Equine Feed Contamination and Toxicology

Dr. Karyn Bischoff reviews common equine feed contaminants, including mycotoxins, weeds, and botulinum toxin.

Speaker Bio:

Karyn Bischoff, DVM, MS, Dipl. ABVT, is a veterinary toxicologist at the New York State Animal Health Diagnostic Center and an associate professor at Cornell University. She graduated with her bachelor's degree in Animal Science from the University of Wisconsin (Platteville campus), and she obtained her DVM from the University of Illinois. She earned her master's degree at Oklahoma State University while completing a residency in toxicology, and she went on to complete a pathology residency at the University of Florida.

Learning Objectives:

1. Understand how feed contamination events can happen on a large or small scale.
2. Understand how contamination occurs due to formulation errors, adulteration, and natural contaminants.
3. Understand how to sample feed, provide proper legal documentation, and submit samples to a diagnostic laboratory.
4. Know what resources are available to veterinarians and horse owners in relation to feed contamination.

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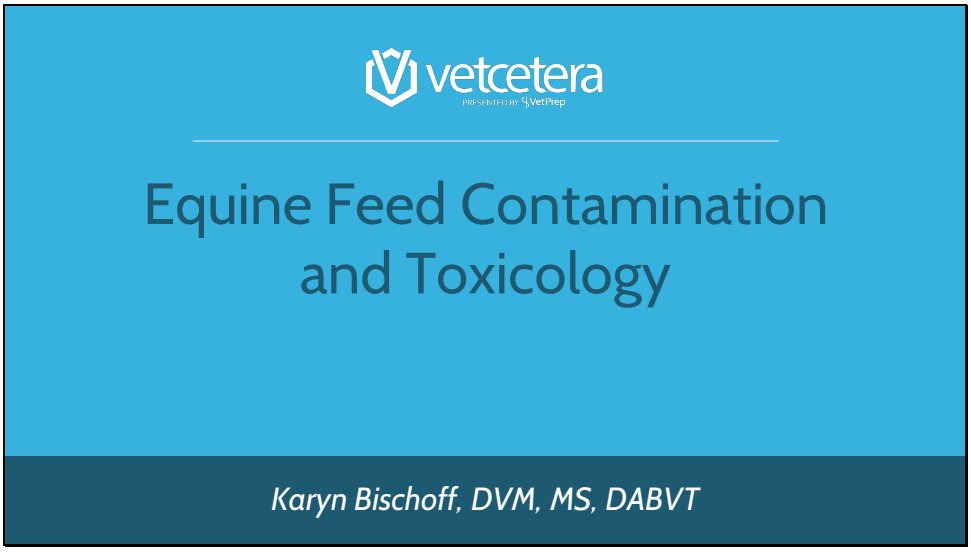

Good evening, everyone. Thank you so much for joining us tonight. My name is Katie Krothapalli. I'm the Director of Veterinary Education for Vetcetera. Our speaker tonight is Dr. Karyn Bischoff.

She's a veterinary toxicologist. She works at the New York State Animal Health Diagnostic Center, and she's also an associate professor at Cornell. She's going to be going over equine feed contamination and toxicology for us tonight. And with that, I will turn it over to Dr. Bischoff.

I'm going to talk a little bit about some equine feed contamination toxicology and then going to use some of the experiences I've had here at Cornell and in other places. I was working in the Midwest for some time as well. So I have a little bit of insight into some of the common horse toxins in the South and in the Midwest as well.

So I'm going to start off-- let's see, trying to move forward. Let's see. Let's try it now.

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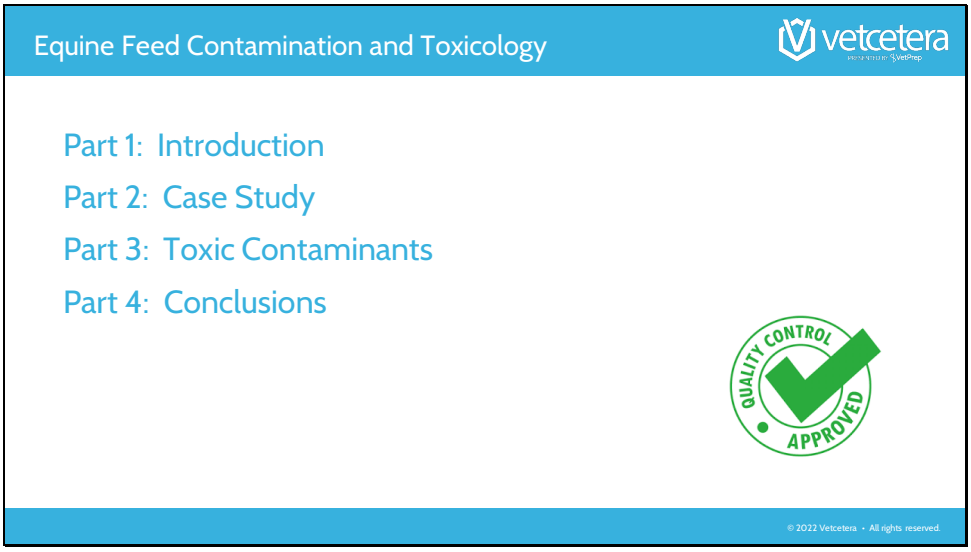

OK, so I'm going to start with an introduction. I'm going to talk about a case study that I've had since I've been here in Ithaca, New York and then talk about some specific contaminants that we worry about. And then just kind of conclude with some general knowledge here.

And just I do have the chat and the questions open in the off chance I might actually see somebody say something, feel free to ask questions during the seminar. And if I see them, I will try to answer them. Otherwise, I can do it at the end of the presentation as well.

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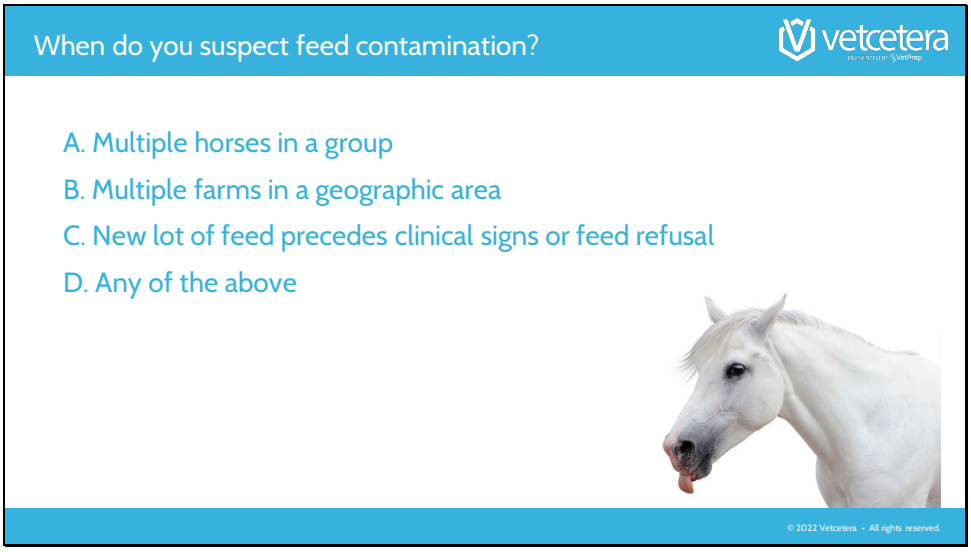

So when do you expect-- and this is a good time to use the chat. When do you start thinking maybe this is a feed problem? When it's multiple horses in one group, when it's multiple farms in a specific geographic area, when they start getting sick right after you got them a new lot of feed, or any of the above. So this is just your wake up question to see if you're out there. I know some of you probably had a long day already.

So OK, we got one answer in the chat. Anybody else want to venture a guess? Yeah, it looks like we have some-- that looks like everybody agrees.

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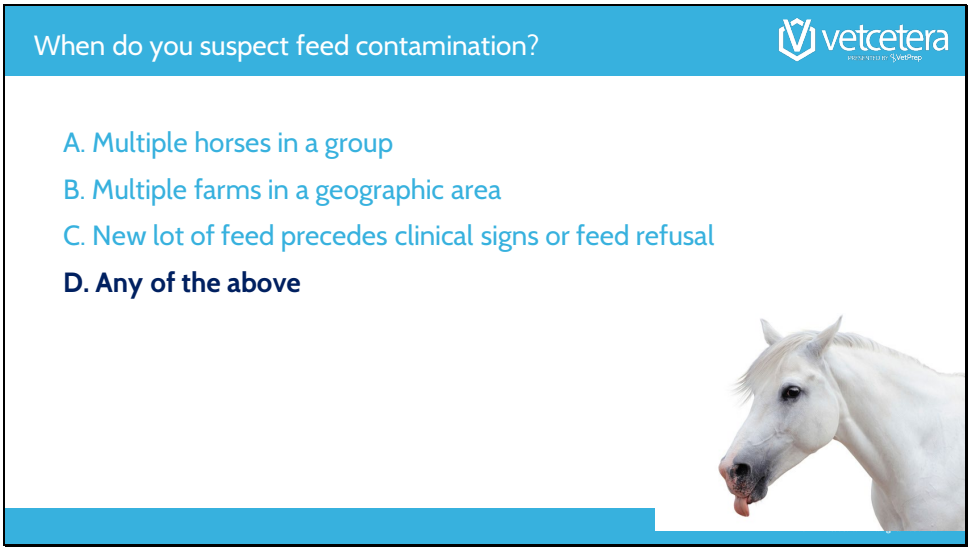

Any of these things would start making you think this is a feed-related problem. So new lot of feed obviously.

Multiple farms in a geographic area, maybe they all use the same feed mill and they are getting exposed to something that was produced at that feed mill, some kind of error. Or one group of horses, multiple horses get sick, well, that could be a bacterial or viral. But it could also mean that they're all in the same feed and having an exposure that way. So any of these things can do it.

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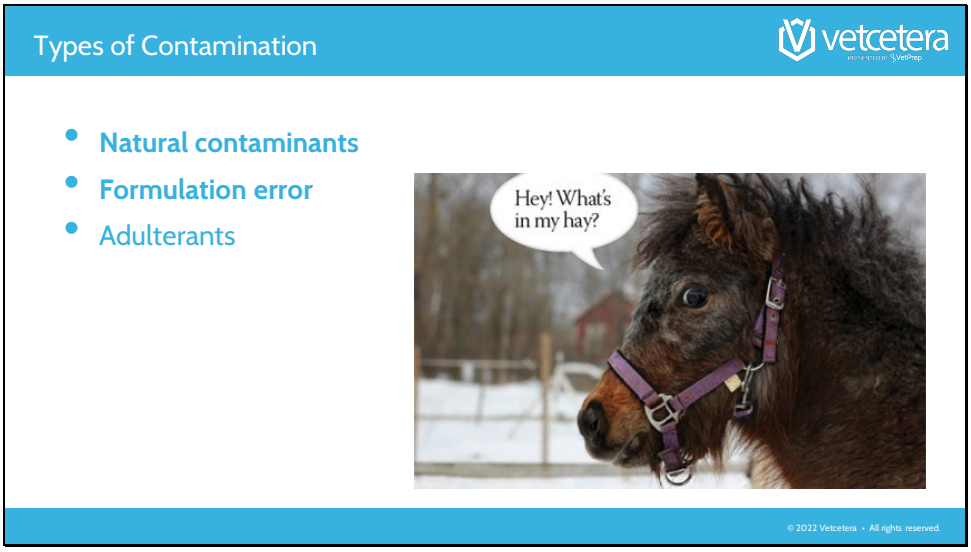

So I'm going to talk about some natural contaminants, and then I'm going to talk about some less natural contaminants. Oops, we made an error in the formulation of this feed. And occasionally, there are also adulterants. I'm not going to talk about those so much with horses. But I've had cases where people added things to horse feeds that were intended to do harm. So that would be kind of those were attended malicious poisoning incidents.

At least in pet foods, there have been adulterants whereby there was fraud involved. An ingredient was labeled as one thing but it turned out to be another. I know in food animals years ago in Michigan and it's happened a few other times in Europe, where a mislabeled bag was added to feeds for livestock and they turned out to be persistent organic pollutants in the bags.

So there was bromo-dibenzyl dioxins in one-- no, actually, no, polychlorinated dibenzo dioxins in one of them. And there was a dioxin contamination event in another and some other things. So these were industrial waste getting accidentally added to animal feed. And certainly there have been some other adulterations in small animals where our euthanized animals got in the feed as well as the melamine incident a few years ago.

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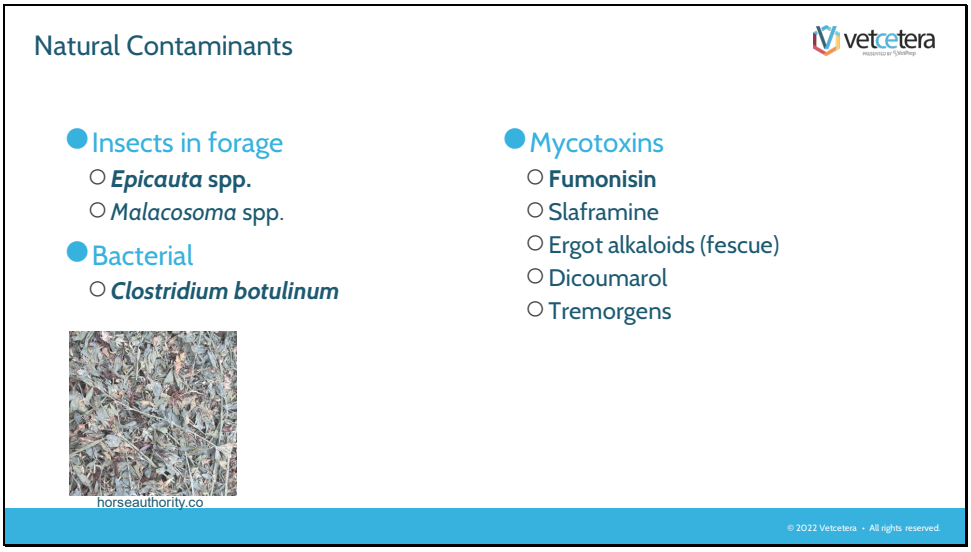

So the natural contaminants, insects-- does anybody remember what the Malacosoma were? That happened in probably 2004-ish. And it was mostly affecting Kentucky. Does anybody remember that incident? It was pretty dramatic at the time. And I'm going to talk about Epicauta as well, which are the blister beetles. I'm going to leave the Malacosoma up there for a little while in case somebody gets a sudden epiphany.

The picture here is alfalfa hay. And if you're going to have blister beetles, it means you're feeding alfalfa hay. And I'll talk more about how that exactly happens. But you might be able to see some blister beetles in here. It's too small on my computer to make them out.

Clostridium botulinum kind of gets into feeds, usually associated with some little animal that got bailed into your hay, big, big problem in silage type things. So if you feed haylage, this is an issue. I remember a few years ago, there was a severe problem in Florida and people couldn't get enough hay. So they started feeding haylage, and they had a lot of botulism issues.

And then mycotoxins, fumonisin is the big bad one out there. I had aflatoxin on this list. I have never seen a horse with aflatoxicosis. And there is zero in the literature about aflatoxicosis on horses. So it doesn't seem to be a major problem, even though corn can definitely get aflatoxins on it and can be fed to horses.

Ergot alkaloids, so this is like the fescue issues that we see in brood mares and then dicoumarol, which is moldy sweet clover. It causes a coagulopathy, just like an anticoagulant rodenticide would, same mechanism. And then occasionally, more problems in Australia, New Zealand but there are the tremorgenic mycotoxins that grow in grasses. They are fungi similar to the fescue.

The Claviceps and the fescue, these organisms grow in the grass, as part of the grass. They're actually symbiotic relationship. They produce toxins. So ergot alkaloids, in the case of fescue, that cause changes that are associated with reproduction. They cause decreased milk release, so decreased prolactin, prolonged pregnancy, and things with the tremorgens. They cause nervous system signs.

So it's mostly a peripheral problem. And it's exactly what it sounds like. It's tremors. They shake like crazy, and they get weak. They fall over, things like that.

So nobody jumped at the bait for Malacosoma, which obviously, I don't spend a whole lot of time saying. So I need more practice. But these were the tent caterpillars. And if you remember the horses, there was a plague of tent caterpillars in the early aughts in Kentucky.

And they were so bad that they covered the fields. They covered water buckets. They were falling into the water buckets. They covered feed buckets. They were just everywhere.

And they had tiny setae, which are hairs, the insect hairs that penetrated the intestines when they were ingested. They penetrated the intestines of the horse and spread gut bacteria all over the body. And so you were seeing abortions secondary to funisitis, which is inflammation of-- and it was that basically funisitis. It was an inflammation of the umbilical cord.

You could get placentitis, as well. They were seeing some ocular damage because the eyes don't have a really good blood supply. So there weren't a lot of white cells to take care of those bacteria and the same with the heart. So those were the things that they were seeing with that.

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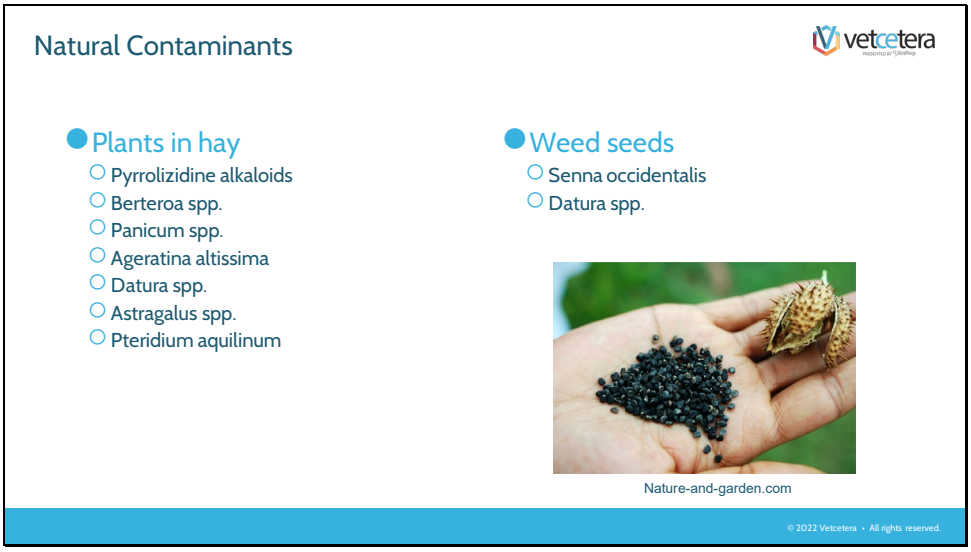

There are lots of weeds. And we'd see Senna occidentalis, which cause which causes contains emodins, can damage the myenteric plexus. So you might worry about some colic with those. But also they can cause muscle degeneration. So you can get almost a white muscle disease kind of issue with that.

The seeds in this person's hand, I believe, are Datura seeds. You will get colic if they eat Datura seeds. Basically, they contain atropine, and they just shut down the GI tract. Plants, pyrrolizidine alkaloids are basically the bane of my existence, because they are very slow-acting. And by the time we see the pyrrolizidine alkaloid effects, which is chronic hepatopathy, it's really hard to trace back the source.

So I've gotten calls on these where I've gone in to try to find the plants. And you ask about the history. And before the animals got hepatic failure, they had been at three different shows. And they had been in three different states. And they had had six different lots of hay from four different sources.

And then of course, they could also be the seeds in the grain. So it's really hard to just trace these back to a source. Berteroa spp. so that one is the one that's associated with founder in these horses. Panicum species can cause hepatogenous photosensitization. It can also cause damage to the liver.

Ageratina, that is the white snakeroot. They changed the genus on me. I want to say it's Eupatorium, but now it's Ageratina. And it has been associated with white muscle type disease as well. It can cause cardiac necrosis as well.

Datura itself, Astragalus out west, these are the locoweeds. They have lots of things that they can do. They can have lots of selenium, which may or may not be an issue. But they can cause locoism, which is a vacuolar storage disease that destroys nerve cells.

It destroys hepatocytes. It destroys all different kinds of cells. And then the Pteridium aquilinum in horses, we usually associate that with polioencephalomalacia, secondary to thiaminase activity. But it causes different things in different species.

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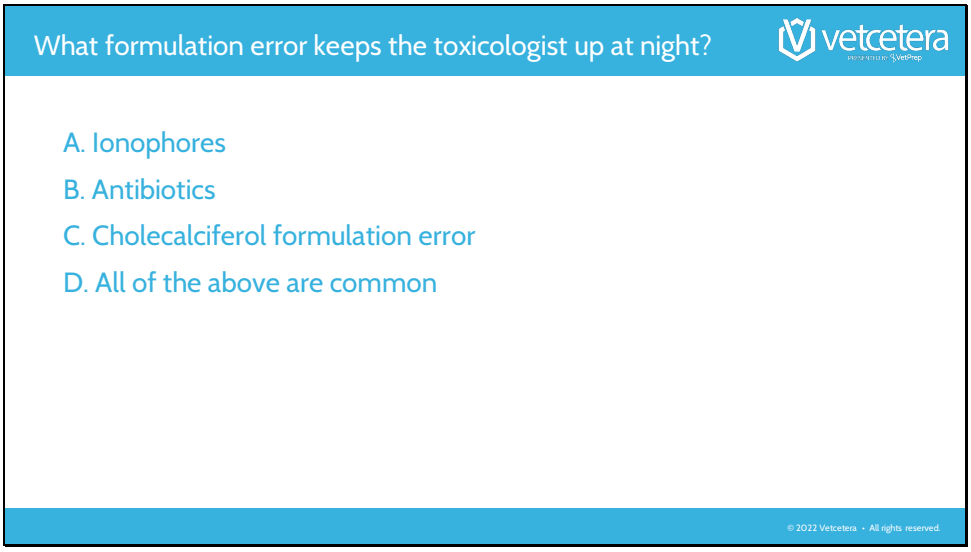

So every now and then, we get cases that-- I have another one that's keeping me up at night right now. But we have some horse cases that do keep me up at night. And I'm going to throw this out there and see if anybody can guess which one of these is most likely to be the source of my insomnia.

OK, I do lose sleep over antibiotics quite honestly. But I don't see them very often.

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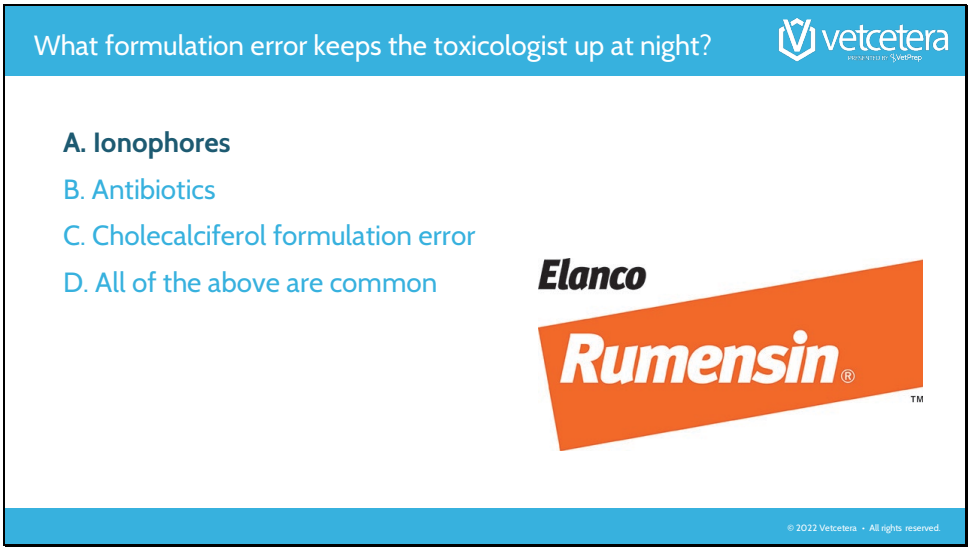

But I do see ionophore poisonings fairly frequently and those I definitely lose a lot of sleep over. Cholecalciferol, I lose sleep over in small animals. I have not had a formulation error in horses. If horses get cholecalciferol poisoning, it's probably going to be from a plant, a toxic plant like Solanum malacoxylon or something like that that's naturally high in vitamin D, but definitely could be an issue.

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So when you suspect the contamination, it's really important to stop it in its tracks. So that requires isolating the source. Obviously, if you're on the farm, you're going to switch and put them on clean feed and clean water sources and maybe keep them off of the pasture. If that's a potential source, keep them away from that hay, keep them away from that feed, just basically change out all the feed to clean feed, change out the water.

You can contact the state veterinarian if you suspect the feed. You can contact the FDA. And there's a phone number, I believe, that will get you to them. But they also have a really great website for reporting feed errors and then contact the manufacturer as well, so they can double check. And if the FDA and/or the manufacturer gets complaints that are similar enough and if it gets multiple complaints, two or more complaints with the same clinical signs from two different owners, they do follow those up to see if it is a feed contamination problem assuming that they're on the same feed.

When you do this, it's super duper important to have the feed tags in your hand. With hay, obviously, you can't do that. But if it's a commercial feed, really I'm talking about commercial feeds with this slide. If it is a commercial feed, you need that feed tag in your hand, so you can tell them what lot it was. You can tell them the manufacture date. You can tell them what the label says it's supposed to be.

So this is Omolene, 14% or whatever, just as an example. It's hard to find Omolene around here. But just as an example of what kind of information, because they will need to back trace that lot of feed and see, a, if other animals are being exposed, and b, if they still have any remaining at the manufacturer for testing.

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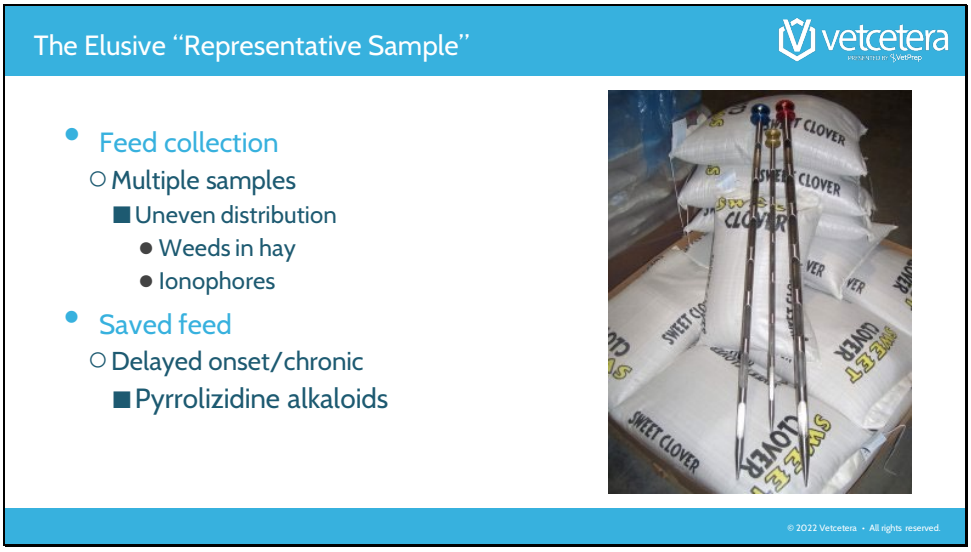

Collect multiple samples, collect samples from different areas of the batch. So there can be uneven distribution. So ionophores or antibiotics, either one, when you have those, when a small manufacturer is producing feed for livestock, they can make an ionophore concentrate to top-dress or to add to the TMR for the dairy cattle. And if they don't clean their equipment well, it'll go into the next lot of feed that they're making. And if that's horse feed, that's where we get into some problems.

So that means that the first bag of horse feed is going to have the highest amount that's produced right after the cattle feed and then the ionophore concentrate or whatever. And then the next bag of feed will have a little less and a little less and a little less as the equipment gets cleaned out through, flow through of the feed. So it may not be distributed. And if you have larger lots than bags, it may not be distributed very well through the lot. So you need to get different samples from different areas.

Hay is hard. Hay is hard. So you actually have to look at the different flakes of hay and see if there's anything in a significant quantity that's there that it's not supposed to be there. So yes, if it's grass hay or legume hay, you can pretty much tell what's grass and what's clover. And if there's a bunch of broad leaves in there that aren't quite grass or clover, then those are the ones that are going to be the most interesting.

And you can sort those out and send them for identification. And I mean, I'll look at them. And if they're really obviously a toxic plant, I might be able to help you out. I have a botanist down campus that I'll refer them to as well. And she's a plant taxonomist and can basically look at a twig of something and tell you what plants it came from, which is pretty amazing.

And then again, with pyrrolizidine alkaloids, it can be really hard because it can be a week. It can be three weeks. It can be a month. It can be three months. It can be a year out before they break with the clinical signs. So who knows what the animals had at that time?

If there's some saved feed, you might be able to tell. And saving feed is helpful in some cases. But sometimes it's not helpful. If you save it too long, it can get rancid and covered with mold and stuff, and

then it's really hard to look at. So if you didn't think to save the hay that the animal ate a year ago, most people don't. I don't, I certainly don't.

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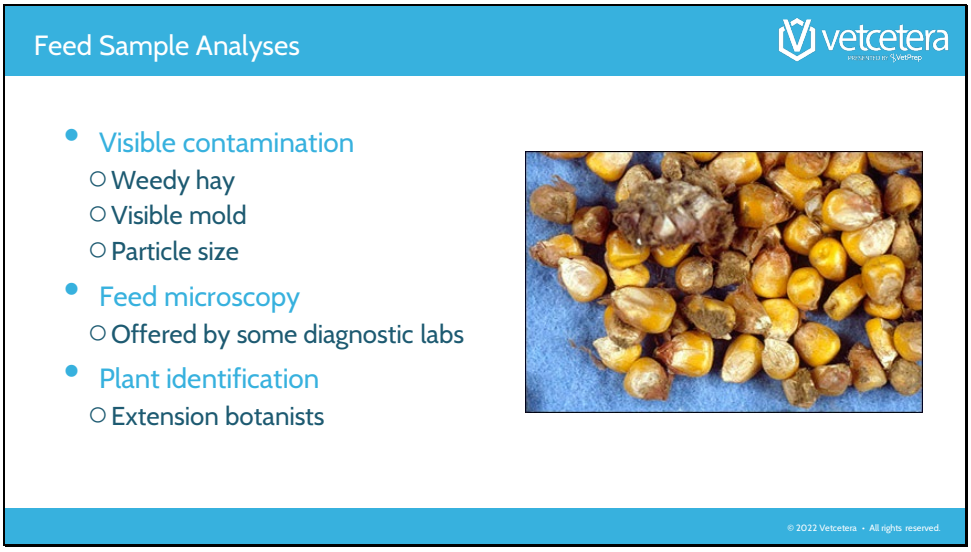

So what samples do you take? You take the visibly weedy stuff from the hay. You take the visible mold from the grain. Particle size, why did I write that in there? Fines are more likely to be moldy in corn.

So corn screenings can be a problem, especially with fumonisin. Feed microscopy is offered by some labs. And that's basically just somebody taking a look through a microscope to tell you what the ingredients in this bag of feed were.

And I had a guy here that used to be able to do this. And you could give him an extruded diet or a pelleted diet. And he could take the pellets apart, tell you exactly what the ingredients were, which blew my mind.

I can't do that anymore unfortunately. But so often can look at something and say OK, that contains this kind of grain or this kind of weed seeds or something like that. So I have some ability to do it and I have a botanist down on campus that's really helpful as well.

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So legal issues, some of these cases are going to be legal cases. If it's a commercial product that's being sold to a farm, there could be lawsuits involved. So sample identification again, have that feed tag in your hand when you report these things and sample handling.

When you take the food sample, use-- I said tamper-resistant in the previous version of this. There is really no such thing. But making it tamper-evident, so using legal tape on things that they have to break to get into. Then you can tell that somebody's tampered with the sample.

Chain of custody sheets are super important. So you start this chain of custody, and you can kind of see it in this piece of paper. So these are just the seals that are tamper-evident. If you break these seals, you can tell that they've been broken.

The chain of custody, basically, after you collect your samples, you label them with who you are, who the samples belong to, the animal's owner, the animal name, the date and time in which it was collected, and the location from which it was collected, et cetera. So that's all part of the evidence. And then you put this chain of custody form on the sample bag.

And that's going to tell-- you're going to use-- as the collector, you're going to be that first person on there. And then the next person you give it to, whether it's a police officer, they assign the next line. And when they sign it over to somebody else, they will sign it over to somebody else.

So the police give it to the postman. The postman signs there and all the way till the final destination if that's a laboratory like mine. And this really helps in tracking, making sure that there wasn't tampering with any evidence.

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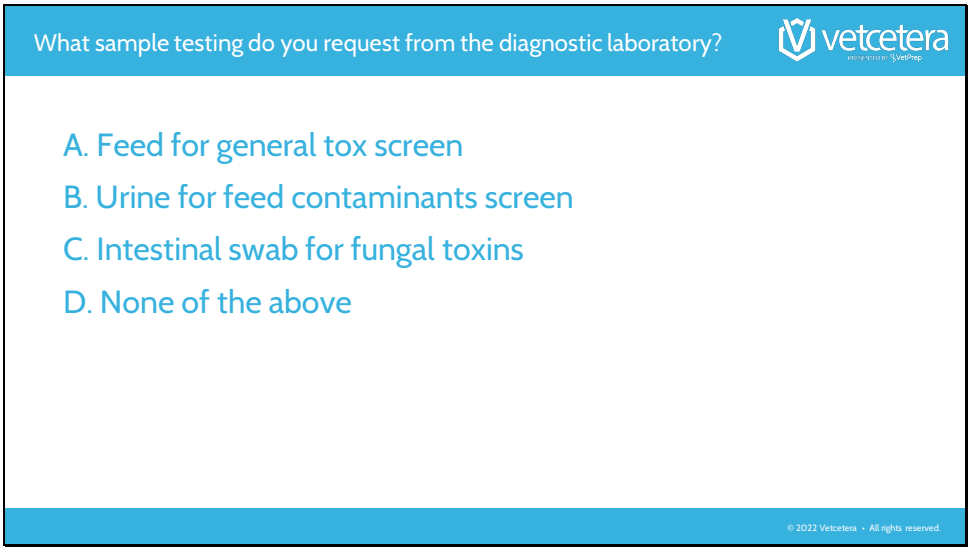

So once you submit it to the laboratory, what are you requesting? Are you requesting the general feed tox screen? And this is where if you answered this one right, we are friends forever. So general tox screen, urine for feed contaminants, intestinal swab for fungal toxins, or none of the above. Wa, wa, as my laboratory technician would say.

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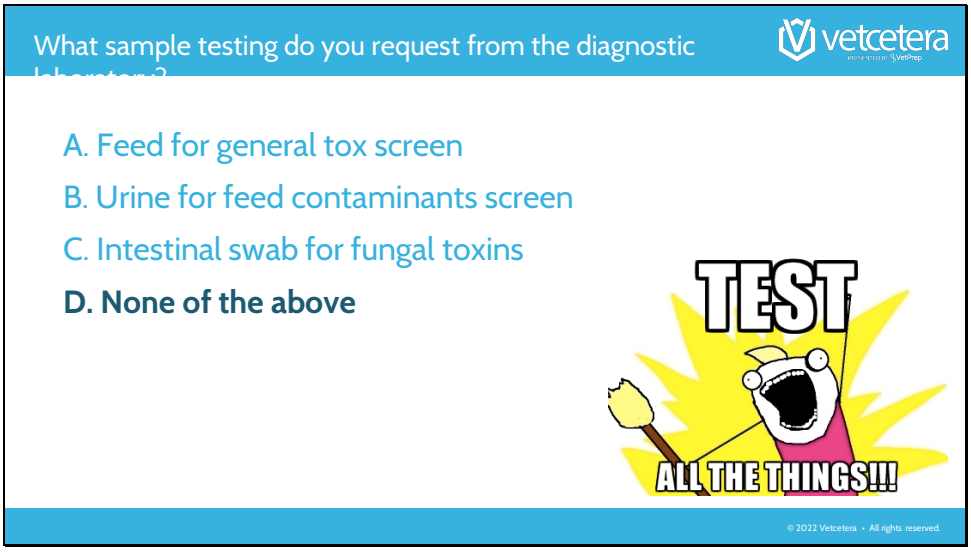

The answer for this is none of these. Any of these that you choose will drive me crazy, because I won't know what to do. There's no such thing as a general tox screen, and obviously, the other two. And I do get stuff like that occasionally are not going to be very helpful. So none of the above.

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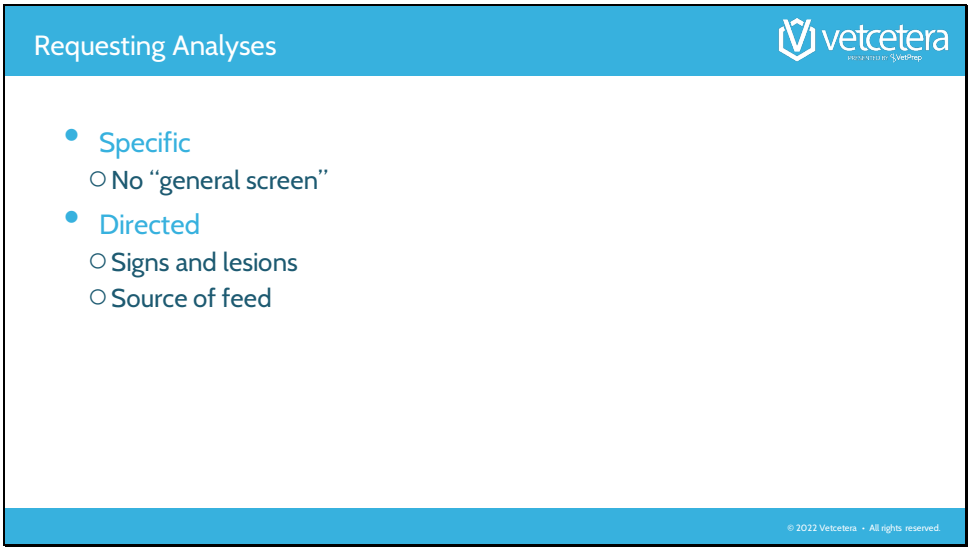

Basically, I need to know what we are expecting, OK, the result to be. I don't like going into these cold, because I've actually done feed testing from cold feed testing. We have no idea what the toxin is, just test for everything.

And it cha-chinged up. And this is somebody with really deep pockets. And it ended up costing them $30,000. And we did not find the contaminant. So test for all the things never works unfortunately in my laboratory. We need some direction.

So is it a hepatotoxin? Do you have chronic hepatopathy, maybe a liver fibrosis? Well, that would point me toward more pyrrolizidine alkaloids. Was this a case-- do you have skeletal muscle damage? Oh, that might be more of an ionophore?

Do you have severe colic? That might point me toward antibiotics or something like that. So knowing what the clinical signs were, knowing what the clinical pathology, the gross pathology, the histopathology, and what kind of feed it was, OK?

If you give me Timothy hay and tell me to test for cantharidin, I mean, I think you're a lunatic, because it's not going to be there. So call the lab, talk to me about what you're seeing, and what kind of things the animals are most likely to have gotten into, a little backstory on where the food came from. Things like that can be really, really helpful in deciding where to go.

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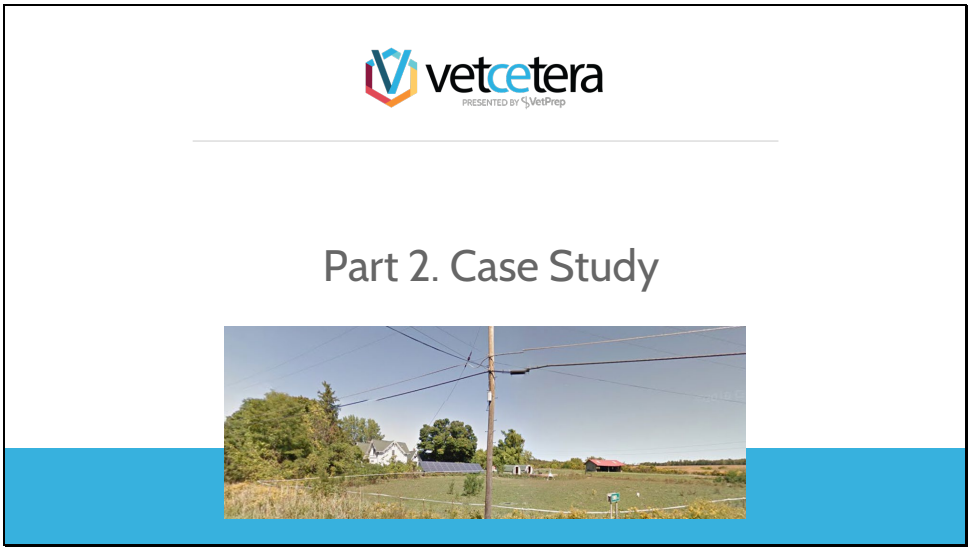

So this is a case study. This is actually my backyard. But we're going to pretend-- and I've actually gotten a better fence since then. But we're going to pretend this is a big horse farm with those two little barns.

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So we are boarding 30 horses in those two little barns.

And day one, a stallion died. And everybody kind of scratched their head. But they didn't notice any clinical signs the day before they just found him dead in the stall. And 1 out of 30, the owners elected to have it buried. And they didn't want to cut into it. So we did not get a post-mortem.

A few days later, about a week and a half later, a pony died. OK, 2 horses out of 30 in two weeks, that's a little much. So they actually had tested five other horses, took blood samples. They sent the feed for mycotoxins. And they did a post-mortem on pony that had died.

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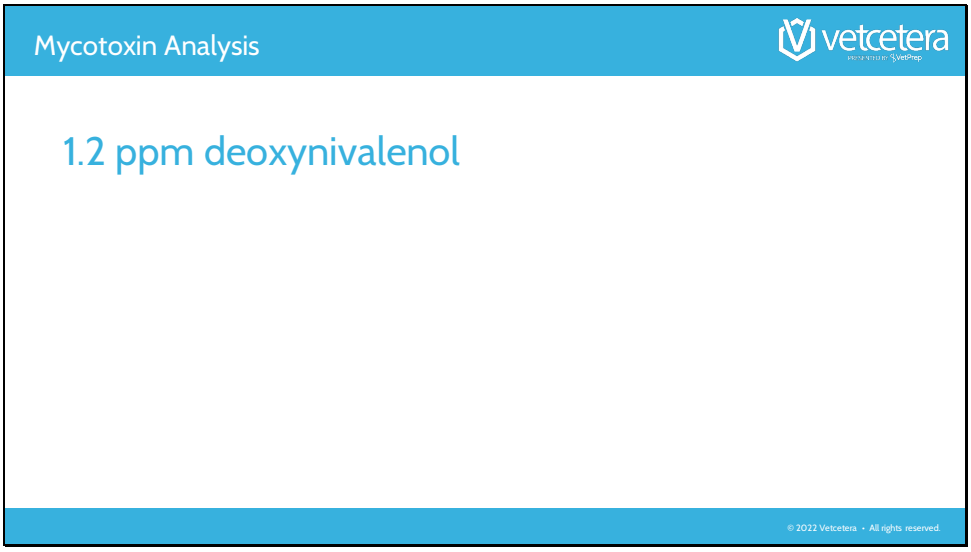

So results, 1.2 part per million deoxynivalenol. Is anybody freaking out over this? No, I can tell you deoxynivalenol did not kill these horses, OK? Deoxynivalenol is vomitoxin. Two part per million, you might get some feed refusal in pigs and maybe in cats and dogs too. Horses don't seem to be very sensitive to it.

And again, this is below the concentration where you'd expect sensitivity even in the most sensitive species, which are swine.

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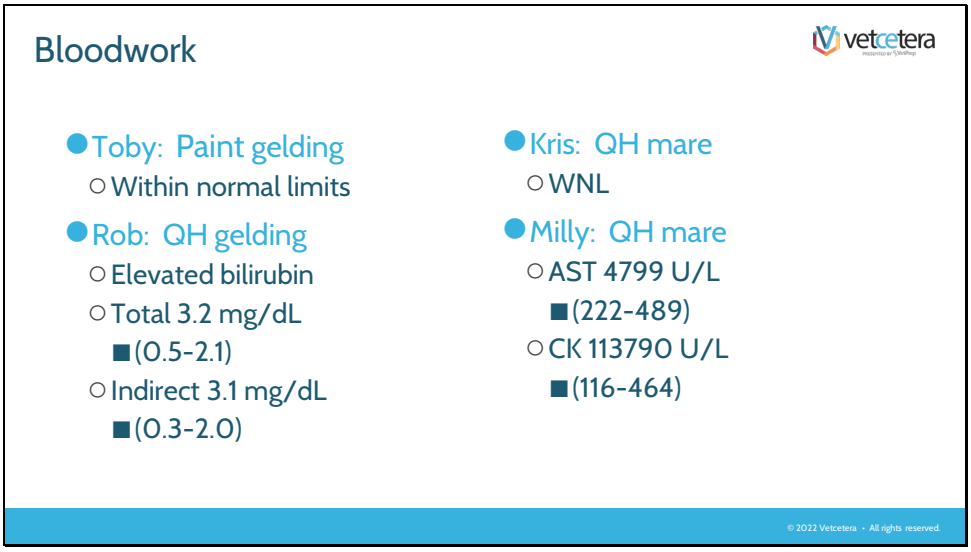

So the bloodwork, everything in the paint gelding was OK. The Quarter Horse gelding had an elevated bilirubin. The Quarter Horse mare, no problems. The other Quarter Horse mare, wow, look at that CK.

The ASC is pretty high too. That's impressive. But the CK kind of blows-- is kind of what's pointing me in one direction. So hopefully, you're pointing in that direction as well.

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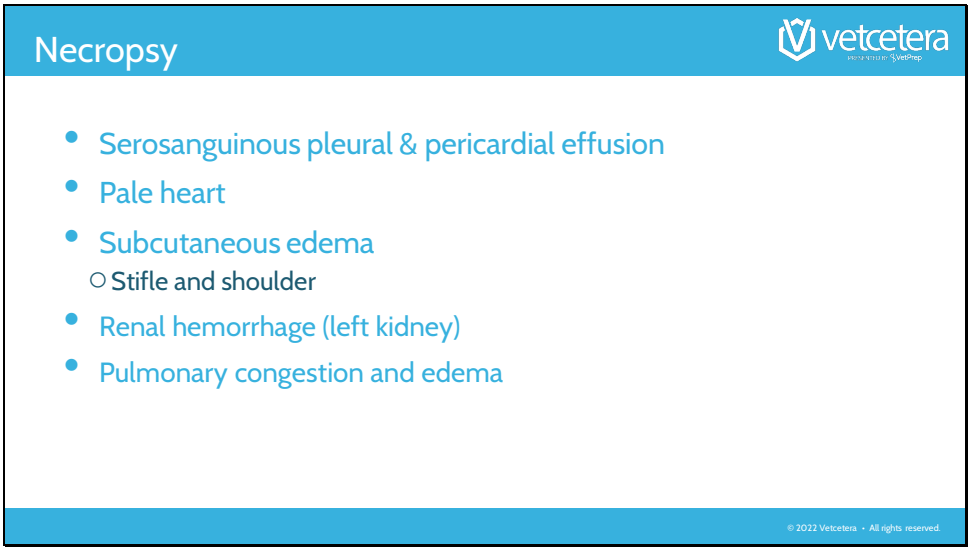

Necropsy on the pony-- yay, we finally have the necropsy results, serosanguinous pleural and pericardial effusion, pale heart. Well, that tells us something. Subcutaneous edema in the stifling left shoulder, renal hemorrhages, and then pulmonary congestion, and edema, so if we put the pericardial effusion and the pleural effusion and the pulmonary edema in one box with the pale heart, we might see. I think we're looking at some heart failure here.

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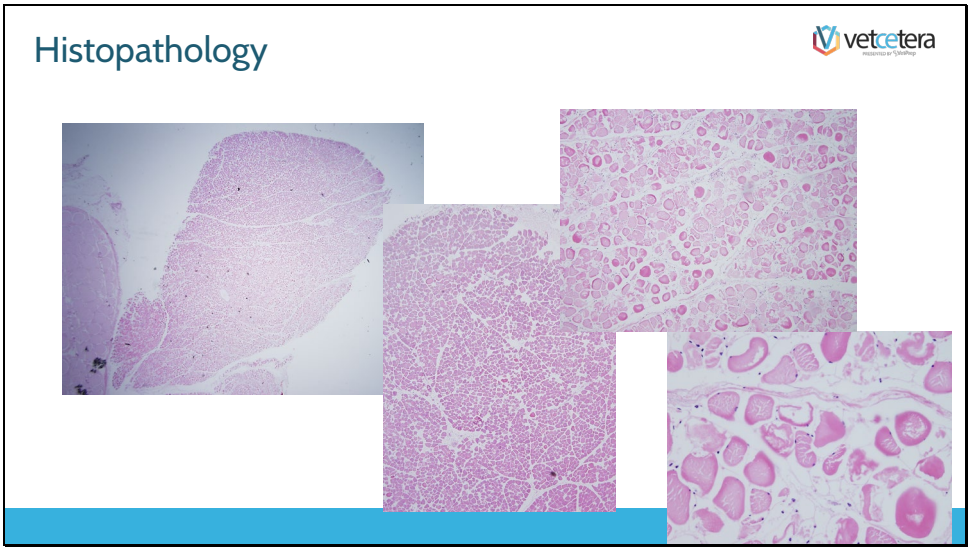

And this is some beautiful histology. There shouldn't be that much. I think I can't even tell what kind of muscle this is. It could be cardiac muscle. It could be skeletal. It honestly doesn't matter that much.

Yeah, it's probably cardiac muscle because of this form, looks like part of the endocardium here. So yeah, our muscle cells aren't supposed to be kind of smudgy and pink. And we've lost a lot of cellular detail. It looks like there's some extra nuclei around these. So there might be some macrophages coming in. But this is not healthy cardiac muscle.

I mean, obviously the animal's dead or wouldn't have a cardiac muscle. But there was something going on in the heart.

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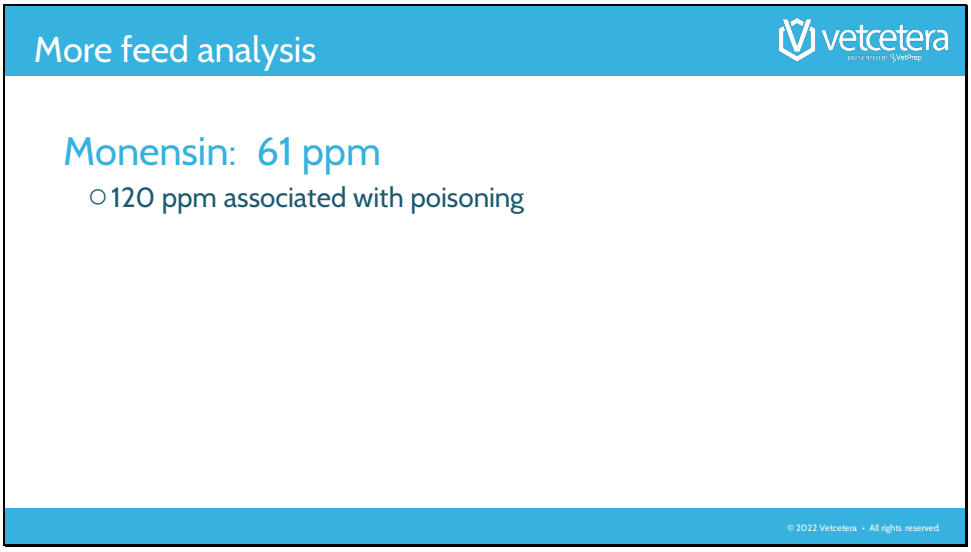


So we've had monensin, 60 part per million, which is about half which would be associated with poisoning in horses. So that's the feed concentration. It depends on how much feed they were getting obviously.

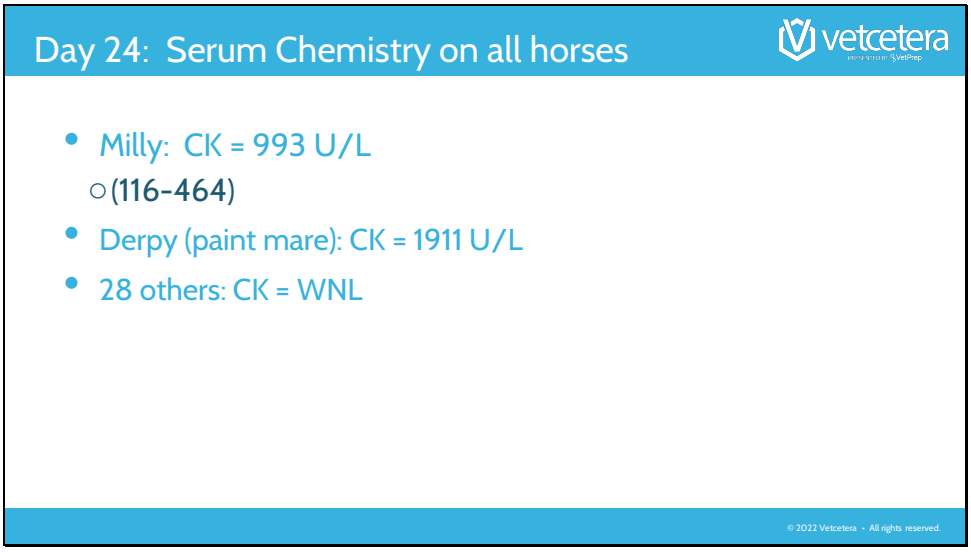
And it also depends on distribution in the feed. Is this a representative sample of the feed? I don't know, but monensin fits a pretty nice picture here. And also this is horse feed, so it ain't supposed to be there. So you can always make that argument.

The monensin, I don't know if that was the only underlying issue in here, but it fits the cardiotoxic effects. That's the rapid onset of death. And the elevated CK, there's probably going to be some high troponins, too, if you tested for that.

And it could very well be that we just didn't get the right feed sample. Because honestly, the feed sample that killed the horse, you're not going to get it because the horse ate it, right? It's gone. So we do the best we can with what we have. So this one wasn't tied up in a pretty little bow.

I am suspicious of monensin poisoning in this case. I couldn't confirm the diagnosis.

Slide 25



The CK increased in one of the horses. Another paint mare also had pretty high CK. And then the other ones were unaffected.

So again, that would go with kind of a sporadic distribution of the ionophores within this lot of feed. Some horses got more than others did. And of course, there's also individual differences in your horses.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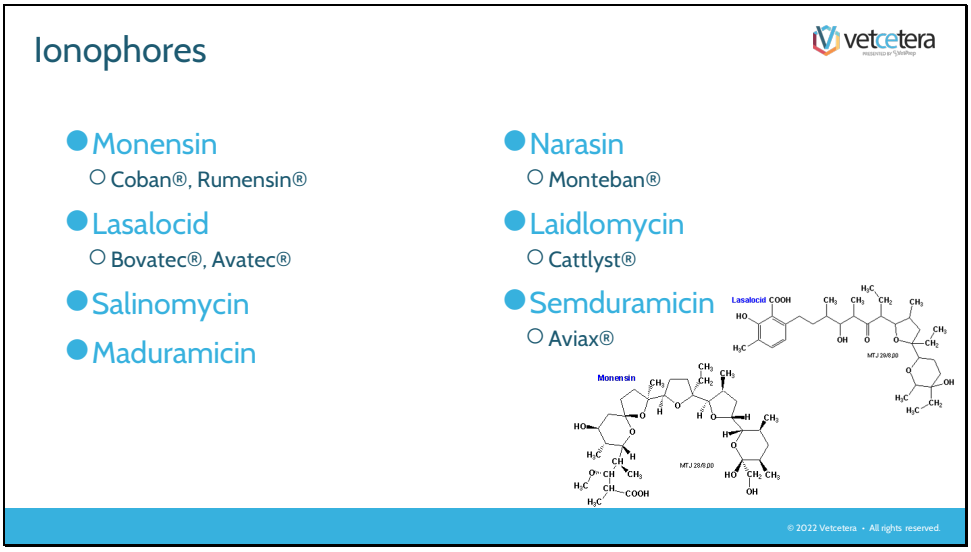
Part 3a: Ionophores

Slide 27



So ionophores, I'm going to start with those as feed contaminants because they segue nicely from the case study. They're pretty interesting. The one we see most is monensin. But we do see lasalocid occasionally and salinomycin occasionally. I don't see too many of the maduramicin or the narasin, laidlomycin, or I don't even know that one, semduramicin.

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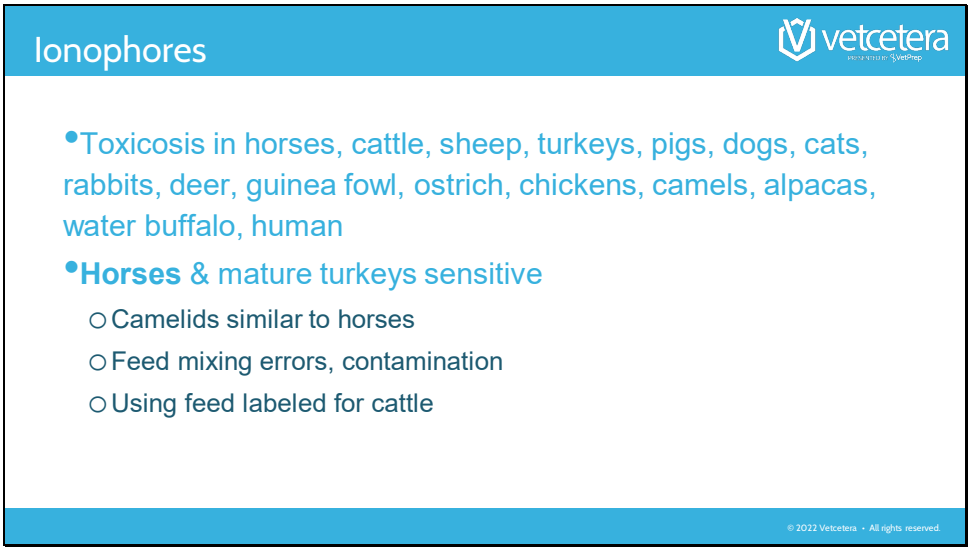
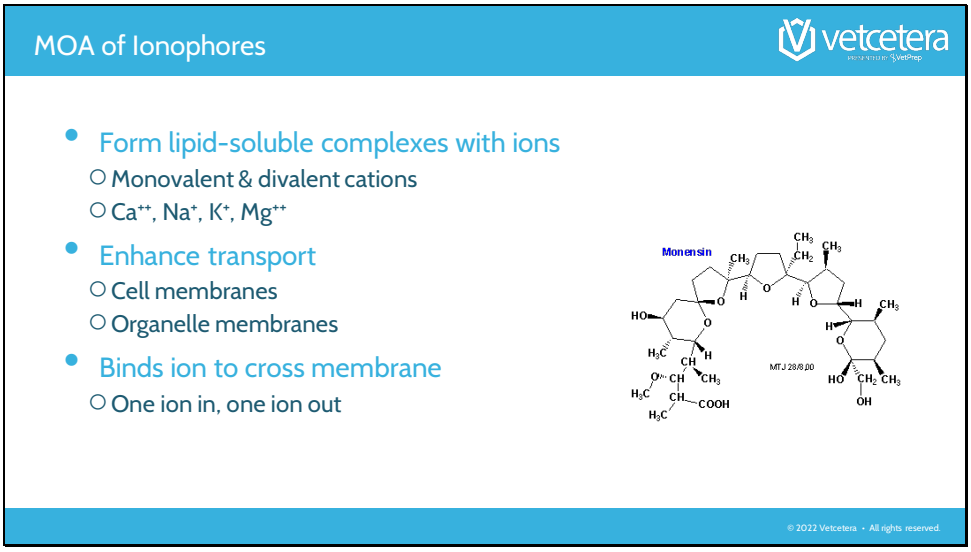


But they have something in common. They're toxic to a lot of critters. They're really toxic to horses. And if anybody also does Camelots, I think Camelots are about the same as horses. I think that the toxic dose of 120 for monensin is probably the same in horses and Camelots.

Turkeys are considered very susceptible. They're really not. It's just that chickens are so very, very resistant. You can put a lot of ionophore in chicken feed. But if the turkeys get into it, you're going to get dead turkeys.

And like I said Camelots are very similar. And there should not be monensin or any of the ionophores in horse feed ever under any circumstances. They can tolerate small doses. But it's not something that you really want to see in your horse feed. And certainly using cattle feed for horses is never a good idea.

Slide 29



So how did these things work? So if you look at this molecule, and I have to move. I have to move something, so that I can see this molecule and point out what I'm looking at here. There it is.

So if you look at this molecule, it is like the stringy molecule. It's got this long chain. And of course, all of these bonds can flip around a little bit. They're not static. Unless there's a double bond or something or unless they're in a ring, they have some ability to maneuver.

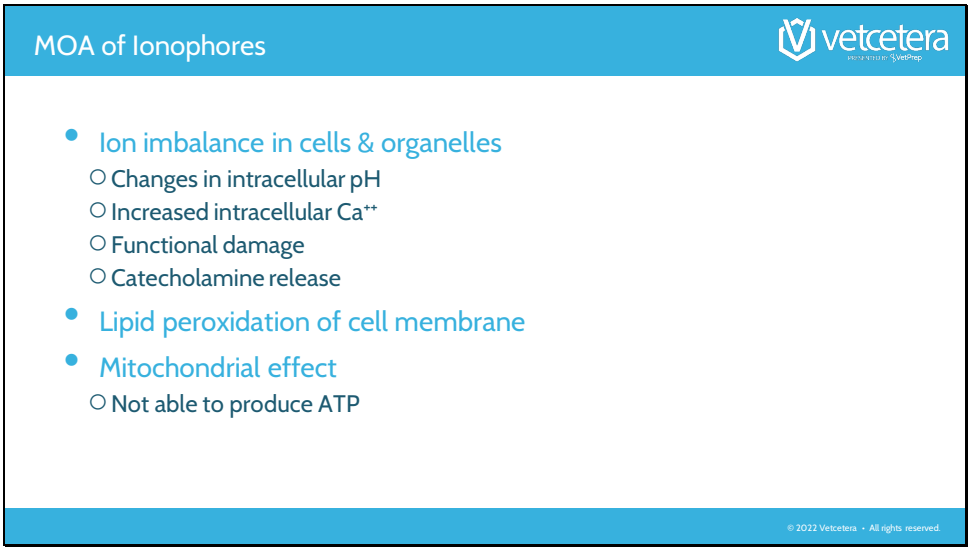
So here, here, and here, here, here, the molecule can flip around. And so it can configure itself, so that all the hydroxyls, all the oxygens, all the charged areas are inside of this molecule. And all of the methyl groups, all of the uncharged things are on the outside of this molecule.

So what happens when you do that? Well, that means whatever's inside can bind to something that's hydrophilic like an ion, whereas everything that's outside can go back and forth across lipid membranes. So basically, these are specific to one cation, whether it's calcium, sodium, potassium, magnesium. And they bind to the inside of this molecule. And then the molecule can go back and forth across lipid membranes, which are like cell membranes and mitochondrial membranes and sarcoplasmic reticulum membranes, all these membranes.

And that kind of messes with your ion balance, because you're supposed to have so much calcium in your sarcoplasmic reticulum. But it's different from what's allowed in the cytosol. And that's different from what's circulating in the serum and the extracellular fluids and things like that. So you're basically messing up these ion gradients with these things.

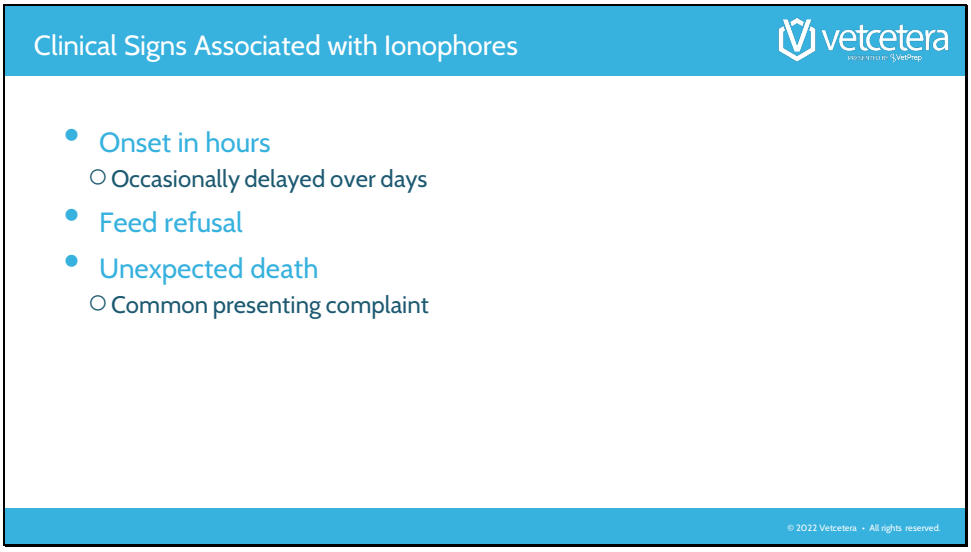
And cells that really need ion gradients, I said sarcoplasma, are muscle cells. So muscle cells and neurologic cells also need ion gradients. But these really seem to focus on the muscle cells. They might not be so good at crossing the blood-brain barrier. They're quite large. So what we really see with these guys are muscle degeneration.

Slide 30



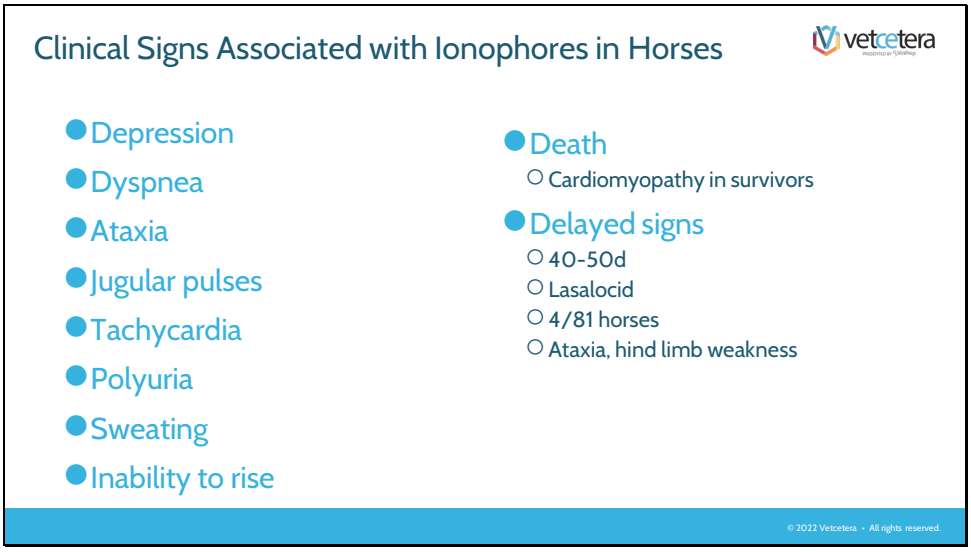
So changes in intracellular pH increase intracellular ions. Catecholamine release, second as a secondary effect, you can cause damage to the cell membranes through the excessive ion actions. And then of course, mitochondria need an ion balance between the inside and the outside of the organelle as well. So without those salt, you can't do cellular respiration.

Slide 31



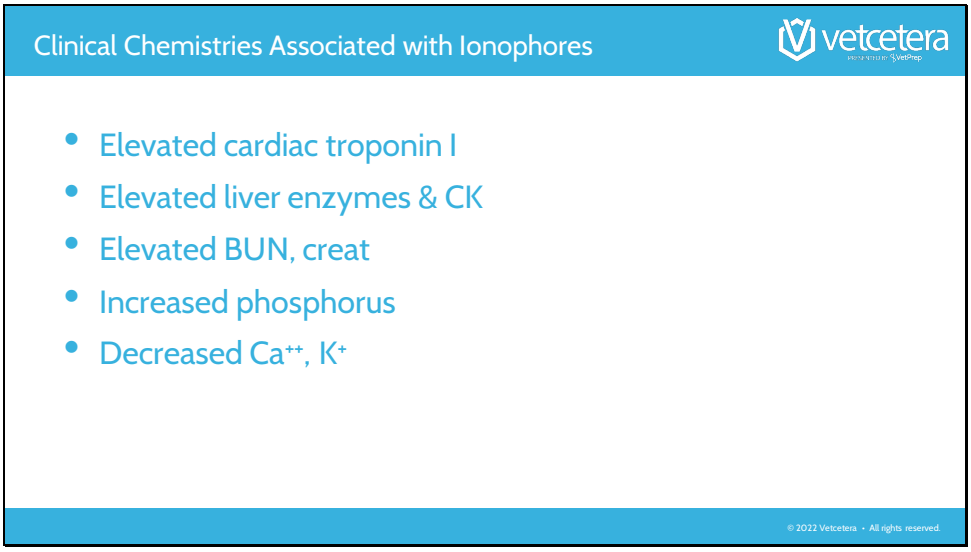
So onset, it can be really fast. So if this was like an enormous dose of monensin that maybe the stallion got an enormous dose and it died right away, maybe that someone that got the undiluted part of the lot, and then the pony got a slightly smaller dose over time. And it was delayed for some days. A lot of them will refuse the food, which is a good thing. They don't eat it, they won't get sick. But the most common presenting complaint in these guys are just found dead.

Slide 32



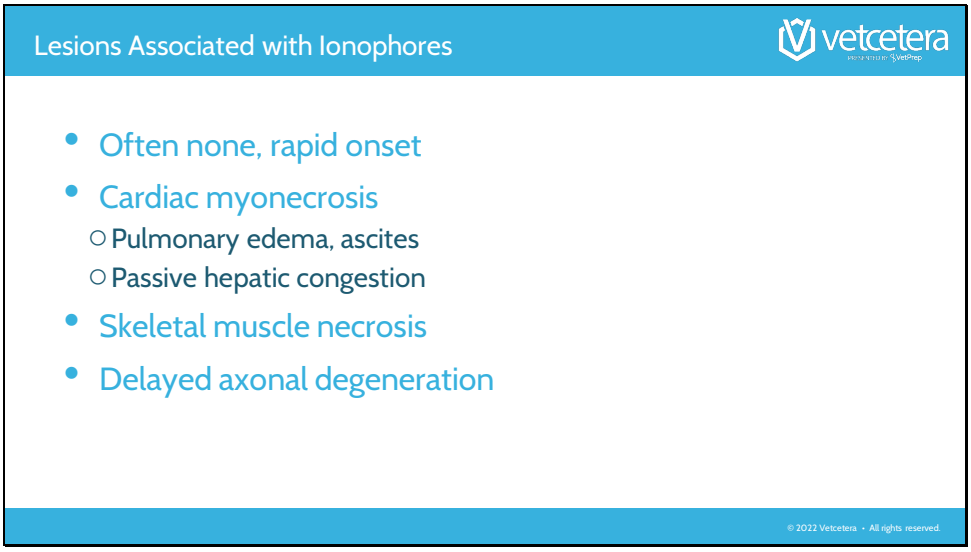
Some other clinical signs, respiratory signs you can imagine secondary to the heart, heart failure jugular pulses, tachycardia, sweating, so stress-related issues. And the survivors, you can't heal the heart muscle very well. So you can get cardiac myopathy. You can get possibly conduction disturbances later on, which can kind of sneak up on you and become a really dangerous situation. And they have seen ataxia and hindlimb weakness and a few horses, as well with lasalocid.

Slide 33



So clinically, you're going to see the elevated liver enzymes and CK that we saw in our group of horses. You can also see elevated cardiac troponin I. You can see some kidney damage, and then ion imbalances as you can imagine because your ion boundaries aren't functioning very well.

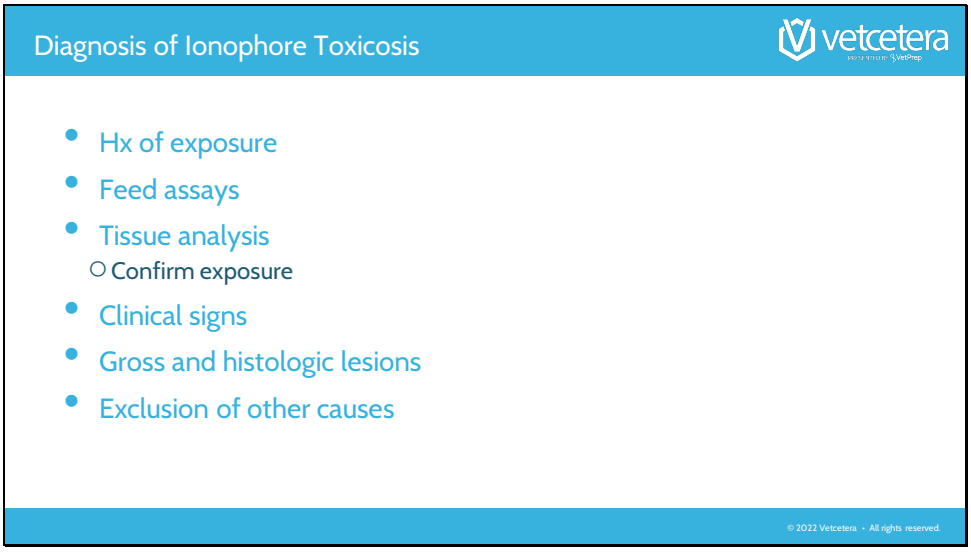
Slide 34



So lesions, you might not see anything. So even if they had done the necropsy on the stallion, they might not have seen anything because it was a pretty acute case.

And so the bottom line is biochemical changes happen a lot faster than morphologic changes. So just the changes on ion channel, you're not going to be able to recognize that grossly or histologically. But as you get later in the disease, you get myonecrosis, which you can see you get the cardiac heart failure kind of clinical signs. And you can also get skeletal muscle necrosis and some external degeneration with these guys.

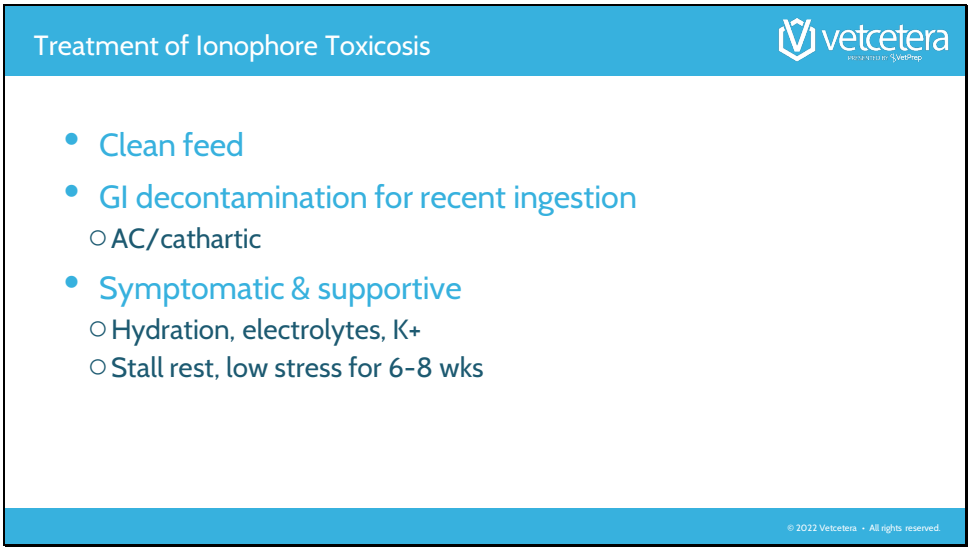
Slide 35



So a lot of times, the diagnosis is going to be on feed analysis. And like I said, that is not 100% useful. You can do tissue analysis to confirm exposure. Ionophores are not supposed to be in horse tissues. If they're there, you can confirm exposure. But making the legal jump that from exposed to poison can be a bit of a difficult situation, because they might be exposed to a small amount and not enough to cause death. And there's really no tissue concentration data out there to sort one thing from the other.

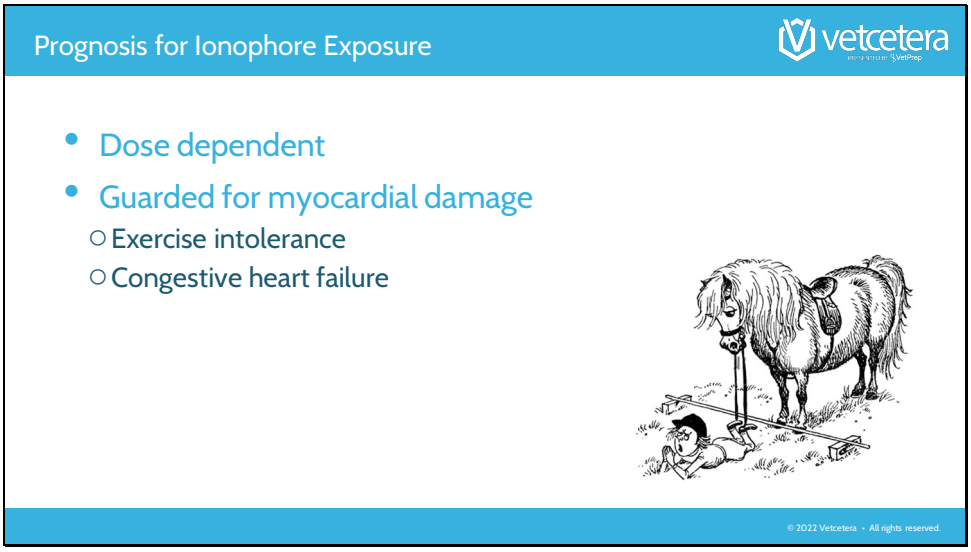
Clinical scientist histologic lesions and exclusion of other possible causes, so things like the Cassia and Senna can cause myonecrosis. Things like selenium deficiency, although that's mostly in youngsters, I have seen it in older animals. Cantharidin can cause cardiac muscle degeneration, but you'd see some other clinical signs as well. So ruling out other potential causes is also helpful.

Slide 36



So these guys obviously with any feed issue, clean feed is your number one priority. You can try gastrointestinal decontamination with activated charcoal plus a cathartic and then symptomatic and supportive care. But again, if they are having cardiac necrosis, myocardial necrosis is going on, you can get later on heart failure. You can get later on conduction disturbances. And those can be pretty significant problems for a performance horse.

Slide 37

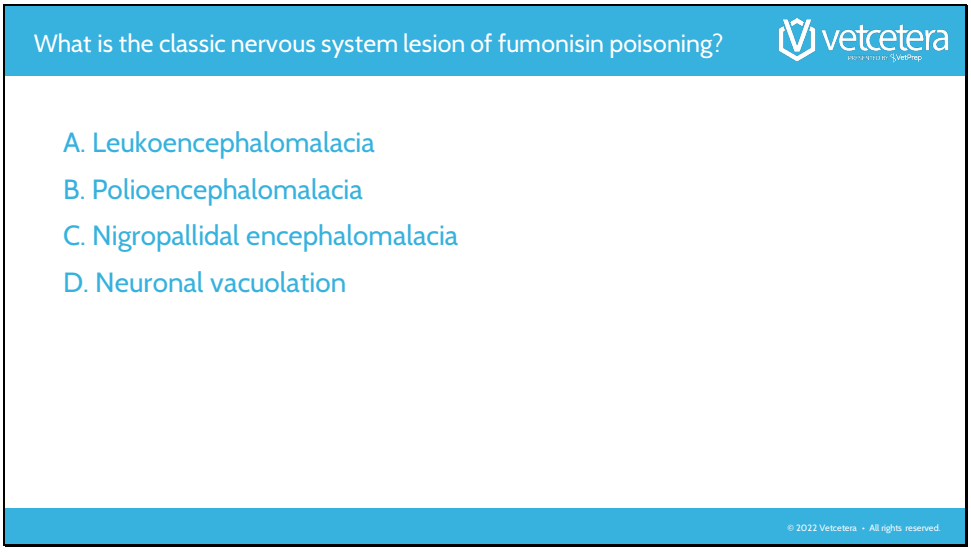


So the prognosis again is really guarded, because you don't know what damage has already been done even to the survivors.

Slide 38

So we're going to talk about fumonisin.

Slide 39



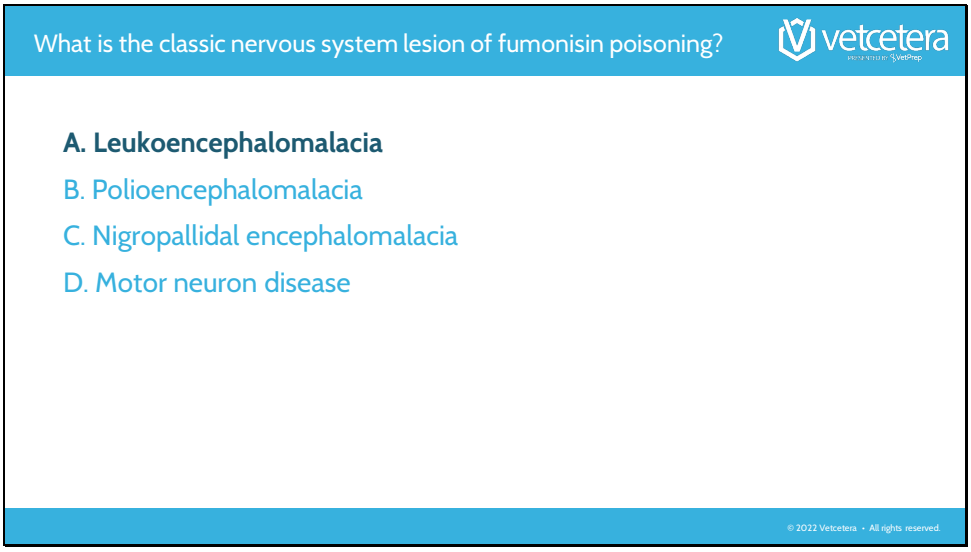
Does anybody remember what the disease associated with fumonisin is? I like these disease names because they're all really, really cool.

So leukoencephalomalacia, so we know leuko is white. Encephalo is head. And malacia is softening. So that is softening of the white matter of the head. Polioencephalomalacia, polio is gray. So that's gray matter softening of the brain.

Nigropallidal encephalomalacia, that one's a little more complicated. Nigropallidal encephalomalacia, so we have softening of the brain. But it's just specifically at the globus pallidus and the substantia nigra. So these two focal areas of the brain.

And then you can have good old-fashioned neuronal vacuolation, which is basically just lysosomes expanding and filling up the cell till they get a nice, foamy appearance. So would anybody care to venture a guess as to which of these we're talking about with fumonisin?

Slide 40



All right, we're running 100% on the guesses with this one. It is leukoencephalomalacia. Excellent work, guys.

Oh, and I changed the last foil on the one. Motor neuron disease is associated with vitamin E deficiency. The neuronal vacuolation is associated with Astragalus, so the locoweeds. And polioencephalomalacia is associated with Bracken fern and Equisetum and some other plants that have thiaminase. And Nigropallidal encephalomalacia is associated with Russian knapweed and yellow star thistle.

And they changed the name. It used to be Centaurea repens with the yellow star thistle. And they changed its name as well. I can't remember what it is.

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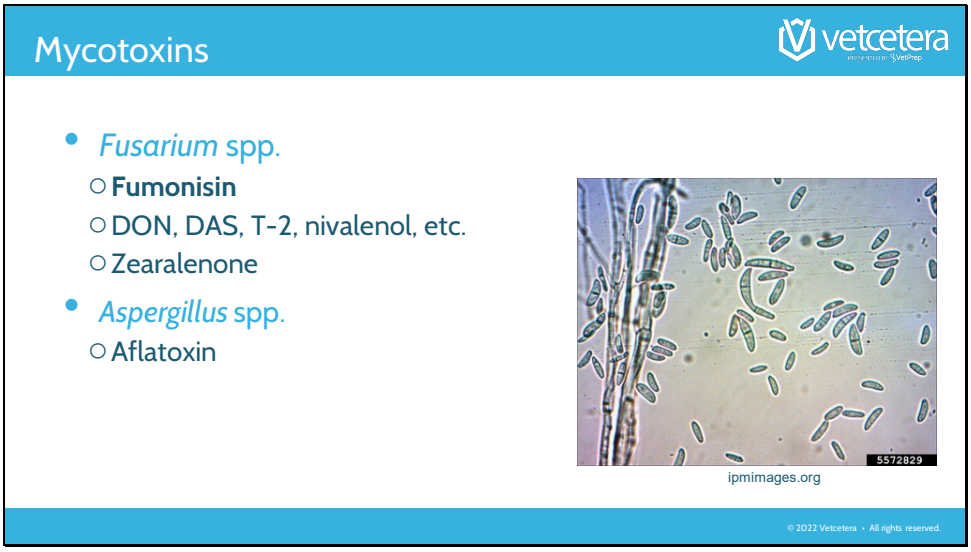

But Fusarium is a mycotoxin. Fumonisin mycotoxin is originally from Fusarium moniliformes, so a fumonisin.

They changed the name of that organism. So it's no longer Fusarium moniliforme. I don't remember what it is. But it is a Fusarium species. And Fusarium also produces the deoxynivalenol I was talking about before, diacetoxyscirpenol, T-2, nivalenol, et cetera.

And zearalenone, which I actually would be a little worried about in horses because it causes reproductive failures. It's an estrogen. It's not a plant estrogen, some old estrogen, but it's an estrogenic compound. And then Aspergillus produces aflatoxin, which I really haven't seen in horses.

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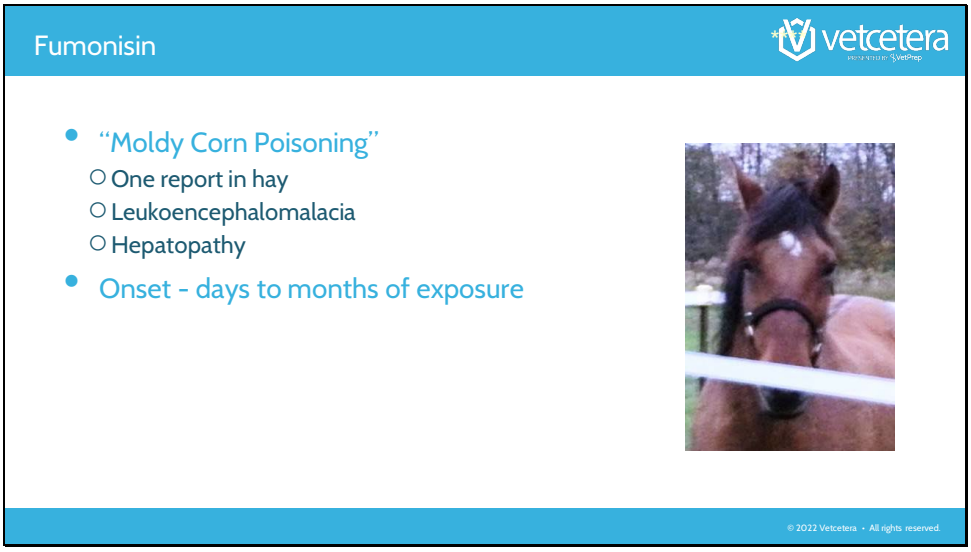

So fumonisin poisoning, also known as moldy corn poisoning, generally associated with corn, but it can be associated with hay. And it can present with brain damage or liver damage although I've never seen a liver damage case. There can be some overlap. You can have both, or you can have either one. But I've mostly seen brain damage in these guys.

And the onset can be a few days after exposure or some way into it. Again, depends on how much fumonisin is in the feed.

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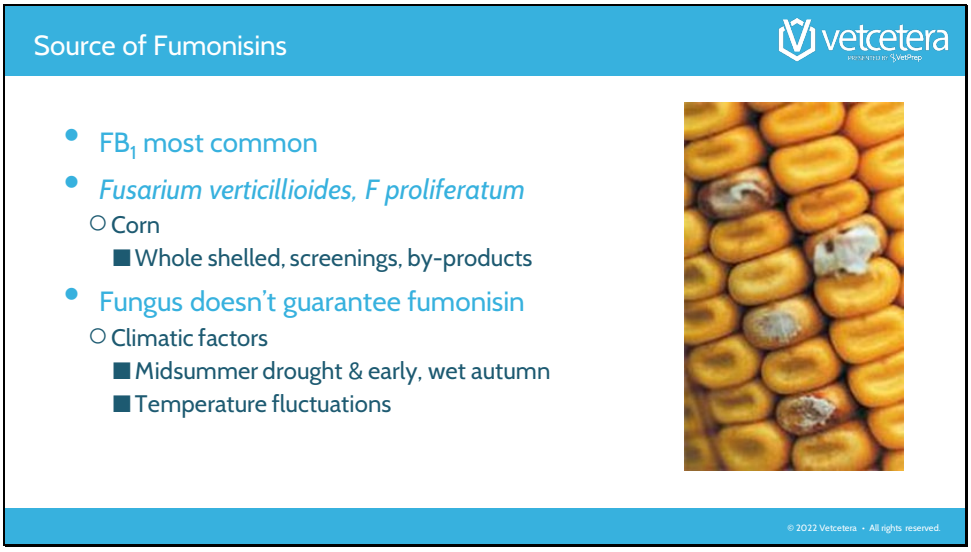

Fumonisin B1 is the most common form. There we go. Fusarium verticillioides is the one that used to be Fusarium moniliforme. And it's found in corn and corn-secreting products.

Any broken kernels are more likely to grow mold. And the Fusarium is pretty much omnipresent. The spores travel by air, and they can be in pretty much any field. Crop rotation helps, but it doesn't entirely prevent it. And there are certain climatic factors, especially droughts. Insect damage can promote it as well.

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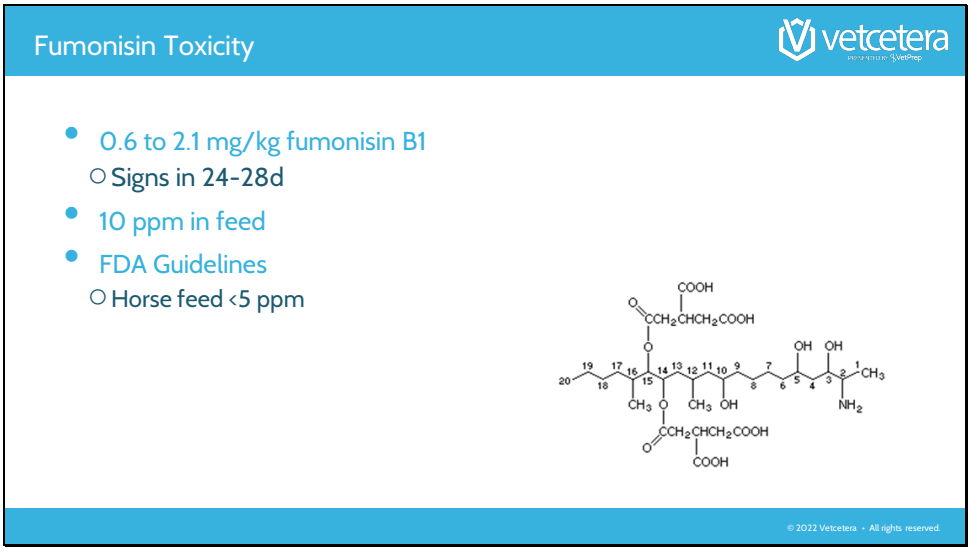


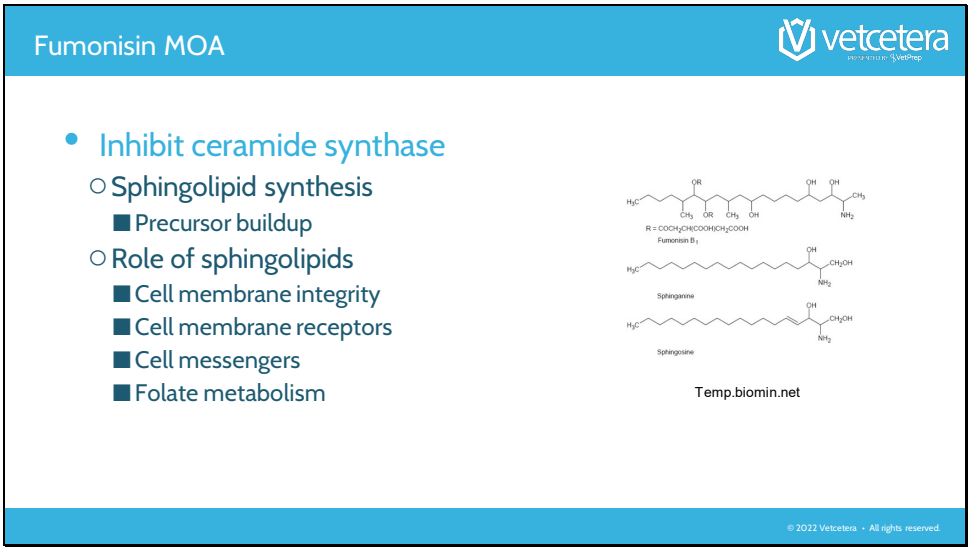
So they say 10 part per million in feed. Yeah, so the dose is 0.6 to 2.1 milligrams of fumonisin to a kilogram of horse. And then you get the signs within a few days. 10 part per million in feed, I don't like to see them above 2 part per million with this one. I know and I would believe 8 part per million would definitely be a problem. So horse feed less than 5 part per million, again, I don't like to see them over a 2 part per million.

And this is the molecule here. And it's this long chain of carbons with some functional groups on it. And what it does is it looks a very lot like sphingolipids.

And you remember sphingolipids from neuroanatomy. They're in your Schwann cells. They're in some of the other-- the oligodendrocytes are in a lot of the white matter cells that accompany neurons. The glial cells is what I'm trying to say. And it looks like that. And they are also used in other functions in the body.

But one of the functions is in fact, neuron basically coating the neurons, so that they can charge better. So that they can move axon potentials faster and things like that.

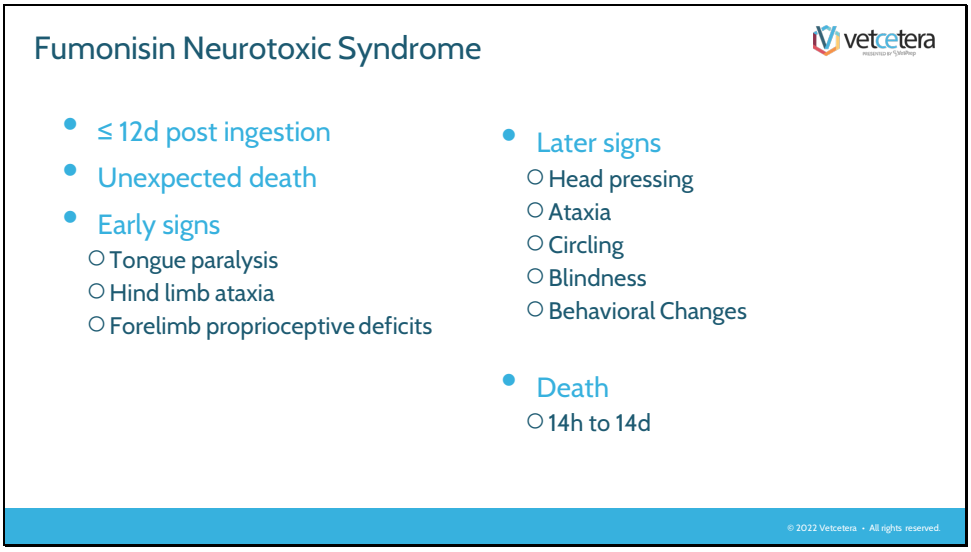
Slide 45



So what this does is inhibits an enzyme that's really important for sphingolipid production.

So the ceramide synthetase cannot function. So you get precursor buildup, which damages-- basically, you don't get your completed sphingolipids, which damages cell integrity, which damages the Schwann cells and the glial cells and the brain and the central and peripheral nervous system. And it's also really important for cellular metabolism.

Slide 46



So the neurotoxic syndrome, less than 12 days of ingestion, sometimes they die. But sometimes they have some clinical signs like tongue paralysis and hindlimb ataxia and forelimb proprioceptive defects. And that's very useful information because I have a case looks a lot like that right now that I should probably contact. I've been kind of mulling it over for a while.

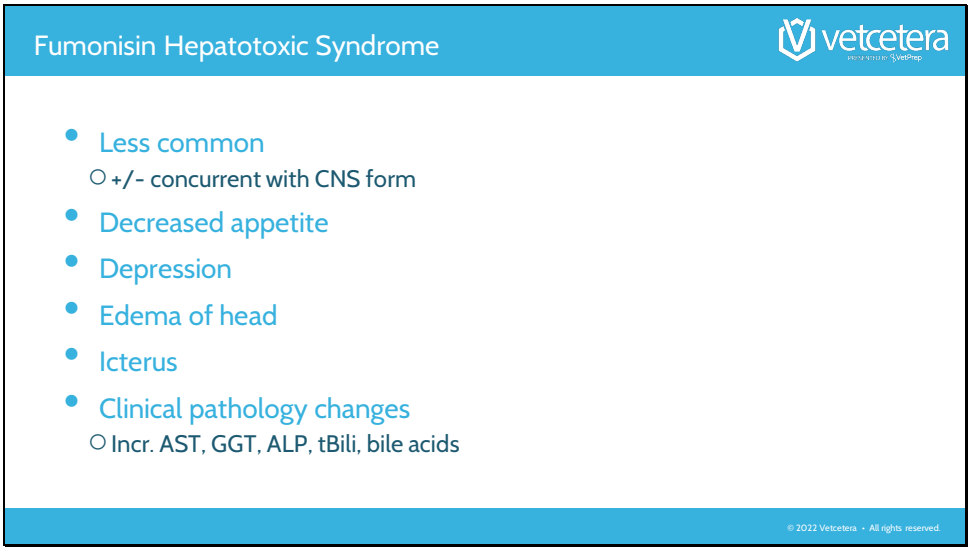
Later, you get head pressing ataxia circling and blindness and behavioral changes. These horses can get really mean. I imagine they're in a lot of pain because when your weight matter starts melting, that just can't be very comfortable. So they can get really belligerent. They can get very dangerous. And they can die in a few weeks.

I had one case that was a pregnant mare that was extremely valuable. And the insurance company would not let them euthanize her even though anywhere near her, she would try to kill. I mean, she was literally a maniac. She just was homicidal. She was just going to stomp anything into the ground that got near her.

And I strongly recommended euthanasia. She wasn't going to get any better. And yeah, I told the owners, maybe you should call the insurance company and ask what they think is going to happen when that foal drops.

If this animal is trying to kill anything that gets close to her, how long do you think it's going to last in that stall with her? So I don't know what happened. That one was lost to follow up. That was pretty scary case.

Slide 47

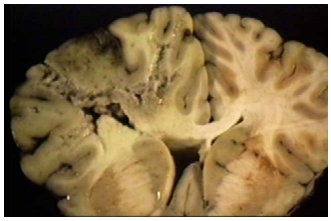


You can get the hepatotoxic form sometimes. I haven't really seen it. But you get a chronic liver disease. So edema of the head is basically from them being unable to lift their head, icterus, elevated liver enzymes, et cetera.

Slide 48

Lesions Associated with Fumonisin

- Leukoencephalomalacia
  - Subcortical liquefactive white matter necrosis
  - Diffuse or multifocal
  - Asymmetric
- Liver changes
  - Hepatomegaly
  - Centrilobular lipidosis, necrosis



Courtesy deLahunta

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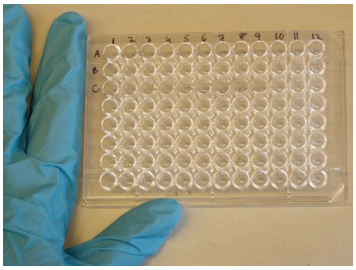
And then leukoencephalomalacia is the lesion, so melting of the white matter. So all of these areas underneath the gray matter are starting to basically just melt away. That's why these horses are not going to get any better. I'm actually astonished that polioencephalomalacia is treatable as it is. But yeah, these myelinized axons are completely gone at this point.

Slide 49

Diagnosis of Fumonisin Toxicosis

- Clinical signs, lesions
- Analytical chemistry
  - Feed analysis
  - No tissue test available
- Sphinganine to sphingosine ratio
  - Not common right now
    - Fresh or formalin-fixed tissue



Jeffrey M. Vinocur

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So diagnosis is usually based on feed testing. I don't see too much of it here where I am. I know we have a lot of Fusarium issues, because we see the deoxynivalenol and whatnot. There is no tissue test available although there are sphinganine to sphingosine ratios available.

They used to operate at Purdue. I don't think they are anymore. Your best bet would probably be Iowa State right now. They may actually run that. And they could tell you if the sphinganine to sphingosine ratio is correct for normal horse, or if there's some inhibition of the ceramide enzyme, ceramide synthetase enzyme.

Slide 50

Treatment of Fumonisin Toxicosis

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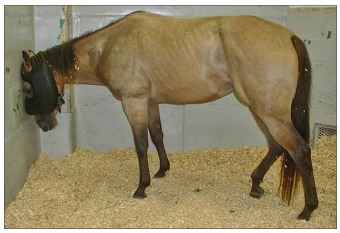
- Prognosis depends on severity
- Clean feed
- Isolate affected horses–dangerous!
- Thiamine
- Supportive
  - Treatment for cerebral edema



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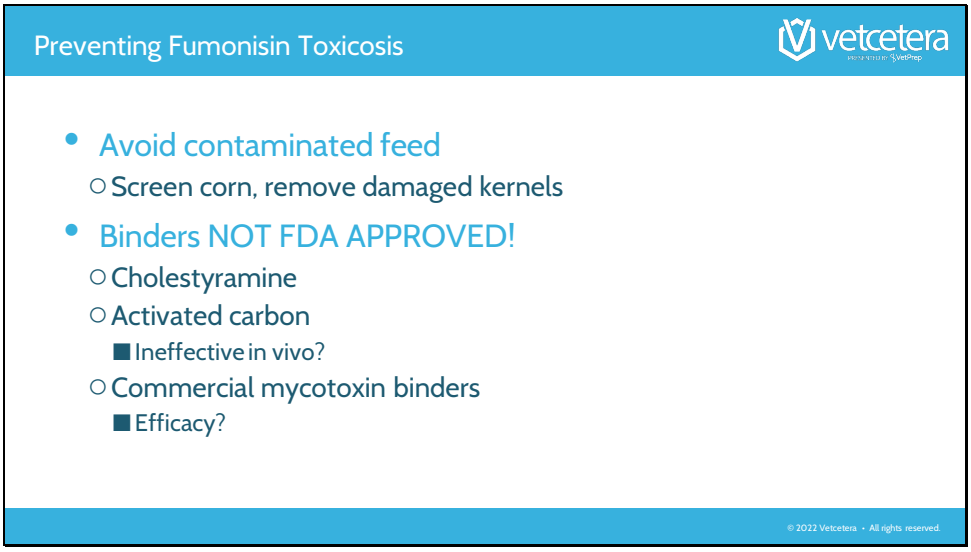
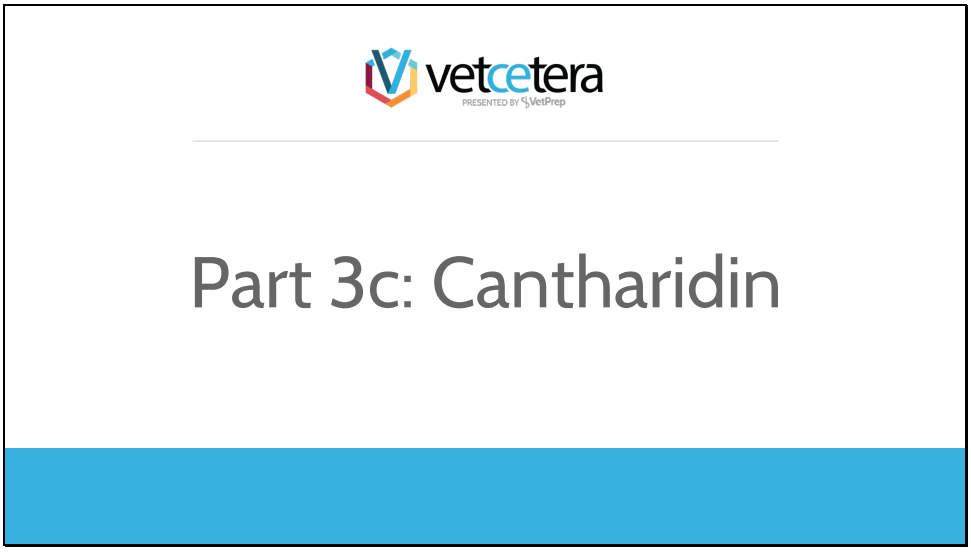
So prognosis depends on severity. But obviously, that brain is not going to heal. These horses are really dangerous. Nothing with neurologic signs should ever be allowed to die without trying thiamine on it in my opinion. But it's going to be of limited use in this particular case and basically supportive care.

Slide 51



So avoid contaminated feed, pre-test the feed. And I think a lot of feed manufacturers are doing this already. Remove damaged corn, screen the corn, remove damaged kernels, or move fines. And there are binders. They are not-- the jury's still out on how efficacious they are. If they are not proven efficacious, then the FDA will not allow binders to be approved, to be sold as mycotoxin binders. They're only to be sold as things to change the consistency of feed and stuff like that.

Slide 52



Slide 53

So the last one I wanted to talk about is the blister beetle. And these are super, super interesting. And I probably don't have time to do them justice, but they're super cool.

These are the ones I used to see, the lemniscata, with beautiful stripes on the backing. You can get the black ones, as well. Those are fairly common in Oklahoma and Texas. But they specifically affect alfalfa, and there's a reason for that.

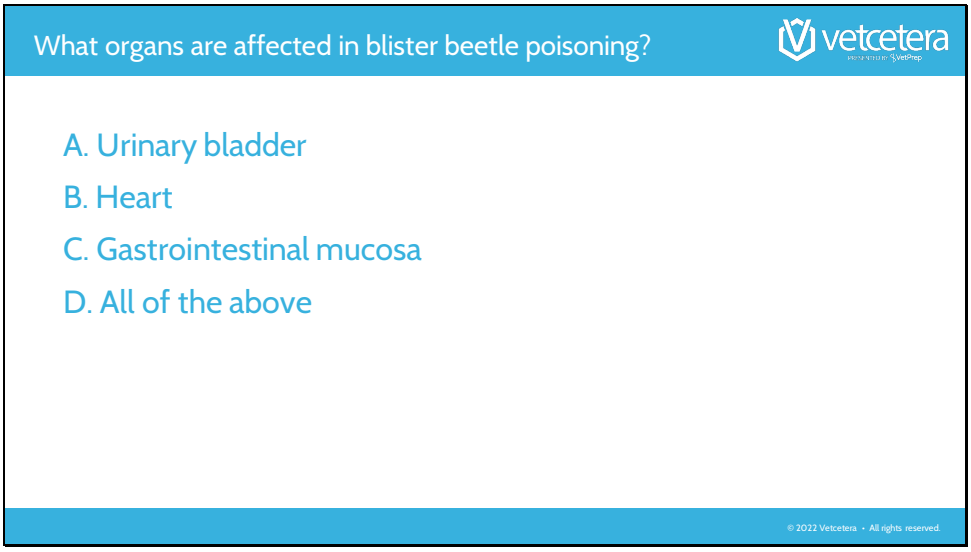
Slide 54

So here's some other pictures of them.

This is the Lytta. This is the actual Spanish fly in Europe. And they are named after the aphrodisiac Spanish fly. They have the same characteristics. People have died from the aphrodisiac, so not a great idea.

And this is just a map of where they can be found in the United States. We have had a few cases in New York. I used to see them all the time in Oklahoma.

Slide 55



I think we just don't feed as much alfalfa in New York.

So where do you see lesions in a cantharidin poisoning? I don't want to take too much time on this, because I'm running out of time. But anybody remember? Is it the urinary bladder? Or is it the heart, is the GI mucosa? Could it be all three?

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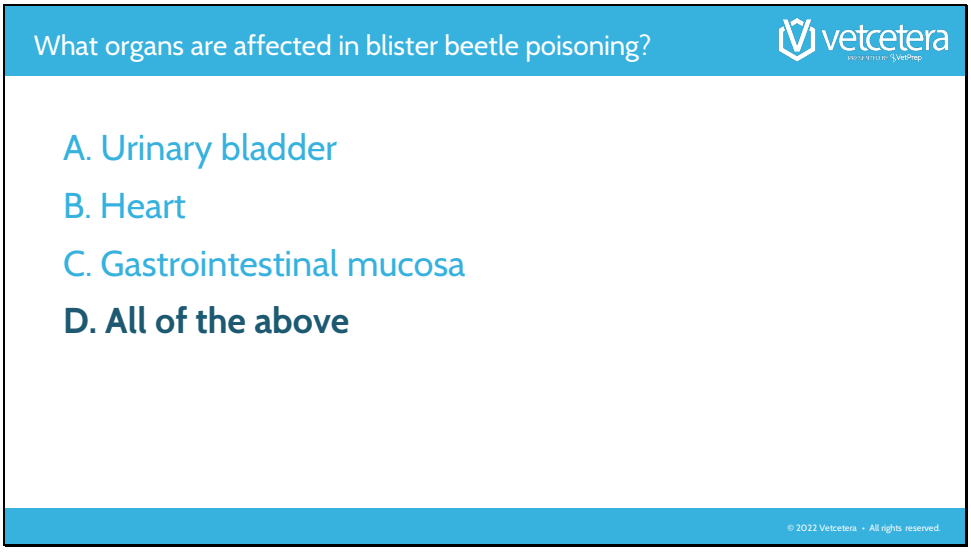

So as soon as one brave person tells me, OK, gastrointestinal mucosa, that is correct. Anybody else? They're all correct. They are all correct.

And the reason is this is a vesicating agent. It causes blisters on everything it touches. So it touches the GI mucosa. It blisters it, causes sloughing, necrosis, et cetera. It touches the urinary bladder, it blisters it, OK?

It's excreted by the kidneys. So it damages the kidneys. It damages the urinary bladder. And it is overtly cardiotoxic. And they don't know if it's the blistering agent that causes that. But all of these things happen.

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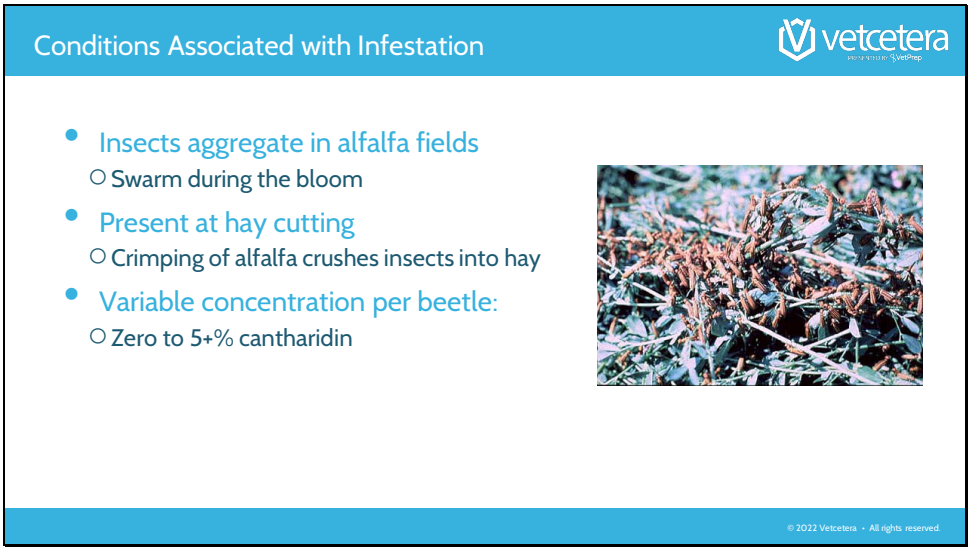
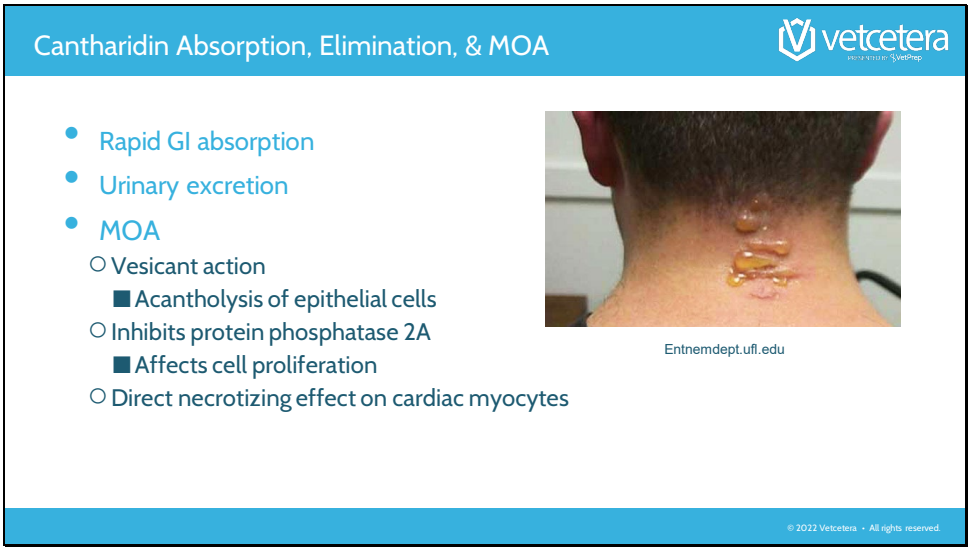


And this is basically what they look like crawling in an alfalfa field. And this is actually a good thing because what happens when you cut the alfalfa and you leave it in the field to dry, the bugs will just fly away. And that's fine. That's what you want. If you go in there and crimp the alfalfa after you cut it, then you smash the bugs into the alfalfa.

So that's why this is kind of a modern farming problem. It used to be they just cut it and leave it to dry and then pull it and bail it. Nowadays, they cut it and crimp it because the flattening helps it dry faster, but it also crushes the insects into the hay. And there's a variable amount of cantharidin in each beetle. The males actually have the highest concentration.

And actually when they fertilize the females, they deliver. They are the ones that produce the cantharidin. They deliver it to the females to protect the eggs. So I heard-- I was reading a paper that called it a nuptial gift, which I thought was just brilliant. So the males produce it. They give it to the females and as a way to protect the eggs.

Slide 58



And this guy, he felt something on the back of his head that was-- and it turned out to be a blister beetle. And he swatted it. So I told you that they're vesicating. Yeah, that's what it looks like. And it's urinary excretion.

So it blisters out the urinary bladder and the GI tract, the oral mucosa, esophagus, stomach, everything. And it causes direct necrosis on cardiac myocytes.

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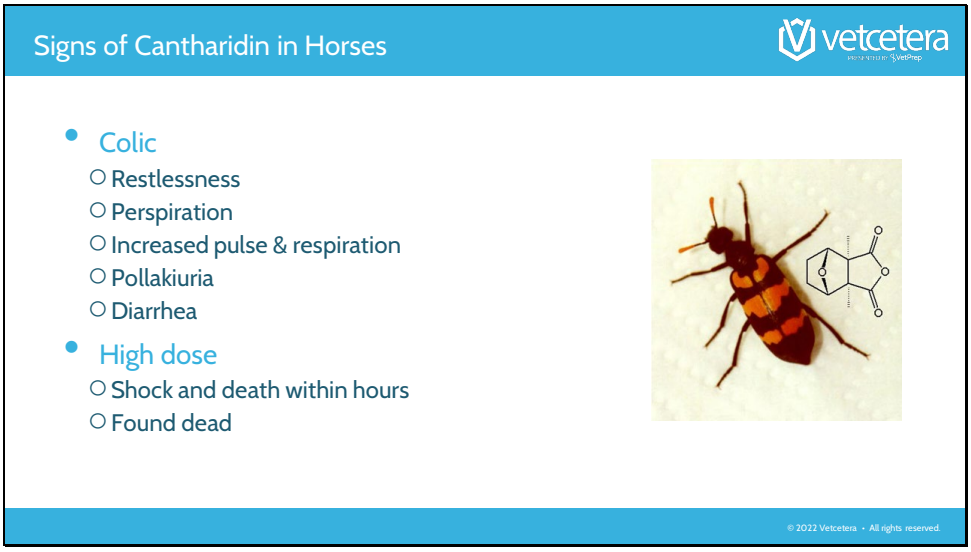

So what you'll see in these guys is pain. They are in pain, GI pain, urinary tract pain, and of course, they can have cardiac necrosis going on as well, which is not cool. So they can actually die pretty quickly from that. But yeah, these guys are in a lot of, lot of pain.

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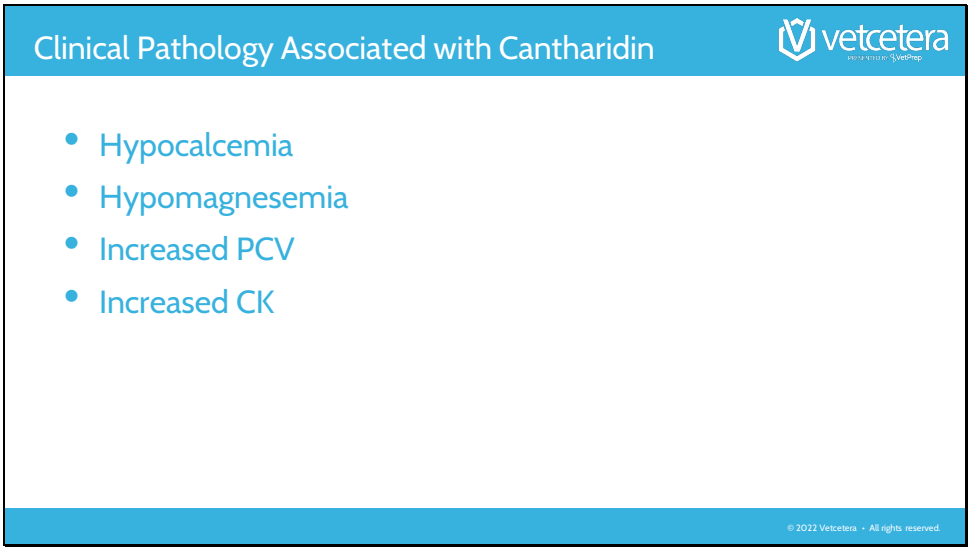
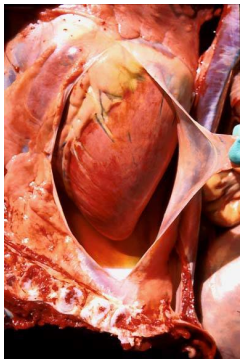


You get hypoglycemia, hypomagnesemia, increased PCV. They're shocky. And increased creatinine kinase probably increased troponin as well.

Slide 61

Lesions Associated with Cantharidin

- Mucosal blistering & ulceration
  - Oral cavity
  - Esophagus
  - Gastric and intestinal mucosa
  - Urinary bladder
- Myocardial changes
  - Necrosis & degeneration



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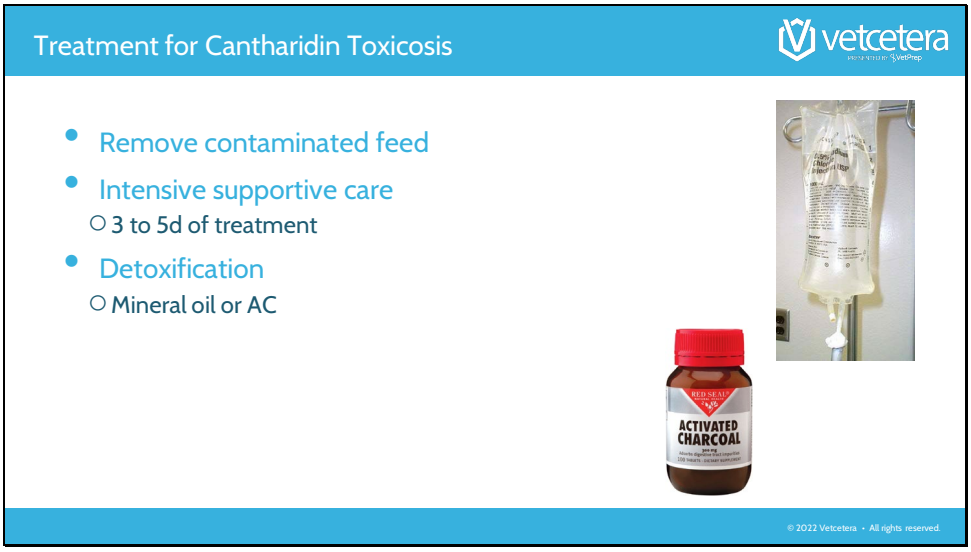
And you can see blisters in the oral cavity, esophagus, et cetera, and the myocardial degeneration as well.

Slide 62

So diagnosis is based on history of eating alfalfa. And you can find the bugs there too.

There are laboratories that do urine analysis. I'm not able to do it right now. Last time I tried, it was a failure. So I ended up sending it to Texas because they have a lot of cantharidin issues there. So they do a pretty good job of analyzing for cantharidin in urine.

Slide 63



You can also test GI contents. Urine is just a cleaner sample to deal with. Need some more water. So remove contaminated feed, always a good idea, and intensive supportive care, three to five days of intensive care.

I'm going to take off mineral oil off the detox list. It's really not recommended. But you might give them some sucralfate. That might make them feel a lot better. Activated charcoal might help find some of the cantharidin to decrease absorption. But the sucralfate may help and lots and lots of pain control.

And these guys are going to need big time pain control. So something like butorphanol or something like that, because flunixin is just not going to cut it with these guys. The NSAIDs aren't going to help. You need to go with big guns on this.

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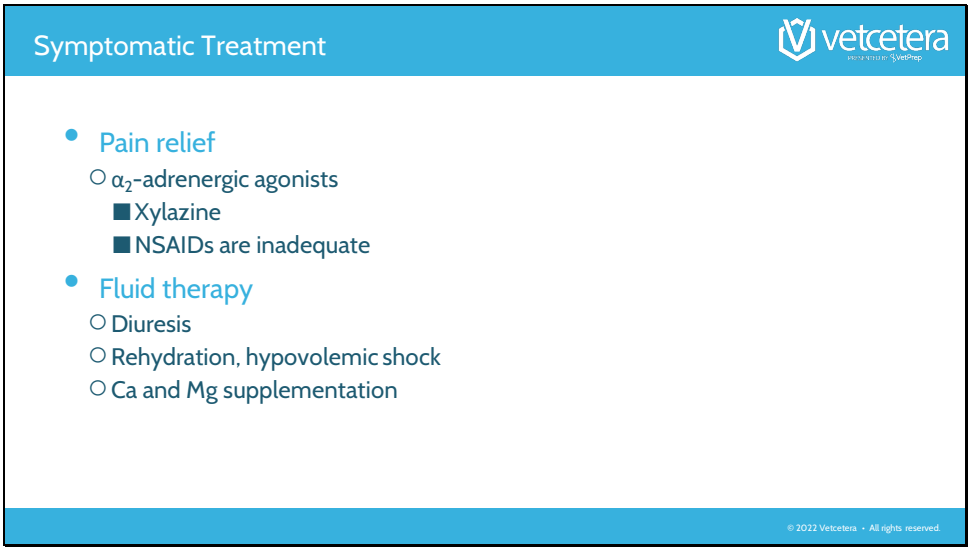
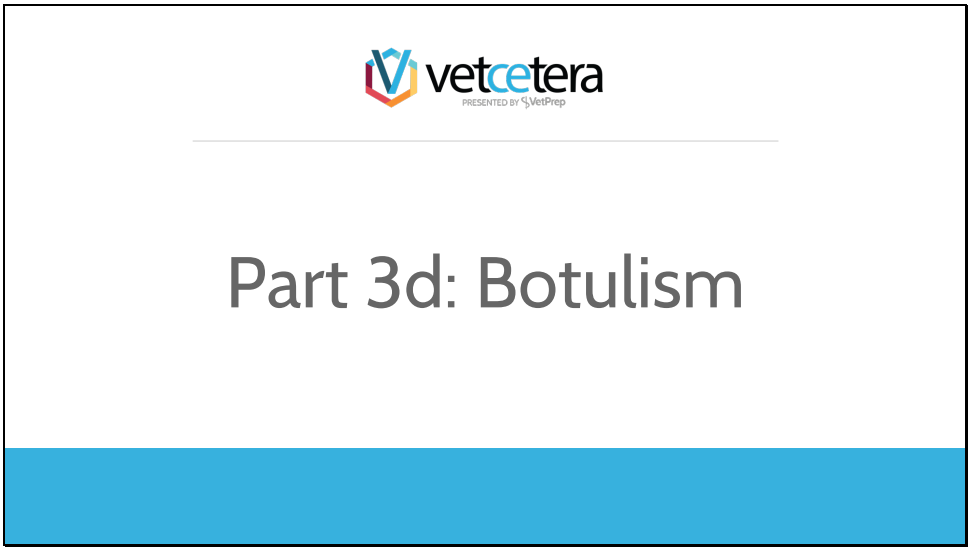


So xylazine, butorphanol has been used and then the diuresis maintain electrolytes, calcium, and magnesium, careful magnesium supplementation, and rehydration.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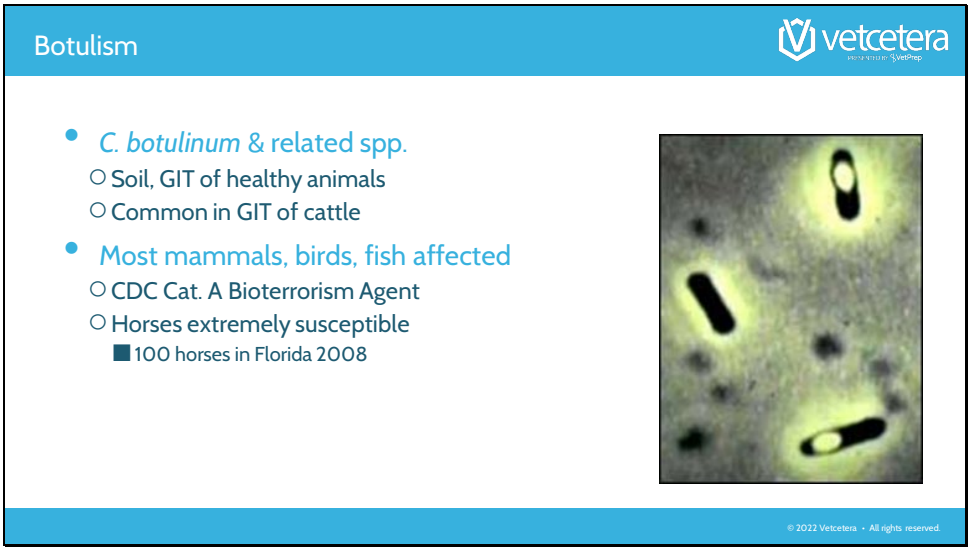
Part 3d: Botulism

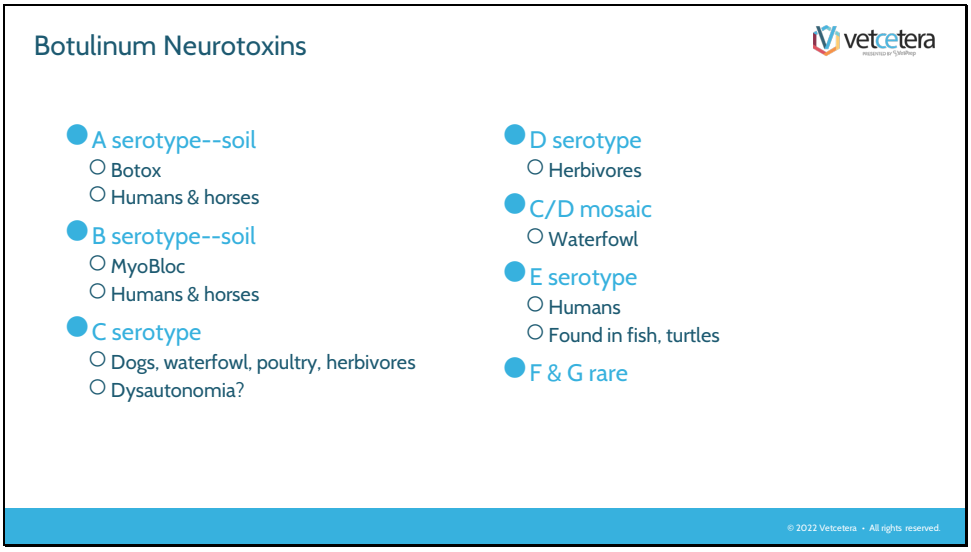
Slide 66



Oh, I guess I have one more, botulism. And this is found in the-- omnipresent in soil. It's found in the gastrointestinal tract of cattle. And horses are, as you probably know, extraordinarily susceptible.

2008 was the year they had hay problems in Florida. So they switched to haylage, and a lot of animals died. It's a bioterrorism agent as well, toxic to a whole bunch of different stuff.

Slide 67



And there's various types. We usually worry about A and B serotypes. And supposedly, there's some difference between A and B serotypes, depending on what part of the country you're in.

But any place in the country can have A and any place in the country can have B. So I don't subscribe to that too much. But there are C serotypes, which has been in Europe associated with dysautonomia. I don't know if it's real or not. The C and D kills a lot of waterfowl, as does C. So these are all some different species susceptibilities.

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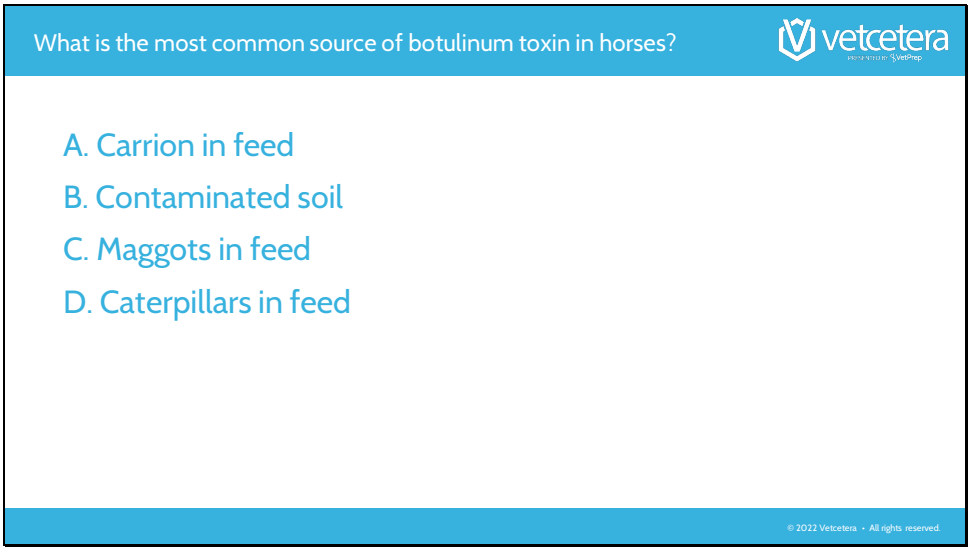

What's the most common source? And I will give this to you. This is going to be the carion getting in the feed. But I've had some cases where I'm pretty sure it was contaminated soil. I had one case-- it wasn't actually my case. I am lying. It was somebody that I worked with had seen it.

And every time they put a horse in a specific stall in the barn, it got botulism. So I think the soil contamination can be pretty significant with this one as well.

Slide 69

What is the most common source of botulinum toxin in horses?

A. Carrion in feed

B. Contaminated soil

C. Maggots in feed

D. Caterpillars in feed

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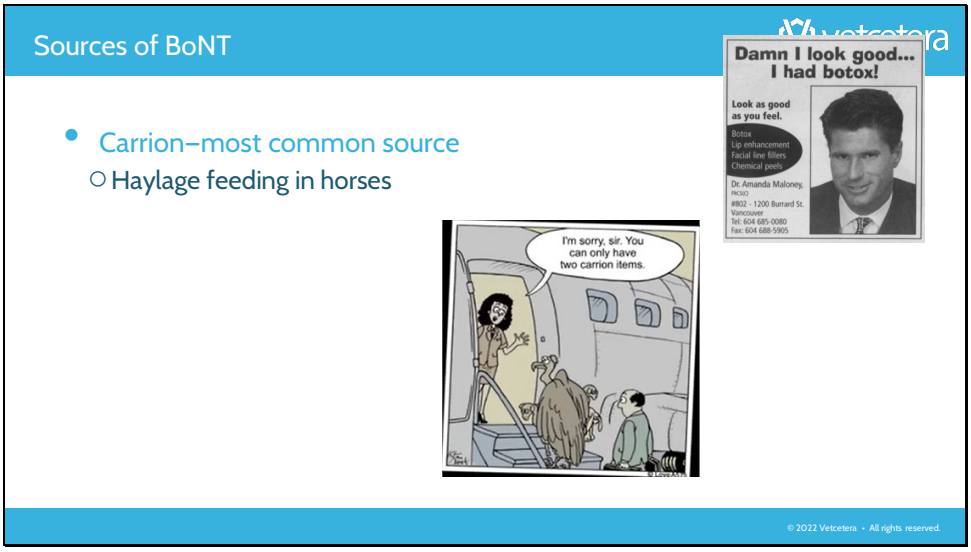

So haylage feeding in horses, but any time yet, I actually, oh, I can't reach it. But I actually, oh, yeah, I can, hang on a second.

All right, this is a sample I received. Snake in the grain, no, this was a snake in a bale of hay. They took that out. So that's possible source of botulism.

Any dead animal that gets in there, bones in the pasture that they can lick, anything like that.

Slide 71

BoNT Toxicity

- Human LD_{50}
  - Parenteral = 1 ng/kg
  - Oral = 0.001 to 1 µg/kg
- Bovine IV LD_{50} = 0.388 ng/kg
- One of most potent toxins, mole/kg
- Denatured by heat, pasteurization

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And it's a big, big protein, so it's actually denatured by heat. So you can kill the protein off with heating and pasteurization. But just one molecule of botulism toxin will kill a cell

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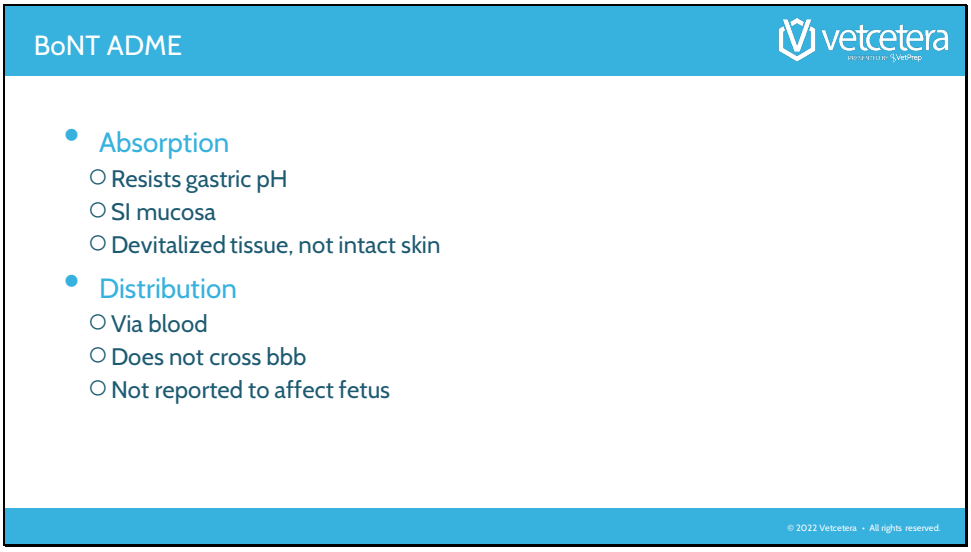


and resists gastric pH absorbed through the small intestinal mucosa.

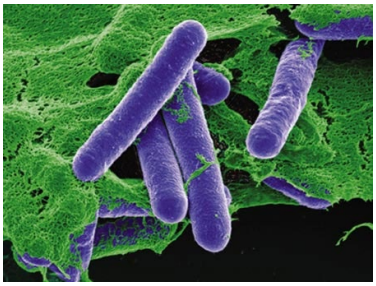
And it can also be absorbed through wound botulism in some animals.

So devitalized tissue can grow the botulina spores. Does not cross the blood-brain barrier. So it's a peripheral neuropathy that you guys see. And it actually can kind of colonize the intestines in very young animals. So you can see the foal trembles and things like that.

Slide 73

Toxicoinfectious & Wound Botulism

- Colonization of intestine
  - Shaker foal syndrome
- Colonization of necrotic tissue
  - Umbilicus, wounds, necrotic tissue
  - Type B toxin



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So that's what I was trying to say, shaker foal syndrome.

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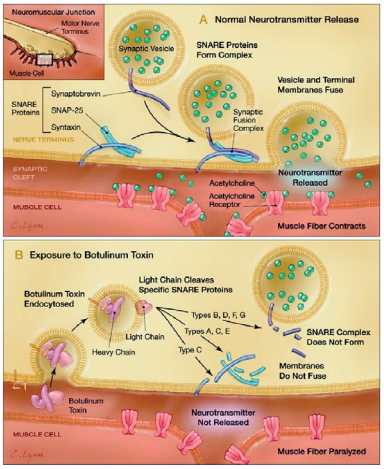
BoNT MOA



JAMA. 2001;285:1059-1070

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And I'm not going to spend a whole lot of time with this. But basically, it prevents the endocytosis of acetylcholine at the receptor. So basically, it stops nerve conduction at the synapse. The nerves can't communicate with each other.

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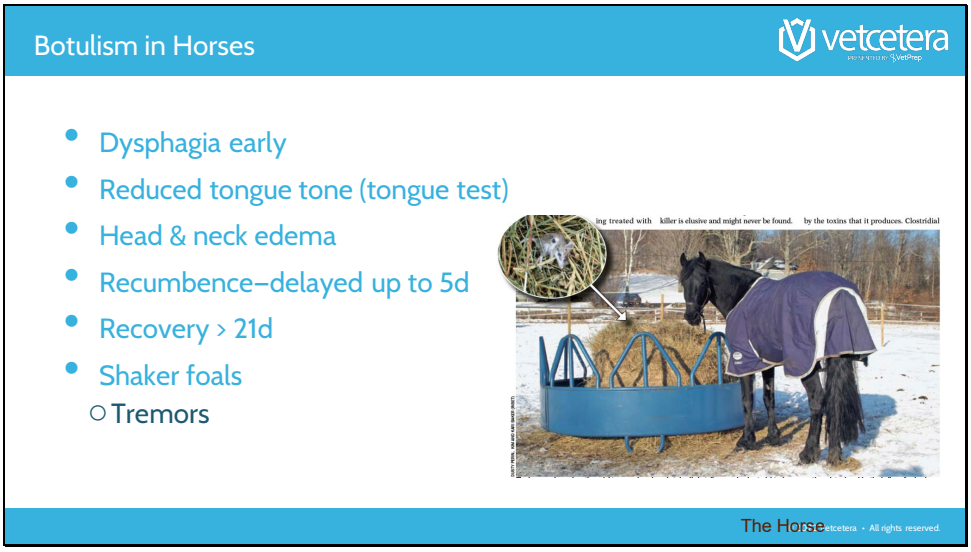


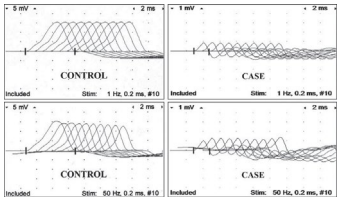
And here's another little baby possum. It looks like it got bailed into the hay. Dysphagia, reduced tongue tone, head and neck edema because they can't hold up their head. So that's where you get the head and neck edema.

And then if they go down, the mature horses aren't going to survive. You might have a chance with foals because they're small.

Slide 76

Diagnostic Assays for Botulism

- Blood, feces, vomitus/stom contents, feed
- Bioassay: mouse inoculation
  - 20-30% positive horses detected
- ELISA serology
  - Wild birds, cattle, horses, dog
- PCR at New Bolton Center
  - 60% positive horses detected
- Repetitive nerve stimulation (RNS) in foals



Prutton et al 2016

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And hard to test for because they're super duper-- Horses are so sensitive. It's like you don't even want to go into a barn and say the word botulism, because they're just that sensitive.

They used to do PCR and mouse tests at New Bolton Center in Pennsylvania. I don't believe they are anymore. There's an ELISA. They're using PCR in other tests as well. Right now, they're looking mostly at testing GI contents and feed and environmental sources, because the concentration in serum is just so low.

And of course, repetitive nerve stimulation, if you put an electrical current on a nerve in a foal and nothing happens, that means the conduction is shut, and that's very suspicious for botulism.

Slide 77

So treatment, antitoxin, symptomatic and supportive, and up to two months in the hospital, and your best bet honestly with these guys is to vaccinate them before they get affected. My horses are vaccinated for botulism.

My regular vet asked me why I was doing this because we don't have botulism in this area. And I said I don't care because if we do get botulism in this area, I don't want to have to deal with it. And then the next year, she actually had a case of botulism locally. And she said I know why you're vaccinating now, because this is a nightmare. These horses do not do well.

Slide 78

Prognosis for Botulism

- Best with early intervention
- Prognostic indicators:
  - 80% mortality if down
  - 5% mortality if standing
  - 4-12% mortality in foals
  - Survival improved with antitoxin

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Slide 79

Botulism Vaccination

- BotVax-B® for horses (Neogen)
  - Botulinum toxin B only
- Expensive
- Swelling and edema at injection site

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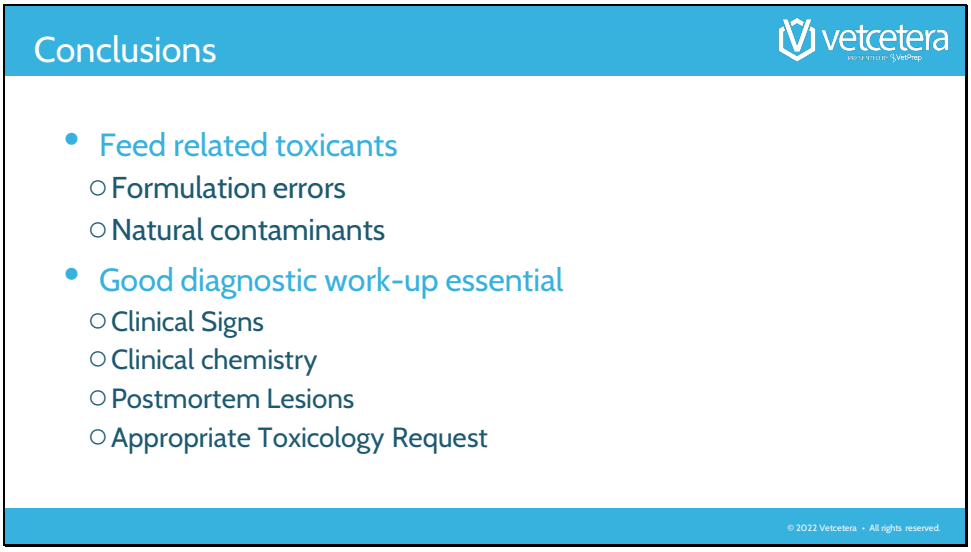
Part 4: Summary and Conclusions

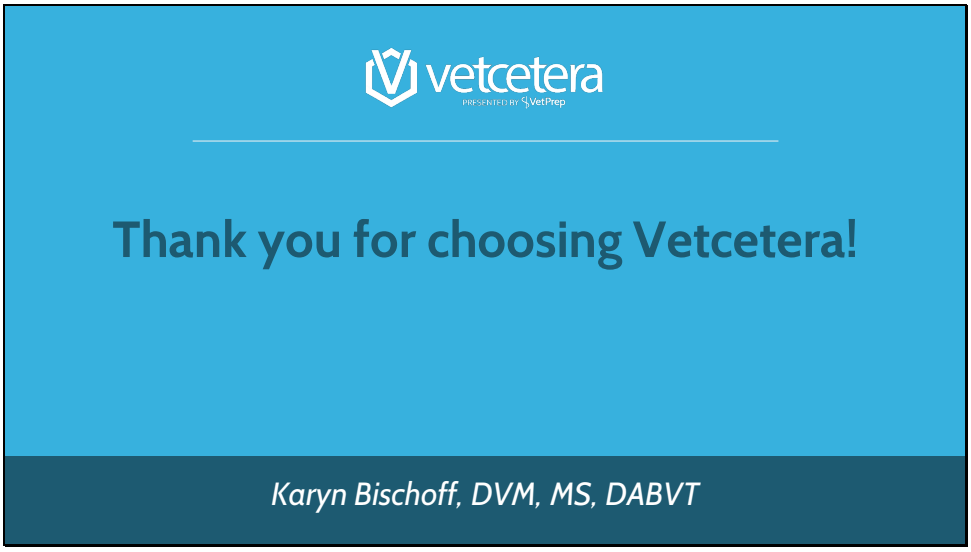
Slide 81



So conclusions, we occasionally do see formulation errors with feed. And most likely the contaminants are going to be something like an ionophore or antibiotics or something along that nature. And then there's a lot of natural contaminants that are kind of the nature of the beast, so cantharidin, weed seeds, weeds themselves, botulism toxin are all natural contaminants. Excuse me, good workup is super essential, putting them on clean feed is super essential, documenting, documenting, documenting especially if this was a commercial feed, because you're going to have to go back and probably worry about compensation and things for the animals and some of the medical bills as well down the line.

Post-mortem lesions, really good workups are always appreciated, so good blood, serum, collection, feed collection. In antemortem cases, feed collection and post-mortem sampling, both for gross post-mortem examination, histopathology, and toxicology testing. And communicating with the toxicologist and knowing kind of what you're looking for is really, really helpful in getting an answer. Otherwise, we can dance around it a lot. But getting an answer is a lot easier when you have some idea what you're looking for.

Slide 82



So I am going to leave it there. And I am sorry I went over like I always do. But it's just toxicology is just so interesting that I can't stop myself, so I apologize for that.

No, you're good. Thank you so much for joining us. We really appreciate it. When you were talking about blister beetles and the pain, I still remember we had a case in vet school. And that was one of the two most painful horses I remember seeing, and it was just horrible to watch. It was terrible, so I definitely will always remember that one.

Again, thank you very much for joining us. We don't have any questions, it looks like. You're free to hop off, and we'll just wrap things up with all of our viewers. Thanks so much, Dr. Bischoff.

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