Genotyping: Applications to TB Control

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and
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Division of TB Elimination
Quick Historical Perspective

- Locally developed capacity in 1990s

- CDC Sentinel Surveillance Project: 1996
  - CDC and 7 laboratories/sites
  - Primary method: RFLP
  - 5-year project: published in 2002
  - Selective regional genotyping services
Current CDC Genotyping Program

• In 2004, two genotyping laboratories funded to cover U.S.: CA, MI
• Program option for either universal or selective genotyping
• All isolates routinely typed by MIRU and spoligotyping
• IS6110-based RFLP upon request
• Packaging/shipping not included
• No additional funding for epidemiologic program support
Expected Program Impact*

• Earlier detection, and thus control, of outbreaks
• Easier identification of incorrect TB diagnoses based on false-positive results
• Identify unsuspected relationships between cases and unusual transmission settings
• More rapid detection of transmission across different jurisdictions
• Evaluation of contact investigations

*CDC, Tuberculosis Genotyping Guide 2004
Number of TB Cases in U.S.-born vs. Foreign-born Persons
San Diego County, 1997-2007

No. of Cases

1997 1999 2001 2003 2005 2007

U.S.-born Foreign-born
San Diego Start-up Challenges

• Identify procedure for creating the CDC required Excel file with new culture-positive cases
  – Solution: delayed, include RVCT number
• Exchange of information with names
  – Solution: Reports via encrypted email
• Duplicates: tracking issues and urgent clinical requests
• Lag time for submissions from non-PH lab
Data Management Process

• CA lab sends reports as results available
  – Cluster designation (e.g., CA_111) and unique PCR identifier
  – Cumulative report with historical data
• Participate in CA data sharing program
• Maintain special request database
• Use Access tool from CA for summary and detail cluster reports
• Await new national information system (GIMS) with RVCT and genotyping data
### Refuting Outbreak Example: Single Room Occupancy Hotels

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<th>Genotype</th>
<th>Epilink</th>
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</tbody>
</table>

*Identified as contact in previous investigation*
Refuting/Confirming Outbreaks

• Example locations
  – Single worksite
  – Multiple schools
  – Housing complex
  – Single room occupancy hotels

• Potential for significant resource savings

• Most valuable local use of genotyping to date
Laboratory Contamination

• Confirm suspected contamination
  – Clinician
  – TB Control Intake nurse
  – Laboratory

• Critical tool to limiting unnecessary treatment for individual patients

• Potential to identify unsuspected laboratory contamination
Monitor High-Risk Populations

• High-risk population examples:
  – Homeless
  – Correctional

• Limited yield to date
  – Anticipated usefulness: established baseline to identify patterns in future

• In progress by local researcher: cohort with HIV coinfection
Review Large Clusters

• First step: identify clustering patterns
• Local experience
  – Approximately 30% clustered
  – 7 clusters account for nearly 85% of clustered cases
  – 3 of the top 7 clusters: \textit{M. bovis}
• Limited yield to date for large \textit{M. tb} clusters: common birth country or ethnicity
Respond to Requests

• Assist in outbreak investigation
  – Usually via state liaison
  – Recent example: homeless shelter outbreak in distant CA jurisdiction

• Review clusters identified in aberration detection algorithms
  – State and CDC in development and testing phases of algorithms
  – No unsuspected transmission identified to date

• Individual inquiries for possible epidemiologic links or missed contact
Other Program Uses

• Identify relapse vs. reinfection, dual infection
  – Clinical relevance: individual patients
  – Improving epidemiologic evidence

• Identify missed opportunities
  – Missed contacts
  – Incomplete evaluation of contacts
  – Contacts with new TB infection who do not initiate or complete LTBI treatment

• Linking to possible origin of infection: *M. bovis*
Genotyping: Practical Applications

• Demonstrated usefulness
  – Outbreaks
  – Lab contamination
  – Gaps in contact investigation

• Potential future uses
  – Identification of unsuspected transmission
  – Identify areas for program improvements

• Challenges
  – New tools for data management/analysis
  – Improve timeliness of submissions