



Cornell University  
College of Veterinary Medicine

## Canine Foodborne Aflatoxicosis Synopsis: 2006

### ***Clinical Signs:***

- insidious in onset, remain vague initially
- inappetence, lethargy, vomiting
- weight loss
- polyuria / polydipsia
- mild jaundice
- hematochezia, melena, hematemesis
- bruising
- abdominal distention:
  - modified transudate progressing to hemorrhagic body cavity effusions
- peripheral edema

### ***Clinicopathologic Features:***

Hematology: non-contributory

Biochemistry:  $\pm$   $\uparrow$  ALT,  $\downarrow$   $\downarrow$  Cholesterol,  $\uparrow$  T. Bilirubin (values hover between 5-9 mg/dL)

Coagulation Profile:  $\uparrow$  APTT,  $\uparrow$  PT,  $\downarrow$   $\downarrow$  Antithrombin,  $\downarrow$   $\downarrow$  Protein C

Urinalysis: dilute urine, granular casts as toxicity escalates

***Liver Cytology:*** microvesicular fatty vacuolation

### ***Liver Histopathology:***

hepatocellular fatty vacuolation, collapse of zone 3 (hepatic venule) associated with perivenular inflammation. Outflow occlusion correlates with acute onset of portal hypertension, abdominal effusion, and bleeding into the distal small intestine and colon.

***Treatment Recommendations:***

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1. ***There is no antidote for this toxin.*** It is rapidly metabolized to toxic adducts that remain within hepatocytes. Toxic effects promote free radical associated cellular injury. There is a linear dose / toxicity relationship. Experimental evidence suggests that the toxin may be retained covalently bound to circulating proteins (e.g., albumin) for up to 60 days.

2. Because dogs have lower liver tissue glutathione (GSH) concentrations than many other species, AFB1 toxicity may be augmented considering that GSH-conjugation has the capacity to produce a water soluble metabolite of the toxin. Consequently, we have recommended that dogs receive medications that foster increased hepatic GSH synthesis.

a. **N-acetylcysteine:** for initial management of overtly intoxicated dogs (jaundiced, vomiting, anorexic). Administer over a 20 minute interval; 20% solutions should be diluted 1:4 before administration.

*Loading Dose:* 140 mg/kg IV given once through an acrodysc syringe filter, 0.2 micrometers, (HT tuffryn membrane, made by Pall Life Sciences).

*Maintenance Dosing:* 70 mg/kg IV (administered as above) every 6-8 hours. Continued empirical dosing has been provided on a case-by-case basis.

b. **s-Adenosylmethionine (SAME):** nutraceutical used to fortify GSH synthesis and as a methyl donor for protein synthesis; also has the capacity to promote cell replication.

*Dose:* 20 mg/kg PO per day, use enteric coated tablets of proven bioavailability, administer on an empty stomach for best absorption.

3. **Silibinin-phosphatidylcholine complex:** use milk thistle derivative with best bioavailability. Although unproven in dogs, this nutraceutical promotes GSH production, directly intervenes in certain toxins, and may promote cell replication / recovery.

*Dose:* 2-5 mg/kg PO per day.

4. **alpha-Tocopherol (Vitamin E):** fat soluble vitamin not synthesized by mammalian cells and the major terminator of lipid peroxy reactions. However, too much vitamin E may be detrimental when given in doses that exceed the balance required for optimal function of the interdependent antioxidant system.

*Dose:* 10 IU/kg per day.

5. **L-carnitine:** a conditionally essential nutrient that can enhance fatty acid mobilization from the liver as well as mitochondrial function in certain conditions. Select a product with proven bioavailability.

*Dose:* 25 to 100 mg /kg per day (adapted from human dosing for individuals with inborn errors of carnitine metabolism and similar to the dose used in feline hepatic lipidosis). There is no information regarding the ability of l-carnitine to assist with mobilization of fatty acids from hepatocytes in canine hepatic aflatoxicosis.

6. **Vitamin K1:** initial dosing for dogs with established coagulation deficiencies.

*Dose:* 0.5-1.5 mg/kg subcutaneously or PO every 12 to 24 hours. Vitamin K administration will not resolve the coagulation problems in aflatoxicosis dogs, but some improvement has been observed. Several vitamin K dependent coagulation proteins are insufficiently produced in this syndrome and there remains a possibility that some inhibition with vitamin K activity is involved (aflatoxin is a coumadin-like derivative and undergoes some metabolism similar to vitamin K).

7. **Water soluble vitamins:** many water soluble vitamins are stored and activated in the liver. Continued supplementation in administered IV fluids is recommended to avoid inconspicuous vitamin deficiency.

8. **Blood component therapy:** constant rate infusions of plasma have controlled bleeding tendencies in some severely affected dogs. Administration of packed red blood cells has provided support through enteric hemorrhage that accompanies acute onset of portal hypertension and transitioning of acquired portosystemic shunts.

9. **Antemetics:** are essential to control vomiting. Start with a metoclopramide constant rate infusion with scaled down dosing in dogs with hepatic injury; dose is then titrated to patient response. If emesis continues, combining ondansetron may be effective. We have not found rectal prochlorperazine suppositories to be helpful.

10. **Sucralfate:** slurry is recommended for dogs with hematemesis or showing signs of esophageal colic.

11. **Nutritional Support:** feeding a balanced canine diet is recommended for recovering dogs. Unless overt signs of hepatic encephalopathy, avoid feeding protein restricted diets.

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***Long Term Patient Outcome:***

It is possible that dogs exposed to foodborne aflatoxin may develop chronic liver disease or be prone to develop neoplastic hepatic disorders. Hepatocarcinogenicity is well recognized as a sequella to chronic aflatoxin exposure in humans, but is not well studied in the dog. Routine health assessments in recovering dogs are advised (i.e., periodic liver function testing and biochemical profiling).

***Poster References***

1. King JM: The correlation of liver function tests with the hepatic lesion in dogs fed toxic peanut meal. PhD Thesis, College of Veterinary Medicine, Cornell University, Ithaca, NY, 1963.
2. Zimmerman HJ: Indirect cytotoxic hepatotoxins. In: *Hepatotoxicity*, 2<sup>nd</sup> ed, Lippincott Williams & Wilkins, Philadelphia, PA, 1999.
3. Center SA, Warner KL, Erb HN: Liver glutathione concentrations in dogs and cats with naturally occurring liver disease. *Am J Vet Res* 2002;63:1187-97.