Collaborating with Commercial Clinical Laboratories

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Speakers

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  – Director, Mycobacteriology Unit, State Microbial Diseases Laboratory (MDL)

Ed, Christy, Grace, Pennan
Outline

- Background
  - Illustrative case example
  - California regulations
- Challenges
- Reaching out to commercial lab partners
- Collaborating / success stories

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Pulmonary sputum culture positive TB cases by laboratory type 2010–2015

What Could Go Wrong

Tissue specimen collected

Day 0

Standard TB treatment started

Request sample to MDL for pyrosequencing (PSQ)

Day 10

Culture ID as MTB

Day 38

Culture positive AFB

Day 49

Hospital admission surgery

Day 59

PSQ: resistance to INH, RIF

MDR regimen started (5 new drugs)

Day 70

MDL receives sample

Day 73

Lab reports DST results: resistance to all first line drugs

Day 74

Lab reports DST results: resistance to all first line drugs

Day 90

Culture positive AFB

>2mo ineffective treatment


Commercial & Other

Public Health

% Cases

0

10

20

30

40

50

60

70

Year

2010 2011 2012 2013 2014 2015
“What Could Go Wrong” is not unique

- Several similar incidents 2016 alone
- Delayed reporting to TB control program additional contributor in other incidents
- Santa Clara County data, 2012–2013 (n=148):
  - TAT from specimen to DST results
    - Regional labs 28-37 days (median)
    - National/commercial labs 62-78 days (median)

Data courtesy Wen Lin

Contributors to delays

- Delays reporting
  - Not reporting results to health department, only to provider*
  - Not reporting preliminary results
  - Complex communication procedures
- Logistical procedures
  - Transport between facilities
  - Batching of cultures and DSTs
  - Sub-culturing each time isolates arrive
  - Not performing DSTs unless ordered*
- Underutilization of rapid tests such as molecular detection of drug resistance

*Required by CA Code of Regulations

California regulations related to tuberculosis (17CCR2505)

- Laboratory shall report any “microscopical, cultural, serological, or other evidence suggestive of” tuberculosis to the local health officer.
- “Laboratory that isolates Mycobacterium tuberculosis from a patient specimen shall” submit it to the designated public health lab (which is the local public health lab).
17CCR Lab Regulations related to TB, cont’d

- “Unless drug susceptibility testing has been performed by the clinical laboratory on a strain obtained from the same patient within the previous three months...” the laboratory shall “perform or refer for drug susceptibility testing...”
- “Whenever a clinical laboratory finds that a specimen... tests positive for acid-fast bacilli staining and the patient has not had a culture which identifies that acid-fast organism within the past 30 days, the clinical laboratory shall culture and identify the acid-fast bacilli...”

Challenges faced by commercial laboratories (a public health view)

- Commercial laboratories should perform laboratory testing requested by ordering physician (and not more as a general rule)
  – Insurance auditors may refuse to pay for services not ordered by the physician
  – But what if the physician ordered only an AFB smear, but not culture, or only a culture but not a drug susceptibility test? CA 17CCR2505 regs can be cited to require follow-on testing.

Challenges faced by commercial labs (public health view, cont’d)

- Commercial laboratories receive specimens from, and need to comply with diverse regulations from many or perhaps all 50 states.
- California’s regulations are difficult to comply with, in that reporting and isolate submittal need to go to many different local jurisdictions.
- Sometimes a patient lives in a jurisdiction which does not have a public health lab—then where does the isolate go???
Challenges faced by commercial labs (public health view, cont’d)
• Not all states will have a regulation requiring follow-on culture (for smear positives) or drug susceptibility testing (for TB complex culture positives).
• Shipping cultures is expensive and time-consuming. A tracking system is required.

Historical relationship between commercial and public health laboratories
• Collegial, cooperative
  – Within legal and fiscal restraints, commercial laboratory staff have uniformly sought to be good citizens
  – Submitting specimens or isolates for expedited testing on request
  – Collaborating with consultation and planning for additional steps in challenging cases
  – IF you can talk to the professional microbiology staff at the commercial laboratory

How to address challenges
• Improve communication
  – Establish direct lines of communication
• Provide information to labs
  – Regulations
  – Role of public health programs
  – Resources in public health labs
• Assist local TB programs
  – Toolkit
  – Case by case assistance
Getting to know each other (conference calls)

- Understand organization and specimen flow
  - Challenges faced by large lab networks
- Share clinical experience from public health
- Exchange contact information

Mycobacteriology Webinar
November 17, 2016

- Invited all laboratories performing mycobacteriology testing in CA
- Attended by >150 laboratorians from >55 laboratories
- 100% (72/72) of evaluation respondents said the lecture increased their knowledge of the subject matter

(Webinar Slide)
Public Health TB Control in California

Local TB control programs: Front line work
- Identification and evaluation of TB cases
  - Reports from providers and laboratories; Hospital discharge approval
- Interruption of transmission
  - Isolation, treatment, directly observed therapy (DOT)
  - Contact investigation
- Detention, legal orders
- Public Health Laboratory

State TB Control
- Supports local programs with funding, consultation, surveillance, statewide issues
Laboratory findings trigger action!

<table>
<thead>
<tr>
<th>Laboratory finding</th>
<th>Possible Clinical or Public Health Actions</th>
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<tbody>
<tr>
<td>Smear positive</td>
<td>Start TB treatment</td>
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<tr>
<td></td>
<td>Place in respiratory isolation</td>
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<tr>
<td></td>
<td>Start contact investigation</td>
</tr>
<tr>
<td>Smear negative</td>
<td>Release from respiratory isolation</td>
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<tr>
<td>Culture positive AFB / MTB</td>
<td>Actions in Smear positive box if not already done</td>
</tr>
<tr>
<td></td>
<td>Expand treatment (if positive after 2 mos)</td>
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<tr>
<td>NAAT positive MTB</td>
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<tr>
<td>DSTs show pan-susceptible (phenotypic)</td>
<td>Stop ethambutol</td>
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<td>Contacts start treatment with standard regimens</td>
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<tr>
<td>DSTs show Rif R or MDR TB (phenotypic or molecular)</td>
<td>Start expanded TB regimen (usu. 5+ meds)</td>
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<td>Place (back) in respiratory isolation</td>
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<tr>
<td></td>
<td>Restart contact investigation if ongoing exposure</td>
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<td></td>
<td>Change treatment of contacts</td>
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Commercial Laboratory Toolkit

- Developed with information gained from
  - Conference calls with commercial laboratories
  - Experience with customer service
  - Reports from TBCB program liaisons and local TB program staff
- Includes contact information for three large commercial laboratories and State MDL
- Tips to guide communication and understand specimen flow

Collaborating on challenging cases

- Molecular detection of drug resistance (MDDR)
  - When pt has known or suspected drug-resistant TB
  - Pyrosequencing (PSQ) at CA lab—detect resistance to INH, rifampin, fluoroquinolones, or injectable drugs by testing culture or smear-positive specimen
  - MDDR at CDC (currently PSQ and Sanger sequencing): adds EMB and PZA to CA menu
  - Both ~ 2 day turnaround time
  - Provided without charge, but shipping incurs cost
Collaborating on challenging cases, cont’d

• Support for investigation of suspected cross-contamination incidents
  – Expedited genotyping
  – Consultation about causes and prevention
  – Training materials

Success stories

• Elderly patient with discordant RIF DSTs → able to troubleshoot quickly, specimen to public health for molecular testing
• Proactive call from commercial lab regarding atypical DST pattern → early notification to local program
• Infant with household MDR contact and transiently abnormal CXR and AFB growth on gastrics → confirmed nonTB organism quickly
• Expedited genotyping to investigate possible false positive culture

Summary

• Communication crucial
• Multiple challenges → multiple activities to address
• Common goals: Obtain accurate information for TB care and public health action rapidly
Acknowledgments

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Resources

- Microbial Diseases Laboratory (MDL) [https://www.cdph.ca.gov/programs/mdl/Pages/default.aspx]
- Laboratory reporting regulations [http://www.cdph.ca.gov/HealthInfo/Documents/Title17Section2505List.pdf]
- Curry International TB Center [http://www.currytbcenter.ucsf.edu/]
  - Warmline: 1-877-390-6682