Extensively Drug-Resistant Tuberculosis—United States, 1993-2006

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1 figure, 1 table omitted

THE WORLDWIDE EMERGENCE OF EXTENSIVELY drug-resistant tuberculosis (XDR TB) and a provisional definition* for this form of TB were first reported in November 2004.1,2 A more detailed description of these findings and preliminary data from the U.S. National TB Surveillance System (NTSS) were published in 2006.3 The U.S. data indicated that 74 TB cases reported during 1993-2004 met the case definition for XDR TB.3 Subsequent reports suggested different definitions for XDR TB.4,5 In October 2006, the World Health Organization convened an Emergency Global Task Force on XDR TB, which revised the case definition to specify resistance to at least isoniazid and rifampin among first-line anti-TB drugs, resistance to any fluoroquinolone, and resistance to at least one second-line injectable drug (amikacin, capreomycin, or kanamycin).5 This report updates the 2006 report on XDR TB in the United States, using the revised case definition and provisional data for 2006. NTSS data were analyzed for reported XDR-TB cases during 1993-2006; a total of 49 cases (3% of evaluatable multidrug-resistant [MDR] TB cases) met the revised case definition for XDR TB. Of these, 17 (35%) were reported during 2000-2006. Compared with 1993-1999, cases from 2000-2006 were more likely to be in persons who were foreign born and less likely to be in persons with human immunodeficiency virus (HIV) infection. XDR TB presents a global threat and a challenge to TB-control activities in the United States. To prevent the spread of XDR TB, renewed vigilance is needed through drug-susceptibility testing, case reporting, specialized care, infection control, and expanded capacity for outbreak detection and response.

TB cases reported to NTSS from 50 states and the District of Columbia (DC) were analyzed for the period 1993-2006.† All culture-confirmed cases with initial drug-susceptibility test (DST) results reported for at least isoniazid and rifampin were included in the analysis. Because susceptibility testing is time consuming, especially for second-line drugs, initial DST results are reported separately to avoid delaying reporting of routine TB case data. At the end of treatment, the outcome is reported in a second follow-up report. The HIV status of TB cases reported to NTSS was available through 2006, except in California, where only data on positive HIV test results§ were available through 2004.

TB cases reported during 1993-1999, a period of rapidly decreasing incidence of both TB and MDR TB, were compared with cases reported during 2000-2006, a period of slower decline in TB and MDR-TB rates. During 1993-2006, a total of 202,436 culture-confirmed TB cases were reported to NTSS; 190,312 of these cases had initial drug-susceptibility test (DST) results reported for at least one fluoroquinolone and one injectable second-line drug. Of these, 49 cases (3%) met the revised definition of XDR TB, including 32 cases reported during 1993-1999 and 17 cases reported 2000-2006.

The 49 XDR-TB cases were reported from nine states and one city, with the largest numbers in New York City (19 cases) and California (11 cases). HIV status was known for 29 (59%) of the 49 persons with XDR TB; 16 (55%) were HIV positive. During 1993-1999, a total of 19 persons with XDR TB had known HIV status, of whom 14 (74%) were HIV positive; during 2000-2006, 10 persons had known HIV status, of whom two (20%) were HIV positive. The number and percentage of persons with XDR TB in the group aged 25-44 years decreased from 21 (66%) during 1993-1999 to six (35%) during 2000-2006.

When the two periods were compared, the number of XDR-TB cases among foreign-born persons did not change substantially, but the percentage of XDR-TB cases among foreign-born persons increased from 39% (12 cases) in 1993-1999 to 76% (13 cases) in 2000-2006 as the number of XDR-TB cases among U.S.-born cases decreased. Among racial/ethnic populations, nine (28%) of 32 XDR-TB cases during 1993-1999 were reported among non-Hispanic blacks, decreasing to two (12%) of 17 cases during 2000-2006. Conversely, the number and percentage of cases among Asians increased from three (9%) during 1993-1999 to seven (41%) during 2000-2006. Spu- tturn microscopy for acid-fast bacilli was positive in 27 (69%) of the 39 cases with known results. Mortality in XDR-TB cases was strongly associated with HIV infection. Among 41 persons with XDR TB and known outcomes, 12 (29%) persons died; 10 of those had HIV infection, and the other two did not have HIV test results reported.

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CDC Editorial Note: After approximately 30 years of declining trends, a TB epidemic occurred in the United States during 1985-1992. From 22,201 cases in 1985 (9.3 per 100,000 population), reported TB increased to 26,673 cases in 1992 (10.4 per 100,000 population).7 Although the in- cidence of MDR TB in the United States

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was largely unknown before 1993, the number of cases began increasing in New York City in the early 1980s, and numerous outbreaks of MDR TB were described in the late 1980s and early 1990s. With implementation of elements of the 1992 National Action Plan to Combat Multidrug-Resistant Tuberculosis, reported MDR-TB cases declined rapidly. TB-control activities included improving laboratory services for rapid, accurate culture and DST, improving infection control, and strengthening NTSS to include DST and HIV test results beginning in 1993. The rapid decrease in MDR-TB cases during 1993-1999 likely correlated with the 34% decline in TB cases overall in the United States to 17,501 (6.3 per 100,000) in 1999.7

Effective treatment of MDR TB requires administration, for 18-24 months, of four to six drugs to which the infecting organism is susceptible, including multiple second-line drugs. Beginning in the 1980s, the use of second-line drugs increased substantially as physicians and TB-control programs treated growing numbers of MDR-TB cases. Increased use of these drugs resulted in MDR-TB strains with extensive resistance to both first- and second-line drugs. Thus, XDR TB in the 1990s likely represented the legacy of the 1985-1992 TB epidemic in the United States and treatments to combat the spike in MDR-TB cases.

Characteristics of XDR-TB cases changed during 2000-2006 in parallel with the changing epidemiology of TB in general and MDR TB in particular. These changes included an overall decrease in the number of cases, a decrease in the proportion of cases in HIV-infected persons, an increase in the proportion of cases among foreign-born persons, and an increase in the proportion of Asians among persons with XDR TB, compared with 1993-1999.7

The findings in this report are subject to at least five limitations. First, the number of XDR-TB cases is a minimum estimate because of incomplete DST data. Although 57% of MDR-TB cases had DST results reported for at least one fluoroquinolone and at least one of the three second-line injectable drugs, only 22% had DST results reported for all drug combinations in the definition of XDR TB, taking into consideration cross-resistance among drugs and data available in NTSS. Initial TB isolates with any resistance to rifampin or resistance to any two first-line drugs should be tested for susceptibility to a full panel of anti-TB drugs, and the results should be reported accordingly. Second, aggregate reporting of drug resistance traditionally has been based on only initial DST results, not on drug resistance that develops during treatment. Because of the complexity of second-line DST, results can be delayed by several months and might not be included in the report of initial DST results. Third, approximately 20% of reported TB cases do not have positive cultures that would enable DSTs to be performed. Fourth, NTSS data for 2006 are provisional, and final case counts, including XDR-TB cases, are subject to revision. Finally, HIV test results usually are reported to NTSS after both TB and HIV surveillance systems have verified their annual case counts. Thus, HIV test results lag behind TB case counts, and data on HIV status are complete through 2005 but provisional for 2006, except for California, which provided data only through 2004. In addition, HIV test results from California are less complete. The NTSS surveillance data summarized in this report represent an updated measurement of XDR TB in the United States. However, surveillance data do not enable a detailed understanding of how many XDR-TB cases arise. For example, the relative importance of person-to-person XDR-TB transmission compared with the emergence of XDR TB in individual patients as a consequence of inadequate treatment cannot be determined.

Use of second-line drugs to treat drug-resistant TB is increasing throughout the world, presaging substantial increases in XDR TB internationally. Accurate measures of the incidence, prevalence, and determinants of XDR TB are needed to target public health responses. Attention to fundamental aspects of TB control (e.g., surveillance, prompt culture and DST, directly observed treatment, contact investigation, rapid containment of outbreaks, and infection control) is needed to control XDR TB in the United States in the same manner that MDR TB was addressed during the previous decade. The Federal TB Task Force is developing a domestic and international response for U.S. government agencies regarding XDR TB. A senior-level interagency meeting will be convened to formulate a comprehensive response and to assign responsibilities for a unified strategic approach. Additional information regarding XDR TB is available at http://www.who.int/tb/xdr/en/index.html.

REFERENCES
Alien and Other Drug Use Among Victims of Motor-Vehicle Crashes—West Virginia, 2004-2005

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2 tables omitted

Alcohol use is a well-established risk factor for motor-vehicle crashes. In 2005, approximately 39% of all traffic fatalities in the United States were alcohol related. Evidence of driver impairment from use of drugs other than alcohol is less definitive. In 2005, an estimated 4.3% of persons in the United States reported driving under the influence of a drug used recreationally during the preceding year, and an unknown percentage drove while impaired by drugs being used for medical reasons. To measure the prevalence of alcohol and drug use among persons killed in motor-vehicle crashes in West Virginia (where test results were available for >80% of fatalities), CDC analyzed 2004 and 2005 data reported by the West Virginia Office of the Chief Medical Examiner (OCME) to the Fatality Analysis Reporting System (FARS) of the National Highway Traffic Safety Administration (NHTSA). This report summarizes the results of that analysis, which determined that the prevalence of drug use (25.8%) was similar to the prevalence of a blood alcohol concentration (BAC) ≥0.08 g/dL (27.7%) among persons killed in motor-vehicle crashes. These results suggest that drug use contributes substantially to driver impairment in West Virginia. Measuring the magnitude of this problem nationally will require better surveillance data. Both surveillance and the development of prevention measures are hampered by difficulties in quantifying and defining drug impairment.

FARS is an active, nationwide, population-based surveillance system for motor-vehicle crashes that occur on public roadways and result in the death of a road user (e.g., driver, passenger, pedestrian, or bicyclist) within 30 days. FARS draws on law enforcement records, which include the results of alcohol and drug tests performed on persons killed in these crashes. In 2005, drug test results were available for fewer than half of all fatalities in FARS. However, in West Virginia, OCME routinely screens all victims of motor-vehicle fatalities for evidence of impairment from alcohol and licit and illicit drugs, including narcotics (e.g., heroin and opioid analgesics), marijuana, stimulants (e.g., cocaine and amphetamines), depressants (e.g., benzodiazepines and barbiturates), and other licit drugs (e.g., antidepressants and antihistamines) that might impair a road user. OCME confirms positive screening tests with gas chromatography/mass spectrometry testing. If multiple drugs are reported, FARS records up to three drugs based on the following priority order: (1) narcotics, (2) depressants, (3) stimulants, (4) marijuana, and (5) other licit drugs. Drugs administered to decedents by emergency medical service providers are not included. Results of hospital toxicology screenings performed on specimens before death are not included in FARS data from West Virginia unless no other valid postmortem specimen is available. In 2004 and 2005, a total of 784 motor-vehicle fatalities resulted from crashes on public roads in West Virginia. Of these, 663 (84.6%) had alcohol test results, 660 (84.2%) had drug test results, and 658 (83.9%) had both. Those not tested were typically persons who did not have a valid antemortem sample available and survived too long after the crash for valid postmortem toxicologic testing. Among all drug tests, 78.6% were conducted on blood or both blood and urine. Nearly all of the remaining tests were urine tests only.

OCME detected alcohol in 32.5% of decedents tested for both alcohol and drugs. Illegal BACs (≥0.08 g/dL) were detected in 27.7% of decedents, and BACs ranging from 0.01 to 0.07 g/dL were detected in 4.9%. The prevalence of detectable blood alcohol was higher in males and highest among persons aged 16-34 years. Drivers were more likely to have detectable blood alcohol levels than passengers. Detectable levels of at least one drug were reported for 170 (25.8%) decedents. Of these, 149 (87.6%) had positive blood tests, and 21 (12.4%) had positive urine tests. The prevalence of detectable drug levels was higher in males and highest among persons aged 35-54 years. Drivers were more likely to have detectable drug levels than passengers. Among women and persons aged ≥55 years, drug levels were more prevalent than alcohol. Nearly half (47.3%) of all decedents had alcohol or drugs in their bodies; 11.1% had both. Among decedents with detectable blood alcohol levels, 34.1% tested positive for drugs. Among decedents with no detectable blood alcohol levels, 21.8% tested positive for drugs.

Opioid analgesics and depressants were each found in 7.3% of tested decedents. The three most common opioid analgesics were hydrocodone, oxycodone, and methadone. The depressants reported were sedatives and muscle relaxants, of which benzodiazepines accounted for 83.3%. The most common benzodiazepines were diazepam and alprazolam. Methamphetamine aminals were involved in four of the five amphetamine reports. Overall, 7.6% of...