Epidemiology & Background

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Tuberculosis is an ancient disease that has caused inestimable suffering and claimed millions of lives over the centuries.

Pathologic evidence of tuberculosis (TB) has been found in Egyptian mummies, and Hippocrates described phthisis (consumption) as the most widespread disease of the times. Some of TB’s more famous casualties include Anton Chekov, Frederick Chopin, Robert Louis Stevenson, George Orwell, and Charlotte and Emily Brontë. It is little wonder that the discovery of effective anti-tuberculosis drugs in the 1940s was hailed as a medical milestone. Tragically, in the last 25 years, the misuse of these “miracle” drugs has resulted in a new public health problem: drug-resistant TB. For various reasons, elimination of tuberculosis has not been achieved, despite the availability of effective chemotherapy.

Global Response

Fortunately, there is renewed energy for control of TB and for treatment of drug-susceptible and drug-resistant TB worldwide.

- With the goal of unifying the approach to diagnosis and treatment of TB globally, a collaboration of international organizations has recently endorsed and published a set of standards of care for tuberculosis. The International Standards for Tuberculosis Care (ISTC) presents a set of widely accepted, evidence-based standards describing a level of care that all practitioners, public and private, should seek to achieve in managing patients with, or suspected of having, tuberculosis. These international standards differ from existing guidelines in that standards present what should be done, whereas guidelines describe how the action is to be accomplished. Two of the 17 standards specifically address drug-resistant disease.
  - Standard 14 advises an assessment of the likelihood of drug resistance for TB patients and culture and susceptibility testing for patients at risk of resistance.
  - Standard 15 recommends use of specialized regimens for MDR-TB, including at least 4 drugs to which the organism is known or presumed to be susceptible for at least 18 months.
- The Patients’ Charter for Tuberculosis Care was developed by the World Care Council in tandem with the ISTC to promote a “patient-centered” approach to tuberculosis care. Initiated and developed by patients from around the world, this document outlines the rights and responsibilities of people with tuberculosis defining what the patient should expect from the provider and what the provider should expect from the patient.
- Around the world, many international organizations are working to control and prevent TB; for a partial list, see Appendix 2, “Contact Information for Selected Organizations Working to Control and Prevent TB in the International Arena.”
- Along the United States–Mexico border, a number of organizations and collaborations exist to address TB control:
• **CureTB** (operated from the San Diego TB Control Program) and **TBNet** (operated by the Migrant Clinicians Network in Austin, Texas) are designed to improve continuity of care and access to health care for TB patients who move between Mexico and the United States.

• **Puentes de Esperanza** is a binational program created to diagnose, treat, and prevent drug-resistant TB in Baja California.

• Many of the state health department TB control programs along the border collaborate with these programs to provide care and continuity for TB patients.

**Long-term control and prevention of TB, including drug-resistant TB, will require:**

- Prioritization of TB by policy makers; political will
- Resources for TB control activities
- Effective, well-organized TB control programs
- Widespread surveillance and accurate reporting systems
- Adequate and accessible laboratory services for timely TB diagnosis and susceptibility testing
- Supervision of therapy—directly observed therapy (DOT) in context of patient-centered management
- Adherence to published protocols and standards, including sound infection control measures (especially in high HIV-prevalence settings)
- Adequate supply of anti-tuberculosis first- and second-line drugs
- Research and development into new diagnostics, drugs, and vaccines
- Access to specialized centers with expertise in use of second-line drugs and alternative therapies

**Two Types of Drug-Resistant Cases: New and Previously Treated**

**Drug resistance in a new TB case:** Presence of a resistant strain of *M. tuberculosis* in a patient newly diagnosed with TB who has not previously been treated with TB drugs (or therapy of less than one month duration). These patients were likely to have been infected with a strain that was already drug resistant. These cases are sometimes referred to as “primary” drug resistance.

**Drug resistance in a previously treated TB case:** Presence of a resistant strain in a TB patient who has previously received at least one month of TB therapy. These cases are likely to have been initially infected with a drug-susceptible *M. tuberculosis* strain, but during the course of anti-tuberculosis treatment, drug resistance emerged (sometimes referred to as “secondary” or “acquired” drug resistance).

Without genotyping of original and subsequent isolates, it is impossible to discern whether previously treated patients have always been infected with drug-resistant strains, were reinfected with a new drug-resistant strain (primary resistance), or whether their strains evolved on treatment (secondary resistance). Hence the current terminology: drug resistance in new vs. previously treated cases.
Multidrug-resistant (MDR)-TB is a strain that is resistant to at least isoniazid and rifampin.

Extremely drug-resistant (XDR)-TB is a strain that is resistant to isoniazid, rifampin, a fluoroquinolone, and at least one of three injectable second-line drugs (amikacin, kanamycin, or capreomycin).

XDR-TB: The Latest Chapter in the Evolution of Drug-Resistant TB

In 2006, details about an outbreak of HIV-associated XDR-TB emerged from Tugela Ferry, KwaZulu-Natal Province in South Africa. Of 221 MDR-TB cases identified during a 14-month period in this isolated community, 53 (23%) were also resistant to kanamycin and ciprofloxacin. Half of the patients were new cases of TB. Among the 53 patients, 44 were tested for HIV, and all 44 were HIV-positive. The mortality rate among the 53 patients was shocking: 52 (98%) of the patients died within weeks of initial sputum collection. The rapid spread of disease was attributed to inadequate infection control in the crowded rural hospital.

The Tugela Ferry outbreak tragically demonstrated both the emergence and dire consequences of XDR-TB. Worldwide health experts mobilized to respond to the crisis, and WHO issued a revised definition of XDR-TB in its 2006 global alert: “TB that is resistant to isoniazid, rifampin, a fluoroquinolone, and at least one of three injectable second-line drugs (amikacin, kanamycin, or capreomycin).

Not all XDR patients die, but high mortality is associated with HIV co-infection, as seen in South Africa. For all XDR patients, the risk of mortality is increased because treatment options are extremely limited and rely on regimens that are less effective, highly toxic, lengthy, and expensive.

In March 2007 a single case of suspected XDR-TB gained worldwide notoriety when an American lawyer disregarded warnings not to travel and boarded several international flights to and within Europe, exposing hundreds of passengers from multiple countries to a TB isolate subsequently diagnosed as XDR (but later confirmed to be MDR.) The case raised urgent issues regarding not only drug-resistant TB and its transmission, but the strength of governmental quarantine and isolation authority.

As of early 2008, XDR-TB was reported from 45 countries.

In the United States, from 1993-2006, 49 cases of XDR-TB were identified, involving 9 states and New York City. During the same period in California, among 425 MDR-TB with complete drug susceptibility reporting, 19 (4.5%) were XDR and 77 (18%) were pre-XDR.

*When considering the burden of MDR and XDR in a given population, a significant but often overlooked category is “pre-XDR,” described as MDR-TB isolates with resistance to a fluoroquinolone or an injectable, but not both. Because pre-XDR is merely one drug away from developing into XDR, some researchers now include this transitional category of resistance in their analyses.
TB Epidemiology Overview

- The World Health Organization (WHO) estimates that each year there are 9 million new TB cases. Annually, TB kills approximately 1.5 million people, making it second only to HIV/AIDS as the leading cause of death from infectious disease.

- Approximately 2 billion people (1 in 3 individuals worldwide) are infected with Mycobacterium tuberculosis. Among those infected with M. tuberculosis, approximately 50 million are infected with drug-resistant strains.

- Worldwide, an estimated 490,000 cases of MDR-TB emerge each year, (5.3% of all new and previously treated TB cases), resulting in 110,000 deaths.

- In the United States, drug resistance in foreign-born persons with TB is much more common than in persons born in the United States, corresponding to the higher rates of drug resistance in the countries of origin. In 2006, 80% of multidrug-resistant TB (MDR-TB) cases in the United States were among foreign-born persons.

- Fortunately, in the United States, drug-resistant TB has been declining in all categories (U.S.-born, foreign-born, previously treated and no previous history of TB) since the early to mid 1990s. For example, among foreign-born individuals not previously treated for TB, resistance to isoniazid (INH) peaked in 1998 at 640 cases (11.3%) and in 2006 was down to 577 cases (10.2%). MDR-TB in previously untreated foreign-born individuals declined from 110 (2.1%) in 1994 to 73 (1.3%) in 2006.

Global Burden of Drug Resistance

Accurate data regarding rates of drug resistance are not universally available. Prior to 1994, rates of drug resistance were mostly based on non-standardized, non-representative samples. Starting in 1994, WHO began to systematically sample countries or regions in order to better assess rates of drug-resistant TB, and new statistical models have recently been developed to approximate the data missing from over 100 countries. The latest estimates portray a sobering snapshot of MDR’s worldwide presence:

- In 2004, there were an estimated 424,203 cases of MDR-TB worldwide, of which 181,408 occurred from previously treated cases. There were 116,000 deaths from MDR-TB.

- With a total of 261,362 cases, China, India, and the Russian Federation accounted for nearly two-thirds of the estimated global MDR-TB burden.

In its 2007-2008 global response plan, WHO identified the top 25 priority MDR-TB and XDR-TB countries, based on their estimated MDR-TB burden and their proportion of MDR-TB among new and previously treated cases combined (see Table 1). The selected countries constitute 85% of the global burden of MDR-TB.

- The five countries with the highest number of MDR cases are China, India, the Russian Federation, South Africa, and Indonesia.

- In the list of countries with the highest proportions of MDR-TB cases among all new and previously treated cases, nations within the Eastern European region—such as Kazakhstan, Estonia, Georgia, Azerbaijan, Uzbekistan, and the Republic of Moldova—dominate the entire first half of the list.

Note: Laboratory capacity in Africa is severely limited, and only 6 African countries were able to provide drug resistance data for WHO’s 2008 report.
<table>
<thead>
<tr>
<th>Country</th>
<th>Estimated proportion of MDR-TB among combined* cases (%)</th>
<th>Estimated total number of MDR-TB cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kazakhstan</td>
<td>23.4</td>
<td>6,718</td>
</tr>
<tr>
<td>Estonia</td>
<td>20.1</td>
<td>147</td>
</tr>
<tr>
<td>Georgia</td>
<td>19.5</td>
<td>980</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>18.9</td>
<td>1,459</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>18.8</td>
<td>1,579</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>18.5</td>
<td>7,043</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>16.8</td>
<td>34,055</td>
</tr>
<tr>
<td>Lithuania</td>
<td>16.4</td>
<td>422</td>
</tr>
<tr>
<td>Ukraine</td>
<td>13.6</td>
<td>7,854</td>
</tr>
<tr>
<td>Latvia</td>
<td>11.5</td>
<td>208</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>10.9</td>
<td>1,394</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>10.6</td>
<td>766</td>
</tr>
<tr>
<td>Belarus</td>
<td>10.4</td>
<td>707</td>
</tr>
<tr>
<td>China</td>
<td>8.9</td>
<td>139,894</td>
</tr>
<tr>
<td>Myanmar</td>
<td>5.2</td>
<td>4,756</td>
</tr>
<tr>
<td>India</td>
<td>4.1</td>
<td>87,413</td>
</tr>
<tr>
<td>Pakistan</td>
<td>3.2</td>
<td>9,306</td>
</tr>
<tr>
<td>Vietnam</td>
<td>3.2</td>
<td>5,033</td>
</tr>
<tr>
<td>South Africa</td>
<td>2.6</td>
<td>10,348</td>
</tr>
<tr>
<td>Democratic Republic of the Congo</td>
<td>2.3</td>
<td>4,941</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>2.2</td>
<td>7,216</td>
</tr>
<tr>
<td>Nigeria</td>
<td>2.0</td>
<td>7,969</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>1.9</td>
<td>5,102</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1.8</td>
<td>10,024</td>
</tr>
<tr>
<td>Philippines</td>
<td>1.8</td>
<td>4,469</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>359,803</strong></td>
</tr>
</tbody>
</table>

*New MDR-TB cases plus previously treated MDR-TB patients.

MDR-TB: multidrug-resistant tuberculosis

XDR-TB: extensively drug-resistant tuberculosis

Drug-Resistant TB in the United States

- In 2006: 13,779 TB cases (4.6 per 100,000) were reported in the United States. There were 646 deaths from TB in 2005 (the latest year for which complete data are available).

- In 2006, among the cases reported that were new cases (no previous history of TB): 7.7% were INH-resistant and 0.9% were caused by MDR-TB strains.

- Among the cases reported with previously treated TB: 13.6% were INH-resistant and 4.2% were caused by MDR-TB strains.

- The number of MDR-TB cases in the United States has declined steadily since 1993 (see Figure 1) after aggressive public health intervention in the early 1990s. Completion of therapy by DOT and effective infection control measures have helped to control the spread of MDR-TB in immunocompromised and hospitalized individuals.

- In 2006, 45 states reported INH-resistant TB cases; 25 states reported MDR-TB.

- California, New York, and Texas contribute the highest number of drug-resistant TB cases to the U.S. total, accounting for just over one-half of the MDR-TB cases reported in 2006.

- California, with nearly 3000 cases of TB annually, has reported the largest number of MDR-TB cases in the nation since 2002. California's MDR-TB cases decreased from 42 in 2005 to 31 in 2006. Given the lengthy period of treatment, the prevalence of MDR-TB cases can be more than twice the number of new cases reported in a given year.

- In 2006, 73 of 91 (80%) new cases of MDR in the United States were foreign-born. In California, more than 85% of MDR cases were foreign-born. In 1993, 25% of patients with MDR-TB in the United States were foreign-born, and the percentage has gradually increased to the current level.

MDR-TB: A Staggering Cost for a Small Percentage of TB Cases

In the year 2004, there were an estimated 424,203 new and previously treated cases of MDR-TB in the world (representing just over 4% of all new and previously treated cases). This figure is in contrast to the 1960s, when rifampin was introduced and not a single MDR case had yet been documented. Appropriate care of these MDR-TB patients would cost more than the care of all drug-susceptible cases combined. A recent survey of local XDR-TB cases in Southern California estimated the cost of inpatient treatment for a single XDR-TB case to be $600,000 in 2006 dollars.
FIGURE 1.

MDR-TB in the United States, 1993-2006

Source: Centers for Disease Control and Prevention
Of the foreign-born patients diagnosed with MDR-TB in the United States from 2005 to 2006, 81% were born in only 14 countries. Table 2 shows the drug resistance pattern for the top 14 countries of origin for United States cases of drug-resistant TB. Younger patients, patients who have recently immigrated, and patients previously treated for TB will have higher rates of resistance. In addition, the true measure of MDR and XDR remains underestimated due to continuing surveillance gaps in many regions of the world.

**TABLE 2.**


<table>
<thead>
<tr>
<th>Country of origin</th>
<th>Total TB cases*</th>
<th>MDR</th>
<th>Any resistance</th>
<th>INH resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Mexico</td>
<td>2969</td>
<td>26</td>
<td>0.9</td>
<td>508</td>
</tr>
<tr>
<td>Philippines</td>
<td>1350</td>
<td>20</td>
<td>1.5</td>
<td>242</td>
</tr>
<tr>
<td>Vietnam</td>
<td>985</td>
<td>19</td>
<td>1.9</td>
<td>280</td>
</tr>
<tr>
<td>India</td>
<td>878</td>
<td>22</td>
<td>2.5</td>
<td>134</td>
</tr>
<tr>
<td>China</td>
<td>612</td>
<td>18</td>
<td>2.9</td>
<td>102</td>
</tr>
<tr>
<td>Guatemala</td>
<td>342</td>
<td>7</td>
<td>2.0</td>
<td>54</td>
</tr>
<tr>
<td>Haiti</td>
<td>334</td>
<td>5</td>
<td>1.5</td>
<td>43</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>312</td>
<td>7</td>
<td>2.2</td>
<td>46</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>276</td>
<td>5</td>
<td>1.8</td>
<td>56</td>
</tr>
<tr>
<td>Peru</td>
<td>253</td>
<td>10</td>
<td>4.0</td>
<td>57</td>
</tr>
<tr>
<td>Somalia</td>
<td>237</td>
<td>4</td>
<td>1.7</td>
<td>50</td>
</tr>
<tr>
<td>Ecuador</td>
<td>203</td>
<td>3</td>
<td>1.5</td>
<td>29</td>
</tr>
<tr>
<td>Laos</td>
<td>122</td>
<td>9</td>
<td>7.4</td>
<td>29</td>
</tr>
<tr>
<td>Russia</td>
<td>68</td>
<td>6</td>
<td>8.8</td>
<td>14</td>
</tr>
</tbody>
</table>

* Total cases with positive cultures and initial susceptibilities performed
Source: Centers for Disease Control and Prevention, National Tuberculosis Surveillance System
TB Drugs and the Development of Resistance

With the widespread and sometimes incorrect use of anti-tuberculosis treatment, the drug resistance situation has changed dramatically. Resistance to streptomycin was documented shortly after it was introduced as monotherapy for TB in the United States in the 1940s. When a single drug is used to treat a large bacillary load of TB organisms, the susceptible organisms are killed, and gradually, the resistant strains multiply and constitute a greater percentage of the population. Subsequently, the patient experiences clinical, microbiologic, and treatment failure.

Multidrug regimens soon became the recommended treatment standard in order to prevent the selection of drug-resistant strains. By 1972, rifampin (RIF) became regularly utilized in anti-tuberculosis regimens, and overall resistance to anti-tuberculosis drugs was uncommon. From 1985 to 1992, TB incidence increased in the United States and outbreaks of drug-resistant TB and MDR-TB occurred. In 1993, the Centers for Disease Control and Prevention (CDC) initiated a national surveillance program for drug resistance to monitor trends and inform interventions.

### Clinical Use of Anti-Tuberculosis Drugs in the United States

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>1945</td>
<td>Streptomycin</td>
</tr>
<tr>
<td>1946</td>
<td>Para-aminosalicylic Acid</td>
</tr>
<tr>
<td>1952</td>
<td>Isoniazid / Pyrazinamide</td>
</tr>
<tr>
<td>1962</td>
<td>Ethambutol</td>
</tr>
<tr>
<td>1967</td>
<td>Rifampin</td>
</tr>
</tbody>
</table>
Evolution and Genetic Basis of Drug-Resistant TB

- Naturally occurring mutations that confer resistance to anti-tuberculosis drugs occur spontaneously and independently.
- Wild-type TB strains are those that have not previously been exposed to anti-tuberculosis drugs.
- Within wild-type *M. tuberculosis* populations, small populations of mutants are found to be resistant to anti-tuberculosis drugs. In a given wild-type population:
  - $3.5 \times 10^{-6}$ are resistant to INH
  - $1.2 \times 10^{-8}$ are resistant to RIF
  - $3.1 \times 10^{-5}$ are resistant to ethambutol (EMB)
  - $3.8 \times 10^{-6}$ are resistant to streptomycin (SM)
- Within wild-type populations, resistance to more than one TB drug is even rarer (as resistance to the various drugs is not linked genetically). Inherent resistance to more than one TB drug is the product of the rates of the individual drugs.
  - INH and RIF: $3.5 \times 10^{-6} \times 1.2 \times 10^{-8}$ equals $4.2 \times 10^{-14}$
- Before the clinical use of TB drugs, *M. tuberculosis* strains were susceptible to the newly discovered anti-tuberculosis drugs.
- Prior to the use of anti-tuberculosis therapy, an individual would need to be infected with a very large population of *M. tuberculosis* to contain any drug-resistant organisms, much less any that would be clinically significant.

- **Selection of the naturally occurring drug-resistant mutants by inadequate TB treatment will cause the population of *M. tuberculosis* bacteria to become increasingly drug-resistant. As the drug-susceptible organisms are killed during sub-optimal treatment, the drug-resistant mutants become an increasing proportion of the disease burden.**

- A large body of knowledge has been accumulated regarding the molecular basis for drug resistance in *M. tuberculosis*.
- Known mutations account for most resistance of strains of *M. tuberculosis* to INH, RIF, pyrazinamide (PZA), SM, EMB, and fluoroquinolones (see Table 3).
- Some strains are drug resistant and do not have any of the known mutations.
### Table 3: Mutations

<table>
<thead>
<tr>
<th>Anti-tuberculosis drug</th>
<th>Gene mutated</th>
<th>% of mutations</th>
<th>Product of that gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>katG</td>
<td>40–60%</td>
<td>Catalase-peroxidase <em>(activates INH)</em></td>
</tr>
<tr>
<td>Isoniazid – ethionamide</td>
<td>inhA</td>
<td>15–43%</td>
<td>Reductase analog <em>(Mycolic acid synthesis)</em></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>ahpC</td>
<td>10%</td>
<td>Hydroperoxidase reductase</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>kasA</td>
<td>unknown</td>
<td>Carrier protein synthase</td>
</tr>
<tr>
<td>Rifampin</td>
<td>rpoB</td>
<td>&gt;96%</td>
<td>Subunit of RNA polymerase</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>pncA</td>
<td>72–97%</td>
<td>Pyrazinamidase</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>embB</td>
<td>47–65%</td>
<td>Arabinosyltransferase</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>rpsL or rrs</td>
<td>50–75%</td>
<td>Ribosomal protein S12/16S rRNA</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>gyrA</td>
<td>75–94%</td>
<td>DNA gyrase A subunit</td>
</tr>
</tbody>
</table>
Factors that Create Resistance

In a previously treated TB case, factors that create or amplify drug resistance include:

- The patient may not take all the drugs prescribed, due to any of the following factors:
  - Lack of resources
  - Intolerance/toxicity
  - Misunderstanding
  - Interrupted drug supply
  - Disbelief in the diagnosis
  - Disbelief in the efficacy or necessity of the treatment
  - Chaotic lifestyle; substance abuse
  - Cultural issues
  - Pregnancy
  - Neuropsychiatric disease

- There may be a dispensing or administration error regarding the correct dose.
- The patient may not be prescribed a large enough dose to be effective.
- The patient may not absorb the full dose of medication and/or have disease in areas where the penetration of one or more of the drugs may be impaired.
- The provider may not prescribe an adequate TB regimen.
- The patient’s organism may already be resistant to one of the TB drugs prescribed, leaving an unrecognized suboptimal TB regimen.
- The patient may have been incorrectly diagnosed as having latent TB infection (LTBI), rather than active TB, and treated with monotherapy.
- The TB patient may be taking therapy for another disease. That therapy may coincidentally contain a single drug active against TB (rifabutin in an HIV patient for *Mycobacterium avium* complex [MAC] prophylaxis; repeated courses of a fluoroquinolone for community-acquired pneumonia).
- The patient may take TB medicines available without a prescription.
- The TB medicines may interact with other drugs being taken by the patient.

If the patient starts an effective TB regimen and then stops taking all the TB drugs at the same time, the population of bacteria usually remains susceptible. This is one of the major advantages of DOT: either the patients take all the drugs or none of them. This is also the benefit of combination formulations such as INH/RIF or INH/RIF/PZA in a single product. The patient either takes all drugs or none—reducing risk of development of resistance.

Clinically significant drug resistance usually emerges after 1 to 2 months of administration of an inadequate drug regimen.
Summary

- Worldwide, there is renewed energy for control of TB and for treatment of drug-susceptible and drug-resistant TB.
- Sustained political will, significant resources, and efficient TB control programs are required to reverse the trend of TB drug resistance.
- There are 2 types of drug-resistant TB cases: “new cases” (infected by an already drug-resistant strain) and “previously treated” TB cases.
- The latest evolution of drug-resistance, XDR-TB, is found in 45 countries, including the United States. High mortality is associated with HIV coinfection.
- Drug-resistant TB in all its variations (monoresistant, polyresistant, MDR, and XDR) is found throughout the world. High-burden areas of the world include China, India, and the Eastern European region.
- Although MDR-TB in the United States has declined over the last decade, 45 states reported drug-resistant cases in 2006. California, New York, and Texas have the highest numbers of MDR-TB cases. Between 2000 and 2006, 17 cases of XDR-TB were reported in the United States.
- The incidence of drug-resistant TB in the United States is highest among foreign-born cases.
- Mutations leading to drug-resistant M. tuberculosis occur spontaneously and independently. The tiny populations of inherently resistant mutants are easily treated during appropriate multidrug TB regimens. Inadequate TB treatment or inadvertent mono-drug therapy allows for the proliferation and eventual clinical significance of drug-resistant populations.
References


