

Investigation of Possible False-Positive *Mycobacterium tuberculosis* Culture Results

Background

Studies have reported that approximately <1–3 percent of cultures positive for *M. tuberculosis* are false-positives.(1; 2) Prompt recognition of false-positive cultures is needed to prevent unnecessary therapy for tuberculosis (TB), financial costs associated with unnecessary public health interventions and clinical care, and human costs of stigmatization and isolation associated with a misdiagnosis of TB. According to Centers for Disease Control and Prevention:

False-positive cultures occur when *M. tuberculosis* bacteria from one specimen, instrument, or culture inadvertently contaminate another specimen or culture or when clerical errors occur and specimens are mislabeled or misreported. Clinical equipment (e.g., bronchoscopes, sputum collection booths, and ultrasonic nebulizers), if inadequately cleaned, can become contaminated and be the source of false-positive cultures (as well as the source of nosocomial transmission). Cross-contamination can occur in the laboratory during batch processing, pipetting, transfer of bacilli from a broth-culture system, work in a faulty exhaust hood, and species-identification procedures. One of the most important advantages of routinely fingerprinting all *M. tuberculosis* isolates is the ability to establish an early warning system to identify suspected false-positive cultures.(3)

When to Suspect a False-Positive

Circumstances which should raise suspicion for a false-positive culture include:

- The health care provider or the clinical laboratory suspects a false-positive culture.
- Only one specimen is culture positive among multiple specimens obtained and all smears are negative for acid-fast bacilli.
- The patient did not have symptoms or radiographic findings consistent with TB.
- The patient had another confirmed diagnosis to explain symptoms.
- The specimen was processed in the same laboratory on the same day as another specimen with matching genotype.
- The specimen was collected in the same facility within three days of another specimen with matching genotype.
- The reported growth on the culture is scant (only a few colonies or growth only in broth) or the time until growth is detected is long (>30 days).
- The specimen genotype matches that of a laboratory control strain.(3) (Note that the commonly used control, ATCC control strain H37Rv, has a known genotype cluster designation: CA_Rv/Ra. However, not all laboratories use this control strain, and control genotypes might drift over time).

It is important to note that true cases of tuberculosis can have many of the characteristics listed above. A thorough investigation is critical to distinguish true-positive from false-positive cultures. Only in exceptional cases should tuberculosis treatment be delayed pending results of this investigation.

Data Collection

Whenever a false-positive culture is suspected, clinical and laboratory information needed to assess the situation should be collected. A data collection form is attached to facilitate this process. Genotype information on all specimens collected or processed around the time (+/- 1–2 days) of the suspected false-positive culture is very useful. If genotyping has not been done, specimens should be sent for genotyping, including the laboratory positive-control strain. Indicate on the request form that a false-positive culture is suspected.

Analysis and Reporting

The following steps should be taken:

1. Compare genotype results for all specimens
2. Review clinical and laboratory records of cases with positive specimens
3. Complete lab cross-contamination investigation worksheet
4. Determine final assessment of laboratory cross-contamination likelihood
5. Inform TB Controller of involved jurisdiction(s) of assessment
6. Submit completed worksheet and any associated reports to:
 - TB Controller(s) involved
 - Laboratories involved
 - California Department of Public Health, Tuberculosis Control Branch (TBCB) (if involved)
 - California Department of Public Health, Microbial Diseases Laboratory (MDL)

Resources Available

The California Department of Public Health Tuberculosis Control Branch can provide assistance with evaluating possible false-positive culture results. TBCB staff can:

- assist with clinical evaluation of suspect patients
- advise on data collection
- assist with interpretation of data
- coordinate laboratory services
- coordinate between local health jurisdictions

The California Department of Public Health, Microbial Diseases Laboratory (MDL) has extensive experience working with laboratories to identify causes of false-positive results and advising on steps to prevent future events. Upon request, MDL can:

- provide consultation to laboratories and TB control staff by phone
- provide a video about how to recognize and prevent false positive results in the TB lab
- make a laboratory site visit to provide assistance

For assistance or more information, please contact the TB Control Branch Outbreak Duty Officer at 510-620-3000.

References

- (1) Jasmer RM, Roemer M, Hamilton J et al. A prospective, multicenter study of laboratory cross-contamination of Mycobacterium tuberculosis cultures. *Emerg Infect Dis* 2002; 8(11):1260-1263.
- (2) Ruddy M, McHugh TD, Dale JW et al. Estimation of the rate of unrecognized cross-contamination with mycobacterium tuberculosis in London microbiology laboratories. *J Clin Microbiol* 2002; 40(11):4100-4104.
- (3) National Tuberculosis Controllers Association/Centers for Disease Control and Prevention Advisory Group on Tuberculosis Genotyping. *Guide to the Application of Genotyping to Tuberculosis Control and Prevention*. 2004. Atlanta, GA, US Department of Health and Human Services.

FALSE-POSITIVE TB CULTURE INVESTIGATION WORKSHEET

Patient name (last, first):

County of residence:

Date of birth:

Date of culture:

Location of specimen collection:

Laboratory processing specimen:

Laboratory culturing specimen:

1. Presentation

a. Describe patient clinical symptoms and findings:

b. Positive TST or IGRA?

YES

NO

c. Is the clinical picture consistent with TB?

YES

NO

2. Radiographic findings

a. Describe patient radiographic findings:

b. Are the radiographic findings consistent with TB?

YES

NO

3. Laboratory findings (complete specimen table)

a. AFB smear results

i. number of smears done:

ii. number of smears positive for AFB:

iii. describe results (scant, 1–4+, etc.):

b. Rapid test results (NAAT, molecular beacons)

i. number of specimens tested:

ii. number of specimens positive for *M. tb* by rapid test:

c. Culture results

i. number of specimens submitted for culture:

ii. number of positive cultures:

d. Pathology results suggestive of TB:

Key to Abbreviations: TST=TB Skin Test; IGRA=Interferon Gamma Release Assay; AFB=Acid Fast Bacilli; NAAT=Nucleic Acid Amplification Test; RVCT=Report of Verified Case of Tuberculosis; RFLP=Restriction Fragment Length Polymorphism

4. Are there any strong alternative diagnoses?
(if yes, describe) YES NO
5. Is the patient being treated for TB? YES NO
6. Does clinician feel the patient has TB? YES NO UNSURE
7. Genotype
- a. What is the genotype cluster designation?
- b. Was RFLP done? YES NO
(if yes, enter band number and genotype cluster designation)
- c. Is there a genotype match to another case with a specimen collected and/or processed around the same time? YES NO
- d. If yes, provide the following information on the other case:
- i. patient name:
 - ii. date specimen collected:
 - iii. location specimen collected:
 - iv. date specimen processed/cultured:
 - v. location specimen processed/cultured:
- e. What is the genotype of the positive control strain?
8. Describe any procedures that could result in cross-contamination or other false-positive report (include laboratory, specimen collection, or clerical procedures):

Assessment:

Likelihood that the result is a false-positive: High Moderate Low None

Date local TB controller notified:
 Date involved laboratories notified:
 Date corrections to RVCT made (if necessary):
 Investigated by (name):

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Specimen Data Collection Table

Patient Name:

Specimen Number	Specimen Type	Date Collected	Facility Collecting Specimen	Date Received in Lab	Laboratory Name	Date Smear Prepared	AFB Smear Result	Rapid Test Type/Result	Date Culture Prepared	Culture System	Culture Result	Culture Result Date