ENVENOMATIONS

ACMT Board Review Course
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CONFLICT OF INTEREST

• NONE

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  • Unless specifically identified are either from Wikipedia or my personal photos

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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
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
- 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
  - Rather attack

Most severe
SCORPAENIDAE

- Venom
  - Inflammatory mediators (lionfish)
  - Stonustoxin, verrucotoxin, catecholamines (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)
  - Anthozoa (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, warm water soak
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
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
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 available
SEA BATHER’S ERUPTION

• AKA ‘sea lice’
• Larvae of Thimble 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
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
- Some evidence for hot water Tx
- Antihistamines / steroids 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
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
SNAKE BITES

- >8000 bites / year in US; <10 deaths
- > 99% venomous bites in US Crotalinae
- Snake Families:
  - Viperidae
  - Elapidae
  - Hydrophiidae
  - Atractaspisidae
  - Colubridae

Subfamilies 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

Rat snake
ATRACTASPIDIDAE

- 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:

Krait (Malaysia, India)
Tiger Snake
Cobra
Mamba
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
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
CROTALINAE

- Pit vipers
- Triangular shaped head
- Heat sensing pits, elliptical pupil
- North, Central, and S. Amer, Asia

- *Crotalus* - Most rattlesnakes
- *Sistrurus* - Massasauga, pigmy
- *Agkistrodon* - Copperhead, cottonmouth
US Pit Vipers

Rattlesnakes

*Crotalus and Sistrurus*

Copperhead

Water Moccasin

*(Agkistrodon)*
US PIT VIPERS

- Venom Toxicity
  - Rattlesnakes > cottonmouths > copperheads

- Venom: cytotoxic, myotoxic, hemotoxic, occasionally neurotoxic
RATTLE SNAKE 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
- Presynaptic neurotoxins
  - $\beta$ neurotoxins
  - Some elapid and viper venoms
  - Inhibit release of acetylcholine at the neuromuscular junction
RATTLESNAKE NEUROTOXICITY

• β neurotoxins
  • Common in Mojave and Southern Pacific (C. scutulatus and C. helleri)
  • Crotoxin, in South American rattlesnake (C. durissus terrificus)
• Fasciculations most common
PHYSICAL EXAM

- Tenderness, swelling, ecchymosis
- Variable # puncture wounds; oozing
- Axillary or inguinal tenderness
- 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 (earlier is better)
• No blood products unless actively bleeding AND giving antivenom
ANTIVENOM INDICATIONS

- Progressive swelling beyond bite site
- 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
- May minimize tissue necrosis
ANTIVENOM

- Goal: gain ‘initial 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-pt 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
• Serum Sickness (type III) common
• 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 no studies

• Children - no AV dose adjustments – Treat to the severity of the bite
EXOTIC SNAKE BITES

• Attempt to identify species and locate appropriate specific AV
  • Patient, local zoo, poison center, Antivenom 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
- 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
BLACK WIDOW SPIDER BITE

- +/- fang marks with surrounding erythema
- 15 min - 6 hrs, “latrodetism”
- 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
- When this fails:
  - 1 vial equine whole IgG AV
    - Antivenin (*Latrodectus mactans*) (Equine)
    - *Analatro* Fab2 antivenom is in clinical trail 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
NON-NATIVE: FUNNEL WEB SPIDER

- *Atrax robustus*
- Australia; Sydney funnel web spider
- Venom neurotoxic
  - Robustoxin (atracotoxin)
  - NT release
- Pressure immobilization
- Rabbit-derived IgG antivenom
SCORPIONS

- 1500 species, 30 dangerous
  - In N. 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 holocyclus*
- 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)
- Remove stingers by any method
FIRE ANTS: SOLENOPSIS SPP

- *Solenopsis invicta*
  - Southern US, imported from S America
  - Venom is 95% alkaloid
  - 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* “Giant Silkworm Moth”
  • 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