Tuberculosis: The Big Picture
And Challenge of Drug-resistance

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National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention
“Those who cannot remember the past are condemned to repeat it”

George Santayana, The Life of Reason, 1905

Conditions

- Deficient infrastructure
- HIV epidemic
- Immigration
- Institutional transmission
- MDR-TB

Profile of Selected HIV-related MDR TB Outbreak Investigations in U.S., 1988–92

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Total Cases</th>
<th>% HIV Infected</th>
<th>% Deaths</th>
<th>Median Wks Dx to Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>65</td>
<td>93</td>
<td>72</td>
<td>7</td>
</tr>
<tr>
<td>B</td>
<td>51</td>
<td>100</td>
<td>89</td>
<td>16</td>
</tr>
<tr>
<td>C</td>
<td>70</td>
<td>95</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td>D</td>
<td>29</td>
<td>91</td>
<td>83</td>
<td>4</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>14</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>F</td>
<td>16</td>
<td>82</td>
<td>82</td>
<td>4</td>
</tr>
<tr>
<td>I</td>
<td>13</td>
<td>100</td>
<td>85</td>
<td>4</td>
</tr>
<tr>
<td>J</td>
<td>28</td>
<td>96</td>
<td>93</td>
<td>4</td>
</tr>
<tr>
<td>Prison</td>
<td>42</td>
<td>98</td>
<td>79</td>
<td>4</td>
</tr>
</tbody>
</table>
Healthcare Worker Union and ACT-UP Demonstrations, 1991
U.S. Response to TB Resurgence

National MDR-TB Action Plan & New Resources

Improved Case Identification & Training

Updated Diagnostic Labs, Real-time Drug Resistance, & Strain Fingerprinting

Rebuilt Research Capacity

Updated Infection Control & Rx Recommendations

DOT & Improved Rx Completion

2HRZE plus 4HR
### Effect of DOT on Drug Resistance & Relapse, Tarrant County, Texas*

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAT (01/80-10/86)</th>
<th>DOT (11/86-12/92)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;o&lt;/sup&gt; Resistance</td>
<td>13.0</td>
<td>6.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Acq. Resistance</td>
<td>14.0</td>
<td>2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Relapses</td>
<td>20.9</td>
<td>5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>During Rx</td>
<td>4.4</td>
<td>1.2</td>
<td>0.003</td>
</tr>
<tr>
<td>MDR TB</td>
<td>6.1</td>
<td>0.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

# TB Laboratory Standards

<table>
<thead>
<tr>
<th>Lab Tools</th>
<th>Max TAT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>• AFB microscopy</td>
<td>≤ 24 hrs</td>
</tr>
<tr>
<td>• NAA</td>
<td>≤ 48 hrs</td>
</tr>
<tr>
<td>• Culture detection</td>
<td>≤ 14 days</td>
</tr>
<tr>
<td>• Culture identification</td>
<td>≤ 21 days</td>
</tr>
<tr>
<td>• 1\textsuperscript{st}-line DST</td>
<td>≤ 30 days</td>
</tr>
<tr>
<td>• 2\textsuperscript{nd}-line DST</td>
<td>≤ 4 weeks</td>
</tr>
</tbody>
</table>

* Turn-around time (TAT) from specimen collection; for 2\textsuperscript{nd}-line DST from date of request

[APC = Annual Percentage Rate Change]

At -3.8%, it would take 100 years to reach the elimination goal of 1 TB case per million population.

An APC of -8.8% would be needed to eliminate TB by 2050, with new Dx tools, new/shorter Rx and a new TB vaccine.
TB Case Rates,* United States, 2007**

- **Cases per 100,000.**
- **Unpublished provisional data, not for citation**

*Cases per 100,000.
** Unpublished provisional data, not for citation
Reported TB Cases by Race/Ethnicity*
United States, 2007**

83% in racial/ethnic minorities

- Hispanic or Latino (29%)
- Black or African American (26%)
- Asian (26%)
- White (17%)
- American Indian or Alaska Native (1%)
- Native Hawaiian or Other Pacific Islander (<1%)

*All races are non-Hispanic. Persons reporting two or more races accounted for less than 1% of all cases.
** Unpublished provisional data, not for citation
Trends in TB Cases in Foreign-born Persons, United States, 1986–2007*

* Unpublished provisional data, not for citation
Countries of Birth of Foreign-born Persons Reported with TB
United States, 2007*

- Mexico (25%)
- Philippines (11%)
- Viet Nam (8%)
- India (7%)
- China (5%)
- Haiti (3%)
- Guatemala (3%)
- Other Countries (38%)

* Unpublished provisional data, not for citation
Global 9.2 million new TB cases, 1.7 million deaths in 2006
Global New TB Cases/100,000 Population, 2006

- **Europe**: case rates up by 40% during 1990s, now falling slowly
- **Africa**: case rates up by 200+% during 1990s, now falling slowly
- **World**: case rates rising during 1990s, now stable or falling slowly

Estimated new TB cases (all forms) per 100,000 population:
- No estimate
- 0-24
- 25-49
- 50-99
- 100-299
- 300 or more
Global Stop TB Strategy

1. Pursue high-quality DOTS expansion and enhancement
   a. Political commitment with increased and sustained financing
   b. Case detection through quality-assured bacteriology
   c. Standardized treatment with supervision and patient support
   d. An effective drug supply and management system
   e. Monitoring and evaluation system, and impact measurement

2. Address TB/HIV, MDR-TB and other challenges
   - Implement collaborative TB/HIV activities
   - Prevent and control multidrug-resistant TB
   - Address prisoners, refugees and other high-risk groups and special situations

3. Contribute to health system strengthening
   - Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems
   - Share innovations that strengthen systems, including the Practical Approach to Lung Health (PAL)
   - Adapt innovations from other fields

4. Engage all care providers
   - Public-Public, and Public-Private Mix (PPM) approaches
   - International Standards for TB Care (ISTC)

5. Empower people with TB, and communities
   - Advocacy, communication and social mobilization
   - Community participation in TB care
   - Patients’ Charter for Tuberculosis Care

6. Enable and promote research
   - Programme-based operational research
   - Research to develop new diagnostics, drugs and vaccines
By 2005 sustain or exceed by 2015
Detect 70% of new sputum smear (SS) + cases
2005 Global 60%
Successfully treat 85% of these cases
2004 Global 84%

By 2015
Reduce TB prevalence and deaths by 50% (relative to 1990)
Reducing prevalence to ≤ 155 per 100,000
2005 Global 217/100,000
Reducing deaths to ≤ 14 per 100,000
2005 Global 24/100,000
“...the issue now confronting the nation is whether we will allow another cycle of neglect to begin or, instead, whether we will take decisive action to eliminate tuberculosis.”
IOM “Ending Neglect”
Recommendations: Eliminate TB in U.S.

1. Maintain control while adapting to declining incidence
2. Speed decline through increased treatment of latent infection
3. Develop new diagnostic, treatment, and vaccine tools
4. Increase U.S. engagement in global efforts
5. Mobilize support for elimination and monitor progress
Interrupting Chain of Transmission for *Mycobacterium tuberculosis* complex

Active TB Source → Treatment TB Disease → Contact → Secondary TB Cases

Infection Control

Treatment LTBI
Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis
Recommendations from the National Tuberculosis Controllers Association and CDC

Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting Mycobacterium tuberculosis Infection, United States

Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005
## Prevalence of Tuberculosis Infection, U.S.


<table>
<thead>
<tr>
<th>Population</th>
<th>% LTBI Prevalence (95% CI)</th>
<th>Estimated No. x Million (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>4.2 (3.3-5.2)</td>
<td>11.2 (8.9-14.0)</td>
</tr>
<tr>
<td>U.S.-born</td>
<td>1.8 (1.4-2.1)</td>
<td>4.1 (3.1-5.6)</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>18.7 (13.5-25.2)</td>
<td>6.9 (5.0-9.3)</td>
</tr>
<tr>
<td>Poverty Index ≥ 1</td>
<td>3.3 (2.5-4.4)</td>
<td>6.5 (4.9-8.6)</td>
</tr>
<tr>
<td>Poverty Index &lt; 1</td>
<td>6.1 (4.0-9.1)</td>
<td>2.8 (1.8-4.2)</td>
</tr>
</tbody>
</table>

**Poverty Index** = Family income / poverty threshold adjusted by family size.  
(Poverty defined as poverty: income ratio < 1)
### Pooled Sensitivity & Specificity of IGRAs and TST

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QuantiFERON-Gold</td>
<td>78 (72-80)</td>
<td>99 (98-100)†*</td>
</tr>
<tr>
<td>QuantiFERON-Gold In-Tube</td>
<td>70 (63-78)</td>
<td>96 (94-98)‡**</td>
</tr>
<tr>
<td>T-SPOT.TB</td>
<td>90 (86-93)</td>
<td>93 (86-100)</td>
</tr>
<tr>
<td>Tuberculin Skin Test</td>
<td>77 (71-82)</td>
<td>97 (95-99)*</td>
</tr>
</tbody>
</table>

† Pooled results for QFN-Gold and QFN-GIT
* Non-BCG vaccinated, ** BCG vaccinated
Multi- and Extensively-Drug Resistant TB
What is MDR and XDR TB?

• **MDR TB** strains are resistant to ≥ INH and RIF (most important 1st-line drugs)

• **XDR TB** = a subgroup of MDR strains with extensive additional resistance to
  – Any fluoroquinolones, and
  – One of the 2nd-line injectable drugs (amikacin, kanamycin, capreomycin)
MDR, XDR TB: Why be Concerned?

• Treatment requires 18–24 mo (vs 6–8 mo)
• Relapse rates ~30-40% (vs 2-3%)
• Prolonged infectiousness
• Adverse events common (fewer with FLDs)
• Higher costs (> 100-fold increase)
• High mortality
Effect of Rifampin Duration and Drug Resistance on Treatment Outcomes

TB Treatment Outcomes, by Selected Drug Resistance Patterns, Latvia, 2000-2003*

Global Estimate of MDR TB

490,000
(95% CI, 455,093–614,215)
incident cases in 2006

4.8%
(95% CI, 4.6%–6.0%)
of all TB cases notified in 2006

Based on 138 settings surveyed in 116 countries between 1994-2007
% MDR TB Among New and Previously Treated Patients, by Region

Countries with XDR-TB confirmed cases as of February 2008

Based on information provided to WHO Stop TB Department - February 2008
## XDR TB in KZN: Patient Characteristics*

<table>
<thead>
<tr>
<th>Characteristics (53 XDR TB Pts.)</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No prior TB treatment (n=47)</td>
<td>26 (55)</td>
</tr>
<tr>
<td>Prior hospitalization [last 2 yrs] (n=42)</td>
<td>28 (67)</td>
</tr>
<tr>
<td>Previous TB treatment (n=47)</td>
<td></td>
</tr>
<tr>
<td>Cured or completed</td>
<td>14 (30)</td>
</tr>
<tr>
<td>Failure or default</td>
<td>7 (15)</td>
</tr>
<tr>
<td>HIV infection (n=44)</td>
<td>44 (100)</td>
</tr>
<tr>
<td>Dead: includes 15 (34%) on ARVs</td>
<td>52 (98)</td>
</tr>
<tr>
<td>Identical genotype (n=46)</td>
<td>39 (85)</td>
</tr>
</tbody>
</table>

Primary MDR TB
United States, 1993–2007*

No. Cases Percent

* Provisional data, not for citation
Note: Based on initial isolates from persons with no prior history of TB.
MDR TB defined as resistance to at least isoniazid and rifampin.

% Resistant

0 1 2 3

1993 1995 1997 1999 2001 2003 2005 2007

U.S.-born ✧ Foreign-born

* Provisional data, not for citation
Note: Based on initial isolates from persons with no prior history of TB.
MDR TB defined as resistance to at least isoniazid and rifampin.
XDR TB Cases, United States, 1993-2007*

*2007 Unpublished provisional data, not for citation
XDR TB Cases by State of Residence, United States, 1993–2007*

<table>
<thead>
<tr>
<th>States (and City)</th>
<th>No. (%) Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York City</td>
<td>16 (33)</td>
</tr>
<tr>
<td>California</td>
<td>11 (23)</td>
</tr>
<tr>
<td>New York State</td>
<td>8 (17)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>3 (6)</td>
</tr>
<tr>
<td>NV, TX (2 each)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Six other states (1 each)</td>
<td>6 (13)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>48 (100)</strong></td>
</tr>
</tbody>
</table>

* Based on Initial DST results; residence N/A for 2 cases
Diagnosing MDR and XDR TB: Requires Heightened Index of Suspicion

The most important predictors of drug-resistant TB are:

- **A previous episode** of TB treatment
- **Progressive** clinical and/or radiographic findings while on TB therapy
- **Origin** from, **history of residence** in, or **frequent travel** to a region/country with high rates of drug resistance
- **Exposure to an individual with infectious drug-resistant TB**, including in facilities where drug resistance has occurred; e.g., correctional institutions, homeless shelters, or other congregate settings
National Standards for Laboratory Turnaround Times

- Clinical specimens should reach the laboratory within 24 hours of collection.
- AFB smear reports should reach physicians within 24 hours of specimen receipt in the laboratory.
- Positive culture identification should occur within 14 days of specimen collection.
- Isolate should be definitively identified as *M. tuberculosis* within 17–21 days of specimen collection.
- Antibiotic susceptibility results should be reported to the physician within 28 days of specimen collection.
National Plan for Reliable Tuberculosis Laboratory Services Using a Systems Approach

Recommendations from CDC and the Association of Public Health Laboratories Task Force on Tuberculosis Laboratory Services
Molecular Analysis of Cross-Resistance to Capreomycin, Kanamycin, Amikacin, and Viomycin in *Mycobacterium tuberculosis*

Courtney E. Maus,¹,² Bonnie B. Plikaytis,² and Thomas M. Shinnick²*

*Antimicrobial Agents Chemotherapy 2005;49:3192-7:*

Evaluation of the TB-Biochip Oligonucleotide Microarray System for Rapid Detection of Rifampin Resistance in *Mycobacterium tuberculosis*

Janice C. Caoili, Angelina Mayorova, David Sikes, Laura Hickman, Bonnie B. Plikaytis, and Thomas M. Shinnick*

*Journal Clinical Microbiology 2006;44:2378-81*

Rapid Detection and Identification of Bacterial Pathogens Using Novel Molecular Technologies: Infection Control and Beyond

Fred C. Tenover
Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

*Clinical Infectious Diseases 2007;44:418-23*
## Examples of Rapid Drug Resistance Methods

<table>
<thead>
<tr>
<th>Test</th>
<th>GenoType® MTBDR</th>
<th>INNO-LiPA Rif.TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Company</strong></td>
<td>Hain Lifescience</td>
<td>Innogenetics</td>
</tr>
<tr>
<td><strong>M. tuberculosis detection</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Detection RMP resistance</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Detection INH resistance</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Strip Assay</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DNA basis: PCR</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Direct assay</td>
<td>No</td>
<td>Yes (modified version)</td>
</tr>
<tr>
<td>RMP resistance: <em>rpoB</em> gene</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>INH resistance: <em>katG</em> gene</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
## Performance of Genotype MTBDRplus assay compared to conventional culture and DST (smear-negative/culture-positive specimens)

<table>
<thead>
<tr>
<th></th>
<th>Rifampicin</th>
<th>Isoniazid</th>
<th>MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity %</strong></td>
<td>98.4</td>
<td>92.2</td>
<td>94.7</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(94.2 – 99.8)</td>
<td>(87.0 – 95.8)</td>
<td>(88.1 – 98.3)</td>
</tr>
<tr>
<td><strong>Specificity %</strong></td>
<td>99.2</td>
<td>99.8</td>
<td>99.7</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(98.4 – 99.7)</td>
<td>(99.2 – 100.0)</td>
<td>(99.1 – 99.9)</td>
</tr>
<tr>
<td><strong>Overall accuracy %</strong></td>
<td>99.1</td>
<td>98.7</td>
<td>99.3</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(98.4 – 99.6)</td>
<td>(97.8 – 99.2)</td>
<td>(98.6 – 99.7)</td>
</tr>
<tr>
<td><strong>PPV %</strong></td>
<td>93.8</td>
<td>98.7</td>
<td>96.8</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(88.1 – 97.2)</td>
<td>(95.4 – 99.8)</td>
<td>(90.9 – 99.3)</td>
</tr>
<tr>
<td><strong>NPV %</strong></td>
<td>99.8</td>
<td>98.6</td>
<td>99.5</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(99.3 – 100.0)</td>
<td>(97.7 – 99.3)</td>
<td>(98.8 – 99.8)</td>
</tr>
</tbody>
</table>
The use of line probe assays is recommended by WHO

MOLECULAR LINE PROBE ASSAYS FOR RAPID SCREENING OF PATIENTS AT RISK OF MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB)

Adoption of line probe assays for rapid detection of MDR-TB should be decided by Ministries of Health within the context of country plans for appropriate management of MDR-TB patients, including the development of country-specific screening algorithms and timely access to quality-assured second-line anti-tuberculosis drugs;

Adoption of line probe assays does not eliminate the need for conventional culture and DST capability; culture remains necessary for definitive diagnosis of TB in smear-negative patients, while conventional DST is required to diagnose XDR-TB. However,

The use of commercial line probe assays rather than in-house assays is recommended to ensure reliability and reproducibility of results, as in-house assays have not been adequately validated or used outside limited research settings. Any new or generic line probe assays should be subject to adequate validation, ie. published laboratory validation studies, adequate data to allow systematic review and meta-analysis (including assessment of data quality), and results from field demonstration projects documenting feasibility and consistent performance equal to conventional methods.

As current line probe assays only detect resistance to rifampicin and/or isoniazid, countries with documented or suspected cases of XDR-TB should establish or expand conventional culture and DST capacity for quality-assured susceptibility testing of second-line drugs, based on current WHO policy guidance;

Adoption of line probe assays for rapid detection of MDR-TB should be phased in, starting at national/central reference laboratories or those with proven capability to conduct molecular testing. Once this has been accomplished, expansion could be considered, within the context of country laboratory strengthening plans, and

Adequate and appropriate laboratory infrastructure and equipment should be provided, ensuring that required precautions for biosafety and prevention of contamination are met:
## TB Clinical Development Pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Development Stage</th>
<th>Sponsor / Coordinator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatifloxacin</td>
<td>Phase III</td>
<td>EC / OFLOTUB Consortium; IRD(^*); WHO TDR(^o); Lupin Ltd.</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Phase II / III</td>
<td>Bayer; TB Alliance; CDC(^\dagger); University College of London; Johns Hopkins University</td>
</tr>
<tr>
<td>Diary/quinoline TMC207</td>
<td>Early Bactericidal Activity</td>
<td>Johnson &amp; Johnson (Tibotec)</td>
</tr>
<tr>
<td>Nitroimidazo-oxazole OPC-67683</td>
<td>Early Bactericidal Activity</td>
<td>Otsuka Pharmaceutical Co., Ltd.</td>
</tr>
<tr>
<td>Nitroimidazole PA-824</td>
<td>Phase I</td>
<td>TB Alliance</td>
</tr>
<tr>
<td>Pyrrole LL-3858</td>
<td>Phase I</td>
<td>Lupin Ltd.</td>
</tr>
</tbody>
</table>

*Novel compounds, highlighted in blue boxes, are active against MDR/XDR TB*

\(^*\) Institut de Recherche pour le Developement
\(^o\) World Health Organization, Tropical Disease Research
\(^\dagger\) Centers for Disease Control and Prevention
Why Control TB and Drug Resistance?

• Reduce personal suffering and death

• Protect others — public health benefit
Technical Tools for TB Control
"Insanity is doing the same thing over and over again and expecting different results."

- Albert Einstein
Acknowledgements

- National TB Controllers Association
- State and Local Health-department TB Programs and Laboratories
- APHL
- Federal TB Task Force
- Global Stop TB Partnership
- OGAC/PEPFAR
- Treatment Action Group
- USAID
- WHO Stop TB Department
- Global XDR TB Task Force
- FIND, Global Alliance
- DTBE Staff (HQ, Field)
Genotype and phenotype correlation in 250 clinical *M. tuberculosis* isolates from Hong Kong.

### Genetic and phenotypic characterization of drug-resistant *Mycobacterium tuberculosis* isolates in Hong Kong

Raphael C. Y. Chan\(^1\)*, Mamie Hui\(^1\), Edward W. C. Chan\(^1\), T. K. Au\(^1\), Miu L. Chin\(^1\), Chun K. Yip\(^1\), Carrie K. W. AuYeang\(^1\), Christina Y. L. Yeung\(^1\), Kai M. Kam\(^2\), Peter C. W. Yip\(^2\) and Augustine F. B. Cheng\(^1\)

<table>
<thead>
<tr>
<th>Drug/resistance gene</th>
<th>Resistance to specific drug (%)</th>
<th>Resistant isolates that harbour mutations (%)</th>
<th>Mutants exhibiting resistance (%)</th>
<th>Drug-susceptible strains that harboured mutations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFX/gyrA</td>
<td>71/250 (28)</td>
<td>55/71 (78)</td>
<td>55/56 (98)</td>
<td>1/179 (0.6)</td>
</tr>
<tr>
<td>RIF/rpoB</td>
<td>221/250 (88)</td>
<td>206/221 (93)</td>
<td>206/208 (99)</td>
<td>2/29 (7)</td>
</tr>
<tr>
<td>EMT/embB</td>
<td>118/250 (47)</td>
<td>98/118 (83)</td>
<td>98/106 (93)</td>
<td>8/132 (6)</td>
</tr>
<tr>
<td>INH/katG</td>
<td>241/250 (96)</td>
<td>159/241 (66)</td>
<td>159/159 (100)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>INH/linA</td>
<td>241/250 (96)</td>
<td>3/241 (1.2)</td>
<td>3/3 (100)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>INH/aphC</td>
<td>241/250 (96)</td>
<td>4/241 (1.6)</td>
<td>4/4 (100)</td>
<td>0/9 (0)</td>
</tr>
<tr>
<td>PNZ/pncA</td>
<td>89/250 (36)</td>
<td>71/89 (80)</td>
<td>71/89 (80)</td>
<td>18/161 (11)</td>
</tr>
</tbody>
</table>