

# Toxicology Part 2

drip 2

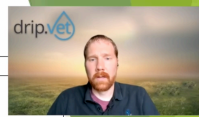
version 1

Instructor: Dr. Adam Lancaster, DVM, DACVECC

Be advised that this document is intended to enhance your learning experience. It is created primarily from an audio transcription of the instructor's lecture. Therefore it is NOT designed to meet the standard of a textbook or proceedings. Please excuse minor grammar and typographical issues. You are welcome to print and use it for notetaking and strengthening your learning.

All rights reserved. Veterinary Information Network, Inc. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without permission in writing from the copyright owner.

## NSAID toxicity



NSAID	Dogs	Cats
Ibuprofen	25-125 mg/kg GI 120-175 mg/kg Renal >400 mg/kg CNS	>50mg/kg renal
Naproxen	>5 mg/kg GI >10 mg/kg renal	Any dose
Carprofen	>20 mg/kg GI >40 mg/kg renal >400 mg/kg CNS	>4 mg/kg GI >8 mg/kg renal
Deracoxib	>15 mg/kg GI >30 mg/kg renal	> 4mg/kg GI > 8mg/kg renal
Meloxicam	>1mg/kg GI >2mg/kg renal	Any dose above therapeutic dose = GI >1.5x therapeutic dose = renal No longer recommended orally in cats
Piroxicam	>1mg/kg	Unknown
Aspirin	25mg/kg GI 100-300mg/kg renal	25mg/kg GI 100-300mg/kg renal

So moving on from marijuana, I want to switch gears a little bit to NSAIDs. So there's a variety of different NSAIDs out there, some of them for use in our patients and then others for use in people. But all of them can be toxic at high enough doses. So, of course, we all know that even the veterinary-prescribed NSAIDs can be toxic at higher doses. And it's certainly the human ones, particularly things like ibuprofen is a pretty common one, Naproxen is quite toxic, things like that.

So they all follow a similar pattern though. So at lowish doses, they tend to cause gastrointestinal signs. At sort of middle range, they tend to cause renal signs, so signs of kidney failure. And then at very, very high doses, they may actually cause CNS signs, seizures, coma, things like that.

## NSAID toxicity

### • Treatment

- Gastric decontamination
  - Emesis
  - Multi-dose AC if sustained release product or massive ingestion
- Prevention of Gastric injury
  - Misoprostol 1-3mcg/kg PO q 8 hrs
  - Sucralfate
  - H2 blockers or Proton Pump inhibitor
- Prevention of renal injury
  - Hospitalization for IV diuresis, dialysis if available and severe
  - Monitoring Renal values for 48-72 hrs
  - Supportive care



Treatment, essentially, is going to consist of gastric decontamination. Again, just the typical gastric decontamination that we talked about. So you're going to want to do emesis. Activated charcoal is certainly effective in these, as I discussed last time.

Multi-dose activated charcoal has historically been recommended. However, there was that recent study that looked at whether it was actually required or not. So, I don't know, I still do it, but it's something that certainly could be debated, I guess, at this point.

And then really going to do prevention of gastric injury, particularly if they just got into say, a gastrointestinal toxic dose, then that may be all that you need to do. So you might not even need to hospitalize them if they just got into a dose that should only cause GI injury, but you can treat them as outpatient. Give them gastric protectant, things like H2 blockers or proton pump inhibitors, sucralfate, or misoprostol.

Misoprostol is something that does need to be specially handled. You're not supposed to break up the tablets. So that's a thing I think people still sometimes do, but you're not supposed to.

So you can only use it in certain sized patients. And then you should make sure that nobody who is handling that is pregnant, or trying to become pregnant as well. So that's actually something I write in my discharges if I'm going to be sending that home, or writing a prescription for that.

And then if they did actually get renal toxic dose, or certainly if they're already azotemic then they're going to need hospitalization for IV diuresis. And then, again, if they're already azotemic and quite sick, then dialysis is something that is quite effective for these patients. And will help not only with the kidney failure portion of things, but if there's still is a toxin in their system, it is dialyzable as well.

Of course most patients aren't going to require that. Most of the time if they got to a renal toxic dose, you're just going to admit them to the hospital, provide them fluid therapy. And then you're going to monitor their renal values for 48 to 72 hours.

Interestingly, it's not a lot of good evidence that IV fluids in the absence of azotemia actually does anything for these patients. I think that if you ask 9 out of 10 doctors if they would do that, they would probably say yes. But there's not a lot of evidence for that. So it's still typically recommended.

It'd be really nice if we could get some clarity around that, maybe doing some studies, looking at a couple of groups of patients where they got into NSAIDs, and some were treated with actually IV diuresis before they were azotemic. And others were maybe just sent home for monitoring, and didn't have that diuresis, and then see how many of them became azotemic. I think that would be a useful study to be done. But to my knowledge, that has not been done, or if it is out there, I haven't seen it.

## Xylitol

- Sugar substitute found in many products
  - Mostly of concern in dogs
- Promotes insulin release leading to hypoglycemia at 0.075 - 0.1 g/kg
- Acute hepatic necrosis also reported at doses of >1 g/kg
  - MOA unknown



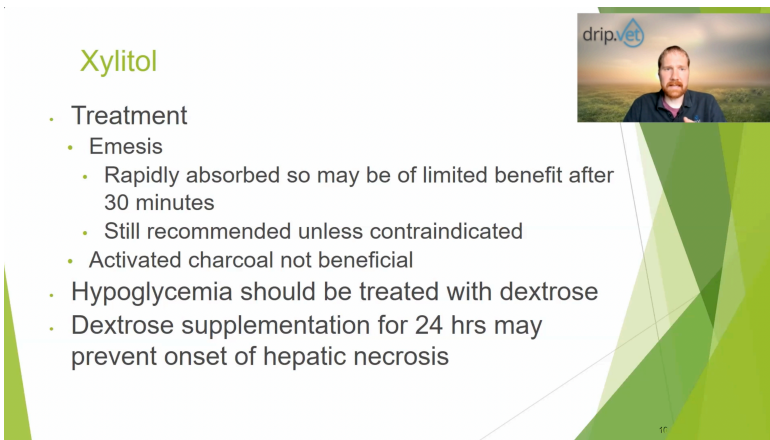
Another pretty common toxin that you may see is xylitol. Xylitol is a sugar substitute. It used to be mostly gum, at least that's where I used to see it primarily. But since it kind of hit the market, it seems to be in tons of stuff now. So even things like peanut butter, other like processed foods, and then of course, gum is still a common space that you're going to find that as well.

One of the difficult things with xylitol is that it can be very difficult to determine the actual dose that the patient got into, particularly if it's some type of a processed food that's not written. It'll say on the package maybe like sugar alcohols, or something like that, explain like how many grams that are in there. But that can still be-- you know, you don't know, especially if it contains multiple different types of sugar alcohols, you don't know how much xylitol is it versus another one. So that can be quite challenging.

A typical stick of gum typically contains somewhere between 0.3 and 0.4 grams of xylitol. So if it's just gum that they got into, that's the number that I use for calculating that. But really if you want actual-- if you really needed the specific amount that was in there, a lot of times you actually have to try to call the manufacturer. And even then, it's difficult to get that information. So that can be one challenge with all of these.

What we do know, though, is that the xylitol, just like when you consume any type of sugar, it is going to promote insulin release, but it doesn't actually increase your blood glucose. So instead of those two things sort of evening each other out, what you end up with is that you have this insulin release without the additional sugar in the blood, and so you end up with actually hypoglycemia.

That's going to be at the lower doses. And then at higher doses you can actually get acute hepatic necrosis that can lead to liver failure. The mechanism of action is not fully elucidated at this point, but it is thought to be from intracellular hepatic hypoglycemia. So basically, hypoglycemia at the cellular level in the liver.



**Xylitol**

- Treatment
  - Emesis
    - Rapidly absorbed so may be of limited benefit after 30 minutes
    - Still recommended unless contraindicated
  - Activated charcoal not beneficial
- Hypoglycemia should be treated with dextrose
- Dextrose supplementation for 24 hrs may prevent onset of hepatic necrosis

The slide features a video thumbnail in the top right corner showing a man with a beard and glasses speaking. The logo 'drip.vet' is visible in the top left of the video frame. The slide has a green geometric background design.

Treatment, gastric decontamination is possible. Emesis is going to be the primary route there because activated charcoal does not actually absorb the xylitol very well. Unfortunate thing with emesis, is that because the xylitol is so rapidly absorbed across the stomach lining, that it's likely to be of limited benefit after about 30 minutes. That being said, particularly with gum, but even in other cases, I still would recommend trying emesis.

A lot of times, especially with a whole pack of gum, you'll get the gum up. Now, whether or not there's any xylitol still left in there or if all of it has been absorbed, I guess I can't say. But I definitely feel better getting that product out.

Sometimes, it can kind of form like a ball and a glob. And I feel like if we can get it out of there, then maybe some of the stuff that's stuck in the middle will have been absorbed. So I still do recommend doing that. But again, activated charcoal, not particularly useful in these situations. If they are already hypoglycemic, it's the same as you would treat any patients with hypoglycemia. So a bolus of dextrose, and then followed by 2 and 1/2 or 5% dextrose IV depending on the severity of the hypoglycemia.

And then, the other thing that's a little bit interesting, because of the proposed mechanism of action for the liver failure, a lot of the toxicologists actually recommend dextrose supplementation for 24 hours, even in the absence of hypoglycemia, to prevent, the onset of hepatic necrosis. So even if you have this guy who comes in and got into the xylitol, and you check some bloodwork and they're not hypoglycemic, the recommendation is actually still to provide extra supplementation for 24 hours if they got into a potentially liver toxic dose.

So that is something that is a little bit interesting. I actually-- this a number of years ago-- I actually called up poison control because I had-- they started doing this and I sort of hadn't heard of this prior to that. And I asked them where that came from and they couldn't tell me. So I don't know where this treatment actually came from but I know that this is recommended all the time by poison control. So that's what, we typically do at the hospital as well.

## Poll #1



- Which of the following is true regarding marijuana toxicosis?
  - It is almost always fatal
  - The only treatment required is Doritos and dark room
  - Lipid therapy is usually required
  - Gastric decontamination is warranted unless contraindicated

OK. Just to see if everybody's awake and to throw up a little poll here. This is a question regarding marijuana toxicosis. So which of the following is true regarding marijuana toxicosis?

So one, it's always fatal. Two, the only treatment requires is Doritos and a dark room. Three, lipid therapy is usually required, or four, gastric decontamination is warranted unless contraindicated.