MDR/XDR TB: An Update

Sundari Mase MD, MPH
Team Lead for Medical Affairs
Division of Tuberculosis Elimination
Centers for Disease Control and Prevention
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Session Objectives

- Definitions
- Epidemiology of MDR/XDR TB
- Building a treatment regimen
- Managing contacts to MDR TB
- MDR TB treatment outcomes
- Adjunctive therapy – surgery
- New TB drug development
- Rapid diagnosis of drug resistance
- Identifying resources for education, training, and expert consultation

Definitions

- MDR-TB
  - Resistance to at least isoniazid and rifampin
  - Importance
    - No short course treatment regimen available
    - Requires use of more toxic drugs
Definitions (2)

• XDR-TB
  - Resistant to at least isoniazid, rifampin, plus resistance to any fluoroquinolone and at least one of three injectable second-line drug (aminoglycosides, kanamycin, or capreomycin)

  - Importance
    ➢ Emerging epidemic of untreatable TB
    ➢ Very high mortality ( >25-40% )

Definitions (3)

• MDR or XDR-TB
  - Primary Resistance: person is exposed to TB which is already drug-resistant and develops disease
  - Secondary (acquired) Resistance: drug resistance develops during the course of treatment

Background

• Enormous resource sink
• Prolonged treatment/monitoring required
• Large cost incurred (drugs, hospitalization, isolation, DOT, lab testing)
• Major impact to individual health
• Pool of clinical experts diminishing
• Increasingly complex healthcare systems to navigate
• No proven therapy for contacts

Which Patients are at Risk of Drug Resistant TB?

• Birth/ residence in country with high incidence of drug resistant TB
• U.S. residents who travel to high risk areas
• Exposure to patient with relapse or failure
• Prior treatment for TB
• Treatment failure
• Relapse in a patient not on DOT
• Poor adherence
• Clinical deterioration during 4 drug therapy
Why Do We Have Drug Resistance?

- Inadequate treatment
  - Incorrect regimen (lack of drugs or knowledge)
  - Poor adherence
- Treatment failure / relapse with drug resistant TB
- Transmission of drug resistant TB

Random Naturally Occurring Resistance

- INH = 1 in $10^6$
- RMP = 1 in $10^8$
- EMB = 1 in $10^6$
- Strep = 1 in $10^6$

Drug Resistant Mutants Selected by:

- Non-adherence
- Malabsorption
- Inadequate drug regimen

Drug-resistant mutants in large bacterial population

Multidrug therapy: No bacteria resistant to all 3 drugs

Monotherapy: INH-resistant bacteria proliferate
Spontaneous mutations develop as bacilli proliferate to >10^8

INH mono-resist. mutants killed, RIF-resist. mutants proliferate → MDR TB

Emergence of Resistance with Single Drug Therapy of Active TB

Start INH alone

INH-S

INH-R

Cost of a single MDR-TB case in the U.S. ranges from $28,217 - $1,278,066
**Epidemiology**

**Tuberculosis in the World**
- People infected: ≈2 billion
- New TB cases: 8.9m (141)
- New ss+ TB cases: 3.9m (62)
- Change in incidence rate: 1% / yr
- HIV prev. in new adult cases: 12%
- MDR prev. in new cases: 3%
- Deaths from TB (inc HIV): 1.8m (29)

**Drug Resistance in the U.S.**
- Current proportions of resistance (U.S.):
  - INH = 8%
  - Rifampin = 3%
  - PZA = 3%
  - EMB = 2%
  - Streptomycin = 6%
  - MDR = 1-2%

**Primary Anti-TB Drug Resistance**
- United States, 1993 – 2010*
Primary MDR TB
United States, 1993 – 2010*

No. of Cases Percentage


No. of Cases U.S.-born Foreign-born

No. of Cases Percentage


XDR TB Case Count Defined on Initial DST* by Year, 1993 – 2010**

Year of Diagnosis

No. of Cases

U.S.-born Foreign-born

No. of Cases Percentage


MDR and XDR: 2010 Global Report on Surveillance and Response - New Cases

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
MDR and XDR: 2010 Global Report on Surveillance and Response - Prior Treatment

MDR-TB among subcategories of retreatment cases (9 settings, 2002-2008)

- Not MDR
- MDR

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>31%</td>
</tr>
<tr>
<td>2003</td>
<td>32%</td>
</tr>
<tr>
<td>2004</td>
<td>15%</td>
</tr>
<tr>
<td>2005</td>
<td>31%</td>
</tr>
<tr>
<td>2006</td>
<td>27%</td>
</tr>
<tr>
<td>2007</td>
<td>28%</td>
</tr>
<tr>
<td>2008</td>
<td>44%</td>
</tr>
</tbody>
</table>

Only ~1-3% of MDR is diagnosed with DST

Only ~1% MDR is treated according to WHO standards
Notified cases of MDR-TB (2006 – 2010) & projected numbers of patients to be enrolled on treatment (2011-2012)

Global TB Control Report 2011, WHO

MDR and XDR: 2010 Global Report on Surveillance and Response  WHO

<16,000 actually treated!

XDR TB in California 1993-2006

- 12 of 18 pts were XDR at time of presentation
- 10 of 12 (83%) were foreign born
  - Disease diagnosed median 0.9 year after arrival in U.S.
  - (MDR 3.7 years, TB in general 9 years)
- 7 of 18 (46.7%) born in Mexico
  - (27% of MDR born in Mexico)
  - Early in study most foreign born from Asia
  - Later in study most were from Mexico

Prevalence of 2nd Line Drug Resistance in MDR TB Patients

- PETTS Study in 7 of 8 countries*
  - 522 MDR isolates
    - 109 (20%) had resistance to either an injectable second line drug (SLD) or FQN – Pre XDR TB
    - 30 XDR
    - 285 resistant to all 1st line drugs

Preserving Effective TB Treatment Study: *Estonia, Latvia, Peru, Philippines, Russia, South Africa, South Korea, and Thailand
Emergence of Totally Drug Resistant (TDR) TB

- XDR TB plus cycloserine, PAS, all injectables
- 15 TDR isolates; 56% Iranian, 30% Afghan
- Cases + smear/culture after 18 months Rx
- VNTR profiles and spoligotyping different
  - Not explained by transmission

TB/HIV: High Incidence Areas

- The dramatic increase in the number of people living with HIV in the past decade has fueled the South African TB epidemic
  - National estimates of HIV among TB patients now range from 60% to 80%
- The Asia and Pacific regions
  - This region has more than half the global burden of TB and 12% of the global burden of HIV
- Only 20% of persons with HIV know their status

MDR and XDR-TB across national borders

WHO and Stop TB HIV TB Newsletter, Oct 2009
Medical Management of MDR/XDR-TB

Treatment Strategies

<table>
<thead>
<tr>
<th>Treatment Strategies</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized treatment</td>
<td>Regimen is designed based on DRS data from a representative patient population</td>
</tr>
<tr>
<td>Empirical treatment</td>
<td>Regimen is individually designed based on patient's previous history of TB treatment and DRS data as above</td>
</tr>
<tr>
<td>Individualized treatment</td>
<td>Regimen is designed based on the patient's previous history of TB treatment and individual DST results</td>
</tr>
</tbody>
</table>

Anti-tuberculosis Drugs

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Rifampin/Rifabutin</td>
<td>Streptomycin</td>
<td>Ethionamide</td>
<td>Clafazime</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Pyrazinamide</td>
<td>Kanamycin</td>
<td>Protonamide</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Rifampin/Rifabutin</td>
<td>Ethambutol</td>
<td>Amikacin</td>
<td>Clofazime</td>
<td>Thiacetazone</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Streptomycin</td>
<td>Capreomycin</td>
<td>Clofazime</td>
<td>Amoxacillin/Clavulanate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Viomycin</td>
<td></td>
<td>Macrolides</td>
</tr>
</tbody>
</table>

Principles of Designing a Treatment Regimen

- Regimens should be based on:
  - History of drugs taken by the patient
  - Drugs and regimens used in the country and
  - Prevalence of resistance
- Regimens should consist of at least 4 effective drugs
- Drug dosage should be determined by body weight
Principles of Designing a Treatment Regimen

- An injectable agent should be used for a minimum of 6 months and at least 4 months past culture conversion
- The minimum duration of treatment is 18 months after culture conversion
- Each dose should be given by DOT
- DST, when available and from a reliable laboratory, should be used to guide therapy
- PZA can be used for the entire treatment if judged to be effective

Building a Treatment Regimen for MDR-TB

**Step 1**
- Begin with any first-line agents to which the isolate is susceptible
- Use any available fluoroquinolones
- Add a fluoroquinolone and an injectable drug based on susceptibilities
- PLUS Pyrazinamide
- PLUS Ethambutol
- PLUS Gatifloxacin
- PLUS Levofoxacin
- PLUS Moxifloxacin
- PLUS Amikacin
- PLUS Capreomycin
- PLUS Streptomycin
- PLUS Kanamycin

**Step 2**
- Add second-line drugs until you have 4-6 drugs to which the isolate is susceptible (and preferably which have not been used to treat the patient previously)
- PICK one or more of these oral second-line drugs:
  - Cycloserine
  - Ethionamide
  - PAS

**Step 3**
- Consider use of these third-line drugs:
  - Clofazimine
  - Imipenem
  - Linezolid
  - Macrolides
  - Amoxicillin/clavulanate
  - High-dose Isoniazid
  - Isoniazid

Building a Treatment Regimen for MDR-TB (2)

Building a Treatment Regimen for MDR-TB (3)
Cross-Resistance Between Anti-tuberculosis Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cross Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
<td>High level cross-resistance with other rifamycins</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Variable cross-resistance; some newer generation drugs remain susceptible when lower-generation drugs are resistant</td>
</tr>
<tr>
<td>Aminoglycosides and polypeptides</td>
<td>Amikacin and kanamycin have high cross-resistance Capreomycin and viomycin have high cross-resistance Variable cross-resistance between other drugs</td>
</tr>
<tr>
<td>Protionamide and ethionamide</td>
<td>High level cross-resistance</td>
</tr>
<tr>
<td>Thiocetazine</td>
<td>Variable and low cross-resistance to isoniazid, ethionamide and PAS</td>
</tr>
</tbody>
</table>

Treatment Regimens for MDR-TB

<table>
<thead>
<tr>
<th>Pattern of drug resistance</th>
<th>Suggested regimen</th>
<th>Minimum duration of Rx</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH, RIF (± SM)</td>
<td>FQN, EMB, injectable, ± another 2nd-line drug</td>
<td>18-24 beyond culture conversion</td>
<td></td>
</tr>
<tr>
<td>INH, RIF (± SM), and EMB or PZA</td>
<td>FQN, EMB or PZA, injectable, plus 2 other 2nd-line drugs</td>
<td>24 beyond culture conversion</td>
<td>Consider surgery</td>
</tr>
<tr>
<td>INH, RIF, EMB, PZA (± SM)</td>
<td>FQN, injectable, ± another 2nd-line drug</td>
<td>24 beyond culture conversion</td>
<td></td>
</tr>
<tr>
<td>INH, RIF, EMB, PZA, injectables</td>
<td>FQN, 2nd-line drugs, injectable, plus consider 3rd-line drug</td>
<td>24 beyond culture conversion</td>
<td>Consider surgery</td>
</tr>
<tr>
<td>INH, RIF, EMB, PZA, injectables</td>
<td>FQN, 3rd-line drugs, plus consider 3rd-line drug</td>
<td>24 beyond culture conversion</td>
<td>Surgery if possible</td>
</tr>
<tr>
<td>INH, RIF, EMB, PZA, injectables</td>
<td>All 2nd-line drugs, injectable, plus consider 3rd-line drug</td>
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Regimens for XDR-TB

- In the face of quinolone and injectable drug resistance, treatment choices are limited
- Linezolid and any remaining injectable become the mainstay of treatment, along with whatever oral medications are left to which there is in vitro susceptibility
- Surgery if disease is localized
- Some patients may not be treatable

MDR-TB Clinical Case Management

- Isolate until 3 consecutive sputa AFB smears are negative and there has been a good response to treatment
- Consider isolation until culture negative in certain situations
- Hospitalization is often helpful when initiating MDR-TB treatment, including placement of PICC line, if used
- Tailor toxicity monitoring to specific drugs employed

CDC
**Recommended MDR-TB Monitoring for Efficacy**

- Collect sputa smears and cultures periodically during treatment once culture negative
- Obtain end-of-treatment sputum for smear and culture
- Perform CXR periodically during treatment and at end of treatment
- Monitor minimum of 2 years following treatment (quarterly during first year, every 6 months during second year)

**MDR-TB Laboratory Monitoring**

- As soon as isolate is known resistant to INH and RIF, order second-line drug susceptibilities
- Repeat susceptibilities on cultures that remain positive after 2-3 months

**Therapeutic Drug Monitoring**

- Renal impairment:
  - Aminoglycoside
  - Capreomycin
  - Ethambutol
- Cycloserine
  - (20-35 mcg/ml)
- Known or suspected malabsorption
- Drug-interactions
- Drug toxicity

**Directly Observed Therapy (DOT) for MDR-TB**

- Essential
- Improved overall cure rates, including MDR cases
- Reduction in community prevalence of MDR
DOT: Effect on Resistance and Relapse

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary R</td>
<td>13%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Secondary R</td>
<td>10.3%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Relapse</td>
<td>20.9%</td>
<td>5.5%</td>
</tr>
<tr>
<td>MDR relapse</td>
<td>6.1%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

*P < 0.001

Source: Weis, NEJM 1994; 330, 1179

Possible Treatment Regimens for MDR-TB Contacts

- Fluoroquinolone + PZA
- Fluoroquinolone + EMB
- PZA + EMB
- Fluoroquinolone monotherapy
- Other combinations?

(Non) Consensus Recommendations for MDR LTBI Treatment

- Assess degree of exposure
- Assess infection
- Assess likelihood of infection with MDR
- Assess risk of progression to active TB
- Offer MDR LTBI treatment to those with significant exposure, likely infected with MDR, and increased risk of progression
  - 2 best drugs for 9-12 months
MDR Tuberculosis
Predictors of Success and Failure

**Success**
- Use of pyrazinamide and/or ethambutol, if susceptible
- Use of a fluoroquinolone
- Use of > 5 drugs
- Sputum conversion by 2 months
- Surgical resection
- Linezolid

**Failure**
- Previous therapy
- Number of drugs resistant
- Presence of cavitation
- Low BMI
- HIV infection
- Poor adherence
- Positive cultures at 2-3 months

XDR-TB treatment success rates from four settings

- **Peru** (1999-2002), 29
- **North China** (2000-2004), 79
- **United States** (1993-2005), 48

XDR-TB treatment success rates from four settings

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- **United States** (1993-2005), 48

**Short, Highly Effective, and Inexpensive Standardized Treatment of Multidrug-resistant Tuberculosis**

- **Shah SN et al.** JAMA 2008;300(18):2153-60.

**Int J Resp Crit Care Med, 2010**

**Int J Resp Crit Care Med, 2010**
Recent Report from Bangladesh
9 month 7 drug regimen

- Used Gatifloxacin as the quinolone
- Initial intensive phase of 4 months of Kanamycin, Gatifloxacin, Clofazimine, High dose INH, Prothionamide, PZA, and Ethambutol
- Continuation phase of 5 months Gatifloxacin, Clofazimine, PZA, and Ethambutol
- 87.8% cure or completion, only 0.5% each failure or relapse

Van Deun A: AJRCCM, May 4, 2010

Outcome of Treatment for MDR-TB by HIV Status

48 MDR-TB patients in San Francisco

<table>
<thead>
<tr>
<th>Outcome measures</th>
<th>HIV-infected patients</th>
<th>HIV-uninfected patients</th>
<th>p</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients treated</td>
<td>41</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of therapy (months)</td>
<td>10-16</td>
<td>12-16</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>No. of drugs taken for new therapy (months)</td>
<td>6-12</td>
<td>6-12</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>No. of drugs taken for all therapy (months)</td>
<td>5-12</td>
<td>6-12</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Time until development of minor results, months</td>
<td>23.9 (2.3-64.5)</td>
<td>23.8 (0.0-166.9)</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Time until development of culture results, months</td>
<td>23.6 (0.3-77.6)</td>
<td>14.4 (0.4-109.5)</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Treatment outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture conversion</td>
<td>6 (44%)</td>
<td>0 (0.0-2.4)</td>
<td>0.05</td>
<td>0.32 (0.04-8.32)</td>
</tr>
<tr>
<td>Cured*</td>
<td>1 (9%)</td>
<td>22 (72%)</td>
<td>&lt;0.001</td>
<td>0.08 (0.01-0.61)</td>
</tr>
<tr>
<td>Relapse or failure*</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&lt;0.001</td>
<td>0.00 (0.00-0.60)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (9%)</td>
<td>1 (4%)</td>
<td>&gt;0.05</td>
<td>3.0 (0.3-30.4)</td>
</tr>
<tr>
<td>Died</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td>&gt;0.05</td>
<td>3.0 (0.3-30.4)</td>
</tr>
<tr>
<td>Mortality decreased by tuberculosis</td>
<td>43 (100%)</td>
<td>10 (100%)</td>
<td>&lt;0.001</td>
<td>3.7 (0.3-6.9)</td>
</tr>
</tbody>
</table>


Treatment of HIV-related MDR-TB

- Rapid diagnosis of drug resistance
- Important to treat with the most active anti-TB regimen available
- Initiate antiretroviral therapy based on CD4 ct and other individual patient variables
- Use therapeutic drug monitoring when drug interactions are possible or malabsorption is suspected

Role of Surgery in Treatment of MDR-TB at NJC

- 205 patients between 1984-1998 with resistance to median of 6 drugs
- Patients treated with a median of 6 drugs
- 130 patients had a least one resectional procedure
- Surgery and use of FQN associated with initial favorable response

Role of Surgery in Treatment of MDR-TB

• Surgery should be considered:
  • When cultures continue to be positive beyond 4-6 months of treatment and/or
  • When extensive drug resistance exist
• To maximize potential success of surgery:
  • Disease should be localized with adequate pulmonary function
  • Surgery should be performed by experienced surgeons preferably after several months of therapy

New Treatments for MDR TB

• TMC 207
• Otsuka
• PA 128
• Linezolid
  – NIH and TBTC studies in progress
  – Already in wide use globally

TMC-207

(1R,2S)-1-(6-bromo-2-methoxyquinolin-3-yl)-4-(dimethylamino)-2-(naphthalen-1-yl)-1-phenylbutan-2-ol
TMC207 - Clinical Safety

- 189 subjects treated with TMC207 in all trials to date (except current trial C208)
- No serious adverse events related to TMC207

Linezolid

- CLASS: Oxazolidinone
- MOA: Inhibition of the formation of a functional 70S initiation complex in the 50S bacterial ribosomal subunit
- ACTIVITY: Gram Positive Cocci (MRSA, VISA, VRSA, VRE), some anaerobic bacteria
- INDICATIONS: community acquired and nosocomial pneumonia, skin and soft tissue infections, UTIs and bacteremia
- Data exists showing utility in treatment of mycobacteria including MDRTB and XDRTB

Linezolid Toxicity

- Cytopenia (Reversible, dose related)
  - Transfusion possible
- Peripheral neuropathy (often after 16 weeks)
  - Cumulative dose-related?
  - Not generally thought to be reversible
- Optic neuropathy
  - Reversible
- Diarrhea
- Lactic acidosis
- Rare serotonin syndrome when combined with SSRIs/Parkinson drugs - weak monoamine oxidase inhibitor
Linezolid: California experience

- 30 patients received linezolid for MDR-TB for a range of 2 - 35 months
- 77% (23/30) of patients treated with linezolid during this period did not experience side effects
- One patient failed treatment, with recurrent positive cultures and progressive radiographic changes, after having been treated for 22 months.
- Of 7 patients who experienced symptoms of anemia/thrombocytopenia, rash, peripheral and optic neuropathy, most (5/7) were able to continue linezolid and combination MDR-TB therapy.

Rapid Tests for Drug Resistance

- Mutation detection
  - GenoType®-Series (Hain Lifescience GmbH, Nehren); not FDA approved
  - “Beacons” (validated in-house tests)
  - Cepheid GeneXpert®
- Gene sequencing

Who is at increased risk of MDR-TB?

- Foreign born
- HIV+
- History of previous TB treatment
- History of exposure to MDR-TB case
- TB treatment failure
Commercial line probe assays for detection of *M. tb* complex & mutations associated with drug resistance

- Genotype MTBDR from Hain Lifescience
  - Detects presence of *M. tb* complex and mutations associated with rifampin & INH resistance
  - Application for U.S. FDA clearance in process
- INNO-LiPA Rif TB from Innogenetics
  - Detects presence of *M. tb* complex & mutations associated with rifampin resistance

Molecular Beacon Testing

- Using real-time PCR technology combined with Molecular Beacons, provides
  - Identification of *M. tb* complex
  - Screening for INH and Rif resistance

Cepheid GeneXpert®

- Rapid detection of MTB/RIF resistance; Point of care test (performed in the field)
- Multicenter, prospective evaluation of the MTB/RIF test
  - 1462 patients; 567 (38.8%) smear and cx+: 174 (11.9%) smear - cx +, 105 (7.2%) clinical, 616 (42.1%) no TB
  - Overall sensitivity of the MTB/RIF test was 97.6%
  - Taking sequencing results into account, the MTB/RIF test correctly detected rifampin resistance in 209 of 211 patients (99.1% sensitivity) and in all 506 patients with rifampin susceptibility (100% specificity).

Progress in the roll-out of Xpert® MTB/RIF, as of June 2011
Resources

- **CureTB**: Binational TB Referral Program for TB patients and their contacts who travel between the United States and Mexico
  http://www.curetb.org/
- **TBNet**: A multi-national TB patient tracking and referral project designed to work with mobile, underserved populations
  http://www.migrantclinician.org/network/tbnet
- **National Jewish Medical Center**

Resources: TB Regional Training and Medical Consultation Centers (RTMCCs)

- **Francis J. Curry National Tuberculosis Center**
  1-877-390-NOTB or 1-877-390-6682
  www.nationaltbcenter.edu
- **Heartland National Tuberculosis Center**
  1-800-TEX-LUNG or 1-800-839-5864
  www.heartlandntbc.org
- **New Jersey Medical School Global Tuberculosis Institute**
  1-800-4TB-Docs or 1-800-482-3927
  www.umdnj.edu/globaltb
- **Southeastern National Tuberculosis Center**
  1-800-4TB-INFO or 1-800-482-4636
  http://snrc.medicine.ufl.edu

Resources

- **MDR-TB Service**
  - Provides clinical consultation, case management, Cl assistance
- **CA Microbial Diseases Lab**
  - Provides MBs for drug resistance; phenotypic DST for first-line drugs and Amikacin, Levofloxacin, Capreomycin, and Ethionamide; genotyping
MDR-TB
Preventable!
Treatable!
Curable!

Acknowledgements
• CDC
• MDR TB experts at the Regional Training and Medical Consultation Centers
• WHO
• Barbara Seaworth, MD
• Gisela Schecter, MD