

Insect Allergy

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November 14th, 2020

Objectives:

- Acquire the knowledge to differentiate the types of insect sting reactions.
- Review the treatments of insect allergy reactions.
- Develop the ability to recognize patients who need allergy testing for insect hypersensitivity.
- Understand the protective benefit of venom immunotherapy.

An 22 y.o. lifeguard is cleaning the pool when she is stung on the left ankle. Within 15 minutes she develops swelling of the left leg and hives of the chest, back, and face. She is treated with benadryl and all symptoms resolve over the next two hours. Which of the following is the best long term management plan?

1. Because her reaction was mild, no follow up is needed.
2. Prescribe epinephrine – remind her to carry it at all times during spring, summer, and fall.
3. Venom immunotherapy for 3-5 years.
4. Perform insect allergy testing followed by venom immunotherapy if positive.
5. Prescribe an epinephrine pen & give the patient detailed instructions on insect avoidance.

Overview

- The vast majority of insect induced anaphylaxis is due to stings from hymenoptera.
- Patients with large local reactions are at minimally increased risk for anaphylaxis.
- Patients with a systemic reaction to a sting must undergo skin testing.
- Inhalant allergy to insect emanations is underappreciated.

Systemic Reaction + Positive Allergy Test = Venom Immunotherapy

Hymenoptera

- Most hymenoptera are beneficial by providing crop pollination or by reducing pest populations.
- The stinging hymenoptera include the vespidae (wasps/yellow jackets), apidae (honey bees), and formicidae (ants).
- Vespidae is further divided into the vespula (yellow jackets) and polistinae (paper wasps). Apidae includes the European honey bee and Africanized honey bee.

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Sting Reactions

- **Normal reaction:** pain, erythema, and < 2 inches swelling. Subsides in 1-2 hours.
- **Large local reaction:** swelling > in size than patients palm
- **Anaphylaxis:** presentation similar to any other cause of anaphylaxis.
- **Toxic reactions:** non allergic reactions due to multiple stings.
- **Unusual reactions:** Serum sickness, nephrosis, encephalitis, Guillan Barre and others.

A 38 y.o. electrician is stung by a yellow jacket on the ankle while working. She develops swelling and extensive erythema of the ankle that gradually progresses up to the knee. Serologic testing for yellow jacket is positive at 8 ku/L. What is the most appropriate short term management?

1. Topical triamcinolone
2. Benadryl & Bactrim for 10 days
3. Prednisone and cefazolin
4. Cetirizine and oral cefazolin
5. Cetirizine and aspirin +/- prednisone

A 38 y.o. electrician is stung by a yellow jacket on the ankle while working. She develops swelling and extensive erythema of the ankle that gradually progresses up to the knee. Serologic testing for yellow jacket is positive at 8 ku/L. Which is the most appropriate **long term** management?

1. Advise her to avoid drinking from a soda can
2. Venom immunotherapy
3. Prescribe epinephrine injector
4. Skin testing followed by immunotherapy if positive
5. Advise use of an insect repellant such as DEET while at work

Large Local Reactions

- Peak at 48 hrs and last up to one week.
- Only dangerous on the head and neck area. Advise patients to drink from a translucent container when outside.
- Large local reactions tend to recur.
- Patients with large local reactions are not at significant risk of anaphylaxis.
- These patients do not *require* skin testing or venom immunotherapy.

Treatment of Large Local Reactions

- The usual treatment is aspirin and antihistamines.
- Severe reactions may be treated with oral steroids.
- The erythema may mimic cellulitis, although infection is rarely present and ***antibiotics are not necessary.***
- Epinephrine emergency kits are generally not required but may be considered.

A 55 y.o. man presents for acute care after a wasp sting with hypotension (70/30), angioedema of the hands, & hives. Current medications include HCTZ, metoprolol, simvastatin, and aspirin. His blood pressure has minimal response (80/30) to ranitidine, diphenhydramine, 2 doses of epinephrine (0.3 and 0.5 mg) and 6 liters of fluid. The next best step would be?

1. 3 more liters saline IV.
2. Dialysis to remove his metoprolol.
3. Intubation
4. Solumedrol 60 mg IV now & every 6 hours
5. Glucagon 3 mg IV over 5 minutes.

Anaphylaxis From Insects

- Have occurred in about three percent of the population.
- Causes about 100 deaths per year in the U.S.
 - mostly in males over age 40.
- The signs of anaphylaxis here are typical of anaphylaxis of any cause.
- Patients with anaphylaxis to an insect sting should undergo both venom skin testing and serologic testing.

Acute Treatment of Insect Sting Anaphylaxis

- Recognize anaphylaxis.
- Epinephrine is the only lifesaving medication.
- If there is no pressor response with epinephrine, give fluids, and consider glucagon.
- Albuterol/atrovent for wheezing that does not resolve with epinephrine.
- Little evidence that steroids help in the acute setting.
- Refer to an allergist for venom testing.

Epinephrine Kits

- They should *rarely* need to be used for insect reactions.
- May be used through clothing.
- 25% of cases of anaphylaxis may require a second dose prior to arrival at the emergency department.
- Carrying 2 doses is usually recommended.

Epinephrine Kits

- Available in 0.10 mg, 0.15 mg and 0.3 mg doses of epinephrine.
- Pediatric dose of epinephrine is ***0.01 mg/kg***
 - 66 pound child @ 2.2 kg/pound = 30 kg.
 - 30 kg x 0.01 mg/kg = 0.3 mg.
 - A child 66 pounds or greater should receive the adult dose epinephrine injector.

Toxic Reactions

- Similar to anaphylactic reactions but are due to multiple stings (10 – 2000) and are not immunologic in nature.
- Signs and symptoms - weakness, vomiting, bronchospasm, pulmonary edema, hypotension or hypertension, rhabdomyolysis, and acute renal failure.
- LD₅₀ is 19 stings/kg body wt. Fatal toxic reactions in adults occur most often after 1,100 to 1,400 stings.
- Severe toxic reactions are most often due to Africanized honey bees.

Treatment of Toxic Reactions

- Avoidance – take care before mowing over an area.
- Assessing the victim is dangerous – encourage them to leave the site and walk/crawl to an enclosed area.
- Epinephrine should not be administered for toxic reactions because patients often present with hypertension and myocardial injury.
- Elderly, pediatric and patients with medical conditions who receive > 50 stings should be admitted – CK-MB /renal panel/IVF/alkalinization of the urine.

Africanized Honey Bees

- The AHB is very similar to the European honey bee except for their very aggressive defense of the hive.
- A healthy adult can generally outrun a group of bees.
- As the 2 groups interbreed a hybrid species is developing that has intermediate characteristics with respect to cold tolerance, aggression, and resistance to colony collapse disorder.

Which of the following is true?

1. Insect sting reactions tend to get progressively more severe.
2. Fire ants are an uncommon cause of anaphylaxis in the U.S.
3. DEET is effective against stinging insects
4. Wearing bright colors is a reasonable bee avoidance measure
5. Venom immunotherapy is 98% effective in preventing insect anaphylaxis

Insect Avoidance

- Knowledge of nesting and foraging behaviors is important.
 - Honey bees generally live in abandoned logs and are aggressive near the nest.
 - Yellow jackets nest in the ground and are attracted to fruit, meats, and sweets.
 - Hornets build large paper Mache nests in trees. Stings are less common than with yellow jackets.
- Repellents such as DEET and permethrin are ineffective for stinging hymenoptera – however they are effective for biting insects.

Insect Avoidance – Honey Bees

- European honey bees are generally docile.
- The defensive area around the hive extends only a few feet.
- Rapid movement, leather, fur, perspiration, bright colors, and perfume attract bees.
- Honey bees eviscerate themselves when stinging and therefore can only sting once.
- If stung, the sac should be removed by flicking it to avoid injecting more venom.

Insect Avoidance – Vespids

- Attracted to food. Drinking from a clear plastic cup is protective.
- All food waste should be enclosed.
- Consider commercially available outdoor traps.
- Have professionals find and remove nests.
- Yellow jackets are not attracted to people.

A Controlled Trial of Venom Immunotherapy in Insect Hypersensitivity

- Previous treatment - whole body extracts.
- Patients placed into 3 groups of 20 patients matched for venom skin test response, venom IgE level, and venom induced histamine release.
- The 3 groups received 6 – 10 weeks of treatment with placebo (histamine), whole body extract, or venom extract and then underwent in hospital sting challenges.¹
- Placebo – 7/12 Whole body extract – 7/11 Venom 1/18 experienced systemic reactions.

Venom Immunotherapy

- Venom immunotherapy is the treatment of choice for anaphylactic insect sting reactions.
- Patients are a candidate if they have a history of a systemic reaction and a positive venom hypersensitivity test.
- Venom immunotherapy **prevents all fatal episodes** of insect sting anaphylaxis.
- Provision of an epinephrine injector is insufficient.

Who is a candidate for venom immunotherapy?

- **Patients with a systemic reaction and a positive skin or blood test for venom allergy** — (with the exception of patients < 16 years of age who had a cutaneous only systemic reaction)
- **Not usually indicated for large local reactors**
- **Screening the general public with insect allergy testing is not beneficial**

How long should patients remain on venom immunotherapy?

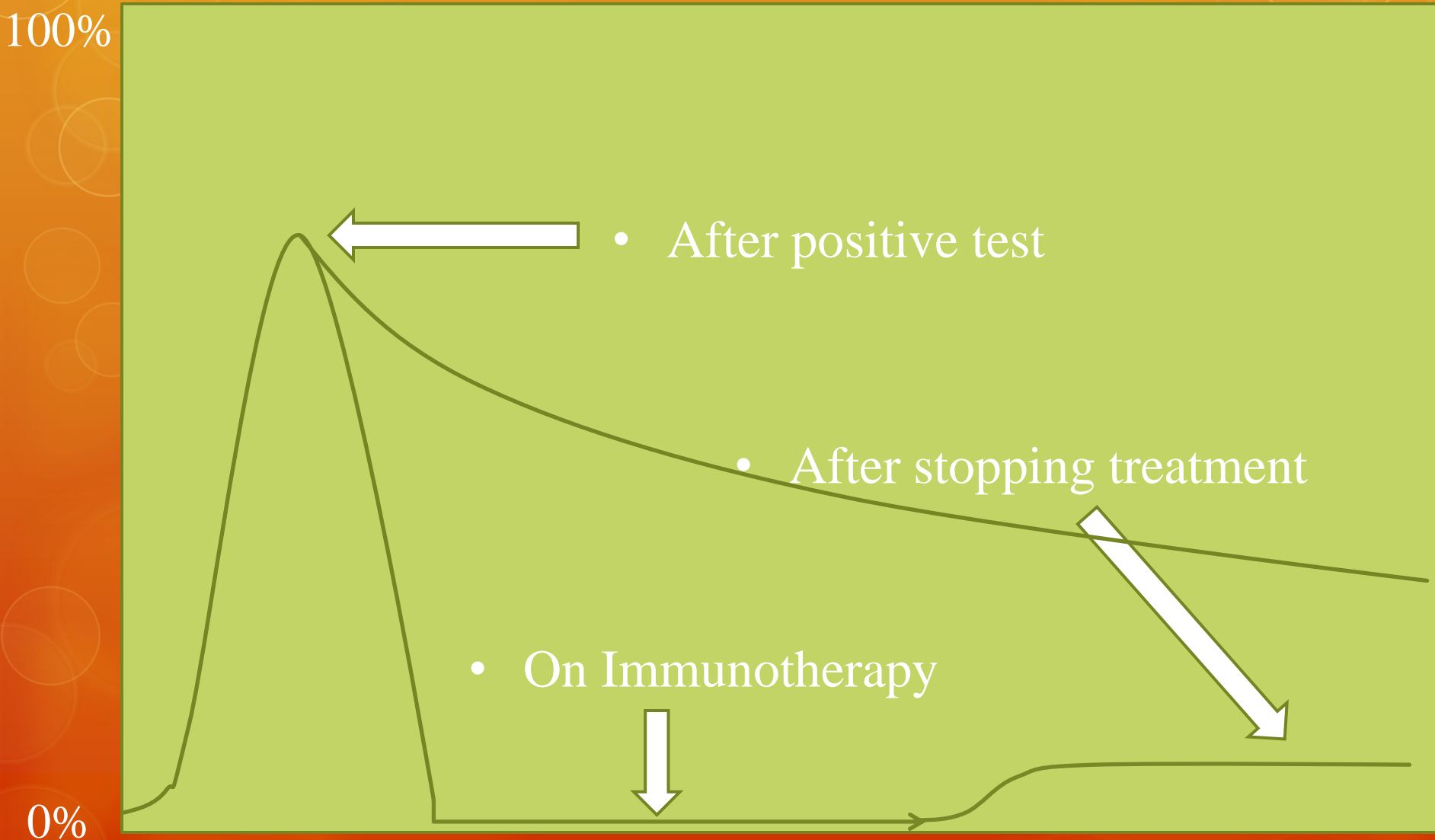
- If patients remain on therapy for 3-5 years and then stop, the risk of anaphylaxis with a future sting is around 5%.
- Generally most patients are encouraged to discontinue after 3-5 years, unless certain risk factors are present:
 - Prior near fatal sting
 - Anaphylaxis to venom immunotherapy
 - Honeybee allergy
 - Patient anxiety

Outcomes of Allergy to Insect Stings in Children, with and without Venom Immunotherapy

David B.K. Golden, M.D., Anne Kagey-Sobotka, Ph.D., Philip S. Norman, M.D.,
Robert G. Hamilton, Ph.D., and Lawrence M. Lichtenstein, M.D., Ph.D.

- Followed children with venom allergy for 20 years.
- Some had received venom immunotherapy and some chose not to and were only observed.
- 20 years after diagnosis, 3% of patients who had received venom immunotherapy reacted to a field sting as opposed to 17% of patients who had not received venom immunotherapy.
- Long term benefit from venom immunotherapy was previously unknown.

Risk of Venom Reaction



Imported Fire Ants

- Imported fire ants (*Solenopsis invicta* & *richteri*) were accidentally introduced into the port of Alabama in the early 1900's.
- Stings from imported fire ants are more common in endemic areas than stings from bees.
- IFA bite produces a sterile pustule – often distributed in a circle.
- Immunotherapy with whole body extract is effective in preventing fire ant induced anaphylaxis.

Imported Fire Ants

- Treatment with antihistamines, antibiotics, NSAIDs, or oral/topical steroids does not affect the evolution of the pustule.
- Anaphylaxis is commonly reported from IFA stings; pustules may become secondarily infected.
- IFA venom does not cause toxic reactions in spite of thousands of stings although fatal anaphylaxis is well described.

A.B. is a 19 year-old man with severe asthma symptoms present in May and June of each year. His symptoms have been getting progressively worse. Skin testing is positive for mold and dust mite. He feels that working on the Lake Erie islands triggers his symptoms but does not feel that vacuuming or musty basements are a trigger. His symptoms are rarely present during other seasons. What is the most likely exacerbating factor underlying his asthma?

1. Ozone exposure
2. Reflux disease
3. Mayfly
(ephemeroptera)
4. Dust mite
5. Cockroach allergen

Inhalant Insect Allergy

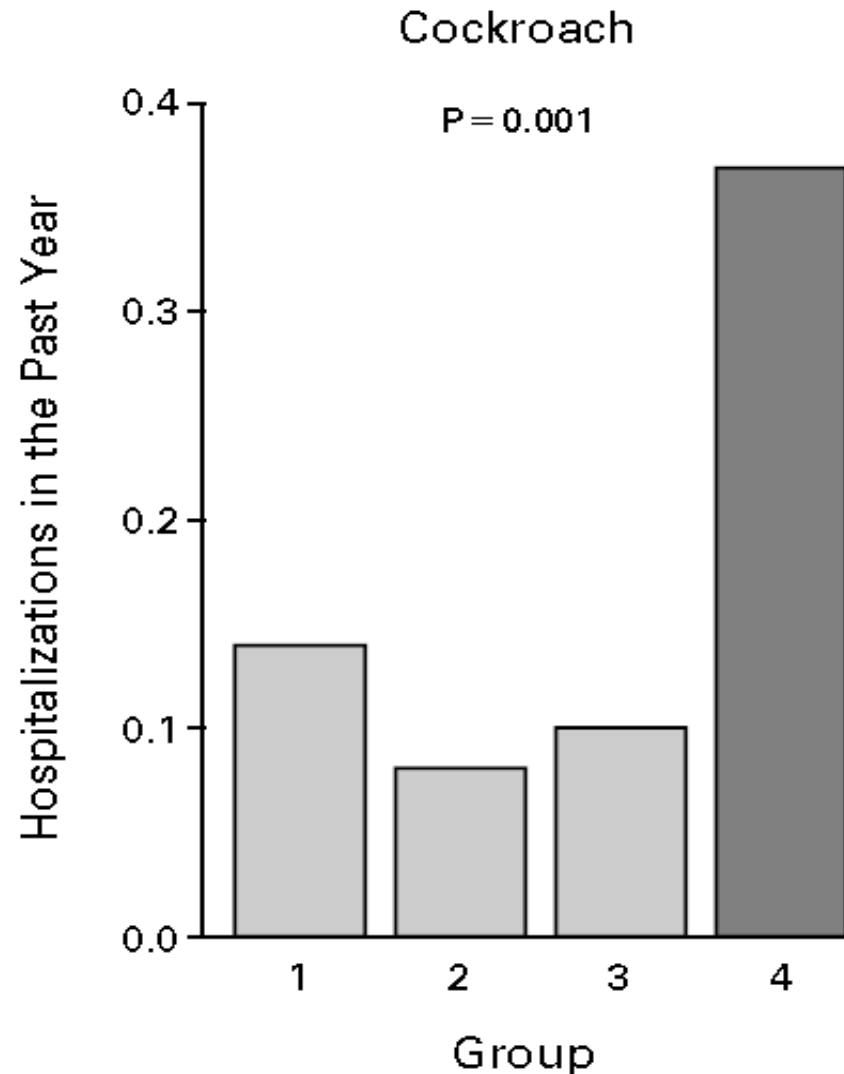
- Almost any insect allergen present in sufficient concentration can cause respiratory allergy.
- The most commonly reported insects are caddisfly, midge, asian lady beetles, and spider (citrus) mites.
- Treatment generally consists of avoidance and in some cases allergen immunotherapy.
- Overall the disease burden from inhalant insect allergy may be greater than from stinging insects.

Allergens in Asthma

Group Characteristics

1. Neither sensitized nor exposed.
2. Exposed but not sensitized.
3. Sensitized but not exposed.
4. Both sensitized and exposed.

NEJM 1997; 336:1356-63



Summary

- Local reactions to bee stings are not a risk factor for future anaphylaxis.
- Patients with systemic reactions to hymenoptera stings should undergo venom testing and need venom immunotherapy if positive.
- Patients experiencing anaphylaxis who are on a beta-blocker should receive glucagon.
- AHB has a strong tendency to swarm in defense of the hive but interbreeding will likely 'soften' the population.
- Fire ant induced anaphylaxis is common and treatable with immunotherapy.

The background is a solid orange color with a gradient from light orange at the top to a darker orange at the bottom. Scattered across the background are numerous thin, white-outlined circles of various sizes, some overlapping each other.

Thank You

Questions?

Mosquito Allergy

- Inject saliva as an anticoagulant in order to facilitate feeding.
- Reactions to mosquito bites are immunologic in nature and caused by reactions to the injected saliva.
- Human IgE and IgG specific for mosquito salivary protein correlate with each other and with the size of immediate and delayed reactions to mosquito bites.
- There are 5 stages of mosquito allergy.

Stages of Mosquito Allergy

Stage	Immediate reaction	Delayed reaction
1	-	-
2	-	+
3	+	+
4	+	-
5	-	-

Mellanby K. Man's Reaction Mosquito Bites. Nature 1946;158:554

Mosquito Allergy

Types of Reactions

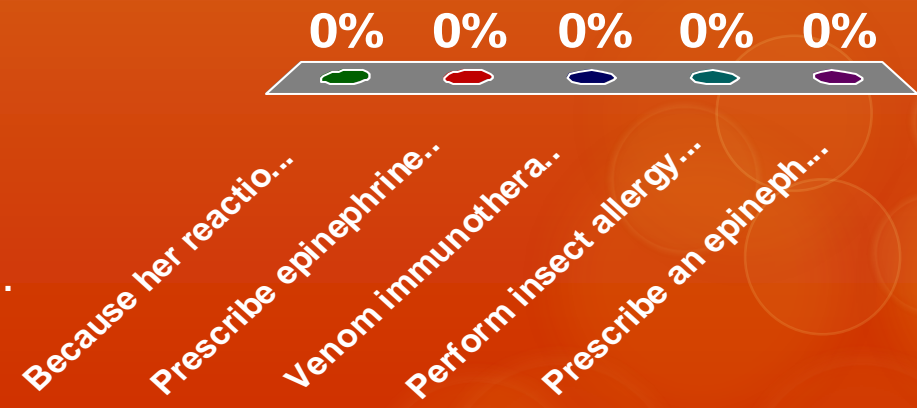
- Immediate reactions
 - Small wheals (normal)
 - Large immediate locals
 - Anaphylaxis (rare)
- Delayed reactions
 - small delayed papule (normal)
 - Skeeter syndrome (very large local reactions)
 - Papular urticaria
 - Large ecchymotic, vesicular, or blistering reactions (rare primary manifestation of NK lymphoma)

Mosquito Allergy

- As the natural history of mosquito allergy with repeated exposure is tolerance, the patients at greatest risk for mosquito allergy are those with low or absent natural immunity (young children or immigrants to a new geographic region.)
- Individuals with primary (congenital agammaglobulinemia) and secondary immune deficiency (HIV) and hematologic malignancy are at increased risk for mosquito allergy.
- Treatment of local reactions to mosquito involves avoidance measures (DEET/permethrin) and antihistamines, +/- oral steroids.

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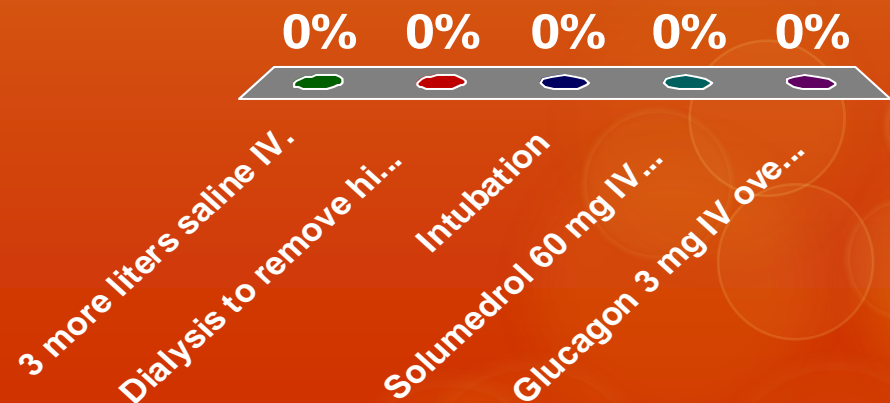
A 38 y.o. electrician is stung by a yellow jacket on the ankle while working on a residential project. She subsequently develops swelling and extensive erythema of the ankle that gradually progresses to involve the lower leg up to the knee. RAST testing for yellow jacket is positive at 8 ku/L. What is the most appropriate short term management?

1. Topical triamcinolone
2. Bactrim for 10 days
3. Lasix
4. Cetirizine and oral cefazolin
5. Cetirizine and aspirin +/- prednisone



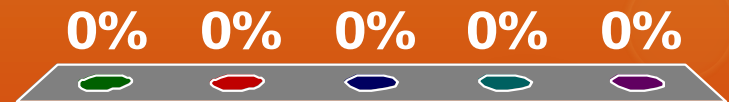
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Insect sting reactions...

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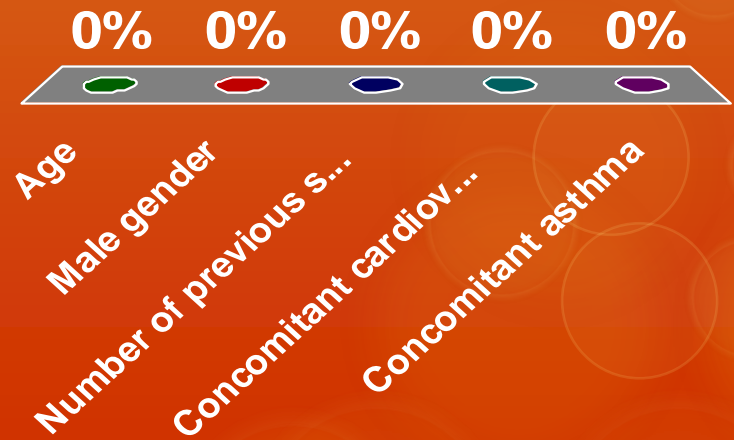
Venom immunothera..

Symptoms of Anaphylaxis

- Shortness of breath, wheeze, cough
- Hives, angioedema, flushing
- Stridor, laryngeal edema
- Hypotension, dizziness, syncope
- Abdominal pain, nausea or vomiting
- Rhinorrhea, lacrimation, sneezing
- Uterine cramping
- Chest pain (ischemia or esophageal edema)

Which of the following does not increase the risk/severity of an insect sting reaction?

1. Age
2. Male gender
3. Number of previous stings
4. Concomitant cardiovascular disease
5. Concomitant asthma



- points to make
- mention the allergy ROS
- mention that we need to perform both skin testing and RAST test and the akron allergist that went to trial for this.9
- • mention the reasons for anaphylaxis anyway in patients with neg skin tests and rast (reasons – too soon testing – too delayed testing – mastocytosis - .
- mention that venom IT is titrated up to about two venom sacs (but that VIT does not contain the bioactive amines.)
- describe a large local versus a systemic
- describe bee avoidance

Insect Sting Allergy

- There are between 50 and 100 deaths in the United States every year from insect stings. The majority of these occur in men.
- MJA 2000 – seven deaths were reported. All occurred in men over the age of 40 working in rural areas.
- JACI 1985 – These researchers examined 158 near fatal insect sting reactions. 118 of these patients were male and 40 were female.
- Insect reactions are probably more common in men because they more frequently work outdoors.

Toxic Reactions to Insect Stings

- Occur from massive envenomation (usually > 100 stings).
- The LD₅₀ for a 70 kg man is about 1,400 stings.
- Can be indistinguishable from anaphylactic reactions.
- Symptoms result from vasoactive amines present in the venom.
- May want to avoid epinephrine/adrenaline in this setting.

The Review of Systems

Review of Systems

gen – denies unintentional weight gain or loss

cardiac - no loc no palpitations

pulm – denies cough - no wheeze no shortness of breath

gi - no n/v/d/c – denies heartburn

neuro - no HA - no seizures – no weakness or

numbnessderm - no skin rash no pruritus

infectious – denies recurrent infections or fevers

allergy - no prior reactions to venoms or foods

Hymenoptera Venom – What is in it?

- Vespula Venom – Antigen 5, phospholipase, hyaluronidase
- Polistes Venom – high sequence homology to vespula
- Honey/Bumble Bee Venom – phospholipase, hyaluronidase
- All hymenoptera venoms contain non-allergenic vasoactive amines such as dopamine and norepinephrine and apamin (a neurotoxin).

Overview

- There are 50 documented deaths in the U.S. each year from venom anaphylaxis. There are likely other undiagnosed deaths from this disease.
- Patients with venom hypersensitivity live in fear.
- Venom Immunotherapy is 98% effective in preventing venom anaphylaxis.
- The best test for venom hypersensitivity is the clinical history.
- 3.3% of adults have a history of venom anaphylaxis (they almost invariably don't mention it.)
- Look for it and you'll find it.

Bee Sting Myths

- In most studies only 3% of patients with a systemic reaction to a sting had a future reaction that was more severe.
- Sting's don't tend to get progressively worse.
- Future reactions tend to be around the same severity as the prior reaction.

Killer Bees in Oklahoma

8/26/2004

OKLAHOMA CITY (AP) -- A swarm of bees that attacked a work crew earlier this month may be of the Africanized variety, which would mark the furthest north the so-called "killer" bees have traveled in the United States, scientists said.

DNA tests show the bees have Africanized traits, said Russell Wright, head of the Department of Entomology and Plant Pathology at Oklahoma State University. "They certainly are more Africanized than European," he said.

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Epinephrine

- Usually comes as a 1:1000 w/v solution
- Expiration date is important (may get a brown discoloration)
- Intramuscular in the lateral thigh (not subcutaneous)
- Adult dose for severe asthma/anaphylaxis is 0.3 to 0.5 mg IM (0.3 – 0.5 ml of 1:1000 solution).

Epinephrine

- Adult dose for cardiac arrest is 1.0 mg (1 ml).
- Pediatric dose for anaphylaxis is 0.01 mg/kg up to 0.3 mg.
- Often need to repeat the dose. WHO guidelines recommend having one dose on hand for every 20 minutes travel time to hospital.
- If giving IV or ET will need to use a 1:10,000 solution

Treatment Schedule – doses given at weekly intervals

1 mcg/ml

1. 0.05 cc
2. 0.1 cc
3. 0.2 cc
4. 0.4 cc

10 mcg/ml

5. 0.05 cc
6. 0.1 cc
7. 0.2 cc
8. 0.4 cc

100 mcg/ml

9. 0.05 cc
10. 0.1 cc
11. 0.2 cc
12. 0.4 cc
13. 0.6 cc
14. 0.8 cc
15. 1.0 cc – maintenance dose

Maintenance dose given monthly for 1 year then every 6 weeks for 3 – 5 years.