MDR-TB CASE MANAGEMENT

LEARNING OBJECTIVES
Upon completion of this session, participants will be able to:

1. Recognize who is at higher risk for MDR TB
2. List the general principles of MDR TB treatment
3. Identify strategies for managing side effects to second-line medications
4. Identify resources for education, training, and expert consultation

INDEX OF MATERIALS

<table>
<thead>
<tr>
<th>MATERIALS</th>
<th>PAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MDR-TB Case Management – slide outline</td>
<td>1-30</td>
</tr>
<tr>
<td>Presented by: Lisa True, RN, MS</td>
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SUPPLEMENTAL MATERIAL

None

REFERENCES

Objectives

• Recognize who is at higher risk for MDR TB
• List the general principles of MDR TB treatment
• Identify strategies for managing side effects to second-line medications
• Identify resources for education, training, and expert consultation
**Terminology**

- **Mono-resistant**: resistant to only one drug
- **Poly-resistant**: resistant to more than one drug, but not the combination of INH and RIF
- **Multidrug-resistant (MDR)**: resistant to at least INH and RIF
- **Pre-extensively drug-resistant (Pre-XDR)**: MDR plus resistance to fluoroquinolone (FQ) or a second-line injectable (Amikacin, Kanamycin, or Capreomycin)
- **Extensively drug-resistant (XDR)**: MDR-TB plus resistance to a FQ and at least one second line injectable

**Global MDR Burden**

- **2014 Estimate**: 480,000 incident cases
  - Half from China, India and Russia
- **Surveillance varies by country and region**
  - Resistance surveys vs continuous surveillance
  - National vs subnational
  - **2015**: Data from 79% of countries since 1994

WHO Global Tuberculosis Control Report 2014
Estimated Number of MDR-TB Cases Among Notified TB Patients, 2014

XDR TB

- 9.7% of MDR TB cases
- 105 countries have reported at least 1 case
- “TDR” reports from Iran and India
Primary Anti-TB Drug Resistance
United States, 1993 – 2014*

*Updated as of June 5, 2015.
Note: Based on initial isolates from persons with no prior history of TB. Multidrug resistant TB (MDR TB) is defined as resistance to at least isoniazid and rifampin.

Primary Isoniazid Resistance in U.S.-born vs. Foreign-born Persons
United States, 1993 – 2014*

*Updated as of June 5, 2015.
Note: Based on initial isolates from persons with no prior history of TB.
Primary MDR TB in U.S.-born vs. Foreign-born Persons
United States, 1993 – 2014*

>90% of MDR cases in foreign-born

*Updated as of June 5, 2015.
Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.

Multidrug-resistant TB Cases
California, 1995-2015

Percent of culture pos cases

Number of MDR cases

0 5 10 15 20 25 30 35 40 45 50

MDR cases

Pct MDR
Origin of Drug Resistance

Random Naturally Occurring Resistance in Bacterial Population

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

$INH \text{ and } RIF = 10^6 \times 10^8 = 1 \text{ in } 10^{14}$
Random drug-resistant mutants in large (> $10^6$) bacterial population

Multidrug therapy works: No bacteria resistant to all 3 drugs

INH
RIF
PZA

INH

Monotherapy: INH-resistant bacteria grow

INH resistant organism
RIF resistant organism
PZA resistant organism

When treated with just one drug, resistant bacteria begin to grow

INH
INH RIF

Spontaneous mutations to other drugs (RIF) develop as bacilli grow to $>10^8$ organisms

INH mono-resist. mutants killed by adding RIF, but RIF-resist. mutants proliferate $\rightarrow$ MDR TB
Spread of MDR TB

- “Biological Fitness” of the M. tb organism is not generally worsened by resistance
  - Studies have shown robust growth among RIF resistant and MDR strains
- Once created, drug resistant TB can spread to other people
  - The majority of global MDR TB (>70%) is among new patients (i.e., was transmitted and not acquired)

Recognition:
Who Is At Higher Risk of MDR-TB?

- History of previous TB treatment, particularly if recent
- Poor response to standard 4-drug treatment
  - Culture remains (+) after 2 months treatment
- Known exposure to MDR-TB case
- HIV (+)
  - Higher incidence of Rifampin mono resistance
Recognition: Who Is At Higher Risk of MDR-TB?

- Foreign born arrived in U.S. within last 2 years
- Immigration from or recent extended travel to country with > 2% MDR among cases from that country diagnosed in California/U.S.
- These countries* are:
  - India  Laos  Russia and other former Soviet states
  - Korea  Peru  Central America
  - Burma  Ecuador  Dominican Republic
- Other state or locally identified risk groups, including:
  - Hmong refugees
  - Persons of Tibetan origin

*California data from 2011-2015 and U.S. data from 2010-2013
† Current U.S. data are available from the CDC, Division of TB Elimination (DTBE) (www.cdc.gov/tb)

High-risk for MDR: Action Steps

- Obtain molecular test for drug resistance
  - Xpert MTB/RIF, (pyro)sequencing, Hain line-probe test, or other
**How is MDR-TB Diagnosed**

- **Growth-based susceptibility tests** = culture-based susceptibility tests = phenotypic susceptibility tests = DSTs
- **Molecular tests for drug resistance**
  - “Molecular susceptibility tests”
  - “Genotypic susceptibility tests”
  - Reduced time to detection of resistance
  - Time from empiric (first-line) treatment to MDR treatment 40 days less (median)

**Molecular Testing for Drug Resistance**
Molecular Testing: Drugs/Loci

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Gene/locus</th>
<th>Sensitivity (Sequencing)</th>
<th>Specificity (Sequencing)</th>
<th>Assays</th>
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<td>Isoniazid (INH)</td>
<td>katG</td>
<td>86.0</td>
<td>99.1</td>
<td>Hain, PSQ, MDDR</td>
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<td>INH and Ethionamide</td>
<td>inhA promoter</td>
<td>4.5</td>
<td>100</td>
<td>PSQ</td>
</tr>
<tr>
<td>INH</td>
<td>ahpC promoter</td>
<td>4.5</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>INH</td>
<td>fabG1</td>
<td></td>
<td></td>
<td>PSQ, MDDR</td>
</tr>
<tr>
<td>Rifampin (RIF)</td>
<td>rpoB</td>
<td>97.1</td>
<td>97.4</td>
<td>Xpert, Hain, PSQ, MDDR</td>
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<td>Ethambutol (EMB)</td>
<td>embB</td>
<td>78.8</td>
<td>94.3</td>
<td>Hain, MDDR</td>
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<tr>
<td>Pyrazinamide (PZA)</td>
<td>pncA</td>
<td>86.0</td>
<td>95.9</td>
<td>MDDR</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>gyrA</td>
<td>79.0</td>
<td>99.6</td>
<td>Hain, PSQ, MDDR</td>
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<tr>
<td>Amikacin (AMK)</td>
<td>rrs</td>
<td>90.9</td>
<td>98.4</td>
<td>Hain, PSQ, MDDR</td>
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<tr>
<td>Capreomycin (CAP)</td>
<td>rrs, tlyA</td>
<td>55.2</td>
<td>91.0</td>
<td>MDDR</td>
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</tbody>
</table>


Types of mutations

Silent (synonymous)
- Nucleic acid change
- No amino acid change
- Not associated with drug resistance generally
  - 514 (TTC→TTT) mutation in rpoB is the most common silent mutation

Missense (nonsynonymous)
- Nucleic acid change
- Amino acid change
- Some are associated with resistance
Molecular Testing for Rifampin ($rpoB$)

- Rifampin cornerstone of TB treatment
  - Resistance requires a longer duration of therapy
  - Rif resistance without INH resistance rare
  Rif resistance $\approx$ MDR

Number and Proportion MDR TB by Country/Region of Origin, CA 2011–2015

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>No.</th>
<th>%</th>
<th>PPV (99% spec)</th>
<th>PPV (98% spec)</th>
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<tr>
<td>Former Soviet Republics</td>
<td>5</td>
<td>12.2</td>
<td>93%</td>
<td>87%</td>
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<td>Laos</td>
<td>6</td>
<td>5.1</td>
<td>84%</td>
<td>72%</td>
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<td>Burma</td>
<td>2</td>
<td>3.4</td>
<td>77%</td>
<td>63%</td>
</tr>
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<td>Japan</td>
<td>1</td>
<td>3.2</td>
<td>76%</td>
<td>61%</td>
</tr>
<tr>
<td>India</td>
<td>12</td>
<td>3.1</td>
<td>75%</td>
<td>60%</td>
</tr>
<tr>
<td>Guatemala</td>
<td>5</td>
<td>3.0</td>
<td>75%</td>
<td>60%</td>
</tr>
<tr>
<td>Korea (N&amp;S)</td>
<td>7</td>
<td>2.9</td>
<td>74%</td>
<td>59%</td>
</tr>
<tr>
<td>Peru</td>
<td>1</td>
<td>2.6</td>
<td>72%</td>
<td>56%</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>1</td>
<td>2.0</td>
<td>66%</td>
<td>50%</td>
</tr>
<tr>
<td>Philippines</td>
<td>47</td>
<td>1.7</td>
<td>64%</td>
<td>52%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>13</td>
<td>1.4</td>
<td>57%</td>
<td>40%</td>
</tr>
<tr>
<td>China (incl Taiwan)</td>
<td>7</td>
<td>1.2</td>
<td>54%</td>
<td>37%</td>
</tr>
<tr>
<td>United States</td>
<td>13</td>
<td>0.8</td>
<td>44%</td>
<td>28%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>1</td>
<td>0.7</td>
<td>40%</td>
<td>25%</td>
</tr>
<tr>
<td>Mexico</td>
<td>11</td>
<td>0.6</td>
<td>36%</td>
<td>22%</td>
</tr>
</tbody>
</table>

- Countries with >20 cases tested for MDR
### MDR TB Cases by Country/Region of Origin and Years in the US, CA 2011-2015

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>Total MDR TB cases</th>
<th>≤ 2 years in US No. (%)</th>
<th>&gt;2 years in US No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Countries (excl US)*</td>
<td>103</td>
<td>30 (3.7)</td>
<td>71 (1.2)</td>
</tr>
<tr>
<td>Former Soviet Republics</td>
<td>5</td>
<td>2 (33.3)</td>
<td>3 (8.6)</td>
</tr>
<tr>
<td>Vietnam*</td>
<td>13</td>
<td>9 (7.9)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>China (incl Taiwan)*</td>
<td>7</td>
<td>5 (8.8)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Philippines*</td>
<td>27</td>
<td>8 (4.0)</td>
<td>19 (1.4)</td>
</tr>
<tr>
<td>Guatemala</td>
<td>5</td>
<td>1 (3.9)</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>India</td>
<td>12</td>
<td>3 (3.3)</td>
<td>9 (3.2)</td>
</tr>
<tr>
<td>All Other Countries</td>
<td>10</td>
<td>2 (1.1)</td>
<td>8 (0.9)</td>
</tr>
<tr>
<td>Mexico</td>
<td>11</td>
<td>0 (0.0)</td>
<td>11 (0.7)</td>
</tr>
<tr>
<td>Korea, North and South</td>
<td>7</td>
<td>0 (0.0)</td>
<td>7 (3.2)</td>
</tr>
<tr>
<td>Laos</td>
<td>6</td>
<td>0 (0.0)</td>
<td>5 (4.6)</td>
</tr>
</tbody>
</table>

* Difference is statistically significant

### How to interpret molecular test for resistance

- Put into clinical and epidemiologic context!
- Confirm non-sequencing tests (e.g., Xpert) with sequencing test (PSQ or MDDR)
- Consider Rif resistance on Xpert to be MDR (not just rifampin monoresistant)
- Can usually treat based on sequencing test results; follow the growth based DST results
Limitations / Areas for Caution

- Molecular tests vs. DST discordance
  - “Disputed” mutations
  - Undescribed mutations outside of loci in current molecular tests → resistance
  - Emerging resistance in mixed populations may not be detected

MDR-TB Treatment Principles

- Perform extensive patient evaluation prior to Rx start
- Obtain expert input
- Use at least 4-6 likely effective drugs (optimally at least 5)
  - 1 bactericidal injectable
  - 1 fluoroquinolone
- Continue injectable for 6 - 12 months post culture conversion
MDR-TB Treatment Principles (2)

- Continue at least 3 oral drugs for full treatment duration
- Treat at least 18 months - 2 years after culture conversion
- Never add a single drug to a failing regimen

Building an Individualized Regimen for MDR-TB

**STEP 1**

Begin with any First-line agents to which the isolate is susceptible

Add a fluoroquinolone and an injectable drug based on susceptibilities

<table>
<thead>
<tr>
<th>First-line drugs</th>
<th>Fluoroquinolones</th>
<th>Injectable agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrazinamide</td>
<td>Levofloxacin</td>
<td>Amikacin</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Moxifloxacin</td>
<td>Capreomycin</td>
</tr>
</tbody>
</table>

1. Not available in U.S.
2. SM: use only if not previously used and if documented susceptibility
Building a Regimen for MDR-TB (2)

**STEP 2**
Add second-line drugs until you have 4-6 drugs (optimally at least 5) to which the isolate is susceptible (and preferably which have not been used to treat the patient previously)

<table>
<thead>
<tr>
<th>Oral second-line drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloserine</td>
</tr>
<tr>
<td>Ethionamide</td>
</tr>
<tr>
<td>PAS</td>
</tr>
<tr>
<td>Linezolid$^3$</td>
</tr>
</tbody>
</table>

3. Although considered a third-line drug, many experts now use LZD as a second-line drug option

Building a Regimen for MDR-TB (3)

**STEP 3**
If there are not 4-6 drugs available in the above categories, consider third-line drugs in consultation with an MDR-TB expert

<table>
<thead>
<tr>
<th>Third-line drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedaquiline</td>
</tr>
<tr>
<td>Delamanid$^4$</td>
</tr>
<tr>
<td>Clofazimine</td>
</tr>
<tr>
<td>Imipenem</td>
</tr>
<tr>
<td>Meropenem/</td>
</tr>
<tr>
<td>Clavulanate</td>
</tr>
<tr>
<td>Amoxicillin/</td>
</tr>
<tr>
<td>Clavulanate</td>
</tr>
<tr>
<td>Clarithromycin</td>
</tr>
<tr>
<td>High-dose INH</td>
</tr>
</tbody>
</table>

4. Awaiting FDA approval
Medication Fact Sheets

- Drug class/trade name
- Activity against TB
- Cross-resistance
- Dose (adult, pediatrics, renal)
- Route of administration
- Preparation/storage
- Pharmacokinetics
- Oral absorption/metabolism
- CSF penetration
- Special circumstances
- Adverse reactions/contraindications
- Monitoring
- Costs/patient education

Role of the Nurse Case Manager

- Team Leader
- Coordinate care with:
  - Treating physician and consultants
  - Other caregivers (primary provider)
  - Hospital staff
  - DOT worker
  - Social worker
  - Disease investigator
  - Providers treating contacts
  - Laboratory
Ensure Appropriate Isolation and Respiratory Precautions

- 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
- Usually outpatient care; hospitalization can be helpful

Patient Centered Care and Ensuring Adherence to Treatment

Provide daily DOT throughout treatment

- Essential
- Improved overall cure rates, including MDR cases
- Reduction in community prevalence of MDR

Anticipate and address barriers
Optimize Management of Other Conditions

- Address underlying medical conditions (e.g. diabetes, Hep C)
- Address nutritional status
- Drug and alcohol use

Provide Patient Education

- Assess current knowledge of diagnosis and understanding of treatment plan
- Focus messages based on treatment stage
  - Phase 1 = ends when isolation discontinued
  - Phase 2 = ends when injectable stopped
  - Phase 3 = ends when treatment completed
  - Phase 4 = post-Rx period
Monitoring for Clinical Response and Toxicity

• Monitor clinical response
  – Conversion of sputum smear and culture
  – Resolution of symptoms
  – Weight gain
• Monitor toxicity
  – Serum creatinine, electrolytes
  – Audiogram and Vestibular function

Use Case Management Tools

• Use drug-o-gram to follow:
  – serial changes in drugs
  – bacteriology
  – chest x-rays
  – drug toxicities
• Use MDR Monitoring Checklist
### Drug-o-gram

<table>
<thead>
<tr>
<th>Date</th>
<th>ML</th>
<th>MEF</th>
<th>PZA</th>
<th>SM</th>
<th>KM</th>
<th>INH</th>
<th>RIF</th>
<th>PAS</th>
<th>CFZ</th>
<th>ETF</th>
<th>LNZ</th>
<th>CS</th>
<th>Date</th>
<th>spec</th>
<th>sm/cult</th>
<th>Comments</th>
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<tbody>
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<td></td>
<td>1/27/11</td>
<td>CDC MDDR results: multiple mutations</td>
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<td></td>
<td>1/27/11</td>
<td>Case Conference—Expanded regimen recommended</td>
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<td></td>
<td>2/12/11</td>
<td>CT stable RUL; w/Amp 2xMIC</td>
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<td>CXR: Enlarging mass LUL</td>
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### Susceptibility Results

<table>
<thead>
<tr>
<th>Date</th>
<th>Spec.</th>
<th>Lab</th>
<th>MEF</th>
<th>PZA</th>
<th>SM</th>
<th>KM</th>
<th>INH</th>
<th>RIF</th>
<th>PAS</th>
<th>CFZ</th>
<th>ETF</th>
<th>LNZ</th>
<th>CS</th>
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<td>R.05</td>
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<td>R.02</td>
<td>R.13</td>
<td>R.15</td>
<td>R.2</td>
<td>R.2</td>
<td>R.05</td>
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<td>R.05</td>
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### Treatment Regimen

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<th>MFX</th>
<th>LNZ</th>
<th>CS</th>
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<tr>
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<td>Case Conference—Expanded regimen recommended</td>
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<td>1/27/11</td>
<td>CXR: Enlarging mass RUL</td>
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</tbody>
</table>

### Susceptibility Results

<table>
<thead>
<tr>
<th>INH</th>
<th>RIF</th>
<th>EMB</th>
<th>PZA</th>
<th>SM</th>
<th>KM</th>
<th>AK</th>
<th>CM</th>
<th>PAS</th>
<th>ETA</th>
<th>LFX</th>
<th>MFX</th>
<th>LNZ</th>
<th>CS</th>
<th>RFB</th>
<th>CFZ</th>
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<tr>
<td>R0.1</td>
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Therapeutic Drug Monitoring

- Cycloserine:
  - absorption highly variable
  - therapeutic and toxic levels are very close
  - drug levels are highly recommended
  - Draw 2 hours after dose

- Injectables:
  - if renal compromise, significantly over or under weight, or elderly
  - Some experts recommend obtaining levels routinely
  - peak and/or trough levels

Recommended MDR-TB Monitoring for Efficacy

- Collect sputum periodically (e.g., monthly) during treatment once culture negative
- Obtain end-of-treatment sputum for smear and culture
- Perform CXR periodically during treatment (e.g., quarterly) 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
- Repeat susceptibility for EMB/PZA if susceptible at baseline and patient received ≥4 weeks of first-line treatment on positive cultures obtained near start of MDR treatment

MDR Monitoring Checklist

| Data | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 |
| Sputum smear and culture* | | | | | | | | | | | | | | | | | | | | | | |
| CB12 | | | | | | | | | | | | | | | | | | | | | | |
| Weight* | | | | | | | | | | | | | | | | | | | | | | |
| Symptom intensity* | | | | | | | | | | | | | | | | | | | | | | |
| DST | | | | | | | | | | | | | | | | | | | | | | 

* Repeat for ATB and DST after 2-3 months

1. Isolate AFB smear and culture specimens every 2 weeks until smear converted, and then 1-3 specimens monthly until cultures have been negative. Sputum specimens obtained at least 1 specimen monthly throughout therapy; chest X-ray or other imaging every 3 months during the first year and 6 months in the second year of treatment.
2. Monitor weight monthly and adjust medications as needed.
4. Give rifampin and ethambutol (ETB) before therapy is started, and after 2-3 months of therapy.
5. Give ethambutol before therapy is started, and after 2-3 months of therapy.
7. Give for 6 months on positive cultures obtained near start of MDR treatment.
Injectable Agent: Why, When, Where, and How

- **Why:** Bactericidal agent
- **When:** 5-7 x/week at start of treatment, drops to 3x/wk
- **Where:** Hospital, home, clinic, infusion center
- **How:** Intramuscular or Intravenous
- **How long:** Aim for 6-12 months post culture conversion unless toxicity develops
Common Side Effects

<table>
<thead>
<tr>
<th>Condition</th>
<th>Medications</th>
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<tbody>
<tr>
<td>G.I. complaints</td>
<td>Ethionamide, PAS, Quinolones, Clofazimine, Rifabutin, Linezolid</td>
</tr>
<tr>
<td>Hearing loss, vestibular toxicity</td>
<td>Injectables</td>
</tr>
<tr>
<td>Renal insufficiency/Electrolyte Abn</td>
<td>Injectables</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>PZA, PAS, Rifabutin, Ethionamide, Quinolones</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Linezolid, INH, Quinolones, Ethionamide, Cycloserine</td>
</tr>
<tr>
<td>Neuropsychiatric: depression, agitation, psychosis, difficulty concentrating, insomnia</td>
<td>Cycloserine, Quinolones, Ethionamide</td>
</tr>
<tr>
<td>Rash</td>
<td>All</td>
</tr>
<tr>
<td>Visual changes</td>
<td>EMB, Rifabutin, Linezolid</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Ethionamide, PAS</td>
</tr>
<tr>
<td>Headache</td>
<td>Quinolones, Cycloserine, Ethionamide, EMB</td>
</tr>
</tbody>
</table>

Chapter 9

Managing GI Side Effects

– Use an anti-emetic/Treat gastritis or acid reflux
– Eat a light snack before taking meds
– Lessen the pill burden
– Allow suspect med to be taken at bedtime
– Mask medication odor
Prevention

- Preventing acquired drug resistance
  - DOT and daily therapy as appropriate
- Preventing transmission of MDR-TB to contacts
  - Effective treatment, Isolation until noninfectious
- Preventing progression to active disease in infected MDR-TB contacts
  - MDR LTBI treatment and monitoring

Preventing Progression to Active TB

- Little published data on LTBI treatment for MDR-TB contacts; No randomized trials
- CDC guidance last in 1992
- Contact investigation and management principles same as drug susceptible:
  - Drug resistant TB is not more infectious, but duration can be longer and consequences are greater
  - Consider infectiousness of index case, duration/intensity of contact, immune status of contact, LTBI test results
  - Rule out active disease prior to starting LTBI treatment
**Treatment Regimens for MDR-TB Contacts**

- FQ monotherapy
- FQ + EMB
- Monitor for 2 years only — acceptable
- FQ + PZA — very poorly tolerated
- PZA + EMB
- Other combinations? Duration?

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**Fluoroquinolones for MDR Contacts**

- Published data from 2 MDR outbreaks in Chuuk:
  - 104 of 119 received LTBI treatment x 12 months
    - Adults: MFX + EMB (n=24) or MFX/LFX alone (n=51)
    - Children: LFX + EMB (N=17) or LFX + Ethionamide (n=12)
  - 11 stopped early; 6 received >6 mos
  - 0 cases in treated vs 3 among 15 refused (36 mo f/u)

Resources

Resources: RTMCCs

- Curry International Tuberculosis Center
  1-877-390-NOTB or 1-877-390-6682
  www.currytbcenter.ucsf.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 1-800-482-3627
  www.umdnj.edu/globaltb

- Southeastern National Tuberculosis Center
  1-800-4TB-INFO or 1-800-482-4636
  http://sntc.medicine.ufl.edu

- Mayo Clinic Center for Tuberculosis
  855-360-1466
  http://centerfortuberculosis.mayo.edu/


**MDR Resources**

- Curry International TB Center and CA Department of Public Health
- Partners in Health Guide (2013):
- WHO MDR Guides:
    http://apps.who.int/iris/bitstream/10665/130918/1/9789241548809_eng.pdf
  - Guideline (2016):
    http://www.who.int/entity/tb/areas-of-work/drug-resistant-tb/MDRTBguidelines2016.pdf?ua=1
- CDC Bedaquiline Guideline (2013):

**California Resources**

- MDR-TB Service
  - Provides clinical consultation, case management, CI assistance – 510-620-3000
- CA Microbial Diseases Lab
  - pyrosequencing for drug resistance
  - phenotypic DST for first-line drugs and amikacin, moxifloxacin, capreomycin, and ethionamide
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