

Pediatric Allergy Update

Chris Cleveland, MD, FAAAAI, FAAAAI, FAAP
Sanford Asthma and Allergy Clinic
Sanford Southpointe
Fargo, ND



1

Disclosures

- No relevant disclosures
- Will be presenting the brand names of biologics for recognition and ease of use

2

Objectives

- Update on food allergy management
 - Review diagnostic strategies for food allergy
 - Outline current infant feeding recommendations
 - Present changes and future directions for food allergy management
- Update on use of biologic medications for atopic disorders
 - Review relevant pathophysiology of atopic disorders
 - Introduce how biologics work
 - Discuss current FDA approved biologics in allergy

3

Food allergy update

- Infant feeding recommendations have changed through the years
 - Dramatic incidence change
 - Delay in science, studies to keep up with the change
 - "Wrong" advice for years
 - Updated advice 2015, 2017, 2021
 - Has incidence actually changed despite new advice?



4

Food allergy update

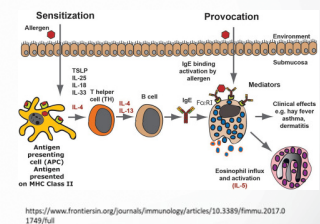
- Hygiene hypothesis
 - Change from agrarian to urban societies
 - Th1 to Th2
 - Daycare
 - Cleaning chemicals
 - Cow's milk formulas
 - Delayed complementary foods
 - Increased atopic dermatitis
 - Allergen introduced through skin rather than gut
 - Epigenetic changes
 - Atopic family history



5

Food allergy update

- Terms:
 - **Immunoglobulin E (IgE):** binds to an amino acid sequence
 - →cross links with high affinity receptor on mast cells, basophils
 - →releasing histamine, vasoactive peptides
 - →resulting in swelling, itch etc.



6

Food Allergy Terms

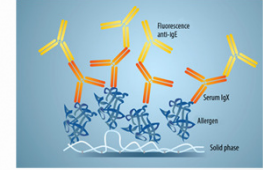


- **Sensitization:** can demonstrate specific IgE to an allergen
- Skin prick testing (personal note- please do not call this 'needle testing')
 - Dermal layer has IgE
 - Measure induration and erythema
 - Limitation on sensitive skin, dermatographia, current AH use

7

Food Allergy Terms

- **Serum specific IgE** or ImmunoCAP testing- FEIA using bound allergen, then serum and fluorescent antibody labeling.
- "RAST" is an outdated term and the modality has been replaced by ImmunoCAP
- Limitations on sensitivity
 - Usually related to high total IgE (Non-specific IgE)



8

Food allergy Terms

- **Allergy:** Sensitization + symptoms occur when a food allergen is ingested
 - Can be mild- oral irritation, rash at mouth
 - Can be severe- anaphylaxis= hypotension, generalized urticaria, angioedema, etc.
 - Proven by oral food challenge (OFC)
- **Tolerance:** can ingest the food without reactions
 - Temporary vs. sustained
- **Desensitization:** through a process of immunotherapy, can tolerate a specified amount of the food

9

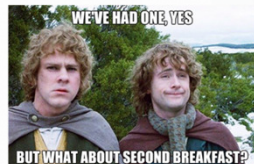
Food Allergy Terms

- **Intolerance or sensitivity:** Non-IgE mediated symptoms with ingested food
 - Varies widely
 - Some are immune-mediated, e.g. celiac due to gluten (IgA/IgG mediated)
- **Very** uncommon to have a clear food reaction without IgE +, but possible
- Both new sensitization and food allergy decline with age

10

Food allergy update

- Current diagnostic strategies
 - Symptoms occur causing concern
 - Symptoms recur on subsequent exposure(s)
 - or depending on severity/enough concern, referral with 1st episode
 - HISTORY, Physical exam
 - Skin testing, serum IgE testing or both
 - Or none
 - OFC if needed



11

Current feeding guidelines-2021

- Fleischer, DM et al.
- A Consensus Approach to the Primary Prevention of Food Allergy Through Nutrition: Guidance from the American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; and the Canadian Society for Allergy and Clinical Immunology
 - [J Allergy Clin Immunol Pract 2021;9:22-43]
- Using data from meta-analyses and 2 pivotal primary prevention studies
 - Learning Early About Peanut Allergy (LEAP) and Enquiring About Tolerance (EAT)

12

Screening advice from 2015-2017

- Based on LEAP data, NIAID and AAP supported screening in high risk children
- Other international societies did not adopt or recommend this
 - Specificity lower for either skin or serum IgE testing
 - Not practical
 - Concern for 'screening creep'
 - Case by case basis

13

Recommendation highlights

- Try to identify infants at high risk
 - AD, family atopy/FA
 - No evidence of younger sibs being at increased risk of developing FA
 - But may be if delayed introduction
- Introduce peanut irrespective of risk around 6 mo (not before 4 mo)
 - At home, when infant and family is ready
 - Continue regular ingestion if tolerated
- Introduce egg irrespective of risk around 6 mo (not before 4 mo)
 - Cooked forms- avoid raw, pasteurized
 - At home, when infant/family ready, continue regular ingestion if tolerated

14

Recommendation highlights

- Do not delay other complementary food introduction
 - Milk, soy, wheat, TN, fish/shellfish, sesame
 - May be harm in purposefully delaying
 - No need to test proactively
 - Once introduced- continue offering regularly
- Cleveland's Caveat: Some kids are going to react
 - Very important to remember that severe reactions from 1st ingestions are SUPER RARE
 - Food allergy anaphylaxis fatal events are tragic and get headlines- but much more common to be bit by a shark or hit by lightning

15

Recommendation Highlights

- A diverse diet may help foster prevention of food allergy
 - Observational, not RCT supported yet
- Do not routinely prescribe or recommend the use of hydrolyzed formula for the specific prevention of food sensitization
- Not recommended for maternal exclusion of common allergens during pregnancy or breast feeding to prevent food allergy

16

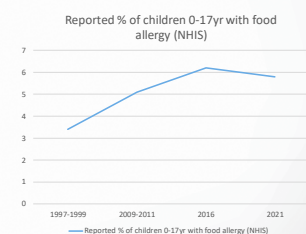
Food allergy incidence

- National Health and Nutrition Examination Survey (NHANES) 2005
 - 28% sensitized to a major food allergen age 1-5 yrs
 - 22% for 6-19 yo
 - Not a significant change from 1988-1994 data
 - * most ingested the food without reaction
- Australian studies from 2005, 2017
 - No change in sensitization (~21%)
 - Essentially no change in proven food allergy (~11%)
- Studies in Sweden had no appreciable change
 - Self reported, included ages 1-18 yrs

17

Food allergy incidence

- Incidence changes
 - National Health Interview Survey
 - Ages 0-17
 - 3.4% in 1997-1999
 - 5.1% between 2009-2011
 - 6.2% in 2016
 - ? Leveling out: 5.8% in 2021



18

Food allergy incidence

- Gabryszewski, SJ, Dudley J, Faerber JA, et al, Guidelines for Early Food Introduction and Patterns of Food Allergy. *Pediatrics*, 2025;156(5):e20240705



19

Gabryszewski, et al

- Multi-site EHR cohort analysis
- 2 yr observation prior to 2015 guidelines based on LEAP advice (2014-2016)
- 2 yr Post advice cohort (2017-19)
- 1 yr Post 2021 addendum cohort (2019-20)
- ~38000-46000 kids in each, age 0-3 yrs
- Children with Peanut FA and 1 or more FAs with or without preceding AD
- ICD-10 code, Epi Rx and 1 food allergy term in the allergy listing

20

Gabryszewski, et al

- Cumulative incidence of peanut FA decreased from 0.92% to 0.67% ($p < 0.0001$) in the post advice group
- Reduced incidence of Peanut FA, 1 or more FA and 2 or more FA in the post addendum group ($p < 0.0001$ in each)
- Reduced peanut FA in the prior egg FA group but not the prior AD group ($P < 0.05$)
- Egg became the most common FA in the postadvice group with.
 - Incidence of egg FA did not change
 - Cows milk FA incidence was reduced as well

21

Practical tips

- Smooth PB 2-3 tsp in 2-3 tbsps hot water, cooled, spoon fed
 - mix in with tolerated pureed foods
 - PN flour or powder
- Peanut teething puffs
 - Aim for 2g 3x/wk
 - 2 rounded tsp PB or 17 g Bamba
- Egg containing cake, muffins, then cookie, homemade waffle/pancakes, French toast
 - Baked egg or baked milk containing foods 350° F for 30 min minimum



22

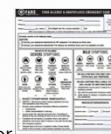
Practical tips

- Milk- formula counts already, baked foods that have milk as an ingredient
- Soy- soy milk, soy yogurt, tofu
 - Soy sauce doesn't have much protein
- Fish/Shellfish- what the family eats
 - If rarely eaten- encourage to at least try some
- Sesame- hummus, tahini (chocolate varieties exist)
- Wheat- soft pasta, bread or what you use for egg-containing foods
- If food allergic parent- ensure safe introduction, reduce possible contamination, maybe out of home.

23

Food Allergy Management Strategy

- Avoidance
 - Food label reading
 - Food allergy plans and medications
 - Prompt treatment of severe symptoms
- OIT (oral immunotherapy or oral induction of tolerance)
- SLIT (sublingual immunotherapy)
- Anti-IgE (omalizumab)



<https://share.google/images/ISGjdngTgzGXxdQ>



24

Food Allergy Management Strategy: New therapy highlights

- (Note: Sanford Fargo allergy clinic is not using OIT/SLIT at this time)
- Palforzia™: FDA approved peanut powder
 - Initial dosing challenge, then every 2 week up-dosing appointments
 - Oral desensitization meant to achieve dose of where accidental exposure of 2-3 peanuts is tolerated
 - Temporary vs sustained
 - 3x rate of reactions requiring epi vs avoidance
 - Frequent GI side effects
- SLIT: not FDA approved- some private clinics may offer
- Omalizumab: Age 1 and older
 - Dosing based on initial total IgE level and weight, SC injections every 2 or 4 weeks
 - Like Palforzia- meant to prevent reaction to accidental exposures, not induce sustained tolerance

25

Food Allergy Management Strategy

- neffy
 - 15-30 kg: 1 mg
 - 30 kg and up: 2mg
 - Mail order pharmacy, poor ins coverage
 - Longer shelf life- 30 months
 - Around \$200/2 devices out of pocket cost
- SL epinephrine film soon to be approved
- EPIT Epicutaneous immunotherapy in stage 3 trials



26

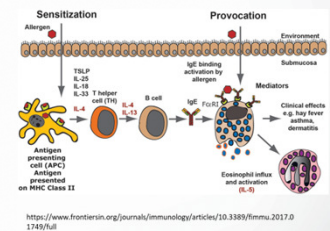
Biologics in atopic disease

- Injectable monoclonal antibody usually targeting a small upstream molecule that results in downregulation of relevant signaling, reducing symptoms, exacerbations, need for additional therapy
- Generally have been reserved for severe asthma, refractory chronic urticaria
- Expanded use with a variety of clinical atopic indications and new FDA approvals seemingly occurring every few months

27

Biologics in Atopic Disease: Pathophysiology

- Certain cytokines facilitate and provide signaling during APC presentation to T helper cells
- Induces differentiation of Th1 (infection) to Th2 (allergic)
- Th2 helps signal B cells to produce IgE producing plasma cells, increased cytokines recruiting eosinophils, mast cells, basophils



28

Where do biologics fit in therapy?

- Asthma: moderate to severe persistent asthma
 - Step 5 and 6 in NHLBI asthma guidelines
- Food allergy
 - High risk for accidental exposure
 - Poorly controlled comorbid diagnosis
 - Prior severe anaphylaxis
 - Studies underway for use with OIT
- Atopic dermatitis refractory to treatment
 - Failed topical steroids, topical calcineurin inhibitors
- Chronic idiopathic (spontaneous) urticaria
 - Failed high dose antihistamines, H2 Blockers, LTRA receptor antagonists

29

Where do biologics fit in therapy?

- Eosinophilic Esophagitis
 - Failed swallowed steroids, PPI, elimination diets
- Chronic Rhinosinusitis with Nasal Polyps
 - Failed intranasal steroids, surgery, polyp recurrence
- COPD
- Hypereosinophilic syndromes
- Eosinophilic Granulomatosis with Polyangiitis (prev. Churg-Strauss)
- Bullous Pemphigoid
- Purigo Nodularis

30

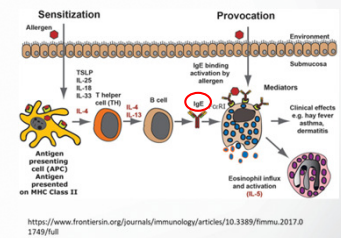
Biologics in Atopic Disease

- Current FDA approved biologics
 - Anti-IgE (omalizumab)
 - Anti-eosinophil cytokines
 - IL4&13 (dupilumab)
 - IL 13 (lebrikizumab, tralokinumab)
 - IL 5 and IL 5 receptor (benralizumab, mepolizumab)
 - Anti-TSLP (tezepelumab)
 - IL-31 blocking (nemolizumab)

31

Omalizumab (Xolair)

- Monoclonal Ab directed against IgE
 - Creates complex that cannot bind to the FCεRI
- Oldest of the atopy biologics
- Indications
 - Moderate to severe persistent asthma age 6 and up
 - Food allergy age 1 and up
 - Chronic Spontaneous Urticaria age 12 and up
 - Chronic Rhinosinusitis with Nasal Polyps (adults)



32

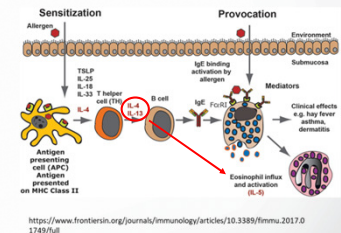
Omalizumab (Xolair)

- Dosing based on total IgE prior to treatment and weight
 - Standard monthly dose for CIU
- Well tolerated, general injection related effects
- Have seen some muscle pain (shoulder, back, thighs) and bone pain issues
- Anaphylaxis was a concern early on- very rare
- Will cause IgE levels to be inaccurate when checked
 - Allergy testing is affected as well
- More used for chronic hives than asthma now

33

Dupilumab (Dupixent)

- Monoclonal Ab vs IL-4/13
 - IL-4 and IL-13 share the IL-4α receptor chain
 - Reduces eosinophil production, recruitment
- Initial indication for AD
- Now AD, CSU, PN, BP, Asthma, COPD, CRS w NP, EoE



34

Dupilumab (Dupixent)

- AD: age 6 months (!) and up
 - Very safe and effective
- Asthma: 6 years and up
- EoE: age 1 year and up
- CSU: age 12 years and up
- CRS w NP: age 12 years and up
- Main adverse effects:
 - May have transient increased eos
 - Conjunctivitis
 - New onset psoriasis being reported
 - Arthritis
- Very well tolerated
- Dosing every 2 or 4 weeks based on weight

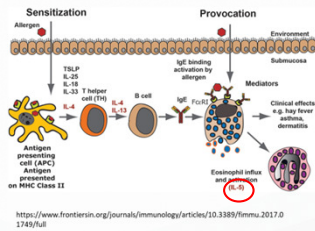
35

Anti-IL 13

- Lebrikizumab (Ebglyss)
 - Monoclonal soluble IL-13 Ab
- Indication for AD only
- Age 12 and up
- Loading dose, then every 2 weeks
- Newer
 - Conjunctivitis, zoster, site reactions
- Allows binding to IL-13Rα to recycle and down regulate receptor but blocks IL-13 signaling
- Tralokinumab (Adbry)
 - Monoclonal IL-13 Ab
- AD only, age 12 yrs and up
- Loading double dose, then every 2 week dosing
- Similar side effect profile

36

Anti IL-5/IL-5 Receptor



37

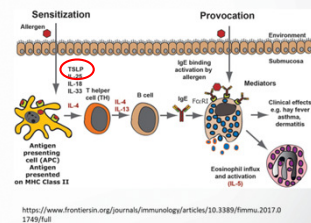
Anti IL-5/IL-5 receptor

- **Benralizumab (Fasenra)**
 - Age 6 and up for asthma
 - EGPA in adults
 - Every 4 weeks x3, then every 8 weeks
 - Site reactions
 - Used less often
 - Trials for other indications failed
- **Mepolizumab (Nucala)**
 - Age 6 and up for asthma
 - Age 18 and up for CRS w NP
 - Adults COPD
 - Adults EGPA
 - Hypereosinophilic Syndromes age 12 and up
 - Not as common, every 4 weeks

38

Anti- TSLP

- Tezepelumab (Tezspire)
- Age 12 and up asthma
 - Th2 high and Th2 low phenotypes
- CRS w NP age 12 and up (new indication)
- Well tolerated



39

Anti IL-31

- Nemolizumab (Nemluvio)
- Receptor present on dorsal root ganglion neurons
- Contributes to sensation of pruritus
 - Increased cytokine release of mediators leading to AD development
- Dosing every 4 weeks
 - New- I don't have experience with it yet
- Age 12 and up

40

Drawbacks

- Injection
- Cost, insurance coverage
- Manufacturer assistance programs can be difficult
- Delivery in rural areas
- Concern for live vaccines
 - Ok to give, but package insert hasn't changed for dupilumab

41

Practical aspects of biologics and benefits

- All current approved medications are SC injections
- "Personalized medicine"
- Initial hope for therapy was to reduce severe exacerbations
 - Dramatic drops in hospitalization for asthma from ICS when they were first approved
 - Now multiple disease, comorbidities being managed with biologics
- OCS sparing medications
- Cumulative adverse effects of OCS now being stressed
- Hope to actually affect disease progression as well

42

Benefits

- Game-changing medications
 - Especially for AD in young infants
- Dramatic difference in oral steroid use
- Management occurring with other specialties
 - Derm for AD, CSU
 - GI for EoE
 - Pulm for asthma, COPD
 - ENT for CRS w NP
- Very safe and effective medications- if called upon to write in care gaps, feel confident they are safe
- Some insurers require Epi Rx in case of reactions
 - Have only ever seen significant reaction with omalizumab once years ago

43

Comparative studies

- Head to head studies being done regarding anti-eosinophil biologics
- Dupilumab seems to be winning
- Few head to head studies in other conditions yet

Hung et al. Comparative Effectiveness of Dupilumab vs Mepolizumab and Benralizumab in Asthma: A multinational Retrospective Cohort Study. J Allergy Clin Immunol Pract 2025;13: 1707-16

44

Objectives

- Update on food allergy management
 - Review diagnostic strategies for food allergy
 - Outline current infant feeding recommendations
 - Present changes and future directions for food allergy management
- Update on use of biologic medications for atopic disorders
 - Review relevant pathophysiology of atopic disorders
 - Introduce how biologics work
 - Discuss current FDA approved biologics in allergy

45

Questions

46