MDR in NDR: Nashville's Trio of Multidrug-Resistant TB Cases

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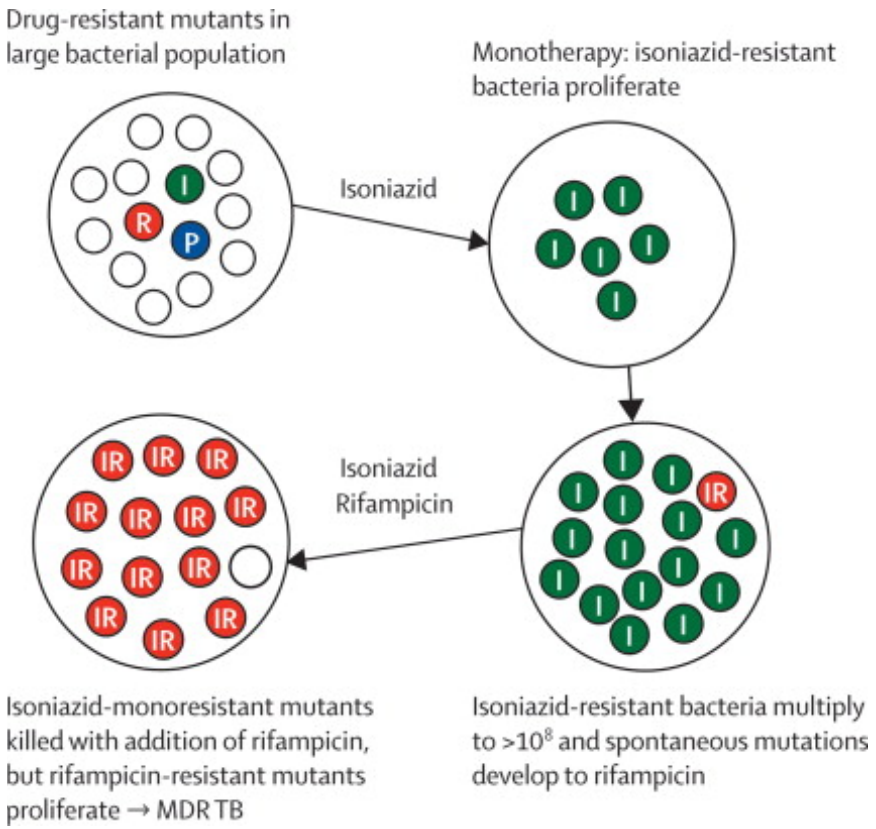
Pansensitive TB vs. MDR-TB vs. XDR-TB

	Pansensitive TB	Multidrug-Resistant TB	Extensively Drug-Resistant TB
Isoniazid	Susceptible	Resistant	Resistant
Rifampin	Susceptible	Resistant	Resistant
Fluoroquinolones (e.g. moxifloxacin)	Susceptible	Susceptible	Resistant
Injectable (e.g. Amikacin)	Susceptible	Susceptible	Resistant

What Causes Drug Resistance?

- Incorrect dosing/use of TB drugs
- Intermittent therapy
- Not finishing treatment
- Poor quality drugs
- When drug supply is insufficient/unstable
- Primary Resistance
  - Infection acquired from a drug resistant case
- Secondary Resistance –
  - Resistance develops within a patient



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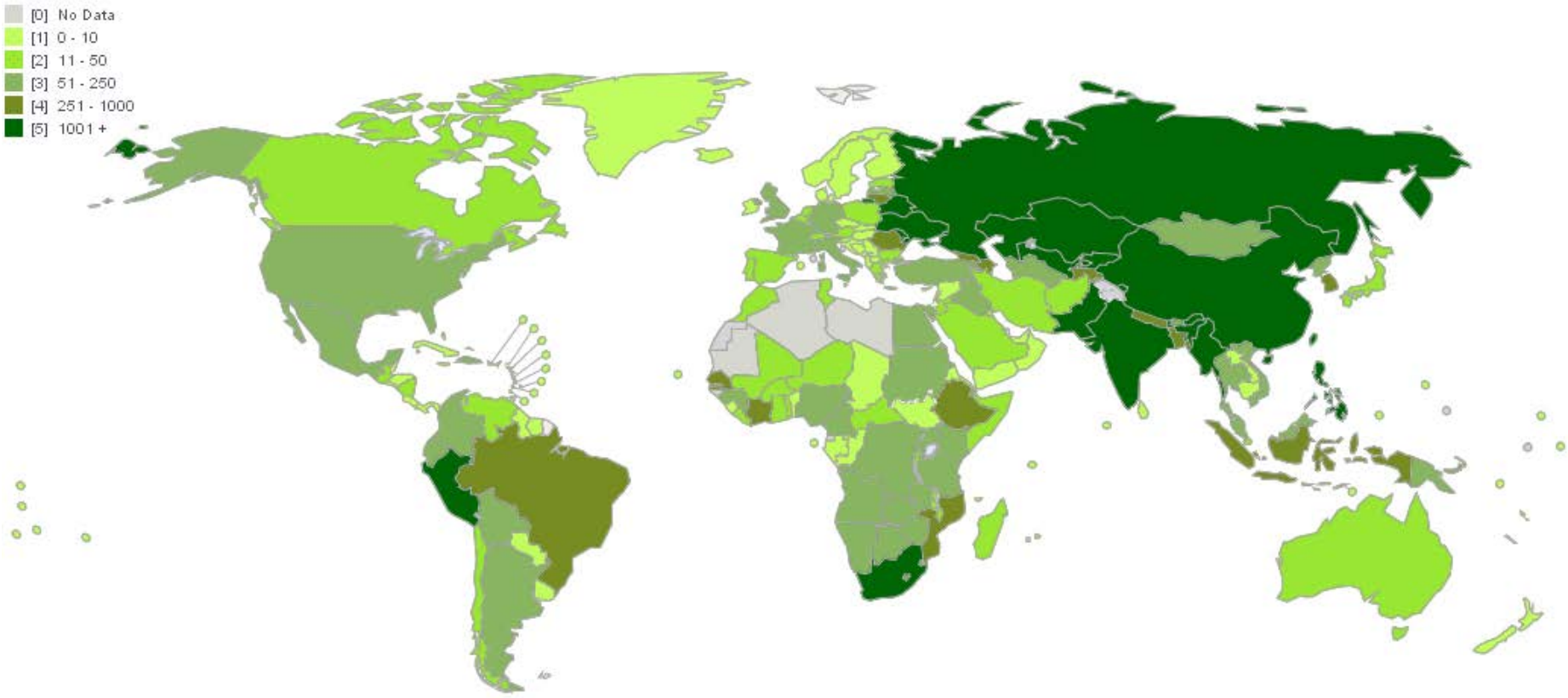
MDR-TB Around the World



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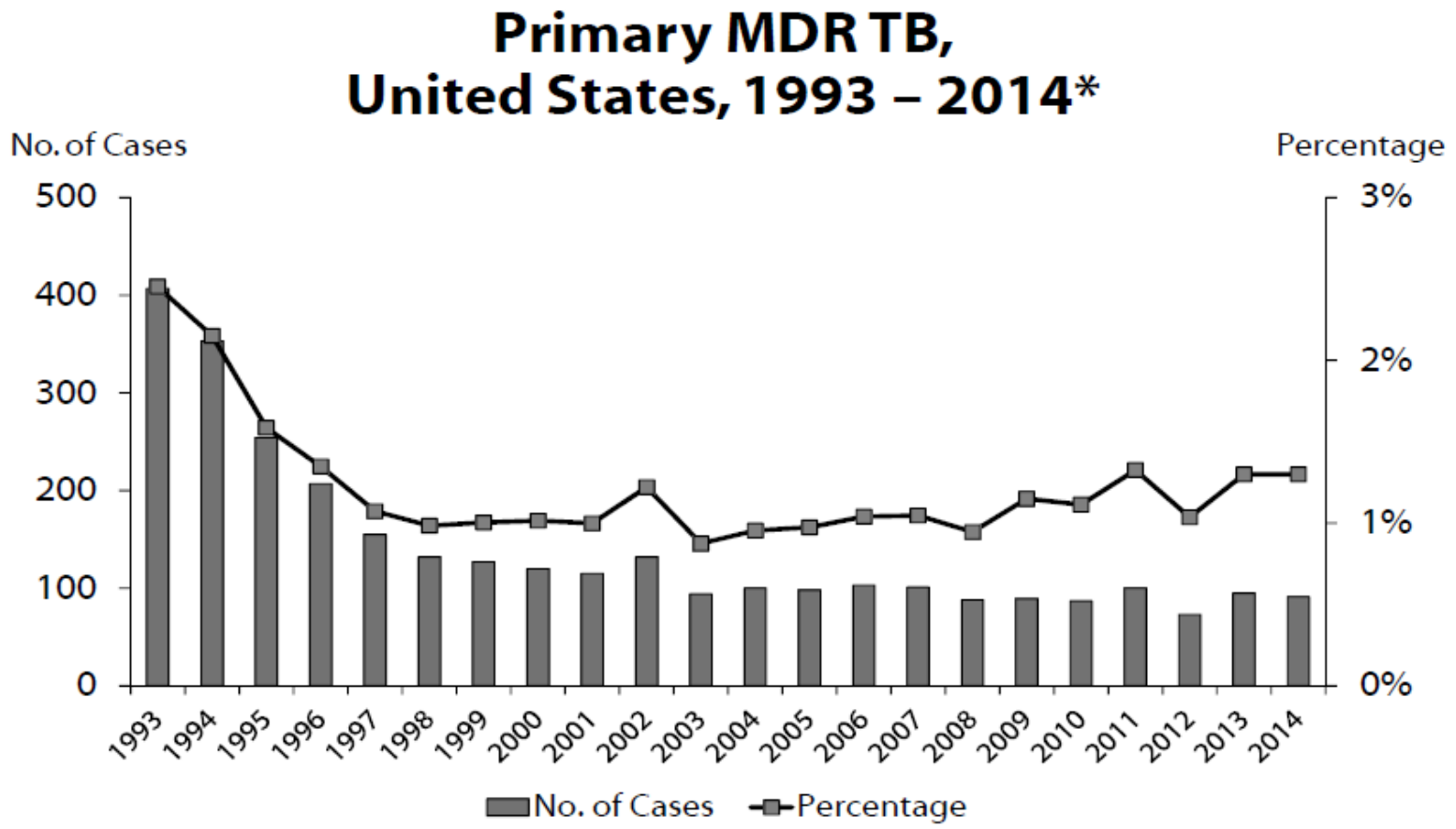
MDR in the U.S.



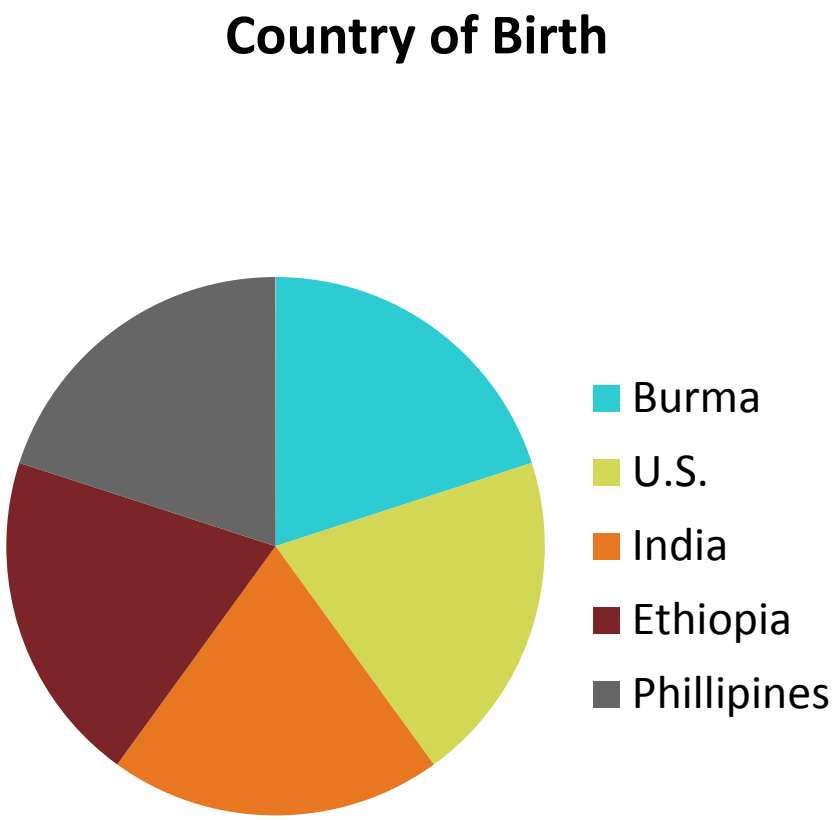
*Updated as of June 5, 2015.

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

Source: CDC. *Reported Tuberculosis in the United States, 2014*. Atlanta, GA: U.S. Department of Health and Human Services, CDC, October 2015.

MDR in Tennessee, 2010-2014

- 5 total cases
- Average Age: 41 yrs., Median Age: 28 yrs., Age Range: 26-89 yrs.
- 100% had pulmonary involvement
- 20% also had extrapulmonary (lymphatic)



Patient 1

- 44 y/o male
- FB
- 5/5/15 – presented to local hospital with cough and abnormal chest x-ray
- 5/7/15 – Smear positive/Nucleic acid amplification test (NAAT) positive (rpoB negative)
- 5/7/15 – IGRA positive
- 5/7/15 – RIPE initiated
- 6/2/15 – Molecular detection of drug resistance (MDDR) showed INH, EMB, and PZA mutations

Patient 1

- 5/7/15 – Rifampin, Isoniazid, PZA, Ethambutol
- 6/4/15 – Rifampin, PZA, Moxifloxacin, Amikacin
- 6/17/15 – Amikacin, Rifampin, Moxifloxacin, PAS
- 7/23/15 – Amikacin, Moxifloxacin, Cycloserine, Ethionamide
- 7/30/15 – Amikacin, Moxifloxacin, Cycloserine, Ethionamide, Linezolid
- 7/25/15 – Culture converted
- 9/11/15 – Removed from respiratory isolation
- Currently still on medication and stable

Patient 2

- 47 y/o female
- FB
- Diabetes Mellitus, Hypertension
- Previous diagnosis 2011 with treatment
- 3/30/15 – TST placed and read 4/3, 16mm
- 4/3/15 – Reported night sweats, weight loss, fatigue, and cough
- 4/4/15 – Smear positive/NAAT positive sample showing resistance to Rifampin
- 4/10/15 – MDDR showed potential resistance to EMB, PZA, Rifampin, and Streptomycin
- 4/13/15 – Cavitary x-ray

Patient 2

- 4/14/15 – Isoniazid, Ethambutol, Amikacin, Moxifloxacin, PAS
- 4/30/15 – Isoniazid, Moxifloxacin, Linezolid, Ethambutol, Cycloserine
- 5/6/15 – Amikacin, Moxifloxacin, Linezolid, Ethambutol, Cycloserine
- 6/5/15 – Request made for Bedaquiline due to intolerance of PAS
- 6/26/15 – Bedaquiline, Linezolid, Moxifloxacin, Cycloserine, Ethionamide
- 5/16/15 – Culture converted
- 7/7/15 – Removed from respiratory isolation
- Currently still on medication and stable

Patient 3

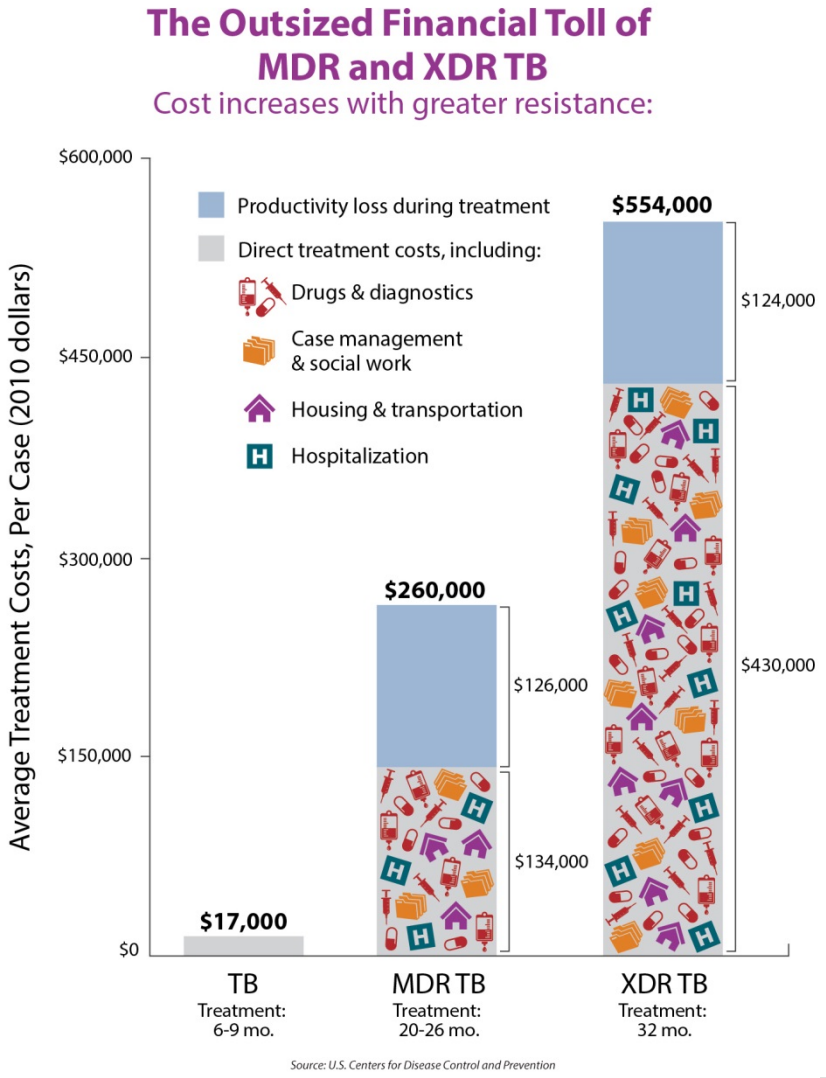
- 28 y/o female
- FB
- Reported TB treatment overseas 2/2013-2/2014 with Isoniazid, Rifampin, and Ethambutol
- 4/14/14 – Sought care related to lump in neck and related medical complaints
- 5/2/14 – Smear positive/culture positive lymph node biopsy
- 5/6/14 – Smear negative/culture positive sputum
- 5/24/14 – Removed from respiratory isolation
- 5/29/14 – Biopsy reported MTb probe positive
- 6/11/14 – Culture converted

Patient 3

- 5/6/14 – Rifampin, PZA, EMB
- 8/25/14 – Amikacin, Bedaquiline, PAS, Cycloserine, Clofazamine,
- 2/12/15 – discontinued Bedaquiline
- 9/9/15 – Cycloserine, Linezolid, PAS
- 9/21/15 – Cycloserine, Linezolid, PAS, Clofazimine
- Currently still on medication and stable

Challenges with MDR-TB

- Cost and availability of drugs
- Requires culture growth or obtaining MTb DNA
- Side effects of treatment
- Long treatment duration 1.5-2 years after culture conversion
- Difficulty creating effective drug regimen
- Treatment for contacts is difficult



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Questions?