The Annual General Pediatric Review & Self Assessment

Nicklaus Children's Hospital

# ALLERGY


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# Disclosure of Relevant Relationship

Dr. Hernandez-Trujillo disclosed relevant conflicts of interests (COIs) and/or financial relationships in the past 24 months with the following ineligible companies:

| Role/ Type of Relationship | Ineligible Company(ies) |
|---|---|
| Advisory Board | Takeda, CSL, Regeneron/Sanofi, ARS, Bryn, Kaleo, Pfizer, Enzyvant/ SMPA, Genentech, Bayer |
| Consultant | Enzyvant, Kaleo, Takeda, Pharming |
| Speaker | CSL, Takeda, Genentech, Kaleo |
| Medical Advisory Committee | Immune Deficiency Foundation |
| Consultant | National Peanut Board |

All COIs have been mitigated prior to this activity

Dr. Hernandez-Trujillo will support this presentation and clinical recommendations with the "best available evidence" from medical literature.

Dr. Hernandez-Trujillo does not intend to discuss an unapproved/investigative use of a commercial product/device in this presentation.

# Outline

- Review of Allergies/ Atopy
- Anaphylaxis
- Bees, Wasps and other Stinging Insects
- Congestion and Coryza (ie: Rhinitis)
- Drug Allergy
- Eczema/Atopic Dermatitis
- Food Allergy
- Diagnosis/ Workup of Allergies
- Treatment
- Referral

# Atopy

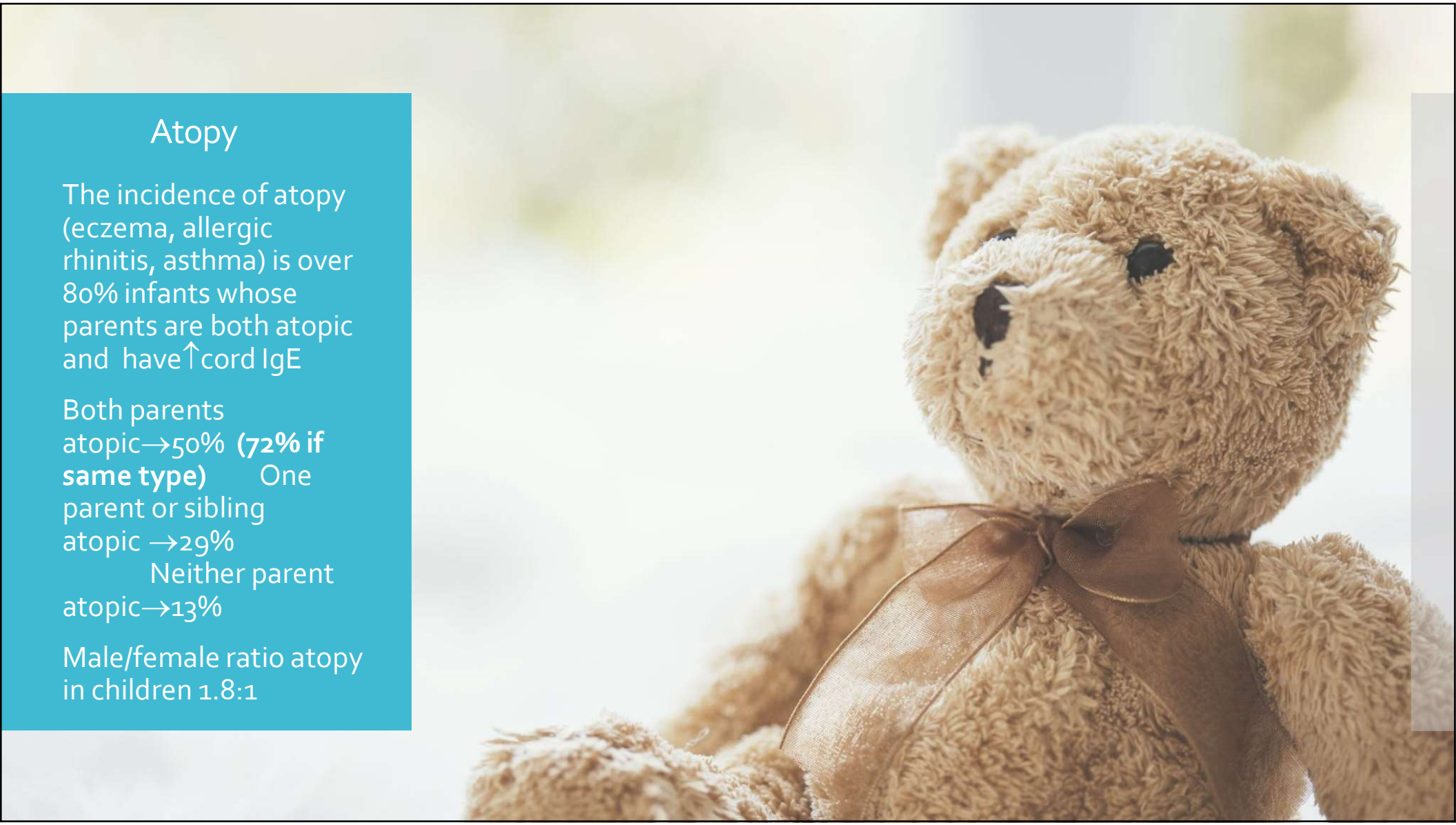
- Results from sensitization to an allergen
- Does not occur without prior sensitization**
- Many times patients are sensitized without knowing it- especially to foods/drugs
- Often seen in families- genetics is important
- 20-30% General Population
- 10-15% Children

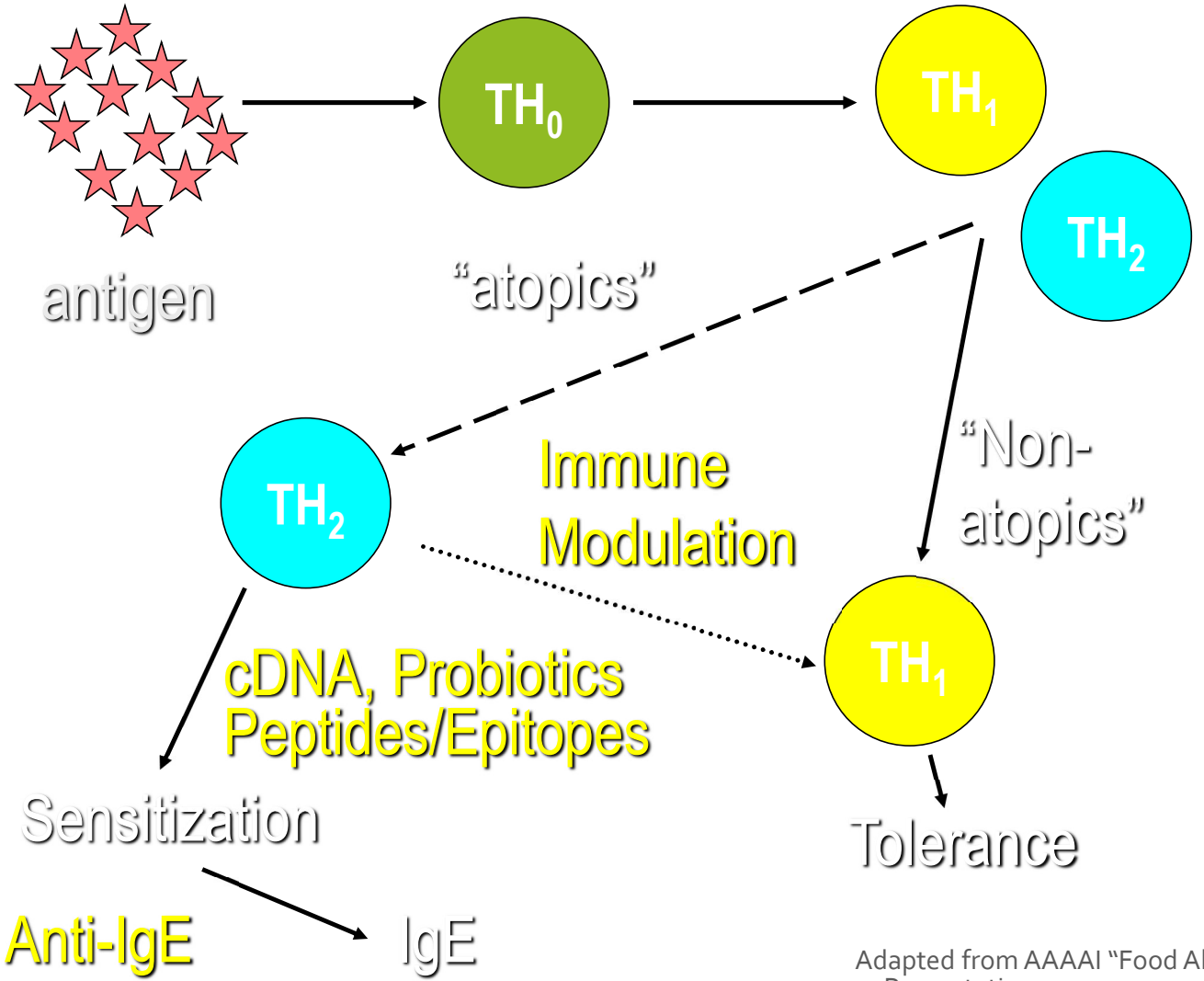
## Atopy

The incidence of atopy (eczema, allergic rhinitis, asthma) is over 80% infants whose parents are both atopic and have↑cord IgE

Both parents atopic→50% **(72% if same type)** One parent or sibling atopic →29%
Neither parent atopic→13%

Male/female ratio atopy in children 1.8:1






Adapted from AAAAI "Food Allergies" Teaching Slides Presentation

# Anaphylaxis

- Severe and life-threatening allergic reaction
- Occurs secondary to food, stinging insect, drugs, other allergens
- Often missed by clinicians- not all patients have hypotension
- Epinephrine is life-saving and first treatment that should be given at onset of symptoms

ARS question Case Study
A 6 year old male is stung by a wasp. He develops urticaria and swelling of the site. What recommendation should you make?

A. Allergy testing for wasp in one week
B. No allergy testing- avoidance
C. Daily antihistamines to avoid possibility of reaction
D. Immediate desensitization

Case Study
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# Stinging Insects

# Bees, Wasps, Stinging Insects

- Stinging insects are common causes of anaphylaxis-yellow jacket, hornet, wasp, honeybee, bumblebee, fire ant
- No workup is needed (or possible) for large local reactions to mosquitoes**
- Care of large local reactions- cold compress; mix hydrocortisone/ topical diphenhydramine/ topical antibiotic ointment; oral antihistamine if very itchy

# Insect Allergy

In children <16 years old, hives, large local reactions after stinging insect bite is not an indication for testing and immunotherapy

In children ≥16 years, generalized hives, shortness of breath, etc is an indication for testing- invasive- if plan is for immunotherapy

# Insect Allergy Recommendations

- Patients with a history of systemic reactions to insect stings should:
  - carry epinephrine for emergency self-treatment
  - avoid areas with possible exposure
  - undergo specific IgE testing for stinging insect sensitivity and be considered for immunotherapy
  - consider obtaining a medical identification bracelet or necklace

# Fire Ant Allergy

- Fire Ants cause large local reactions
- One ant will bite several times, often in a circle, leading to a toxic reaction
- Cellulitis can result- treat with oral antibiotic- many will improve

# Insect Allergy

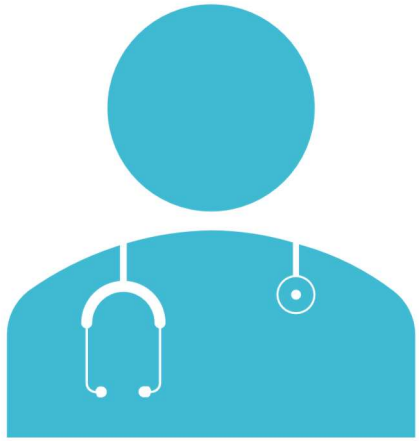
In patients with true allergy to stinging insects, should be given a prescription for epinephrine autoinjector and referral for testing/immunotherapy

Immunotherapy 5-7 years

Patients with systemic mastocytosis have higher likelihood of severe anaphylaxis to stinging insects

# Congestion (ie: Rhinitis)

- Part of the allergic triad (along with atopic dermatitis and asthma)
- 10-15% General Population
- Frequently seen in patients with environmental allergies
- Common causes include house dust mite, pet dander, cockroach, molds and pollens
- May influence ability to sleep-quality of life
- Seasonal Allergic Rhinitis- due to pollens
- Perennial Allergic Rhinitis- due to dust mite, pet dander, cockroach, indoor molds



# Look at my Allergic Shiners!!

- Dennie Morgan Lines or allergic shiners

# Drug Allergy

Often challenging

Diagnostic testing is not easy- resources/materials needed for reliable testing to antibiotics are not available

Avoidance of suspected drugs leading to reaction

Reliable testing is now available to penicillin if IgE mediated- not serum sickness or Stevens Johnson **

Desensitization necessitated if antibiotic absolutely needed

Many alternatives are available these days

# Gell and Coombs' Classification of Allergic Reactions

| | |
|---|---|
| Type I | Type I: IgE-mediated immediate-type hypersensitivity (anaphylaxis to antibiotics, allergic asthma) |
| Type II | Type II: IgG and IgM cytotoxic antibody (hemolytic anemia, granulocytopenia, thrombocytopenia from penicillin, Goodpasture's) |
| Type III | Type III: antibody-antigen immune complex (serum sickness from penicillin or heterologous antisera, SLE) |
| Type IV | Type IV: delayed-type cell-mediated hypersensitivity (contact dermatitis from neomycin, poison ivy, granuloma) |

ARS question Case study

A patient has a severe allergic reaction during a CT Scan with contrast media. Which of the following recommendations would you make?

A. Avoid all use of contrast media in the future
B. Avoid all iodine-containing seafood products
C. Avoid premedication prior to the next study
D. Premedicate with antihistamines and steroids

Case study
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# Contrast Media Reactions- Non-IgE Mediated

- Mediated through a mechanism other than IgE
- Patients should have low osmolar contrast agent used
- Patients should be premedicated with steroids 13, 7 and one hour prior to study, diphenhydramine one hour prior and ephedrine one hour prior to avoid reaction
- No correlation exists between shrimp allergy/iodized salt and contrast allergy!!

# Eczema/ Atopic Dermatitis

- Common in infants and young children
- 1-3% General Population
- In patients with moderate to severe eczema, 1/3 will have food sensitivity
- Hydration, Moisturization, use of antihistamines for itching, and avoidance of known allergens are essential
- Recent studies reveal use of emollients helps decrease the risk of eczema
- Important for above to be continued when skin clears- skin is not "normal" even when no lesions are visible

# Food Allergy

- Frequent cause of allergic reactions and anaphylaxis in children of all ages
- Allergy confirmed:  Children 6-8%  Adults 2-3.5%
- Cow milk**, soy, egg, wheat and peanut are the most common allergens in children
- Most common, outgrow cow milk, soy, wheat and egg allergy
- 85% Wheat, soy allergy remit by 3 yrs
- Rarely lose allergy to peanut, tree nuts, seafood
- Avoidance is imperative

# ARS Question

- What is the current recommendation regarding infant feeding in a child with mild eczema?

- A Introduce solids at 3 months
- B Exclusive breastfeeding until 6 months
- C Introduce Peanuts at 6 months
- D Introduce Peanuts at 24 months

# ARS Question

- What is the current recommendation regarding infant feeding?

- A Introduce solids at 3 months
- B Exclusive breastfeeding until 6 months
- **C Introduce Peanuts at 6 months**
- D Introduce Peanuts at 24 months

# New diets for infants





# Peanut Allergy Recommendations

- Study by G Lack and G DuToit 2015 LEAP study Feb 2015 NEJM
- Look at infants with severe eczema, egg allergy or both, considered at risk for developing PN allergy
- Randomized infants between ages of 4 and 11 months into 2 groups- consume versus avoid peanuts

# LEAP study NEJM 2015

"The early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk"

# Food Allergy

- New Guidelines have revolutionized our recommendations!
- **No longer recommended to avoid "highly allergenic" foods in hopes of decreasing prevalence of food allergy**
- Infants 4-6 months recommended to introduce solids- even egg, peanut, fish after traditional solids introduced
- No new food introduction if patient is sick***

# Food Allergy

- Food Introduction Guidelines
- Infants with either egg allergy, severe eczema or both, should be evaluated by testing to peanut prior to introduction- depending on results, determine whether should introduce and/or perform supervised oral challenge
- Infants with mild to moderate eczema should be introduced to peanut protein at 6 months
- Infants with no eczema or egg allergy should be introduced at the preference of the parents – no earlier than 4 months
- Always keep in mind the form of food for infant- discuss choking risk

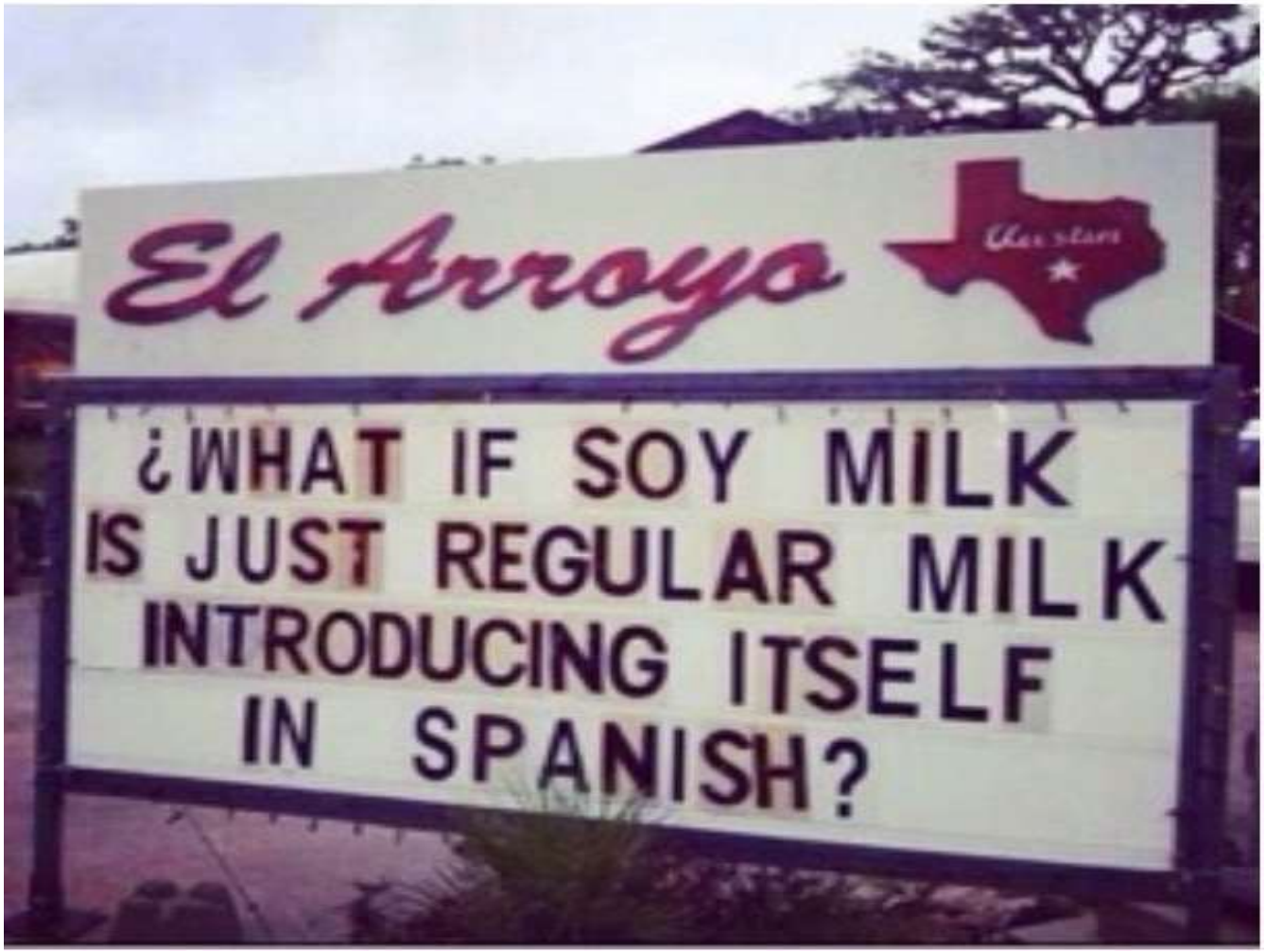
# New treatments for Food Allergy

- In 2020, first FDA approved oral immunotherapy for peanut for patients age 4-17 years old
- In Feb 2024, FDA approved treatment of food allergy- omalizumab starting at 12 months old
- Avoidance of food allergen is still needed- no "free eating" of the food allergen
- **Reminder- if patient reacts to food and has food allergy- need for strict avoidance exists **

# Challenge with Anaphylaxis to **known food allergen**

- Recent stories of children dying due to food allergy reaction treated with oral antihistamine either before epinephrine or never receiving epinephrine due to "masked" signs and symptoms- **beware** of recommending oral antihistamine in child with known anaphylaxis to food

- Anaphylaxis Action plans- Epinephrine first, then ER www.aaaai.org


El Arroyo
¿WHAT IF SOY MILK
IS JUST REGULAR MILK
INTRODUCING ITSELF
IN SPANISH?

ARS question Case Study

A 1 year old with egg allergy is due for the MMR? What is your recommendation for the patient?

A. Do not give the MMR
B. Skin testing to MMR, give if negative
C. Skin testing to MMR, desensitize if positive
D. Give MMR without testing

## Case Study
## A 1 year old with egg allergy is due for the MMR? What is your recommendation for the patient?

A. Do not give the MMR
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✓ D. Give MMR without testing

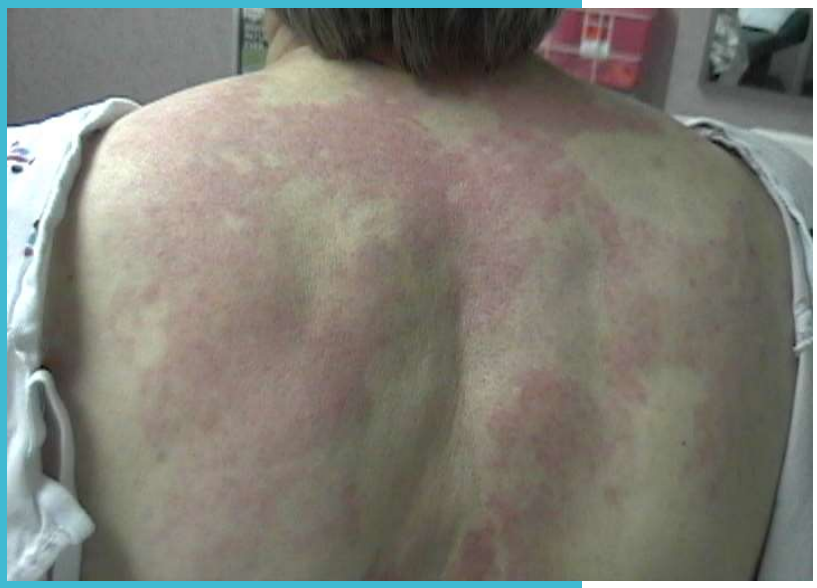
# Egg allergy and vaccines

- MMR can be given to egg allergic patients (AAP Red Book)
- Recent changes and reports of patients with egg allergy tolerating influenza vaccine- recommendations include giving influenza to egg-allergic patients. If anaphylaxis to egg, observe after influenza vaccine administration.
- Vaccines that should be avoided in egg allergic patients: Yellow fever

# Hives/Urticaria

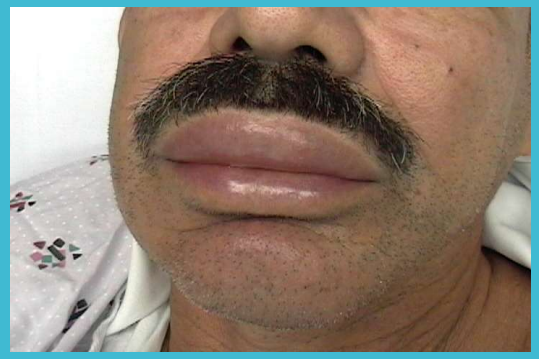
- The challenge for allergists, pediatricians and patients alike
- Often difficult to treat because no clear allergen is found
- Important to consider quality of life
- May need multiple medications to ensure symptomatic relief
- Up to 6-8 weeks- Acute
- More than 6-8 weeks- Chronic

# Acute Urticaria and Angioedema
(< 6 wk)



- Usually develops a short time from ingestion of allergen, resolves within hours
- More commonly IgE mediated
- Increased likelihood of finding etiology
- Beware- may be early sign of anaphylaxis

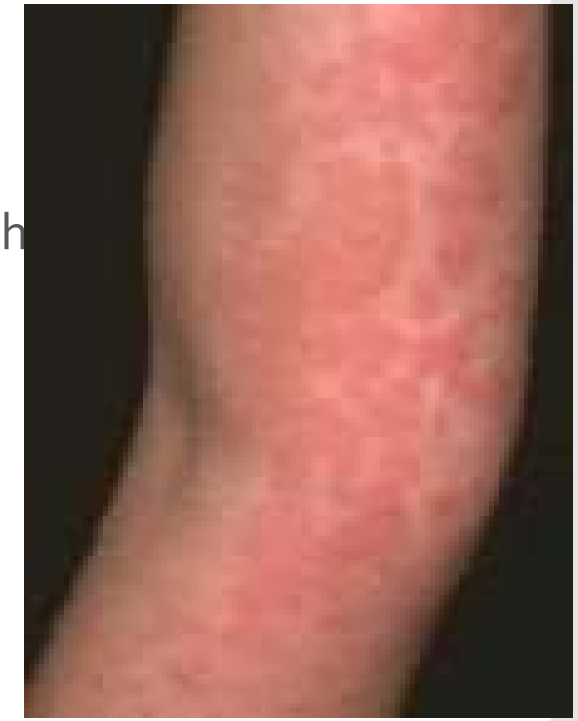
# Acute Urticaria and Angioedema: Etiology



- Viral syndromes (especially in young children)
- Insect bites or stings (fire ants, scabies)
- Food induced reactions (eat this- get that)
- Medication related (antibiotics, NSAIDs, narcotics, angioedema due to ACE inhibitors)

# Chronic Urticaria /Angioedema (> 6 wk)

- Chronic Urticaria – lasting longer than 8 weeks
  - Physical urticarias (dermographism, cholinergic, cold)
  - Urticarial vasculitis ****
  - Urticaria/angioedema associated with autoimmunity
  - Autoimmune urticaria (Autoantibodies to high affinity IgE receptors )
  - Idiopathic urticaria
- Chronic Idiopathic Urticaria Only 10% etiology defined
- Biopsy if lesion persists in same location for > 24 hours or purpuric



Urticaria

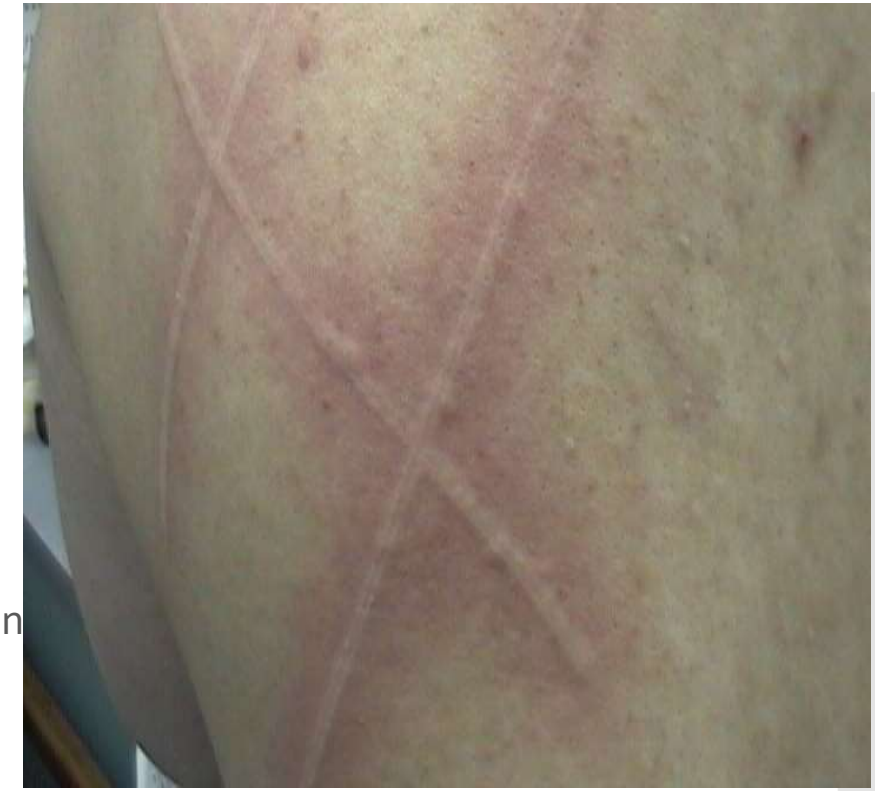
- Image from health-pictures.com

# Physical Urticaria

- Symptomatic Dermatographism
- Cholinergic
- Cold Induced (Familial or Acquired)
- Vibratory (angioedema)
- Pressure – induced, Solar, Aquagenic

# Dermatographism

- Simply scratching the skin promotes linear hives within minutes
- Delayed form described
- Typically is short-lived in duration (1/2 to 3 hours) and responds readily to antihistamines



AAAAI Urticaria and Angioedema Committee

# Workup of hives

- Acute hives  Observe
- Ask about ibuprofen/NSAID use prior to hives
- Infections are #1 cause of hives
- **Do not order random food tests** due to pressure from the families- this will bring more problems in the long run due to false positives and likelihood of missing true cause
- May treat with oral antihistamine course of 5-30 days to see if hives resolve

# Workup of chronic hives

- **Chronic Urticaria**

- Not likely to find cause
- No reason to perform Immunocap to food or environmental allergens on every patient
- Thyroid, Acute Hepatitis, Lupus Analyzer and Urine analysis

ARS question Case Study

A three year old girl presents with episodes of facial swelling and abdominal pain. The episodes have occurred on four separate occasions. No other symptoms- ie: urticaria seen.

The initial workup should include:

A. C1
B. C3
C. C4
D. C6

Case Study
A three year old girl presents with episodes of facial swelling and abdominal pain. The episodes have occurred on four separate occasions. No other symptoms- ie: urticaria seen. The initial workup should include:

A. $C_1$
B. $C_3$
C. $C_4$
D. C6

# Hereditary Angioedema

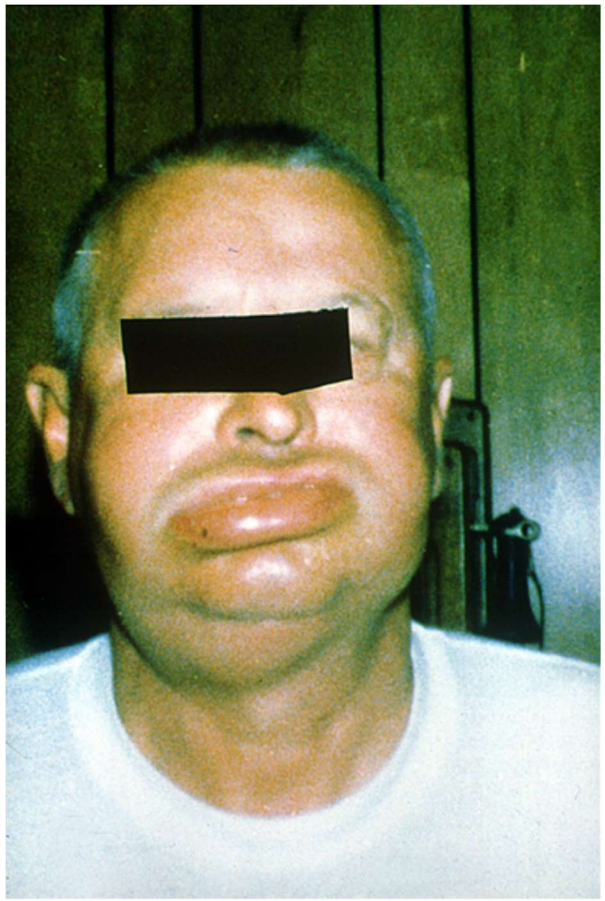
- Autosomal dominant with incomplete penetrance
  - Spontaneous mutations in 50%
  - Diminished $C_4$ between attacks
  - Very low $C_4$ during attacks
  - C1 esterase inhibitor protein low in about 85% of cases
  - C1 esterase inhibitor only functionally deficient in about 15%

Image from **health-pictures.com**

from AAAAI Urticaria and Angioedema Committee Slide Set

# Hereditary Angioedema

Image adapted from AAAAI Urticaria and Angioedema Committee Slide Set



- **Treatment**:

- No regular medication needed in many cases
- Prophylactic stanozolol or danozol; C1 esterase inhibitor for adults and children 12 years and older
- Epsilon aminocaproic acid (EACA) an option
- Fresh frozen plasma before emergency surgery
- C1 esterase inhibitor and kallikrein inhibitor- available for adults and children
- Symptomatic treatment during attacks

# Importance of IgE

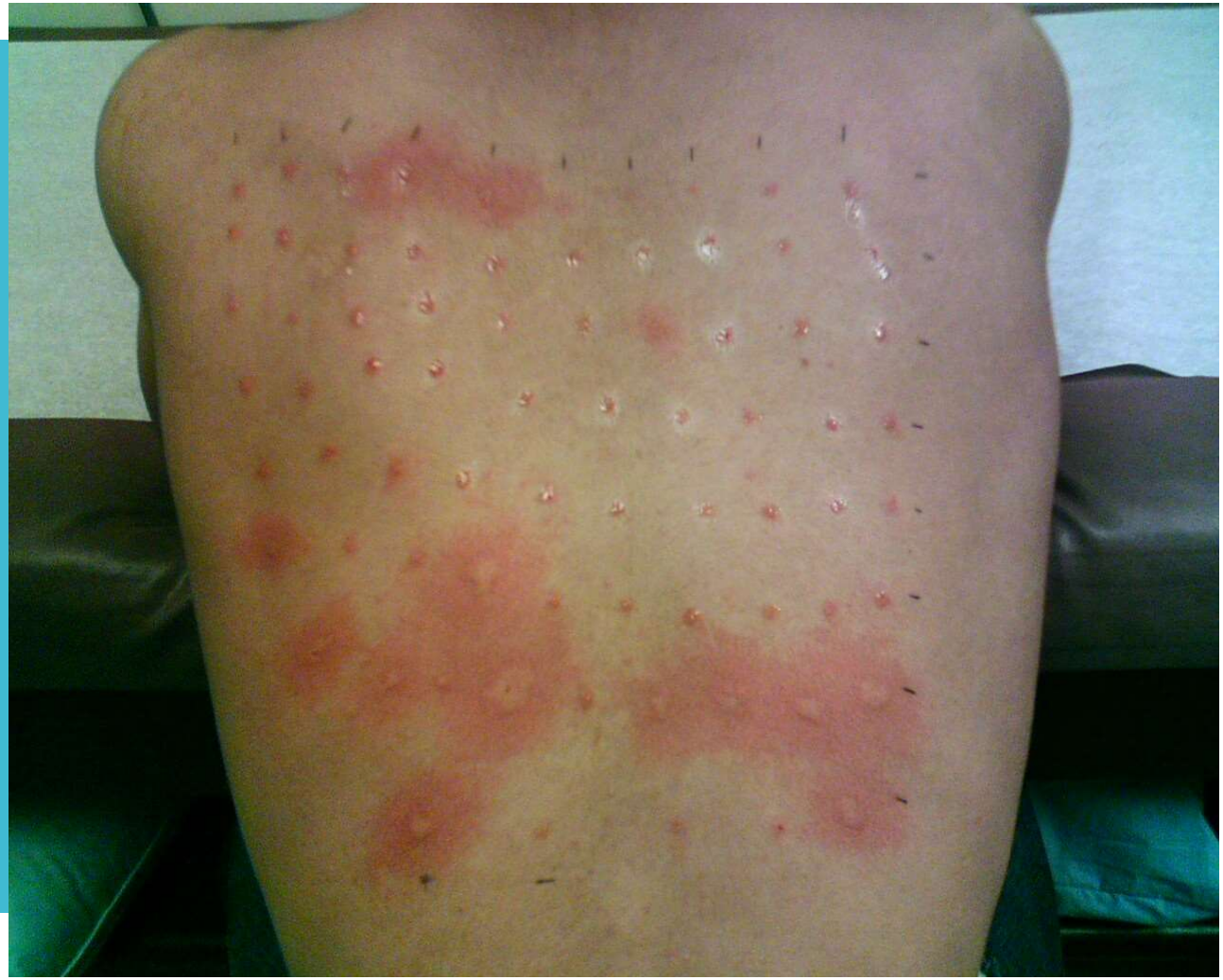
Obtain Total IgE when Specific IgE tests are ordered- if Total IgE is very high, may have nonspecific binding therefore use care with interpretation

Useful for diagnosis in patients with severe skin disease, patients unable to stop anitihistamines or tricyclic antidepressants, when risk of anaphylaxis if great based on history, uncooperative patients- behavior/autism

# Importance of IgE

Epicutaneous/ skin prick testing (SPT) is sensitive- more so than specific IgE- therefore the preferred method/ standard of care

Total IgE is elevated in several diseases including Atopic Dermatitis, Parasitic Diseases, Hyper IgE syndrome, HIV, Allergic Bronchopulmonary Aspergillosis



# Diagnosis of Allergies

- Testing is often needed to clarify whether a suspected allergen is indeed the cause of the reaction
- Skin prick testing is most sensitive test
- Prick skin test confirms the absence of IgE: negative predictive accuracy > 95%
- Immunocap/Specific IgE is specific- confirms **sensitization (not necessarily clinically significant allergy) to a food**- scale of Class 0 (negative) to Class VI (>100) very positive
- Beware of children with elevated IgE- "all" specific tests may look positive
- Interpretation in these cases requires careful review of history and correlation with Immunocap results

# Diagnosis of Allergies

In patients with one allergen Class I- may be clinically significant

In patients with elevated IgE, class I may not be significant. Either way, observation with the food is essential to confirm this.

Class VI more likely to be a significant allergen

# ARS question- Case Study Which of the following is an indication for immunotherapy?

A. Food Allergy
B. FPIES
C. Asthma
D. Urticaria

Case Study
Which of the following is an indication for immunotherapy?

A. Food Allergy
B. FPIES
✓ C. Asthma
D. Urticaria

# Indications for Immunotherapy

- The indications for immunotherapy include:
- Asthma
- Allergic Rhinitis- seasonal and perennial
- Hymenoptera
- Atopic Dermatitis- Dust

- Subcutaneous immunotherapy/ desensitization;
- Sublingual tablets approved for 5 grass mix in children 10 years and older for allergic rhinitis

# Diseases NOT Indications for Immunotherapy

- Urticaria/Angioedema
- Migraines
- Behavior Issues

# Treatment

**Avoidance, Avoidance, Avoidance** in Anaphylaxis, Stinging insects, Drug Allergy, Atopic Dermatitis, Food Allergy and Urticaria

Epinephrine in Anaphylaxis, Stinging Insects

New FDA approved treatment option in peanut allergy only: oral immunotherapy

New FDA approved treatment option food allergy: omalizumab

# Treatment

**<u>Other medications in:</u>**

Atopic Dermatitis- antihistamines/topical creams

Urticaria- antihistamines- often multiple; Chronic idiopathic urticaria refractory to treatment- Omalizumab

Rhinitis- Topical steroids** Gold standard/antihistamines-oral +/-topical/antileukotrienes

# Treatment

- Immunotherapy in Stinging Insect Allergy
- Allergic Rhinitis
- Asthma
- Atopic Dermatitis to Dust
- No immunotherapy in urticaria/angioedema at this time

# References


- AAAAI website. www.aaaai.org