

Pet Food: Recalls and Product Safety

Dr. Karyn Bischoff reviews pet food safety, including common sources of contamination.

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 the role of veterinarians and the FDA in pet food recalls,
2. Understand the HACCP approach used by manufacturers.
3. Know examples of types of contaminants and the associated clinical symptoms of exposure.




Pet Food: Recalls and Product Safety

Karyn Bischoff, DVM, MS, DABVT


Good evening, everyone. Thank you so much for joining us. I'm Katie Krothapalli, the Director of Veterinary Education for Vetcetera.

Our speaker tonight is Dr. Karen Bischoff. She is a veterinary toxicologist with the New York State Animal Health Diagnostic Center and an associate professor at Cornell University. We wanted to focus on some toxicity topics for this month, in observation of Pet Poison Prevention Month. So we hope you enjoy it. And with that, I'll turn it over to Dr. Bischoff.

Well, some toxicologist I am, I had no idea it was Pet Poison Prevention Month. But I guess, in my life, every month is Pet Poison Prevention Month. So we'll go from there. Let's see.

Pet Food: Recalls and Safety 

- Recalls
- Contaminants and Formulation Errors
 - Natural contaminants
 - Formulation errors
 - Adulteration
- Preventing Contamination



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So I'm going to talk first a little bit about recalls. I put some stuff in there about collecting samples when you suspect the pet food problem or something like that. But I'm not going to go too much into that today. And then I'm going to talk about the different kinds of errors that lead to pet food recalls, what gets into stuff into the pet food, why it gets into the pet food.


And then last, I'm going to talk about, from the pet food industry standpoint, what kinds of things they are able to do to deal with some of these issues and prevent them. So kind of going a little bit backwards starting from what happens when there is a recall to why there is a recall and how do you prevent recalls.



Recalls

So recalls.

What is the most common cause of a pet food recall?

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- A. Mycotoxin contamination
- B. Adulteration
- C. Formulation error
- D. Bacterial contamination


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And I just put this up here. If anybody wants to write in the chat what they're thinking about the most-- what would you think is the most common cause of pet food recalls? What is the most common error that leads to pet food recalls? And you have your choice between, A, which is mycotoxins, like aflatoxin, or B, which is adulteration, so something like melamine or barbiturates, something that gets in there really isn't supposed to be in there ever and is not a natural contaminant, or a formulation error, which is when they mix up the ingredients or put the wrong amount or put none in or something along those lines, or bacterial contamination.

And I have one vote so far. And I'll just give it a few seconds for you guys to think about it, and see if anyone agrees or disagrees. And while they are all-- they've all happened in the recent history. That's for sure.

OK. And I should put with a caveat in here that this is actually for all animal food and feed products. So it's a little bit beyond pet foods. It would include sheep feed and horse feed and stuff like that because that's the data that I have, as well as dog and cat foods, ferret foods, rabbit foods, bird food, stuff like that.

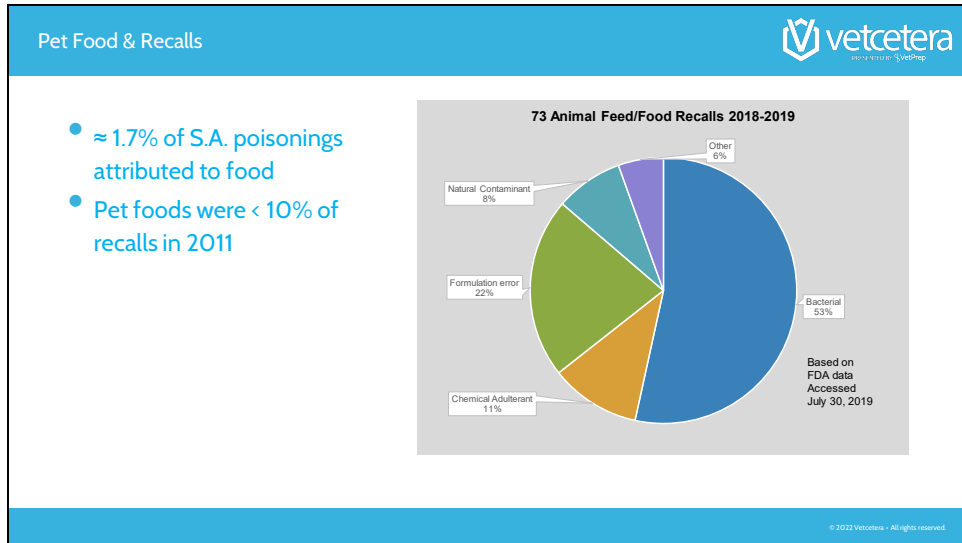
What is the most common cause of a pet food recall?

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- A. Mycotoxin contamination
- B. Adulteration
- C. Formulation error
- D. **Bacterial contamination**

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But actually, and this is unfair, and somebody did get it. This is kind of unfair because this is a toxicology seminar. But actually, it's microbial contaminants. So if you are reading about pet food recalls, it's always salmonella, the salmonella that-- salmonella in pig's ear, salmonella in raw foods, salmonella-- sometimes, there's some listeria or some E. coli as well. But it's usually a lot with the raw pet foods and sometimes with other pet food products and occasionally with processed pet food products.




So we'll just kind of move on to this pie chart. So you can see like, I just made this pie chart over the 2018-2019 pet food recalls because that's the data I had readily available. And about half of them are actually bacterial contamination cases. So that means the other half or something else and usually, are contaminated contaminant errors, adulterants. And other just means that there was like a labeling error. Or there was, and especially in humans, they worry about allergen errors not as big a deal in our pet foods normally. But some kind of ingredient that was in the wrong concentration or wasn't listed on the label or something like that.

So while the bacteria are common and there are things that I don't know a whole lot about, the other contaminants, the toxicants, and things like that are also pretty common. And it's interesting because I actually have recently taken a food safety class for human food safety, public health food safety. And we were talking about contaminants. And the class was all against salmonella this, listeria that, Campylobacter this, et cetera.

And I said, what about chemicals and contaminants? And the professor said, well, we only talk about important things here. So I thought that kind of blew my mind. Currently, his definition of important is not as broad as mine. But I definitely consider the chemical contaminants to be quite important. And I think I'll give you a feel for that today.

Contaminants reported to the FDA 2018-2019



Bacterial contaminants	Chemical contaminants	Formulation error	Natural Contaminants	Other					
Salmonella	31	Foreign material	4	Vitamin D3 (low)	17	Aflatoxin	6	Compliance or labelling	2
				Thiamin (low)	3				
Listeria	13	Unspecified	2	Calcium (high)	1	Thyroxin	4	Quality standards	1
				Copper (high)	4				
Salmonella + Listeria	6	Pentobarbital	4	Choline Cl (high)	1	Lead	1		
		Herbicide		Ionophore	3	C. botulinum	1		
				Salt (high/low)	2				
		"Chemical"	1	"Ingredient level"	1	Deoxynivalenol	1		
Salmonella + E coli	2	Aluminum phosphide		NPN	3				
			1	Magnesium (high)	1				
Total	50		13		36		13		3

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So bacteria, salmonella, salmonella listeria, salmonella and listeria, salmonella and E. coli, and then chemical Contaminants and some of it's like foreign material, like little pieces of metal that fell off the equipment into the feed bag or something like that. That happens occasionally. Unspecified pentobarbital, so that's when, unfortunately, a euthanized food animal gets into the mix. There's this rumor that it means that there's dead dogs and cats in the pet food, but that's kind of nonsense because we euthanize large animals as well. So it just means something that was euthanized got into the batch.

And usually, if it's like a large company, like the Big Smucker's recall a few years ago due to pentobarbital, it was traced contamination. It was very, very low concentrations. The one case that we'll get into later where some animals actually were affected was one a very small boutique dog food manufacturer that basically took one whole cow and cut it up. And all of it was all of the pet food from that batch was contaminated.

One unknown chemical, one herbicide, and then there was an aluminum phosphide, which is probably a horse feed issue that occurs when they use aluminum phosphide tablets as an agent. When you add water to them, they produce phosphine gas which is deadly to basically everybody, including insects. So they'll use it as a fumigate. And if they don't add enough water, then the aluminum phosphide can end up in the horse feed. So that's a real issue.

So formulation areas, we see a lot of vitamin D3. I think there's two on the books right now when I check the FDA website earlier today. Too high calcium, too high copper, that was probably a sheep feed. Too high choline, that was a new one on me. And that was in a cat food a few years ago. Ionophores, too much salt, too little salt, ingredient misformulation, too much ingredient, too little ingredient. Non-protein nitrogen, that's a bovine issue, and too much magnesium.

That's all US stuff. There were a couple of really interesting ones internationally in the past year that I'll get into a little bit later. Natural contaminants, aflatoxin. This was before the 2021 outbreak that started in the Midwest from Missouri, in particular, was affected and Oklahoma, I think. Thyroxine, so when they are

using food animals and when they're taking meat, sometimes they get the thyroid gland in there. And they'll be big chunks of thyroid gland. That'll actually cause hypothyroid in animals that ingest it.

There was one lead contamination, that's kind of weird. Clostridium botulinum, that is improper processing issue. And then deoxynivalenol, which is another mycotoxin that I'll talk about a little bit later. And then others were just the labeling problems and quality control problems that didn't lead to a specific contaminant or anything like that.

What contaminant caused the 2020/21 Sportmix/Midwestern Pet Foods recall? 

- A. Deoxynivalenol
- B. Thyroid hormone
- C. Aflatoxin
- D. Pentobarbital

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So what was the one that was very recent in the Midwest? The one associated with SPORTMiX. And this is to see if you were paying attention. A, deoxynivalenol, B, thyroxine, C, aflatoxin, or D, pentobarbital. I've probably put you all to sleep. That's amazing. Nobody's going to be brave? Not after that last question, right? There is no judgment here. OK, got a guess for thyroid. And we get a guess for aflatoxin. Anybody else want to weigh in?

What contaminant caused the 2020/21 Sportmix/Midwestern Pet Foods recall? 


- A. Deoxynivalenol
- B. Thyroid hormone
- C. **Aflatoxin**
- D. Pentobarbital

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OK. Well, I'm trying to use a poker face and probably not doing very well. It was in fact aflatoxin. Timothy Evans, the veterinary toxicologist at Missouri was on top of that one.

Submitting Samples for Analysis
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- “Representative Sample” of food
- Container/lot number/bar code/label
- Antemortem samples
- Postmortem samples



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So if you do suspect a pet food contaminant because you have multiple animals in the same household or you have multiple animals from other households that happen to be on the same diet or something like that, what do you do? And I generally recommend that you start by contacting the FDA and the manufacturer. So the manufacturer's phone number will be on the lot on the product bag. And then the FDA, I believe, is 1-888-FDA-VETS. But they also have a website where you can file a consumer complaint either as a consumer or as a veterinarian.

So those are two things you can do. If the manufacturer or the FDA get credible complaints, they will act on them. And a credible complaint means multiple animals from different locations that have the same clinical signs. So that's basically how they decide if it's real or not as opposed to like, one person fed their animal dog food, and then the dog died a day later. And I can pretty much guarantee you that just about every patient that you see will have had dog food-- every dog patient that you've seen would have eaten dog food at some point or something before they died. So it's always-- correlation and causation can be a bit difficult to assess and approve.

So make sure you keep the containers, especially keep lot numbers, especially keep barcodes and the expiry dates and all that kind. They need to know exactly what the kind of food was. You have to read the whole label to them. If it was dog food for senior dogs with chicken and fish and rice, and it was whatever brand. So they need all those details.

And then hopefully, you'll be-- and you'll be getting a representative sample of the food, which generally, I'd say, hang on to whatever is left of that particular batch of food that you have. You can put it in the freezer. You can subsample it. But you want to take some samples from various areas of the bags that may not be homogeneously contaminated. We'll get to why that is later on.

Hopefully, you have add more samples available to you. So blood, urine, serum, plasma, those are probably going to be the big ones. Occasionally, feces, don't use them so much as much in toxicology, as


the guy upstairs move back in-- parasite does, but sometimes we can figure things out with those. Stomach contents, vomitus, sometimes we use those. I have found bad things that animals ate that way.

And then if unfortunately, it comes to a postmortem samples are needed, so just your usual stuff, but take two samples, take one, less than 1 centimeter, cubed size to put in formalin and one larger size. So you take liver, kidney, brain, half a brain, and formalin, half a brain safe frozen. Let's see, bone marrow. So you can-- I probably am not going to test it in my lab, I do sometimes test bone in my lab for vitamin D and calcium-phosphorus issues. But you can snip off some rib for that.

So liver, kidney, rib, brain, those are the big ones. Sometimes myocardium more of a problem, not usually a big problem in feeds except for ionophores. So that's a pretty good sample basis. Intestine if it's a GI irritation disease, but it's really good if you can get those samples really, really fresh, and those can be sent to postmortem So when I say take a small sample for pathology, I explained what that was, maybe a centimeter-- any aspect of it. Whereas toxicology we like big samples. OK? I will ask for at least 50 grams of everything, and more is better. And I understand you can't get 50 grams from a parakeet, but what we'll work with you and try to figure something out. Because more is better. We have a lot of equipment, we have a lot of tests we can do, but they tend to use up the sample. So if we do one test comes back negative, we want to have enough sample that we can do another test. If we do one test and it comes back positive but weird, we want to be able to retest it. So more sample is always better for us.

Antemortem Samples


- Blood
- Serum
- Urine
- Vomitus/lavage fluid
- Feces



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Oh, and here we go. These are the samples that you can take. And I actually did something for a pet food company years ago that paid a little bit. But I've cleverly tried to obliterate the names and some of the pictures, but this is my cat, Holly, looking a cat food bag.

Postmortem Samples



- Fixed in formalin
 - Brain
 - Liver
 - Kidney
 - Bone marrow
 - Lung
 - Heart
 - Spleen
 - Skeletal muscle
- Fresh/frozen
 - Brain
 - Liver
 - Kidney
 - Heart blood
 - Adipose
 - GIT contents
 - Others?

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And then here are the formalin-fixed tissues. So I definitely want half of-- well you definitely want to collect half a brain, liver, kidney, you can try heart blood, sometimes we can do stuff with that, sometimes not. I don't do a lot with adipose tissue in my lab, but some fat-based chemicals can accumulate their GIT contents et cetera.



Pet Food Contamination

So pet food contamination issues.

Which are possible types of pet food contamination?


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- A. Natural contaminants
- B. Formulation errors
- C. Adulteration
- D. All of the above

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So this is back to earlier, what are some of the pet food contamination issues that we worry about from a toxicology standpoint, is it just natural contaminants, or formulation errors, or adulteration issues, or all of the above. And hopefully, this is easy, but I'm afraid we're starting to get pretty groggy at the last question so maybe-- thank you.

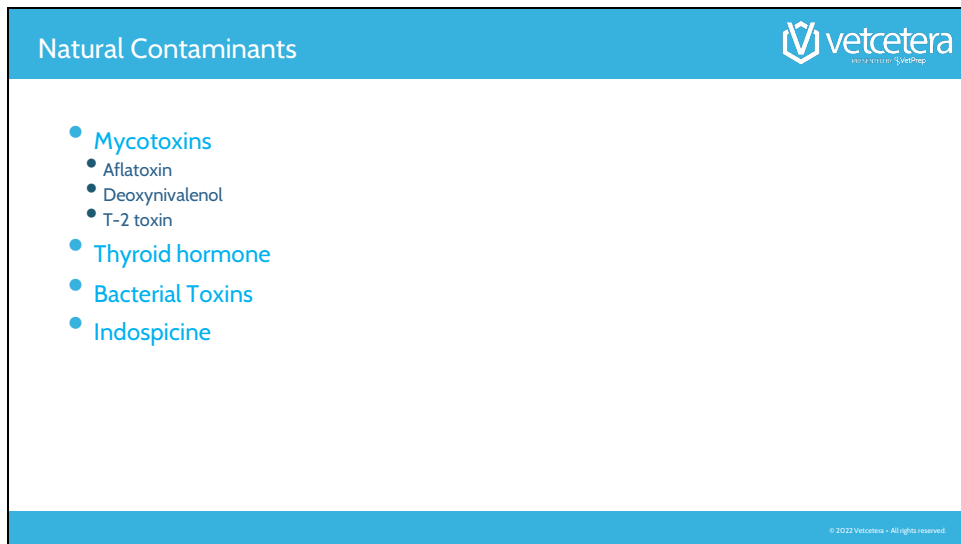
What are types of pet food contamination?

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- A. Natural contaminants
- B. Formulation errors
- C. Adulteration
- D. **All of the above**

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OK. Yey! You guys woke up. And all of the above. Guys are on it. All of these things can happen, and there's probably some things that can happen that I don't know about. But these are the ones that I've worked on.



The slide is titled "Natural Contaminants" and features the VetCetera logo in the top right corner. The content is organized into a bulleted list:


- Mycotoxins
 - Aflatoxin
 - Deoxynivalenol
 - T-2 toxin
- Thyroid hormone
- Bacterial Toxins
- Indospicine

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So mycotoxins, aflatoxin, that was the big outbreak in Missouri. Deoxynivalenol, that is also known as D-O-N, because people like to call it DON instead of saying Deoxynivalenol which doesn't always roll off the tongue. Deoxynivalenol is also called vomitoxin because it makes animals puke. And it gives them diarrhea too. So basically this is one that can cause some significant morbidity, it does not usually cut's mortality in an otherwise healthy animal, but this is one where they are going to pay for the supportive care at the veterinarian, the pet food company, and pay for supportive care at the veterinarian, that they're going to pay to have the carpets cleaned. And the animal is probably be just fine unless it's got some underlying issue. Always have to be careful.

And then T2 toxin is a new one on my list this year, because there was a big outbreak of something that appears to have been T2 toxin that killed a lot of cats in Great Britain last year. So I'll talk a little more about that. Thyroxine thyroid hormone, ground-up thyroid in the dog food can. And that's kind of a sporadic one. It's kind of a weird one because sometimes some cans will get more thyroid than others. Even though they tend to be pretty well homogenized, some are going to get more than others just because of the nature of the beast, the nature of the thyroid gland.

Bacterial toxins again, which I'm not going to talk too much about but Botulinum toxin would be the one that comes to mind. And then indospicine, this is a new one on me that-- again, happened last year in Australia, I know that the plant is called Indigofera, it's also called creeping indigo, its present in California. No, I don't know if it's present in California, it's definitely present in Florida. It's a plant toxin and it ended up in dog food.

History of Mycotoxins in Pet Foods


- **2021 T-2, cat food, UK**
 - 570 cases
 - 64% mortality
- **2020/1 aflatoxin, dog food**
 - Morbidity 200+
 - Mortality 110
 - Evans, Pers. Comm.
- **2005 aflatoxin in dog food**


- **1998 aflatoxin, dog food**
 - Texas
 - 45 deaths
- **1995 DON, dog food**
 - National
 - \$20 million losses
- **1970s aflatoxin**
 - Georgia

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So the T2 570 cases in cats, 64% mortality, then this suggests mycotoxins in general. The 2021 case, 2020-2021 was Tim Evans case that had a pretty high morbidity and about 50% mortality. The 2005 aflatoxin outbreak that happened around me, that happened in the Northeastern United States, it actually hit the news pretty hard that year because we weren't at war with anybody at the time, well we weren't-- I guess we probably were at war in Afghanistan, but we actually didn't have-- it was a slow news cycle. So it became national news when we had that particular little recall. And I don't know how many dogs were killed. There were definitely 100 and the mortality rate was about 50% to 60%. So it was quite high. Aflatoxin are not fun to deal with. The aflatoxin outbreak in dog, in dog food in Texas. So those two aflatoxin outbreaks were associated with bad ingredients. The one in Texas was associated with post-manufacture issues. It was stored in a humid, hot place, in a warehouse in Texas and the aflatoxin mold *aspergillus* grew on the dog food right there.

Deoxynivalenol, 1995, high morbidity, low mortality, and about \$20 million in fees that the pet food companies had to pay to help people clean up their homes and deal with their sick dogs. And then in the 1970s is really when aflatoxin came in and of its own. Excuse me, I'm going to have a little sip of water before I cough. I have already talked for an hour today so my voice is a little iffy. So in the 1970s, actually they were using peanut meal in dog food, and they discovered that it had quite a bit of aflatoxin.

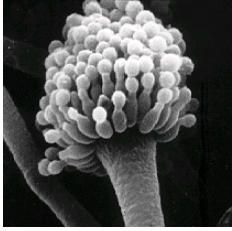
Source of Aflatoxin



- *Aspergillus flavus*, *A. parasiticus*, others
- Field crops or stored grain, food, & feed



Pat Lipps




Wikipedia


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So aflatoxin is a toxin produced by *Aspergillus flavus*. Afla, aflatoxin. And it grows both on crops and in storage conditions. So it can be in the grain when you harvest it, or it can be in the grain car, could grow in the grain car as it's being transported to your pet food place, or it can grow in the feed after it's already been produced for food, in the case of dog foods.

Sources of Aflatoxin



- Peanuts
- Corn
- Walnuts
- Pecans
- Almonds
- Cottonseed
- Sorghum grain
- Rice
- Sweet potatoes
- Potatoes
- Wheat
- Oats
- Barley
- Millet
- Sesame
- Cocoa beans




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It grows on all kinds of things that we love to eat, it's in peanut butter, I'm sorry. It's in corn chips, they've detected it and in some of the name brand corn chips like Doritos and things like that. Walnuts, pecans, anything that's really good, it's probably in there.

But humans don't have as many problems with it because we tend to eat a varied diet. So we don't have peanut butter sandwiches every day, we don't have popcorn every day, most of us. We don't have the same meal over and over again. Whereas dogs and cats, they eat out of the same lot of the dog food bag, right? And this is usually a dry pet food, dry dog food, dry cat food issue. They eat out of the same bag every day. So if they're going to be exposed, they're going to be exposed over, and over, and over, and over again.

And this is also true in humans there are parts of the world where people have a stapled crop. There have been several outbreaks of aflatoxin toxic in people in Kenya because they eat a lot of corn and the way they ferment it to make different products can lead to aspergillus outbreaks.

Source of Aflatoxin and Government Regulations 

- Factors affecting *Aspergillus* spp growth
 - Moisture > 15%
 - Humidity > 75%
 - Warm environment
 - Damage to grain
 - Insects, drought
- Uneven growth within substrate

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So factors suspecting, moisture, humidity, warm environment, damage to grain. So on the one hand, you don't want to use a lot of insecticides because insecticides themselves are toxic. But if you don't use enough insecticides, you can get insect damage to your crops that can lead to mold formation. So it's a very delicate balance on producing these.


And then the fact is that these things don't grow in the same-- grow in the same way throughout the patch of corn, right? Mold is focal. Multifocal. It's not homogeneously spread out. So that makes it really hard to test things, and that's why I said you might want to take samples from several parts of a dog food bag or something like that. Because one area might be a hot spot, and the other areas ice cold. So and if you see something that looks abnormal, like, this clump of dog food that's clumped together and looks a little fuzzy, that is definitely the worst-case scenario sample that you want to take. So definitely take those samples, but if you don't see anything on these, take multiple samples from different areas of the batch.

And I use blue cheese as an example because the blue in the blue cheese is actually penicillium, but it doesn't grow homogeneously throughout the cheese, it grows in veins. And oranges always making-- I always think of oranges because I'll go out and buy those giant bags of oranges, and I'll be eating them in the second day I reach in and grab the squish that's all green and fuzzy and soft and it just kind of grosses me out. And I'm sitting here going, was that in the bag when I bought it? Did it grow since I bought it? How long has it been it-- but all the other oranges are perfectly fine, right? So it's just that one hot spot that is the problem. And you don't know when it occurred, but there it is.

So that's the problem that we sometimes get into with these dog foods is they do the testing of the ingredients, but they kind of miss stuff.

Aflatoxin Basics

- Dogs extremely sensitive
 - 60 ppb in food can be toxic
 - $LD_{50} \approx 1 \text{ mg/kg}$
 - Cats similarly sensitive
 - No clinical reports in cats
- Increased susceptibility
 - Pregnant females
 - Young males
 - Certain individuals




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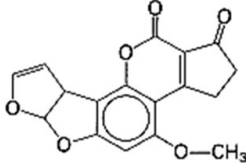
So I'm finally going to have to cough, sorry about that. So this is Simon puppy, he's my little guy. He's a lot bigger now, actually. So dogs are super duper sensitive, 60 part per million-- sorry, 60 parts per billion with a B. Most of the times when I talk about toxic concentrations, I'm talking parts per million with an M. So for that idea if you were to spit into an Olympic sized swimming pool that would be one part per million. But if you were to spit into a lock on the Erie Canal that is one part per billion. With a so these are tiny, tiny, tiny concentrations.

Cats appear to be similarly sensitive but they don't tend to be as affected as dogs and it's probably be-- well I'll get into why it is, but it's probably a palatability issue. And Dr. Evans followed some of the dogs out that were pregnant at the time they were given the contaminated dog pet food and there were definitely some issues with the neonates, they were much and frailer than the other neonates, they didn't grow as well as pups from other litters. Young males are a little more sensitive and then there's individual differences and susceptibility.

Aflatoxin Basics



- **Absorption**
 - Rapid, duodenal
- **Distribution**
 - Minimal accumulation
- **Metabolized to epoxide**
 - Hepatic P450
 - Glutathione conj.



Aflatoxin B₁
(*Aspergillus flavus*)

- **Excretion**
 - Urine, bile, milk
 - 90% urinary excretion within 12 hours

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So this is the aflatoxin molecule. And it is pretty well absorbed it goes into the circulation it gets picked up by the liver through the first pass effect. So intestine portal tract, portal vein liver. And then it's taken up and P450 microsome and enzymes act on it, the phase one enzymes attack it. And what they do is they attack right here, where this double bond to. See this double bond? So what happens is they break this double bond and shove an oxygen there. So they'll be this oxygen in between these two carbons. So the confirmation is like this, because you have these two carbons on a horizontal plane and then they've got this oxygen at a weird angle, and these are unstable glands. This is not comfortable for the carbons to be doing. They like to have 90 degree angles, but they've got-- well not really 90 degree because there's 3-dimensions. But they like to have that they're bonds as far apart as possible.

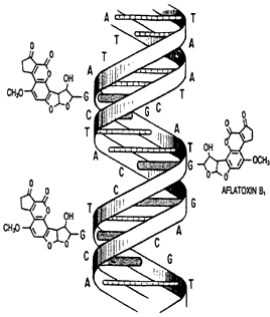
But now you've got these two bonds coming together and this is unstable. So it's going to fly apart when it hits a macromolecule. So it might cause lipid peroxidation, or it might bind to a macromolecule, an enzyme, or something like that. But what it really likes to do is interpolate itself into DNA. The other thing I did want to bring to mind on this slide is most of the aflatoxin is eliminated within 12 hours. So we're talking about something that is a 60 parts per billion with a B, in the feed already. And then it's diluted by the body. So by now, we're getting the parts per trillion with a T, tiny, tiny concentrations. And then most of that's excreted. So there is going to be some stuck in the tissue because it binds to stuff. But most of it is going to be eliminated by the time the animal shows clinical signs. So they can-- and usually they go off feed for several days before they present to the veterinarian in these cases.

So getting a tissue sample is not going to be helpful in most situations for finding aflatoxin. I know, I think, Steve Hoosier in Purdue, because if your name is Steve Hoosier you're probably going to be in Indiana, right? He's been doing some work on trying to do an immune method of detecting aflatoxin in liver, but it's very, very hit or miss as far as I know.

Mechanism of Action

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- Reacts with DNA, RNA
- Reacts with protein
- Reacts with membrane



Systems Affected Approach
To Toxicology, Beasley


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So this is the DNA, what it does to DNA, it finds here at the guanine residues. And then you basically-- you can't reproduce your DNA, you can't make RNA and therefore protein manufacture shuts down.

Acute Aflatoxicosis

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- Weakness & depression
- Vomiting & diarrhea
- Hemorrhage
 - Intestine
 - Elsewhere
- Jaundice
- Death




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And this is pretty much because it's the liver that's doing the detox here, and because of the portal effect the fact that it goes right from the intestines to the liver. Liver is the most affected organ, it's going to affect kidneys and other things too, but the liver is the primary site of effects. And so you get liver failure. Very acute liver necrosis. You can have vomiting, diarrhea.

A lot of times though when they first are exposed to this pet food they will go off feed, because there's something about the aflatoxin, whether it's a related chemical that's also in the feed that's produced by *Aspergillus*, I'm not sure, but they won't want to eat it. So people will try to doctor it up to make it more palatable to dogs. Cats still aren't going to eat it. So we don't see as many problems in cats just because they don't seem to interested in eating it.

So we can see some GI irritation and stuff, but then, we start having synthetic liver failure. And that's a big deal. So your liver enzymes actually aren't going to go up very much because you're not going to have a lot of cell rupture, a lot of bile stasis, but what you're going to have is liver cells that don't have functional DNA. And therefore, they're not making proteins. So they're not making clotting factors, they're not making proteins seed, they're not making cholesterol, which isn't a protein but it's also synthesized by the liver. So these things are going to go down in the serum and the circulating concentrations.

Diagnosis of Aflatoxicosis


- **Aflatoxin analyses**
 - Foods, grains, etc.
 - Tissue testing?
- **Diagnostic testing**
 - Protein C
 - Cholesterol
 - Bilirubin
 - Liver enzymes?



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So you can do the aflatoxin analysis on tissues, not always very helpful. Very hit or miss, lots of false negatives in that case. Food and grain, but that's hard too. And the reason it's hard, and I will tell you a story. We had the aflatoxin outbreak in '05, it was brought to my attention by some veterinarians in Rochester, New York that there was a problem. And I went down there and we collected pet food from the dogs that were very sick and the dogs that were dying, and it all came back negative for aflatoxin. There was one healthy dog, and she was on the same pet food. So we took her pet food and tested it. It was lit up for aflatoxin, it was probably 100 part per billion or something like that. That dog got sick three weeks later.

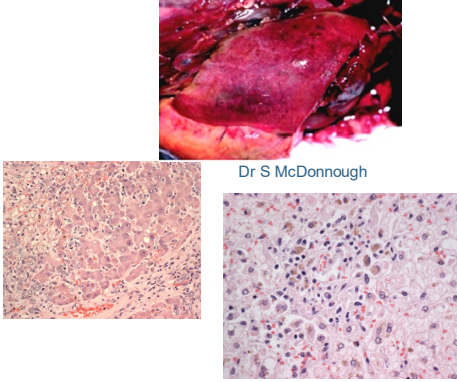
So there is a lag time between exposure and clinical signs. So if you have a bunch of big dogs and if you have your herd of dogs, that pet food bag is going to get gone through really fast. And so you're not going to have the aflatoxin there. If you get a little Yorkie poo or something like that, that's eating a big bag of dog food, then you got a chance of actually catching the aflatoxin, but it can be really hard to find it even when you know it, when you have a pretty good feeling it's there.

And then the dogs, you're looking for synthetic liver failure. So protein C, cholesterol, hypo-- low protein C, low cholesterol, the bilirubin is variable in these guys. Liver enzymes aren't very impressive in these guys. So it helps to know what you're looking for and none of these tests of course is going to be diagnostic as much as finding the actual aflatoxin.

Postmortem findings in aflatoxicosis

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- Characteristic changes
- Early lipid storage
- Cell death
- Later fibrosis




Dr S McDonnough

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So characteristic changes in the liver. This is one of the dogs-- this one was a little bit farther along, there's a little bit of inflammation and there's some hemosiderophages here suggesting hepatic congestion. There's a little bit of a microvascular hepatic lipidosis.

So instead of getting those nice big lipid vacuoles, but with the nucleus gets squished onto one side. You tend to get foamy or looking cells with these guys. This one has some fibrosis in it. So this one's also a little bit further along. So you're starting to get a cirrhotic effect, this is a long term issue. This is a more acute one with areas of hemorrhage and some tail areas which are probably the lipidosis.

Deoxynivalenol



- Produced by *Fusarium* spp on grain
- One of many tricothecenes
- Feed refusal at 4-8 ppm (dogs, cats)
- Predominantly GI effects
 - Vomiting, diarrhea
 - Self-limiting




ipmimages.org

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So I'm going to also talk about the Fusarium Mycotoxins. Briefly this is, the Deoxynivalenol and T2 producing fungus. And generally with the Deoxynivalenol, you have vomiting and diarrhea, which is predominantly self-limiting. And I used to say that for all of them,

T-2 Toxin, United Kingdom, 2021



- Cat Food
 - 217 ppb T-2 & HT-2
 - 364 ppb DAS
- Pancytopenia
- Glanemann & Humm, personal communication

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but now we know that T2 seems to be lethally toxic to cats. And this one is another one where we're talking about part per billion. So this kind of shocked me, because T2 is usually toxic at low part per million concentrations, but here we're seeing 10 cytokines in these cats.

So the Trichothecene are-- they basically attack rapidly dividing cells, cells with a high metabolic rates, so they get your GI, mucosal cells, and another rapidly dividing population of cells of course is the bone marrow. So it actually kind of mimics radiation sickness, because it's the rapidly dividing cells that get hit first. And usually with the Deoxynivalenol you get recovery, with the T2 maybe not. So they've lost quite a few of patients with this. And part of the problem was, of course, they had no idea what they were dealing with because this had never seen before.

So Dr. Gladman and Dr. Hum were really, really helpful from the Royal College in London, were really, really helpful in figuring this stuff out. They did the figuring out and they were very helpful in informing me of all the stuff they figured out.

Indospicine, Victoria Australia, 2021




- *Indigofero spicata* (creeping indigo)
- Accumulates in grazing animals
 - Horses resistant
 - Dogs extremely susceptible
 - 42 affected
 - 26 died
- Salmon, personal communication

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And then indospicine is creeping indigo. And it turns out that horses are very resistant to indospicine, so they can eat creeping indigo to an extent without adverse clinical signs. However, if you then slaughter that horse and put it in the dog food you can poison the horses, and that's exactly what happened. They had a pretty high death rate, it was pretty much-- as with the cat food and the previous one this was semi-boutique, so they weren't feeding thousands of animals but maybe tens or hundreds, so thankfully that limited the dispersion.

But Dr. Salmon in-- trying to remember what town. She was in Australia. I don't remember which town. But she was kind enough to share this information with me. So this information is hot off the press. Because I don't think it's available anywhere else unless you know these particular veterinarians.


Formulation Errors 

- Ingredient errors
 - Too much
 - Too little
 - Wrong one

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So then you get into the feed ingredients that are supposed to be there, but they're not in the right amount. And this is usually nutrient supplements,

What is the most common formulation error associated with adverse effects?




- A. Thiamin
- B. Vitamin D
- C. Vitamin A
- D. None of the above

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which is the most common nutrient supplement error that you would see in these guys. Too much thiamine, too little thiamine, too much vitamin D, too little vitamin D, too much vitamin A, too little vitamin A, or none of the above.

Give me a break from talking so I can try to make my throat feel better. Vitamin A, we get a vote for vitamin A? Or too little thiamine? I do believe too little thiamine is under diagnosed I will throw that right out there. But it's not the most frequently reported, probably because it's under diagnosed.

What is the most common formulation error associated with adverse effects?


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- A. Thiamin
- B. Vitamin D**
- C. Vitamin A
- D. None of the above

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So it's actually-- in this case, it's going to be a vitamin D. Thank you. Just in time guys.

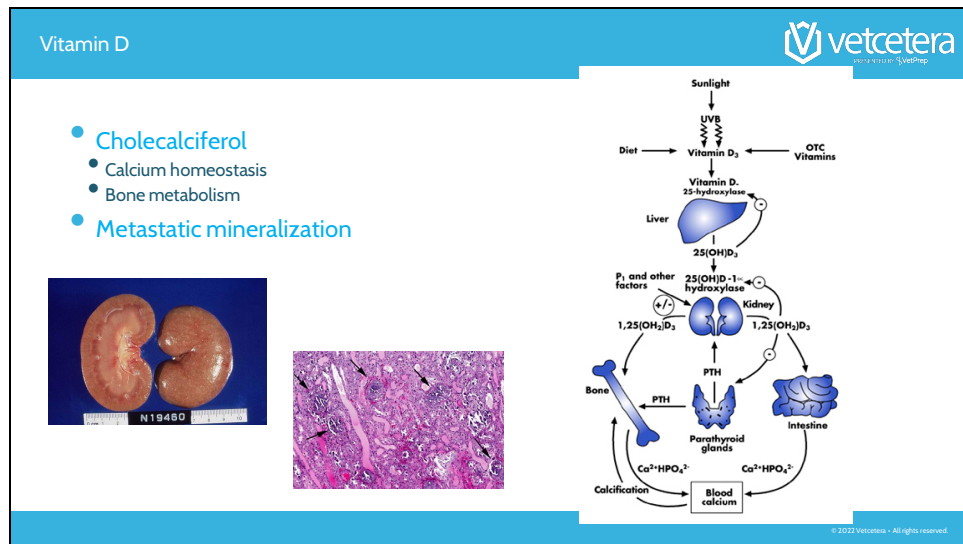
Major Historical US Pet Food Recalls Due to Formulation Errors



- Elevated vitamin D
 - 2012 bird formula
 - 2010 dog food
 - 2006 cat & dog food
 - 1999 dog food
- Deficient Thiamin
 - 2013 cat food
 - Eastern US
 - 2009 cat food
 - Eastern US


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So elevated vitamin D in bird formula. So this is like the stuff they feed, the baby birds, baby parrots, and stuff that are hand-reared. There was a 2010 in dog food, there is 2006 cat and dog food, in 1999 in dog food. There are a couple open right now, then there was one a few years ago in rabbit food as well. But I don't know what the source of that was. So I don't know if it was a commercial or a feed mill kind of thing. Thiamine deficiency, there was a recall in 2013, caused by it and one in 2009 caused by it, and there was one in Australia that I believe was caused by thiamine deficiency a few years ago as well.



So Cholecalciferol vitamin D3, isn't super important for calcium homeostasis. So what happens if you have too much Cholecalciferol in the pet food? Well you get high circulating concentrations of calcium because you have increased absorption of calcium from the intestines, you have bone resorption, and so these things increase the amount of calcium. Your kidneys are filtering out, the blood, and they are condensing this calcium and phosphorus, in their tubules, in their glomeruli, and this these concentrated calcium and phosphorus ions bind together and cause mineralization. Particularly in the kidneys but in other parts of the body as well. So wherever they kind of get concentrated together, that's where they're going to come out.

And so you get what's called metastatic mineralization. So there's really two kinds of mineralization, there's this dystrophic, when some body parts-- so this is like calcinus escudos, where the body part gets rubbed on a lot and eventually the insults lead to cell death, and the cell death leads to mineralization. This is different. This is a multifocal mineralization, although, I did hear about a case of calcinus escudos in a dog that had exposure to a vitamin D ointments multiple times in the same spot. It was like the people were using it on their hands and then touching the dog kind of thing, so it might actually increase the risk of that as well from topical exposure. But from oral ingestion, you're going to get mineralization. The intestines, you're going to get mineralization of blood vessels, kidneys, and other places.

2009 Recall 

- Between 13 and 20 cats affected
- First cases mid-Sept
- Ages 18 months to 9+ years
- Lot of cat food restricted to NE US

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So the 2009 recall between-- and this one I was not directly involved in. Rosama who's now in California shared some of this. Between 13 and 20-- Oh, wait. Wait, wait, wait. This is a different one. OK. I am moving on to-- Oh, yeah. This is the Thiamine related recall. Because I actually haven't been very involved in vitamin D recalls, but Thiamine I have. 13 of 20 cats were infected in mid-September, 18 months to nine years old.

Review of Thiamin vetcetera
vetcetera.com

- **Vitamin B1**
 - Required water soluble vitamin
- **Cofactor of pyruvate dehydrogenase**
 - Pyruvic acid \rightleftharpoons acetaldehyde
- **Deficiency diseases**
 - Beriberi
 - Polioencephalomalacia
 - Chastek paralysis
 - Polyneuritis


The chemical structure of Thiamine (Vitamin B1) is shown. It consists of a pyrimidine ring fused to a thiazolium ring. The pyrimidine ring has an amino group (NH₂) at position 4 and a methyl group (H₃C) at position 5. The thiazolium ring has a methyl group (H₃C) at position 2 and a 2-hydroxyethyl group (-CH₂-CH₂-OH) at position 4.

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You know what, I think that slide is out of place. I'm going to skip that slide right now and talk about Thiamine.

So Thiamine is vitamin B1, it is really important for pyruvate dehydrogenase in the Krebs cycle. And deficiency diseases is associated with-- it's got a bunch of names to it. In humans it's Beriberi, in cattle it's polioencephalomalacia, and horses it's polioencephalomalacia. In mink and fox, for you fur bearing animals, it is Chastek paralysis. And then in chicks it's Polyneuritis.

Clinical Signs in Cats

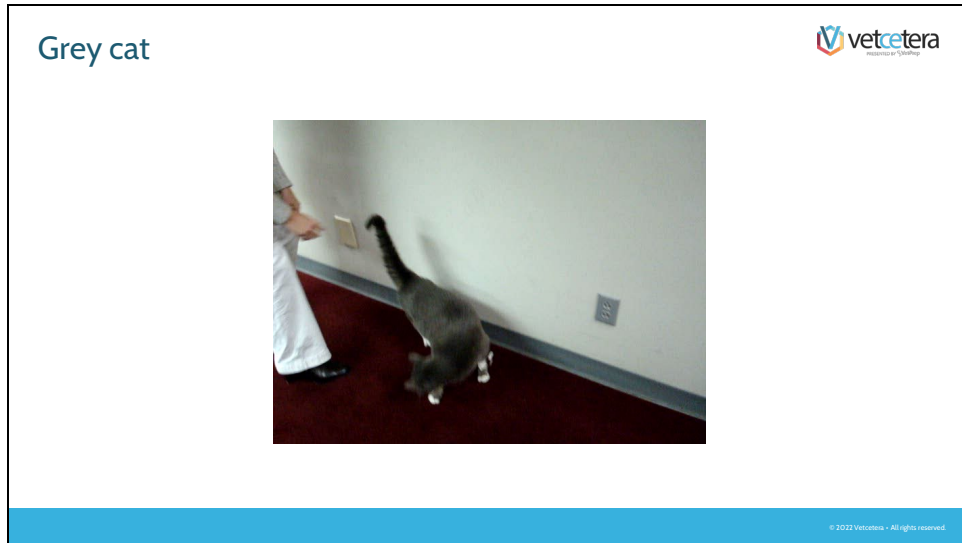


- Neurologic defects
 - Limb ataxia to rigid paralysis
 - Wide-based stance
 - Flaccid neck
 - Apparent blindness
 - Circling
 - Seizures
 - Nystagmus



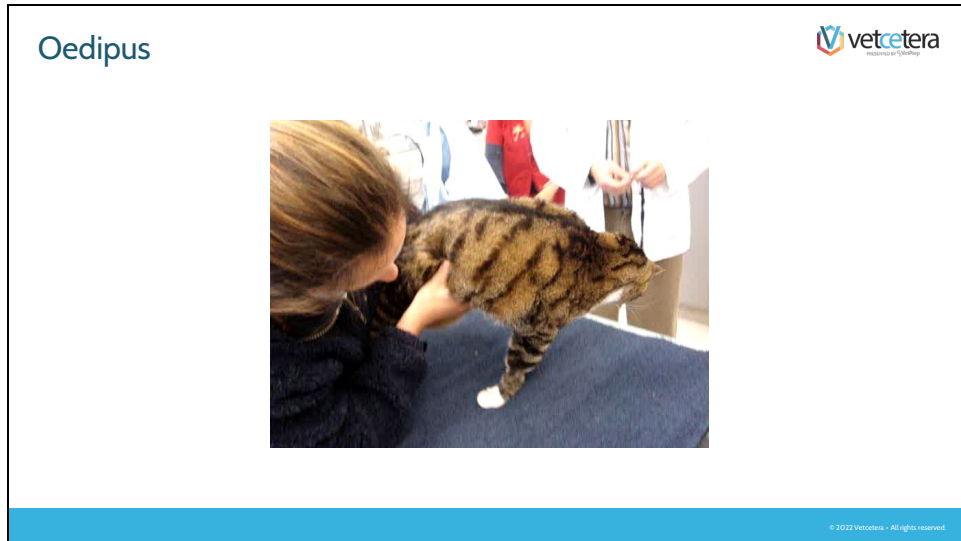
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And it's associated with limb ataxia, usually they start off with a slow ataxia, maybe some neurologic signs, and a wide base stance, flaccid neck, so when you pick them up their knuckles flop down. It's called the prayer sign. And apparent lines, circling, seizures, nystagmus has been seen in some of them, and then they go to this tetanic spasm situation.



So I actually have images for that if they're going to work, so fingers crossed let's see if this works.

This is a cat with thiamine deficiency, and this is Dr. Hubbard. I think she's changed her mind since then, but it was Dr. Hubbard at the time. And I have to give her a whole lot of credit because she was the one that really figured this one out. If this cat had been a cow, I'd have been all over it because we do see polio encephalomyelitis a lot of cows, but I don't see it a lot in cats. But it turns out it's the same kind of thing.



Now this one is more advanced, this cat's name was Oedipus. So you can see those are some pretty stiff limbs, and you can also see his neck is a little bit floppy here, at some point he's going to turn to face the camera and I want you to look into his eyes when you have that opportunity. So basically stiff as a board legs, and look at the face, the cat is there. This cat is present, this cat knows what's happening to him-- well, he doesn't know what's happening and he knows that he's suffering. So this doesn't affect the cerebral cortex, they are aware, they are alert, but they are in bad shape.

And once they get to this point, so this cat is going to survive. This cat did well. This cat, there wasn't anything that we could do, this is the cutoff point. When they get to this tetanic spasm, tetanic paralysis issue, we are not going to be able to save them, unfortunately. Learned this the hard way.

Grey cat




And once they get to this point, so this cat is going to survive. This cat did well.

Oedipus



This cat, there wasn't anything that we could do, this is the cutoff point. When they get to this tetanic spasm, tetanic paralysis issue, we are not going to be able to save them, unfortunately. Learned this the hard way.

Diagnosis of Thiamin Deficiency



- Polioencephalomalacia
- Associated with low thiamin diet
 - 1.5 ppm
 - Serum thiamin?
 - Erythrocyte transketolase activity?

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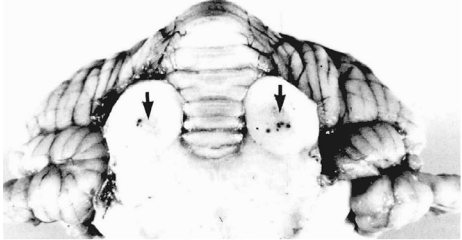
So Polioencephalomalacia, is associated with low thiamine, and the reason I think it's under-reported is because thiamine breaks down easily. So the rendering process, the extrusion process, the heating process, the pasteurization process, they all cut the thiamine concentration in the foods.

So over time-- well basically, during processing, I don't know how long it lasts in the can, or in the kibble, but over processing it is going to dissipate. And so you have to put huge amounts of thiamine into the batch to make it come out the other side. Unfortunately. So that is why it is-- I think it's under-reported. I think after discussing with Dr. Hubbard, she had started seeing neurologic cats sometime before she started suspecting that it was the pet food and some of them had been unvaccinated. So they were euthanized for rabies suspects, so something to think about obviously if you suspect rabies, euthanasia it's the right thing to do. But after a while she started saying why am I seeing these weird neurologic cats, and that's when it came out.

So this is something that's treatable, until you get to the state where Oedipus was give them Thiamine. You give them thiamine and it's almost a miracle cure for these guys.

Lesions of PEM vetcetera
Institute of Veterinary


- Neuronal necrosis in the brainstem
 - Periaqueductal grey matter
 - Caudal colliculus
 - Other nuclei
 - +/- Cerebellum



Read et al, 1977

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Just like it is in cattle, just like you learn about polioencephalomyelitis in cattle, same thing, give them Thiamine, they recover. So this is just showing some of the areas of the gray matter that are specifically affected.

Treatment & Prognosis for PEM 

- Thiamin supplementation
 - Most will respond
- Prognosis good
 - Generally good to excellent
 - Poor if severely affected

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And it is basically treated, with thiamine supplementation it may take them a few weeks to get back to normal. But they do recover very nicely and almost miraculously with Thiamine, which is amazing to me because the nerves are not supposed to regenerate, but this actually works really, really well.

So I think that a lot of animals are probably running a little bit low on the thiamine status, and then when you get a lot a bag that's really low and thiamine because of a formulation error, that's when you get into a crisis situation. But I think a lot of animals are probably on the verge of crisis. And we just don't know it because it is really hard to keep thiamine in pet foods.

Vitamin A

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Innovation in Vet Prep

- Associated with hyperostosis
- Permanent skeletal lesions

Photo courtesy
Dr Rosama Pusoonthornthum




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And this is actually a vitamin A toxicosis in a cat, normally you get axillary bone-- axillary hyperostosis. So you get it in the sacrum and the vertebral column, and the skull barium and stuff, you start seeing bony proliferation. But in this particular instance, it was older cats and they got it in the axial skeleton.

And they do improve when you take the vitamin A out of their diet, but they don't do 100% well. And this was a recall that was in Thailand. So Doctor Rwashana was very kind enough-- very kind to share me with me some pictures.

Adulteration



- Addition of a contaminant
 - Accidental
 - PBBs in Michigan
 - Intentional
 - Fraud
 - Melamine

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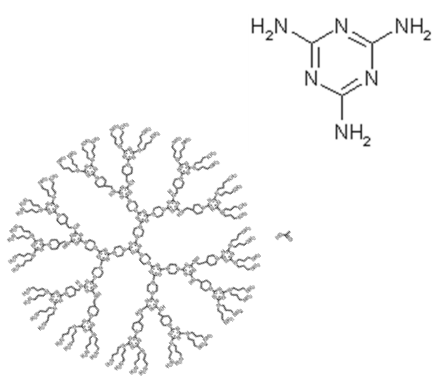
And then contaminants that really, really had no business being there, they're not natural contaminants, they're not natural ingredients, they should not be there. So there are big cases like polybrominated biphenyls got into a lot of animal feed in Michigan in the 1970s, and it was a disaster. Hundreds of thousands of livestock were destroyed, millions of poultry were destroyed. And they were toxic waste at that point because these are forever chemicals Polybrominated biphenyls.

Phenobarbital should never be in a pet food. If it gets into pet food it is the T2 fraud, because you are not supposed to steal euthanize animals for food under any circumstances. So this is a fraud situation. And then there was the-- but it can also be-- I mean, it really should be fraud. I probably should have put it under fraud. And then there was the intentional case in pet foods of fraud due to melamine.

Melamine

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- Industrial uses
 - Melamine resin
 - Combined with formaldehyde
 - Plastics
 - Resins
 - Glues
 - Textile dyes
 - Yellow colorant
 - Pharmaceuticals




Neerman et al 2004

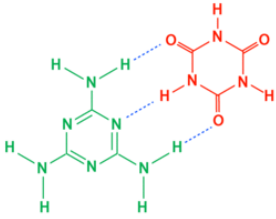
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So what is melamine? Back in-- I think it was '07, we had this outbreak of nephropathy in cats, and I think that's what that previous slide that I was trying to figure out was about. It is an industrial component of plastics. You mix melamine with formaldehyde and get back light. So it's used in plastic manufacturers using dyes and things like that. And some polymers of melamine can be used in pharmaceutical delivery, but very specific uses for it.

Cyanuric acid



- Polymerizes with melamine
 - pH = 5.8
 - 50.58% cyanuric acid
- Detected in urinary crystals
 - ≈ 30% melamine/70% cyanurate (Hoff)



Wikipedia

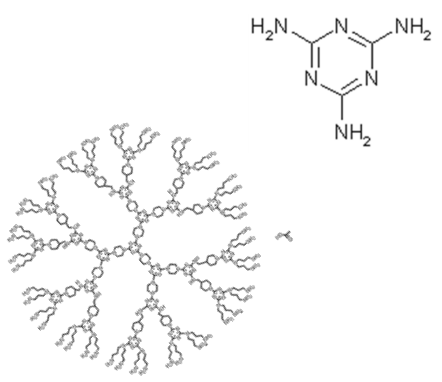
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So in addition to melamine, there's this thing that was-- so the problem with the pet food is the melamine is high in nitrogen.

Melamine

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veterinarian | VetDip

- Industrial uses
 - Melamine resin
 - Combined with formaldehyde
 - Plastics
 - Resins
 - Glues
 - Textile dyes
 - Yellow colorant
 - Pharmaceuticals



Neerman et al 2004


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You see all that nitrogen? So pet food needs to have protein in it. You want your pet food to have protein in it. So how do we measure protein in food? We measure nitrogen, and then we calculate the amount of protein and nitrogen--- based on the nitrogen. So nitrogen-- protein is 16%, nitrogen-- so if you get this much nitrogen, 1% nitrogen, you can calculate that at 16% protein in that batch of whatever.

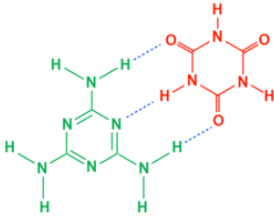
So instead of using-- so they sold things as protein supplements specifically as gluten meals, wheat gluten meals, and corn gluten meals, that are high in protein. Whereas, they actually were flour in the case of wheat gluten meal, that was spiked with melamine to make it look like gluten. Or corn starch that was spiked with melamine to make it look like corn gluten. And so this was fraud.

Now this had been done before. There had been an outbreak actually in Southeast Asia few years before. And there had probably been other contamination. And the one in Asia did not get diagnosed for a few years until we looked at it honestly. And then before that, there had been other issues, and probably what was going on was that they were using high grade melamine to spike this stuff. And it was just getting peed out. So high-quality melamine, it will crystallize, so you get a little bit of crystal urea, but most of it doesn't cause blockages, it actually gets peed out.

Cyanuric acid




- Polymerizes with melamine
 - pH = 5.8
 - 50.58% cyanuric acid
- Detected in urinary crystals
 - ≈ 30% melamine/70% cyanurate (Hoff)




Wikipedia

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If you have low-quality melamine, you can have this other thing that looks like melamine that's got some oxygen stuck to it. So this is actually cyanuric acid. It is part of the manufacture melamine-- part of the manufacture process of melamine. And when you add it to melamine it crystallizes. And this is what was killing cats and dogs in '07. So the melamine, the industrial melamine this was-- previously, they'd been using higher quality melamine, and they've gotten away with it, I think. And then they added this low quality melamine and animal started getting sick.

Melamine/Cyanuric Acid: Preliminary Investigation & Clinical Signs 

- **Palatability trials**
 - 20 cats fed for 6 d (Group 1)
 - Decreased consumption after d 1
 - Elevated BUN/Creat observed d 7-9
 - 4/20 died (eventually 9/20)
 - First death at the end of the test



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So what happened was we had-- and this is the same slide. So here it is again, and this is really what happened. There 20 cats on a feeding trial for a pet food, and they stopped eating the pet food after about a day, they started having some hyporexia, then they had increased BUN and creatinine about seven days. The first cat that died was 20 years old, died of kidney failure, nobody raised any eyebrows. But then the younger cats started to die as well. And eventually, 9 out of the 20 cats died.

Diagnosis of Melamine Toxicosis




- Analytical chemistry
 - GC/MS of foods, tissues, urine
 - Microscopy
- Urine crystals
- Postmortem lesions



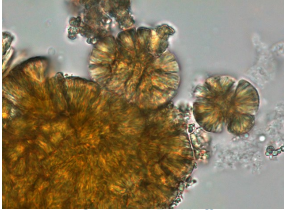
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And we had no idea what we were looking at the time because nobody had ever heard of melamine.

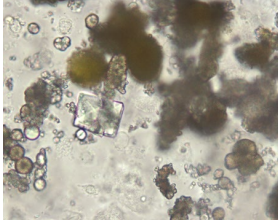
But we finally, based on-- what was in the crystals, based on what was in the pet food, it was tracked down to be melamine,

Urine Melamine/Cyanurate Crystals 

- Large “broken dinner plate” crystals



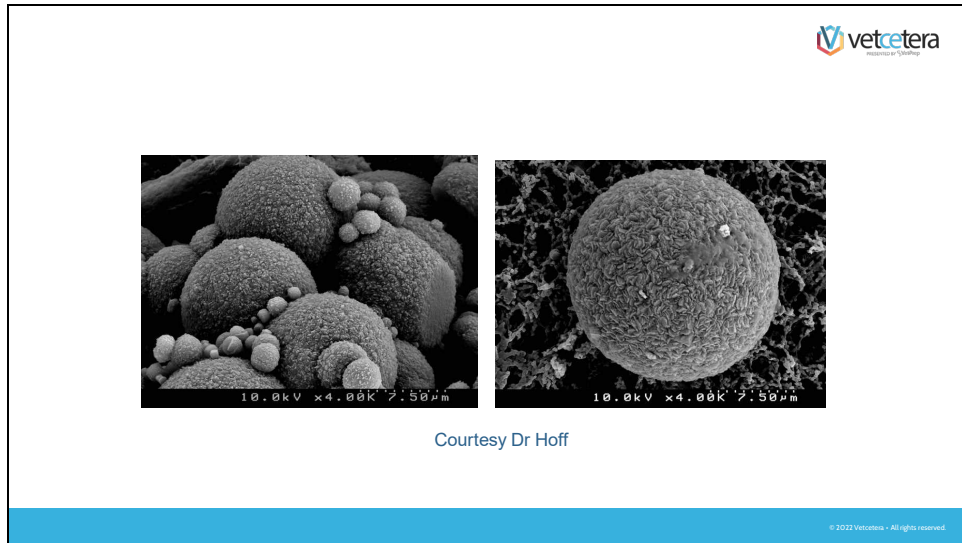
Courtesy Dr Hoff



Courtesy Dr Goldstein

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and these are the crystals. They're really-- they look like hedgehogs to me, they're kind of fluffy and brown. And here are some in the urine, they're a little bit not great focus. But that was what we were dealing with.




And these are what they look like, again, they look like hedgehogs to me, and scanning electron microscopy. The late Dr. Huff was very kind and sharing these images.

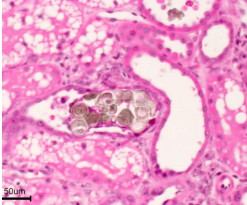
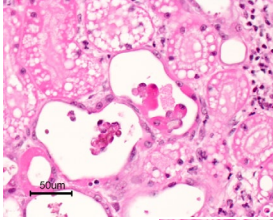


Why I talked too much. And these are-- actually, this was from the original corn gluten meal that they had purchased years before and still had some left. This was from the new batches of wheat gluten that the company had been using. And it turned out that this particular wheat gluten had been used by every pet food company out there. So all of the products were pretty much contaminated.

Postmortem Lesions with Melamine/Cyanuric acid




- Renomegaly
 - Pale tan kidneys
- Uremic plaques in oral cavity
- Histology
 - Subacute tubular necrosis
 - Regeneration
 - Intratubular crystals
 - Perivascular inflammation in cortex



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These are the kidneys. So you can see here, there are some crystals that look like the broken dinner plates hedgehog crystals that you saw.

These kidneys-- this is a cat, so you can see all the evacuation of the epithelium here because cats have evacuated renal epithelium, so that's actually normal in this species. But having all your cells slough off, and having their basement remain in your tubules is not cool. There's a little bit this is a big plump cell. So it might be trying to regenerate, but these kidney tubules have been stripped bare. They're not doing-- they're not functioning. There's no cells left. So that is what we saw with these guys.


Treatment 

- Supportive care for renal failure
- Poor prognostic indicators
 - Aged animals
 - Underlying conditions

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The ones that got really good supportive care, so if you could take them off the feed and put them on the fluids, they did really, really well. As long as they weren't 20 years old or something like that, these actually-- so bicarbonate and fluids. And a lot of-- maybe some furosemide, a lot of them did really, really well.

Melamine in Children



- Cyanuric acid not necessary
 - Neonates excrete uric acid
- Predominantly causes renolithiasis

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But the sign uric acid was really necessary for this to happen in dogs and cats. It turns out, a year later, I was at a conference at my Alma mater, University of Illinois. And when I was there, they had a representative of the FDA, his name was Stephen Sundlof, he was actually head of the FDA for a little bit. But because he was a veterinarian, that was hushed up a little bit. But he was there receiving a Lifetime Achievement Awardee, he's also a graduate of the University of Illinois.

And so the day before, I had turned on the radio, and they were talking about baby deaths in China. Babies had been dying from urolis. And I happened to walk up to Dr. Sundlof, and said, hey, do you know anything about what's going on in China? And he said, yeah. And I said, is it what I think it is? And he said, yeah. So it turned out that they had put the mela-- this was a year after the pet food recalls. The melamine had ended up in being used in baby formula to increase the apparent protein content. Previous years they've had some babies that actually died from not enough protein because the baby formulas were too dilute, so the manufacturer decided to pretend there was more protein by putting the melamine in there. These babies don't need cyanuric acid, because uric acid does pretty much the same thing, except the crystals form farther down the urinary tract so they form in the renal pelvis and they form in the urinary bladder. 300,000 babies in China drank this formula. 300,000 babies got sick, and 6 didn't survive. Which is tragic, but it could have been so much worse if we hadn't done all the work on the dog food stuff the year before. So by the time this happened, everybody had seen it before, they knew what to look for and they knew how to treat. So most of the babies actually survived this. So that was a miraculous story for me. It really-- I went into this business to save cats because I fully support the feline overlords, but knowing that some of our work went to saving hundreds of thousands of babies was a good experience for me. And this is why I think that contaminants-- unlike my professor in food sciences, I think that chemical contaminants are pretty darn important.



Preventing Contamination



Association of American Feed Control Officials (AAFCO) GMP

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Innovation in FeedTech

- Training
- Maintenance
- Ingredients
- Packaging/labeling
- Storage/inventory
- Inspection
- Record keeping



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So I have like two minutes to tell you all about how to deal with-- how to prevent these things. And it comes down to a whole bunch of stuff. Training, maintenance, ingredients, record keeping, inspections,

Cleanliness/Sanitation 

- **Pest control**
 - Insects
 - Rodents
- **Cleanliness**
 - Surfaces
 - Personnel



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pest control. You do not want rodents or insects getting into your pet food manufacturing process. OK?
Cleanliness,

Hazard Analysis and Critical Control Point (HACCP): Step 1

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- Consider manufacturing
 - Ingredients
 - Equipment
 - Processes
 - Storage
 - Distribution



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people in these places, culture, surfaces, all day long if you go into a pet food manufacturing facility, you have to put on an immune suit, and these places are sterile. And that's good. Ingredients, quality ingredients. That's where we went wrong with melamine, that's where we've gone wrong with the aflatoxin contamination, there was something wrong with the original ingredients. You also have to be able to put them in the right formulation or else you can get into trouble.

So how does it work? Hazard analysis and critical control points. Hazard-- So I'm not going to go-- I'm going to make my professor not proud because I'm not going to go into great detail, there's 11 steps to pass up, not going to go through them all. I'm going to hit the high points. So hazard analysis, what can possibly go wrong? Think of all the things that can go wrong. Critical control points, where are they going to go wrong? And which of them are going to be a bigger deal? So Deoxynivalenol, that can go wrong, easily. Is it a big deal? Kind of, but it's not as big a deal as aflatoxin. aflatoxin is going to kill a lot of animals. So aflatoxin is your chosen critical control point.

HACCP: Step 2

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- Analyze potential hazards
 - High probability
 - High morbidity/mortality




After the cat scan comes the lab work


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So potential hazards, high probability, high morbidity and mortality considerations.

HACCP: Steps 3 & 4



- **Control hazards**
 - Critical Control Points (CCP)
- **Document**
 - Monitoring of CCPs
 - Handling of problems




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And then you figure out those critical control points, where are you going to look for this problem so that you can prevent it? So this is going to require a lot of automation, a lot of cleanliness, a lot of routine. Equipment maintenance, routine recording, et cetera.

Example 1 of CCPs: Raw ingredients



- **Potential hazards**
 - Natural contaminants
 - Aflatoxin
 - Deoxynivalenol (DON)
 - T-2
 - Adulteration
 - Melamine
 - Phenobarbital
 - Formulation errors
 - Vitamin D
 - Thiamin



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So these are some of the natural hazards that I've talked about already. These are some of the critical control-- or some of the things you're going to be looking to control.

Natural Contaminants in Raw Ingredients vetcetera
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- Aflatoxin screens
- DON screening
- T-2 screening



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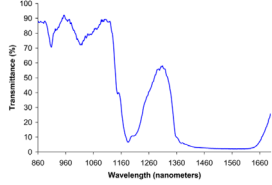
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One thing you can do is screen the ingredients before they go into the pet food. So this is an HPLC, this is an ELISA test kit for aflatoxin. These things are going to help you-- these things are going to help you test the ingredients in the feed, so you don't get a contaminated feed but I also recommend you test after the feed is manufactured. So that if something slip by because these mycotoxins don't tend to be homogeneously distributed in a lot, things can get by and you don't want to sell a contaminated product.

Adulteration of Raw Ingredients

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powered by VetDrop

- **Ingredient ID**
 - Near Infrared Spectroscopy
 - Feed Microscopy
- **Other analyses**
 - GC/MS
 - LC/MS-MS
 - HPLC
 - ICP, AA, X-ray fluorescence




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And these are just some ways of looking at it. I had to feed microscopist here years ago, who could take a piece of kibble and break it up and tell you what all the ingredients were which blew my mind. So that's a neat science infrared. This is you take a fingerprint of the ingredient using this NIR, and then you compare it to the new ingredient and they should match precisely. If you looked at this with melamine, they did not match. The wet gluten meal that was pre-melamine, did not look anything like the post-melamine. So something like this could have told them that the ingredient was not safe.

Formulation Errors

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- Automated equipment
 - Excellent maintenance
 - Cleanliness
- Record keeping
 - Can be automated
 - Easily accessed
 - Reviewed before release



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Making sure your equipment works, making sure your records are kept and going through them to make sure everything is right.

CCP Example 2: Pasteurization




- Heating during production
 - Extrusion (bagged)
 - Retorting (canned)
- Coating process
 - Certified pathogen free
- Cleanliness
 - Surface culturing
- Record keeping



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There are processing procedures that prevent contamination, so pasteurization is a big one. And then, of course, again, cleanliness. They are constantly swabbing these equipment down to make sure that there is no bacterial contamination. These are very sterile facilities.

Monitoring 


- Data can be automatically recorded
 - Temperature monitors
- Accessible at any time
- Reviewed & analyzed before release of lot
- Subsamples of all lots held

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Automated data collection and transfer can be accessible to anyone at any time and reviewed. Lots are held for a time until the records are reviewed to make sure everything is safe and ready to go.

Error Handling vetcetera
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- Stop production
- Analyze records
- Consultation
 - On-site experts
 - Outside experts
- Solution initiated
 - Discard or salvage



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And then when something does happen you stop production. And you go through the records, you figure out what happened, you find the experts, you do the testing, and you probably discard the feed or maybe you're going to end up salvaging some of it by feeding it to a less affected species.

So with the melamine, they ended up feeding a bunch of it to swine, which turned out to be a big mistake because then they had to recall. They basically had to slaughter and destroy all of the swine because it was a potential human contaminant. So carefully deciding what to do is super important.

The slide features a blue header with the word "Conclusions" on the left and the VetCetera logo on the right. The logo consists of a stylized 'V' icon followed by the text "vetcetera" and "VetPrep" in smaller text below it. The main content area is white and contains a bulleted list under the heading "Recent recalls". The list items are: "Natural contaminants" (with sub-bullets for "Mycotoxins", "Thyroid hormone", and "Bacteria"), "Formulation errors" (with a sub-bullet for "Vitamins"), and "Adulteration" (with a sub-bullet for "Melamine/cyanuric acid"). A thin blue footer bar at the bottom right contains the text "© 2022 VetCetera - All rights reserved."

So these are basically just a rundown of the things that I've talked about. I am like 1 minute over, but I am stuck here for another 40 minutes anyway. So I will hang out as long as anybody has questions or wants to talk about anything.

Conclusions vetcetera
Korea's #1 VetPrep

- Preventing future recalls
 - Regulations
 - Consumers & vets
 - <https://www.fda.gov/animal-veterinary/report-problem/how-report-pet-food-complaint>
 - HACCP & automation



우주비행사는 HACCP로 관리되는 안전한 식품만 먹습니다
농림부 국립수산물품질관리원 HACCP인증 표시제품의 안전한 사용을 꼭 지켜주세요.

HACCP(위생관리)
위생관리를 위해 HACCP(위생관리) 인증 표시제품을 꼭 지켜주세요.

HACCP(위생관리)의 원칙

1. HACCP(위생관리)의 목적	2. HACCP(위생관리)의 범위
3. HACCP(위생관리)의 책임	4. HACCP(위생관리)의 절차
5. HACCP(위생관리)의 기록	6. HACCP(위생관리)의 교육
7. HACCP(위생관리)의 점검	8. HACCP(위생관리)의 개선

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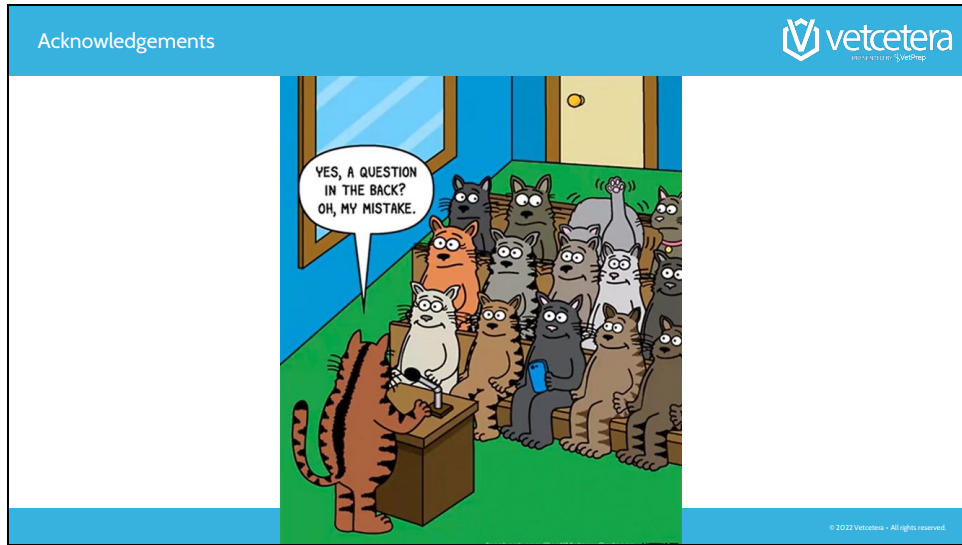
I took this picture when I was in Korea and it basically says that everybody needs HACCP, and it's true.

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These are like the millions and millions of people who've helped me on this. So I'm so grateful.



And I opened it up for any questions, chat time, anything you guys want to bring up.

All right. So, yeah. It looks like we don't have any questions tonight. So I'll let you go. Thank you so much for joining us. We really appreciate it.

Thank you. It was really fun.

Thank you for joining us. Have a good night.



Thank you for choosing Vetcetera!

Karyn Bischoff, DVM, MS, DABVT

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