were somewhat greater among children who owned both a cat and a dog. Since no evaluation of indoor levels of cat/dog allergens was carried out in that study, the stronger association observed between dog ownership and worsening of respiratory symptoms has been attributed to higher levels of indoor endotoxins associated with dog, in comparison to cat, ownership. This contrasts with the fact that the role of endotoxins in respiratory allergy is still controversial. Recent studies have confirmed that microbial communities, such as *Proteobacteria* spp., *Actinobacteria* spp., *etc.*, may also be higher in homes containing dogs in comparison with homes with cats where fungal exposure is prevalent [3]. The authors speculate that the increased bacterial amount and diversity could be associated with a protective effect.

CARLSTEN *et al*. [1] studied the effects of combined exposure to Can f 1 and indoor pollution, and found an increasing risk of incident asthma. We think that in ''real life'', it is not realistic to separate the role of dog allergens from that of other allergens commonly found indoors, such as house dust mite and cat allergens; some studies have shown that indoor air pollution, particularly NO_2, enhances the risk of asthma exacerbations in asthmatic children sensitised to dust mite allergens.

Although no defined data exist on the relationship between the main cat allergen (Fel d 1) and indoor air pollution, Fel d 1 is widely distributed in all private and public indoor environments with or without the presence of cats. Indeed, Fel d 1 contamination of some public places, such as day care centres and schools, constitutes an important source of allergen exposure for children in addition to domestic exposure. The amount of cat allergen found in domestic/public environments without cats may be of sufficient magnitude to induce allergic sensitisation in susceptible children and to trigger exacerbation of respiratory symptoms in already sensitised individuals. It has been shown that clothing of cat owners constitutes the main mode of transfer of Fel d 1 to cat-free environments [4]. As a consequence, a higher number of cat owners in a given community is associated with higher levels of Fel d 1 in cat-free homes. The same mechanisms could explain the presence of dog and sometimes also of other animal allergens in animal-free environments.

The importance of both cat and dog allergens as risk factor for induction of allergic sensitisation and bronchial asthma is not limited to shared indoor environments. *In vitro* studies have shown a degree of cross-reactivity between cat/dog allergens; in addition, lipocalins and serum albumins have been indicated as animal ''pan-allergens''. These latter factors could explain the common clinical finding that allergic sensitisation to cat/dog co-exist in the same individual.

We have recently suggested the possibility that allergic sensitisation to common pets (cat/dog) and other furry animals could be considered as a definite ''allergic phenotype''. In our study, >75% of all cat/dog-sensitised subjects exhibited a skin prick test positivity to both cat and dog allergens. Moreover, individuals sensitised to these common pets showed an ~14-fold increase in the risk of developing sensitisation to other mammals, such as horses, cows, rabbits, rats, mouse, guinea pigs and hamsters [5].

In conclusion, we think that the relationship between dog ownership and air pollution in enhancing symptomatic responses in children with asthma may be somewhat attributable to the greater amounts of endotoxins associated with the presence of a dog at home. In addition, it is unrealistic to hypothesise that at home exposure to Can f 1 could be completely independent of simultaneous exposure to other common indoor allergens, particularly those of mite and cat. Considering the relevant implications of pet–human relationships, especially in children, we think it is important to avoid unjustified incrimination of dogs and dog ownership for children nonspecifically sensitised to dog allergen and not symptomatic after dog contact.

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From the authors:

We thank G. Liccardi and co-workers for their interest in our work. In our article [1], we recognised the potentially important role of endotoxin. Furthermore, we agree that allergenic exposures other than dog may be important, and we agree that dog exposure is likely not to be completely independent from simultaneous exposure to other common indoor allergens; nothing in our paper suggests otherwise. However, given the concerns of G. Liccardi and co-workers, we note that when we have examined the potential for cat or house dust mite to synergise with environmental tobacco

smoke or nitrogen dioxide exposure, in an analysis analagous 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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