

## What's New in Toxicology

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1

## Outline

- Toxicokinetics review
- Decontamination
  - Emesis
  - Activated charcoal
  - Intravenous lipid emulsion
- Common toxicants

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## Toxicokinetics

Toxicokinetics = what the body does to a toxin

- Absorption
- Distribution
- Metabolism
- Excretion

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## Absorption

Time	Rapid Concentration	Slow Concentration
0	0	0
1	50	5
2	30	25
3	10	20
4	5	15

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## Distribution

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- Volume of distribution ( $V_D$ )

$V_D$	Plasma Concentration	Tissue Concentration
Small	High	Low
Large	Low	High


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## Metabolism

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- Increased water solubility → increased excretion
- BUT some substances will be made more toxic!
- Some substances never metabolized



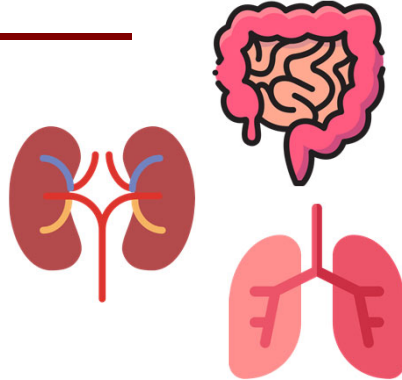
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## Excretion

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- Clearance (CL)



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## Half Life ( $T_{1/2}$ )

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- Dependent on  $V_D$  and CL

	$T_{1/2}$
Small $V_D$	Decreases
Large $V_D$	Increases
Low CL	Increases
High CL	Decreases

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## Toxicodynamics

- Toxicodynamics = what a toxin does to the body
- Mechanism of action
- Concentration
- Dose-response relationship

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## Emesis

- Dopamine agonist
- Effective in dogs



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## Emesis

- Apomorphine
  - SC or IV!
  - 0.03 mg/kg

**Evaluation of subcutaneous versus intravenous administration of apomorphine for induction of emesis in dogs**

Christiana Fischer VMD  
Kenneth J. Drobatz DVM, MSCE  
Vincent J. Thawley VMD



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## Emesis

- Dexmedetomidine 7 mcg/kg IM
- OR**
- Hydromorphone 0.1 mg/kg SC



ORIGINAL STUDY

**Assessment of hydromorphone and dexmedetomidine for emesis induction in cats**

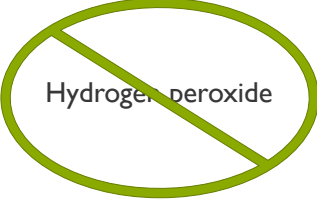
Michael R. Nystrom DVM, Adesola Odunayo DVM, MS, DACVECC, Chika C. Okafor DVM, MS, PhD, DACVPM

First published: 25 June 2019 | <https://doi.org/10.1111/vec.12866>

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## Emesis



Hydrogen peroxide

**JOURNAL OF Veterinary Emergency AND Critical Care**

Original Study  
**Effects of oral 3% hydrogen peroxide used as an emetic on the gastroduodenal mucosa of healthy dogs**

Alicia H. Niedzwiecki DVM, Bradley P. Book DVM, DABVP, DACVECC, Kristin M. Lewis DVM, MS, DACVIM, J. Scot Estep DVM, DACVP, Joseph Hagan ScD

First published: 14 December 2016 | <https://doi.org/10.1111/vec.12558> | Citations: 8

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## Activated charcoal

- Risk of hypernatremia
- Monitor sodium
- Give fluids

**JOURNAL OF Veterinary Emergency AND Critical Care**

ORIGINAL STUDY  
**Effect of single dose administration activated charcoal containing sorbitol on serum sodium concentration and hydration status in dogs**

Katherine A. Mix DVM, Jennifer Stafford DVM, DACVIM, DACVECC, Erik Hofmeister DVM, MA, DACVAA, DECVAA


First published: 29 August 2019 | <https://doi.org/10.1111/vec.12887> | Citations: 1

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## Intravenous lipid emulsion (ILE)

- Lipid shuttle versus lipid sink
- Improves cardiac function in cardiovascular toxicoses



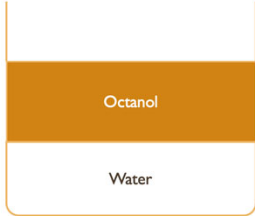
Intralipid® 20% 500 ml

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## Intravenous lipid emulsion (ILE)

- $\log P$  = measure of lipophilicity



Octanol

Water

**NIH** National Library of Medicine  
National Center for Biotechnology Information

**PubChem**

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## Top 10 Toxicants




1. Over-the-counter medications
2. Human prescription medications
3. Human foods
4. Chocolate
5. Bouquets and plants
6. Household toxicants
7. Rodenticide
8. Veterinary products
9. Insecticides
10. Garden products

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## OTC Medications

- Decongestants
  - Pseudoephedrine
  - Phenylephrine
- Adrenergic stimulants

- Cardiovascular 
- CNS 
- Gastrointestinal 



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## OTC Medications

- Decongestants
  - Pseudoephedrine
  - Phenylephrine
- Sedation
- Beta blockers
- Anti-hypertensive agents
- Supportive care






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## OTC Medications

- NSAIDs
- Inhibitors of prostaglandin synthesis

- Gastrointestinal 
- Renal 
- CNS 
- Platelet function




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### OTC Medications

- NSAIDs
- Gastroprotectants
- IV fluids
- Supportive care
- ILE?
- Therapeutic plasma exchange





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### Human Prescription Medications

- SSRIs/SNRIs
- Increase serotonin or norepinephrine in the presynaptic membrane

• CNS 

• Gastrointestinal 




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### Human Prescription Medications

- SSRIs/SNRIs
- Cyproheptadine
- Sedation
- Supportive care





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### Human Prescription Medications

- Cannabis
- Binds to CB1 and CB2 receptors

• CNS 

• Urinary 



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## Human Prescription Medications

- Cannabis
- Most pets do not require therapeutic intervention
- If severely affected:
  - ILE
  - Supportive care




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## Human Foods

- Grapes and raisins
- Tartaric acid?
- Idiosyncratic

• Renal 



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## Human Foods

- Grapes and raisins
- IV fluids



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## Human Foods

- Xylitol
- Stimulates spike in insulin
- Acute hepatic necrosis

• Hepatic   
• Hypoglycemia




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## Human Foods




- Xylitol
- +/- dextrose
- +/- N-acetylcysteine, SAME/silymarin
- Supportive care




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## Chocolate

- Methylxanthines
- Catecholamine release
- Increased calcium entry into the cells
- Gastrointestinal 
- Cardiovascular 
- CNS 




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## Chocolate



- Methylxanthines
- IV fluids
- Frequent walks
- Anxiolysis
- +/- beta blockers
- Supportive care




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## Bouquets and Plants

- Cycad palms
- Cycasin
- B-methylamino-L-alanine (BMAA)
- Hepatic 
- Gastrointestinal 




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### Bouquets and Plants


- Cycad palms
- N-acetylcysteine or SAMe/silymarin
- Supportive care




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### Bouquets and Plants

- Hops
- Unknown MOA
- Malignant hyperthermia 




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### Bouquets and Plants




- Hops
- Active cooling
- Dantrolene
- Cyproheptadine
- Supportive care




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### Household Toxicants

- Liquid potpourri
- Cationic detergent
- Essential oils
- Burns 
- Lungs
- Gastrointestinal 
- CNS 



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## Household Toxicants

- Liquid potpourri



- No emesis!
- Gastroprotectants
- Topical burn therapy
- Analgesia
- +/- oxygen

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## Rodenticide

- Bromethalin
- Uncouples oxidative phosphorylation



- CNS 

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## Rodenticide

- Bromethalin

- ILE?
- Mannitol
- Gingko biloba?
- Supportive care





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## Veterinary Products

- Pimobendan
- PDE III inhibitor




- Cardiovascular 
- Gastrointestinal 

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## Veterinary Products

- Pimobendan
- IV fluids
- Vasopressors





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## Insecticides

- Pyrethroids
- Slow sodium channel closure
- May also affect GABA

- CNS 




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## Insecticides

- Pyrethroids
- Slow sodium channel closure
- May also affect GABA

- IV fluids
- Methocarbamol
- ILE





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## Insecticides

- Macrocylic lactones
- GABA<sub>A</sub> channels
- ABCBI (MDRI) mutation

- CNS 




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## Insecticides

- Macrocyclic lactones
  - ILE
  - Supportive care






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## Garden Products

- Tremorgenic mycotoxins
- Penitrem A
- Roquefortine C

- CNS 
- Gastrointestinal 




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## Garden Products

- Tremorgenic mycotoxins
- Methocarbamol
- IV fluids
- ILE



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## Questions?



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