Envenomations

ACMT Board Review Course
September 9, 2012

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Special Acknowledgement

• Thanks to Michelle Ruha and other previous presenters for their efforts on this topic.
What to Review?

• Natural Products: 5% of tox boards
  – Includes food and marine food poisonings, herbals, plants, fungi, toxic envenomations

• Toxic Envenomations
  – Marine, snakes, lizards, scorpions, spiders, bees, ants, caterpillars, other random things (blister beetles, toads, newts, etc…)
  – Native AND non-native!!!
Keep in Mind

• This presentation attempts to include most important points for the boards
  – A lot of things not included

• All venoms are ‘complex’
  – Will leave out lists of components and try to include the ones to remember (for the most part)
Marine Envenomations

- Stingrays
- Scorpaenidae
- Sea snakes

- Cnidaria
  - Jellyfish
  - True, ‘not’ true
  - Fire coral
  - Anemones
  - Corals

- Echinodermata
- Mollusks
- Sponges
Stingray / *Dasyatis* spp

- Most common stinging fish
- Atlantic / Mediterranean / Indian Ocean
- Spine on dorsum of tail has sharp tip and barb, with venom glands under spine
  - Lacerates and envenomates
  - A sheath surrounds the spine and may become embedded in wound
Stingrays

- Extremity injuries - deep ulcers and secondary bacterial infections
- Chest injuries - death
- Venom produces edema and pain out of proportion to visible tissue injury
  - Peaks at 60 min, may last 48 hours
  - Systemic: cramping, weakness, N/V/D
- Wound initially cyanotic or dusky, becomes erythematous, necrotic
Management

• Cleanse, explore, debride wound
• Tetanus prophylaxis
• Prophylactic antibiotics (Cipro, Bactrim, Tetracycline okay)
• Pain control: hot water, analgesics
• Don’t suture
Scorpaenidae

- Next most common fish envenomations
- Over 350 species; found in coral reefs
- Spines with venom glands
- More venomous: Gulf of Mexico, Pacific & Indian oceans
- Less venomous: Ca and SE US coasts
- Victims: scuba divers, snorkelers, fishermen; people with imported fish in home aquariums
Scorpaenidae

Least severe
- **Pterois**
  - Lionfish
  - Rather escape
- **Scorpaena**
  - Scorpionfish
- **Synanceja**
  - Stonefish

Most severe
- Rather attack
Scorpaenidae

- Venom
  - Inflammatory mediators (lionfish)
  - Stonustoxin, verrucotoxin, catecholamines (stonefish)
- Clinical: spectrum, ranges from local with Lionfish to severe with Stonefish
  - Local - Erythema, pain, induration
  - Systemic - N/V, syncope, arrhythmia, seizure, pulmonary edema, death
Management

- Hot water (110-115°F) inactivates toxin
- Analgesic or digital nerve block
- Remove barbs or spines
- Tetanus
- Consider prophylactic antibiotics
- Antivenom for life-threatening stonefish envenomation - equine Fab
- Don’t suture
Sea Snakes

- Hydrophiidae
- >50 species – all venomous
- None in Atlantic or Caribbean
- Some relevant species:
  - *Enhydrina schistosa* (beaked)
  - *Pelamis platurus* (pelagic)
  - *Astrotia stokesii*
  - *Hydrophis ornatus*
  - *H. cyanocinctus* (banded)
Sea Snakes

- Front fixed fangs, 80% dry bites
- Similar to Australian Elapids
- Venom extremely toxic
  - Neurotoxins, myotoxins
- Symptoms within minutes to hours
- Minimal local reaction
- Ascending paralysis, rhabdomyolysis
- No coagulopathy
Antivenom

- Treat symptomatic envenomations
- Equine-derived, available in Australia
- Prepared against *Enhydrina schistosa* (beaked sea snake) and *Notechis scutatus* (terrestrial tiger snake)
Cnidaria

- Formerly Coelenterata
- > 9000 species, grouped:
  - Hydrozoans (man-of-war)
  - Scyphozoans (true jellyfish)
  - Cubozoa (box jellyfish)
  - Anthozoans (corals, anemones)
- Most contain nematocysts
**Nematocysts**

- Dart-like structures enclosed within venom sacs
- Stimulated by pressure / chemical signals
- Shoot out of containment sacs, injecting venom as they penetrate flesh
Cnidaria

- Venom: inflammatory mediators, proteases
- Spectrum of severity
  - Mild: dermatitis, pain
  - Severe: multi-organ toxicity, death
  - Anaphylactoid reactions may occur
- May be inactivated by 5% acetic acid solution (vinegar)
- Antihistamines or steroids prn
Jellyfish

- Long tentacles contain hundreds of thousands of nematocysts
- Stinging sensation, pruritus, paresthesias, central radiation of pain
- Red-brown-purple lesion in a linear whiplike pattern
- Blistering, edema, violaceous petechial hemorrhages
Box Jellyfish

- *Chironex fleckeri*
- Off Australia and SE Asia
- Most venomous of all stinging marine life
- Venom produces catecholamine surge
Box Jellyfish

- Most victims with severe pain only
- Wounds may become necrotic
- May develop acute and/or delayed hypersensitivity
- Severe: Hypotension, cardiac arrhythmias, respiratory failure, anaphylaxis
- Death more common in kids, occurs fast
- Sheep derived whole IgG AV in Australia
Portuguese Man-Of-War

- *Physalia physalis*
- Waters along the Florida coast
- Tentacles up to 10 feet, nearly transparent
- Venom may cause excruciating pain
- Rare cardiac arrhythmia, respiratory failure, anaphylaxis, death
Irukandji Jellyfish

- *Carukia barnesi*
- Peanut-sized, translucent jellyfish
  - Australia’s north coast, Pacific, Florida (different species?)
- Relative of the box jellyfish
- Catecholamine surge, with cardiac and pulmonary effects, death may occur
- No antivenom
Sea Bather’s Eruption

• AKA ‘sea lice’
• Larvae of jellyfish *Linuche unguiculata*
• Between March and June, SE Florida
• Pruritic, erythematous, maculopapular rash in areas covered by bathing suit
• Symptoms resolve spontaneously hours to days, up to 2 weeks
Fire Coral

- *Millepora spp*
- Not a true coral
- Most commonly found in shallow tropical waters
- Sharp skeleton, contain nematocysts
- Divers at risk: contact may result in burning pain, urticaria, pruritis
- Wheals may take weeks to resolve and may leave a hyperpigmented scar
Anemones

- Flowerlike appearance
- Modified nematocysts known as spirocysts
- Humans stung when handling them
- Varies in severity, from stinging sensation to vesiculation, necrosis
Cnidaria Treatment

- Supportive care / tetanus
- Vinegar often first line
  - Inhibits d/c of nematocysts from *C fleckeri*
  - May increase d/c in some species
- Irrigation with seawater may be better in US
- Pain may resolve spontaneously in 30-90 min
- Antihistamines / corticosteroids prn
- No prophylactic antibiotics
Echinodermata

- Starfish
- Sea urchins
- Sea cucumbers
Mollusks: Cone Snails

- 300 *Conus* species
- Stings with a modified tooth fired from the proboscis
- Venom contains conotoxins
  - neurotoxins which target multiple specific ion channels
- Ziconotide, a conotoxin derivative, is being used to treat neuropathic pain
Cone Snails

• Local pain, burning sensation, numbness, ischemia, paresthesias
• Most cases only local manifestations with resolution in 6-8 hours, although deaths have been reported
• Progression to generalized paresthesias, paralysis, respiratory failure, coma, cardiac failure
• Treatment – hot water, supportive
Mollusks:
Blue Ringed Octopus

- Found in Indo-Pacific shallow waters
- Small, up to 20 cm
- Usually harmless, bites rare
- Two sets of salivary glands that release venom from a powerful parrotlike beak
- Venom contains tetrodotoxin (aka maculotoxin)
  - Blocks sodium channels
Blue-Ringed Octopus
(_Hapalochlaena spp_)

- Initially mild local pain, burning, numbness, ischemia; local progressing to perioral and distal paresthesias
- May rapidly progress to paralysis, respiratory failure
- Treatment supportive
Snakebites

• >8000 bites / year in US; <10 deaths
• > 99% venomous bites in US
  Crotalinae
• Snake Families:
  – Viperidae
  – Elapidae
  – Hydrophiidae
  – Atractaspididae
  – Colubridae
  
  Crotalinae
  Viperinae
Colubridae

- Rear fixed fangs
- Found in most parts of the world
- Most species harmless
  - garter, gopher, sonoran vine snake
- Some dangerous, even lethal
  - Clinical effects: swelling and coagulopathy
Atractaspidae

- Rear/lateral – directed front fangs
- Africa, Middle East
- Pain, swelling, lymphadenopathy, vomiting, diaphoresis, fever, coagulopathies

African Burrowing Asp
Elapidae

- Front, fixed fangs
- 60% bites dry
- Often neurotoxic venom
- Some non-native species:

  - Cobra
  - Mamba
  - Tiger Snake
  - Krait (Malaysia, India)
US: Eastern Coral Snake

- *Micrurus* spp
- Red on yellow complete bands
- Neurotoxic venom: paralysis, symptom onset may be delayed many hours
- Treat with antivenom early, if available

- Sonoran coral snake (*Micruroides*) - not dangerous
Red on yellow, kill a fellow

Red on black, venom lack
Viperidae

- **Viperinae** - old world vipers
- **Crotalinae** - new world or ‘pit’ vipers
- Front, mobile fangs
- 25% bites dry
- Venom into dermis/SQ, to lymphatics
- Local tissue effects, hematotoxicity, some neurotoxic
Viperinae

- Old World Vipers
- Found in many European and Asian countries, Middle East, Africa
- No heat sensing pits

Russell’s Viper
Asp Viper
African Gaboon Viper
Puff Adder
Crotalinae

- Pit vipers
- Triangular shaped head
- Heat sensing pits, elliptical pupil
- North, Central, and So America, Asia
- In US: all states except ME, AK, HI
  - *Crotalus* - Most rattlesnakes
  - *Sistrurus* - Massasauga, pigmy
  - *Agkistrodon* - Copperhead, cottonmouth
US Pit Vipers

Rattlesnakes (*Crotalus* and *Sistrurus*)

Copperhead (*Agkistrodon*)

Cottonmouth
US Pit Vipers

- Venom Toxicity
  - Rattlesnakes > cottonmouths > copperheads

- Venom: cytotoxic, myotoxic, hemotoxic, occasionally neurotoxic
Rattlesnake Venom
(a few of many components)

• Fibrinolytic, fibrinogenolytic enzymes
  – Defibrination, coagulopathy
• Thrombin-like enzymes
  – Coagulopathy
• Metalloproteinases
  – Tissue damage
• Phospholipases
  – Thrombocytopenia, neurotoxicity
• Bradykinin-potentiating peptides
  – Anaphylactoid reactions
Venom Neurotoxins

- Postsynaptic neurotoxins
  - $\alpha$ neurotoxins
  - Most elapid and sea snake venoms
  - Competitively bind nicotinic acetylcholine receptors and produce a nondepolarizing neuromuscular blockade
- Neostigmine may reverse
Venom Neurotoxins

• Presynaptic neurotoxins
  – β neurotoxins
  – Some elapid and viper venoms
  – Inhibit release of acetylcholine at the neuromuscular junction
Rattlesnake Neurotoxicity

• $\beta$ neurotoxins
  – Common in Mojave and Southern Pacific (C. scutulatus and C. helleri)
  – Crotoxin, in South American rattlesnake (C. durissus terrificus)

• Fasciculations most common
• Severe cases progress to weakness and paralysis with respiratory failure
Physical Exam

- Tenderness, swelling, ecchymosis
- Variable # puncture wounds; oozing
- Axillary or inguinal tendernessness
- Possibly: vomiting, diarrhea, bleeding, tachycardia, fasciculations, erythema near bite, hypotension, angioedema
- Rare: DIC, compartment syndrome, anaphylaxis
- Labs: low platelets, low fibrinogen, high PT, high FSP; hemoconcentration
Local: oozing at bite site, ecchymosis

Severe swelling, third spacing
Tissue necrosis, hemorrhagic blisters at bite site – usually with bites to digit
Management

- IV fluids
- No pressure bandages, incision, suction, tourniquet, extractors, etc…
- No prophylactic antibiotics
- Pain meds
- Occasional epinephrine drips prn
- Consider antivenom
- No blood products unless actively bleeding AND giving antivenom
  - Not ‘nuisance bleeding’
Antivenom Indications

- Progressive swelling
- Thrombocytopenia
- Coagulopathy
- Neurotoxicity
- Shock

- No contraindications
Antivenom: CroFab
Crotalidae Polyvalent Immune Fab (ovine)

- Sheep derived using Mojave, Western and Eastern Diamondbacks, Cottonmouth
- Stops progression of swelling
- Usually reverses hematologic toxicity
- May prevent compartment syndrome
- No evidence that prevents tissue loss
Antivenom

• Goal: gain ‘control’ of envenomation
  – Stop progression of swelling and reverse hematologic abnormalities
  – May need to give maintenance doses after establishing control to prevent recurrent venom effects in first 24 hours after control
Management

• Beware
  – Late onset coagulopathy or thrombocytopenia
  – Recurrence of hematologic findings
  – May be many days after AV, requires close out-patient follow up
All Antivenoms May Produce Hypersensitivity Reactions

- Acute anaphylactoid
  - Most common, rate-related
- Acute anaphylaxis
  - IgE mediated, type 1, pre-sensitized
- Above treated with antihistamines, epi prn
- Delayed (type IV) serum sickness
  - 3 - 21 days, rash / fever / arthralgias
  - Treat with steroids / antihistamines
Special Populations

• Pregnant - case reports suggest poor fetal outcome if first trimester
  – Most would aggressively treat with AV although not studies

• Children - no AV dose adjustments
Exotic Snakebites

• Attempt to identify species and locate appropriate specific AV
  – Patient, local zoo, poison center, Antivenin Index, etc…
  – Do not reflexively administer CroFab

• Supportive care
Venomous Lizards

• Gila Monster - *Heloderma suspectum*
  – Desert areas of southwestern US
• Beaded Lizard - *Heloderma horridum*
  – Mexico
• Large, nocturnal, slow, shy
• Forceful bite - only if handled
  – Difficult to disengage, teeth may break off in the wound
Gila Monster

- Venom contains helothermine
- Poor delivery system (grooved teeth)
- Local pain, tenderness, and edema
- Occasional anaphylactoid reactions
- No antivenom
- Treatment: antihistamines, steroids, epinephrine; airway protection
Angioedema after gila monster bite
Arthropod Envenomations

• Native Spiders
  – Black widow
  – Brown Widow
  – Brown recluse

• Non-native
  – Funnel web

• Scorpions

• Hymenoptera
Widow Spiders

- Many species worldwide
- US: ‘Black widow” = *Latrodectus mactans, L hesperus, L variolus, L geometricus*
- *L mactans*: shiny black with ventral red hourglass on belly
- Venom neurotoxic: $\alpha$-latrotoxin
  - Causes release of neurotransmitters from presynaptic nerve terminals
Black Widow Spider Bite

- +/- fang marks with surrounding erythema
- 15 min - 6 hrs, “latrodectism”
- Characteristic feature: pain
- **Neuromuscular**: cramps, rigidity, tremor, weakness, priapism, uterine contractions
- **Cardiopulmonary**: HTN, tachycardia
- **Systemic**: nausea, diaphoresis, salivation, urinary retention
- **Latrodectus** facies: periorbital swelling, grimacing
Black Widow Treatment

• Recovery usually in 24 to 48 hours
• Supportive care
  – Analgesics
  – Benzodiazepines

  – If this fails:
    • 1 vial equine whole IgG AV
      – Antivenin *(Latrodectus mactans)* (Equine)
      – Analatro Fab2 antivenom is in clinical trial phase presently
Brown Recluse Spider

- *Loxosceles reclusa*
  - AKA Fiddleback Spider
- Violin-shaped mark on cephalothorax
- Other *Loxosceles*: unlikely to interact with humans as much but can probably produce wound
- Very reclusive spider, bites uncommon and over-diagnosed
Brown Recluse Spider

• Venom
  – sphingomyelinase D: necrosis, hemolysis
  – Hyaluronidase: facilitates spread of venom

  – Leads to neutrophil migration to bite site, inflammation, clotting of small vessels, ischemia, necrosis
Brown Recluse Spider

- May have only mild and transient skin irritation
- May develop dermonecrosis
  - Blisters, bleeds, ulcerates in 2-8 hours (red, white, and blue lesion)
  - Lesion may enlarge for a week
  - Healing may take months
- Erythema is gravitational
Brown Recluse Spider

• Systemic involvement uncommon
  – More frequent in children
  – Usually 1-3 days after bite
• Fever, chills, nausea, rash, arthralgias, DIC, hemolytic anemia, and renal failure
• Treatment: supportive care, delayed debridement for large necrotic wounds; steroids recommended for hemolysis
• Evidence does not support dapsone, HBO use in humans
Non-native: Funnel Web Spider

- *Atrax robustus*
- Australia; Sydney funnel web spider
- Venom neurotoxic
  - Robustoxin (atraxotoxin)
  - NT release
- Clinical: no necrosis; autonomic storm, with AMS, HTN, pulmonary edema, muscle writhing, salivation.....
- Pressure immobilization
- Rabbit-derived IgG antivenom
Scorpions

- 1500 species, 30 dangerous
- All dangerous in Family Buthidae
  - In No America, all Centruroides
    - In US, single species dangerous
      - Centruroides sculpturatus
- All have venom that affects neuronal sodium channels and causes excessive NT release
Clinical Effects

- Neurotoxic venom produces
  - Pain, paresthesias
  - Neuromuscular agitation

- Most dangerous species
  - Autonomic storm, cardiovascular collapse, pulmonary edema, death
The Bark Scorpion

- 15-20,000 calls/year to AZ PCCs
- 95% mild, managed at home
  - Grade 1, local pain
  - Grade 2, distal paresthesias
- Severe (Grade 3, 4) mostly peds
  - Roving eye movements (opsoclonus)
  - Neuromuscular agitation
  - Hypersalivation, tachy, fever
The Bark Scorpion

• Management
  – Supportive, with benzodiazepines, opioids, airway protection
  – Monitor for rhabdomyolysis, aspiration pneumonia
  – In August 2011 Anascorp® (produced from the Mexican Centruroides species) was approved by the FDA
Tick Paralysis

- US - *Dermacentor andersoni*
- US - *Dermacentor variabilis*
- Australia - *Ixodes holocylus*

- Cases in US in northwest
- As tick feeds on blood, secretes venom into host which is absorbed systemically
- Neurotoxin: inhibits release of ACh at NMJ
Tick Paralysis: Clinical

- Tick on person for 4-6 days
- Initially: weakness, lethargy, ataxia,
- Then: ascending paralysis beginning in lower extremities, can progress to bulbar within 48 hours, can lead to respiratory weakness, death
- Absent or decreased DTRs
- Treatment: remove tick, supportive
Hymenoptera

- Apidae: honeybees, bumblebees
  - Can sting only once
- Vespidae: Wasps, hornets, yellow jackets
- Formicidae: Fire Ants

Most common reactions are allergic
Africanized Honeybees

- *Apis mellifera scutellata*
- Aggressive, can attack in thousands

- Venom:
  - Melittin - main component, disrupts cell membranes
  - Phospholipase A2 - major allergen
Africanized Honeybees

• > 50 stings may cause systemic toxicity
  – Vomiting, edema, rhabdomyolysis, hemolysis, DIC, death (>500 stings)
• Treatment: supportive care with IVF and pain control, antihistamines and steroids prn, epinephrine prn
• Remove stingers by any method
Fire Ants: Solenopsis spp

- *Solenopsis invicta*
  - Southern US, imported from S America
- Grabs skin with mandibles and stings in a circle around bite
- Burning pain, wheals evolve to pustules, can necrose
- Can have systemic and anaphylactic reactions
Caterpillars / Lepidopterism

• US most important is *Megalopyge opercularis*
  – AKA puss caterpillar or wooly slug
  – an urticarial toxin can produce severe pain, swelling and erythema

• In South America, the most medically important in the world: *Lonomia obliqua*
  – pain, coagulopathy, renal failure, DIC
  – Antilonomic serum (SALon) in Brazil
Toads

• *Bufo spp*
  – *Bufo marinus* - Cane toad
  – *Bufo alvarius* - Colorado River toad

• Bufotoxins
  – Indolealkylamines: hallucinogenic
  – Bufadienolides: inhibit Na-K-ATPase

• Toad licking, toad soup, aphrodisiac preps – cardiac toxicity

• Can treat arrhythmias with digibind
Major Summary Points

- Stinging fish – hot water inactivation
- Nematocysts – acetic acid inactivation
- Rattlesnakes – cyto and hemotoxicity
- Black widow – pain and hypertension
- Brown recluse – necrotic wounds
- Bark scorpion – hypersalivation, opsoclonus, neuromuscular toxicity
- Massive honeybee - toxic reaction to mellitin – rhabdo, DIC