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
  • Acknowledgements: Special thanks to Michelle Ruha for contributions from previous versions

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

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

ENVENOMATIONS
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

• Pterois
  • Lionfish
  • Rather escape
• Scorpaena
  • Scorpionfish
• Synanceja
  • Stonefish
  • Rather attack

Most severe

ENVENOMATIONS

• Venom
  • Inflammatory mediators (lionfish)
  • Stonustoxin, verrucotoxin, catecholamines (stonefish)
  • Local - Erythema, pain, induration
  • Systemic - N/V, syncope, arrhythmia, seizure, pulmonary edema, death

ENVENOMATIONS 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)

ENVENOMATIONS

- 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

ENVENOMATIONS

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
• 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

Envenomations
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

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

Snake Families:
- 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:
  - Cobra
  - Mamba
  - Krait (Malaysia, India)
  - Tiger Snake

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*

**ENVENOMATIONS**

**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
  - α neurotoxins
  - Most elapid and sea snake venoms
  - Competitively bind nicotinic acetylcholine receptors and produce a nondepolarizing neuromuscular blockade
    - Neostigmine may reverse
- Presynaptic neurotoxins
  - β
  - 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)
  - Crototoxin, 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
ENVENOMATIONS

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

Local: oozing at bite site, ecchymosis

Severe swelling, third spacing
**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-patient follow up

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**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

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**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 SNAKEBITES

• 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: α-latrotoxin
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
• When 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

ENVENOMATIONS

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

ENVENOMATIONS

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 (atraxotoxin)
  - 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

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