Toxicities

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Lecture Overview

• Basic principles of toxicology
  • Common terms
  • Route(s) of exposure
    • Oral, inhalation, dermal
• Decontamination therapy
• Selected toxicants of Interest
Definitions

• **Poison**: Any solid, liquid, or gas that, when introduced into or applied to the body, can interfere with the life processes of cells of the organism

  • **Occurs by its own inherent chemical properties**
    • Without acting mechanically and regardless of temperature
    • Type of HAZARD
Definitions

• **Poison = Toxicant**
• **Xenobiotic**: Any substance, harmful or not, that is foreign to the body
• **Toxin** = Poison of biological origin
Definitions

• **Toxic** = chemical has the properties of a poison
• **Toxicity** = amount of poison that, under a specific set of conditions, will cause a detrimental effect.
  • Agents are usually compared on a *mg/kg* basis
  • LD$_{50}$ is an estimate of a dose required to kill 50% of the animals given that dose
Exposure Dose

Small Amounts Matter!

Exposure dose =
5 ml × 100 mg/ml = 500 mg
500 mg/30 kg = 16.7 mg/kg
LD50 (dog) = 9 mg/kg
Exposure Dose

30 kg

Exposure dose = $\frac{6000 \text{ mg}}{30 \text{ kg}} = 200 \text{ mg/kg}$

Small Amounts Matter!
### Exposure Dose

**30 kg**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Toxic dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>100-200</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>&lt; 20-30</td>
</tr>
<tr>
<td>C4</td>
<td>~ 100</td>
</tr>
<tr>
<td>Caffeine</td>
<td>&lt; 100-200</td>
</tr>
<tr>
<td>Cocaine</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Heroin</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>100</td>
</tr>
<tr>
<td>MDMA (Ecstasy)</td>
<td>&lt;10-100</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>&lt;10</td>
</tr>
<tr>
<td>VX</td>
<td>0.003-0.010 (est)</td>
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</tbody>
</table>

**6 grams**

Exposure dose = 200 mg/kg
Common Routes of Exposure: Working Dogs

Oral exposure
- Most common
- Allows for decontamination

Inhalation exposure
- Uncommon
- Gases and inhaled particles
- Respiratory support

Dermal exposure
- Common
- Mixed skin and oral (grooming)
<table>
<thead>
<tr>
<th>Exposure Scenarios</th>
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</thead>
<tbody>
<tr>
<td><strong>Ingestion</strong></td>
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<tr>
<td>Explosives</td>
</tr>
<tr>
<td>Drugs</td>
</tr>
<tr>
<td>Pesticides</td>
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<tr>
<td>Commercial products</td>
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<tr>
<td><strong>Inhalation</strong></td>
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<tr>
<td>Smoke</td>
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<tr>
<td>Combustion products</td>
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<tr>
<td>Carbon monoxide</td>
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<tr>
<td>Cyanide</td>
</tr>
<tr>
<td>CWAs</td>
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<tr>
<td><strong>Injection</strong></td>
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<tr>
<td>Snake</td>
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<tr>
<td>Ants</td>
</tr>
<tr>
<td>Bees</td>
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<tr>
<td>Drugs</td>
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An ounce of prevention is worth a pound of cure
- Ben Franklin

Prevention is Critical!
An Exposure Happened What Can We Do Next?

WELL, THIS IS AWKWARD...
When to Suspect a Poisoning

- Acute onset of clinical signs in a previously normal animal
- Multiple animals affected in the same household
- “Odd” or severe clinical signs involving one or more organ systems
  - Seizures
  - Hepatic failure
  - Renal dysfunction
- EXPOSURE HISTORY
Management Goals

• Prevent Ongoing Human and Animal Exposure
  • Human first aid
  • Safely remove animal from source

• Assess Chemical Exposure
  • Evidence of exposure
  • Try to identify the agent

• Seek Veterinary Advice
  • Tailored decontamination approaches
    • Skin (e.g., bathe)
    • Gastrointestinal tract (e.g., emetics)

• Transport to Veterinary Facility
General Principles

• Goals for the management of acutely poisoned animals include:
  • Stabilization of vital signs
  • Ongoing clinical evaluation
  • Prevention of continued exposure to the toxicant
  • Administration of an appropriate antidote
  • Facilitation of the removal of the absorbed toxicant
  • Supportive therapy
Toxicology Help is Available

• ASPCA Animal Poison Control Center
  • $65 consultation fee
  • (888) 426-4435
• The Pet Poison Hotline
  • $49 consultation fee
  • (800) 213-6680

All 24/7
Toxicological Hazards

Medical PPE may be inadequate for many chemical agents!

Graniteville, SC (2005)
60 tons chlorine

Maryville, TN (2015)
Acrylonitrile
INHALATION EXPOSURE

Management goals
- Respiratory protection!
- Remove from source
- Oxygen
  - Supplemental oxygen given by mask or in an unconscious animal via an endotracheal tube
- Flush the animal’s eyes with saline solution and apply eye ointment/lubricant (NO steroids)
ORAL EXPOSURE

Management goals
• Remove source
• Decrease absorption
  • Dilution
  • Emetics
  • Activated charcoal

Depends on agent, time since ingestion, and animal's condition
Dilution

• Rapid dilution
  • Water or milk
• Management of corrosive ingestions
  • Acid or alkali ingestion
    • Sodium hypochlorite, sodium hydroxide, “button batteries”
  • Gastrointestinal protectorants and demulcents
• Neutralization of the corrosive with vinegar, sodium bicarbonate, etc. is contraindicated
Batteries

• Dry cell
  • Grey/black powder inside
  • Look for evidence on teeth
• Button
  • Size of pencil eraser
• Lithium ion
  • Risk of fatality if ingested!
Lithium Batteries

• Human poison centers:
  • 2000-2009, 92% of disk batteries from fatal ingestions or those with major outcomes were 20-mm lithium cells
  • Most were imprint code CR 2032 (71%) or CR 2025 (21%)
    • "CR" represents the battery chemistry, "20" is the diameter, and "32" indicates the thickness (3.2 mm) of the battery.
Batteries

• Corrosive to GI mucosa due to electrical discharge and contents

• Li batteries
  • Higher voltage
  • More tissue necrosis than button alkali batteries

• Onset of signs: within 1-12 hr

Courtesy of the Arizona Poison & Drug Information Center
Batteries

• Diagnostics
  • Physical exam
  • Radiograph

• Treatment:
  • Remove foreign body
  • Administer GI protectants
  • Re-radiograph
Emetics Update (DOGS)

• Administration recommendations
  • < 2 hr after toxicant ingestion
  • Feed small meal (bread, weight dog food)

• Contraindications
  • CNS depression, seizures
  • Ingestion of:
    • Corrosives
    • Hydrocarbon/petroleum distillate
    • Anti-emetic drugs
Emetics Update (DOGS)

- Hydrogen peroxide (3% solution)
  - 1 ml/lb body weight; per os
  - Up to 45 ml
  - Repeat once if emesis does not occur after 10-15 minutes

- Apomorphine
  - 0.03 mg/kg; IV
  - Crushed tablet dissolved in saline – administer via conjunctival sac – rinse eye once vomiting occurs
Emetics Contraindications

• Difficulty breathing (dyspnea), hypoxia, seizures, coma, or abnormal pharyngeal reflexes
• Corrosive agents
• Volatile hydrocarbons
  • Emesis is rarely recommended with ingestion of low viscosity hydrocarbons (e.g., gasoline, xylene, toluene, lighter fluid, and mineral seal oil)
• Species that can not vomit
  • Horses, rodents or rabbits
Removes 30-50% of stomach contents

Time < 2 Hours?
- Yes
  - Corrosive?
    - Yes
      - Dilution
    - No
      - Volatile hydrocarbon?
        - Yes
          - Dilution
        - No
          - Vomited?
            - Yes
              - Induce vomiting
            - No
              - Normal airway control?
                - Yes
                  - Toxic dose?
                    - Yes
                      - Induce vomiting
                    - No
                      - Seizures?
                        - Yes
                          - Induce vomiting
                        - No
                          - Don't use

- No
  - Too late
Emetics

• Salt
  • NEVER USED
• 3% hydrogen peroxide (2 mL/kg, PO)
• Apomorphine (0.03 mg/kg (IV) or 0.04 mg/kg (IM))
  • Some eye drop formulations are marketed
# Emetic Efficacy

<table>
<thead>
<tr>
<th></th>
<th>3% Hydrogen peroxide</th>
<th>Apomorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to onset of emesis</td>
<td>15 min</td>
<td>19 min</td>
</tr>
<tr>
<td>Duration of emesis</td>
<td>42 min</td>
<td>27 min</td>
</tr>
<tr>
<td>% Toxicant recovered</td>
<td>48%</td>
<td>52%</td>
</tr>
<tr>
<td># Emetic events</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>% Emesis (1 dose)</td>
<td>86%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Khan et al., 2012
Activated Charcoal and Cathartics

• Medical grade activated charcoal
• Charcoal tablets are much less effective
• May cause constipation and cathartics may be needed
Activated Charcoal

• Most recent (< 6 hr) ingestions
• Use a 10:1 activated charcoal-to-toxicant (mass) ratio
• 1-4 g/kg (PO, q 4-6 hr)
• Repeated administration of activated charcoal is commonly recommended for many toxicants

**CL in:** Caustic agent
DERMAL EXPOSURE

Management goals
• Remove source
• Decrease dermal exposure (bathe)
• Decrease oral absorption
  • Emetics
  • Activated charcoal

{ Depends on agent, time since ingestion, and animal’s condition }
DERMAL EXPOSURE

Non-pesticide detergent shampoo

LOTS of water to rinse

Oral exposure from grooming
Pepper Spray

The active ingredient in most pepper sprays is capsaicin (oily extract of pepper plants of the genus Capsicum).

Dermal exposure to pepper spray causes tingling, intense burning pain, swelling, redness, and, occasionally, blistering in people and may have similar effects with dogs.
Pepper Spray

Most commonly causes:

- Eye irritation (redness, swelling, severe burning pain, stinging, conjunctival inflammation, lacrimation, blepharospasm and involuntary or reflex closing of the eyelids)
- Respiratory effects including cough, bronchoconstriction (asthma-like signs), laryngospasm, and respiratory arrest
Pepper Spray

First Aid:
• Flush eyes
• Bathe skin (mild detergent shampoo and water)
• Oxygen
• Seek veterinary care if ocular (eye) or respiratory signs persist or worsen
Toxicants of Interest
Police dog accidentally ingests crystal meth during drug raid

Koda, of the El Cerrito Police in California, accidentally ingested the drug. His handler Joshua Del Prado rushed him to a veterinarian who was able to save the K-9 and get him back to work quickly.

Police dog ate hamster after knocking over its cage during raid on man's home

- Manchester Police were raiding 46-year-old Musa Kham's house in Oldham, Greater Manchester

A police dog ate a hamster during a raid on the pet's owner's home. Officers from Greater Manchester police were raiding the home of a man who has since been prosecuted by the RSPCA.

Musa Khan, 46, had his home in Oldham searched by officers last May.

Star RCMP puppy in training dies after eating rope and rocks

MICHAEL TUTTON
HALIFAX — The Canadian Press
Published Tuesday, Jan. 19, 2016 9:18PM EST
Last updated Tuesday, Jan. 19, 2016 9:20PM EST
Toxicants Encountered in Veterinary Practice

• Pesticides
• Drugs (veterinary and human)
• Household chemicals
• Workplace chemicals
• Feed additives
• Poisonous gases
Marijuana (*Cannabis sativa*)

- All species affected
- Toxic principle:
  - The cannabinoid δ-9-tetrahydrocannabinol (THC) is the major psychoactive constituent
  - There are two specific cannabinoid receptors in humans and dogs, CB₁ (primarily in central nervous system) and CB₂ (peripheral tissues)
Marijuana

• Clinical signs
  • Mentation changes
  • Vomiting
  • Ataxia
  • Bradycardia
  • Increased respiratory rate
  • Tachypnea

• Onset of clinical signs usually occurs within 1-2 hours of exposure

• Duration of clinical signs can range from 1-3 days
Marijuana Toxicity

• The minimum lethal oral dose for dogs for THC is more than 3 g/kg
  • This dose is 1000 times the dosage where behavioral effects are observed
• Plants can contain up to 1-6% THC and extracts as much as 28% THC
• THC can be detected using analytical chemistry methods

A typical marijuana cigarette (a “joint”) generally contains 500-1000 mg of crude plant material and 15-30 mg of THC
Marijuana Ingestion Management

• Activated charcoal
• Hypotension: begin intravenous (IV) fluid administration
• CNS agitation: benzodiazepines
• Intralipid therapy to bind the highly lipophilic THC has been utilized to help reduce clinical signs
• The majority of dogs experiencing intoxication after marijuana ingestion recover completely without sequelae
Cocaine

• Clinical signs
  • Vomiting
  • Ataxia
  • Tremors/seizures
  • Tachycardia
  • Increased respiratory rate
  • Dilated pupils
Amphetamines

- Clinical signs
  - Vocalization
  - Ataxia
  - Hypersalivation
  - Tremors/seizures
  - Increased respiratory rate
  - Tachycardia/bradycardia
  - **Hyperthermia**
Amphetamine

Warning from Europe: "Superman" pills

An alert was recently issued in The Netherlands warning about pills with a distinctive Superman logo, sold as MDMA (also called ecstasy or Molly) but actually containing a lethal dose of another substance, PMMA (paramethoxymethylamphetamine). These pills have not been reported in the U.S., but four people in the UK are thought to have died after taking these pills.

http://www.drugabuse.gov/
Amphetamine

• Mode of action
  • Increase catecholamine release
  • Inhibit catecholamine reuptake
  • Increase release of serotonin
Amphetamine

- Clinical signs
  - Agitation
  - **Hyperthermia**
  - Tremors
  - Seizures
  - Tachycardia
  - Hypertension
  - Cardiac arrhythmias
  - Coma
Amphetamine

• Treatment
  • Gastric decontamination
    • Activated charcoal
  • Tranquilization (chlorpromazine or acepromazine)
    • May potentiate other agents and induce severe hypotension
  • Signs may be seen for 12 to 48 hours or more
  • Often good prognosis
Explosives

• Smokeless powders
• More “reactive” the material the more likely to cause:
  • Decreased blood pressure
  • Methemoglobinemia
  • Nervous system depression
Explosives

- RDX/C4*
  - Seizures
  - Nausea
  - Vomiting
  - Reddened mucous membranes
- Signs can be delayed due to slow GI absorption

*Cyclotrimethylenetrinitramine
Hymenoptera (Bees, Wasps)

- Local reaction (wheal/urticaria)
  - Sharp, burning pain
  - Pruritis
  - Edema
    - Extensive reactions may involve entire extremity
    - Stings to tongue/throat may cause loss of airway
Hymenoptera

- Systemic reactions
  - Mild: Diffuse itching, urticaria, swelling distant from sting site, flushing
  - Severe: Laryngeal edema, severe bronchospasms, profound hypotension
Hymenoptera

• Systemic reactions
  • Most deaths (75%) occur within 4 hours of the sting
Hymenoptera

• Treatment
  • Local Reactions
    • Remove retained stinger (flick, or remove with tweezers)
  • Ice to site
  • Oral antihistamines
  • Mild analgesics
Hymenoptera

• Treatment of Severe Reactions (Anaphylaxis)
  • Epinephrine should be immediately administered, SC, at a dosage of 1:1,000 (0.1–0.5 mL). This dosage can be repeated every 10–20 min.
• IV fluids (shock)
• Antihistamines such as diphenhydramine (10–50 mg, SC or IV) and corticosteroids should also be given.
• Supplemental oxygen.
• Water or alcohol or ice compresses
Hymenoptera

• Severe Reactions
  • Hemolysis
  • Cardiac arrhythmias
  • Vomiting, diarrhea
  • Others (rare)
  • Fatalities (very rare)
Fire Ants
(Solenopsis spp)

• Toxin = piperidine alkaloid (Solenopsin A)

http://www.ars.usda.gov/
Fire Ants

• Clinical signs
  • Swelling, redness, itchiness, and pain around the site of bite
  • Pustule formation

• Allergic reactions (people)
  • Dyspnea

• All veterinary species affected
  • Dogs, others
Fire Ants

• **Management**
  • Steroids
  • Antihistamine
  • Analgesics
  • Antibiotics
Snakes

• Humans
  • 45,000 bites per year in U.S.
  • 8,000 bites from venomous snakes
  • 25% are “dry strikes”

• Most common victims:
  • Children
  • Intoxicated adults
  • Snake handlers and collectors
Venomous Snakes

• **Elapidae**
  - Cobra, mamba, kraits, coral snakes
  - Small to moderate sized fangs at the front of the mouth

• **Viperidae**
  - Well developed fangs on hinged maxillae
  - Two subfamilies:
    - Viperinae ("true" or typical vipers)
    - Crotalinae (pit vipers)
Poisonous Snakes

• **Species of poisonous snakes found in North Carolina**
  
  • **Pit Vipers**
    • Copperhead (*Agkistrodon contortrix*)
    • Cottonmouth (*Agkistrodon piscivorous*)
    • Timber Rattlesnake (*Crotalus horridus*)
    • Eastern diamondback rattlesnake (*Crotalus adamanteus*)
    • Pygmy rattlesnake (*Sistrurus miliarius*)

  • **Elapidae**
    • Eastern coral snake (*Micrurus fulvius fulvius*)
Pygmy Rattlesnake
*Sistrurus miliarius*

36-96” long

Elliptical pupil

Pit organ
• Retractable fangs
Timber Rattlesnake
Canebrake Rattlesnake
(\textit{Crotalus horridus})

• Subspecies:
  • \textit{Crotalus horridus horridus} (Timber Rattlesnake)
    • Mountains
  • \textit{Crotalus horridus atricaudatus} (Canebrake Rattlesnake)
    • Piedmont
    • Coastal plains
Timber Rattlesnake
Canebrake Rattlesnake
(*Crotalus horridus*)

35-74” long
36-96” long

Eastern Diamondback Rattlesnake
*Crotalus adamanteus*
Cottonmouth
*Agkistrodon piscivorous*

20-75” long
Cottonmouth
*Agkistrodon piscivorus*
Copperhead
(*Agkistrodon contortrix*)
Copperhead
(*Agkistrodon contortrix*)

22-53” long

juvenile
Eastern Coral Snake
(*Micrurus fulvius fulvius*)

“Red touch yellow bad for fellow.
Red touch black good for Jack”

22-48” long
Snake Bite

• Snakebite, with envenomation, is a true emergency
  • Not all snake bites result in envenomation
    • “Dry bites” account for ~ 25 to 50% of all US pit viper bites
  • Rapid examination and appropriate treatment are paramount
Grading of Pit Viper Envenomation

• Dry Bite
  • Local abrasion or bite mark without severe pain or swelling
  • Normal vital signs
  • Normal coagulation studies
  • Normal platelet count
Grading of Pit Viper Envenomation

• Mild Envenomation
  • Local pain and swelling
  • Normal vital signs
  • Normal to mildly abnormal coagulation studies
  • Platelet count > 100,000
Grading of Pit Viper Envenomation

• Moderate Envenomation
  • Local pain and moderate swelling (>12” from bite site)
  • Normal vital signs
  • Abnormal coagulation studies
  • Thrombocytopenia
Grading of Pit Viper Envenomation

• Severe Envenomation
  • Initial presentation often consistent with shock
  • Altered mental status with or without normal vital signs and/or poor peripheral perfusion
  • Abnormal coagulation studies (PTT > 50; INR > 3; fibrinogen < 50)
  • Thrombocytopenia (platelets < 20,000)
Crotalidae Snake Bite – Clinical Signs

• Pain and edema around the bite site
• Swelling
• Dyspnea
• Nausea, vomiting, or diarrhea
• Coagulopathy
  • Thrombocytopenia
  • Hematemesis, hematochezia
• Neurologic symptoms:
  • Weakness
  • Paresthesias
  • CNS depression
• Hypotension/hypertension
• Tachycardia
• Muscle fasciculations
Crotalidae Snake Bite – Clinical Signs

- Late phase (> 24 hours)
  - Active and alert after 24 hours, death due to the direct effects of the venom is unlikely
  - Infection (possibly anaerobic) may be of concern
  - Tissue necrosis may occur
Crotalidae Snake Bite - Diagnosis

• Typical pit viper bites are characterized by severe local tissue damage that spreads from the bite site
• The tissue becomes markedly discolored within a few minutes
• Dark, bloody fluid may ooze from the fang wounds if not prevented by swelling
• Skin sloughing
• Fang marks
  • One fang mark
  • Multiple punctures
Poisonous Snake Treatment

• Preventing or controlling shock
• Neutralizing venom
• Preventing or controlling coagulopathy
• Minimizing tissue necrosis
• Preventing secondary infection
• Pain control
Crotalidae Snake Bite Vaccinations

Red Rock Rattlesnake Vaccines: Protection when danger strikes

Rattlesnake bite is a veterinary emergency that results in serious injury or even death to thousands of dogs and horses each year. Rattlesnake venom is a complex mixture of toxins that spreads through an animal’s body following the bite. Red Rock has developed vaccines to defend both dogs and horses from the dangerous effects of rattlesnake venom. That’s rattlesnake protection that will put you and your animals at ease.
Crotalidae Snake Bite Vaccinations

• Protective immunological response possible
• Red Rock product
• Efficacy and safety studies are lacking.
• Positive reports could be due to:
  • Vaccination works?
    • False sense of security?
  • “Dry bites”
  • Not effective for the Mojave rattlesnake
  • May have limited or no immunity for the Eastern species of rattlesnakes (and other members of the Crotalidae family)
“No statistically significant difference in morbidity or mortality between vaccinated and unvaccinated dogs was found. The findings of this study did not identify a significantly protective effect of previous vaccination in the cases of moderate to severe rattlesnake envenomation that require treatment with antivenin.”