

Experimental model for peanut allergy by epicutaneous sensitization in atopic beagle dogs

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Background

Atopic dermatitis (AD) and food allergies are increasingly common in westernized countries. Peanut allergy affects more than 3 million Americans. Yet, treatments are still limited and testing is potentially very risky. Safe testing is needed before implementation in the clinics.

Animals have been used as models for food allergy but the routes used for sensitization were not biologically relevant (e.g. injections [1,2], gavage using tubes that bypass the oral cavity to place foods directly into the stomach) and the allergen is frequently presented in conjunction with powerful adjuvants [3]. Epicutaneous sensitization to food can occur and can be clinically relevant in humans [4]. Recently, mice have been epicutaneously sensitized to peanuts [5]. Unfortunately mice models do not always predict behavior in humans and typically only reproduce some aspects of the human condition [6]. Dogs are a good model as food allergies frequently coexist with AD [7]. Dogs naturally develop AD which is strikingly similar to human AD [8] and are genetically closer to people than mice are. An experimental model of AD in atopic beagles has been described [s1]. In this model epicutaneous sensitization to environmental allergens is easily accomplished without any prior tape stripping due to the fact that these dogs have skin barrier defects [8].

Questions addressed

This pilot study aimed to investigate whether atopic dogs could be epicutaneously sensitized to peanuts and whether flare-ups of dermatitis could be elicited after epicutaneous and oral challenges.

Experimental design

Detailed methods are described in Data S1 Briefly, normal and atopic dogs without prior known exposure to peanuts received epicutaneous application of peanut paste for 8 weeks and were then orally and epicutaneously challenged with peanuts. Severity of dermatitis was scored and compared between groups at various time points. Presence of systemic signs was noted. Circulating allergen-specific IgE and number of IgE+ cells in skin biopsies was compared between groups after 8-week peanut exposure.

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Results

After 8-week peanut exposure pruritic erythematous macules and papules developed in the area of paste application in all atopic dogs and in two of the control dogs. After oral challenge, pruritic dermatitis developed in all atopic dogs (Figure 1) starting at 15 minutes and peaking one hour after ingestion. Temporary mild erythema was seen in one of the control dogs who was very excitable and easily stressed but no pruritus was observed. Mild diarrhea developed in one atopic dog. No other systemic signs were observed. Total clinical scores were significantly different between groups (Figure S1). ANOVA showed significant effects of group ($p=0.0139$), time ($p<0.0001$) and group x time interaction (0.0067).

After epicutaneous challenge macules and papules developed at the site of patch in all atopic dogs (Figure S2) and in one control dog. In three of the atopic dogs, erythematous macules were also noted around the muzzle and the eyes.. No distant signs were noted in the controls.

After 8-week exposure IgE were detected in the serum of all atopic dogs and two control dogs. Mild positive results were also detected in both groups at baseline (Figure S3). H&E of skin samples taken after oral challenge showed marked superficial perivascular eosinophilic dermatitis with eosinophilic pustules in atopics (Figure S4). No changes were seen in the controls except for one dog that had mild eosinophilic dermatitis. The number of IgE+ cells was significantly higher in the skin biopsies from atopic dogs compared to the controls ($p=0.033$, Figure 2).

Discussion and conclusions

Flare up of dermatitis could be induced in this model after oral challenge with peanuts. No anaphylaxis developed in this model. This is different from previous reports of nut allergy in dogs which described severe vomiting, diarrhea and anaphylaxis within 10 minutes of challenge [1]. A possible reason for this difference may be in the different route used for sensitization. In our model we used epicutaneous route while in Teuber study the subcutaneous route was used. This model thus would best fit to mimic a food aggravated AD type of disease rather than gastro-intestinal or anaphylaxis manifestations of food allergy.

After 8 week exposure, an IgE response was detectable in all atopic and some control dogs. The IgE response in the controls did not have clinical relevance as it was not accompanied by dermatitis or pruritus upon challenge. The positive results present in some dogs at baseline may be due to a cross reactivity with soybean [s14] as all these dogs had been exposed to soybean since this is a common ingredient in dog food. The local reaction noted in some of the normal dogs was not due to irritation but was indeed a mild allergic reaction as the H&E showed mild eosinophilic dermatitis. Thus a mild allergic response can be obtained also in non-atopic individuals. The atopic status just amplifies the magnitude of the immune response. This is probably due to the fact that allergens applied to damaged skin are more likely to elicit a T helper 2 response [s8, s9, s10].

In this study, the serology aimed to detect IgE to peanuts and not to the specific peanut allergens. In preliminary western blot studies (data not shown here) the serum of the atopic dogs contained IgE against Ara h2. Additional work with larger number of dogs is needed to further characterize the immunologic response of dogs to peanut allergens. This pilot study was intended as a proof-of-concept and used a very small number of animals. Future studies will involve epicutaneous exposure to purified allergens relevant to humans so that these dogs can be used to test strategies aimed at specific allergens relevant to humans.

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Conflict of interest

The author has no conflict of interest to declare.

Figure 1

Clinical picture of the ventral abdomen of an atopic dog 2 hours after the beginning of oral challenge. Erythema, macules and papules were noticeable. The animal was pruritic and had developed erythema also on the muzzle and feet.

Figure 2

Mean and standard deviation of the total number of IgE positive cells detected by immunofluorescence in biopsies taken from atopic and normal beagles at the end of 8 weeks of epicutaneous exposure to peanut paste. T test showed a significant difference between normal and atopic dogs with atopic samples having a higher number of IgE+ cells ($p=0.033$).

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