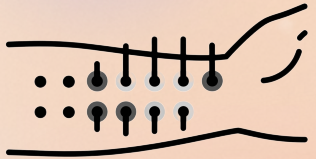
Interpreting Food Allergy Testing

Katie Larson, PA-C

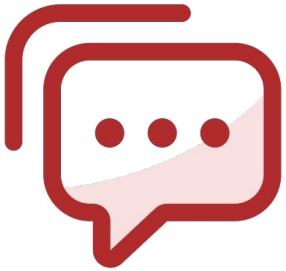


No disclosures

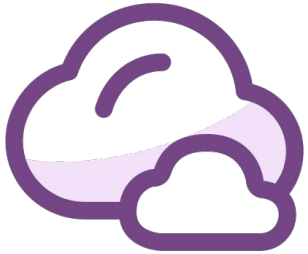
But I would love some ;). . .

Objectives

- Learn the three main types of food allergy testing and their benefits and limitations.
- Properly interpret both skin prick and allergen specific serum IgE testing to aid in diagnosis and management of food allergy.
- Determine when an oral food challenge may be needed to further elucidate a diagnosis of food allergy.



Audience Q&A



In a single word, describe your thoughts or feelings about food allergy testing.

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Meet our Case Study

Cole is a 15 year-old male with a history of severe eczema in early childhood. He was full panel food tested to the top nine allergens as an infant due to his eczema. He tested positive for wheat, egg, milk, peanuts, and tree nuts. He has been avoiding these foods since toddlerhood. Mom reports an accidental exposure to milk at the age of 4, which resulted in peri-oral hives and an accidental exposure to peanut at the age of 8, which resulted in facial swelling, vomiting, and diffuse hives. No exposure history to his other allergens. He has never tried milk or egg in baked goods.

In a few words, what is your first impression about Cole's food allergies?

You decide to repeat food testing on Cole.

What type of tests do you run?

And are these tests going to help us in decision making?

2

Types of Tests

Let's Define Some Statistical Terms:[1]

Sensitivity

- A test's ability to detect everyone with the disease.
- Negatives on sensitive tests help rule out disease.
- Not dependent on patient population.

Positive Predictive Value

- Percentage of patients testing positive who truly have the disease.
- Can change with patient population.

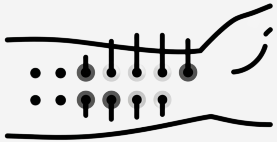
Specificity

- A test's ability to exclude those who do NOT have the disease.
- Positives on specific tests help rule in disease.
- Not dependent on patient population.

Negative Predictive Value

- Percentage of patients testing negative who truly do NOT have the disease.
- Can change with patient population.

Three Main Food Allergy Tests

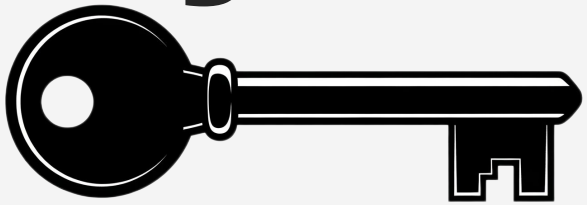


Allergen Specific Serum IgE Testing	Percutaneous (Skin) Prick Testing	Oral Food Challenge
Blood draw, measures free floating IgE (results in days to a about a week)	In office test, measures skin histamine response (results in 20 minutes)	In office oral test (results in 4 hours)
No need to avoid antihistamines	Avoid antihistamines 5-7 days prior	Avoid antihistamines 48-72 hours prior
Lowest risk	Low risk	**Higher risk**
High sensitivity, **low specificity**[2]	High sensitivity, **low specificity**[2]	High sensitivity, high specificity, **gold standard**[2]

Serum IgE and Skin Prick Testing: The Specificity Problem

- **This is not a pregnancy test**– these tests will NOT give you a “yes/no” “allergic/not allergic” answer.
- **A positive test result** only indicates sensitization to the allergen, and **does not indicate clinical reaction.**[1]
- The **false positive rate** of both forms of testing **is upwards of 50%.**[3]
- This false positive rate is why we **NEVER PERFORM FULL PANEL FOOD TESTING ON PATIENTS**.[4]
- Increasing SPT wheal size and increasing serum IgE numbers **indicate an increased likelihood of a clinical reaction** to the food.[1]
- Increasing SPT wheal size and increasing serum IgE numbers **DO NOT indicate severity** of an allergy.[1]
- Because sensitivity is high, **negatives for both tests are fairly reliable**.[2]

History is KEY to food allergy diagnosis.



Testing should generally only be performed to confirm an allergy after a convincing history of reaction, but often, we are faced with patients who have an unclear history of reaction or who were full panel food tested by another clinician. It’s at these times we need a deep knowledge of food testing interpretation and its limitations.

3

Test Interpretation

The goal of skin prick and serum IgE testing is to is place allergens in one of three buckets:

Introduce Allergen at Home

- Completely negative testing AND
- No or questionable reaction history

In Office Oral Food Challenge

- Minimally positive testing and/or
- Convincing distant reaction history

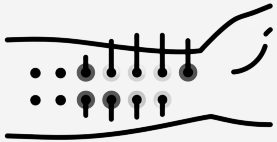
Avoidance vs Treatment

- Strongly positive testing and/or
- Convincing recent reaction history

What constitutes a “convincing” history of reaction?

- **True IgE mediated reactions to food are:**
  - **RELIABLE:** the **reaction occurs EVERY TIME** a sufficient amount of the food is eaten[1]
  - **RAPID:** the reaction occurs **within minutes to about two hours of eating the food**[5, 6]
  - **REGULAR: 90% of allergic reactions** to food occur with the **same 9 foods**[5]
    - Milk, egg, wheat, soy, peanut, tree nuts, sesame, fish, shellfish[5]

What Constitutes Negative Testing?



Skin Prick Test

Wheals <3mm are considered negative.[1]

Serum IgE

Measurements <0.1 kU/L are considered negative.[7]

Patients with negative SPT and allergen specific serum IgE with little to no reaction history can likely trial foods at home safely.

What constitutes “Strongly Positive” Testing? 95% Positive Predictive Values

Allergen	Allergen Specific Serum IgE 95% PPV	Skin Prick Test Wheal 95% PPV
Egg White[1,8]	≥7 kU/L (≥2 kU/L if under age 2)	≥7 mm ≥4 mm (infants)
Cow’s Milk[1]	≥15 kU/L (≥5 kU/L if under age 1)	≥8 mm
Peanut[1]	≥14 kU/L	≥8 mm
Tree Nuts[9]	≥15 kU/L	≥8 mm
Fish[1]	≥20 kU/L	not established
Shellfish	not established	not established
Sesame[8, 10]	Best PPV 86% @ 50 kU/L (infants)	≥14 mm ≥8 mm (infants)
Wheat[2]	Best PPV 75% @ 100 kU/L	not established
Soy[2]	Best PPV 50% @ 65 kU/L	not established

These patients likely need to avoid or treat their allergens.

What stands out to you about these positive predictive values?

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What constitutes “Strongly Positive” Testing? Recent Meta Analysis of Cut Offs[11]

Allergen	Allergen Specific Serum IgE 95% PPV	Skin Prick Test Wheal 95% PPV
Egg White	≥7 kU/L (meta analysis only 70% specificity) (≥2 kU/L if under age 2)	≥7 mm (meta analysis only 68% specificity)
Cow’s Milk	≥15 kU/L (≥5 kU/L if under age 1)	≥8 mm
Peanut	≥14 kU/L	≥8 mm
Tree Nuts	≥15 kU/L	≥8 mm
Fish	≥20 kU/L	not established
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Meta Analysis Specificity[11]
Green = >90%
Yellow = 80-90%
Red = <80%

What constitutes “Strongly Positive” Testing?

Component Resolved Diagnostics	
Allergen	**Allergen Specific Serum IgE: High Risk of Reacting**
Egg White: Ovomucoid[12]	≥11 kU/L* (heated egg white reactivity) *95% specificity
Cow’s Milk: Casein[13]	≥5.4 kU/L* (baked milk reactivity ≤ 24 months of age) *95% specificity
Peanut: Ara h 2[14]	≥42 kU/L (95% PPV) ≥14.4 kU/L (90% PPV)
Cashew: Ana o 3[15]	≥2 kU/L (95% PPV)
Hazelnut: Cor a 14[14]	≥47.8 kU/L (90% PPV)
Sesame: Ses i 1[16]	Best PPV 50% @ >32 kU/L

These patients likely need to avoid or treat their allergens.

What constitutes “Minimally Positive” Testing?

- Consider **50% negative predictive values** as a **rough guide for offering in office oral food challenges.**

50% Negative Predictive Values		
Allergen	**Allergen Specific Serum IgE 50% NPV**	**Skin Prick Test Wheal 50% NPV**
Egg White[1]	≤2 kU/L	≤3 mm
Cow’s Milk[1]	≤2 kU/L	not established
Peanut[1]	≤2 kU/L (hx of rx) ≤5 kU/L (no hx of rx)	≤3 mm
Tree Nuts[17]	≤5 kU/L* *58% OFC pass rate	not established
fish, sesame, wheat, soy	not established	not established

Unless there is a recent history of a convincing reaction, these patients likely need to undergo in office oral food challenges.

What constitutes “Minimally Positive” Testing?

Using Component Testing to Guide OFC Decision Making		
Allergen: Component	**Component Information**	**Consideration for Oral Food Challenge**
Egg White: Ovomucoid[12]	heat stable protein in egg	Optimal cut off point for heated egg reactivity: 4.4 kU/L (sens 76%, spec 81%)
Cow’s Milk: Casein[13]	heat stable protein in milk	Optimal cut off point for baked milk reactivity: 4.68 kU/L (sens 75%, spec 84%)
Peanut: ara h 8[18]	associated with oral allergy syndrome	Consider challenge if ara h 8 is the ONLY positive component
Hazelnut: cor a 1[18]	associated with oral allergy syndrome	Consider challenge if cor a 1 is the ONLY positive component
All other peanut and tree nut components	may be associated with systemic reaction	Use shared decision making, challenge may be higher risk at even low IgEs

Unless there is a recent history of a convincing reaction, these patients likely need to undergo in office oral food challenges.

Other considerations for Oral Food Challenges

- Consider challenges at **higher allergen specific IgEs** for patients with **atopic dermatitis and/or high total IgE.**[1]
- Use **shared decision-making** with families, explaining that **challenges with higher sIgEs and/or SPT are higher risk.**[1]
- Remember that **history is KEY.** If a patient has a convincing recent reaction, they have already performed (and failed) their own oral food challenge.
- Consider the natural history of each allergen: **milk, egg, wheat and soy are commonly outgrown in childhood.** If no recent reaction and declining testing, especially below 50% NPV, consider challenge.[1]
- Remember that **wheat, soy, and sesame often yield high allergen specific IgEs with no clinical reactivity.**[2, 8, 10] Consider challenges of these foods with even high IgEs if no recent reaction.
- Sometimes, the decision is made based on ***VIBES*** – we use fancy words for this like “expert opinion” and “pattern recognition.” **Asking a more experienced clinician their thoughts is never the wrong thing to do!**

Unless there is a recent history of a convincing reaction, these patients may need to undergo in office oral food challenges.

4

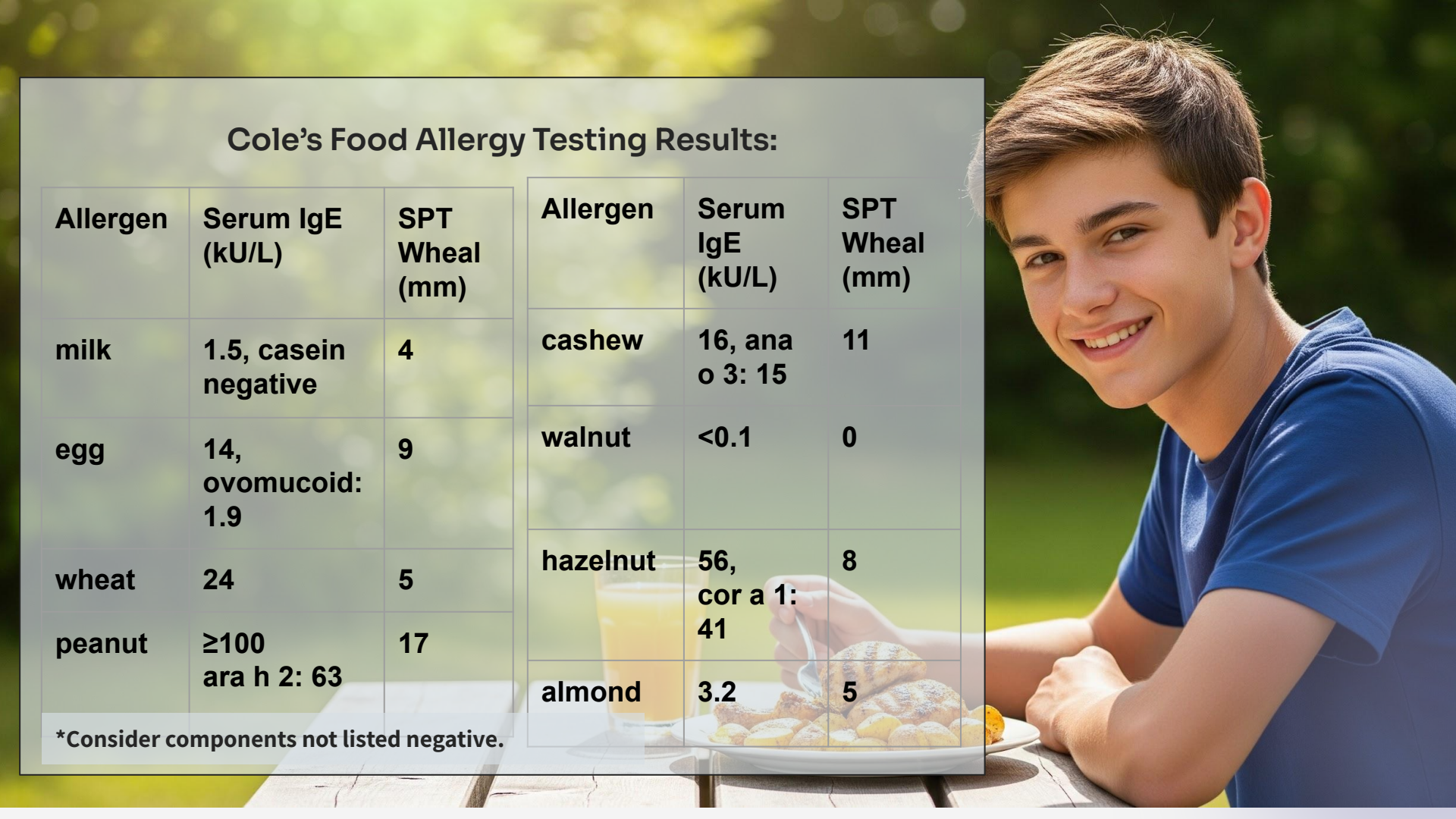
Putting it all Together

Cole's Food Allergy Testing Results:

Allergen	Serum IgE (kU/L)	SPT Wheal (mm)
milk	1.5, casein negative	4
egg	14, ovomucoid: 1.9	9
wheat	24	5
peanut	≥100 ara h 2: 63	17

Allergen	Serum IgE (kU/L)	SPT Wheal (mm)
cashew	16, ana o 3: 15	11
walnut	<0.1	0
hazelnut	56, cor a 1: 41	8
almond	3.2	5

*Consider components not listed negative.



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Introduce Allergen at Home

- Completely negative testing AND
- No or questionable reaction history

Which allergen(s) would you recommend for home introduction? (select all that apply)

Cole's Food Allergy Testing Results:

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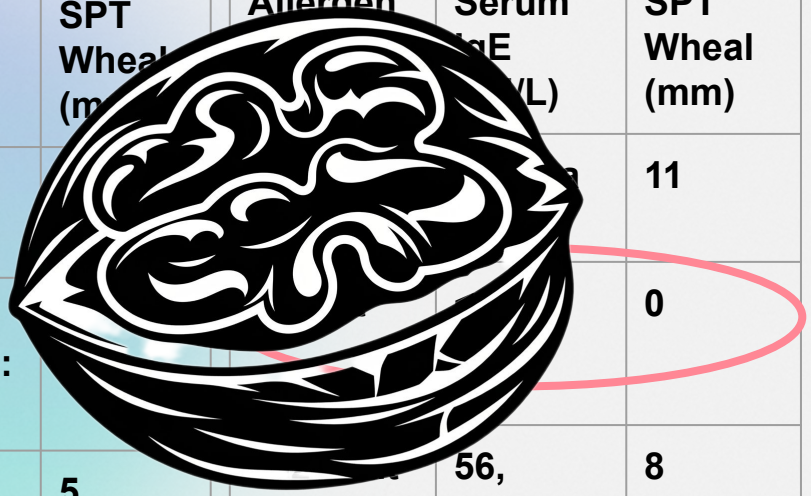

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Avoidance vs Treatment

- Strongly positive testing and/or
- Convincing recent reaction history

Which allergen(s) would you recommend that Cole either treat or avoid? (select all that apply)

Cole's F… g Results:

Allergen	Serum IgE (kU/L)	SPT Wheal (mm)
milk	1.	11
egg	coi	0
wheat	24	5
peanut	≥100 ara h 2: 63	17

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	…a 15	11
		0
hazelnut	56, cor a 1: 41	
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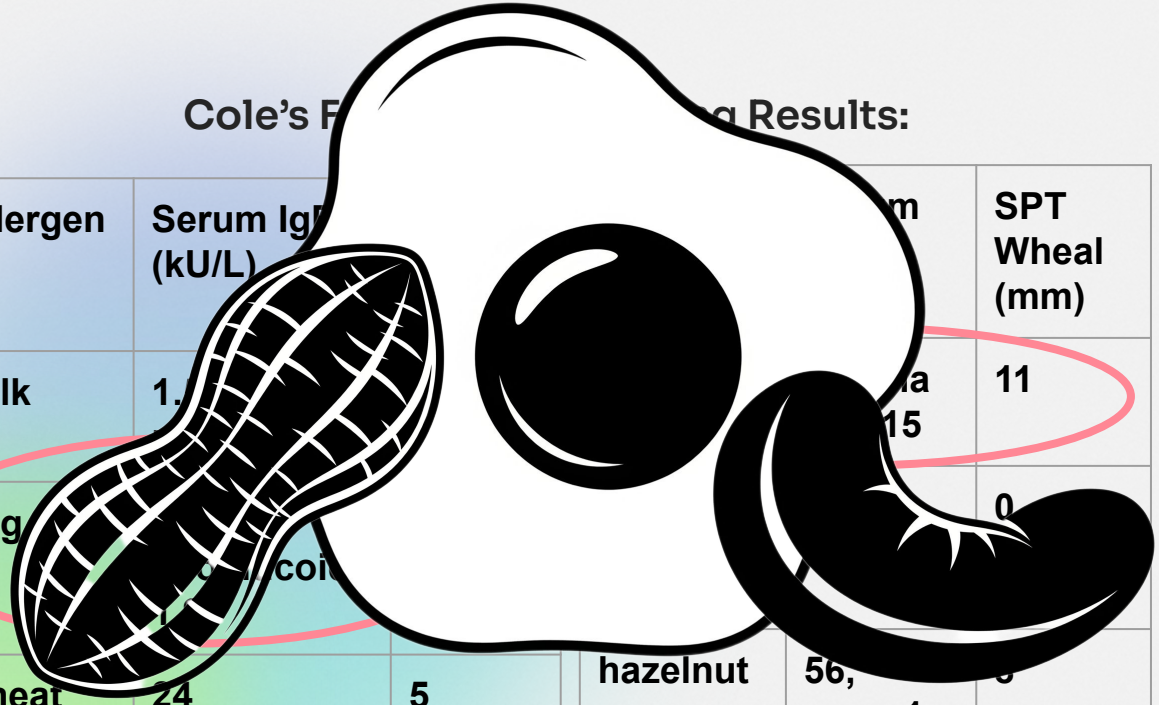

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walnut	<0.1	0
hazelnut	56, cor a 1: 41	8
almond	3.2	5

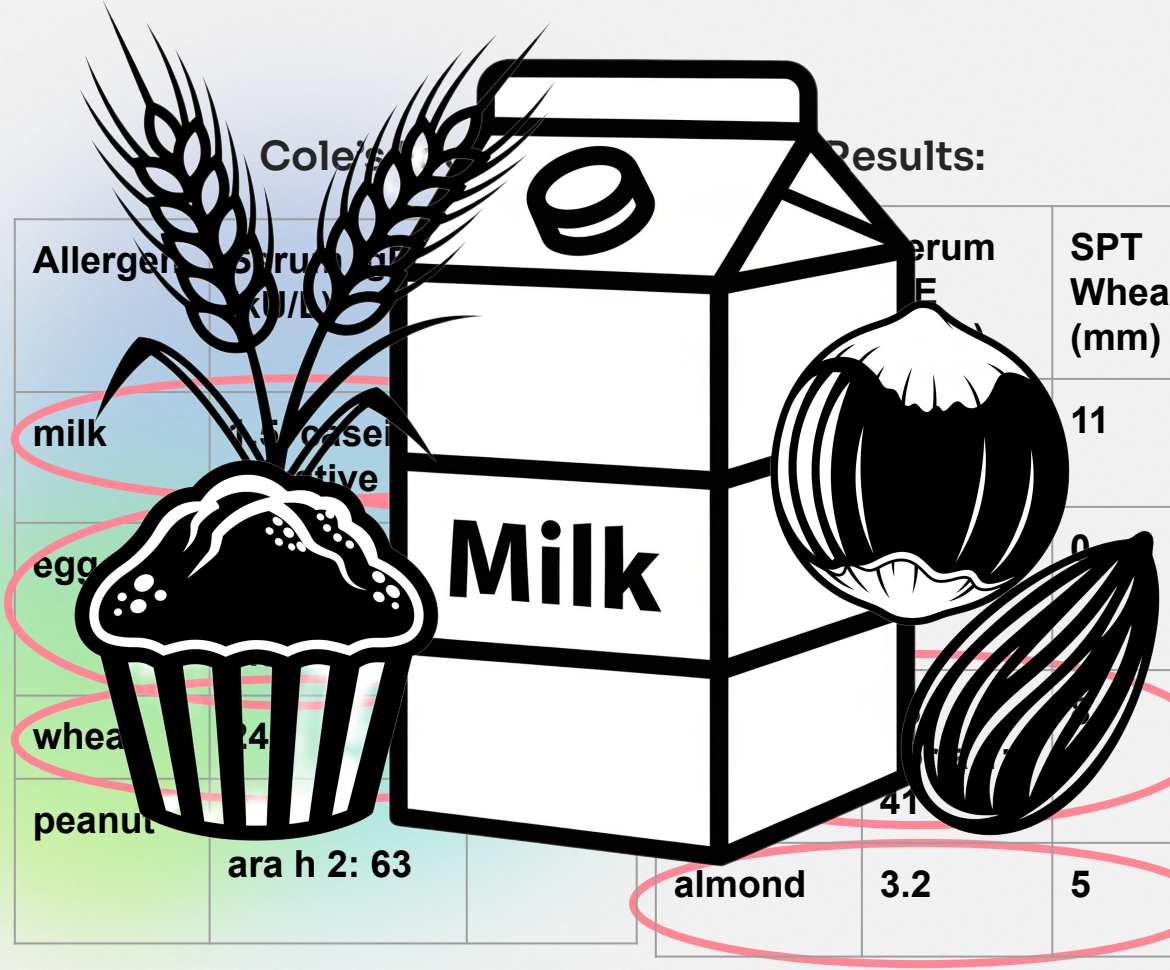
In Office Oral Food Challenge

- Minimally positive testing and/or
- Convincing distant reaction history

Which allergen(s) would you recommend for an in-office oral food challenge? (select all that apply)

Cole's [illegible] Results:

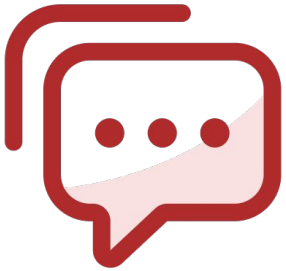
Allergen	[illegible]	[illegible] Serum IgE	SPT Wheal (mm)
milk	11.5; casein positive		11
egg			0
wheat	24		
peanut	ara h 2: 63	41	
almond		3.2	5



In Office Oral Food Challenge

- Minimally positive testing and/or
- Convincing distant reaction history


Cole completes home introduction of walnut and passes all of his food challenges. He decides to undergo OIT for peanut and cashew, graduating after a year. Two years later, his egg IgE has declined, and he passes a liquid egg white challenge. He now has no food restrictions. His family is so grateful that he can go off to college without worrying about his food allergies.



Audience Q&A

Thanks!

Do you have any questions?
katie.larson@aspireallergy.com

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