Lab Monitoring for Outcome Prediction & Maintenance Dose & Frequency Modification

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NY Food Allergy & Wellness

What We Want To Know

Johnny - 4 Yr old, Peanut Allergy, starting PN OIT

Desired Outcomes: Freedom
Desensitization
Sustained Unresponsiveness
Tolerance

- **What tests? How often?**
- **Predicting outcomes**
- **Predicting potential issues**

Modify:
Dose, Frequency, Duration

Patient's Journey

1. HISTORY
2. SKIN TESTS (SPT)
3. LABS
4. ORAL CHALLENGES
5. OIT
6. MAINTENANCE
7. DS
8. SU TOLERANCE

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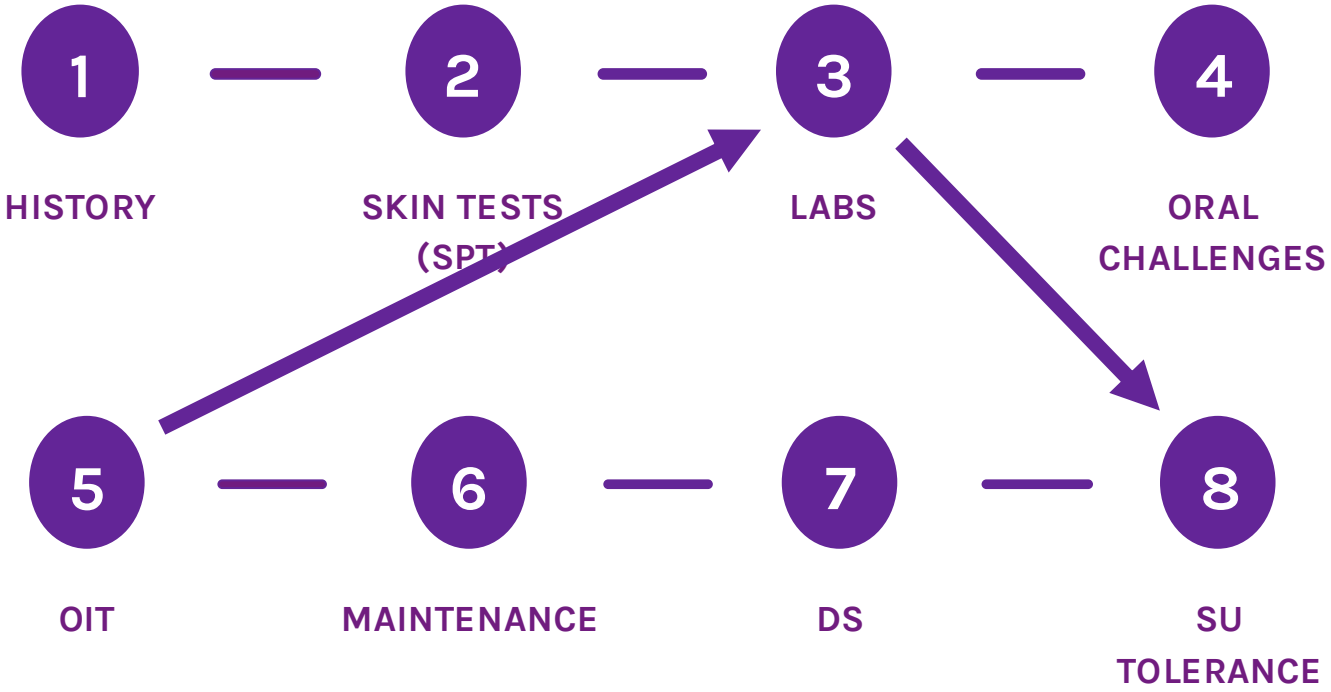
Discussion



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Labs

- Pre-OIT testing
- Monitoring tests
- Outcome Prediction with each tests
- Frequency of testing
- Adjusting OIT Dose and Frequency
- Published
- Clinical Observations
- Experience

- Skin Tests
- CBC with Diff
- sIgE, Total IgE
- Components IgE
- IgG4
- Vitamin D Level
- BAT, MAT
- Epitope testing
- EoP

Skin Tests

PPOIT trial -

There was a significant longitudinal reduction in median peanut SPT and Ara h 2 sIgE along with an increase in median sIgG4 to peanut and Ara h 1,2,3 in children who achieved SU in PPOIT trial.

915 **Predicting Acquisition of Sustained Unresponsiveness Following Peanut Oral Immunotherapy Using Skin Prick Test Size and Serum Levels of Immunoglobulins Specific to Peanut**

Lalita Jindal[1,2], Anne-Louise Ponsonby, PhD[3,4], Paul Licciardi, PhD[4,5],

NYFA: We do NOT use ST data for treatment decisions

CBC - with Differential

- WBC, Hb, Platelets
- Peripheral Eosinophils (pEos) - baseline
- EoE (no relation to pEos)
- ELORS (elevation in pEos)
- Needed with BAT, EoP and SIP

NYFA:
CBC is used with BAT & EoP to get accurate results

Food sIgE, IgG4, Components

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Lancet -

Association with SU
When Pre-OIT values:

- **Higher baseline peanut-specific IgG4/IgE**
- **Lower Ara h 2 IgE**
- **Lower basophil activation responses**

Sustained Outcomes in a Large Double-blind, Placebo-controlled, Randomized Phase 2 Study of Peanut Immunotherapy. R. Sharon Chinthrajah, MD...
Lancet. 2019 October 19; 394(10207): 1437–1449. doi:10.1016/S0140-6736(19)31793-3.

High Risk Components List

1. Peanut	▸ Ara h 2, 6, (1, 3, 9, 8)
2. Brazil Nut	▸ Ber e 1
3. Walnut	▸ Jug r 1, (3)
4. Hazelnut	▸ Cor a 9, 14, (1, 8)
5. Cashew	▸ Ana o 3
6. Pistachio	▸ Cashew
7. Pecan	▸ Walnut
8. Milk	▸ Casein, (ALA, BLG)
9. Eggs	▸ Ovomucoid, (OA)
10. Soy	▸ nGly m 5, (6, 4)
11. Wheat	▸ rTri a 19 Omega-5 Gliadin
12. Sesame	▸ Ses i 1

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sIgE vs Components

NYFA:

Reduction in sIgE for high risk components is more helpful in reducing OIT dose and frequency (when total and sIgE are high)

BAT shifts to non reactive despite no major changes in sIgE/Components

Components - more reliable

New York Food Allergy & Wellness								
ATUL N. SHAH, MD, FACAAI, FAAAAI								
NYFoodAllergy.com		631-446-1436						
OIT	Food	Day 1 Date	Challenge	Daily Dose		**Infancy**		
1	Milk	09/08/2020	3/2/2021	240mL		**Atopic March**		
2								
3								
Food	**Components**	11/11/2016	04/28/2017	07/21/2020	04/02/2021	07/08/2021	12/18/2021	06/08/2022
				Pre-OIT	**POST-OIT**			
Total IgE		1612	1443	915	1194	967	1075	**1577**
Vit D 25OH		14.7	14.7	37	42.1	39	39.3	40.2
AEC								
Milk	SPT							
	sIgE	87	>100	>100	42	26.3	21.3	13.4
	Alpha-Lactalbu	0.7	39.8	12.4	8.29	4.95	4.46	3.12
	Beta-Lactoglob	8.96	50.8	7.82	3.19	2.25	2.1	1.46
	CASEIN*	>100	>100	>100	43.7	24.9	23.4	11.8
Birch	sIgE / SPT	<0.10	1.32		0.81			**52.3**

Epitope - BAT - MAT

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Bringing the Next Generation of Food Allergy Diagnostics Into the Clinic

Alexandra F. Santos, MD, PhD[a,b,c,d], Michael D. Kulis, PhD[e], and Hugh A. Sampson, MD[f] *London, United Kingdom; Chapel Hill, NC, and New York, NY*

TABLE I. Diagnostic performance of next-generation food allergy diagnostic tests

Diagnostic test	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Epitope testing				
Bead-based epitope assay peanut[11]	92%	94%	91%	95%
Basophil activation test				
To peanut[12,13]	83% to 98%	96% to 100%	95% to 100%	83% to 98%
To cow's milk[14]	91%	90%	81%	96%
To egg[15]	90%	100%	100%	92%
Mast cell activation test to peanut[16]	75%	99%	95%	92%

Epitope Assay - PN OIT

Baseline Epitope Profiles are Predictive of Sustained High Threshold in the POISED Trial

Using epitope profiles to predict sustained unresponsiveness of peanut OIT.

Epitopes are 81% predictive

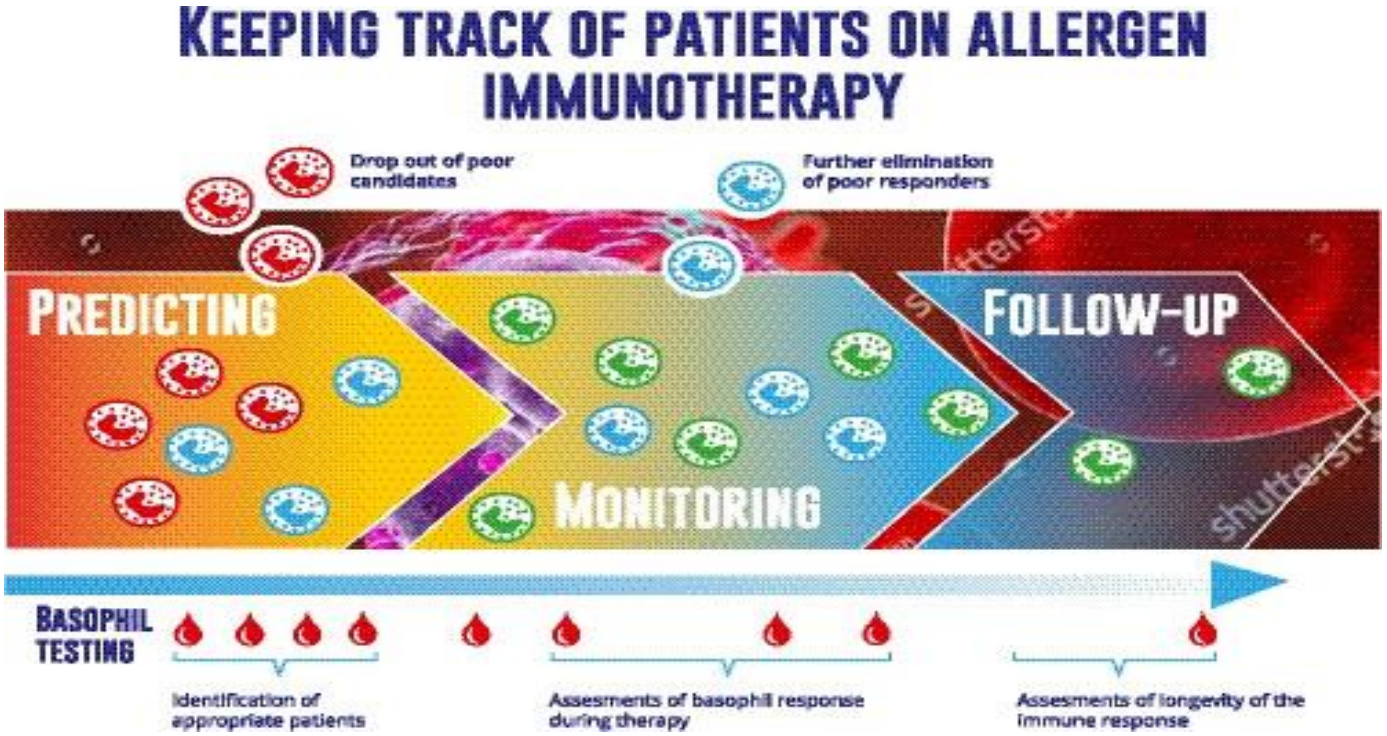
Abstract at AAAAI 2023: Mt. Sinai School of Medicine, Ashley San Eun Lee

BAT- AIT

EDITORIAL

Allergy

Basophil activation test: A diagnostic, predictive and monitoring assay for allergen immunotherapy



BAT as a predictive tool

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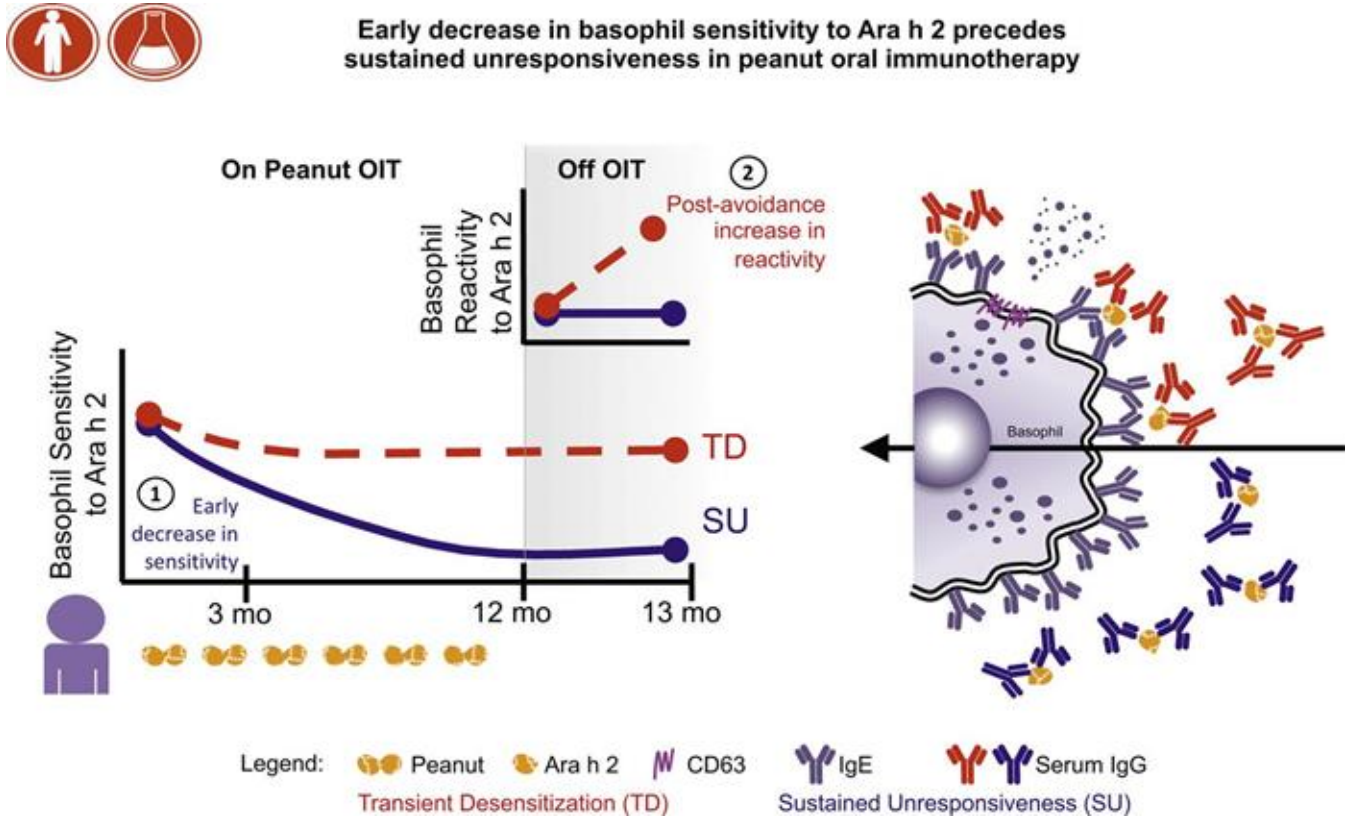
Early decrease in basophil sensitivity to Ara h 2 precedes sustained unresponsiveness after peanut oral immunotherapy

Check for updates

Sarita U. Patil, MD,[a,b,c,d] Johanna Steinbrecher, BS,[a] Agustin Calatroni, MS,[e] Neal Smith, MS,[a] Alex Ma, BS,[a] Bert Ruiter, PhD,[a,b,c,d] Yamini Virkud, MD, MPH,[a,b,d] Michael Schneider, BS,[f] and Wayne G. Shreffler, MD, PhD[a,b,c,d]

Boston, Mass, Chapel Hill, NC, and Schönenbuch, Switzerland

BAT - PN OIT


Early decrease in basophil sensitivity to Ara h 2 precedes sustained unresponsiveness in peanut oral immunotherapy
On Peanut OIT
Off OIT
2
Post-avoidance increase in reactivity
Basophil Reactivity to Ara h 2
Basophil Sensitivity to Ara h 2
TD
SU
1
Early decrease in sensitivity
3 mo
12 mo
13 mo
Basophil
Legend:
Peanut
Ara h 2
CD63
IgE
Serum IgG
Transient Desensitization (TD)
Sustained Unresponsiveness (SU)

PN BAT in OIT

- Peanut OIT suppresses basophil activation
- BAT can help to differentiate those who will achieve TDS from those who will achieve SU and tolerance after peanut OIT.
- Basophil non/low responders exhibit higher treatment success to peanut OIT
- 80% to 90% suppression of peanut-specific basophil activation is required to maintain long-term clinical tolerance after peanut OIT.

Sustained successful peanut oral immunotherapy associated with low basophil activation and peanut-specific IgE. Mindy Tsai... JACI 2020 Mar;145(3):885-896.e6

NYFA - BAT Experience

- No “one” biomarker
- Clinical: History and other parameters
- Lag: Immunological parameters (sIgE, sIgG4) often lag months behind clinical desensitization.
- BAT: Functional assay is more reliable to support the decisions

NYFA - BAT Experience

- Use CD63 and CD203c with proper controls
- 8-10% non-reactive basophils at baseline
- 0.1 nano gram, 1ng, 10ng, 100ng, 1000ng, 10,000ng incremental reactivity data is more helpful
- As patients progress through SLIT and OIT, the reactivity at lower concentrations clears
- We reduce dose frequency with every change

NYFA - BAT Experience

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BAT - Reactive to ALL concentrations
Bell Shaped

ALLERGEN	% Positive CD63	CD63 Reference Range
Allergen: 10,000ng/ml (CD63)	26.4	<1
Allergen: 1000ng/ml (CD63)	21.1	<1
Allergen: 100ng/ml (CD63)	30.7	<1
Allergen: 10ng/ml (CD63)	45.8	<1
Allergen: 1ng/ml (CD63)	11.3	<1
Allergen: 0.1ng/ml (CD63)	2.2	<1

NYFA - BAT Experience

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As patients progress through SLIT and OIT, the reactivity at lower concentrations clears

ALLERGEN	% Positive CD63	CD63 Reference Range
Allergen: 10,000ng/ml (CD63)	9.7	<1.40
Allergen: 1000ng/ml (CD63)	12.1	<1.40
Allergen: 100ng/ml (CD63)	16.6	<1.40
Allergen: 10ng/ml (CD63)	3.7	<1.40
Allergen: 1ng/ml (CD63)	0.9	<1.40
Allergen: 0.1ng/ml (CD63)	0.6	<1.40

NYFA - BAT Experience

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Reactivity at lower concentrations cleared

ALLERGEN	% Positive CD63	CD63 Reference Range
Allergen: 10,000ng/ml (CD63)	4.7	<1
Allergen: 1000ng/ml (CD63)	2.6	<1
Allergen: 100ng/ml (CD63)	0.2	<1
Allergen: 10ng/ml (CD63)	0.3	<1
Allergen: 1ng/ml (CD63)	0.5	<1
Allergen: 0.1ng/ml (CD63)	0.4	<1

NYFA - BAT Experience

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Post OIT BAT
Non reactive cells - SU / Tolerance

ALLERGEN	% Positive CD63	CD63 Reference Range
Allergen: 10,000ng/ml (CD63)	0.6	<1.20
Allergen: 1000ng/ml (CD63)	0.5	<1.20
Allergen: 100ng/ml (CD63)	0.2	<1.20
Allergen: 10ng/ml (CD63)	0.3	<1.20
Allergen: 1ng/ml (CD63)	0.4	<1.20
Allergen: 0.1ng/ml (CD63)	0.3	<1.20

NYFA - BAT Experience

- Sequential BATs are needed to predict SU
- Completely non reactive basophils at all concentrations - time to consider free-eating, off the maintenance dose and discuss clinical SU and Tolerance

EoP - Eosinophil Progenitors

1. Flow Cytometry - Whole Blood
2. CD34+ cells
3. EoPs elevated with EoE
4. Not increased with ELORS (observation)
5. EoP numbers match with endoscopic biopsy numbers
6. EoPs decrease with improved EoE symptoms and reduction in biopsy Eos

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EoP - Eosinophil Progenitors

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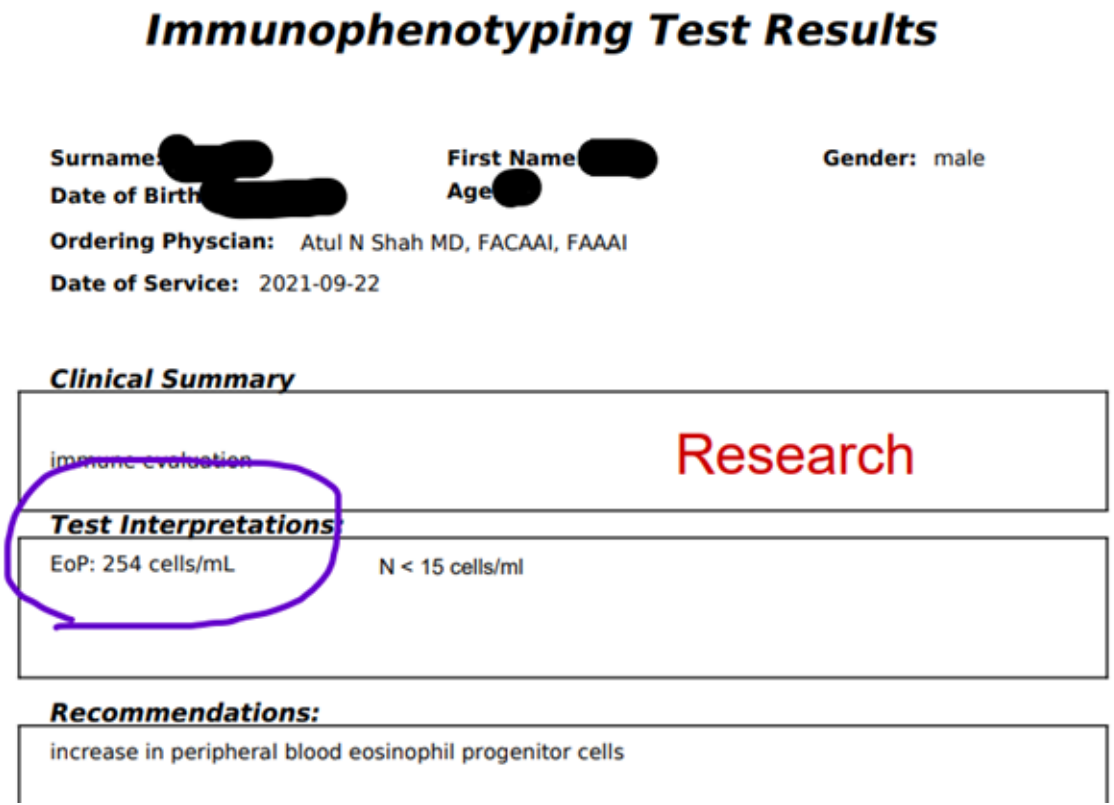
1. **Eosinophil progenitor levels are increased in patients with active pediatric eosinophilic esophagitis**

2. Monitoring Eosinophilic Esophagitis Disease Activity With Blood Eosinophil Progenitor Levels

*Anna Henderson, †Adam Magier, †Justin T. Schwartz, ‡||Lisa J. Martin, §||Margaret H. Collins,

3. **Eosinophil progenitor levels correlate with tissue pathology in pediatric eosinophilic esophagitis**

NYAIRL - EoP Results



Immunophenotyping Test Results

Surname: [redacted] **First Name** [redacted] **Gender:** male

Date of Birth [redacted] **Age** [redacted]

Ordering Physcian: Atul N Shah MD, FACAAI, FAAAI

Date of Service: 2021-09-22

Clinical Summary

immune evaluation

Research

Test Interpretations:

EoP: 254 cells/mL N < 15 cells/ml

Recommendations:

increase in peripheral blood eosinophil progenitor cells

Modify Dose & Frequency

- Post OIT - 6 week, 3 months, 6 months, Yearly
- Expect significant increase of total IgE, sIgE, components
- Drop 1 day with every 10% reduction of sIgE/Components or increase in sIgG4/sIgE
- Drop 1 day per week for every 1 yr completed (when sIgE and components are >100)
- When sIgE or components reach below 10% of pre-OIT levels, dosing 2 x a week is sufficient

Modify Dose & Frequency

- Reduction in frequency more appreciated than dose reduction
- Reduce dose when taste aversion is an issue
- Basophil reactivity reduction with lower concentrations (0.1, 1, 10 nanogm) on BAT allows to reduce the frequency sooner
- The rate of reduction varies per food in multi-food OIT patients
- Younger age (<4 years) higher rate of sIgE reduction - faster dose frequency reduction

Credits - Thank You

- Dr. Wasserman
- Dr. Jones
- Dr. Windom
- Dr. Detjen
- Dr. Agrawal
- Dr. Alpan

- My Team at:

- New York Food Allergy
- NYAIRL
- Center 4 Asthma & Allergy
- Global Food Therapy

Lab Monitoring for Outcome Prediction & Maintenance Dose & Frequency Modification

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