HIV, TB and Substance Use
Triple Trouble

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Tugela Ferry Care and Research Collaboration
HIV, TB and Drug Use

- Epidemiology of HIV, TB and drug use
- “Perfect storm” of drug resistant TB
- Prevention and Treatment

- Historical and geographic examples
Global TB/HIV Epidemics

- 35 million persons infected with HIV
  - 5 million new infections, 3 million deaths per year
  - >90% in resource limited countries
  - IDU major risk in many European countries
  - 2.5-3 million IDUs living with HIV
- 2 billion people are infected with M.TB
  - 8 - 9 million new active TB cases, ~2 million deaths per year
  - > 90 % in developing countries
  - >500,000 in Europe
- 12-14 million persons are TB/HIV co-infected
- TB epidemics have followed in wake of rising HIV rates
HIV Co Infection in New TB cases

5-20% HIV co infection rate in TB cases
Recent Recognition of growing threat of drug resistant TB

- **MDR-TB** multiple drug resistant TB
  - resistance to at least isoniazid and rifampin
  - requires TB laboratory infrastructure for diagnosis
  - two most potent first line TB therapies

- **XDR-TB** extensively drug resistant TB
  - MDR+ resistance to fluoroquinolones and at least one injectable
  - requires TB laboratory infrastructure for diagnosis
  - two most potent second line therapies
M/XDR TB Definitions

• **Acquired resistance**
  – Resistance as a result of treatment failure
    • The predominant mechanism in past and many areas
    • A consequence of program and/or patient limitations

• **Primary resistance**
  – Resistance resulting from transmission of resistant organisms
    • The predominant mechanism in areas of high HIV prevalence
    • A consequence of increased susceptibility, rapid progression to disease and absence of infection control
### HIV-related MDR-TB Outbreaks in Industrialized Countries, 1988-1995

<table>
<thead>
<tr>
<th>Location</th>
<th>Total cases</th>
<th>% HIV infected</th>
<th>% Death</th>
<th>Median time to death (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital, New York City, USA, 1989-1990</td>
<td>51</td>
<td>100</td>
<td>89</td>
<td>16</td>
</tr>
<tr>
<td>Hospital, New York City, USA, 1990-1991</td>
<td>70</td>
<td>95</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td>Hospital, New York City, USA, 1991-1992</td>
<td>32</td>
<td>91</td>
<td>83</td>
<td>4</td>
</tr>
<tr>
<td>Hospital, Florida, USA, 1988-1990</td>
<td>65</td>
<td>93</td>
<td>72</td>
<td>7</td>
</tr>
<tr>
<td>2 Hospitals, Italy, 1991-1995</td>
<td>116</td>
<td>98</td>
<td>95</td>
<td>6-8</td>
</tr>
<tr>
<td>Hospital, Madrid, Spain, 1991-1995</td>
<td>48</td>
<td>100</td>
<td>98</td>
<td>7</td>
</tr>
<tr>
<td>Hospital, Buenos Aires, Argentina, 1994-1995</td>
<td>68</td>
<td>100</td>
<td>93</td>
<td>5</td>
</tr>
<tr>
<td>Prison system, New York State, USA 1990-1991</td>
<td>42</td>
<td>98</td>
<td>79</td>
<td>4</td>
</tr>
</tbody>
</table>
Tugela Ferry KwaZuluNatal Province Rural South Africa

- 1800 sq km rural district
- Population 200,000 traditional Zulu people
- TB case rate
  1,100/100,000/yr
  >1200 new cases/yr, ~50% completion rate
- TB laboratory/Durban
  culture and 1st and 2nd line DST
TB/HIV Integration
MDR/XDR TB in Tugela Ferry
2005 – 2006

• MDR/XDR TB – major cause of death

• 53 cases XDR TB
  – All tested HIV+
  – 98% rapid mortality
    • Median 16 days
  – Strong evidence for nosocomial transmission
    • >50% no previous Rx
    • 83% single strain
    • HCW deaths

Recognition that MDR/XDR TB are Widespread in South Africa and Beyond

- > 600 cases M and XDR TB Tugela Ferry
- XDR TB from ~60 KZN facilities in KZN
- Mortality XDR TB 85%, MDR TB 65%
- XDR TB cases in all 9 South African provinces and neighboring countries
  - Botswana, Mozambique, Lesotho, Swaziland, Namibia, ? Zimbabwe
- Full extent unknown; no denominator, culture and DST limited
Etiology of M and XDR-TB Epidemic in KwaZuluNatal

- High prevalence *M. tb*; weak TB control program
  - Low cure and completion rates
  - Acquired, previously treated drug resistance
- Arrival and progression of the HIV epidemic
  - Massive increase in TB cases
  - Increasing population and individual immuno-compromise
  - Rapid progression to disease
  - New, transmitted drug resistance
- Absent/limited infection control
  - Nosocomial transmission
  - Community transmission in congregate settings (prisons)
Global surveillance indicates substantial and rising numbers of M and XDR TB

• **MDR** 489,000 (5%)  
  (95% CI 455,000-614,000)

• **XDR** 40,000 (8%)  
  (95% CI 4.6-6.0%)
FIGURE 1.6
Countries with the highest numbers of estimated MDR-TB cases, 2007. Horizontal lines denote 95% confidence intervals. The source of estimates is drug resistance surveillance or surveys (DRS, in red) or modelling (in grey).
% MDR TB among new and previously treated patients by region

- Multidrug resistance (MDR) more frequent in the Baltic States (combined MDR: 10–21%) than in the other countries
**MDR-TB and HIV in Ukraine**

<table>
<thead>
<tr>
<th>Civilian sector</th>
<th>Penitentiary sector</th>
</tr>
</thead>
<tbody>
<tr>
<td>New cases</td>
<td>New cases</td>
</tr>
<tr>
<td>n=924</td>
<td>n=78</td>
</tr>
<tr>
<td>Previously treated cases</td>
<td>Previously treated cases</td>
</tr>
<tr>
<td>n=369</td>
<td>n=125</td>
</tr>
<tr>
<td>MDR rates</td>
<td>MDR rates</td>
</tr>
<tr>
<td>(95% CLs) (13.1 to 17.8)</td>
<td>(95% CLs) (12.4 to 31.2)</td>
</tr>
<tr>
<td>15.5</td>
<td>21.8</td>
</tr>
<tr>
<td>(36.4 to 46.5)</td>
<td>(43.9 to 61.7)</td>
</tr>
</tbody>
</table>

- **Independent predictors for MDR-TB**
  - History of previous treatment: OR: 4.0 (95%CLs 3.1-5.1)
  - Imprisonment: OR: 1.5 (95%CLs 1.1-2.0)

- **HIV status:** OR: 1.7 (95%CLs 1.3-2.3)

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Abstract to the 38th World Conference on Lung Health, 8-12 November 2007. Cape Town, South Africa
Countries with confirmed cases of XDR-TB as of November 2008

Based on information provided to WHO Stop TB Department - June 2008
Treatment and Prevention Challenges and Opportunities in HIV, TB and Substance Use

- Triple stigma
- Access to prevention, care and treatment
- Organization of services
- Integration and co-location of services—best strategy to reduce morbidity and mortality from HIV and TB in drug users
  - Three I’s
  - Medication Adherence
  - Drug-drug interactions
  - M/XDR TB treatment
Current Approaches to Treatment

TB

HIV/AIDS

Drug Treatment
Treatment and Prevention Challenges and Opportunities in HIV, TB and Substance Use

- Hidden population, avoidance of traditional health care system
  - Community outreach
  - Non-traditional care sites
  - Prison health

- 3 I’s
  - Intensive case finding
    - HIV C and T of all TB cases
    - TB screening of all HIV+ pts
  - Infection control
  - Isoniazid prophylaxis therapy (IPT)
Superiority of Directly Administered Antiretroviral Therapy over Self-Administered Therapy among HIV-Infected Drug Users: A Prospective, Randomized, Controlled Trial

Frederick L. Altice,† Duncan Smith-Rohrberg Maru,‡ R. Douglas Bruce,§ Sandra A. Springer,† and Gerald H. Friedland,‡

CID, 2007

VL Response

CD4 Response
Antiretroviral Agents, TB and Substance Use Therapies’ Drug Interactions

- Antiretroviral and methadone/buprehorphine interactions
  - Marked induction of methadone metabolism by efavirenz and nevirapine with severe opiate withdrawal
  - Milder but unpredictable induction methadone metabolism by some protease inhibitors
  - Milder reduction in buprenorphine levels
  - Decreased methadone levels with raltegravir

- TB and methadone and antiretroviral interactions
  - Rifampin induces methadone, protease inhibitor and NNRTI metabolism
FIRST APPROACH TOWARD SUCCESSFUL INTEGRATION

**TB Program**
- DOT
- Adherence Support
- Sputum Collection
- Drug Interactions
- Latent TB Prophylaxis
- Contact Tracing

**HIV Program**
- Antiretroviral Treatment
- Drug Interactions
- VCT
- Toxicity Monitoring
- Prophylaxis of OIs
- Adherence Support
- Secondary Prevention
- Syringe Exchange

**Drug Treatment**
- Opioid Substitution Therapy
- Effective Counseling
- DOT
- Urine Monitoring
- Drug Interactions
- Syringe Exchange

Sylla et al, 2007
LATER APPROACH TOWARD SUCCESSFUL INTEGRATION

- **TB Program**
  - DOT
  - Adherence Support
  - Sputum Collection
  - Drug Interactions
  - Latent TB Prophylaxis
  - Contact Tracing

- **HIV Program**
  - Antiretroviral Treatment
  - Drug Interactions
  - VCT
  - Toxicity Monitoring
  - Prophylaxis of OIs
  - Adherence Support
  - Secondary Prevention
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  - Effective Counseling
  - DOT
  - Urine Monitoring
  - Drug Interactions
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Communication Collaboration

Sylla et al, 2007
The aim is to provide a strategic approach to reducing TB- and HIV-related morbidity and mortality among drug users and their communities in a way that promotes holistic and person-centered services. Thirteen recommendations covering issues of joint planning, prevention and treatment of TB and HIV in drug users and service delivery
“TB claims 1.7 million lives each year, and eliminating it will be a global challenge - but it's a challenge we must take on....”

Barack Obama,

October 3, 2008