

Correspondence

Shorter “time to peanut introduction” can prevent peanut allergy and avert false Ara h 2 screening results in infants

To the Editor:

We echo the importance of estimating precise pretest probabilities based on the degree of appropriate risk factors—a task potentially enabled by data presented by Keet et al.^{1,2}—to fully evaluate the utility of screening tests for the purposes of infant peanut introduction. Diagnostic test operating characteristics are central to the screening controversy in peanut allergy prevention.³ Assuming the authors’ data are generalizable to the US population of infants with moderate to severe eczema, Ara h 2 component IgE appears to be superior to skin prick testing and to peanut-specific IgE testing, with Ara h 2 having the greatest area under the receiver-operating characteristic curve.¹ With a 20% peanut allergy prevalence at time of first peanut ingestion, an Ara h 2 cutoff of greater than or equal to 0.1 kUa/L (92% sensitivity, 98% specificity) resulted in a 92% positive predictive value (PPV) and 98% negative predictive value (NPV). Under these test characteristics and conditions, false positives and false negatives appear to be minimal and balanced (1.6% vs 1.2%, respectively) at the end of this proposed screening cascade, which does not incorporate confirmatory oral food challenges.

However, Keet et al.² also show that the prevalence of already-developed peanut allergy in an infant is a function of age and eczema severity. Different point prevalences emerge when the authors’ data are disaggregated into subgroups on the basis of age and eczema severity. Different prevalences are effectively different pretest probabilities, and thus produce

diverse test predictive values. Table I presents the extrapolated natural frequencies of Ara h 2 screening outcomes among these subgroups with different prevalences, along with respective PPVs and NPVs. Natural frequencies have intuitive advantages over probabilities in making diagnostic inferences, and thus might be more useful than using predictive values alone in decision making.⁴ Ten percent of infants who were younger than 6 months with moderate to severe eczema had already developed peanut allergy, a prevalence lower than the 20% period prevalence across the entire cohort from which the authors’ presented PPV and NPV values are derived. A 10% prevalence would lead to 18 false positives and 8 false negatives in 1000 infants, at an Ara h 2 cutoff of greater than or equal to 0.1 (Table I). Yet, as prevalence increases, NPV categorically decreases. Using Ara h 2 at the same cutoff to screen 6-month or older infants with moderate to severe eczema, a 30% to 50% prevalence would actually produce more false negatives than false positives (24–40 vs 10–14, respectively). This pitfall, as well as other screening program concerns,⁵ deserves consideration before incorporating indiscriminate use of Ara h 2, or any screening test, into prevention recommendations.

Regardless of the operating characteristics of any screening cascade, the data presented by Keet et al, as well as by other groups, emphasize that “time to peanut introduction” is an important modifiable risk factor in peanut allergy development.² Introducing peanut-containing food reasonably early enough (ie, before age 6 months regardless of eczema severity) would prevent both peanut allergy and the consequences of false screening results.

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TABLE I. Ara h 2 screening outcomes of 1000 infants based on peanut allergy prevalence

Natural frequencies out of 1000 infants								
Prevalence of peanut allergy	Clinical scenario*	Allergic		Nonallergic		PPV	NPV	Percent misclassified
		True positive	False negative	False positive	True negative			
Ara h 2 ≥ 0.1 kUa/L (92% Se, 98% Sp)								
2%	Family history of peanut allergy	18	2	20	960	49%	100%	2%
10%	<6 mo with moderate to severe eczema	92	8	18	882	84%	99%	3%
20%	4-11 mo with moderate to severe eczema (aggregated cohort)	184	16	16	784	92%	98%	3%
30%	>8 mo with moderate eczema	276	24	14	686	95%	97%	4%
50%	>6 mo with severe eczema	460	40	10	490	98%	93%	5%
Prevalence of peanut allergy	Clinical scenario	Allergic		Nonallergic		PPV	NPV	Percent misclassified
		True positive	False negative	False positive	True negative			
Ara h 2 ≥ 0.35 kUa/L (89% Se, 99% Sp)								
2%	Family history of peanut allergy	18	2	10	970	64%	100%	1%
10%	<6 mo with moderate to severe eczema	89	11	9	891	91%	99%	2%
20%	4-11 mo with moderate to severe eczema (aggregated cohort)	178	22	8	792	96%	97%	3%
30%	>8 mo with moderate eczema	267	33	7	693	97%	95%	4%
50%	>6 mo with severe eczema	445	55	5	495	99%	90%	6%

Se, Sensitivity; Sp, specificity.

*Clinical scenario and corresponding prevalences are extrapolated and estimated from Keet et al.²

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