

Glaucoma and allergies: 'should I get rid of my cat?'

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This question was posed by an elderly patient with severe glaucoma who recently adopted an adorable kitten. To my cat-loving patient's dismay, the headline of an article in *The Telegraph* admonished: 'why owning a cat could lead to blindness'; while another online commentary advised: 'keep your dog, get rid of your cat'. In view of her advanced glaucoma, should her kitty make way for a little pooch?

This uproar can be traced to a recent study by Tseng *et al*.¹ In a retrospective cross-sectional study of 1652 participants in the National Health and Nutrition Examination Survey (NHANES), the authors analysed the association between IgE levels for a panel of common indoor allergens and glaucoma. Weighted estimates were calculated based on the multi-stage NHANES sampling design for a weighted total of 83 308 318 participants. It was concluded that sensitisation to the cat and cockroach antigens were associated with increased odds of glaucoma, while the dog antigen was associated with decreased odds of glaucoma.

The theory that the cat and cockroach antigens may trigger autoantibodies targeting the optic nerve may be a plausible one. Immune-mediated mechanisms for the development of glaucomatous optic neuropathy have been previously proposed, and the immune system has been implicated in both neuroprotection and neurodegeneration.² IgG deposition and plasma cells have been detected in human glaucomatous retina.³ Upregulation (eg, anti-HSP60, anti-nuclear antibody) and downregulation (eg, anti-14-3-3) of certain autoantibodies have been associated with glaucoma,⁴⁻⁶ though it remains unclear whether these autoantibodies are causative or an epiphenomenon. Autoimmune damage of the optic nerve

may be particularly relevant to patients who have glaucoma with normal intraocular pressure, and may occur when optic nerve antigens are similar to a sensitising antigen.⁷ Serum interleukin (IL)-4 and IL-6 cytokines, produced by the T helper cell 2, are found to be raised in patients with glaucoma, and these cytokines also activate B cells to produce IgE.⁸ These proposed mechanisms provide a potential, although tenuous, immunological link between IgE and glaucoma.

The study by Tseng *et al*¹ is the first to propose an association between glaucoma and IgE subtypes for common indoor allergens. Arguably, this study raised more questions than it answered, and the authors were much more cautious in recognising the limitations of the study compared with the media who have sensationalised the findings. Even if the inherent deficiencies of a retrospective study are overlooked, ultimately NHANES was not designed to investigate glaucoma risk factors. Hence, the logistic regression models used to examine the association between allergen-specific IgE and glaucoma were only adjusted for age, ethnicity and steroid use. The authors have acknowledged that information on established glaucoma risk factors, such as intraocular pressure and a family history of glaucoma,⁹⁻¹⁰ were not available, and therefore, could be possible confounders in the analyses. The diagnosis of glaucoma was made merely based on the cup:disc ratio determined on non-stereoscopic retinal images and frequency-doubling threshold perimetry, and could not be validated by additional data or by clinical examination. Information on glaucoma subtypes was also not available within NHANES. Moreover, the ORs for the association between glaucoma and the IgE subtypes for the cat and dog antigens were remarkably wide (1.10–10.67 and 0.06–0.96, respectively), suggesting a low precision for these study estimates.

Even if the results presented by Tseng *et al* were entirely valid, they proposed that cat allergy (indicated by the IgE subtypes for cat antigens), and not cat ownership, was associated with glaucoma in their study population. Airborne cat allergens are ubiquitous in the environment, and are found in homes with and without

cats.¹¹⁻¹² Many individuals become sensitised to cats without having lived around cats, suggesting that environmental levels of cat allergens may be high enough to sensitise individuals who do not own cats. Hence, removal of cats from homes often does not result in the anticipated symptomatic improvement in individuals with allergies.¹³ In fact, cat ownership may be associated with a lower rate of sensitisation, as exposure to high levels of cat allergen induces IgG4 antibodies to the cat antigen without an IgE response, resulting in 'tolerance'.¹⁴ Furthermore, the risk of sensitisation is highest in young children, while most patients with glaucoma are in their adulthood, and are less likely to develop new allergies.¹⁵

To conclude, we unreservedly commend Tseng *et al* for their thought-provoking and hypothesis-generating study. However, cat lovers should be reassured that having feline companions do not necessarily spell glaucoma in their future. On the other hand, I think most would agree that the extermination of cockroaches does not require further justification.

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