Approach to the Envenomated Patient

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Disclosures

No relevant commercial relationships to disclose

Learning Objectives

At the conclusion of this session, participants should be able to:

- **Recognize and distinguish the clinical manifestations of rattlesnake, scorpion, black widow and massive honeybee envenomations**
- **Explain the action and pathophysiology of venom and the resultant clinical signs**
- **Demonstrate knowledge of the proper laboratory evaluation and management of envenomated patients**

Case #1

- 4 year old male presents following rattlesnake bite to left lower extremity
- Pain and swelling at the bite site initially
- Patient reports pain is moving proximally

Case #1

- VS: HR 96 RR 18 BP 116/66 T 37
- Alert, awake no acute distress
- Left lower extremity tenderness
- Edema rapidly progressing

Rattlesnake Bites (RSB)

- Found throughout the U.S. except Maine, Alaska and Hawaii
- Mortality is rare ~5-15 deaths per year
- Most bites occur May to October
- Extremity bites are most common
- Face bites are seen on occasion…

Tongue bite #1

Kissing the snake….

Tongue bite #2

Calming the snake…

Arizona Rattlesnakes

- Western Diamondback (*Crotalus atrox*)
- Western Rattlesnake (*Crotalus viridis*)
- Blacktail rattlesnake (*Crotalus molossus*)
- Rock Rattlesnake (*Crotalus lepidus*)
- Twin-spotted Rattlesnake (*C pricei*)
- Ridgenose Rattlesnake (*C willardi*)
- Speckled rattlesnake (*Crotalus mitchellii*)
- Massasauga (*Sistrurus catenatus*)
- Mojave rattlesnake (*Crotalus scutulatus*)
- Tiger rattlesnake (*Crotalus tigris*)
- Sidewinder (*Crotalus cerastes*)

Arizona Rattlesnakes

Western Diamondback

(*Crotalus atrox*)

Mojave

(*Crotalus scutulatus*)

Massasauga

(*Sistrurus catenatus*)

Sidewinder

(*Crotalus cerastes*)

Tiger Rattlesnake
(*C tigris*)

Western Rattlesnake
(*C viridis*)

Speckled Rattlesnake
(*C mitchellii*)

Northern Blacktail Rattlesnake
(*C molossus*)

Ridgenose rattlesnake
(*C willardi*)

Rock rattlesnake
(*C lepidus*)

Twin-spotted rattlesnake
(*C pricei*)

What Determines Severity of Envenomation?

- # of strikes
- Depth of envenomation
  - Typically occur subQ
  - IV can be life-threatening
- Size of snake
- Potency and amount of venom
- Children or adults with co-morbidities may have more severe presentation

Venom

- Complex heterogeneous solution
- Varies between and within species, depending on geographic location, age, diet, and health
- Contains hemotoxins, cardiotoxins, neurotoxins, myotoxins

Rattlesnake Venom

- Peptides
- Lipids
- Kinins
- Leukotrienes
- Histamine
- Metals
- Phospholipase
- Serotonin
- Hyaluronidase
- Acetylcholinesterase
- Collangenase
- Proteolytic enzymes

Envenomation

- Venom is deposited in dermal or subcutaneous tissue
- Spreads via lymphatics and venous drainage
- ~20% of bites are dry: no venom deposited

History & Physical

- Co-morbidities
- Atopic individual
- Previous RSB or exposure
- Previous anti-venom administration
- Beta-blocker
- Tenderness
- Variable # puncture wounds
- Maybe: N/V, diaphoresis, hypotension; anaphylaxis
- Swelling
- Pain (axillary or inguinal tenderness)

Effects of Venom

- Local Tissue Effects
- Hematologic Effects
- Sytemic Effects
- Anaphylaxis

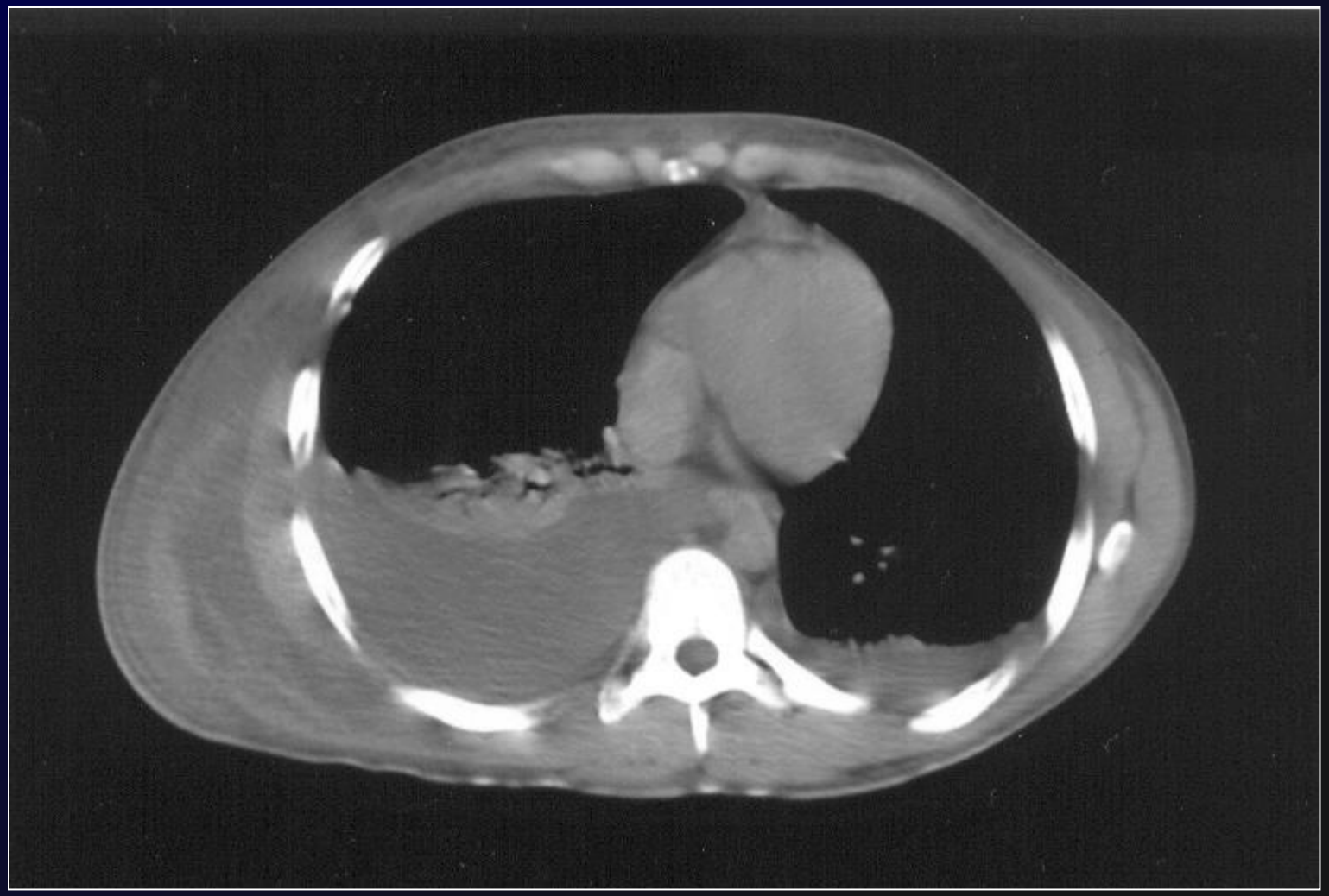
Tissue Effects

- Edema from alteration in blood vessel permeability
  - Within minutes at the bite site
  - Involve entire extremity over next several hours
- Tissue Damage due to digestive enzymes metalloprotease
- Local necrosis
  - Blebs
  - Tissue loss
  - Amputation

Local Tissue Effects

Extensive swelling and ecchymosis

3 patients - not treated with AV



Wrist bite, not treated with antivenin, resulting in pleural fluid collection.

Wrist Bite

Extensive third spacing resulting in scrotal edema and swelling extending to the knees

Extensive bleb formation involving envenomed digit.

Bleb formation distal to the site of envenomation (hand) - rare.

Local Tissue Effects

Upper and lower extremity bites in the same patient.

Mimic Compartment Syndrome

- Tense profound edema
- Pain on passive motion
- Paresthesias
- Subfascial envenomation is rare
  - More common in kids
- Most edema does not occur in compartmentalized areas

Myotoxicity

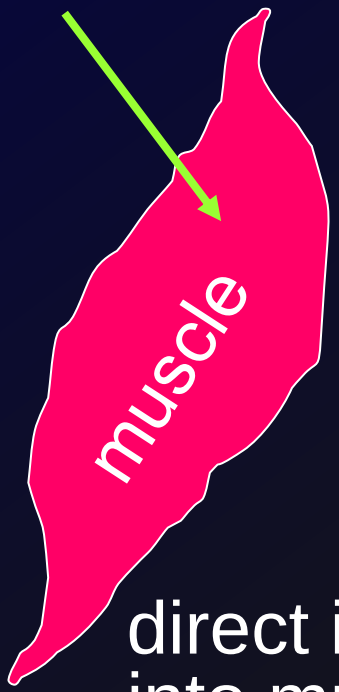
digestive enzymes

metalloproteinases

myotoxins

venom

venom



subcutaneous

systemic absorption

direct injection into muscle produces local myonecrosis

Rhabdomyolysis

Compartment Syndromes are Rare

- Noninvasive vascular studies demonstrate increased blood flow in envenomated extremities
- Fasciotomies and SQ decompression do not prevent myonecrosis in animals receiving IM or SQ venom injections
- If concerned measure compartment pressures

Back to Our Patient

- Has not received anti-venom previously
- No history of atopy or asthma
- No systemic symptoms
- Swelling appears to be rapidly progressing
- Severe pain persists and worsening
- Inguinal tenderness is noted

Lower extremity bite

- **Compartment pressures ranged from 75 to 101 mmHg**

Hematologic Effects

- Attributed to complex variety of anticoagulants, procoagulants, fibrinolysin and hemorrhagins in venom
- Thrombin-like enzymes results in poorly constructed fibrin chain and fibrin mesh cannot be formed

Moderate to Severe Envenomation

- Fibrinogen levels are low or undetectable
- Prothrombin time and partial thromboplastin time may be immeasurably high
- Platelet counts drop (10,000-50,000)
- NOT DIC; bleeding rare but can occur

Thrombocytopenia

- Phospholipase damage to platelet membrane
- Platelet aggregating proteins important in some species
- Questionable consumption of platelets in envenomated extremity
- Platelets may drop dramatically
- Nadir 72 to 96 hours
- Bleeding rare

Disseminated Intravascular Coagulation

- Extremely uncommon
- Labs similar to venom-induced thrombocytopenia and defibrination, with additional findings of:
  - Hemolysis
  - Red cell fragmentation
  - Organ infarction
  - Diffuse bleeding

Systemic Effects

- Mild effects include:
  - Non-specific weakness, malaise, nausea restlessness
- More severe effects include:
  - Confusion, abdominal pain, vomiting, diarrhea, sweating, dyspnea, tachycardia, hypotension, metallic taste
- Rarely respiratory compromise with obstruction or bronchospasm may occur
- Hypotension and cardiovascular collapse
- Multiorgan system failure

Severe swelling of tongue, but minimal swelling at bite site

Rhabdomyolysis

Neurotoxicity

- β-bungarotoxin
- Inhibits acetylcholine at the neuromuscular junction
- Most commonly seen in the Mojave rattlesnake
- Cranial nerve dysfunction
- Profound weakness and respiratory paralysis is unusual

Anaphylaxis

- May occur in individuals who have been sensitized to crotalids
  - Previous bite
  - Sensitization via inhalation or dermal exposure
- May be difficult to distinguish from severe systemic envenomation
- Pruritus, urticaria, wheezing may suggest anaphylaxis

Prehospital Care

- DON'T: Tourniquets, ice, compression bandages, incision and suction, shock
- DO: Immobilization and rapid transport
- CAUTION: Decapitated and "killed" snakes
- IVFs and occasionally epi drips may be needed en route

Management

- No physical evidence of envenomation
- Initial CBC with Plts, PT, PTT, fibrinogen are normal
- Monitor 8-12 hours if no physical findings and repeat labs are normal can discharge
- Exception is a leg bite (especially in children)
- Admit for observation

Management

- Elevate and immobilize extremity
  - Splint in full extension
- Monitor extremity circumference
- Neurovascular checks
- IV fluids
- Pain control
  - Fentanyl best choice
- Wound care/tetanus
- Antivenom?
- Tongue bites- intubate early

Wound Care

- Update tetanus
- Clean wound/bite site
- Empiric antibiotics unnecessary
  - Infection rates exceedingly low
- Debridement of blebs for comfort
- Dermotomy/fasciotomy
  - Rarely needed

Fasciotomy

Hand initially placed on ice

Fasciotomy

RSB often produce severe swelling and pain.

Suspect compartment syndrome if very tense, loss of color or cap refill in digits, severe pain but anesthetic.

Check pressures if concerned

Administer Antivenom

- Progressive swelling
- Significant thrombocytopenia
- Coagulopathy
- Neurotoxicity
- Shock
- Assuming no contraindications

Antivenom

2 Options

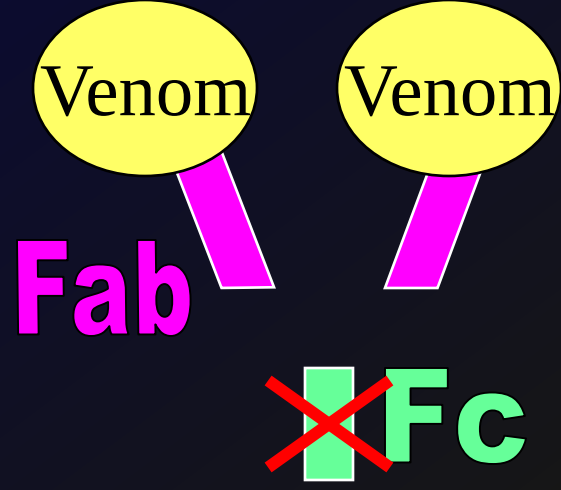
- Anavip (Crotalidae Immune Fab_2) FDA approved 2015 now becoming more widely available

- CroFab (Crotalidae Polyvalent Immune Fab) approved by FDA in 2000

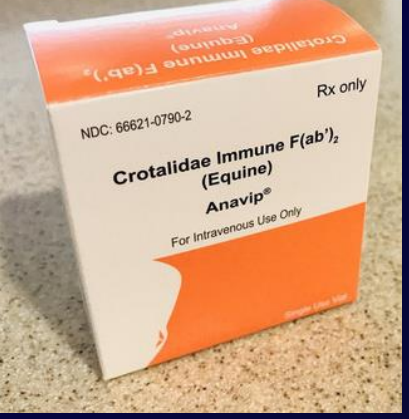
Anavip

- Fab_2 Derived from horse serum
- Longer elimination half-life
- Decreased late/recurrent hemotoxicity
- Initial dose 10 vials, may repeat
  - Dose in 4 vial increments until control achieved

CroFab



- Made by immunizing sheep with venoms from Mojave, Western and Eastern diamondbacks, Cottonmouth
- Purified → <3% Fc fragment
- Less immunogenicity



Antivenom

- Stops progression of swelling
- Reverses hematologic toxicity
- No evidence that prevents tissue loss
- Dosing
  - Control dose reconstituted in normal saline
    - Crofab 6 vials; Anavip 10 vials
  - If swelling progressing or labs not improving, administer another 4 vials
  - Maintenance when envenomation ‘controlled’
    - 2 vials q 6 hours X 3 doses

Antivenom

- Acute hypersensitivity reactions do occur
  - Mainly rate-related anaphylactoid
- Always administer in monitored unit
- Have epinephrine, antihistamines at the bedside
- Initiate at slow rate, increase as tolerated to allow infusion over 1 hour

Problems

- **Recurrence**
  - **Swelling and/or hematotoxicity following apparent resolution with treatment**
  - **Detected within 72 hours post-treatment**

Current Management

- Continue to check labs as out-patient until steadily improving
- Isolated coagulopathy not retreated
- Thrombocytopenia in range of 15,000/mm^3 $\rightarrow$ retreat with CroFab
- Combined severe coagulopathy and platelets <30,000/mm^3 $\rightarrow$ retreat with CroFab

Inform Patients…

- May lose the finger despite early antivenom administration
- May develop allergic reaction to antivenom
- Antivenom will arrest swelling and reverse coagulopathy but the blood abnormalities may return
- Recovery may take weeks to months despite antivenom

Take Home Points

- There is currently no ideal treatment
  - AV does not prevent necrosis
  - Must monitor for recurrence
- As tempting as it may be, don't ever put a snake in your mouth
- Do not attempt to suck the venom from a recently envenomated individual no matter how much they beg you

Case #2

- Mother brings in 4 yo child after she became agitated and inconsolable
- She is diaphoretic, writing in mom's arms and salivating
- Mom states she vomited prior to arrival
- This is what you see…..

The Bark Scorpion

- *Centruroides sculpturatus*
  - Yellow/tan/brown
  - Up to 5 cm in length
  - Hard exoskeleton
  - Segmented tail curves up, ends in a telson, containing venom glands and stinger

Bark Scorpion

Centruroides sculpturatus

Exoskeleton

Telson

Scorpions

- 40 species of scorpions in the US
- Only one is neurotoxic
  - Found in Arizona, areas of Texas, New Mexico, California, and Nevada
- >6000 calls/year to Banner Poison Control Center
- Most managed at home

The Bark Scorpion

- Body fluoresces under UV light
- Resides in or near trees; wood
  - Climbs, but not up glass

Envenomation

- Most stings cause only local pain
- Onset of symptoms immediate, progress up to 5 hours
- Children tend to be most severely affected

Venom

- Complex mixture of:
  - Mucopolysaccharides
  - Hyaluronidase
  - Serotonin
  - Histamine
  - Protease inhibitors
  - Histamine releasers and other neurotoxins
- No enzymes producing tissue destruction
- Neurotoxicity without cardiotoxicity

Venom

- Blocks inactivation of Na^+ channel resulting in increased influx
- Increased duration and amplitude of the neuronal action potential
- Enhanced release of neurotransmitters
  - Acetylcholine
  - Norepinephrine
  - Others (dopamine, glutamate, aspartate, GABA)

Clinical Effects

- See cholinergic and adrenergic stimulation
- Skeletal motor and parasympathetic stimulation
  - Tongue and muscle fasiculations
  - Gross skeletal motor hyperactivity
  - Salivary gland, gastric and pancreatic hypersecretion
  - Rarely may see priapism

Grades I and II

- I
  - Pain and paresthesias at sting site
- II
  - Local symptoms plus remote pain or paresthesias or both

Grade III

- Cranial nerve abnormalities OR
  - Blurred vision
  - Roving eye movements
  - Slurred speech
  - Tongue fasciculations
  - Hypersalivation
  - Upper airway dysfunction
- Somatic skeletal neuromuscular dysfunction
  - Restlessness
  - Fasciculations
  - Shaking and jerking of the extremities

Grade IV

- Both cranial nerve abnormalities and neuromuscular dysfunction
- Other complications include:
  - Respiratory failure
  - Aspiration pneumonitis
  - Fever
  - Rhabdomyolysis

Management

- Most symptoms improve within 9 to 30 hours without treatment
- Pain and paresthesias may last up to 2 weeks
- Options:
  - Supportive care with sedation and pain control
  - Antivenom

Antivenin Therapy

- 1965 to 2004 ASU produced a goat serum derived antivenom
  - Immunogenic, serum sickness occurred in >50% of patient who received antivenom
- Supportive care was only option until study using horse derived Fab fragment made in Mexico completed
- FDA approval granted for Anascorp 2011

Dosing Antivenom

- Give initial dose of 3 vials, additional vials if symptoms persist
- Have Epinephrine drip, steroids, H_1 and H_2 blocker at the bedside
- Absolute contraindication is horse serum allergy
- Dose is the same for adults and children

Recent Case #3

- 39 yo man was hiking in the Superstition mountains with a friend
- They were swarmed by bees
- Friend escaped to get help
- Patient stranded on cliff
- On EMS arrival patient found supine with vomiting and diarrhea

Case Presentation

- VS HR 120 BP 140/palp RR 16 O2 sat 96% GCS 15
- Significant facial edema noted
- Able to stand and walk to assist in rescue effort
- 2 L NS and Zofran 4 mg IV given
- More than 200 stings were counted
- Transported to ED

Hymenoptera

- Phylum Arthropoda
- Order Hymenoptera
- Includes
  - Bees (honey, bumble, sweat etc.)
  - Wasps
  - Ants

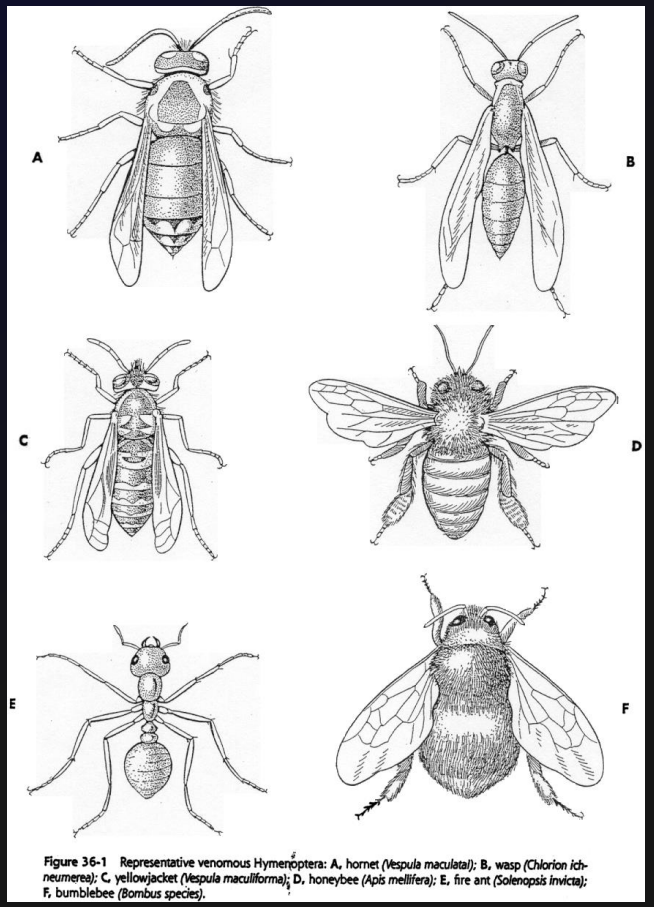
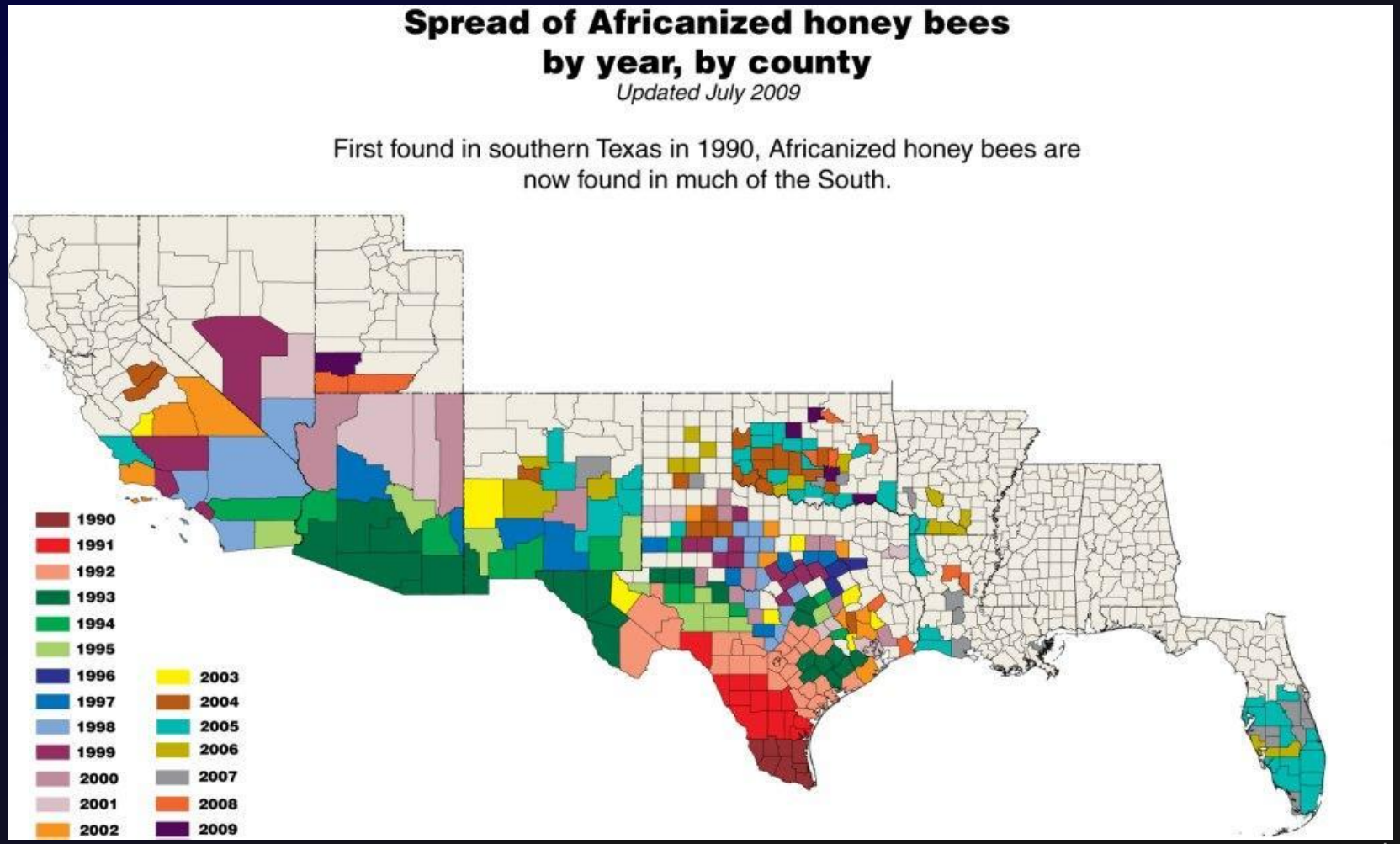


Figure 36-1 Representative venomous Hymenoptera: A, hornet (*Vespula maculata*); B, wasp (*Chlorion ichneumerea*); C, yellowjacket (*Vespula maculiforma*); D, honeybee (*Apis mellifera*); E, fire ant (*Solenopsis invicta*); F, bumblebee (*Bombus species*).

OOPS!

- African species brought to Brazil- 1956
- Crossbreed with the European honeybee
- 26 swarms of African honeybees (AHB) and their queens accidentally released
- Interbreeding and “Africanization” of the domestic species occurred

Distribution



Emergency Department Course

- BP 150/110, HR 105, RR 16, 100%, T 37, BG 95
- Diffuse pain, nausea, vomiting, and facial edema
- Given 2L NS, methylprednisolone 125 mg, zofran 4 mg, morphine 5 mg, (Unasyn 3 gm)*
- Progression of facial edema and protracted vomiting prompted RSI

Initial Labs

	15	
23		239
	44	

139	109	32	
			150
3.9	22	1.7	

- **AST 90**
- **ALT 37**
- **T bili 2.6**
- **CK 1836**
- **PT 13.6**

Venom Components

- Melittin 40-60%
- Phopholipase A_2 15-20%
- Apamin 2-3%
- Mast cell degranulating protein 2%
- Hyaluronidase 1-2%
- Acid phosphatase 1%
- Lysophopholipase 1%
- Histamine 0.7-1.6%

Clinical Effects of the Venom

- Lethality of venom is similar in AHB and EHB
- Sytemic Toxicity is due to sheer number of stings
- Study of beekeepers revealed systemic reactions occur with as few as 50 stings
- > 500 stings may result in death

Local Venom Effects

- Minor
  - Wheal at sting site
  - With edema, erythema, pruritus
- Major
  - Spread > 15 cm beyond sting site
  - Persists > 24 hours

Anaphylaxis

- Most immediately life-threatening
- Estimated 40-50 deaths in U.S. annually
- Flushing, pruritis and urticaria remote from sting site
- Bronchospasm, airway edema and respiratory failure
- Loss of consciousness
- Hypotension
- Cardiac dysrhythmias

Systemic Toxicity After Massive Envenomation

- Immediate reaction
  - Headache
  - Dizziness
  - Edema
  - Nausea
  - Vomiting
  - Hypotension or hypertension

Systemic Toxicity After Massive Envenomation

- Rhabdomyolysis
- Hemolysis
- Acute renal failure
- Hepatic dysfunction
- Thrombocytopenia
- DIC
- Myocardial infarction/ cardiovascular collapse

Clinical Course

- Supported on vent, sedated on propofol, significant facial edema
- Acute kidney Injury with oliguria
  - Cr 1.7 GFR 48
- Rhabdomyolysis
  - Peak CK 20,352 IU/L
  - Alkalization therapy
- Hemolysis
- Elevated Transaminases
  - AST 291 ALT 81

What Do You Do If You Encounter a Swarm of Honeybees?

Remain calm and don’t make any sudden movements

Remain calm and don't make any sudden movements

Diagnostic Approach

- Asymptomatic with < 100 Stings
  - Baseline labs (CBC, CK, coags, CMP, EKG and U/A)
  - 6 hour observation period
  - Re-evaluate and repeat labs
- Asymptomatic with > 100 Stings
  - Baseline labs
  - Admit for 24 hr observation due to possible delayed toxicity

Treatment of Symptomatic Patients

- Analgesia
- Aggressive hydration
- Antihistamines
- Pressor support if necessary
- Ventilatory Support
- Blood products as needed

Treatment Continued

- Steroid Therapy
  - See increased edema, flushing pruritus day 2 post-envenomation
  - Franco et al confirmed presence of venom >50 hrs after envenomation
- Hemodialysis for ARF or hyperkalemia
- Case report describing benefit of plasmapheresis
  - Not sufficient evidence to recommend

What about Stinger Removal?

- A. Remove immediately to reduce venom load
- B. Remove immediately to reduce patient discomfort
- C. Remove after stabilization to reduce foreign body reaction
- D. Do not remove due to increased risk of secondary infection
- E. Timing is irrelevant as long as you scrape and do not pinch the stinger

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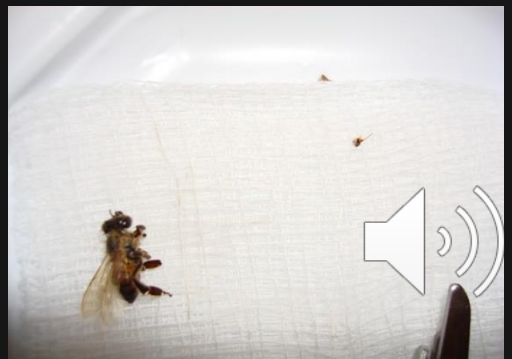
What about Stinger Removal?

- Contents of venom sac injected in < 60 sec.
- No effect in reducing envenomation
- Removal may be desirable to prevent foreign body reaction but is not a high priority acutely

Our Patient Treated With:

- Methylprednisolone 60 mg q 6h
- Diphenhydramine 25 mg q 6 hrs
- Famotidine 20 mg bid
- Urine alkalization for rhabodmyolysis
- While on fentanyl and propofol infusions attempt made to remove stingers
- Dead bee removed from ear



Outcome

- Patient extubated after facial edema improved on hospital day 3
- Urine output improved and Creatinine normalized
- CK decreasing
- Continued to obsess about the location of his beloved friend

Case # 4

- 33 yo male brought in by family
- Moaning and writhing in pain
- Symptoms began 30 minutes ago and have progressively worsened
- Patient non-communicative secondary to pain and distress

Physical Exam

- T-98.9 HR-126 BP-164/98 RR-20 O_2 sat-98%
- Awake, alert, moaning, writhing
- NC/AT OP: clear
- Chest: CTA B
- CV: tachy RR no m/g/r
- Abd: rigid, non-distended

Latrodectus Envenomation

- 5 species in the US
- *Latrodectus mactans*
- Males felt to be harmless
- Female is larger, black with red hourglass mark on ventral surface
- Inhabit large untidy webs close to the ground
- Live in woodpiles, crevices, barns

Envenomation

- Bite may produce a sharp pain or go unnoticed initially
- May see erythema with central pale area (target lesion)
- Symptoms typically evolve 15 to 60 minutes following the bite

Venom

- 6 active components
- α-latrotoxin important in human toxicity
  - Potent neurotoxin
  - Results in transmembrane pore formation and Calcium influx
  - Induces neurotransmitter release from nerve terminals
    - Acetylcholine
    - Norepinephrine
    - Others (dopamine, neuropeptides, glutamate etc)

Latrodectism

- Evolves over 30-60 minutes
- Spreads contiguously from bite site
- Systemic and severe neuromuscular symptoms
- Typically resolves in 24-48 hours

Latrodectism

- Systemic
  - Nausea
  - Diaphoresis
  - Salivation
  - Urinary retention
- Cardiopulmonary
  - Hypertension
  - Tachycardia
  - Bronchorrhea

Latrodectism

- **Neuromuscular**
  - **Muscle spasm**
    - **chest, thighs, abdomen (may mimic acute abdomen)**
  - **Rigidity**
  - **Tremor**
  - **Weakness**

Other Clinical Manifestations

- Pavor mortis (fear of death)
- Priapism
- Pregnancy
  - May be complicated by uterine contractions and premature delivery
- "Facies latrodectismica"
  - Sweating, contorted, grimaced face
  - Periorbital edema

Management

- ABC's, IV, O_2, monitor
- Tetanus prophylaxis
- Opioids
- Benzodiazepines
- Calcium Gluconate
  - Historically recommended
  - Chart review of 163 patients found it largely ineffective
- Dantrolene and Methocarbamol
  - No evidence to support use

Management

- **ABC's, IV, O_2, monitor**
- **Tetanus prophylaxis**
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XXX

Black Widow Antivenin

- Crude hyperimmune horse serum
- Can be highly effective
- Deaths from antivenin administration
- Use is discouraged given low risk of mortality from black widow envenomation
- Contraindications
  - Horse serum allergy
  - Asthma, beta-blocker use, CAD
  - Previous *Crotalidae* or *Latrodectus* antivenin

Questions?