Knowledge Gaps in OIT

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Things We Know

- Many foods have been used in OIT, all over the world
- Success rates in reaching Maintenance 75-90%
- Epi used by 5-20% in 1st year
- Immunologic markers mimic SCIT and other forms of desensitization
- EoE is rare and reversible, if due to OIT food
- Early childhood OIT, < 3 yo, is safe and more likely to achieve tolerance

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Age as Predictor of Sensitivity

- Cumulative dose of peanut in 3 age groups:

Age group (yrs)	Peanut (median, mg)	n
< 5	790 (716-864)	29
5 – 10	310 (160-460)	61
> 10	70 (40-100)	36

van der Zee. J Allergy Clin Immunol 2011; 128:1031-6

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- Younger age and lower peanut sIgE improve chances of reaching Maintenance

Wasserman RL. J Allergy Clin Immunol Pract 2019;7:418-26

- No ≥ moderate reactions through build up, more likely to reach SU by 4 years (egg)

Jones SM. J Allergy Clin Immunol 2016;137:1117-27

- Low baseline sIgE/total IgE strongest predictor of SU with up to 5 years of OIT (peanut)

Vickery B. J Allergy Clin Immunol 2014;133:468-75

Things We Need to Know

(from more than 1 small study)

- A better diagnostic gold standard than OFC
- Buildup phase failures – how to rescue them
  - Low and slow, SLIT, biologics
- Maintenance phase
  - Dose and frequency
  - Rescue reactors – lower dose, more frequent dosing
  - Biomarkers to guide the above

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Duplicate Food Skin Tests

- >1,000 patients had duplicate skin prick tests over 7-year period
- Discordent 14% of time, i.e. one positive, one negative
- Using positive predictive value for a + OFC, 10-15% of tests, depending on food, were discordent

Nelson RW. J Allergy Clin Immunol Pract 2019;7::675-7

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Sustained Outcomes with Peanut OIT

- POISED study: N=120, 8-17 y.o., + OFC at ≤ 2 peanuts (cumulative), sIgE > 4
- 3 groups: OIT to 16 peanuts over 2 years then stop (peanut-0), same OIT for 2 years then 300 mg peanut protein QD (peanut 300), and placebo throughout
- Measures: basophil activation test, sIgE, total IgE, components, and sIgG4; OFC every 3 mo. in year 3

Chinthrajah RS. Lancet 2019;394:1437-49

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POISED Study Results

- 85% reached maintenance 4 gm peanut protein, median time 1 yr, 19% used Epi in 1st year
- Peanut-0 group less likely to pass 4 gm OFC at year 3: 13% vs 37% in peanut-300 (same result at 900 mg)
- Adverse events associated with higher sIgE, sIgE/IgE ratio, and araH1 and H2; high araH2/sIgE ratio associated with treatment failure
- Low BAT, sIgE, & ara H1 and H2 associated with SU

Tsai M. J Allergy Clin Immunol 2020;145:885-96

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Epitope-specific Antibody Binding

- 2 years of milk OIT, n=57, 7-35 y.o.
- SU tested 8 weeks off milk, 40% passed
- Lower binding and lower diversity of sIgE to a set of 66 allergenic milk peptides was strongest predictor of SU

Suarez-Farinas M. J Allergy Clin Immunol 2019;143;1038-46

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Two Year Palforzia Trial

- 4-17 y.o. from PALISADE trial, 256 active 300 mg peanut protein and 102 placebo were treated for 1 more year with Palforzia
- Active group randomized to ongoing QD dosing vs. taper to QOD then twice weekly
- Placebo group started OIT and continued QD x 1.5 yrs
- Exit DBOFC: 3-10-30-100-300-600-1,000-2,000 mg

Vickery B.. J Allergy Clin Immunol Pract 2021;9;1879-89

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Two Year Palforzia Trial

- exit OFC: 80-95% QD dosed reached 1 gm vs 58-68% twice weekly dosed subjects
- 18 twice weekly were changed to QD due to AE's, seemed to become less frequent and mostly mild
- Epi use 8.6% QD dose, 10.8 % twice weekly
- 73% epi reactions occurred < 2 hours after dosing
- 2 EoE's by EGD, resolved with d/c Palforzia

Vickery B.. J Allergy Clin Immunol Pract 2021;9;1879-89

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Editorial to Palforzia Trial

"In our experience, patients frequently elect to return to strict avoidance rather than have to take a daily treatment," due to dosing fatigue and potential for reactions

Real world response:

- study fatigue > dosing fatigue

- 8-11% patients having an Epi reaction after year 1 is often tolerable (QOL not assessed in this study)

Dunlop JH. J Allergy Clin Immunol Pract 2021;9;1890-91

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Registry Goals

- Demographics of OIT patients – age, gender, atopic history, reaction history, and baseline ST and labs
- Single food vs Multi-food experiences
- Day One reactions and top dose(s)
- % reaching Maintenance and time to do so
- Reasons for and predictors of early termination
- Epi use

Registry Reality

- Unfunded, multi-year, multi-center private practice trials are challenging
- 1,500 -2,000 OIT patient experiences is impressive, but if the data is incomplete/inaccurate, it is unpublishable
- Stay tuned

Conclusions

- Much is known about OIT, much more to learn
- How one defines success alters perception
- While huge projects like the Registry are complicated, smaller, focused reports are not
- When it come to daily practice, statistics are helpful, but each patient is unique
- Early is the key: Introduction (LEAP) and OIT (Vickery, Ly)

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