

Authors' response



We appreciate the comments¹ about our article on dog allergen immunotherapy published in the *Annals*.² The scientific data supporting the clinical efficacy of dog allergen immunotherapy are lacking. However, anecdotal reports suggest many dog allergic patients seem to derive substantial benefit from immunotherapy. At least 2 theories may explain this observation: lack of standardized potency and dog allergen diversity.

Published data regarding the effectiveness of dog allergen immunotherapy began in 1967 with an unmasked, uncontrolled case series of dog allergic patients who benefited from a specifically prepared dog extract.³ Although the clinical trials methodologically improved (yet often remained underpowered) during the next 40 years, they continued to use unstandardized and highly variable dog extracts, resulting in conflicting efficacy results. Even the landmark study in dog allergy lamented the quality of their extract as a potential explanation for suboptimal results.³

No studies have directly compared the clinical outcomes after immunotherapy with different dog extracts, so the most effective dog extract remains conjecture. However, a 2001 study compared skin prick results with aqueous epithelial dog extract and acetone precipitated (AP) dog extract. AP dog extract was superior at eliciting skin prick test positivity in dog allergic patients, hypothesized to be secondary to the higher potency of AP dog extract (80–400 µg/mL of Can f 1).^{4,5}

The current immunotherapy practice parameter recommended a target dose of 15 µg of Can f 1^{4–6} originated from a 2006 trial designed to determine the most effective dose of Can f 1 for dog immunotherapy by administering AP dog extract at differing doses (0.6, 3, and 15 µg) of the allergen. Although nasal challenge symptom scores remained unchanged at all doses, researchers noted similar immunologic outcome changes at the 15-µg dose to the patients with significant symptomatic improvement in the antecedent cat study.⁷ This similarity suggested that this dose of Can f 1 is also “likely effective” for dog immunotherapy, but the data were again underwhelming. Of note, this quantity can only currently be achieved in a 0.5-mL dose with AP dog extract.

Can f 1 is not as predominant of an allergen as the major cat allergen Fel d 1 (70% vs 95% sensitization rates),^{8,9} suggesting that multiple allergens are likely important to dog allergic patients, whereas most cat allergy can be explained by a single allergen. Can f 5 was identified in 2009 as one such dog allergen to which 70% of

symptomatic patients were sensitized. Interestingly, 38% of patients were monosensitized to Can f 5.¹⁰ This information argues that standardizing dog extracts on Can f 1 alone may not be sufficient to produce an extract that would be effective for all dog allergic patients.

Additional dosing trials with standardized dog extracts, possibly supplemented with standardized quantities of the newly characterized dog allergens, are needed produce conclusive data revealing the efficacy of modern dog allergen immunotherapy.

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References

- [1] Liccardi G, Salzillo A, Calzetta L, et al. Dog allergen immunotherapy and allergy to furry animals. *Ann Allergy Asthma Immunol*. 2016;116:590.
- [2] Smith DM, Coop CA. Dog allergen immunotherapy: past, present, and future. *Ann Allergy Asthma Immunol*. 2016;116:188–193.
- [3] Tuft L, Torsney P. Experience in the hyposensitization treatment of animal dander allergic patients with alum-precipitated pyridine extracts. *Am J Med Sci*. 1967;253:19–22.
- [4] Meiser J, Nelson H. Comparing conventional and acetone-precipitated dog allergen extract skin testing. *J Allergy Clin Immunol*. 2001;107:744–745.
- [5] Cox L, Nelson H, Lockey R, et al. Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol*. 2011;127(1 suppl):1–55.
- [6] Hedlin G, Graff-Lonnevig V, Heilborn H, et al. Immunotherapy with cat- and dog-dander extracts, V: effects of 3 years of treatment. *J Allergy Clin Immunol*. 1991;87:955–964.
- [7] Lent AM, Harbeck R, Strand M, et al. Immunologic response to administration of standardized dog allergen extract at differing doses. *J Allergy Clin Immunol*. 2006;118:1249–1256.
- [8] Schou C, Svendsen U, Lowenstein H. Purification and characterization of the major dog allergen, Can f 1. *Clin Exp Allergy*. 1991;21:321–328.
- [9] van Ree R, van Leeuwen WA, Bulder I, Bond J, Aalberse RC. Purified natural and recombinant Fel d 1 and cat albumin in vitro diagnostics for cat allergy. *J Allergy Clin Immunol*. 1999;104:1223–1230.
- [10] Mattsson L, Lundgren T, Everberg H, Larsson H, Lidholm J. Prostatic kallikrein: a new major dog allergen. *J Allergy Clin Immunol*. 2009;123:362–368.

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