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From the authors:

We thank R.P. Young and co-workers for their comments on our recent article [1]. As we highlighted in our article, there are two recent reports indicating that single-nucleotide polymorphisms in the advanced glycosylation end product-specific receptor (AGER) gene, which encodes the receptor for advanced glycation end-products (RAGE), are associated with changes in measurements of airflow obstruction [2, 3]. The findings reported by R.P. Young and co-workers in their correspondence add to these earlier studies and shed light on the genetic basis by which cigarette smoke exposure leads to chronic obstructive pulmonary disease (COPD) in some individuals, while “resistant smokers” maintain normal lung function.

Our finding that circulating levels of soluble RAGE (sRAGE) are lower in COPD subjects than healthy controls has since been reproduced in a study reported recently by Miniati et al. [4]. Within an individual, circulating levels of sRAGE may be determined by polymorphisms in the AGER gene, but are also susceptible to environmental factors, especially as plasma sRAGE levels are very low during acute exacerbations of COPD and rise during convalescence [1]. There is now a need for longitudinal studies to define the relationship between polymorphisms in the AGER gene and circulating levels of sRAGE in patients with COPD, and to assess the extent to which this predicts rate of decline in lung function over time.

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Can dog allergen alone, if combined with indoor pollution, be responsible for asthma in children?

To the Editors:

We read with interest the article by Carlsten et al. [1] showing the increasing risk of incident asthma in a high-risk birth cohort after early co-exposure to dog allergen (Can f 1) and nitrogen dioxide (NO₂) or environmental tobacco smoke. The topic is highly relevant because most studies on the interaction between allergens and air pollution regard outdoor environments and very few articles have been published on the possible allergen–pollutant relationship in indoor places.

Nevertheless, we think that other limitations to the study should be considered in addition to those already acknowledged by the authors. In their study, they referred to the article of McConnell et al. [2] that showed a significant association between “bronchitis symptoms” and particulate matter only in the subset of asthmatic children who owned dogs. However, McConnell et al. [2] examined the relationship of both dog and cat ownership with air pollution, and reported that effects
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 NO₃, 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-allergic exposed individuals. 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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**REFERENCES**


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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