

RESEARCH LETTER

The yield of different pleural fluid volumes for *Mycobacterium tuberculosis* culture

We prospectively compared the culture yields of two pleural fluid volumes (5 and 100 ml) inoculated in liquid culture medium in 77 patients of whom 58 (75.3%) were diagnosed with pleural tuberculosis. The overall fluid culture yield was high (60.3% of cases with pleural tuberculosis). The larger volume had a faster time to positivity (329 vs 376 h, $p=0.055$) but its yield was not significantly higher (53.5% vs 50%; $p=0.75$). HIV-positive patients were more likely to have positive cultures (78.9% vs 51.5%; $p=0.002$).

Pleural tuberculosis is a common form of extra-pulmonary tuberculosis particularly among HIV-infected individuals.¹ Mycobacterial cultures from pleural fluid have a reported average yield of 24%–58%, which is the highest when liquid culture media are used.^{1–2} Recent evidence suggests that a higher volume of pleural fluid submitted for cytological analysis or for bacterial culture does not increase the rate of detection of malignant cells or bacteria, respectively.^{3–4} We

compared the yields of 100 ml or 5 ml of pleural fluid inoculated in liquid culture medium in 77 patients with a high suspicion of pleural tuberculosis. Pleural tuberculosis was diagnosed in 58 (75.3%) following extensive examination including pleural biopsy, of whom 35 (60.3%) had positive fluid cultures (table 1). Time to culture positivity (TTP) was considerably shorter with the larger volume (329 vs 376 h, $p=0.055$) but the absolute yield was not significantly greater (53.5% vs 50%; $p=0.75$). HIV-positive individuals had culture-positive fluid more often, and spontaneously expectorated sputum had a remarkably high yield. Detailed descriptions of the methods and results can be found in the online supplement.

The fact that larger volume cultures had a lower TTP confirms that a higher number of viable bacteria were recovered from the larger volume. In vitro titration curves confirm that the TTP decrease found corresponds to a 10- to 20-fold increase of colony forming units inoculated.⁵ But why would this not translate into a significant increase in culture positivity? Bacterial concentrations among tuberculosis effusions could be distributed in dichotomous rather than continuous fashion. After initial invasion of the pleural space mycobacteria are either cleared from pleural fluid rapidly, thus leaving cultures negative irrespective of

technique, or the clearing process is insufficient or incomplete leaving behind bacteria in numbers large enough for culture positivity. It is in this group that the shorter TTP can be demonstrated. This theory would also explain the fact that HIV-positive patients, in whom bacterial clearance might be impaired, have higher yields for pleural fluid culture.

In conclusion, we confirmed that liquid mycobacterial culture has a high yield in pleural fluid. The volume of fluid used for inoculation in liquid culture did not seem to influence the proportion of positive cultures. Further studies are required to investigate if more than one pleural fluid sample should be submitted for mycobacterial culture. This study confirmed that HIV infected patients have a higher proportion of positive fluid cultures and that a substantial proportion of patients with pleural tuberculosis can be diagnosed on sputum.

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Table 1 Patients and pleural fluid

Parameter	All	TB	Non-TB	p Value
Number of patients (N)	77	58	19	NA
Age (years) \pm SD	33.4 \pm 12.8	30.8 \pm 11.4	41.1 \pm 14.1	0.002
Male gender (%)	59.7	60.3	57.9	1
HIV-positive, n (%)	23 (29.9)	19 (32.8)	4 (21.1)	<0.001
Effusion size				
Small or moderate, n (%)	39 (50.6)	25 (43.1)	14 (73.7)	0.01
Large, n (%)	38 (49.4)	33 (56.9)	5 (26.3)	0.03
Pleural fluid				
pH \pm SD	7.34 \pm 0.17	7.34 \pm 0.12	7.34 \pm 0.26	0.92
Protein (g/l) \pm SD	60.3 \pm 20.3	64.5 \pm 17.3	47.9 \pm 25.5	0.015
LDH (IU/l) \pm SD	1178 \pm 2466	947 \pm 1425	1859 \pm 4259	0.37
ADA (IU/l) \pm SD	88.1 \pm 45.3	98.5 \pm 37.5	53.8 \pm 52.5	0.004
Lymphocytes (%)	62.5 \pm 28.5	66.8 \pm 25.9	48.6 \pm 32.9	0.056
Lymphocytic effusion* (%)	80.9	84.6	68.16	0.16
Pleural fluid culture yield for MTB				
100 ml volume, n (%)		31 (53.5)		0.75
5 ml volume, n (%)		29 (50)		
Time to culture positivity for MTB				
100 ml volume (h) \pm SD		329 \pm 102		0.055
5 ml volume (h) \pm SD		376 \pm 160		

Continuous data were compared using Student t test as data were normally distributed and equal variance was assumed. Proportions were compared using χ^2 test and Fisher's exact test for non-matched proportions and McNemar's test for matched proportions.

*Lymphocytes/neutrophils >1.

ADA, adenosine deaminase; LDH, lactate dehydrogenase; MTB, *Mycobacterium tuberculosis*; TB, tuberculosis.

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