

Bee Sting Allergy

What You Need to Know

Hymenoptera Venom Allergy

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Bee Sting Allergy

- Case Report
- Definition and Scope
- Allergic reactions
- Other conditions that may mimic
- Prevention and Treatment, epinephrine injection
- How venom shots work
- Questions

Patient B

- 62 yo beekeeper developed generalized urticaria (hives) 5-10 minutes after stung on the neck once
- Head felt hot, flushed and 'under pressure'. Lips felt numb and swelled
- No respiratory, cardiovascular or GI symptoms.
- Symptoms resolved over 30 minutes after 50 mg diphenhydramine (Benadryl)
- Patient had an Epi-Pen and driver on hand
- 3rd season as beekeeper, app. 24 stings/year with large local reactions (LLR)

What to do?

Give up beekeeping
and find a new hobby?

Seek medical solution
to keep bees?



Patient B

- Allergy tests highly reactive to honey bee venom and mildly to 2 wasp venoms
- Immunotherapy begun to all three. Minor local reactions only
- 9 weeks buildup to maintenance level.
- Schedule then switched to every 4 weeks. Over 3 years reduced to every 7 weeks.
- Keeping bees again.
- Prior large local reactions are smaller.
- No systemic symptoms to stings.

Definition

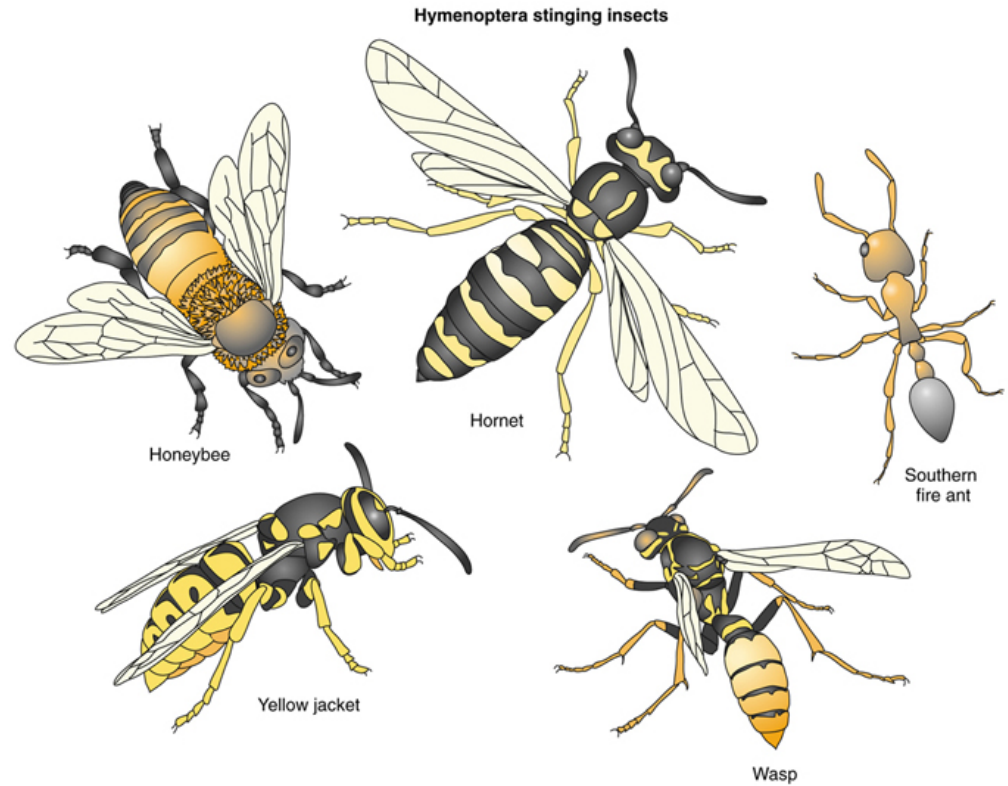
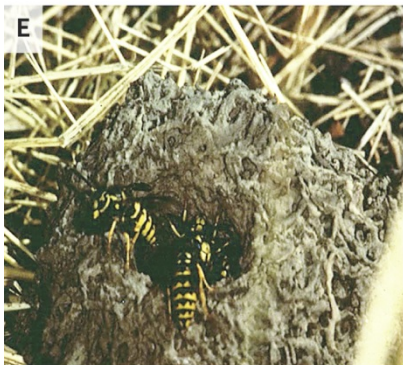
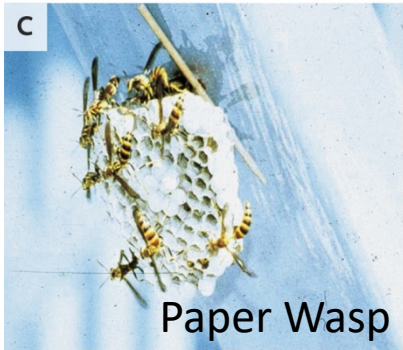
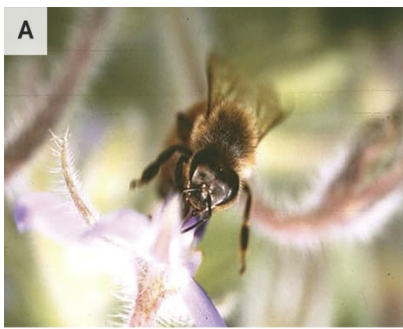
- Immunoglobulin E (allergic antibody IgE) mediated
- Only in previously sensitized individuals
- Multiple species in Hymenoptera order

Classification

- Kingdom: Animalia
- Phylum: Arthropoda
- Class: Insecta
- Order: **Hymenoptera**
- Family: Apidae, Vespidae, Formicidae
- Genus and species: *Apis mellifera*, *Dolichovespula arenaria* (yellow hornet), *Dolichovespula maculata* (white-faced hornet), *Vespula vulgaris* (yellow jacket), *Polistes* sp. (wasp), *Solenopsis invicta* (imported fire ant)

Hymenoptera Order

- Apidae family- includes Honey Bees, European and Africanized, and Bumblebees. Single barbed sting in Honey Bees.
- Vespidae family- includes yellow jackets, hornets and wasps. Can sting repeatedly.
- Formicidae family- includes species of fire ants, native and imported (more aggressive and prolific)



Paschall V; Cleveland Clinic Medical Pubs

Casale TB and Burks AW; NEJM 2014; 370:1432-39

What Stung You?

- 35% identified what stung with certainty.
31% had no idea
- 47% yellow jackets
- 27% honey bees
- 14% wasps
- 6% bumble bees
- 6% hornets

Venom Anaphylaxis in the United Kingdom

- 70.6% wasps and yellow jackets
- 23.4% bees
- 4.1% hornets

Magnitude of Problem

- If reported systemic allergic symptoms, then confirmed by testing-occurs in **2% of adults** (1 in 50), lower in children at 0.5% (1 in 200)
- More in men
- More reported in beekeepers, according to allergists? Stay tuned...
- At least 40 deaths/year in United States confirmed (may be an underestimate)
- Half had not reported prior allergy to stings

In Perspective in the United States 2016

- Hymenoptera allergy deaths- 50 to 100/year (at most 25 from honey bees)
- Lightning deaths- 33/year
- Traffic deaths- 37,461/year (NHTSA)
- Firearm deaths- 36,252/year (CDC) and rising, at least in NC
- Opioid deaths- 42,249/year (CDC) and rising rapidly across the US

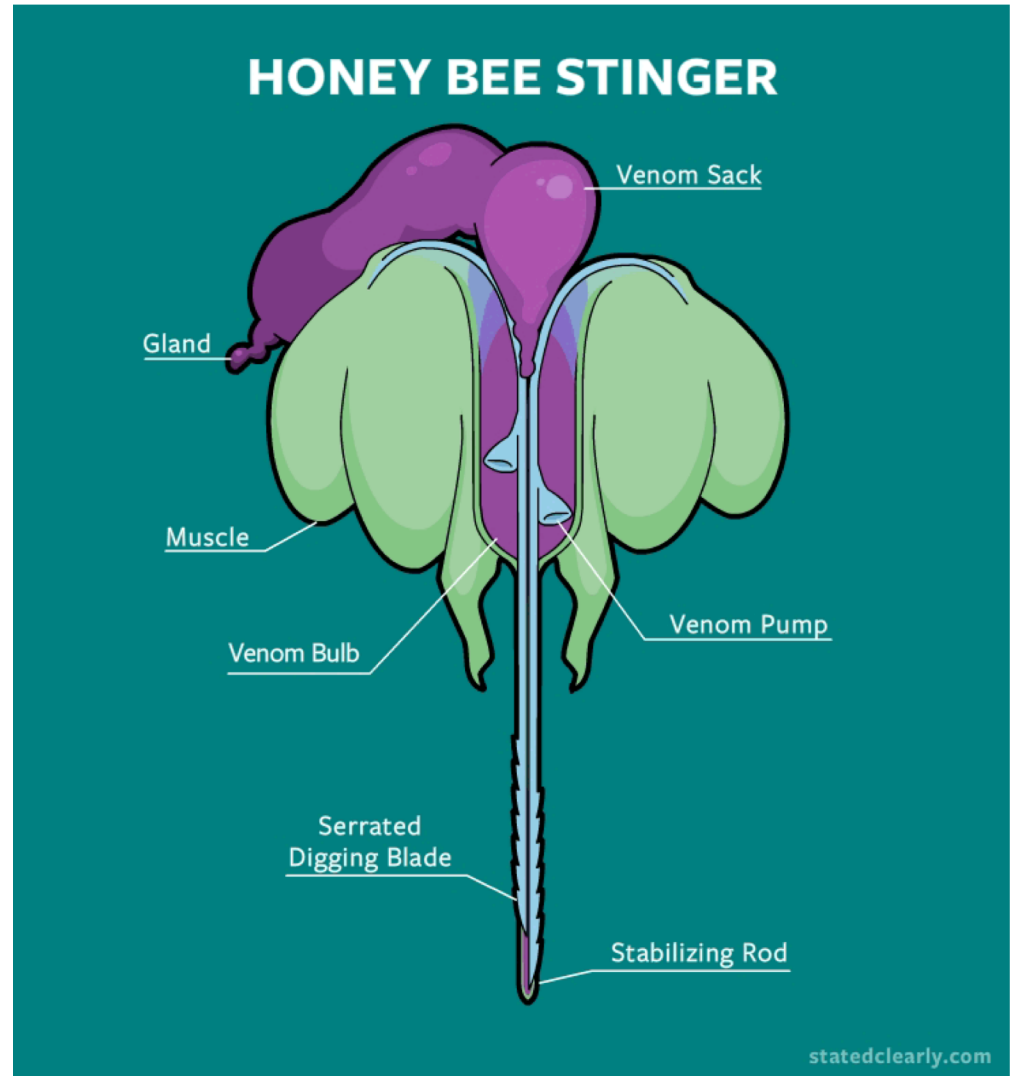
After First Systemic Reaction

- 30-60% chance of recurrence overall
- 50-60% early years after reaction
- 35% if 3-5 years since reaction
- 25% if >10 years since reaction
- 20% if reaction was only cutaneous

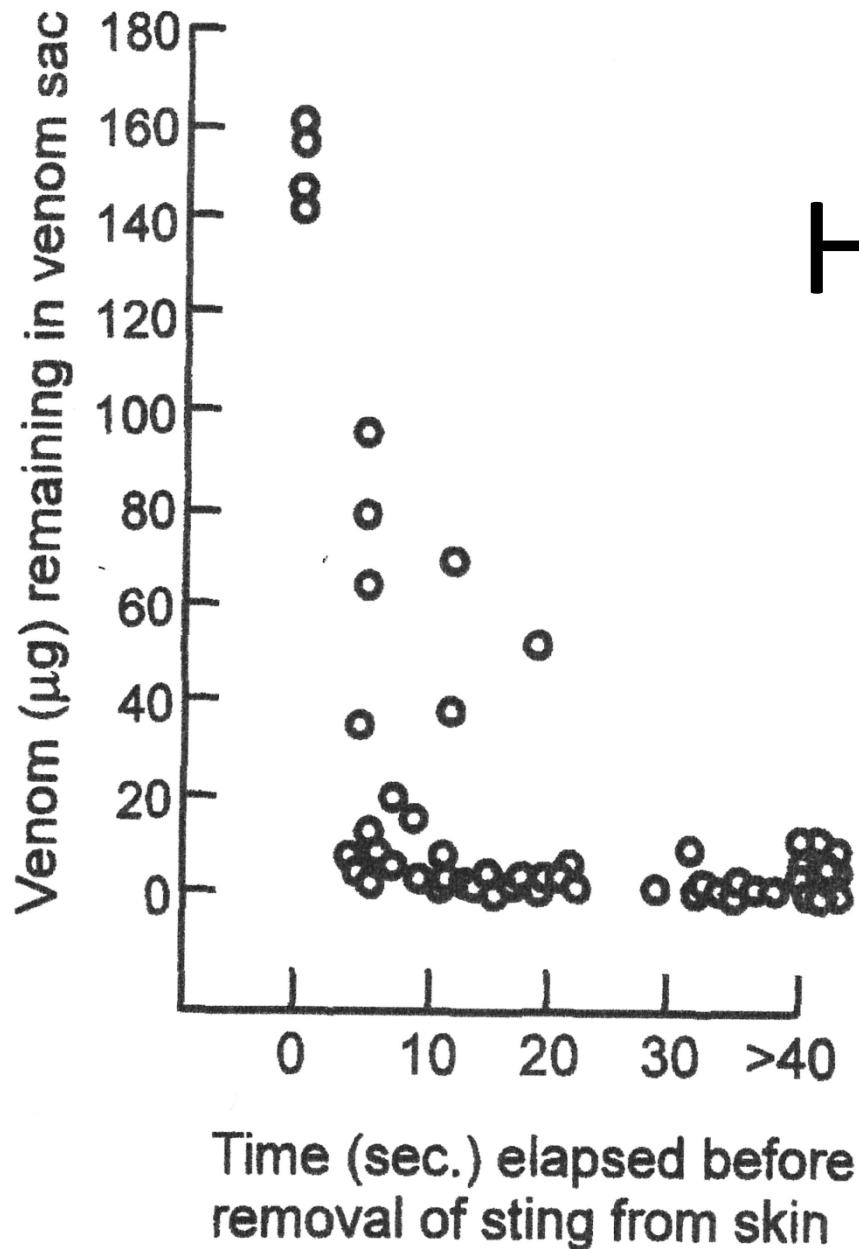


Honey Bee Sting Apparatus

Venom



Honey Bee Sting



Schumacher MJ et al.
J Allergy Clin Immunol
1994; 93:831-835

Venoms

- 50-160 mcg per honey bee sting
- 90% of honey bee venom delivered in first 20 seconds, so scrape stinger off immediately
- 2-20 mcg per vespid sting, 10-100 yellow jacket
- 0.66 nanoliters of fire ant venom containing 0.57 mcg of alkaloids and protein (UpToDate)

CHEMICAL COMPONENTS OF INSECT VENOMS



Bee Venom



Wasp Venom



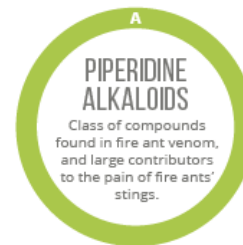
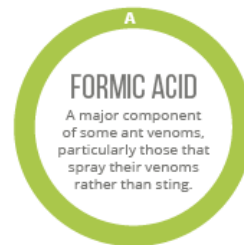
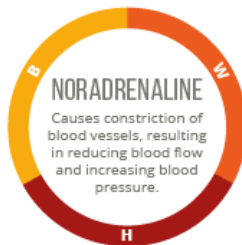
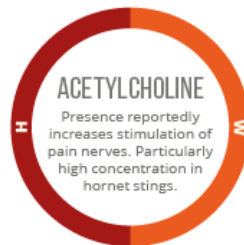
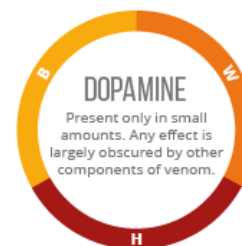
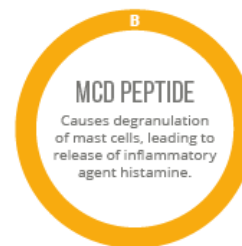
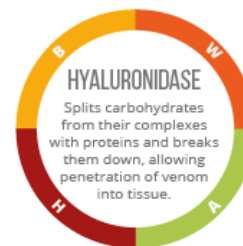
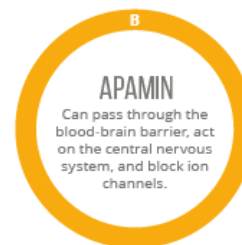
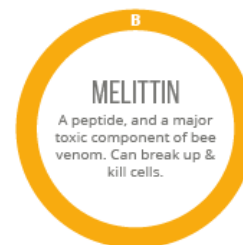
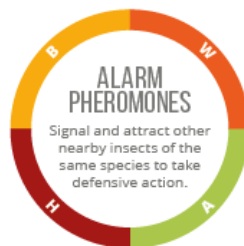
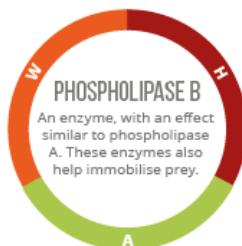
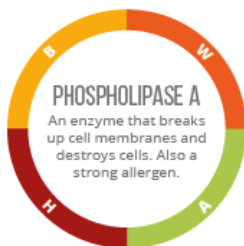
Hornet Venom



Ant Venom

Insect venoms can vary significantly in their composition. They commonly contain a complex mix of proteins, peptides, and enzymes, as well as smaller molecular weight components. This graphic aims to give a broad overview of some of these components.

The circle surrounding each component is colour coded to indicate whether it is present in bee, wasp, hornet, or ant venom. Note that this represents a general overview, and venoms will vary from species to species.



LETHAL DOSES OF VENOM

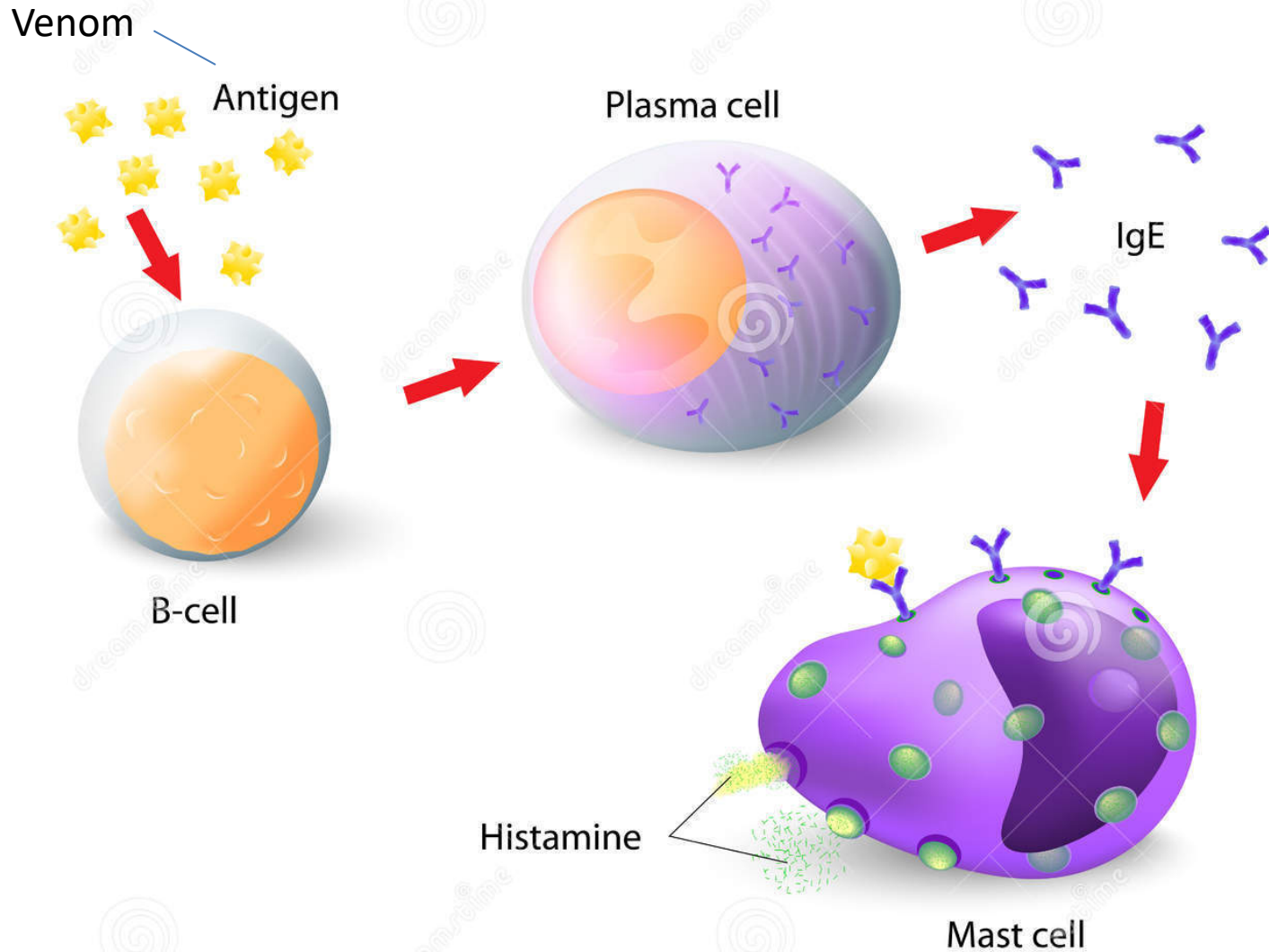
Honey Bee	2.8mg/kg
Yellowjacket	3.5mg/kg
Giant Hornet	4.6mg/kg
Harvester Ant	0.12mg/kg

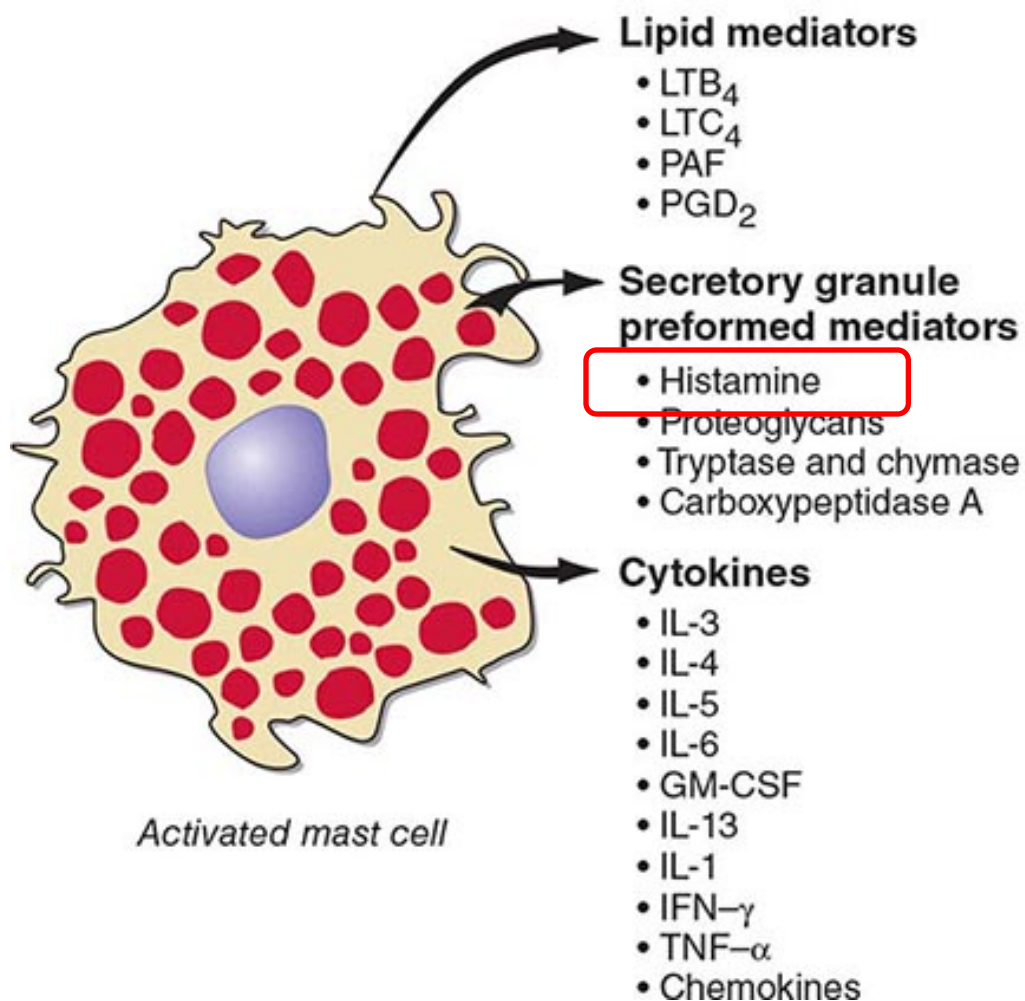


Definition

- Immunoglobulin E (allergic antibody IgE) mediated
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ANAPHYLACTIC REACTION





Leukocyte responses

- Adherence
- Chemotaxis
- IgE production
- Mast cell proliferation
- Eosinophil activation

Fibroblast responses

- Proliferation
- Vacuolation
- Globopentaosylceramide production
- Collagen production

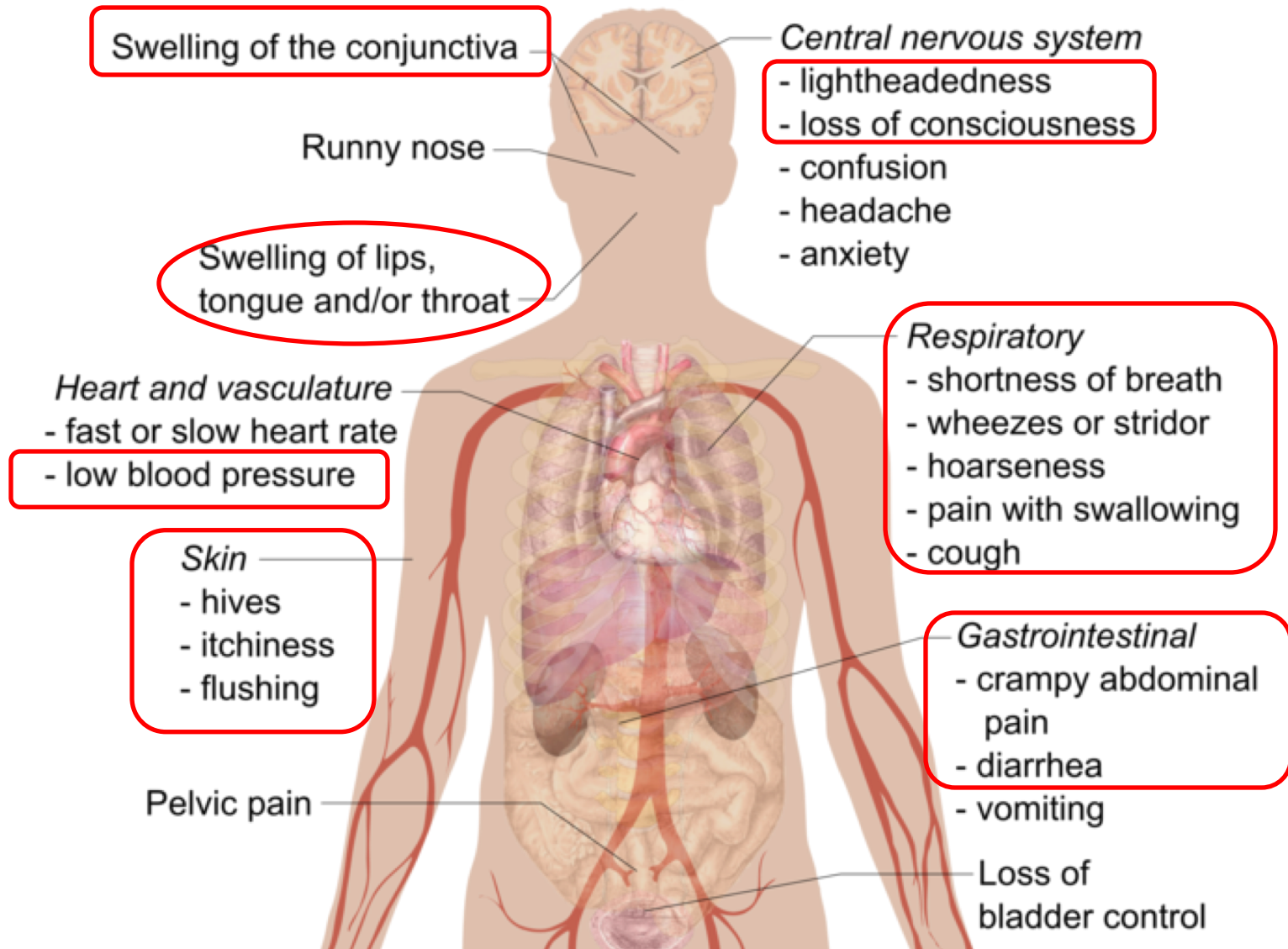
Substrate responses

- Activation of matrix metalloproteases
- Activation of coagulation cascade

Microvascular responses

- Augmented venular permeability
- Leukocyte adherence
- Constriction
- Dilatation

Signs and symptoms of Anaphylaxis



Toxic Reaction (not IgE mediated)

- Can occur after multiple stings (eg. Beekeeper working multiple hives in a day)
- Does not prove allergy
- Can cause headache, hives, nausea and diarrhea
- Numerous stings (eg. AHB attack) venom toxins can lead to kidney, liver, cerebral dysfunction and red blood cell lysis

Heat Exhaustion and Heat Stroke

Exhaustion

- Cool, clammy skin with goose bumps
- Sweating
- Temperature 100-104
- Dizzy, lightheaded
- Muscle cramps
- Headache
- Nausea

Stroke

- Flushed, hot dry skin
- Not sweating due to dehydration
- Temperature 105
- Confusion, fainting, coma
- Rapid breathing, pulse
- Low or high BP

Heat Exhaustion and Heat Stroke

Exhaustion

- Avoid sunburn
- Move to a cooler place
- Rest
- Remove jacket
- Cool drinks and external applications
- Some medications may increase risk
- Age and alcohol increase risk

Stroke

- Measures similar to Exhaustion
- Emergency care including external and core cooling, and IV fluids
- Laboratory studies-electrolytes, kidney, muscle

Systemic Allergic Reaction means allergic symptoms away from the sting site

- Usually start within minutes
- Skin involvement (hives) in most (80% adults and 95% of children) with systemic reactions
- Skin may be only manifestation in 15% adults, but 60% of children
- Throat and/or breathing systems in 40-50%
- Dizziness, low BP in 60% adults, 10% children
- Loss of Consciousness in 30% adults, 5% children



Urticaria (Hives)
and Angioedema





Pustules from Fire Ant Stings



Casale TB and Burks AW:
NEJM 2014; 370:1432-39

Large Local Reactions



- Only at area of sting (>10 cm)(**take off rings!**)
- Can last 5-10 days
- Can respond to steroids, if warranted
- Low risk for systemic reaction (5-10%)
- Possibly helped by immunotherapy, but usually not an indication
- Often confused with infection, but infection is rare



<http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/allergy/hymenoptera-venom-allergy/>

Management



Medical Alert



Avoidance

Bright colors and perfume

Barefoot and open toe shoes

Eating (bananas!) and drinking outdoors

Lawn and garden sites

Trash bins



Treatment of Systemic Reaction

- Carry cell phone
- If only mild cutaneous, antihistamine
- Otherwise, epinephrine 0.3-0.5 mg for adults, 0.01 mg/kg children, without delay
- Call EMS
- May need to repeat epinephrine in 15 minutes
- Patients on beta blockers may be resistant to epinephrine and need glucagon
- Consider venom immunotherapy (VIT)

EpiPen®



**EpiPen®
Junior**

EpiPen
(brand name)

For both, note expiration date
and temperatures for storage

AdrenaClick
(generic version)



How to use an EpiPen



Form fist around EpiPen® and pull off
BLUE SAFETY RELEASE



Push **ORANGE** end hard into outer thigh
so it 'clicks' and hold for 10 seconds[‡]

[‡]After administration of EpiPen® Adrenaline Auto-Injector
always seek medical attention – call 911

3. Then massage injection site for 15 seconds

Testing

- Venoms available for skin testing include, yellow jacket, yellow hornet, white-faced hornet, wasp and honey bee
- Whole body extracts of fire ants available
- Can start with skin prick tests of 1-100 mcg/mL
- Venom intradermal tests start with 0.001 mcg/mL and advance to 1.0 mcg/mL if negative
- RAST for specific IgE may be positive in 10% with a clinical history and negative skin tests
- Tests at least 1-2 months after reaction to avoid false negatives

Does Venom Immunotherapy Work?

Table 2. Summary of Sting Challenges with Venom (Group I), Whole-Body Extract (Group II) and Placebo (Group III).

GROUP	PATIENTS TREATED	PATIENTS STUNG	SYSTEMIC REACTIONS
I	19	18	1 (5%)
II	20	11	7 (64%)
III	20	12	7 (58%)

Decisions for Systemic Reactions

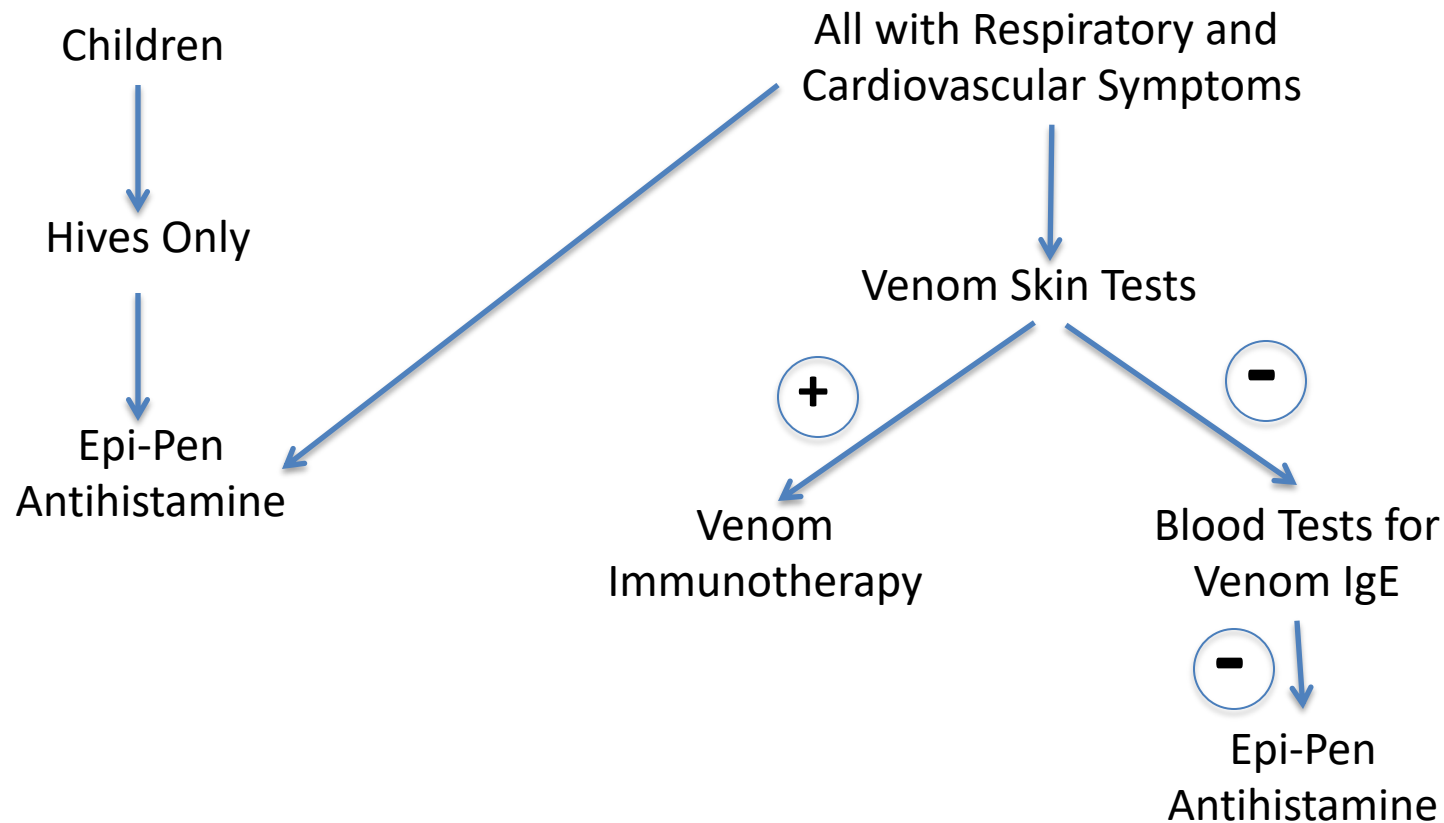
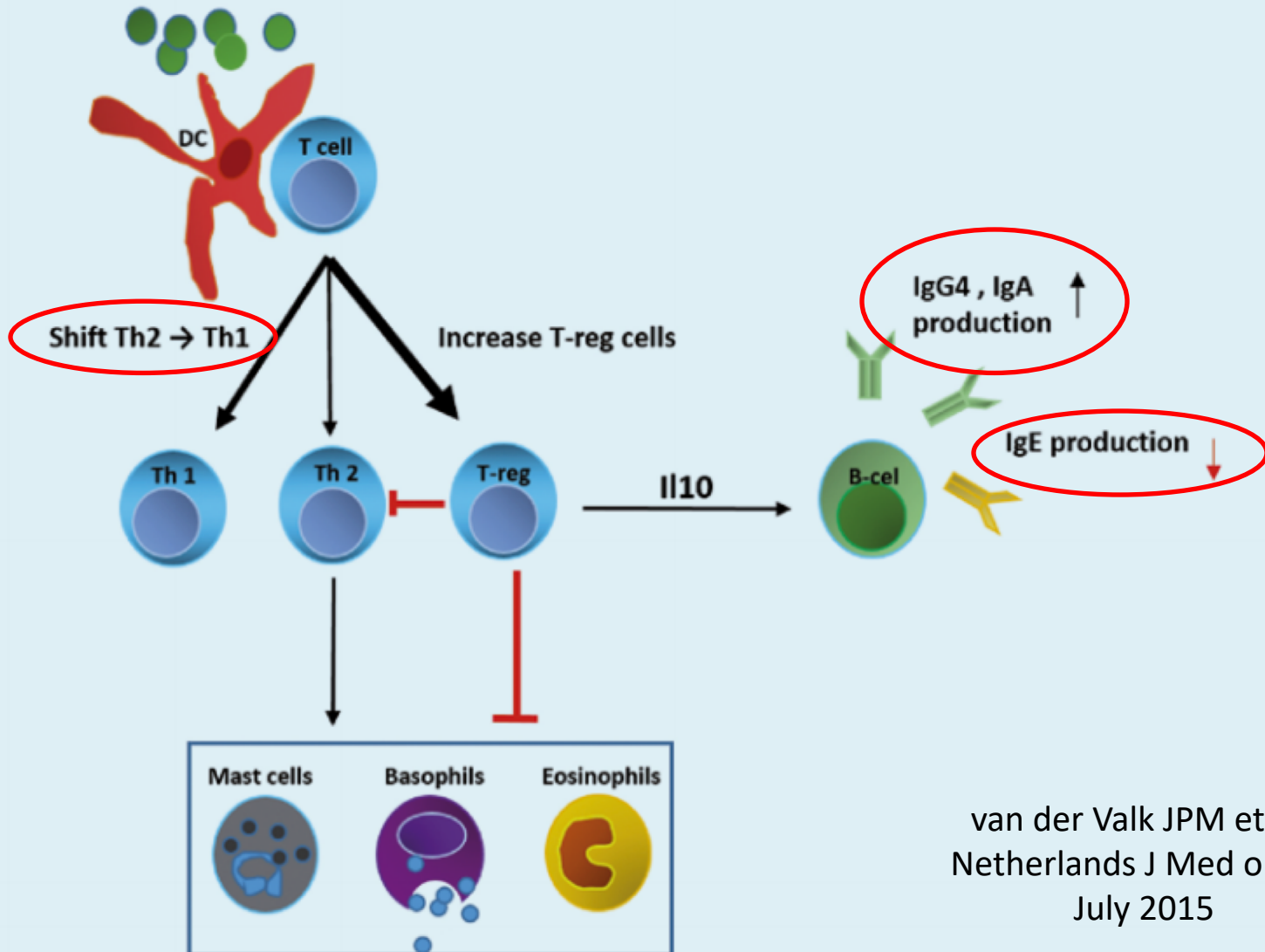


Figure 1. The mechanism of immunotherapy is shown in this figure. The number of mast cells, basophils and eosinophils decreases and the production of IgG4 and IgA increases. A shift from Th2 cells to Th1 cells and an increase of T-reg cells occurs during immunotherapy. IL 10 plays a important role in this induction of immune tolerance

Allergen immunotherapy



van der Valk JPM et al,
Netherlands J Med online
July 2015

Systemic Reactions in Beekeepers

- 200 Seasonal French Beekeepers with at least 3 years experience recruited
- BKs excluded if they reported toxic reaction symptoms
- 14% reported systemic allergic symptoms by questionnaire
- Those with the highest number of stings (>200/year) had highest IgG levels and no systemic allergy
- Those with lower number of stings (0 to 25/year) had more reported systemic allergy (15 of 30 BKs) and lower IgG levels
- Venom IgE could be present without allergic reaction to sting

Systemic Reactions In Beekeepers

- 3 out of 158 (2%) Spanish Beekeepers reported systemic reactions
- Those with systemic reactions had the highest total and venom specific IgE levels
- They also had the lowest specific IgG levels

Venom Immunotherapy (VIT)

- VIT begins with 0.1 mcg SQ 2/wk and builds to 100 mcg of each venom, eventually every 4 weeks
- Fire Ant maintenance is 0.5 mL of 1:100 wt/volume
- 95% preventive of systemic reactions (may be 75% for honey bee). Reactions less severe. Dose may be increased if failure.
- If continued over 5 years, 90% will be free of systemic reactions after sting after stopping VIT
- Consider >5 years VIT depending on severity of prior reaction and likelihood of sting. Consider whether beta blockers or ACE Inhibitors are needed.

Other Considerations

- Protocols-Traditional (up dosing 4-6 mos.), Semi-rush (8 weeks), Rush (2-3 weeks), Ultra-rush (2 days)
- Up to 14% systemic reactions for honey bee VIT, lower for wasps
- Future-Sublingual (SLIT)?

Summary Bee Sting Allergy

- Venom allergy is caused by allergic antibodies (IgE) in a sensitized individual
- Symptoms (hives, swelling, respiratory, low blood pressure) occur away from the sting site
- Venom immunotherapy is effective at preventing reactions
- All beekeepers should be familiar with allergy symptoms and have a plan for prompt treatment for themselves and others

Questions?



© Bill Ballenberg

SNAPS

References

- 1) Hunt KJ et al; NEJM 299:157-161. July 27, 1978
- 2) Bousquet J et al, J Allergy Clin Immunol 1984; 73:332
- 3) Ludman SW and Boyle, RJ; J Asthma Allergy 2015; 8: 75-86
- 4) <https://www.dovepress.com/> by 54.191.40.80 on 30-Jun-2017.
Ludman SW
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- 6) Carballo I et al. J Investig Allergol Clin Immunol 2017; 27:146-8
- 7) compoundchem.com/2014/08/28/insectvenoms/
- 7) Golden DBK et al; Stinging insect hypersensitivity:
A practice parameter update; JACI 2011; 127:854.e1
- 8) Graft DF; Med Clin N AM 2006; 90:211-232.
- 9) Casale TB and Burks AW; NEJM 2014; 370:1432-39\

THE SCHMIDT INSECT STING PAIN INDEX

The Schmidt Pain Index was developed by Dr. Justin Schmidt, an entomologist, as a method for comparing the pain of various different insect stings he experienced during his work. The scale runs from 1 to 4, with four being the most painful. Pain can be subjective, varying from person to person, and this scale is therefore not absolute.

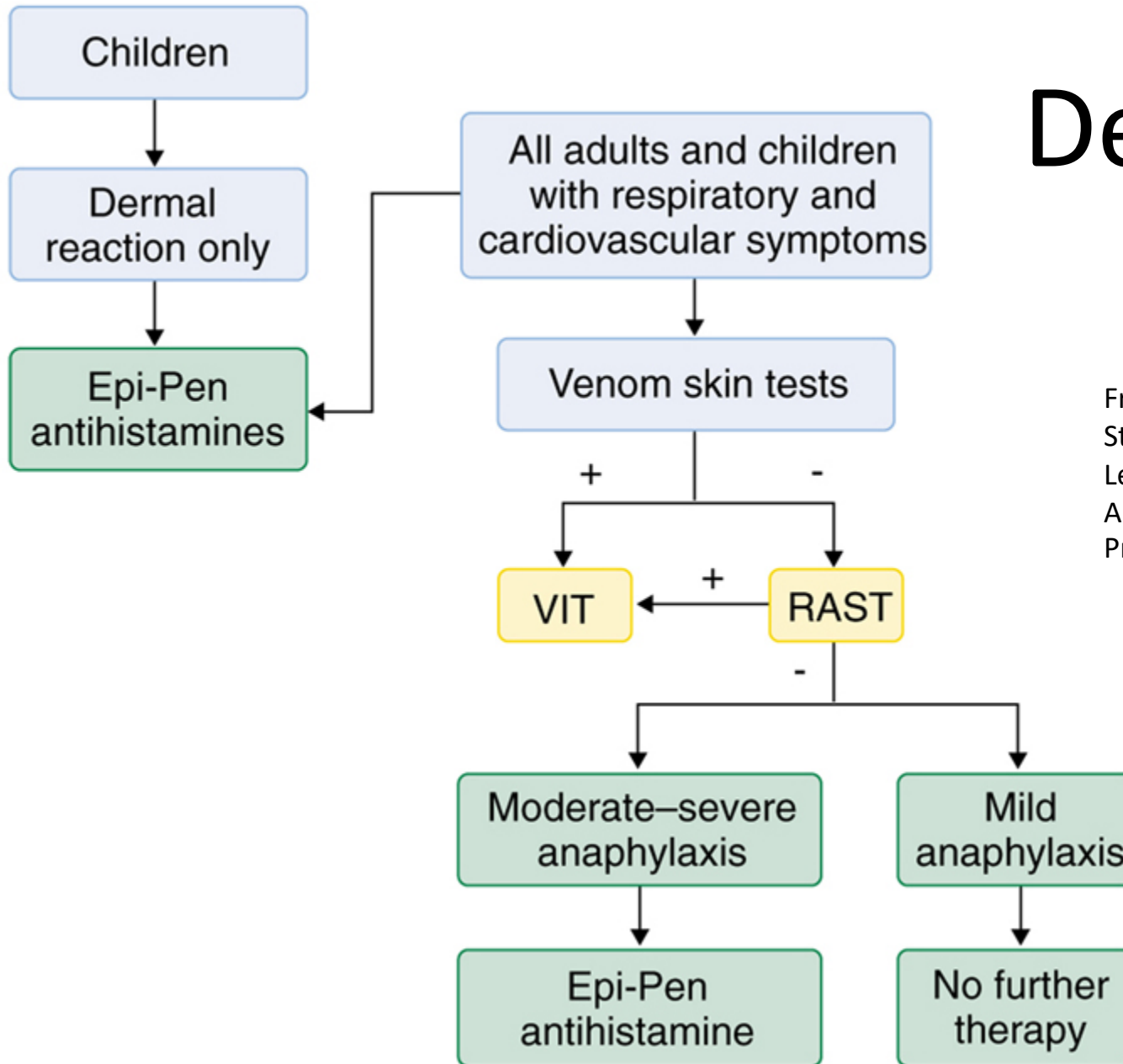
Key Pain: 1 2 3 4 **Type:**  BEE  WASP  HORNET  ANT **SIZE** **APPROXIMATE DURATION**



Note: circles sizes relate to duration, but are for purposes of comparison only, and are not to scale. All durations are an average, and as with pain, are subject to variation.



Decisions



From Reisman RE. Insect Sting Anaphylaxis in
Leung DYM et al; Pediatric Allergy; Principles and Practice 2003, pp 633-642