccination is recommended for all adults

- Sexually transmitted disease treatment facilities
- Human immunodeficiency virus testing and treatment facilities
- Facilities providing drug-abuse treatment and prevention services
- Health-care settings targeting services to injection-drug users
- Correctional facilities
- Health-care settings targeting services to men who have sex with men
- Chronic-hemodialysis facilities and end-stage renal disease programs
- Institutions and nonresidential day care facilities for developmentally disabled persons

Program Spotlight:

Perinatal Hepatitis B Prevention Program

Breakout Session at the Perinatal Hepatitis B Prevention Conference held at the J.J. Pickle Center in Austin, TX on February 22, 2007.

The goal of the Texas Department of State Health Services Perinatal Hepatitis B Prevention Program (PHBPP) is to eliminate hepatitis B infections in Texas. The PHBPP function is to identify hepatitis B surface antigen (HBsAg)-positive pregnant women. The program ensures that the infants of any HBsAg-positive pregnant women receive hepatitis B immune globulin (HBIG) and the hepatitis B vaccine at birth, and, subsequently, complete the hepatitis B vaccine series and serological testing. Finally, the program identifies the mother's contacts and household members to provide immunization, serological testing, and educational services, as needed.

Texas Law requires:

- Providers and hospitals to screen all pregnant women for HBsAg at their first prenatal visit and at delivery (Texas Administrative Code Title 25, Part 1, Chapter 97, subchapter A § 97.135)
- Perinatal hepatitis B and all positive HBsAg mothers to be reported to DSHS (Texas Administrative Code Title 25, Part 1 Chapter 97, subchapter A, §97.3)

Perinatal hepatitis B is highly preventable by:

- Screening pregnant woman at the first prenatal visit and at delivery
- Giving a birth dose of hepatitis B vaccine and HBIG to babies born to HBsAg-positive women
- Giving birth doses to all babies before hospital discharge

In Texas, up to 1,200 children are born to HBsAg-positive women every year (National Health and Nutrition Examination Survey estimate).

In 2004, only 455 cases were reported. Up to 90% of infants born to HBsAg-positive women will become infected if they do not receive hepatitis B vaccine and HBIG within 12 hours of delivery. If not treated at birth, it's estimated 25% of these infants will die from liver-related diseases such as cirrhosis, liver failure, and hepatocellular carcinoma.

Program services

On February 22, 2007, a group of 140 health care professionals attended the program's statewide conference at the J.J. Pickle Center in Austin. The conference provided education and training on screening, reporting and case management activities.

Prepared by Carole Donsbach, RN, Perinatal Heaptitis B Prevention Program, DSHS. For more information, visit our website at http://www.dshs.state.tx.us/idcu/disease/hepatitis/hepatitis%5Fb/perinatal/fact_sheet/ , send e-mail to carole.donsbach@dshs.state.tx.us or call (512)-458-7111, extension 6535.

Quick*Links*

Disease Reporting in Texas

CDC Hepatitis B Resources

Interpretation of the Hepatitis B Panel Tests Results

Hepatitis B Coordinators

Public Health in Action:
Hansen's Disease Program

The Hansen's Disease Program supports ambulatory services to treat Hansen's disease to prevent deformity and disability through early diagnosis and treatment. It is a reportable condition in Texas and services are provided through Dallas County Health and Human Services, Houston Department of Health and Human Services, Texas Center for Infectious Disease, and Health Service Region (HSR) 11.

Hansen's disease

Hansen's disease (leprosy) is a chronic communicable disease caused by *Mycobacterium leprae* and is considered a major pathogen among the mycobacteria species, next to *M. tuberculosis*. (There are more than 70 species of *Mycobacterium*). A Norwegian scientist, Gerhard Armauer Hansen, MD, first discovered the bacterium in 1873. *M. leprae* is a gram-positive, aerobic rod surrounded by the characteristic waxy coating unique to Mycobacteria. Due to its thick, waxy coating, Ziehl Neelsen stain is used to identify *M.leprae* bacilli rather than the traditional Gram staining method. The bacterium cannot be grown in an artificial culture medium.

Most specialists agree that greater than 95% of the world's population has a natural immunity to the disease; therefore, Hansen's disease is not considered to be highly infectious. Humans are the host carriers and persons with untreated *M. leprae* in the upper respiratory tract are thought to be the main source of infection. In the past, it was believed that transmission required prolonged close contact with an infected person. However, about 75% of patients in the United States have no known contact.

Hansen's disease affects the skin, peripheral nerves, and mucous membranes of the upper respiratory tract, particularly the nasal mucous membranes. The symptoms of *M. leprae* are varying types of skin lesions on the face, trunk, and extremities; absence of sweating; hair loss; and/or changes in the texture of the skin. Damage to the peripheral nerves includes nerve enlargement (Photo 1), neuropathy, diminished sensation of the hands and feet, pain and a burning sensation in the soles of the feet, repeated injury, ulceration, muscle atrophy, and deformity of the hands and feet (Photo 2). Involvement of the eye results in inflammation and incomplete closure of eyelids.

Hansen's disease cases are classified into two groups, paucibacillary and multibacillary:

Paucibacillary cases have few bacilli with the following presentation:

1. Indeterminate lesions
    a. A lesion that appears early in the course of the disease, usually a hypopigmented macule (flat area that is lighter than the rest of the patient's skin)
2. Tuberculoid type (Photo 3)

a. A limited form of the disease
b. Characterized by few lesions
c. Hypo or hyper pigmented
d. Well defined borders
e. Lesions are usually anesthetic
f. Peripheral nerve involvement is common, resulting in severe disabilities
g. Considered non-contagious

Multibacillary cases have many bacilli with the following presentation:

1. Borderline type (borderline tuberculoid or borderline lepromatous) (Photo 4)
    a. Lesions are characteristic of both tuberculoid and lepromatous types, respectively.
2. Lepromatous (Photo 5)
    a. A generalized form of the disease
    b. Many small lesions, symmetrically distributed on the body
    c. Hypo or hyper pigmented
    d. All organs can be involved
    e. Possible inability to perspire
    f. Possible loss of eye lashes and brows
    g. Lobular ear lobes and enlarged folds of skin of the forehead
    h. Considered to be contagious to household contacts of the untreated case. Contacts are at greatest risk, possibly because of genetic factors relating to susceptibility and/or prolonged intimate contact.

Texas ranks among the top five states (California, Louisiana, Florida, and New York) reporting the largest number of diagnosed cases in the United States. Between 2002 and 2006, Texas reported 98 Hansen's disease cases. Forty seven percent (47) were diagnosed with multibacillary lepromatous disease, 23% (23) paucibacillary tuberculoid, and 13% (13) with multibacillary borderline lepromatous. Twenty nine percent of reported cases were identified in HSR 6, with HSR 3, 8, and 11 each reporting 17%. Forty seven percent (47) of cases were United States born and 25% (25) reported Mexico as their country of origin. Fifty three percent (52) of cases are female and 46.9% (46) were male. The racial/ethnic presentation of Hansen's disease in Texas was 44.8% (44) white/Hispanic, 26.5% (26) white/non-Hispanic, 19.3% (19) Asian-Pacific Islander, 4% (4) African American, and 2% (2) American Indian/Alaska Native

Prepared by Linda J. Brown, RN, Nurse Consultant, Infectious Disease Intervention and Control Branch. For more information call: (512) 458-7447.

Photos

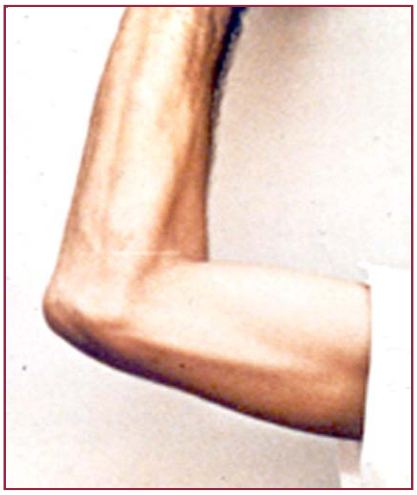


Photo 1. Enlarged peripheral nerve in patient's arm indicating invasion of the bacillus into the nerve creating anesthesia from the point of nerve enlargement to the fingertips. This presentation is often seen among persons diagnosed with tuberculoid type Hansen's disease; however, it may also be present among persons diagnosed with lepromatous or dimorphous type Hansen's disease. The nerve involvement can result in deformity of the hands from muscle wasting and repeated unintentional injury due to loss of sensation. (Return to article)

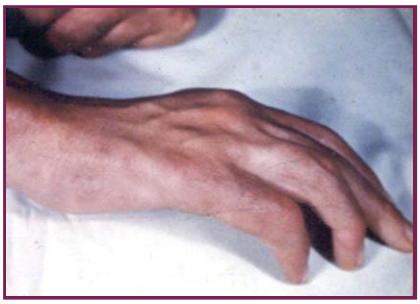


Photo 2. Disfiguration of the hand results from the invasion of the bacillus into the nerve, creating anesthesia from the point of nerve enlargement to the fingertips. This presentation is often seen among persons diagnosed with tuberculoid type leprosy; however, it may also be present among persons diagnosed with lepromatous or dimorphous type Hansen's disease. The nerve involvement can result in deformity of the hands from muscle wasting and repeated unintentional injury due to loss of sensation. Both the ring and little finger demonstrate an enlarged joint, flexor contracture, clawing of the fingertip and shortened digit due to repeated injury and bone absorption.The myth of Hansen's disease is that fingers and toes "fall off"; however the truth is that fingers and toes are shortened by bone absorption when there are repeated injuries due to loss of sensation in the hands and feet. (Return to article)

(continued ☞)

Photos

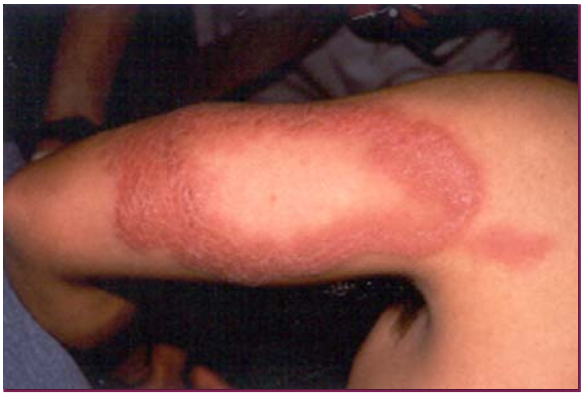


Photo 3. In the **tuberculoid** type of Hansen's disease there are few (1 to 3) skin lesions; these are large (3 to 30 cm) macules. The lesions are hypopigmented or erythematous. They have a well defined border and are rough and scaly. The periphery is raised and erythematous or hyperpigmented; the center is flat and hypopigmented. (Return to article)

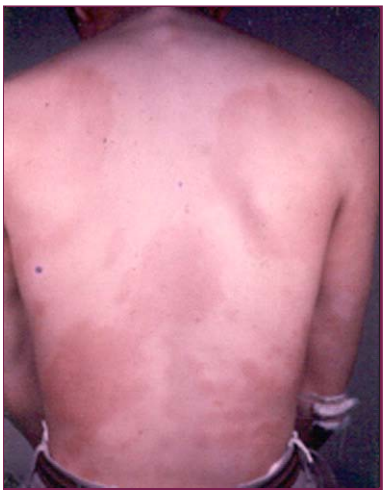


Photo 4. Clinically and histologically **borderline** Hansen's disease has features of both the lepromatous and tuberculoid types. The majority of Hansen's disease cases are borderline, but for particular purposes, they are often classified as Tuberculoid or Lepromatous. The term **dimorphous** is sometimes used instead of borderline. (Return to article)

Photos

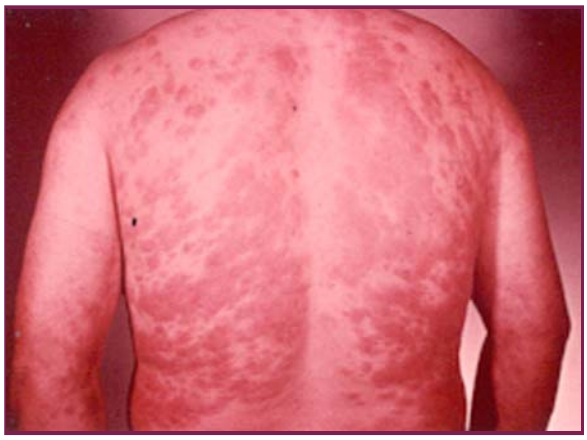


Photo 5. In the **lepromatous** type of Hansen's diease, the skin lesions are very numerous small macules. They appear copper colored or erythematous. Their margin is vague and they tend to coalesce. They are symmetrically distributed over the body. They are not necessarily anesthetic. There is a generalized infiltration of the skin, often noticed by palpation rather than by visual inspection. (Return to article)

Public Health in Action:
Refugee Health Program

Official refugees are persons admitted to the United States because of actual or well-founded fear of persecution in their country of origin.

In year 2006, 3,683 program-eligible clients, including 2,949 official refugees, arrived in Texas. Previously, there had been a noted decline in the arrival numbers following September 11, 2001. Since the program's inception, the numbers from Vietnam (once a majority of arrivals) have declined and those from Africa (Somalia, Liberia, Sudan, Congo, Ethiopia), the Middle East and South Asia (Iran, Afghanistan), and the Far East (Burma) have increased. Recently, most arrivals have come from Cuba. More than 60 other countries have also been represented, in smaller numbers, in the last few years.

The Department of State Health Services Refugee Health Program (RHP) supports local health departments in seven principal refugee resettlement areas with resources to provide health assessments to refugees and other eligible clients.

Eligible for services are newly arrived official refugees (within 90 days of arrival to the United States), Amerasian immigrants, Cuban and Haitian parolees or entrants, asylees (from date-granted asylum), and victims of severe forms of trafficking (from date certified).

Health screening processes

The program supports screening and referral for various health conditions. Newly arrived refugees are screened for tuberculosis (TB), hepatitis B, HIV, sexually transmitted diseases (STDs), and lead and receive vision, hearing and dental testing, a review of immunization status, and initiation of required immunizations. They are also screened for intestinal parasites and receive treatment, if diagnosed. Additionally, a physical exam is provided to identify, educate, and refer for other health problems, which would impede the refugee resettlement process or have significant personal consequence. All program-contracted health departments are guided by the Office of Refugee Resettlement *Medical Screening Protocol for Newly Arriving Refugees*, 1995.

Refugees and all applicants for permanent immigration undergo an overseas Visa Medical Examination, which looks for "excludable medical conditions." These conditions may delay or prevent refugees from traveling to the United States, unless treated, or 'waivered' in with a declaration that identified medical care will be provided in the United States. Excludable conditions include infectious TB disease, HIV, STDs, severe mental illness, and drug addiction. Refugees are usually waivered in for TB and HIV and are treated for STDs overseas.

The overseas medical exam is a limited physical exam. It is not comprehensive and serves primarily to identify excludable medical conditions. The Texas Department of State Health Services Refugee Health Program (RHP) provides a more complete health assessment and when appropriate, will refer refugees for comprehensive medical services.

Refugee health conditions

Tuberculosis

One of the most important public health problems among refugees is tuberculosis infection. With large

number of refugees arriving from TB endemic countries, 30% to 60% of refugees are infected. Up to 10% of these will eventually become active cases if not treated for latent TB infection. Although the actual number of newly arrived refugees diagnosed with TB disease each year is relatively small (15-20), it represents a case rate of about 300 per100,000 population. The Texas case rate is 6.7 per 100,000 population, while the U.S. is 4.8 per 100,000 population. All program-contracted RHPs screen refugees for TB infection and refer them into existing TB programs for evaluation and treatment. Other local and regional health departments are notified of refugee arrivals and target them for screening and evaluation through their tuberculosis programs.

During calendar year 2006, the TB infection rate was approximately 37% among refugees tested. Countries with high infection rates were mainly Africa, especially Congo (49%), Ethiopia (60%), Liberia (48%), but also Afghanistan (52%) and Uzbekistan (46%).

Overall, males were diagnosed more often with latent TB infection than females (43% vs. 31%), however in some populations the disparity is greater (for example, Uzbekistan: M=63% vs. F=27%; Afghanistan M=68% vs. F=36%).

Parasitic infections

Intestinal parasites are also a common health problem among refugees. Forty percent to 70% of refugees are infested with one or more types of parasite. Each of the following is commonly found: hookworm, roundworm (*Ascaris*), whipworm (*Trichuris*), *Giardia lamblia* and *Strongyloides stercoralis* (which can become a generalized fatal infection in immunosuppressed persons). These and other species (e.g. *Entamoeba histolytica*) are of concern, due to inadvertent transmission within households, in day care settings, or food-handling settings. The RHP provides treatment for identified infections.

In 2006, Sherri Khatami, a student from the University of Texas at Austin, reviewed data from the Department of State Health Services laboratory on parasitic infections among refugees who arrived in Texas from 2000 to 2004. Her report indicates that one-third of approximately 14,000 refugees had infection with a pathogenic species. Among protozoan pathogens, *Giardia* was more common for all countries, and Somalia had a higher prevalence rate for *Entamoeba histolytica* and *G. lamblia*. *Giardia*, however, had a higher prevalence rate for children between 0-9 years of age.

The Refugee Health Program data also finds that in 2006, *Giardia*, *Dientamoeba fragilis*, and *E. histolytica* were among the most reported pathogenic protozoan parasitic infections, with *Giardia* reported most often in those 11 years of age and under. Higher percentages of helminthic infections were seen in refugees from Africa, yet helminthic parasites were less common than protozoan parasites. Vietnam and Burma showed higher rates of *Ascaris* and hookworm infections.

Hepatitis B

Approximately 13% of refugees from Southeast Asia are chronically infected with Hepatitis B and may infect newborns or other closely exposed persons. Refugees from other world regions (Africa, Mid-east, and Eastern Europe) are also at increased risk. Local RHPs screen and vaccinate, as

indicated, all arrivals. The program is working to incorporate appropriate testing and follow-up for Hepatitis A, C, D, and E, into the assessment protocol.

Immunizations

Refugees may arrive with incomplete or undocumented immunization histories. Enrollment in immunization clinics and continuation of immunization schedules, especially for children, is an important public health measure. Local RHPs usually provide initial susceptibility testing and immunizations in refugee-specific clinics or coordinate with regular immunization clinics. Some immunizations (varicella especially) not currently available for adults through the Immunization Program are purchased and provided through local RHP programs and budgets.

HIV

In recent years, more arrivals are either HIV positive or diagnosed with HIV/AIDS. These arrivals require specialized management and health assessment procedures and must take into account their immune status (live vaccines, interpretation of tuberculin skin tests, health risk of parasite infections, etc.). When possible, these arrivals are immediately enrolled into specialized HIV programs, where careful medical case management and coordination of health assessment activities and referrals are required.

Other conditions

Additional medical conditions may be noted in records accompanying each arrival, or are identified in the domestic health assessment. The most commonly reported medical conditions are dental problems, defective vision, chest conditions other than TB, and hypertension. These conditions are not more prevalent in one sex than the other. Refugees are referred to local health department clinics or other community health providers for follow up.

Elevated lead levels in some refugee children, who are malnourished and/or underdeveloped, has resulted in the recommendation that children *up to 16 years of age* be given an initial test for elevated lead levels, with retesting for children *under 6 years of age.*

Traumatic experiences overseas, which may include torture, and the immediate and long-term difficulties of adjustment to a new culture may also result in stress or more serious mental problems, including post-traumatic stress disorder on arrival or years after arrival. Challenges to the program include how to address mental health issues at initial screening and identifying culturally appropriate resources for referrals.

Prepared by Sam Householder, MPH, Department of State Health Services Refugee Health Program. For more information, call (512) 458-7111, extension 6976, or e-mail at: sam.householder@dshs.state.tx.us.

Vaccine Preventable Diseases, 2002-2006

Disease	2000	2001	2002	2003	2004	2005	2006*
Congenital Rubella Syndrome	0	0	0	0	0	0	0
Hepatitis A	1,937	1,154	960	613	640	461	306
Hepatitis B	1,059	714	1,110	965	673	742	794
*Hepatitis B, Perinatal	n/a	11	3	1	0	8	1
Hib	4	3	7	5	2	8	11
Measles	0	1	1	0	0	3	0
Mumps	27	14	15	18	24	25	55
Pertussis	327(2)	615(5)	1,240(4)	670(6)	1186 (2)	2224 (9)	913(1)
Rubella	6	2	2	0	1	0	0
Tetanus	5(1)	3(1)	2	1	2	0	0
Varicella	7,003(4)	5,741(1)	6,047(1)	5,465(0)	8657 (0)	8336 (0)	11,094
*Beginning in 2001, Perinatal Hepatitis B w ere counted in children less than 2 years of age.							
( ) Deaths							

*Provisional as of March 21, 2007. Source DSHS Infectious Disease Control Unit. For more information, go to: http://www.dshs.state.tx.us/idcu/health/vaccine_preventable_diseases/

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How to submit manuscripts for publication

The *EpiLink* welcomes the submission of articles on a variety of public health and medical topics for publication. In addition, the newsletter will focus on a different health topic each month, such as maternal and child health and border health issues. If you are interested in contributing articles for the monthly health focus, please read the chart for topics and deadlines.

Issue	Topic	Articles due by
June	Preparing for the 2007 Hurricane Season	May 28, 2007
July	Maternal and Child Health	July 2, 2007
August	Chronic Diseases	July 30, 2007
September	Mental Health	August 28, 2007
October	Influenza	October 1, 2007
November	Border Health Issues	October 29, 2007
December	Communication and Information Technology in Public Health	December 3, 2007
January	Environmental Issues and Occupational Diseases	January 2, 2008
February	Social Marketing in Public Health	January 25, 2008

TEXAS Department of State Health Services