Case Studies on Updates in Allergy and Asthma

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Disclosures

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Case 1

A 26-year-old Caucasian female while hiking in a wooded area is stung on her left foot. Within minutes she has itching at the site. Her symptoms progress to generalized hives, shortness of breath and chest tightness. There is no phone service so her hiking partner attempts transport to the nearest emergency department. She becomes unresponsive on the way so her partner drives into your parking lot. Upon her arrival she is cyanotic.
Case 1 (continued)

She has no significant past medical history. She takes no medications. She is an avid hiker. She has never had a similar reaction.

Assuming this is anaphylaxis, how should you treat?
A. Evaluate ABC’s then immediately administer (1:1,000) 0.3-0.5 ml SubC or IM to her upper arm.
B. Evaluate ABC’s then immediately administer epinephrine (1:1,000) 0.3-0.5 ml IM to her thigh.
C. Evaluate ABC’s then immediately administer (1:10,000) 0.3-0.5 ml IM to her upper arm.
D. Evaluate ABC’s then immediately administer (1:10,000) 0.3-0.5 ml IM to her thigh.
E. Tell them to leave because this isn’t an emergency department.
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D. Evaluate ABC’s then immediately administer (1:10,000) 0.3-0.5 ml IM to her thigh.
E. Tell them to leave because this isn’t an emergency department.
Peak plasma epinephrine concentrations were significantly higher (P < 0.01) after epinephrine was injected intramuscularly into the thigh than after intramuscular or subcutaneous injection into the upper arm.

A previous study revealed 34% of people required a subsequent dose of epinephrine.
14% of those requiring any epinephrine required more than one dose.
Patients with a history of previous anaphylaxis, and those presenting with flushing, diaphoresis, or dyspnea, were more likely to require multiple doses of epinephrine to control symptoms.

Predictors of Repeat Epinephrine Administration for Emergency Department Patients with Anaphylaxis.
Anaphylaxis

• Anaphylaxis is a serious, life-threatening IgE mediated reaction.
• The most common anaphylactic reactions are to foods, insect stings, medications and latex.
• The immune system overreacts to this allergen by releasing chemicals that cause allergy symptoms.
Anaphylaxis

- **Cutaneous**: Pruritus, urticaria, flushing, angioedema.
- **Respiratory**: Bronchospasm, dyspnea, hypoxemia, laryngeal edema.
- **Cardiac**: Hypotension, shock, vascular collapse
- **Gastrointestinal**: Pain, nausea, vomiting, diarrhea.
- **Neurologic**: “Impending doom,” dizziness, loss of consciousness.
Clinical criteria for diagnosing anaphylaxis. Anaphylaxis is highly likely when any **one** of the following 3 criteria are fulfilled:

1. Acute onset (minutes to hours) with involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips–tongue–uvula)

**AND** AT LEAST ONE OF THE FOLLOWING

A. Respiratory compromise (eg, dyspnea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia)
B. Reduced BP or associated symptoms of end–organ dysfunction (e.g., hypotonia [collapse], syncope, incontinence)
Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

A. Involvement of the skin–mucosal tissue (eg, generalized hives, itch–flush, swollen lips–tongue–uvula)
B. Respiratory compromise (eg, dyspnea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia)
C. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
   A. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP*
   B. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person’s baseline
NIAID/FAAN anaphylaxis diagnosis Criteria cont’d

The study results showed that the NIAID/FAAN criteria were 96.7% sensitive, meaning that most patients who have anaphylaxis will meet NIAID/FAAN criteria. They also showed that the criteria were 82.4% specific, indicating that most patients who do not have anaphylaxis will not meet the NIAID/FAAN criteria.

Management of Anaphylaxis

• Evaluate ABC’s.
• Epinephrine (1:1,000) 0.3–0.5 ml IM lateral: may repeat in 20–30 min. IV epinephrine (1:10,000) used in profound shock.
• Diphenhydramine 50 mg or equivalent.
• More severe reactions may require vasopressors, intravenous fluids, oxygen, corticosteroids, and bronchodilators.
• Referral to allergist.
Case 2

A 30–year–old African–American female presents with exertional shortness of breath and wheezing which have gotten progressively worse over the last three spring seasons. She was treated with allergy shots (AIT) for two years as a child. She works as a national sales representative and travels frequently sometimes as much as 2–3 weeks at time. She is currently taking loratadine and albuterol daily for chest symptoms.
Case 2 (Continued)

Physical Examination:
Vital signs are stable.
Nose: pale 3+ turbinates.
Lungs: diffuse wheezing with fair excursion and prolonged expiratory phase.

Spirometry

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<tr>
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<td>FVC</td>
<td>1.558</td>
<td>1.635</td>
<td>105</td>
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<tr>
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<td>1.456</td>
<td>1.385</td>
<td>95</td>
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<tr>
<td>FEV1/FVC</td>
<td>0.934</td>
<td>84</td>
<td>8994</td>
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<td>FEf25%–75%</td>
<td>1.866</td>
<td>1.635</td>
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Can she have asthma with normal spirometry?
Case 2 (continued)
Spirometry Post bronchodilator

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<td>8994</td>
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<tr>
<td>FEf25–75%</td>
<td>1.866</td>
<td>1.635</td>
<td>88</td>
<td>2.304</td>
<td>123</td>
<td>40.92</td>
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A. She has moderate persistent asthma based upon daily symptoms and daily albuterol use.
B. She requires daily treatment with a low dose inhaled corticosteroid.
C. She requires daily treatment with a combination inhaler and short course of oral steroids.
D. She requires an allergy evaluation for probable allergic asthma.
E. She doesn't have asthma because her spirometry is normal.
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B. She requires daily treatment with a low dose inhaled corticosteroid.
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D. She requires an allergy evaluation for probable allergic asthma.
E. She doesn't have asthma because her spirometry is normal.
Asthma Triggers

IgE
- Pollen
- Dust
- Mold
- Pets
- Pests
- Food

Non IgE
- Infections
- Temperature Changes
- High Emotion
- Cold Air
- GERD
- Pregnancy
- Medications
- Irritants
- Exercise
Management of Asthma

• Avoidance Measures
• Medications
• Allergen Immunotherapy
Allergen Immunotherapy (AIT)

• AIT is the only treatment directed at resolving the underlying cause of allergy symptoms.
• Prevents asthma in 50% of children with allergic rhinitis. *(Jacobson)*
• Decreased asthma symptoms.
• Decreased asthma medications
Indications for Allergen Immunotherapy

- Allergic rhinoconjunctivitis
- Allergic asthma
- Hymenoptera hypersensitivity
- Possible prevention of asthma in children with allergic rhinitis

Subcutaneous Immunotherapy for Allergic Rhinoconjunctivitis: General Considerations

- In allergic rhinitis, immunotherapy is indicated for subjects:
  - In whom antihistamines and topical medications insufficiently control symptoms.
  - Who do not wish to be on pharmacotherapy.
  - In whom pharmacotherapy produces undesirable side effects.
  - Who do no desire to receive a long–term pharmacologic treatment.

Subcutaneous Immunotherapy for Allergic Asthma: General Considerations

- In allergic asthma, immunotherapy is indicated for subjects:
  - Who do not present a severe form of the disease, FEV1 levels should be over 70% from predicted values after adequate pharmacologic treatment
  - In whom symptoms are not adequately controlled by allergen avoidance and pharmacologic treatment
  - Who have both nasal and bronchial symptoms
  - Who do not wish to be long-term pharmacotherapy
  - In who pharmacotherapy produces side effects
Sublingual Immunotherapy

- Sublingual immunotherapy is a method of allergy treatment that uses a dissolvable allergen tablet given under the tongue.

- Approved by FDA in April 2014

- Three products: Grastek and Ragwitek (Merck) Oralair (Greer)
• Prescription medicine to treat Timothy and related grass pollen allergies.

• Reduces sneezing, runny or itchy nose, stuffy or congested nose, or itchy and watery eyes.

• 5 through 65 years of age who are allergic to grass pollen.

• 12 weeks before the grass pollen season and throughout the grass pollen season OR daily for 3 years to provide a sustained effect for a fourth year.

• NOT a medication that gives immediate relief of symptoms of grass allergy.

• Prescribe auto-injectable epinephrine

• First dose must be taken in the doctor’s office.

• Monitor for least 30 minutes for symptoms of a serious allergic reaction.
RAGWITEK®

- prescription medicine used to treat ragweed pollen allergies.
- Reduces sneezing, runny or itchy nose, stuffy or congested nose, or itchy and watery eyes.
- 18 through 65 years of age who are allergic to ragweed pollen.
- Begin treatment 12 weeks before the ragweed pollen season and throughout ragweed pollen season.
- NOT a medication that gives immediate relief of symptoms of ragweed allergy.
- Prescribe auto-injectable epinephrine
- First dose must be taken in the doctor’s office.
- Monitor for least 30 minutes for symptoms of a serious allergic reaction.
• Prescription medicine used to treat allergy symptoms.
• Reduces sneezing, runny or itchy nose, nasal congestion or itchy and watery eyes due to allergy to these grass pollens.
• 10 to 65 years old. NOT a medication that gives immediate relief of symptoms of ragweed allergy.

• Prescribe auto-injectable epinephrine

• First dose must be taken in the doctor’s office.

• Monitor for least 30 minutes for symptoms of a serious allergic reaction.
Case 3

A 52-year-old white male presents for evaluation of anaphylaxis. He is a bird watching enthusiast and on a recent camping trip woke up with generalized hives, SOB and near syncope which warranted an evaluation in the ED. He denies NSAIDS, pepto bismol, alka-seltzer.

Denies previous reaction to stinging insects. Denies being bit, stung or eating anything out of the ordinary. Over the past 15 months he has been taking Hydroxyzine, Afrin and loratadine for episodic hives and angioedema.
Case 3

PMHx – remote 6 year hx of frequent hives/angioedema 30 years prior.
He admits to searching the web for an explanation for his symptoms and asks if his hives/angioedema and anaphylactic reaction could be due to ticks.

What do you recommendation?
Case 3 (Continued)

A. Leave the research to the experts and refrain from reading entomology journals.
B. There is a relationship between tick bites and anaphylaxis.
C. He requires an evaluation for Type I, II and III Hereditary Angioedema.
D. He has Idiopathic Anaphylaxis, should carry autoinjectable epinephrine and return in 1 year for a follow-up.
Alpha Gal Allergy (galactose-α-1,3-galactose)

- Alpha Gal is a carbohydrate (sugar) found in all non-primate mammals.
- Humans have natural IgG and IgM antibodies against it.
- Is major antigen preventing hematologic transplants.
- (Lone star) tick saliva contains a substance which causes an IgE mediated reaction to Alpha Gal (galactose-α-1,3-galactose).
Lone Star Tick

Images of Ticks
Alpha-gal Allergy

- Delayed hypersensitivity reaction that occurs 3–6 hours after the ingestion of non primate mammalian meat.
- Presence of sIgE to cats, dogs and parasites.
- Characteristic geographical distribution in the US. (Southern states).
- Tick bites seem to underlie many cases of alpha-gal sensitization.

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Alpha gal Allergy

• IgE mediated reaction to alpha-gal may result in anaphylaxis.
• Prick to prick skin test to fresh mammalian meat.
• Obtain galactose alpha1,3 galactose level. Lab is commercially available.
Treatment of Alpha-gal Allergy

- Avoid tick bites.
- Avoid non-primate mammalian meat
- Emergency readiness
  - Autoinjectable epinephrine.
  - Medical alert bracelet.
  - Inform family and friends of allergy.
## Venom Hypersensitivity

<table>
<thead>
<tr>
<th>Genus</th>
<th>Common Names</th>
</tr>
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<tbody>
<tr>
<td><strong>Bees</strong></td>
<td><strong>Apis</strong> Honeybee <strong>Bombus</strong> Bumblebee</td>
</tr>
<tr>
<td><strong>Vespids</strong></td>
<td><strong>Vespula</strong> Yellow Jacket <strong>Dolichovespula</strong> Hornets <strong>Vespa</strong> European, oriental hornet</td>
</tr>
<tr>
<td></td>
<td><strong>Polistes</strong> Paper wasp species</td>
</tr>
<tr>
<td><strong>Ants</strong></td>
<td><strong>Solenopsis</strong> Fire Ants</td>
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Natural History

- 60% of patients with prior anaphylaxis and positive venom skin tests have repeated anaphylaxis on re-sting
- No relation between occurrence or severity of reaction and level of serum venom-specific IgE or concentration of venom that produces positive skin test
- Repeat anaphylactic episodes tend to be similar to initial reaction
Prevalence of Venom Sensitization

• History of systemic reaction in 0.5% – 3.0% of the population.
• Positive venom skin test or RAST in 15% – 25% of the population.
• Transient positive skin test or RAST may occur after uneventful sting.
• Presence of IgE venom antibody not necessarily predictive of clinical sensitivity.
Yellow Jackets are more abundant in the summer/fall, are aggressive and are responsible for the majority of responses to venom. They live in nests underground or in walls.
Bumblebees are not aggressive and rarely cause anaphylaxis.
Honey Bees

Honeybees are docile except when provoked.

Honeybee stinger, having multiple barbs, detaches from abdomen leading to bee’s death.
Honey Bee

Honey Bee Nests

Honey bees nest in hives and hollow trees.
Yellow Jackets are aggressive, more abundant in the summer or fall, and are responsible for most **allergic reactions**.
- They live in nests under the ground or in walls.
White and Yellow–faced Hornets

Both yellow hornets and white-faced hornets are aerial nesters that build large oval nests resembling Japanese lanterns in trees, shrubs, roof overhangs, or undersurfaces of wooden decks. The Vespa family of hornets are similar in most ways but are significantly larger.
Fire Ants

- Fire ants are non-winged Hymenoptera
- Reside in southeast and south central US
- Large subterranean nests
- Multiple stings common
- Sterile pustule at sting site
Examples of sterile pustules
Diagnostic Tests

- Purified, standardized venom from single insect and/or mixed vespids (YJ, YH, & WH)
- Prick skin test, then intradermal (0.01 mcg/ml)
- RAST for venom–specific IgE less sensitive
Diagnosis of Insect Sting Allergy

- Careful history to classify the reaction
- Venom skin tests
- Do not substitute *in vitro* assays of IgE for skin test
Insect Sting Reactions

- Usual reaction consists of localized pain, swelling, and erythema at the site.
- Peak at 48 hours, may last 7 days.
- Associated fatigue and nausea.
Management of Insect Sting Reactions

- Remove stinger and attached venom sac with blunt object (e.g., credit card, table knife).
- Avoid squeezing venom sac and injecting more venom.
- Managed with analgesics, cool compresses, antihistamines and oral steroids.
- Antibiotics and tetanus rarely needed.
Anaphylaxis to Stinging Insects

- May occur at any age; most frequent under age of 20
- 2:1 male: female incidence
- Symptoms usually start within 10–20 minutes
- Most fatalities reported in adults
- Subsequent stings often produce symptoms of similar severity
Toxic Reactions

- Occur after many simultaneous stings
- Similar clinical presentation to anaphylaxis
- Frequently stimulates production of IgE antibodies
- Potential risk for allergic reactions to subsequent single stings
Type III Immunologic Venom Reaction

- Venom–induced serum sickness may occur
- Urticaria, joint pain & fever 7–10 days after sting
- Both venom–specific IgE and IgG found
- Increased risk for acute anaphylaxis
- Venom immunotherapy protective for subsequent anaphylaxis
Prevention/Prophylaxis

- Minimize exposure to stinging insects: protective clothing, dark colors, minimal cosmetics/perfumes, avoid outdoor cooking/eating.
- Self-administered epinephrine.
- Antihistamines and Medic Alert bracelet.
- Venom immunotherapy highly effective in preventing recurrent anaphylaxis.
Indications for Venom Immunotherapy

- Positive venom skin test.*
- Requires documentation of venom-specific IgE.
- Hx of systemic reaction—Anaphylaxis.
- Serum sickness reactions.
- Toxic reactions.
- NOT indicated in cutaneous reactions in children or large local reactions.