The value of determining pleural adenosine deaminase activity for the diagnosis of non-tuberculous diseases: a cohort study from a TB-low-prevalence area

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Objectives
Adenosine Deaminase Activity (ADA) is a cost-effective and well evaluated pleural fluid marker for ruling out pleural TB in low prevalence settings. However, ADA is also known to be elevated in exudative effusions due to non-tuberculous diseases like lymphoma and in pleural empyema. The purpose of the study was to evaluate the benefit of determination of ADA for non-tuberculous diseases in a setting with a low TBC incidence.

Methods
In total 65 patients of three styrian hospitals (South-East Austria) with exsudative pleural effusions of unknown origin tested for ADA between March 2011 and February 2013 were retrospectively enrolled in the study. Along with the conventional analysis of the pleural fluid the ADA level was measured on the Cobas 8000 system at the Medical University of Graz, Austria. The cause of the pleural effusion was established by reviewing all results of the conventional analysis, microbiologic results and medical files at the end of the study. Finally, the diagnostic accuracy of ADA was evaluated for TB, pleural empyema and lymphoma.

Results
Four of the included patients had tuberculous pleuritis while 61 had non-tuberculous pleuritis. Only 2 out of 4 TB cases were above the proposed diagnostic cut-off of 40 U/L. Using a cut-off level of 25 U/L the sensitivity, specificity, positive and negative predictive values of ADA for TB pleuritis were 100%, 87%, 33% and 100%, respectively. ADA resulted also positive in 6 patients with pleural empyema, and each one patient with non Hodgkin lymphoma and squamous cell carcinoma of the lung. With a cut-off level of 25 U/L sensitivity, specificity, positive and negative predictive values for either TB, pleural empyema or lymphoma were as follows: 92%, 98%, 92% and 98%, respectively. Receiver-operating-characteristic (ROC) anaylysis revealed an area under the curve of 0.987 (95% CI 0.964-1.00) for differentiating between patients with either TB pleuritis, empyema or lymphoma from those without.

Conclusion
In countries with low TBC prevalence pleural fluid ADA above 25 U/L may be a very sensitive and specific marker for pleural effusions caused by TB, empyema or lymphoid malignancy.