Number of Negative Acid-Fast Smears Needed To Adequately Assess Infectivity of Patients With Pulmonary Tuberculosis*

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Study objectives: **To investigate the relationship between the number of negative acid-fast bacilli (AFB) smear results and infectivity of pulmonary tuberculosis (TB).**
Design: **Retrospective analysis.**
Methods and subjects: **We examined 122 index cases in Harris County, TX, reported in 1998 and 1999. All cases had only negative AFB smear results during the infectious period and were categorized in two groups: group A consisted of cases with only one or two sputum specimens collected and processed, and group B consisted of cases with at least three sputum specimens or at least one bronchoscopic specimen. Tuberculin skin test (TST) results of contacts were ascertained from the results of contact investigations performed by the City of Houston Department of Health and Human Services, Tuberculosis Control Division. Univariate and multivariate analyses were done to explore index case and contact attributes associated with tuberculosis (TB) transmission using positive TST results of contacts as a measure of recent transmission.**
Results: **We found male gender and younger age of index cases along with Hispanic ethnicity of contacts to be independently associated with positive TST results, while younger contacts were less likely to be TST positive. Smear category of the index case (group A vs group B) was not independently associated with transmission. We also found that the first two sputum specimens in cases where three or more were performed yielded 90% of all positive culture results for *Mycobacterium tuberculosis* (MTB).**
Conclusions: **We conclude that two sputum specimens negative for AFB stain are adequate for both assessing infectivity and for isolating MTB from patients with pulmonary TB.**
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Key words: infectivity; sputum smear; transmission; tuberculin; tuberculosis

Abbreviations: AFB = acid-fast bacilli; CI = confidence interval; HTI = Houston Tuberculosis Initiative; IP = infectious period; MTB = *Mycobacterium tuberculosis*; OR = odds ratio; OTC = other than close; TB = tuberculosis; TB Control = Tuberculosis Control Division; TST = tuberculin skin test

Patients with pulmonary tuberculosis (TB) having consistently negative smears for acid-fast bacilli (AFB) are less infectious than patients with positive smear results as shown by various epidemiologic studies.[1–3] A positive AFB smear result is considered a major determinant as to whether a pulmonary TB case will transmit the bacilli to a contact.[4] However, according to a study[5] that utilized molecular characterization of *Mycobacterium tuberculosis* (MTB) isolates, smear-negative cases are still responsible for approximately 17% of recently transmitted TB. The

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latter observation lends support to the current Centers for Disease Control and Prevention recommendations stating that in order to discontinue airborne precautions, patients with pulmonary TB in addition to having three negative, consecutive, sputum smear results must be receiving efficacious therapy and show adequate clinical response.[6] However, there is a paucity of data supporting a specific number of negative smear results as adequate in assessing the infectious potential of such patients. In addition, some authors have suggested that airborne precautions be discontinued after two negative smear results have been collected before[7,8] or during adequate treatment,[9] although direct evidence that this would not result in higher disease transmission is lacking.

In order to investigate the impact of the number of negative smear results on transmission of pulmonary TB, we conducted a retrospective study of patients (index cases) and their corresponding contact investigations. We included cases with only negative AFB smear results collected during a specified infectious period. We then grouped and compared the index cases according to the number of specimens collected from each. The rationale for such a study design is as follows: When the initial two sputum specimens collected from an active pulmonary TB case are smear negative, according to current guidelines[6] at least one more specimen is needed in order to fully assess whether a patient is infectious. In theory, this third specimen can be smear positive and can thus signify a case with a higher infectious potential, information that would be missed if this third specimen is not collected. However, if disease transmission from cases in which a third specimen is not collected is similar to that of cases with three or more negative smears results, one may conclude that in practice a third or later specimen adds little information on evaluating the infectious potential of the patient.

Methods and Materials

Index Case Selection

All index cases meeting the following criteria were initially included in this study: (1) culture-proven pulmonary TB; (2) no positive smear results for AFB from pulmonary specimens collected during the infectious period (as defined below); and (3) reported to the City of Houston Tuberculosis Control Division (TB Control) during 1998 and 1999. The infectious period (IP) was defined as the time from the start of cough and/or hemoptysis until 14 days after the start of effective therapy (at least two drugs with *in vitro* activity) or, if therapy was not started, until the time the patient died or moved out of Harris County. When neither cough nor hemoptysis were reported, the date of the first specimen collection was considered the start of the IP. The above information was extracted from the Houston Tuberculosis Initiative (HTI) database. The HTI is an ongoing population-based project involving TB patient interview, medical record review, and molecular characterization of MTB isolates. The HTI has been enrolling Harris County (Houston), TX, TB cases since October 1995.[10] Cases were cross-referenced with the City of Houston TB Control database to confirm that no positive AFB smear results were ever reported (during the period noted above) and that all specimens collected and processed were captured. Patient demographics and additional factors potentially related to disease transmission and severity were extracted from the HTI database. Culture results together with the timing and type of respiratory specimens were also recorded. The HTI project was approved by the Baylor College of Medicine and Affiliated Hospitals Institutional Review Board, and all enrolled cases signed informed consent, allowing access to contact investigation data for each index case.

Index Case Groups

For the purpose of statistical analysis, index cases were classified in two groups: group A included those with one or two sputum smears for AFB collected and processed during the IP, and group B included those with three or more sputum AFB smears or at least one smear from a bronchoscopic specimen collected during the IP. In cases in which more than one specimen was collected the same day, the specimens were considered as one for the purpose of the above classification, but all had to be smear negative in order to be included in the study.

Contact Investigation

Trained workers from City of Houston TB Control performed contact investigation on index cases according to the American Thoracic Society recommendations.[4] Briefly, the investigation protocol was as follows: all index cases were interviewed to identify all possible contacts. Then, all household contacts were investigated as well as anyone who shared the same closed space with an index case for at least 4 h/wk during a period of at least 3 months prior to TB diagnosis. Household contact was defined as anyone staying in the same house as his/her permanent residence at the time of TB diagnosis. The above contacts were defined as *close contacts* for our analysis. The remaining contacts were defined as *other than close* (OTC). Contact investigation was expanded if $\geq 30\%$ of the close contacts were positive tuberculin skin test (TST) reactors. The first TST is administered within 2 weeks of identification of a contact using five tuberculin units of purified protein derivative of standard strength. The TST was repeated in 3 months if the first test result was negative. Contacts with previously documented positive TST results or contacts treated for TB in the past were not tested with TST, but underwent chest radiography to assess for active disease. These individuals were classified for our analysis as *nonsusceptible.*

Contact Classification

Contacts with at least a 5-mm induration on the first or second TST were considered positive (infected by the index case).[11] Those with both TSTs 0 to 4 mm were considered negative (not infected). If only one TST was performed, was 0 to 4 mm, and was performed at least 8 weeks after the end of the IP, a contact was also considered negative.[12] If only one TST was performed with 0- to 4-mm induration < 8 weeks from the end of the IP, or no TSTs were done, the contact was classified as *incompletely investigated.*