smoke or nitrogen dioxide exposure, in an analysis analogous to that presented in our article, no such synergy is apparent. Again, given the limited sample size and specific context of our analysis, no definitive conclusion can be drawn from these results, but it is possible that dog/endotoxin may synergise more powerfully with indoor air pollutants, relative to other exposures. If so, it may be important to understand the biology that underlies this effect.

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Interferon- γ release assays for diagnosis of active pleural tuberculosis: a developing world perspective

To the Editors:

We read with interest the article by SESTER *et al.* [1]. The results are clinically helpful, but there are some points that need to be highlighted from the perspective of the physician practising in tuberculosis (TB)-endemic areas in the developing world, where TB remains by far the commonest cause of an exudative pleural effusion [2].

Determining the aetiology of pleural effusions is a challenging problem in these clinical settings. Conventional diagnostic tests for pleural TB include microscopic examination of fluid, mycobacterial culture and histopathological examination of pleural tissue for granulomatous inflammation. However, these tests have several limitations.

The interferon- γ release assays (IGRAs) are technically more complicated and expensive than established biomarkers and their diagnostic performance for active TB is highly variable between studies. A study comparing the cost-effectiveness of performing interferon (IFN)- γ estimation in comparison to adenosine deaminase (ADA) for pleural effusion found that even though it was more sensitive, the cost of using IFN- γ for detecting one additional patient was equivalent to the cost of complete TB treatment for six patients [3, 4]. In developing countries where the burden of TB is high and cost is a major issue, pleural fluid IFN- γ does not seem to be an attractive means of differentiating TB from non-TB aetiology. In fact, the World Health Organization Strategic and Technical Advisory Group for Tuberculosis (WHO STAG-TB) has not yet endorsed the use of IGRAs in resource-limited countries [5].

In contrast, pleural fluid ADA measurement has good sensitivity and specificity. It is inexpensive, simple and easy to perform and does not require any special equipment. These qualities make it an ideal inflammatory marker in resource-limited settings where there is a high burden of TB incidence. A high diagnostic accuracy of ADA measurement has been reported in several studies. A meta-analysis by GRECO *et al.* [6] found that among 31 studies, which included ~4,700 patients, the pooled sensitivity was 92% and specificity was 89%.

In conclusion, IGRAs, although potentially useful tools for diagnosing extrapulmonary TB, are still not suitable for high-TB burden, low-resource countries. A possible practical solution would be to use ADA measurement as the test of choice at the community level and IFN- γ in tertiary referral institutions.

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