Transmission of XDR TB

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Background

2006: 53 XDR TB cases in South Africa

• 52 of 53 (98%) died
  – median survival 16 days

• All HIV-infected, if status known

• Transmission of XDR TB likely
  – 51% never previously received TB treatment
  – 85% with genetically similar TB strains
Local Outbreak vs Epidemic

• 2001-2002: MDR TB prevalence low: 2-4%
• 2006: KwaZulu-Natal: 2654 MDR TB cases
  – MDR TB Prevalence: 26 cases per 100,000
  – US 2005: 124 MDR TB cases total
    Prevalence of any TB: <5 per 100,000
Rapid Emergence of MDR & XDR TB

- What can explain rapid rise in MDR TB cases?
- Emergence of XDR TB provides insights into rise of both MDR and XDR TB
Tugela Ferry

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MDR & XDR TB Widespread in South Africa

- XDR TB cases in all 9 South African provinces
- MDR and XDR TB prevalence rates are similar among all provinces
- XDR TB cases reported from all of South Africa’s neighbors
  - Namibia, Botswana, Lesotho, Swaziland, Mozambique
What’s driving this epidemic?

- Traditional Dogma
  - Selection for drug-resistant TB strains in setting of poor adherence or incorrect treatment
    “Acquired or Amplified Resistance”

- Neglected mechanism
  - Transmission of drug-resistant TB strains
    “Primary or Transmitted Resistance”
Acquired vs. Transmitted Resistance

- Acquired or amplified resistance may explain original genesis of first XDR TB strains

- Current magnitude and spread of XDR TB difficult to explain by acquired resistance alone
  - Tugela Ferry alone 2005-2007: 382 XDR TB cases

- High likelihood of primary or transmitted resistance
  - 30% Never previously treated for TB
  - Prior Treatment Relapse: due to new infections
    - Majority were cured or completed treatment course
    - Molecular genotyping data
Transmission of MDR & XDR TB?

• Molecular fingerprinting to determine acquired vs primary resistance in relapses with MDR and XDR TB

• Compared genotypes between initial susceptible isolate and follow-up MDR or XDR TB isolate
  – If genotypes differ, resistance due to new infection
  – If genotypes same, resistance due to acquired resistance from ineffective treatment
Baseline Characteristics

17 patients: susceptible TB Ë MDR or XDR TB

• Baseline & follow-up isolates available for genotyping
• 15 of 17 tested for HIV: 100% HIV-infected
• Inpatients and outpatients enrolled
  – 17 (100%) hospitalized at time of susceptible TB or before relapse with MDR or XDR TB
  – Median 25.5 days in hospital
Genotyping Results

• All 17 (100%) follow-up MDR/XDR genotypes different from initial isolate
  – All cases re-infected with MDR or XDR strain
  – No cases of acquired resistance
Four TB Strains in Single Patient

Susceptible TB  ‡  MDR TB  ‡  XDR TB
Genotypes of Patients with XDR TB Relapse

Initial Isolate

Follow-up Isolate

- ST 60
- ST 1218
- ST 26
- ST A4
- ST A3
- ST 244
- ST 172
- ST 53
- ST 4
- ST 1
- ST A2
- ST 33
Conclusions

• Transmission of drug-resistant strains is the principal source of MDR & XDR TB in South Africa

• High rates of HIV co-infection and hospitalization may have contributed to risk

• Re-infection with MDR and XDR TB attributable to relatively few TB strains
  – Suggesting common sources of transmission
Implications

- Efforts must focus on creating infection control programs to prevent the transmission of drug-resistant TB strains
  - Most settings worldwide with no infection control
- Early diagnosis necessary to facilitate infection control
  - Hampered by lack of laboratory capacity and lack of simple, rapid diagnostic test
- Further studies to characterize transmission patterns needed
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