Objectives

- Know the available treatment options for allergic rhinitis
- Understand clinical features, diagnostic testing and natural history of IgE mediated food allergy
- Become familiar with the recent LEAP study on the prevention of peanut allergy
- Know the available treatment options for chronic urticaria
- Understand clinical features, diagnostic testing and natural history of IgE mediated penicillin allergy

Allergic Rhinitis

- 10-30% of children and adults have environmental allergies
- Allergic rhinitis has a significant impact on quality of life
- Direct and indirect costs are high
  - Estimated 3.5 million lost workdays per year

Nathan, 2007
Cuffel et al, 1999

Allergic Rhinitis

- Treatment
  - Allergen avoidance
  - Oral antihistamines, oral leukotriene inhibitors, nasal antihistamines, nasal steroids
  - Short courses of oral steroids
    - Injections of steroids are not recommended
  - Nasal irrigation
Allergic Rhinitis

- Treatment
  - Subcutaneous immunotherapy
  - Sublingual immunotherapy
    - 1 year ago the FDA approved sublingual tablets for ragweed and grass allergy

Sublingual Immunotherapy

- Ragweed allergy
  - Ragweed pollen is one of the most common allergens
  - 26% of people in the U.S.
  - Symptoms occur in the fall

Sublingual Immunotherapy

- Ragweed allergy
  - Ragwitek
    - Indicated for ages 18-65 years
    - Dissolve tablet under tongue daily from May-November
    - First dose given in physician’s office

Sublingual Immunotherapy

- Grass allergy
  - Timothy grass is one of the most common grasses in the U.S.
  - Symptoms occur in the summer

Sublingual Immunotherapy

- Grass allergy
  - Grastek
    - Indicated for ages 5-65 years
    - Dissolve tablet under tongue daily from February-July
    - First dose given in physician’s office
    - Year round treatment for 3 years provided sustained benefit 2 years after cessation of treatment

Didier et al, 2011
Sublingual Immunotherapy

- Grastek

Grass allergy

- Oralair
  - Indicated for ages 10-65 years
  - Dissolve tablet under tongue daily from January-July
  - If >18 years old, first dose given in physician’s office
  - If <18 years old, first 3 doses given in physician’s office

Oral Allergy Syndrome

Due to cross-reactive allergens in pollen and plant foods

- Onset typically within 5 minutes of food ingestion
- Symptoms
  - Pruritus, tingling and angioedema of lips, palate, tongue or oropharynx
  - Rarely systemic symptoms

Common food triggers

- Raw fruits or vegetables
- Cooked forms are well-tolerated
IgE Mediated Food Allergy

- Prevalence
  - 3-4% of adults and 6% of children
  - Onset typically within seconds to 2 hours of food ingestion

- Symptoms should occur every time the food is ingested
- Exceptions
  - Small, sub-threshold quantities
  - Extensively baked, heat-denatured foods
- Symptoms
  - Skin
    - Pruritus, flushing, urticaria, angioedema
  - Respiratory tract
    - Rhinitis, sneezing, shortness of breath, cough, wheeze, chest tightness, laryngeal edema
## IgE Mediated Food Allergy

### Symptoms
- Gastrointestinal tract
  - Nausea, emesis, diarrhea, cramping abdominal pain
- Cardiovascular system
  - Dizziness, headache, syncope, shock

### Common food triggers
- **Children**
  - Milk, egg, peanut, soy, wheat, tree nuts, fish and shellfish
- **Adults**
  - Peanut, tree nuts, fish and shellfish

### Diagnosis
- **History**
- Specific food IgE testing or skin testing
- Oral food challenge

**Skin Prick Testing**
- Negative predictive value is >95%
- Positive predictive value is 30-50%
  - Larger size increases likelihood of clinical allergy

**Intradermal Testing**
- Not predictive and high risk for systemic reactions

**Serum IgE Testing**
- 10-25% of patients with negative IgE levels may have clinical reactions
- Elevated serum IgE alone is not diagnostic
- Higher levels increase likelihood of clinical allergy
- Level does not correlate with severity

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*Boyce et al, 2010*

*Petres et al, 2013*

*Bird et al, 2015*
IgE Mediated Food Allergy

- Unproven allergy tests
  - Serum IgG testing
    - Sign of a normal functioning immune system
  - Cytotoxic and ELISA/ACT testing
    - Evaluates changes to WBCs in the presence of allergens
    - Scientific studies have determined that WBCs change by many mechanisms, whether an allergen is present or not

- NAET (Nambudripad's Allergy Elimination Technique)
  - Evaluates changes in muscle strength as foods are placed in contact or close proximity with the body
  - There are no standards for consistent testing and no scientific studies have proven reliability

- Resolution
  - Wheat and soy
    - 85% outgrown by five years
  - Peanut
    - 20% outgrow
    - 7-9% redevelop allergy if peanut is avoided
  - Tree nuts
    - 9% outgrow
  - Seafood/Fish
    - Typically lifelong

Sampson, 1999

- Egg allergy
  - 53% outgrow by age 10 and 82% outgrow by age 16

Milk allergy
  - 80% outgrow by age 5

Savage et al, 2007
Sampson, 1999

- Heating milk and egg can denature conformational epitopes
- Many children with milk and egg allergy can tolerate baked milk or egg over time
- Children should continue eating baked milk and egg if already tolerating

Kim et al, 2011
Leonard et al, 2015

- Adding baked milk and egg to the diet
  - Increases quality of life by expanding the diet
  - Boosts nutrition
  - Promotes inclusion in social activities
  - May hasten the development of tolerance to lesser cooked or raw forms of milk and egg

Kim et al, 2011
Leonard et al, 2015
IgE Mediated Food Allergy

- Baked milk versus no baked milk

- Baked egg versus no baked egg

- History of reaction
- Milk IgE or egg IgE
- Component testing
  - Milk proteins
    - Whey (alpha-lactalbumin, beta-lactoglobulin) – heat labile
    - Casein – heat resistant
  - Egg proteins
    - Ovalbumin – heat labile
    - Ovomucoid – heat resistant

Vaccines
- MMR/MMRV
  - May be administered to children with egg allergy/anaphylaxis
  - However allergy evaluation and testing is recommended if gelatin allergy

- Rabies Vaccine
  - Innovax does not contain egg protein and can be used if egg allergy/anaphylaxis
  - RabAvert can also be administered if egg allergy/anaphylaxis

- Inactivated influenza vaccine
  - Egg allergy with hives only – administration by PCP with 30 minute observation
  - Egg anaphylaxis – administration by allergist
  - 28 published studies with 4315 patients with egg allergy including 666 patients with anaphylactic reactions to egg, received influenza vaccine with no serious reactions
  - Live attenuated influenza vaccine
  - Recent study of 68 children with egg allergy had no allergic reactions

Kelso et al, 2014
IgE Mediated Food Allergy

- Vaccines
  - Yellow Fever Vaccine
    - Allergy evaluation and testing is recommended if egg allergy/anaphylaxis

Kelso et al, 2014

Oral Immunotherapy

- Oral immunotherapy (OIT) for foods date back to 1905
- In the United States OIT is not a standard treatment
- However a recent article proposed that practicing allergists may consider OIT for treatment of patients with peanut allergy

Wasserman et al, 2014

Oral Immunotherapy

- Study Methods
  - Retrospective record review of 5 allergy practices
  - More than 350 patients treated for peanut allergy with 240,000 doses

Oral Immunotherapy

- Study Methods
  - Initial dose of peanut flour
    - Below the threshold dose for a reaction
  - Patients would continue the same dose 1-2 times daily for a defined period of time and then return to the site for dose increases
  - Dose increases were administered under direct observation
  - Once maintenance dose was reached the patients would continue dose 1-2 times daily for a prolonged period
  - Patients were instructed to avoid exercise for 2 hours after the dose and call if ill for dose adjustments
Oral Immunotherapy

- Study Results
  - 85% reached maintenance dose
    - Withdrawal was due to GI symptoms, taste aversion, anxiety, poor adherence, mild reactions, systemic reactions or uncontrolled asthma
  - 95 systemic reactions required epinephrine
    - 0.2 per 1000 doses

Future Immunotherapy Options

- Studies undergoing for sublingual food immunotherapy and epicutaneous food immunotherapy
- Maximal dose administered is limited by the small volume/surface area
- Small dose will protect against accidental exposures only

Food Allergy Prevention

- In 2000 recommendations for exclusion of allergenic foods from the diets of infants at risk for allergy and from diets of their mothers during pregnancy and lactation
- Studies have consistently failed to show that early elimination of foods from the diet prevents food allergies
- In 2008 the recommendations for avoidance were withdrawn

In February the LEAP (Learning Early about Peanut Allergy) study favored early introduction of peanut for infants at high risk for allergy

Du Toit et al, 2015
Food Allergy Prevention

Study Methods
- Randomized, open-label, controlled trial of 530 infants ages 4-11 months (Mean 7.8 months) with severe eczema, egg allergy or both

Infants underwent skin testing to peanut:
- >4mm were recommended to avoid peanut
- 1-4mm were challenged to peanut
  - If positive recommended to avoid peanut
  - If negative were randomly assigned to consume peanut or avoid
- <1mm were randomly assigned to consume peanut or avoid

Peanut puffs (Bamba) or smooth peanut butter was recommended three times per week until age 60 months

Study Results
- In infants with negative skin test results
  - At 60 months of age, 13.7% of avoidance group and 1.9% of consumption group were allergic to peanut (P<0.001)
  - 86.1% relative reduction in prevalence of peanut allergy

- In infants with positive skin test results
  - At 60 months of age, 35.3% of avoidance group and 10.6% of consumption group were allergic to peanut (P<0.004)
  - 70.0% relative reduction in prevalence of peanut allergy

Unanswered questions
- Is early peanut introduction indicated for low risk infants?
- Would infants who consumed peanut need to continue consuming consistently to prevent peanut allergy?
  - Under investigation in the LEAP-On study (Persistence of Oral Tolerance to Peanut)
- After prolonged cessation of peanut would children need to be challenged by an allergist in the office prior to reintroduction?
- Should early introduction of other allergenic foods be considered as well?

Current clinical practice guidelines have not yet changed in light of these studies
- Consider referral of infants with high risk for food allergies to an allergist for skin testing and further recommendations
Chronic Urticaria

- Hives that spontaneously present and re-occur for >6 weeks
- In 80-90% of children and adults no external allergic cause or contributing disease is identified
- Duration
  - 70% last >1 year
  - 14% last >5 years

Sheikh, 2005
Toubi et al, 2004

Chronic Urticaria

- Treatment
  - H1 antihistamines, H2 antihistamines, leukotriene inhibitors, systemic steroids
  - Antiinflammatory agents, immunosuppressant agents
  - Biologic agent
    - One year ago the FDA approved Omalizumab
    - >12 years of age symptomatic despite H1 antihistamines

Chronic Urticaria

- Omalizumab
  - Monoclonal antibody directed against IgE
  - Typically 300mg SubQ every 4 weeks
  - 53% were hive free and 66% had suppression of hives to a minimum level after 12 weeks
  - Hives can improve within days

Maurer et al, 2013
Penicillin Allergy

- Most commonly reported medication allergy
- Up to 5-10% of patients
- Large-scale studies found that 85-90% were negative on penicillin skin testing and tolerated penicillin

Park et al, 2006
Gadde et al, 1993

Penicillin Allergy

- IgE mediated reaction
  - Typically begins within one hour of the first dose
  - May take up to one hour especially if administered with food
  - May occur later in the course of treatment if not already sensitized
  - Should be within 1 hour of the dose and symptoms typically escalate quickly
  - Must rule out other severe drug reactions such as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)

Penicillin Allergy

- Symptoms
  - Pruritus, flushing, urticaria, angioedema, wheezing, laryngeal edema, emesis, diarrhea, hypotension

Wong et al, 2006
Solensky et al, 2000
Pattarca et al, 1987

Penicillin Allergy

- Diagnosis
  - History
    - Several studies show that IgE mediated penicillin allergy cannot be accurately predicted based upon history alone
  - In vitro testing
    - Sensitivity may be as low as 45% and specificity unknown
Penicillin Allergy

- Diagnosis
  - Skin testing
    - 1/3 of patients with vague reaction histories had positive skin testing
    - 50% lose sensitivity 5 years after reaction
    - 80% lose sensitivity 10 years after reaction
    - Includes both skin prick testing and intradermal testing

- Graded oral challenge
  - May be performed without testing depending on history
  - Performed after skin testing
    - Skin testing may miss 10% of penicillin allergy

Should I refer to an Allergist?

Consider referral

- Allergic rhinitis which is uncontrolled or interest in subcutaneous immunotherapy or sublingual immunotherapy
  - For evaluation, allergy testing and/or providing further treatment

Consider referral

- Concern for IgE mediated food allergy
  - For evaluation, allergy testing and/or possible oral food challenge
- Known diagnosis of IgE mediated food allergy with need for further education, testing or monitoring
  - For in-depth education on food allergies
  - For allergy testing to cross reactive foods
  - Monitoring for development of tolerance to baked egg or milk
  - Monitoring for outgrowing food allergy
  - If not outgrowing food allergy considering OIT

Consider referral

- Infant with high risk for food allergies
  - For allergy testing
- Chronic urticaria which is uncontrolled
  - For evaluation and providing further treatment
- History of penicillin allergy
  - For penicillin testing and/or oral challenge
Questions?