EVE 491/591
Toxicology

Lecture #4
1. Haiti update
2. Biological Poisons
3. Case study – Part III

Haiti Update
1. 5.9 aftershock yesterday; a few more buildings down
2. New casualties unknown; estimates still range up to 200,000
3. 2 million homeless
4. $1 billion in worldwide aid pledged
5. 16,000 US troops on the ground...Too many?
6. International rescue teams pulling back

Biological Poisons
• There are MANY
  – Holly berries, daffodils, oleander, hemlock
  – Tiger snake venom, blue-ringed octopus venom, dart frogs
• Purposes
  – Defense
  – Predation
• Typically much more toxic than man-made chemicals
  (effective in small amounts)
• Human utility
  – Physiological research
  – Pharmacologic prototypes
Toxins

- Toxic substances of biological origin
- Categorized based on the organism that produces them:
  - Bacteria
  - Fungi: mycotoxins
  - Algae: phycothoxins
  - Plants: phytotoxins
  - Animals: zootoxins
- Venom: an animal toxin that is produced in a poison gland and is delivered to another animal through a bite or sting

LD_{50} Values of Some Common Animal Toxins

<table>
<thead>
<tr>
<th>Species</th>
<th>Hosts</th>
<th>LD_{50} (mg/kg)</th>
<th>Locality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frogs</td>
<td>South America</td>
<td>0.26</td>
<td>South America</td>
</tr>
<tr>
<td>Fly Tadpoles</td>
<td>Subadult</td>
<td>0.22</td>
<td>Subadult</td>
</tr>
<tr>
<td>Sea Creatures</td>
<td>Subadult</td>
<td>0.26</td>
<td>Subadult</td>
</tr>
<tr>
<td>Antarctic shrimp</td>
<td>Adult</td>
<td>0.28</td>
<td>Australia</td>
</tr>
<tr>
<td>Sea Otter</td>
<td>Adult</td>
<td>0.26</td>
<td>Adult</td>
</tr>
<tr>
<td>Sea Turtle</td>
<td>Adult</td>
<td>0.26</td>
<td>Adult</td>
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Animal Toxins

• Spider Venoms
  – Black widow spiders (*Lactrodectus* spp.)
    • Venom is neurotoxic
    • Effect: “Latrodectism” (pain, nausea, muscle contractions and cramps)
  – Brown recluse spiders (*Loxosceles* spp.)
    • Venom is cytotoxic and hemolytic
    • Effect: “Loxoscelism” (local and systemic effects associated with necrosis)

Animal Toxins, cont.

• Scorpions
  – Very painful sting
  – Venom is generally neurotoxic
  – Most species relatively harmless to humans
• Bees and Wasps
  – Moderately painful sting
  – Venom is generally myotoxic (muscular)
  – Minimal toxic effect unless
    • Multiple stings
    • Individual is allergic to venom

Animal Toxins, cont.

• Cnidarians (jellyfish, corals, and anemones)
  – Nematocysts (thread-like “tentacles”)
    • Capable of discharge even if animal is dead!
  – Box Jellyfish, *Chironex fleckeri*
    • Extremely toxic
    • Excruciating sting can produce shock and drowning
  – Portuguese Man-of-War, *Physalia*
    • Less toxic
    • Painful sting that leaves welts
Animal Toxins, cont.

• **Mollusks**
  – Blue-ringed octopus, *Hapalochlaena lunulata* and *Hapalochlaena maculosa*
    • Capable of killing a human (painless) within 5 minutes
    • No known antidote
  – Bivalve mollusks: consumption may lead to
    • Amnesic shellfish poisoning
    • Diarrheic shellfish poisoning
    • Neurotoxic shellfish poisoning
    • Paralytic shellfish poisoning
  – Cone snails: several dozen humans confirmed killed

Animal Toxins, cont.

• **Amphibians**
  – Poison dart frogs, *dendrobates* and *phylobates*
    • >100 toxins have been identified in secretions
    • Weaponized by native Central/South Americans
    • Secretions may also have medicinal value
  – “Frog licking”
    • An hallucinogenic effect of the toxin
    • MANY hospitalizations

Animal Toxins, cont.

• **Reptiles**
  – Venomous snakes
    • Venom may be proteolytic, hemotoxic, neurotoxic, cardiotoxic and/or cytotoxic
    • Approximately 125,000 deaths annually
      – The Russell’s viper kills more than any other (moderately toxic venom; although irritable and wide-ranging)
      – Inland Taipan has most toxic venom (very, VERY shy, however; no deaths ever documented)
    • Most inject venom; a few spit!
Animal Toxins, cont.

• **Lizards**
  – Gila Monster, Mexican Bearded Lizard
    • SW USA and Mexico
    • Painful bite with neurotoxic or hemotoxic venom
    • Few (if any) deaths documented
  – Monitor lizards, Komodo dragons
    • Likely "some" venom (debatable)
    • Komodo dragon has septic bacteria in saliva
    • Few human deaths recorded; most as a result of blood loss and/or shock

Bacterial Toxins

• **Botulinum Toxin**
  – Neurotoxic protein that is produced under anaerobic conditions by the bacterium *Clostridium botulinum*.
  – **LD₅₀**: approximately 0.25 - 1 ng/kg
  – Likely the most acutely toxic substance known
  – *Clostridium* spores are ubiquitously found in soil globally
  – Used in very small amounts both as a cosmetic treatment (Botox) and to treat painful muscle spasms (Dysport)

Comparison of the Toxicity of Botulinum Toxin with Several Other Chemical Substances

<table>
<thead>
<tr>
<th>Toxin</th>
<th>LD₅₀ (µg/kg)</th>
<th>Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum toxin</td>
<td>0.00025</td>
<td>150,000</td>
</tr>
<tr>
<td>Botrachotoxin (amphibian dart poison)</td>
<td>2</td>
<td>538</td>
</tr>
<tr>
<td>Tetrodotoxin (puffer fish poison)</td>
<td>9</td>
<td>319</td>
</tr>
<tr>
<td>Sodium cyanide</td>
<td>10,000</td>
<td>65</td>
</tr>
</tbody>
</table>
Bacterial Toxins, cont’d

• **Tetanus Toxin**
  – Described by Hippocrates 2500 years ago
  – Neuromuscular toxin produced by the bacterium *Clostridium tetani*
  – LD₅₀: approximately 2 ng/kg
  – Introduced into the body through skin lacerations, abrasions, and occasionally from body piercing or tattooing

Fungal Toxins

• **Mushroom Toxins**
  – Food processing (cooking, freezing, etc) will not “detoxify”
  – LD₉₀
    • Death cap: 0.1 mg/kg
    • Psilocybins: 285 mg/kg
  – Four categories of toxic effect based on the primary toxicity
    • Gastrointestinal Effects
    • Disulfiram-Like Effects (anxiety, high BP)
    • Neurotoxic Effects
    • Cytotoxic Effects

Algal Toxins

• Cyanobacteria commonly known as blue-green algae.
  – Primitive photosynthetic organisms
  – Approx. a dozen are toxic
  – Some of these are responsible for “swimmers itch”
  – Others linked to liver cancer
  – Still others produce a very dangerous neurotoxin
• Other algal bacteria (eg. red tide) associated with massive fish kills and shellfish contamination
Higher Plant Toxins

• Many higher plants produce harmful substances that can produce injury and death if ingested
• Toxins are present in fruit, vegetable, garden, outdoor ornamental, and wild plants
• Plant toxins can be classified based on their general chemical structure:
  – Alkaloids (e.g., Yew, Poison Hemlock, Nightshade, Jimsonweed)
  – Proteins and amino acids (e.g., Castor bean)
  – Glycosides (e.g., Lily of the Valley, Foxglove, Oleander)
  – Oxalates (e.g., Philodendron, Dieffenbachia, Rhubarb)
  – Phenols, resins, and volatile oils (e.g., Poison Ivy, Poison Oak, Poison Sumac, Rhododendrons)
  – Phototoxins (e.g., St. John’s wort)

Case Study #1 “Mary Beth”

Refer to the handout provided (Part III).

Questions:
1. Do you agree with Mary Beth that something seems off-base with the number of cancer cases? How would you determine if there were more cancer deaths than could be accounted for by chance?
2. What information about Mary Beth’s mother and the other victims of cancer would be needed for us to evaluate the cause of her cancer?
3. List potential carcinogens linked to coal mining and all possible routes of exposure.
4. What are the logical target organs for cancer related to coal mining? Can you think of others?
5. Describe a mechanism for one of the potential cancers that were suggested in questions 3 and 4.