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# Incremental yield of bronchial washing for diagnosing smear-negative pulmonary tuberculosis

## Aumento do rendimento do lavado brônquico para diagnóstico da tuberculose pulmonar com baciloscopia negativa

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### ABSTRACT

**OBJECTIVE:** To assess the increased diagnostic yield for pulmonary tuberculosis using bronchial washing cultures compared with sputum cultures.

**METHODS:** Study conducted with 61 adults in Lima, Peru, from January 2006 to December 2007. The yield of sputum cultures was compared with the yield of acid-fast bacilli smears and cultures of bronchial washing for diagnosing pulmonary tuberculosis in suspected cases of clinical tuberculosis with negative acid fast bacilli sputum smears.

**RESULTS:** Twenty seven (95%CI 32;58) of the cases were eventually diagnosed with smear-negative pulmonary tuberculosis. Bronchial washing samples detected 23 (95%CI 72;99) of the smear-negative pulmonary tuberculosis cases compared with 15 (95%CI 37;74) for sputum cultures ( $p = 0.02$ ). The incremental diagnostic yield of acid fast bacilli smear and culture of bronchial washing specimens over sputum culture was 44% (95%CI 25;65).

**CONCLUSIONS:** In function of the epidemiological context and the resources available, bronchoscopy should be deployed as part of a comprehensive work up that optimizes smear-negative pulmonary tuberculosis diagnosis and minimizes risk and costs.

**DESCRIPTORS:** Bronchoalveolar Lavage. Tuberculosis, diagnosis. Diagnostic Techniques and Procedures. Sensitivity and Specificity.

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## RESUMO

**OBJETIVO:** Avaliar o aumento do rendimento do diagnóstico de tuberculose pulmonar mediante cultura de lavado brônquico em comparação ao rendimento da cultura de escarro.

**MÉTODOS:** Estudo realizado com 61 adultos da cidade de Lima, Peru, a partir de janeiro de 2006 a dezembro de 2007. Foi comparado o rendimento de culturas de escarro com o de esfregaço de bacilos ácido-resistentes e cultura de amostras de lavado brônquico para diagnóstico de tuberculose pulmonar, em casos suspeitos de tuberculose clínica, com esfregaço de escarro de bacilos ácido-resistentes negativo.

**RESULTADOS:** Vinte e sete (IC95% 32;58) dos casos foram diagnosticados com tuberculose pulmonar de baciloscopia negativa. As amostras de lavado brônquio detectaram 23 (95%; IC95% 72;99) dos casos de tuberculose pulmonar de baciloscopia negativa, comparados com 15 (IC95% 37;74) de cultura de escarro ( $p = 0.02$ ). O diagnóstico da tuberculose pulmonar mediante o uso do esfregaço de bacilos ácido-resistentes e da cultura de lavado brônquico tiveram um rendimento adicional de 44% (IC95% 25;65) em relação à cultura de escarro.

**CONCLUSÕES:** Em função do contexto epidemiológico e dos recursos disponíveis, a broncoscopia deve ser adotada como parte de trabalho abrangente que otimize o diagnóstico de tuberculose pulmonar de baciloscopia negativa e minimize riscos e custos.

**DESCRIPTORIOS:** Lavagem Broncoalveolar. Tuberculose, diagnóstico. Técnicas e Procedimentos Diagnósticos. Sensibilidade e Especificidade.

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## INTRODUCTION

According to World Health Organization (WHO), smear negative pulmonary tuberculosis (SNPT) is defined as a case with at least two negative sputum acid fast bacilli (AFB) smears and either a positive culture or radiographic abnormalities consistent with tuberculosis and failure to respond to an antibiotic trial.<sup>5</sup> Microbiological tests on flexible bronchoscopy samples are considered useful for the diagnosis of SNPT, but their indication is not standardized. The procedure is performed on the premise that the bacillary load is higher in samples from bronchial secretions than in sputum. However, bronchoscopy is not without risk for patients and may be associated with nosocomial transmission of tuberculosis.

The reported sensitivity in patients with clinical suspicion of tuberculosis varies from as low as 6.5% to up to 77%.<sup>2</sup> However, evaluations of bronchoscopy are scarce, specifically for the detection of SNPT in prospective studies. Additionally, culture in liquid media is seldom performed. It is more sensitive than culture in conventional solid media of sputum and recommended by the WHO,<sup>4</sup> but whether this is also the case for bronchoscopy samples is less clear.

Further evaluation of the yield of bronchoscopy is needed in order to generate evidence-based recommendations for the use of the procedure in patients with clinical suspicion of SNPT. This study aimed to prospectively assess the incremental diagnostic yield of acid fast bacilli (AFB) smear and culture of a bronchial washing sample over the yield of sputum sample culture in such patients. We also compared the yield of liquid culture compared to conventional solid culture in bronchial washing samples.

## METHODS

Study conducted in adults that attended the *Hospital Nacional Hipólito Unanue*, a tuberculosis reference hospital in Lima, Peru, from January 2006 to December 2007. We included patients with clinical suspicion of pulmonary tuberculosis (cough for 14 days or more) and two or more negative AFB sputum smears and one additional negative concentrated smear, who did not improve after a two week antibiotic trial. Patients with high clinical suspicion of tuberculosis who were put on anti-tuberculous treatment without further investigation by the treating pneumologist were excluded from the analysis.

All patients underwent bronchoscopy with bronchial washing, without bronchoalveolar lavage. The procedures were executed by trained pneumologists. Patients were pre-medicated with 0.5 mg atropine and then sedated with midazolam. Bronchial washing was performed by instilling 20 to 50 ml of 0.9% isotonic saline in the tracheobronchial tree up to the sub-segmental level. The sample was obtained by aspiration into a trap connected to a suction tube.

The sputum sample taken prior to the procedure was concentrated, decontaminated and cultured in solid Ogawa medium using standard methodology<sup>1</sup> and in mycobacteria growth indicator tube, manually read as previously described.<sup>3</sup> Bronchial washing samples were concentrated, directly examined for AFB and cultured in the same way.

We classified patients as SNPT cases when they had a positive bacteriological result in cultures of sputum or in AFB smears or cultures of bronchial washing specimens. We calculated the overall diagnostic yields of the different sputum and bronchial washing examinations. Incremental diagnostic yield was defined as [(number of additional cases diagnosed by the test / all detected cases)\*100]. The McNemar test was used for comparing the proportion of positive results.

Written informed consent was obtained from all participants. Patients were offered HIV counseling and voluntary testing. The study followed the Declaration of Helsinki principles and was approved by the Ethics Committee of the *Hospital Nacional Hipólito Unanue* and of the Institute of Tropical Medicine of Antwerp (Registration number 4525842, July 5 2005).

## RESULTS

Sixty-one patients were recruited. The median age was 33 (interquartile range 26 to 43 years old) and 52% were males; 21% had a previous history of tuberculosis. Fourteen patients refused HIV testing and one out of the 47 patients tested had a positive test. SNPT was diagnosed in 27/61 (95%CI 32;58) suspected cases. There were no complications from the procedure and bronchial washing samples were able to be obtained from all recruited patients.

Bronchial washing AFB smears and cultures detected 23/27 cases of SNPT (95%CI 72;99), a significantly higher proportion ( $p = 0.02$ ) than the 15/27 (95%CI 37;74) cases detected by sputum cultures (Table 1). Nine of the 27 SNPT patients (95%CI 17;54) had a positive solid sputum culture and 13/27 (95%CI 29;68) a positive liquid sputum culture. This difference was not significant ( $p = 0.16$ ). The incremental diagnostic yield of bronchial washing examinations over sputum cultures was 12/27 (95%CI 25;65). AFB smears from bronchial

**Table.** Comparison of the diagnostic yield in sputum smear-negative pulmonary tuberculosis suspects of sputum culture, bronchial washing smear acid fast bacilli staining and bronchial washing culture. Lima, Peru, 2006 to 2007.

Variable	Bronchial washing AFB smear and culture		
	Any positive	Both negative	Total
Sputum culture			
Positive	11	4	15
Negative	10	33	43
Contaminated	2	1	3
Total	23	38	61
Bronchial washing culture			
	Positive	Negative	Total
Bronchial washing AFB			
Positive	10	1	11
Negative	12	38	50
Total	22	39	61

AFB: acid fast bacilli

washings were already positive in 6/15 (95%CI 16;68) cases eventually detected by sputum culture.

Bronchial washing AFB smears were positive in 11 of the 23 (95%CI 27;69) SNPT cases detected through bronchoscopy while cultures of bronchial washing specimens were positive in 22 of these cases (95%CI 78;100) ( $p < 0.001$ ). The incremental diagnostic yield of culture over AFB smears in bronchial washing specimens was 12/23 (95%CI 31;73).

Positivity of bronchial washing culture was higher in liquid media (19/22; 95%CI 65;97) than in solid media (14/22; 95%CI 41;83) ( $p = 0.06$ ). The incremental diagnostic yield of liquid culture from bronchial washing over solid cultures was 8/22 (95%CI 17;59).

## DISCUSSION

The incremental yield of AFB smear and culture of bronchial washing specimens over sputum cultures (44.0%) is substantial in suspected cases of SNPT, and the diagnostic yield (85.0%) is high. The latter finding is consistent with the literature, but yield is highly dependent on the setting. Nevertheless, a few patients with positive sputum cultures have negative bronchial washing examinations. This may be due to the bacteriostatic effect of the local anesthetic, xylocaine<sup>2</sup> or to delays in processing the bronchial washing samples. Bronchoalveolar lavage could possibly result in an even better diagnostic yield but is not frequently performed in resource constrained settings.

A considerable proportion of bronchoscopies could be foregone if the results of sputum cultures became more rapidly available: half of patients with SNPT diagnosed through bronchoscopy eventually had a positive sputum culture. Liquid media cultures give faster results and are more sensitive than culture in standard solid media and should be made more generally available.<sup>4</sup> The diagnostic yield of bronchial washing samples is better than that of sputum samples, but they are complementary and should be included in the work-up in function of the epidemiological context, patient presentation and resources available. Sputum induction, post-bronchoscopic sputum samples and the deployment of molecular techniques could all further

contribute to rationalizing the use of bronchoscopy and to optimizing SNPT diagnosis.

While substantially augmenting diagnostic yield, it remains unclear at which step in the diagnostic workup of suspected cases of SNPT bronchoscopy could best be used and further research is needed to define its precise place and role. It should be deployed as part of a broader, comprehensive approach towards diagnosing SNPT that maximizes yield while minimizing risks and costs. Nevertheless, AFB smears from bronchial washing specimens detect almost half of all SNPT cases and allow for a very rapid diagnosis. This justifies the use of the procedure in critical situations where a treatment decision is urgently needed, particularly if avoiding tuberculosis drug related morbidity is of concern.

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