Predicting probability of tolerating discrete amounts of peanut protein in allergic children using epitope-specific IgE antibody profiling

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ARTICLE SUMMARY

- Existing diagnostic testing is not predictive of severity or the threshold dose of clinical reactivity, and many patients still require an Oral Food Challenge (OFC). While OFCs are very useful for making an allergy diagnosis and determining clinical reactivity, they often cause anaphylaxis, which can increase patient anxiety. and are time and resource intensive.[1]
- An extensive validation was performed across 5 cohorts (all with confirmed oral food challenge results) across six different countries. Cohorts used: BOPI, OPIA, CAFETERIA, CoFAR6, and PEPITES with specimens from Australia, UK, US, Ireland, and Germany.
- This paper reports the first validated algorithm using two key peanut specific IgE epitopes to predict probabilities of reaction to different amounts of peanut in allergic subjects and may provide a useful clinical substitute for peanut oral food challenges.
- Using the algorithm, subjects were assigned into "high", "moderate", or "low" dose reactivity groups. On average, subjects in the "high" group were 4 times more likely to tolerate a specific dose, compared to the "low" group.[1] For example, 88% of patients in the high dose reactivity group were able to tolerate ≥ 144 mg of peanut protein whereas only 29% were able to tolerate the same amount in the low dose reactivity group.[1-2]

CLINICAL CONSIDERATIONS

- The new epitope test offers more granular information to help clinicians stratify treatment and peanut avoidance plans for their patients.
- See below for summary of clinical considerations based on threshold reactivity level.[1]

allergenis peanut diagnostic result	clinical considerations[1]
likely allergic – low dose reactor	• inform or avoid oral food challenge to reduce risk of anaphlyaxis • confirm strict avoidance of peanut • consider immunotherapy to reduce risk of reaction
likely allergic – moderate dose reactor	• consider a single oral food challenge (30 to 100 mg) to reduce anxiety and improve quality of life • less stringent avoidance of peanut regime • consider inclusions of precautionary labeled foods such as 'May contain peanut' • consider immunotherapy to reduce risk of reaction
likely allergic – high dose reactor	• consider a single oral food challenge (100 to 300 mg) to reduce anxiety and improve quality of life • less stringent avoidance of peanut regime • consider inclusions of precautionary labeled foods such as 'May contain peanut' • consider starting immunotherapy at higher doses to shorten time to maintenance dose
unlikely allergic	• oral food challenge to rule out the diagnosis of peanut allergy

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Title: Indoor visible moulds and rhinitis in adults: the EGEA study

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To the Editor,

Although rhinitis is among the most common diseases worldwide,(1) few studies have investigated among adults the association between past and current exposure to indoor mould, a modifiable environmental factor, and current rhinitis.(2,3) Furthermore, even if rhinitis and asthma often coexist, the potential modifying impact of asthma on this association has never been studied.

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We investigated the cross-sectional association between mould exposure and rhinitis among 410 adults with asthma and 556 without asthma from the first follow-up of the case-control and familial study on the Genetics and Environment of Asthma (EGEA2) (https://egeanet.vjf.inserm.fr/index.php/en/; see Methods and Figure S1, Online supplement 1 for details). Current rhinitis was defined as a confirmatory response to: "*Have you had problems with sneezing, runny nose or stuffy nose when you did not have a cold or flu in the last 12 months?*". As we focused on current rhinitis, we considered all participants who had had rhinitis symptoms in the past 12 months regardless of the duration of the symptoms, and participants who reported non-current rhinitis were excluded from the analyses. Participants with current rhinitis and with at least one positive skin prick test (SPT) were classified as allergic rhinitis (AR), otherwise as non-allergic rhinitis (NAR). Ever exposure to visible mould was defined based on confirmatory response to "*Has there ever been mould on any surface inside the house (excluding food)?*" Among participants with ever exposure, those who responded positively to "*Did this happen in the last 12 months?*" were classified as having current exposure, otherwise as past exposure. We performed logistic regression analyses accounting for familial dependence by Generalized Estimating Equation (GEE) and adjusted for age, sex, smoking status, education and furry pet's ownership 1) according to ever-asthma status (410 with asthma and 556 without asthma), and 2) in all participants (pooled sample) by adjusting for asthma. We tested potential additive and multiplicative mould-asthma interactions, as interaction may be present on one scale but absent on the other(4) (see Online supplement 1).

Among the 966 participants (mean 42 years, 52.7% women, 24.2% smokers, 42.4% ever-asthmatics, Table 1), 61.6% reported current rhinitis (41.4% AR, 20.2% NAR), and 27% reported mould exposure (9% past, 18% current). In analyses according to asthma status (Figure 1A and 1B), positive associations between ever and current mould exposures with current rhinitis and AR were observed, with stronger evidence among never- than in ever-asthmatics

(all p for interaction>0.23, Online supplement 2, Table S1). In all participants, similar patterns were observed: ever and current exposures to moulds were significantly associated to current rhinitis (adjusted(a)odd-ratio(OR)[95% confidence interval]=1.51[1.10-2.08] for ever and 1.75[1.18-2.60] for current exposures, respectively, Figure 1C and Online supplement 2, Table S1), the associations being statistically significant only for AR (aOR=1.80[1.25-2.60] and 2.01[1.30-3.10], respectively).

Sensitivity analyses using alternative definitions of AR and NAR, or further adjustment for centre showed consistent findings both in all participants (Online supplement 2, Table S2) and according to asthma status (data not shown).

Assessing mould exposure is complex, and applying a self-reported qualitative definition of mould exposure may lead to some misclassification, however it is probably non-differential which would lead to lower statistical power. We acknowledge that an anamnesis and tests carried out by a specialized health professional would be the best possible diagnosis. Using alternative definitions of rhinitis showed the robustness of our results, even if we cannot exclude some misclassification bias. The limited number of participants in some strata may have resulted in insufficient statistical power. Despite these limitations, we observed significant associations between ever and current mould exposures with current rhinitis and AR, that were stronger among never asthmatics. In this study, participants had extensive asthma characterisation,(5) and rhinitis definitions were based on standardised questions(6) and on performance of gold standard SPT. Furthermore, the participants were unaware of the specific hypotheses under study, which diminishes potential for differential misclassification of mould exposure. The stronger mould-rhinitis association observed in participants without asthma as compared to those with ever-asthma, could be related to the avoidance of mould exposure among ever-asthmatics, or to the hypothesis that rhinitis and rhinitis asthma multimorbidity represent distinct diseases with different risk factors.

In conclusion, this study provides evidence that ever and current exposure to indoor visible moulds is related to an increased risk of current rhinitis and of allergic rhinitis among adults. These results emphasize the need for preventive measures against indoor mould growth.

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Table 1. Characteristics of the study population: total population and according to exposure to visible moulds

Characteristics	All	Exposure to visible moulds					
		Never	Ever		Past	Current	
	(n=966)	(n=710, 73.5%)	(n=256, 26.5%)	p^a	(n=87, 9.0%)	(n=169, 17.5%)	p^b
Age, years, mean ± SD	42.7 ± 16.4	43.5 ± 16.8	40.5 ± 14.9	*0.04*	43.1 ± 15.3	39.2 ± 14.5	*0.11*
Sex, women, n (%)	509 (52.7)	376 (53.0)	133 (52.0)	*0.85*	47 (54.0)	86 (50.9)	*0.79*
Smoking status, n (%)				*0.27*			*0.08*
Non-smokers	485 (50.2)	366 (51.6)	119 (46.5)		47 (54.0)	72 (42.6)	
Ex-smokers	247 (25.6)	180 (25.3)	67 (26.2)		17 (19.5)	50 (29.6)	
Current smokers	234 (24.2)	164 (23.1)	70 (27.3)		23 (26.4)	47 (27.8)	
Educational level, n (%)				*0.02*			*0.38*
Low	221 (22.9)	178 (25.1)	43 (16.8)		17 (19.5)	26 (15.4)	
Medium	264 (27.3)	192 (27.0)	72 (28.1)		25 (28.7)	47 (27.8)	
High	481 (49.8)	340 (47.9)	141 (55.1)		45 (51.7)	96 (56.8)	
Fury pet's ownership, yes, n (%)	401 (41.5)	276 (38.9)	125 (48.8)	*0.33*	46 (52.9)	79 (46.8)	*0.19*
Ever-asthma, n (%)	410 (42.4)	299 (42.1)	111 (43.4)	*0.51*	37 (42.5)	74 (43.8)	*0.61*
SPT (all), at least 1 test > 3 mm, n (%)				*0.34*			*0.08*
No	402 (44.0)	306 (46.0)	96 (38.5)		29 (34.5)	67 (40.6)	
Yes	512 (56.0)	359 (54.0)	153 (61.5)		55 (65.5)	98 (59.4)	
Rhinitis, n (%)				*0.07*			*0.30*
Never	371 (38.4)	288 (40.6)	83 (32.4)		33 (37.9)	50 (30.0)	
Current	595 (61.6)	422 (59.4)	173 (67.6)		54 (62.1)	119 (70.4)	
NAR	195 (20.2)	150 (21.1)	45 (17.6)		13 (14.9)	32 (18.9)	
AR	400 (41.4)	272 (38.3)	128 (50.0)		41 (47.1)	87 (51.5)	

NAR: non-allergic rhinitis; AR: allergic rhinitis. [a]: comparison between participants with *ever* vs. *never* exposure to visible moulds. [b]: comparison between participants with *past* vs. *current* exposure to visible moulds.

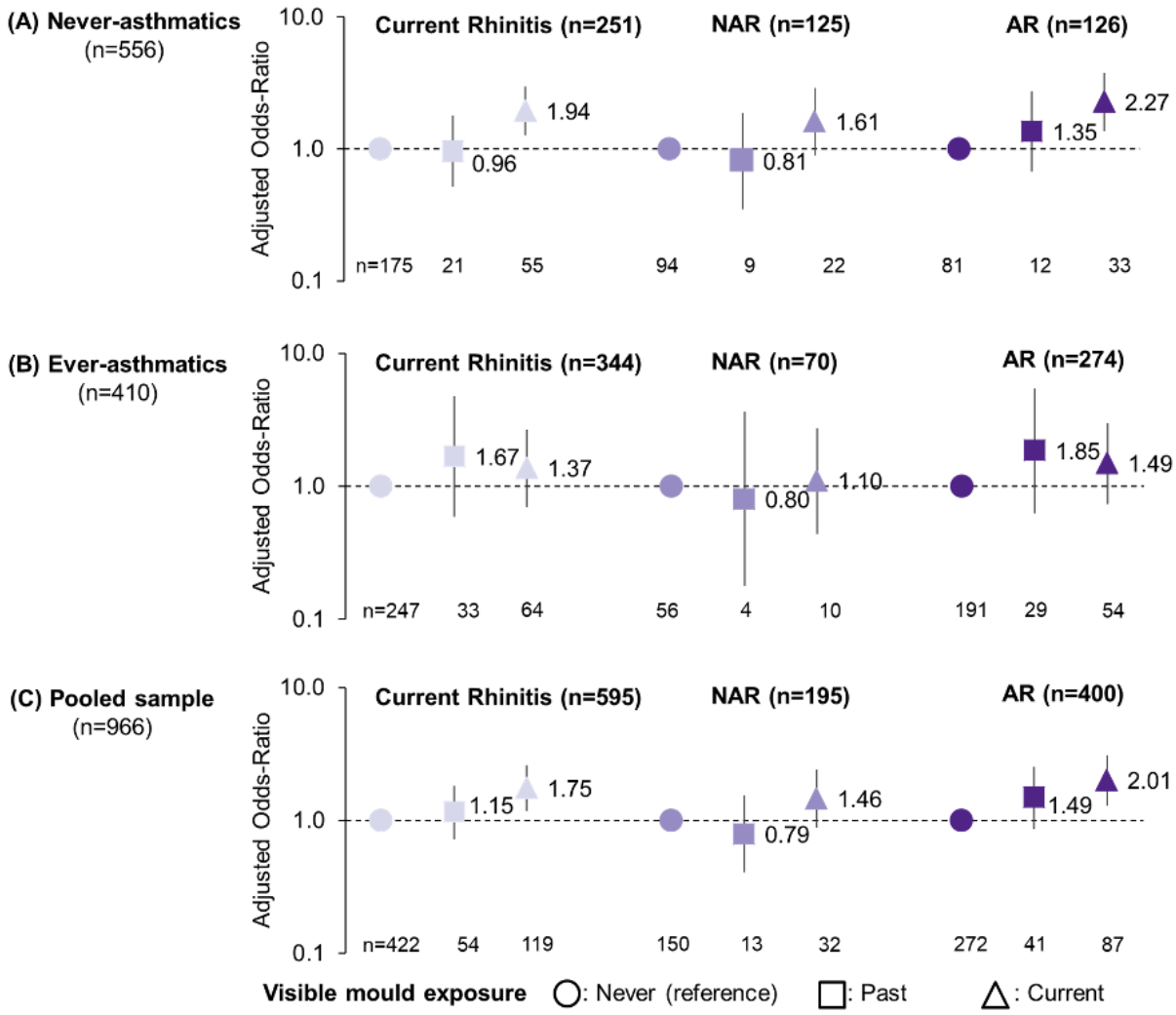

Figure 1. Associations between exposure to visible moulds at home and current rhinitis, non-allergic (NAR) and allergic (AR) rhinitis, according to ever-asthma status (A and B) and in the pooled sample (C)

Adjusted Odds-Ratios were estimated using binary or polytomous logistic models including age, sex, smoking, education and furry pet's ownership, considering familial dependence by GEE. Models also included ever-asthma status (yes/no) for analysis in the pooled sample.

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