All patients said that the project should be continued and expanded.

The present data[2,4] and this study suggest that singing does produce specific benefits and that participation in singing classes should be encouraged where these are available.

Acknowledgements

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Pleural adenosine deaminase in the diagnostic workup of tuberculous pleural effusion

Adenosina deaminase do liquido pleural na abordagem diagnóstica do derrame pleural tuberculoso

To the Editor,

Adenosine deaminase (ADA) has been promoted as a quick, efficient and cost-effective method in the diagnosis of tuberculous effusions.[1] However, the predictive parameters of ADA, in the diagnostic workup of tuberculous effusions, depend on the prevalence of the disease in the population[2] and no such analysis has been published in Portugal, a country of intermediate tuberculosis (TB) incidence (25.9 per 100,000 in 2010).[3]

In response to this situation, we carried out a cross-sectional analysis over a 4-year period, beginning in January 2006, in which we evaluated pleural fluid results from all patients admitted to our department with a pleural effusion of unknown etiology. Only the results obtained from the first thoracocentesis were included and samples from empyema were excluded from our analysis. Pleural ADA was measured using Giusti's colorimetric method. Mann–Whitney test was performed to compare medians and a Receiver Operating Curve (ROC) was used to determine the predictive parameters of different cutoffs. Prism 6 from Graphpad Software was used for the statistical analysis.

A total of 107 pleural samples were analyzed, including TB ($n = 20$), malignant ($n = 54$), parapneumonic ($n = 20$) and idiopathic ($n = 13$) effusions. Of the 107 patients, 57.9% were males, median age was 72.5 (interquartile range: 59.7; 80.2) and all the patients were of European ethnicity. TB pleural effusions were found to have the highest median ADA value (98.55 U/L), which were significantly higher than malignant effusions (17.99 U/L) ($p < 0.0001$) – the group with second highest median ADA value. Using the ROC curve we found that an ADA cutoff of 40.5 U/L had the best performance in the diagnosis of pleural TB (see Table 1), with a sensitivity of 95%, specificity of 91.55%, positive predictive value (PPV) of 73.08% and negative predictive value (NPV) of 98.77%. Seven nontuberculous exudates (8.0%) reached the diagnostic cutoff. Using a >50% lymphocyte count criteria in the diagnostic workup, only 4.5% nontuberculous exudates were misclassified – 2 malignant (plasmocytoma and lymphoma) and 2 parapneumonic. The association of these two criteria increased specificity (95.40%) and PPV (82.61%). Using an ADA cutoff level of 74.6 U/L and the >50% lymphocyte criteria further increased specificity (98.85%) and PPV (93.75%), and only one (1.1%) nontuberculous exudate was misclassified.

The diagnosis of tuberculous pleural effusion is a common diagnostic challenge due to low mycobacterial detection rates and to the frequent need for invasive, sometimes technically difficult, operator dependent techniques like the pleural biopsy or thoracoscopy.[4] In this context, a rational interpretation of pleural fluid characteristics, particularly ADA level and differential leukocyte count, is essential to the diagnostic workup. In our research, an ADA level < 40 U/L can virtually exclude pleural TB with a NPV of 98.7%, while an ADA level > 74.6 U/L with >50%lymphocyte has a very high PPV of 93.75 and can thus be used to safely confirm pleural TB with a very small error rate of 1.1%. The

	40 U/L	40 U/L + >50%lymph.	74.6 U/L + >50%lymph.
Sensitivity (%, 95%CI)	95.24 (76.11–99.21)	95.00 (75.05–99.17)	75.00 (50.89–91.25)
Specificity (%, 95%CI)	91.95 (84.12–96.69)	95.40 (88.63–98.71)	98.85 (93.74–99.81)
PPV (%, 95% CI)	74.07 (53.71–88.84)	82.61 (61.20–94.94)	93.75 (69.69–98.86)
NPV (%, 95%CI)	98.77 (93.29–99.79)	98.81 (93.52–99.80)	94.51 (87.63–98.17)

PPV: positive predictive value; NPV: negative predictive value; lymph.: lymphocytes.

performance of the cutoff value of 40 U/L and the error rate of 4.5% (for ADA > 40 U/L and >50% lymphocytes) and 1.1% (for ADA < 74.6 U/L and >50% lymphocytes) is in line with other publications.[2,5,6] In our analysis, one patient with pleural TB had an ADA level < 40 U/L; however, in a sample collected just 3 days later, ADA level was now 90 U/L which reaffirms the diagnostic utility of ADA. Also, as we have shown, hematological malignancies are frequent causes of error, and they should be excluded by this analysis of the pleural lymphocyte populations.[2,6] However, the usefulness of ADA in the diagnosis of tuberculous effusions depends on the prevalence of the disease in the population.[2] If tuberculosis is highly prevalent, as in the African continent and Southeast Asia, then a high value of pleural ADA is more likely to be due to tuberculosis, thus increasing the PPV of pleural ADA in the diagnosis of pleural TB. If, however, the disease is less prevalent, the probability of a high ADA being due to other causes, such as cancer, increases, and PPV of pleural ADA is lower. This is most evident in countries with a low prevalence of tuberculosis and an aging population, as it is in old age that malignant effusions are more prevalent.

In conclusion, pleural ADA is a valuable tool in the diagnostic workup of pleural TB in Portugal and should routinely be used in the exclusion or confirmation of TB in the differential diagnosis of patients with a pleural effusion of unknown cause. Furthermore, in order to make a correct interpretation of its values, we have highlighted: potential false-positives; the usefulness of different ADA cutoffs for the exclusion or confirmation of TB; and the impact of TB prevalence on the predictive parameters of this tool.

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EBUS in pulmonary sarcoidosis: What to expect?

EBUS (ecografia endobrônquica) na sarcoidose pulmonar: o que esperar?

Dear Editor,

The utility of EBUS-TBNA in the diagnosis of sarcoidosis has recently been reported.[1,2] Studies published have shown a higher diagnostic yield in favour of EBUS-TBNA, compared to standard bronchoscopic diagnostic techniques, particularly for stage I sarcoidosis.[3–6] The main advantages identified, beside the high diagnostic yield, are the low complication rate and being able to avoid invasive procedures, like mediastinoscopy.

Several recent editorials reviewed the value of EBUS-TBNA in excluding other diagnoses in patients with suspected sarcoidosis. In a recent editorial published in the *Journal of Bronchology and Intervention Pulmonology*, Reich and colleagues estimated that 10,000 patients with stage I sarcoidosis would have to be submitted to an invasive diagnostic procedure to identify, at most, 5 people with an alternative pathology, and questioned the need for tissue confirmation in asymptomatic stage I sarcoidosis.[7]

Among the series published with patients in suspected stage I and II sarcoidosis that have undergone EBUS-TBNA, only 10% obtained an alternative diagnosis.[8] However, these alternative diagnoses should not be ignored. A delay in this context can be harmful to the patient.

What data exists that is available in relation to these questions?