Hot Topics in Pediatric Allergy

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Disclosures

• No financial conflicts
• I will provide some trade names as well as generics for some medications
Objectives

• Provide relevant updates in pediatric allergy topics related to diagnosis, management and prevention

• Discuss potential “pit-falls” in relation to evaluating pediatric allergy in the general pediatric practice

• Discuss evidence based treatment and new treatment modalities in allergy and immunology
Topics

- Allergic rhinitis (AR)
- Food allergy (FA)
- Urticaria
- Drug allergy (DA)
- Atopic Dermatitis (AD)
- Asthma
- Immunodeficiency
Allergic rhinitis

• “Hay-Fever”: itchy, stuffy, runny nose/eyes
  – Perennial: animal, dust mite, indoor molds, +/- cockroach
    • Asian Lady Beetle (*Harmonia axyridis*): cross reactivity with cockroach
  – Seasonal: “distinct” patterns, last longer than colds
    • Spring: trees, +/- molds
    • Late spring/summer: grasses
    • Summer/fall to frost: weeds, molds
    • Severe late summer, early fall, severe sudden onset asthma exacerbations: *Alternaria alternata*
      – Outdoor running in gym class
Allergic rhinitis

• Diagnosis: clinical history, testing
  – Current gold standard: Skin prick testing (IT’S NOT NEEDLES)
    • IgE response in the skin
    • Is affected by medications that have H1 blocking effects (TCAs, Benzos, atypical antidepressants, sedatives, +/- H2 blockers)
    • Not affected by oral steroids
    • Topical steroid could blunt response, but generally ok
  – Serum IgE testing/ImmunoCAP (old term: RAST)
    • Less reliable for aeroallergens
    • Negative results have good negative predictive value.
    • Not affected by antihistamines or steroids

Allergic rhinitis

• Pitfalls:
  – Intradermal testing (the needles): high false positive rate
  – Patients with atopic dermatitis/eczema or dermatographism
    • Sensitive skin, high overall IgE levels
  – Positive IgE does not equal clinical allergy in all cases
    • Tolerance to household animal, dust mites
  – Age may affect aeroallergen skin testing
    • 0-2 yrs: generally not enough exposure to seasonal allergens
    • Some children up to 6-7 years do not have + skin testing despite good clinical history of AR, + serum or asthma history
Allergic Rhinitis

• Try to avoid “I just want to know” testing
  – Test for things they can do something about: pets, dust mites or if interested in shots
  – Prior “house dust” tests are not common now
    • Swept up dust mixed with diluent from pet containing houses
    • Actual allergens are dust mites, cat, dog and cockroach, so they are tested for separately now
    • Everybody is bothered by dust, few people are allergic to the allergens in dust
AR Treatment$^{1,2}$

• H1 Blocking Antihistamines (AH)
  – 1$^{\text{st}}$ gen: diphenhydramine, hydroxyzine; sedating, OTC, cheap;
    • no role for these medications now with cheap, non-sedating medications available
  – 2$^{\text{nd}}$ gen: cetirizine (2yr+), loratadine (2+), fexofenadine (2+); non-sedating, OTC, safe
    • Desloratadine and Levocetirizine: No more efficacious and more $$; better results with urticaria
AR treatments

• Nasal steroids: 1st line therapy; aqueous sprays; drying, epistaxis
  – OTC: triamcinolone (2+), fluticasone (Flonase, 4+)
  – Rx: mometasone (2+), fluticasone (Veramyst, 2+); beclomethasone (4+, MDI-like device), $$

• Nasal decongestants
  – Caution with extended use: Rhinitis medicamentosa is generally worse than what you started with

• Oral Antihistamine/Decongestant combinations
  – Short term use with colds is about the only recommendation
AR treatments

• Nasal antihistamine: azelastine (5+)
• Nasal steroid/Antihistamine combination
  – Azelastine/fluticasone (12+), $$, rare ins. coverage
• Leukotriene receptor antagonist
  – Montelukast (1yr+); 20-30% non-responsive, psych effects, use with caution in ASD, behavioral or mood issues
  – Zafirluklast (5+); higher side effects, less convenient, $$
Treatment summary

- Most effective: intranasal steroids
- Intranasal steroids > AH + LTRA
- No benefit to adding LTRA or AH to Intranasal steroid in most studies
- Intranasal steroid + intranasal AH > than either alone (conflicting results)
- Europeans take an either/or approach
- US usually takes a step-up/additive approach
Subcutaneous Immunotherapy (SCIT)

• Only treatment that is curative (induces tolerance)
  – Improved rhinitis, conjunctivitis symptoms and asthma control
• Safe
  – 1 anaphylactic event/1 million injections given
• Cons:
  – Commitment
    • Build up phase, q3-10 days (x 30 doses)
    • Maintenance, q4 weeks x3-5 years
  – expense
  – (most) allergists desire willing participants
  – Wide variation in prescribing, even among allergists
    • formulation
    • schedules
Sublingual Immunotherapy (SLIT)

- Liquid drops:
  - Theoretically should be effective
  - not FDA approved
  - same solution as SCIT, hence billed the same but most not covered by insurance
  - Poor adherence rates
  - Popular with ENT providers
    - Specialty clinic in La Crosse, WI
Sublingual tablets

- FDA approved in spring 2014 for Timothy grass (Grastek), 5 grass mix (Oralair), and ragweed (Ragwitek)\(^4,5\)
- Good track record in Europe
  - Studies show efficacy, but slow to catch on in US\(^6\)
- Uncertain length of treatment
  - Can have lasting effects if taken year-round
- First dose taken in allergy office
  - Daily doses taken at home
  - Started 8-12 weeks prior to season
- Poor insurance coverage
- Adherence likely not better than drops
New therapies

• Pet, dust mite, cockroach SL tablets (eww...)
• Patches
  – Trouble with contact derm
• Intralymphatic (IL)\(^7\)
  – 3 total IL doses under ultrasound guidance into inguinal LN
    • Effective in trials in Europe
    • 15 US teens in randomized, D-B, placebo controlled trial demonstrated safety and tolerance using US extracts
• Little effect with air cleaners, HEPA filters on HVAC, frequent washing of pets
  – NO SUCH THING AS A HYPOALLERGENIC PET!!
Food Allergy Updates

• Most common cause of anaphylaxis in children
  – Anxiety provoking for parents
• Skin prick and serum IgE/ImmunoCAP testing
  – ISAC or “component” testing; maybe useful in future to determine risk of anaphylaxis or in cross-reactivity
• Still no role for IgG4 (Alcat) testing in food allergy
  – Popular with alternative practitioners
• Still can’t evaluate food intolerance
• Avoid curiosity testing
  – Caveat: new information on peanut allergy
Food Allergy Update

• Celiac disease: measure total IgA with TTG
  – Selective IgA deficiency est. incidence around 1/500
    • If IgA deficient: TTG IgA labs will be normal, but could still have celiac (IgG mediated)
  – Gluten free diet fad; possible non-IgE mediated pathology

• Eosinophilic Esophagitis
  – Children and teens with food impaction, dysphagia
  – Biopsy based diagnosis
  – Skin prick testing rarely helps identify foods to eliminate
    • Results on patch testing are mixed
    • Basophil activation assays may be the next step in diagnosis
  – Treatment with food elimination (4 vs 6 food), elemental diets, PPIs and swallowed MDI-delivered corticosteroids
“Red Meat” allergy

• IgE to galactose alpha 1,3 galactose on mammalian meats (alpha-gal)
  – carbohydrate attached to protein
• Delayed anaphylaxis 3-6 hours after ingestion
  – Fattier meats, more raw
  – Usually starts with palmar itching, redness
  – Can progress to anaphylaxis, treated in same way as immediate anaphylaxis with Epi, H1 blockers
• Association with tick bites
  – May resolve over time
  – Increased risk/recurrence with subsequent tick bites
Food Allergy Update

• Complementary food introduction in infants
• Feb 23 NEJM article, Du Toit et al.⁸
  – Randomized, open trial with no control group
  – 640 infants with severe AD, egg allergy or both
  – 4-11 months old
  – Skin prick to peanut
    • 2 groups: no skin reaction or 1-4 mm wheal
      – >5mm were excluded
    • Those groups were then randomized to receive or avoid peanut in specified amount
    • Consumption group had oral challenge to peanut
      – Positive oral challenge were placed in avoidance group, included in intention to treat but not per-protocol analysis
Peanut introduction article

- Consumption group
  - At least 6 g of peanut protein/week divided in 3 meals until age 5 years
    - 30 g of peanut = 2 Tbsp, 5-6 g = 1 tsp
  - Preferred source: Bamba snack
    - Alternative smooth peanut butter
  - Assessed adherence via questionnaire
    - At least 2 g in first and 2nd years on 1 or more occasions AND
    - At least 3 g (25g of Bamba or 12 g peanut butter) per week for 50% of the data collection weeks
Results

• 98.4% retention rate
• Primary prevention trial
  – Intervention meant to protect from a disease state not already present
• Primary outcome: % of patients with peanut allergy at 60 months of age.
Results (per protocol)

- SPT Negative Cohort (n=500): 13.9%
- SPT Positive cohort (n=89): 34%
- Both cohorts (n= 589): 17.3%

- Adapted from Du Toit, et al.
Discussion

• “...early sustained consumption of peanut product was associated with a substantial and significant decrease in the development of peanut allergy in high risk infants.”

• Wholesale change in complementary food introduction strategy coming? (opinion: yes)
  – More food allergy reactions at home at younger ages
  – More labs, more tests

• Advising caution at this time
Food Allergy Update

• Food recalls/allergy alerts:
  – Almost 1 a day
  – Most common items: the big 8
    • Peanut, tree nuts, milk, egg, fish, shellfish, wheat, soy

• Food immunotherapy
  – Oral (OIT)
    • Concern for causing EoE
  – Probiotics with OIT: good results with egg OIT
  – Epicutaneous (patch)
  – Chinese herbal preparations
Epinephrine delivery devices

• Epi-Pen®/Epi-Pen Jr®
• Auvi-Q™; voice direction like AED; current ND Medicaid preferred device
• Change dose at ~30kg from 0.15 to 0.3 mg
• Stability in heat/cold\textsuperscript{9,10}
  – Store room temp, away from light
  – 59-86\textdegree F
  – If frozen: may use if unthawed completely
  – If >38\textdegree C consistently: replace every 3-4 months
• Concerns about emergency departments or urgent care facilities unwillingness to use Epi during witnessed anaphylaxis
Urticaria

• Frequent referrals; frustrating results
  – Viral etiology, AD
  – Physical urticaria
    • Sun, cold, pressure, vibration, exertion, scratching, sweating
    • Good history for cold-induced hives: Give Rx for Epi-Pen and advise no swimming alone
  – The need for labs/testing...
    • Apart from history, extensive food/inhalant allergy testing and/or blood work is not cost effective and does not improve outcomes
    • Limited labs may be appropriate/optional, not necessary
      – CBC with diff, CRP/ESR, TSH, LFTs
Urticaria

- Chronic idiopathic; main treatments stay the same
  - usually resolves but can take years
  - H1 blockers: 2\textsuperscript{nd} gen AH (needs 2-4x normal dose most times for control), 1\textsuperscript{st} gen AH, doxepin
  - Dapsone, sulfasalazine, hydroxychloroquine: poor evidence, high side effects, lab monitoring
  - Omalizumab (12+); Anti-IgE treatment; FDA approved, good evidence, every 4 week injections, $$$$$
Drug Allergy Update

• Serum IgE tests exist; questionable utility
  – If positive: would certainly avoid
  – If negative: does not rule out either immediate or delayed reactions

• Penicillin testing
  – Good negative predictive value
  – Necessity vs. curiosity; willing participation
  – 6 skin prick tests, 7+ intradermal tests, takes ½ day to complete

• Local anesthetic skin testing/challenge
  – Similar to PCN testing; necessity vs. curiosity
  – Amide group and ester group
Drug Allergy Update

• Challenge vs. desensitization
  – Challenge: sketchy history, low likelihood of reacting, can be graded, open vs. blinded, generally office based; access to epinephrine auto-injector
  – Desensitization: good history or positive challenge AND necessity for medication (no alternative)
    • ICU or 1:1 nursing, IV based, 1-2 days to complete
    • Only desensitized for that course of medication
Food allergy and vaccines

• Egg allergy
  – MMR: safe. Negligible or no egg in vaccine
    • Skin tests not indicated
  – Influenza: safe. No contraindication
    • No testing needed
  – Skin prick testing: would grudgingly do if no other way to get parents to give vaccine
    • What to do if positive test that is likely irritation or due to atopic dermatitis??

• Component allergy: gelatin, neomycin, etc.
  – Avoid vaccine or consider graded challenge/desensitization
Atopic Dermatitis Updates

• Mainstay remains moisturization and topical steroids
  – Topical calcineurin inhibitors: pimecrolimus, tacrolimus
• Immunotherapy
• New medications on horizon:
  – Biologics: Anti-IgE, Anti-IL5, anti-TNF, anti-CD11a: mixed results
  – Barrier restoration with moisturization (Atopiclair, EpiCeram)
  – Anti-Staphylococcal treatments: bleach, intranasal mupirocin
• Pitfall: Serum IgE levels are high in AD: sometimes in thousands
  – Hyper IgE (Job) syndrome due to STAT 3 mutation is incredibly rare (1/1 mil)
  – Creates headaches for determining true allergy vs. sensitization or false positive due to non-specific IgE binding in ImmunoCAP assays
Atopic Dermatitis Update

- Wet wrap therapy
  - Soak/seal
  - Barrier to scratching
- Child bathes
  - 5-15 min, lukewarm
  - No soap
  - Bleach (capful) ok 1-2 times a week, not cracked skin
  - Pat dry
- Apply steroid to affected areas
  - Do not apply moisturizer/barrier cream over steroid
  - Light cotton pajama soaked in warm water, cover with warm sweatshirt/pants, blankets
  - Leave on 2 hours, take off, reapply moisturizer to all areas
  - Do not use wet wraps with TCIs
  - Can be done 2-3 times daily if severe
  - Can be limited to extremities
  - Eucerin, Cetaphil, Aquaphor, Vanicream
  - Use Aquaphor or Vaseline if white-based creams burn, create redness
  - Use antihistamines for pruritus
Asthma Update

• Success story, much fewer lengthy hospital stays with inhaled corticosteroids over last 20+ years
  – Asthma deaths still persist, worse in inner city, racial disparities

• Terminology
  – Asthma vs. reactive airways
  – Mild, moderate, severe
  – Intermittent, persistent
  – Allergic (eosinophilic) vs. neutrophilic phenotypes

• Diagnosis:
  – Spirometry (pre/post), Full PFT (with DLCO)
  – Methacholine challenge
  – Exercise challenge (treadmill, cycle)
  – Impulse Oscillometry
  – Exhaled Nitric oxide
Asthma Update

• Main treatment remains inhaled steroids for persistent asthma
  – Guideline update soon (?)
  – Concerns regarding growth velocity and steroids
  – LABAs and heart attacks (adults)
  – Discouragingly few new medications on horizon
    • biologics
  – Omalizumab (12+) for severe
  – Do medications affect long term prognosis?
  – Anticholinergics
Asthma Update

• Step down therapy if stable for 3-6 months
  – Difficult to justify prior to or during viral season
• Inhaled corticosteroids/Combination ICS+LABA
  – Beclomethasone
  – Fluticasone
  – Ciclesonide
  – Budesonide + Formoterol
  – Mometasone + Formoterol
  – Fluticasone + Salmeterol
Asthma treatment pitfalls

- Medication delivery
  - Kids don’t do DPI/diskus well
  - Same medication amounts with MDI + aerochamber vs. nebulizer
  - Aerochamber + mask can be more successful in young children who won’t sit for nebs
  - Caution using Advair diskus with milk allergy

- Medication adherence
- Diagnosis in preschoolers
- Obesity
Vocal Cord Dysfunction vs EIB

- **VCD Exercise symptoms:**
  - starts within just a few minutes of exercise
  - can have stridor +/- wheezing
  - rest resolves symptoms within a few minutes
  - may not occur again during exercise session
  - albuterol +/- effect, generally no effect with pretreatment
  - Teenager, anxious, “type-A”
  - Sensitivity to noxious odors
    - Choked up easily
  - Can occur while sitting quietly as well as exercise

- **Exercise induced bronchospasm (exercise asthma):**
  - usually does fine during exercise
  - cough + wheezing start 5-20 minutes after stopping
  - abated with pre-treatment of albuterol
  - Only occurs with exercise
  - Often has allergy history
Vocal Cord dysfunction

• Inspiratory flow loop flattened
• Laryngoscopy can confirm
• Breathing exercises
  – Refer to knowledgeable SLP

Immunodeficiency update

• Still very rare to find a true immunodeficiency
  – Truly sick kid vs. snotty, daycare kid with school aged siblings

• Finding Selective IgA deficiency more due to celiac testing
  – No specific treatment, most patients are asymptomatic
  – Concern regarding anaphylaxis with blood products or IVIG due to IgG against IgA

• IVIG (gamma globulin)
  – Transitioning more to SQ, home delivered, once weekly, higher trough levels
Immunodeficiency update

• New severe combined immunodeficiency (SCID) screening on newborn screens
  – Both ND and SD to team with Univ. of Iowa
  – SD: plan in place to start
  – ND: working on logistics/legislation and would like to start in 2016

• TREC assay
  • True SCID will be 0
  • Will pick up many lymphopenic disorders
When to work up immunodeficiency

- 8 + new ear infections in 1 year
- 2 + serious sinus infections in 1 year
- 2 + months on antibiotics without effect
- 2 + pneumonias in 1 year
- Failure to gain weight/grow in infancy
- Recurrent, deep skin or organ abscesses
- Persistent thrush in mouth or elsewhere after age 1
- Need for IV antibiotics to clear infections
- 2+ deep seated infections
- A family history of primary immunodeficiency
Basic work up

• CBC w/ diff
• ESR/CRP
• Immunoglobulins: IgG, IgA, IgM, IgE
• T, B and Nk cell enumeration (sometimes called immunodeficiency panel)
• Vaccine titers: diphtheria, tetanus, HiB, pneumococcal (send to Mayo)
• HIV 1/2
• Consider empiric GERD treatment in young children with recurrent sinus issues
References


