Evidence-based Tuberculosis Diagnosis
One-page plain language summaries of systematic reviews - #2

Title: Serial sputum specimen examinations for the diagnosis of pulmonary tuberculosis
This *systematic review* presents *evidence* from a collection of studies evaluating tests or strategies for the diagnosis of tuberculosis (TB). Terms in *italics* are defined in the TB Evidence Glossary.

Why this review is important: Early diagnosis and timely treatment are principles of TB control, leading to reductions in illness, death, and spread of TB. The examination of 3 sputum specimens for TB diagnosis became routine following studies conducted in India in the 1950s that showed that 3 specimens collected over 2 days identified the highest number of patients with the lowest number of visits. Many patients, however, are unable to complete this diagnostic process. Increased *sensitivity* of the 3rd specimen may be offset by increased laboratory workload and burden on patients who are required to return to the health center with an additional sputum specimen. Is there still a need for 3 specimens to diagnose TB?

Objective: To quantify the contribution of the microscopic examination of the 1st, 2nd, and 3rd sputum specimens for the diagnosis of TB.

Main findings: 37 studies were included in the review. The average percentage of all smear-positive TB cases (using culture or smear as the *reference standard*) detected with the 1st sputum specimen was 86%. In 20 studies using culture as the reference standard, the average *sensitivity* of the 1st specimen was 54%; the average increase in sensitivity of the 2nd specimen was 11%; and the average increase in sensitivity of the 3rd specimen was 3%. Subgroup analysis showed an average gain in positive smears and/or increases in sensitivity ranging from 2% to 5%. There were only 3 studies in the review directly comparing results in people with and without HIV, too little information from which to draw conclusions. However, a recent paper showed that, for people with HIV, the minimal gain from the 3rd specimen makes it not worth doing (reference 2).

Table. Average increase in sensitivity of the third sputum specimen (95% confidence intervals); number of studies

	Overall	**Prospective Studies**	**Retrospective Studies**	**Direct Smears**	**Processed Smears**	**Ziehl-Neelsen Microscopy**	**Fluorescence Microscopy**
Increase in Sensitivity	3.1% (2.1,4.2); 20	3.1% (1.3,5.0); 9	3.1% (1.8,4.4); 11	2.3% (0.6,4.0); 6	4.1% (2.7,5.5); 14	4.7% (3.3,6.0); 8	2.4% (1.1,3.58); 12

Authors' conclusions: The majority of TB patients can be diagnosed with the 1st sputum specimen. The increase in the average sensitivity gained by examining a 3rd sputum specimen appears to be low. Reducing the recommended number of specimens examined from 3 to 2 could benefit patients and TB control programmes, particularly if 2 specimens could be collected on the same day.

Policy implications: In 2007, WHO revised the definition of a sputum smear-positive pulmonary TB case to be based upon the presence of at least one acid-fast bacillus in at least one sputum sample in countries with a well functioning external quality assurance (EQA) scheme. In addition, the minimum number of sputum specimens to be examined was reduced from 3 to 2 in settings where a well-functioning EQA scheme exists, the workload is high, and human resources are limited.

Comments: Although, several studies had shortcomings, the authors found consistent results among studies with different study designs, microscopy stains, and sputum processing methods, increasing confidence in the findings.

Systematic review: Mase SR et al. Yield of serial sputum specimen examinations in the diagnosis of pulmonary tuberculosis: a systematic review. International Journal of Tuberculosis and Lung Disease 2007 11(5):485-495 Available at www.tbevidence.org

Publications and other resources of related interest
1. http://www.who.int/tb/laboratory/policy_diagnosis_pulmonary_tb/en/index.html 2.Monkongdee P et al. Yield of acid-fast smear and mycobacterial culture for tuberculosis diagnosis in people with human immunodeficiency virus. Am J Respir Crit Care Med. 2009 Nov 1;180(9):903-8. Epub 2009 Jul 23. 3. Bonnet M et al. Reducing the number of sputum samples examined and thresholds for positivity: an opportunity to optimise smear microscopy. Int J Tuberc Lung Dis. 2007 Sep;11(9):953-8

Contact: Karen R Steingart, MD, MPH karenst@uw.edu, Evidence Synthesis & Policy Subgroup, NDWG, Stop TB Partnership