THIRD EDITION

Tuberculosis Laboratory Aggregate Report

CDC

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Introduction

The Laboratory Capacity Team (LCT) in the Laboratory Branch (LB) of the Division of Tuberculosis Elimination (DTBE) at U.S. Centers for Disease Control and Prevention (CDC) is pleased to present the "Tuberculosis Laboratory Aggregate Report." This report, the third edition, includes a comparison of the aggregate workload data for calendar years 2010 and 2011, select 2011 data, and four year trends (2008–2011) for turnaround time (TAT) and other data. See Technical Note #1. Data are self-reported by public health laboratories (PHL) supported in part by the CDC TB Elimination Cooperative Agreement. Current PHL methods and practices (2010 compared to 2012) are also included in this report. These data serve as a tool to assess benchmarks and make peer comparisons. Providing the self-reported data back to grantees in a meaningful format is an important mission of LCT.

How to Get the Most from this Report

An important aspect of a quality assurance program for laboratories is to monitor workload and TAT indicators. By assessing these indicators over time internally, as well as externally against peer data, laboratories can track progress and set realistic yet ambitious interim goals. The aggregate report provides the nationally aggregated data for comparison and acts as a guide to define your laboratory's TAT goals using national averages and trends. The aggregate report also contains data that is stratified by laboratory volume for a more applicable comparison across laboratories. For details regarding data sources and abbreviations and terms used in this report, please see the Technical Notes section and Glossary.

Use the data in this report to your advantage. This report can serve as evidence to substantiate change within specific activities in your laboratory, possibly in methodology, protocols, or staffing. Use this report to document your laboratory's accomplishments and to increase awareness of your program's impact.

Please contact your LCT consultant with any questions regarding the data requirements for the CDC TB Cooperative Agreement or your laboratory's specific data. Also any recommendations concerning the aggregate report and its content are welcomed.

Laboratory Workload

Table 1. Comparison of 2010 and 2011 National Workload Data

Variable	2010			2011			% change	p value[a]
	Total number	Sites reporting	Median (Range)	Total number	Sites reporting	Median (Range)		
Clinical specimens[b] received	257,005	58	2,643.5 (251–23,250)	239,982	58	2,515 (283–21,943)	−6.6	≤0.05
Patients for whom a specimen was submitted[c]	114,700	58	1,249.5 (126–10,404)	107,144	58	1,182.0 (94–10,057)	−6.6	≤0.05
Patients culture positive for MTBC	4,285	58	43.0 (0–599)	4,399	58	40.5 (2–586)	2.6	0.33
Patients for whom a reference isolate was submitted[d]	18,905	58	195.0 (0–2,619)	17,944	58	200.5 (0–2,496)	−5.1	0.19
Patients with a reference isolate identified as MTBC	3,343	58	27.0 (0–406)	3,331	58	26.0 (0–368)	−0.4	0.105
Patients for whom DST was performed	7,217	58	71.0 (0–758)	6,822	58	66.5 (1–705)	−5.5	≤0.05
Patients tested by NAAT or other rapid test	14,081	58	78.5 (0–6,253)	15,077	58	100.5 (0–6,450)	6.6	≤0.05
Patients NAAT positive for MTBC	2,507	58	16.0 (0–408)	2,430	57	18.0 (0–361)	−3.1	0.33

[a]Wilcoxon signed-rank test, [b]Processed and cultured, not including isolates referred from other laboratories, [c]Processed and a TB culture inoculated, [d]Received to either rule out or confirm the identification of MTBC

From 2010 to 2011, PHLs reported statistically significant (p value ≤ 0.05) decreases in the number of clinical specimens received, patients for whom a specimen was submitted, and patients for whom a DST was performed. However, there was no significant change in the number of patients that were culture positive for MTBC. There was a significant increase in the number of patients for whom a clinical specimen was tested by either NAAT or other direct detection assay.

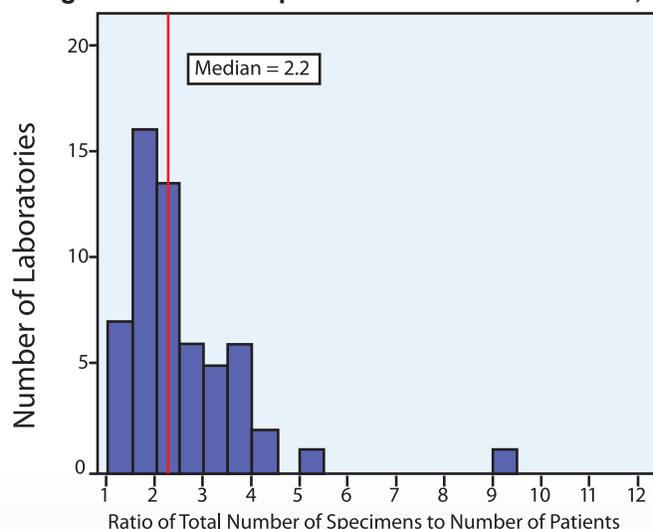### Figure 1. Ratio of Specimens to Patients Tested, 2011

Figure 1 represents the number of total specimens received in relation to the number of patients from whom the specimens were collected. In 2011, the median ratio of specimens to patients across laboratories was 2.2, and this median has been consistent over the last four years (see Technical Note #2). A ratio less than 2 indicates that only a single specimen per patient was submitted for many patients. A high ratio indicates excess specimens are received per patient. Laboratories should work with TB control programs and clinicians to develop guidelines for accepting diagnostic and repeat specimens from patients that ensure effective patient management while reducing unnecessary testing.
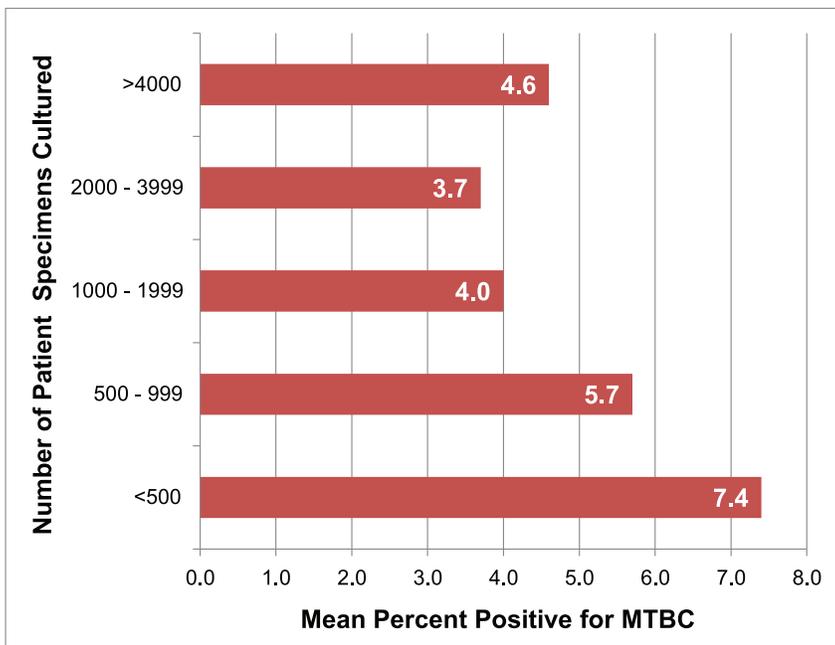
Positivity of Cultures and Isolates for MTBC

Figure 2. Trends in Positivity of Cultures and Isolates, 2008–2011
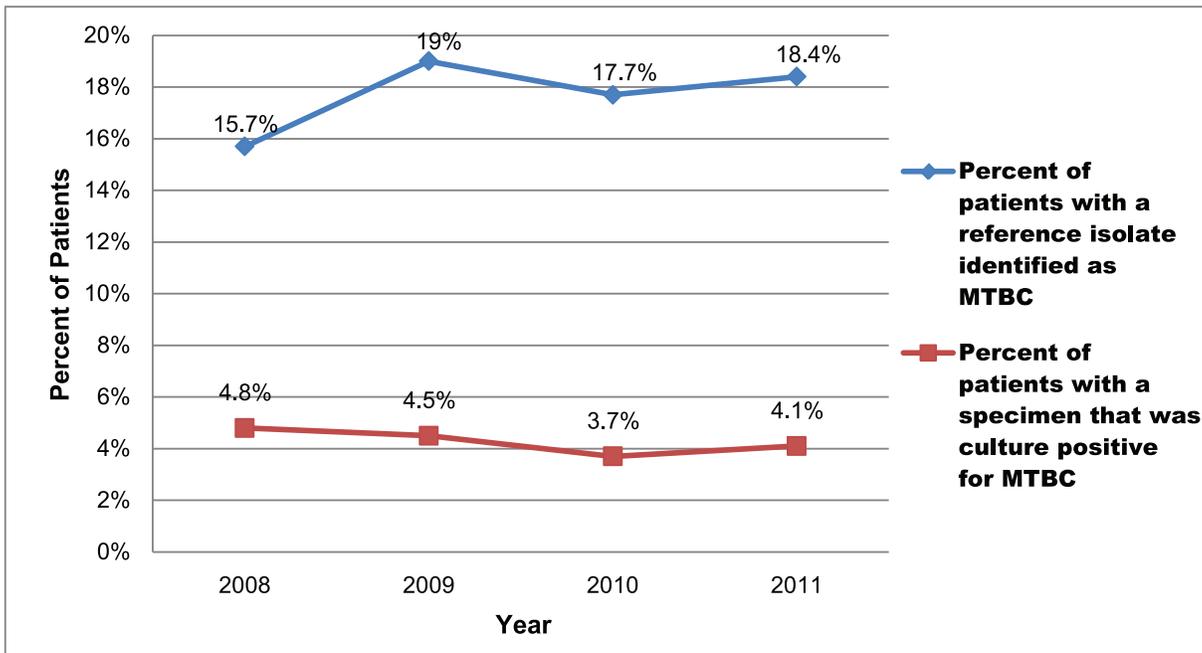
Positivity of patient specimens and reference isolates has remained fairly stable from 2008–2011.

Figure 3. Positivity of Cultures Stratified by Volume of Patient Specimens Tested, 2011

In 2011, culture positivity increased as volume decreased (except for the highest volume laboratories). This indicates that although low-volume laboratories may see relatively few MTBC-positive patients, they are finding a higher proportion of positive results among patient-specimens received. For all public health laboratories, 4.1% culture positivity was seen for MTBC in 2011, and is similar to previous years (see Technical Notes #2 and #3).

Trends in Nucleic Acid Amplification Testing (NAAT)

Table 2. NAAT volumes 2009–2011

Year	Number of PHL	Percent of patient specimens processed at PHL that also had NAAT performed	Percent of patients with NAAT performed that were NAAT positive for TB	Percent of patients with culture confirmed MTBC with a NAAT positive result reported within 48 hours (HP 2020)	Percent positive NAAT results reported within 48 hours of specimen receipt
2009	45	8%	24%	36%	76%
2010	36	16%	13%	40%	72%
2011	43	16%	13%	42%	81%

The percent of patients that had NAAT performed did not change in 2011 when compared to 2010; however, the percent of patients did increase significantly in 2010 compared to 2009. Increasing access to this type of testing in PHL may be due in part to the Association of Public Health Laboratories one-time grant funding for the expansion of NAAT in 2010. Please see Technical Note #4 for explanation of how Number of PHL was derived.

Table 3. NAAT numbers stratified by NAA testing volume, 2010-2011

Number patients NAAT performed	Number of PHL		Percent of patient specimens processed at PHL that also had NAAT performed		Percent of patients with NAAT performed that were NAAT positive for TB		Percent of patients with culture confirmed MTBC with a NAAT positive result reported within 48 hours (HP 2020)		Percent positive NAAT results reported within 48 hours of specimen receipt	
	2010	2011	2010	2011	2010	2011	2010	2011	2010	2011
≤25	6	8	0.7%	2%	32%	26%	8%	21%	65%	75%
26-100	13	13	4%	6%	28%	19%	32%	37%	67%	86%
101-200	6	9	4%	5%	29%	31%	27%	34%	68%	71%
201-500	7	9	11%	12%	21%	23%	25%	36%	51%	80%
>500	4	4	58%[*]	64%[*]	9%	7%	70%	63%[*]	88%	87%

[*]For the highest volume laboratories, data are likely skewed because of inclusion of data from 2 laboratories receiving referred sediments for NAAT only without culture.

In general, as NAAT volume increased, positivity decreased. Prompt reporting of NAAT results has increased for all laboratories in 2011 compared to 2010. Please see Technical Notes #3 and #4 for explanation of years used for comparison and how Number of PHL was derived.

Turnaround Times

Figure 4. Time[a] to Specimen Receipt, 2011
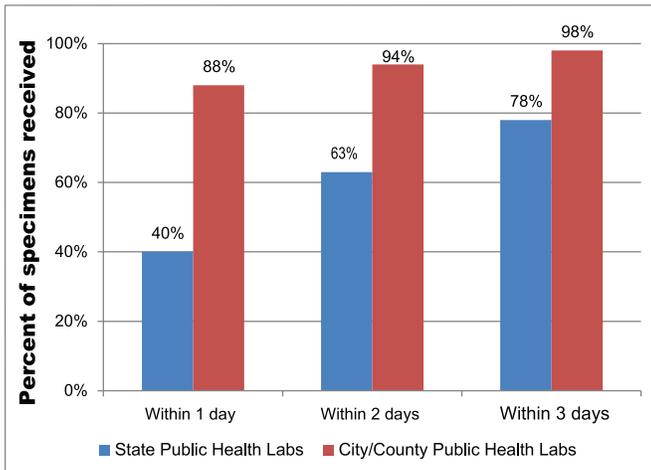
[a] Times represent days from collection of specimen to receipt in laboratory.

State PHLs continue to face challenges in receipt of specimens within one calendar day, while city and county PHLs remain at high levels for this indicator, as seen in previous editions of this report[1]. Please see Technical Note #2.

Figure 5. National Trends in Meeting TAT Recommendations, 2008–2011
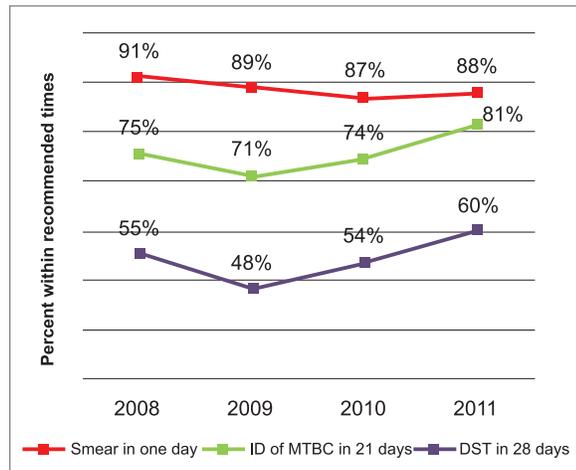
Laboratories saw improvements in meeting TAT recommendations for ID of MTBC within 21 days but, although progressing, still face challenges for DST within 28 days from 2008 to 2011. Providing smear results within one day continued at high levels.

Figure 6. Association of ID TAT with DST TAT for MTBC in 2011
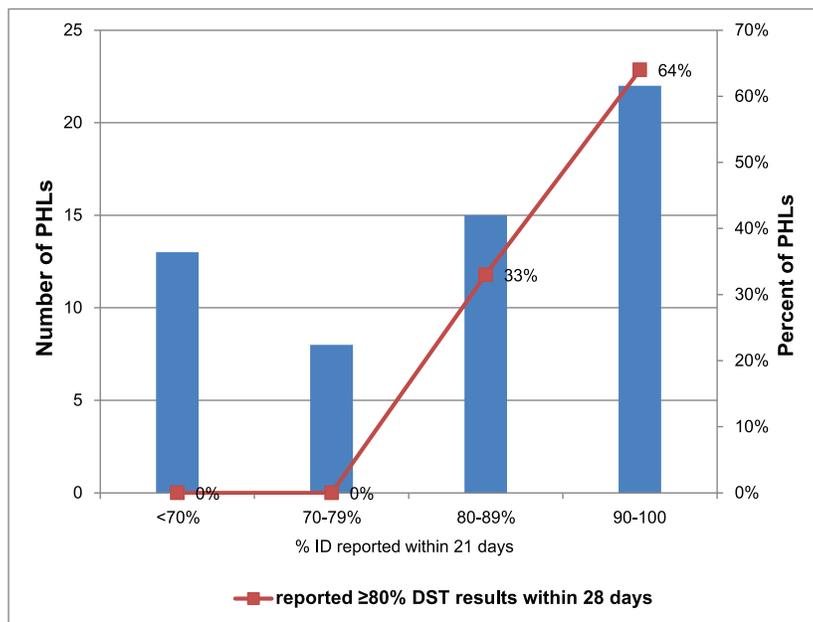
Delays in DST TAT are often a result of delays in obtaining upstream testing results. For example, none of the laboratories reporting ≤79% of their ID results within 21 days are able to report at least 80% of their DST results within 28 days, while 64% of laboratories reporting ≥90% ID results within 21 days were able to report at least 80% of their DST results within 28 days. Upstream delays could occur because of low bacterial load in initial specimen, slow growth of extrapulmonary specimens, or contamination issues. Please see Technical Note #2.

Testing Performed in PHL when Compared to National Surveillance Data

Table 4. Proportion of TB testing done in PHLs

Year	Total culture confirmed TB cases[a]	MTBC-culture positive patients in PHL[b]	Proportion of culture confirmed cases tested by PHL	Total culture confirmed cases with DST reported[a]	Patient DST performed by PHL[b]	Proportion of DST performed by PHL
2008	10,030	5,745	57%	9,365	8,255	88%
2009	8,876	5,005	56%	8,495	7,531	89%
2010	8,413	4,285	51%	8,063	7,213	89%
2011	8,070	4,399	55%	7,727	6,822	88%

[a]Surveillance data, Reported Tuberculosis in the United States[2], 2008–2011. [b]TB Laboratory Aggregate Report Data, 2008–2011

PHL performed a significant proportion of culture and DST for TB cases reported in the United States. The proportions shown include self-reported data. Duplication of testing may have occurred possibly resulting in an overestimate.

**Table 5. NAAT positivity among culture confirmed TB cases reported through national surveillance**

Year	Total culture confirmed TB cases[a]	NAAT positive patients for MTBC in PHL[b]	Proportion of culture confirmed TB cases detected by NAAT in PHL
2008	10,030	2,533	25%
2009	8,876	2,355	27%
2010	8,413	2,506	30%
2011	8,070	2,430	30%

[a]Surveillance data, Reported Tuberculosis in the United States[2], 2008–2011. [b]TB Laboratory Aggregate Report Data, 2008–2011

The proportion of culture confirmed TB cases in the United States detected by NAAT in a PHL appears to be increasing. The proportion shown includes self-reported data. Duplication of testing may have occurred possibly resulting in an overestimate. One barrier to continued progress in rapidly detecting cases is that many laboratories do not routinely perform NAAT on smear-negative specimens. Laboratories should collaborate with TB control programs to provide NAA testing for all TB suspects and devise algorithms that are not dependent on smear status, but rather focus on clinical suspicion of TB.[3]
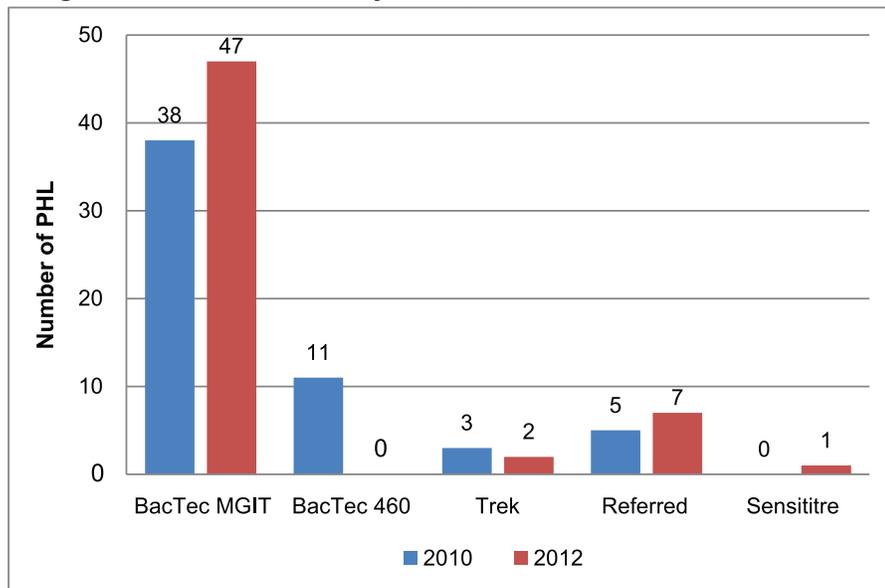
Trends in Laboratory Methods

Figure 7. NAAT Methods, 2010 and 2012
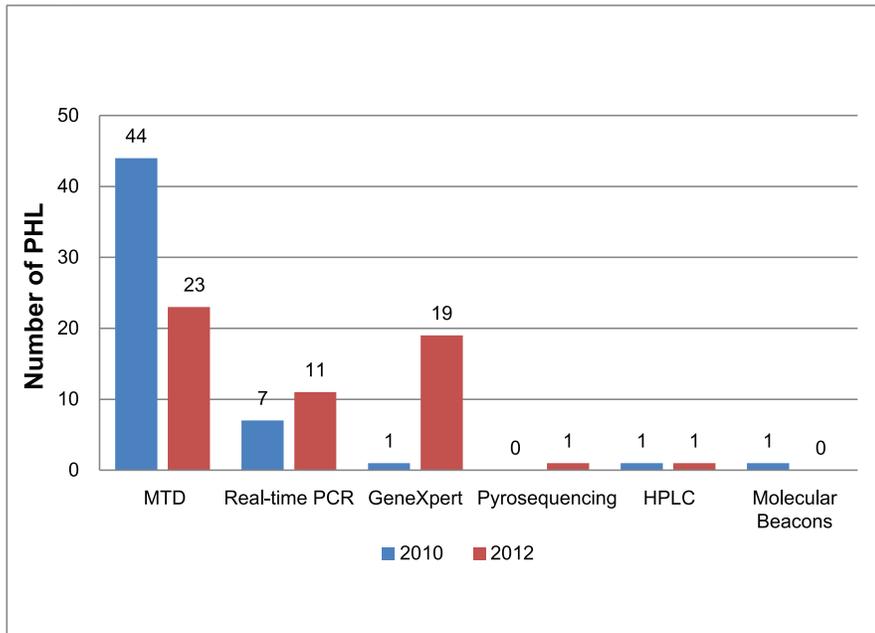
NAAT technology methods changed, with a decrease in the use of the MTD™ test and an increase in use of the GeneXpert™ MTB/RIF assay and laboratory developed real-time PCR.

Please see Technical Note #5 for description of source of data.

Figure 8. First-Line DST Systems, 2010 and 2012

As the BacTec 460™ media became commercially unavailable, laboratories shifted to use of the BacTec MGIT™ for their culture system and first-line DST method. Please see Technical Note #5 for description of source of data.

Technical Notes

1. Unless otherwise specified, the source of all data and information for the tables and figures in this report comes from the Interim and Final Progress Reports of the TB Elimination and Laboratory Cooperative Agreement submitted to CDC by U.S. Public Health Laboratories.

2. Figures 1, 3, 4, and 6 show data for 2011 only because data were not notably different from 2010.

3. Data were not aggregated for years 2010 and 2011 because of a shift between categorical levels (i.e., testing volume) by some laboratories between years.

4. For Tables 2 and 3, laboratories had to report data for all categories described for inclusion in analysis.

5. Figures 7 and 8 compare laboratory methods between 2010 and 2012. The data from 2012 were used to indicate changes in methodology that occurred in 2011, when many laboratories were in a transition period evaluating newer techniques.
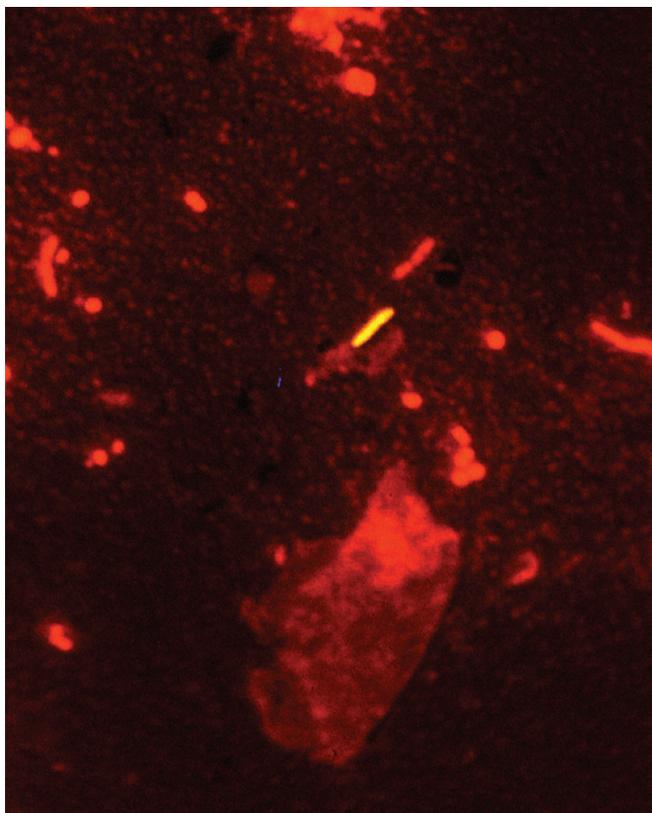
Glossary

BacTec 460™: Becton Dickinson and Co. A commercial radiometric broth-based mycobacterial culture system

CDC: U.S. Centers for Disease Control and Prevention

DST: Drug susceptibility testing

DTBE: Division of Tuberculosis Elimination

GeneXpert™ MTB/RIF, Cepheid, Inc. A commercial molecular assay for the direct detection of MTBC and mutations associated with rifampin resistance in clinical specimens

HP 2020: Healthy People 2020 TB Goal is to increase the percent of TB cases detected within 48 hours to 77% of those later culture-confirmed.

ID: Bacterial species identification of MTBC

LB: Laboratory Branch, DTBE

LCT: Laboratory Capacity Team, LB, DTBE

MGIT™, BacTec MGIT ™: Mycobacterium Growth Indicator Tube, Becton Dickinson and Co. A commercial non-radiometric broth-based mycobacterial culture system

MTBC: Mycobacterium tuberculosis complex

MTD™: Mycobacterium Direct Test, Gen Probe, Inc. A commercial molecular assay for the direct detection of MTBC in clinical specimens

NAAT: Nucleic Acid Amplification Test. Generic terminology for molecular method used for the direct detection of MTBC in clinical specimens

PCR: Polymerase Chain Reaction

PHL: Public Health Laboratory

Positivity (in reference to culture, isolate, or NAAT): Percent positive for MTBC of all specimens or isolates assayed, determined on a per-patient basis

Reference isolate: A growing culture of mycobacteria, for example, a positive MGIT™ tube or growth on a Lowenstein-Jensen slant

TAT: Turnaround time

TB: Tuberculosis (disease)

References

1. CDC. Tuberculosis Laboratory Aggregate Report. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2010 and 2011. http://www.cdc.gov/tb/publications/reportsarticles/labreports.htm

2. Reported Tuberculosis in the United States, 2008 to 2011, CDC. Atlanta, GA http://www.cdc.gov/tb/statistics/default.htm

3. Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis http://www.ncbi.nlm.nih.gov/pubmed/19145221

Resources

APHL Resources

APHL TB page http://www.aphl.org/aphlprograms/infectious/tuberculosis/pages/default.aspx

APHL TB Core Services http://www.aphl.org/aphlprograms/infectious/tuberculosis/Documents/ID_2009Dec_Core-TB-Services.pdf

APHL Self-assessment tool http://www.aphl.org/aphlprograms/infectious/tuberculosis/Pages/TB-Self-Assessment-Tool.aspx

Essentials for the Mycobacteriology Laboratory: Promoting Quality Practices http://www.aphl.org/aphlprograms/infectious/tuberculosis/tb-core-curriculum/Pages/default.aspx

APHL Fact Sheet for Cepheid Xpert MTB/RIF Assay http://images.magnetmail.net/images/clients/APHL/attach/CepheidXpert_FactSheet_090913.pdf

CDC Resources

CDC TB Website http://www.cdc.gov/tb/

CDC Molecular Detection of Drug Resistance (MDDR) Service http://www.cdc.gov/tb/topic/laboratory/guide.htm

Regional Training and Medical Consultation Centers http://www.cdc.gov/tb/education/rtmc/default.htm

Report of Expert Consultations on Rapid Molecular Testing to Detect Drug-Resistant Tuberculosis in the United States http://www.cdc.gov/tb/topic/laboratory/rapidmoleculartesting/default.htm

Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection—United States, 2010: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_w

Guide to the Application of Genotyping to Tuberculosis Prevention and Control http://www.cdc.gov/tb/programs/genotyping/manual.htm

TB Notes Newsletter http://www.cdc.gov/tb/publications/newsletters/notes/default.htm

CDC Model Performance Evaluation Program http://www.cdc.gov/tb/topic/laboratory/mpep/

MMWR on use of GeneXpert http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6241a1.htm?s_cid=mm6241a1_e

Other Resources

TB Education and Training Resources http://www.findtbresources.org/

Evidence-based TB Diagnosis http://tbevidence.org/
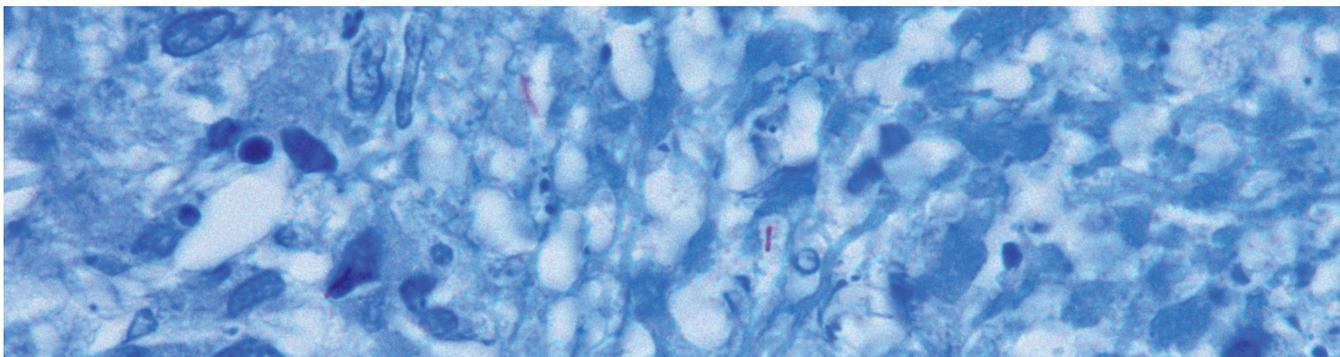
Journal Articles of Interest

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Tyrrell, F. C., G. E. Budnick, et al. (2012). "Probability of negative mycobacterium tuberculosis complex cultures based on time to detection of positive cultures: a multicenter evaluation of commercial-broth-based culture systems." J Clin Microbiol 50(10): 3275-3282. http://www.ncbi.nlm.nih.gov/pubmed/22837326