Equine Feed Contamination and Toxicology

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

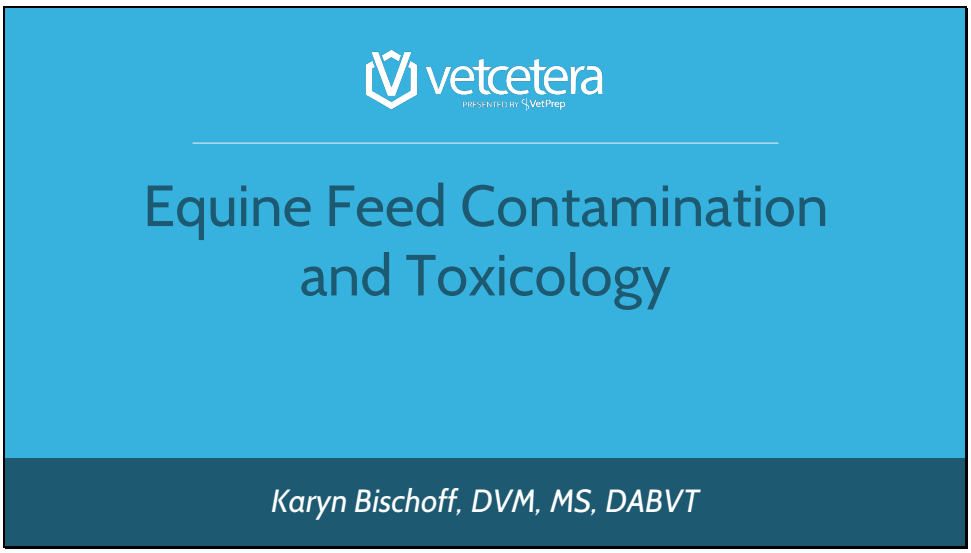
Speaker Bio:

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.

Slide 1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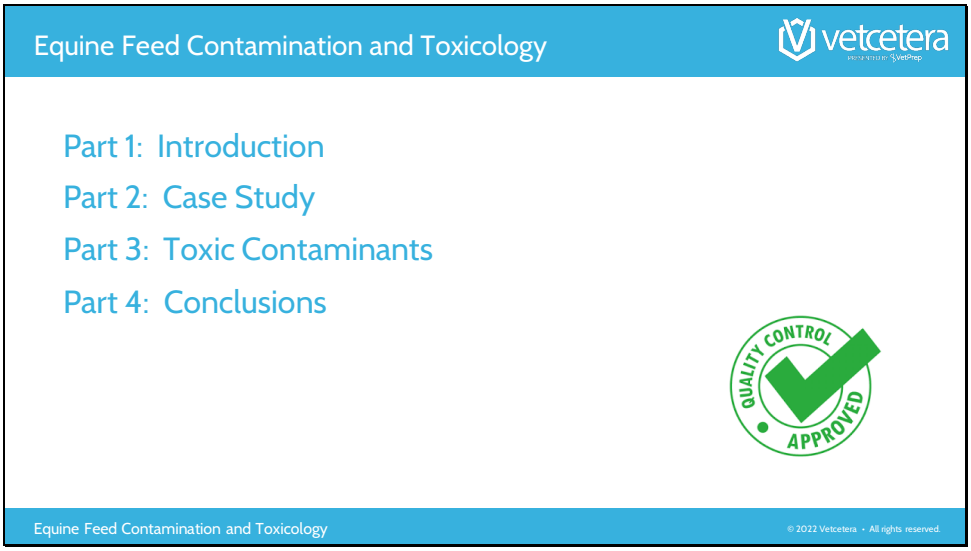
Equine Feed Contamination and Toxicology
Karyn Bischoff, DVM, MS, DABVT

Slide 2


Equine Feed Contamination and Toxicology
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Part 1: Introduction
Part 2: Case Study
Part 3: Toxic Contaminants
Part 4: Conclusions
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Slide 3

Slide 4

When do you suspect feed contamination?

A. Multiple horses in a group

B. Multiple farms in a geographic area

C. New lot of feed precedes clinical signs or feed refusal

D. Any of the above

Slide 5

When do you suspect feed contamination?

A. Multiple horses in a group

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Slide 6

Types of Contamination

- **Natural contaminants**
- **Formulation error**
- Adulterants

Slide 7

Natural Contaminants

- Insects in forage
  - ***Epicauta* spp.**
  - *Malacosoma* spp.
- Bacterial
  - ***Clostridium botulinum***

horseauthority.co

- Mycotoxins
  - **Fumonisin**
  - Slaframine
  - Ergot alkaloids (fescue)
  - Dicoumarol
  - Tremorgens
  - Aflatoxin

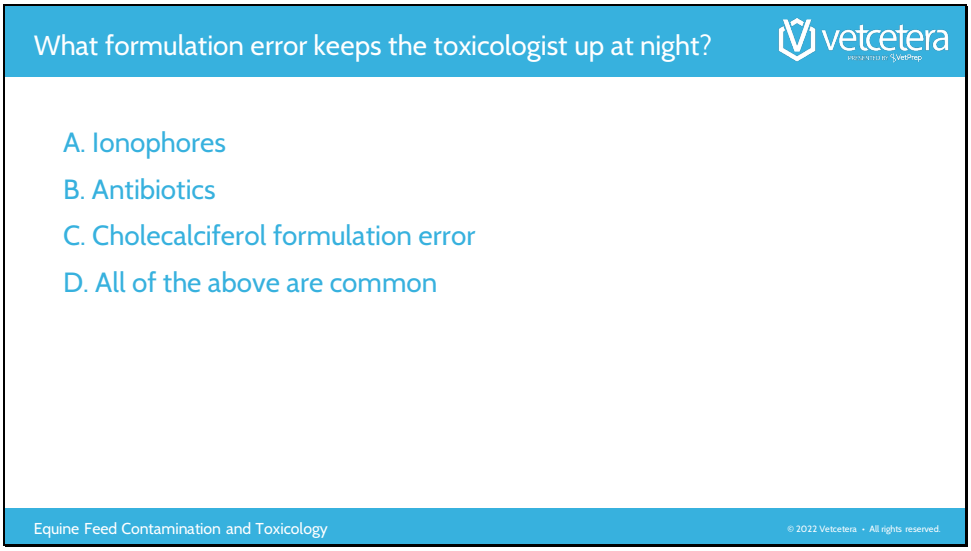
Slide 8

Natural Contaminants

- Plants in hay
  - Pyrrolizidine alkaloids
  - Berteroa spp.
  - Panicum spp.
  - Ageratina altissima
  - Datura spp.
  - Astragalus spp.
  - Pteridium aquilinum
- Weed seeds
  - Senna occidentalis
  - Datura spp.

Nature-and-garden.com

Slide 9


What formulation error keeps the toxicologist up at night?
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A. Ionophores
B. Antibiotics
C. Cholecalciferol formulation error
D. All of the above are common
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Slide 10

What formulation error keeps the toxicologist up at night?

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A. Ionophores

B. Antibiotics

C. Cholecalciferol formulation error

D. All of the above are common

Slide 11

When Commercial Feed Contamination Suspected

- Contact the State Veterinarian
- Contact FDA
  - 877-689-8073
- Contact manufacturer

Slide 12

The Elusive "Representative Sample"

- Feed collection
  - Multiple samples
    - Uneven distribution
      - Weeds in hay
      - Ionophores
- Saved feed
  - Delayed onset/chronic
    - Pyrrolizidine alkaloids

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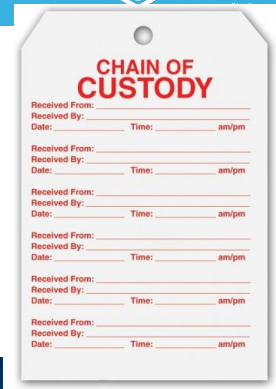
Feed Sample Analyses

- Visible contamination
  - Weedy hay
  - Visible mold
  - Particle size
- Feed microscopy
  - Offered by some diagnostic labs
- Plant identification
  - Extension botanists

Slide 14

Legal Issues

- Sample identification
- Sample handling
  - Tamper-resistant
  - Chain-of-custody



Slide 15

What sample testing do you request from the diagnostic laboratory?

A. Feed for general tox screen

B. Urine for feed contaminants screen

C. Intestinal swab for fungal toxins

D. None of the above

Slide 16

What sample testing do you request from the diagnostic laboratory?

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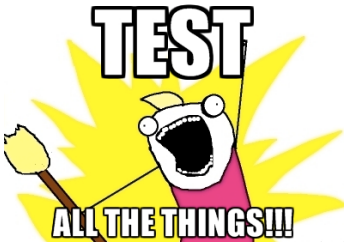

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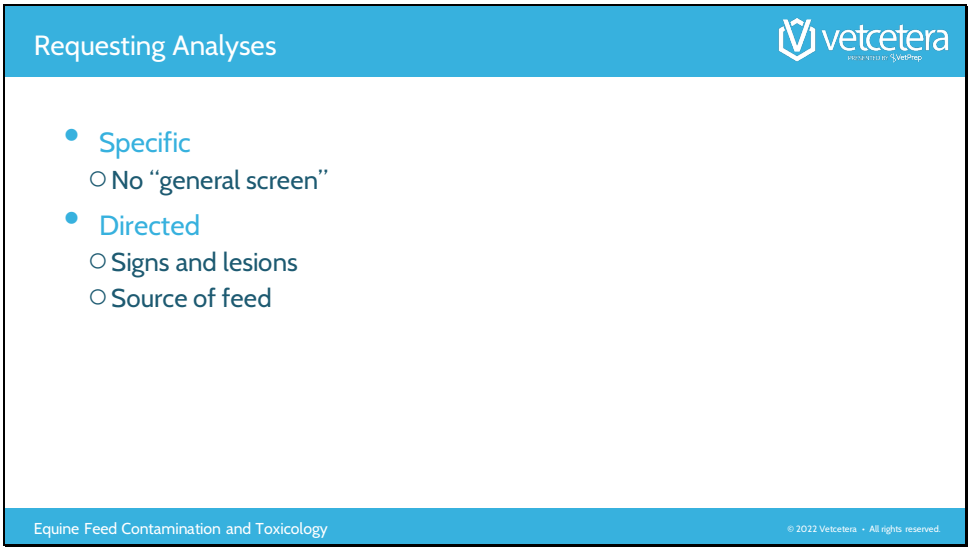
Requesting Analyses
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Specific
No "general screen"
Directed
Signs and lesions
Source of feed
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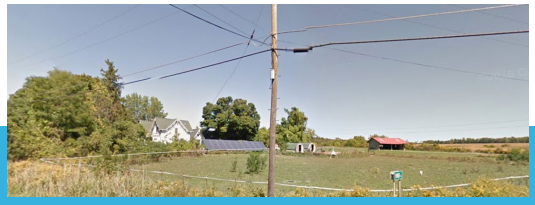
Part 2. Case Study

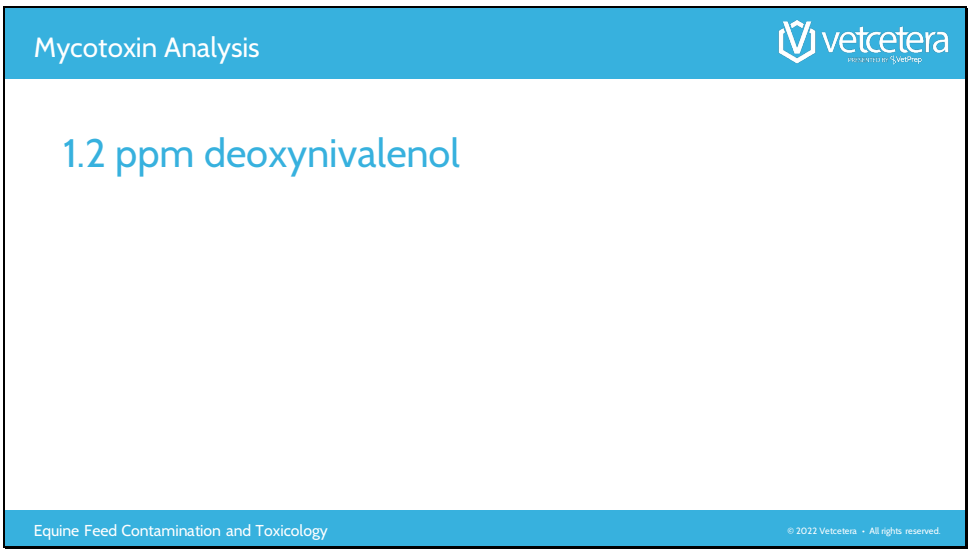


Slide 19

Stable in Western New York, Nov 2016

- Boarding and performance horses
  - 30 horses currently
- Day 1: stallion died
  - No clinical signs noted
- Day 12: pony died
  - Necropsy
  - Bloodwork from 5 others
  - Feed for mycotoxin analysis

Slide 20


Mycotoxin Analysis
vetcetera
1.2 ppm deoxynivalenol
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Bloodwork

- Toby: Paint gelding
  - Within normal limits
- Rob: QH gelding
  - Elevated bilirubin
  - Total 3.2 mg/dL
    - (0.5-2.1)
  - Indirect 3.1 mg/dL
    - (0.3-2.0)
- Kris: QH mare
  - WNL
- Milly: QH mare
  - AST 4799 U/L
    - (222-489)
  - CK 113790 U/L
    - (116-464)

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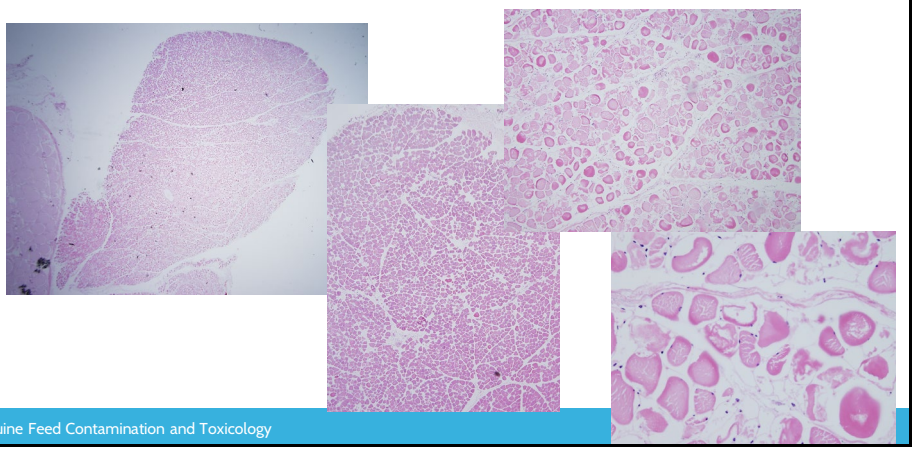
Necropsy

- Serosanguinous pleural & pericardial effusion
- Pale heart
- Subcutaneous edema
  - Stifle and shoulder
- Renal hemorrhage (left kidney)
- Pulmonary congestion and edema

Slide 23

Histopathology



Equine Feed Contamination and Toxicology

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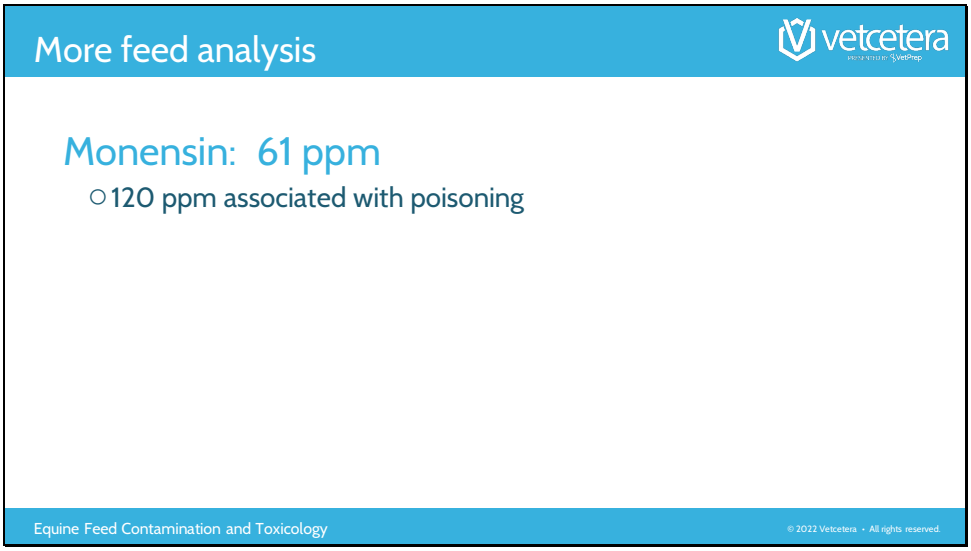
More feed analysis
vetcetera
Monensin: 61 ppm
120 ppm associated with poisoning
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Day 24: Serum Chemistry on all horses

- Milly: CK = 993 U/L
  - (116-464)
- Derpy (paint mare): CK = 1911 U/L
- 28 others: CK = WNL


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Part 3a: Ionophores

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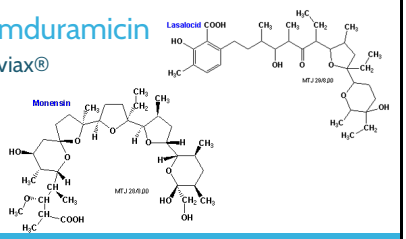
Ionophores

- Monensin
  - Coban®, Rumensin®
- Lasalocid
  - Bovatec®, Avatec®
- Salinomycin
- Maduramicin
- Narasin
  - Monteban®
- Laidlomycin
  - Cattlyst®
- Semduramicin
  - Aviax®



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Ionophores

- Toxicosis in horses, cattle, sheep, turkeys, pigs, dogs, cats, rabbits, deer, guinea fowl, ostrich, chickens, camels, alpacas, water buffalo, human
- **Horses** & mature turkeys sensitive
  - Camelids similar to horses
  - Feed mixing errors, contamination
  - Using feed labeled for cattle

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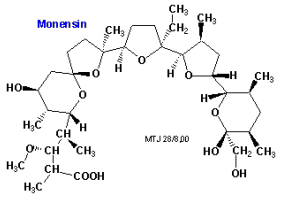
MOA of Ionophores

- Form lipid-soluble complexes with ions
  - Monovalent & divalent cations
  - Ca^{++}, Na^{+}, K^{+}, Mg^{++}
- Enhance transport
  - Cell membranes
  - Organelle membranes
- Binds ion to cross membrane
  - One ion in, one ion out



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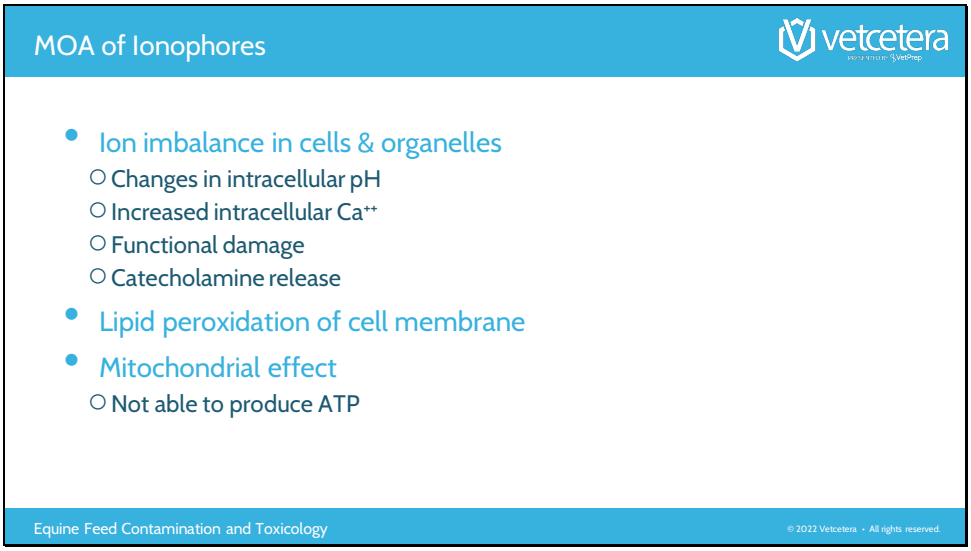
MOA of Ionophores
vetcetera
Ion imbalance in cells & organelles
Changes in intracellular pH
Increased intracellular Ca++
Functional damage
Catecholamine release
Lipid peroxidation of cell membrane
Mitochondrial effect
Not able to produce ATP
Equine Feed Contamination and Toxicology
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Slide 31

Clinical Signs Associated with Ionophores

- Onset in hours
  - Occasionally delayed over days
- Feed refusal
- Unexpected death
  - Common presenting complaint

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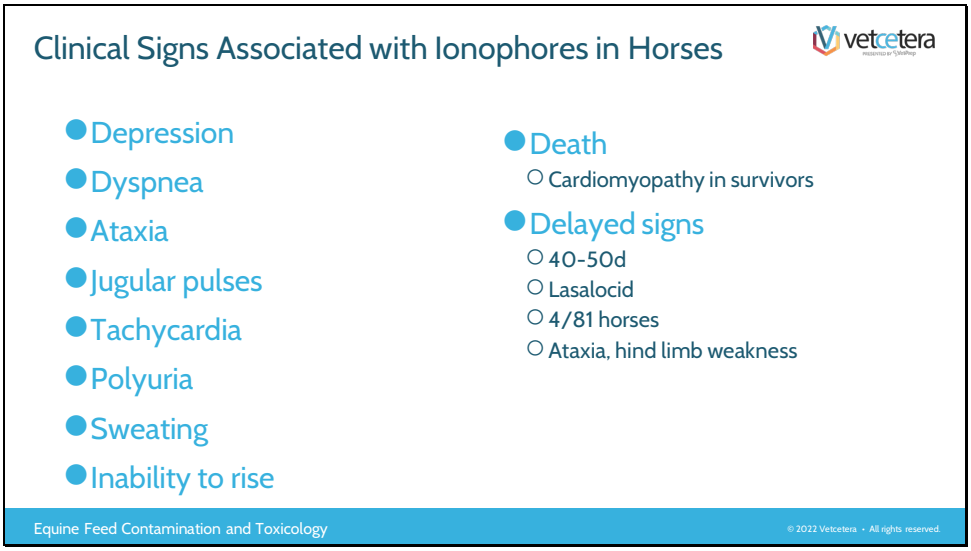
Clinical Signs Associated with Ionophores in Horses
vetcetera
Depression
Dyspnea
Ataxia
Jugular pulses
Tachycardia
Polyuria
Sweating
Inability to rise
Death
Cardiomyopathy in survivors
Delayed signs
40-50d
Lasalocid
4/81 horses
Ataxia, hind limb weakness
Equine Feed Contamination and Toxicology
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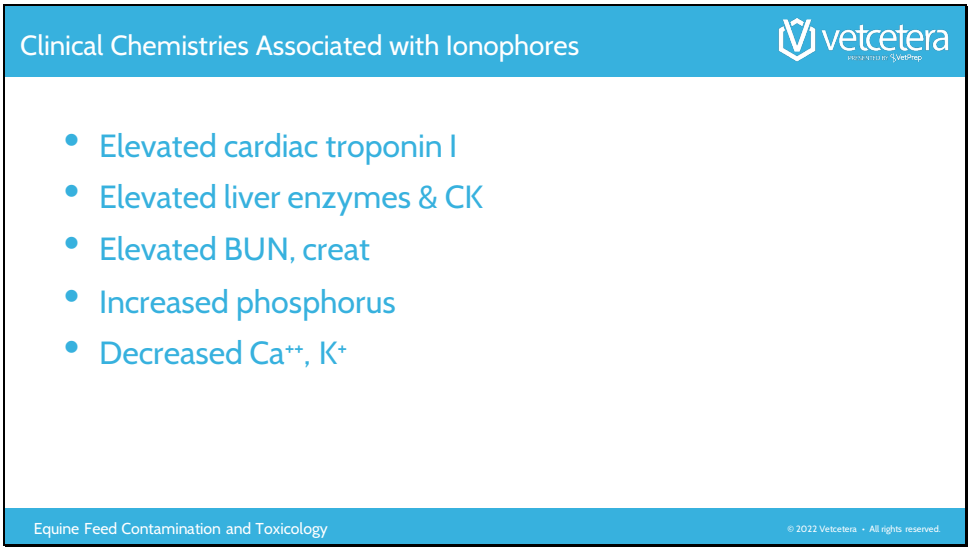
Clinical Chemistries Associated with Ionophores
vetcetera
Elevated cardiac troponin I
Elevated liver enzymes & CK
Elevated BUN, creat
Increased phosphorus
Decreased Ca^{++}, K^{+}
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Lesions Associated with Ionophores

- Often none, rapid onset
- Cardiac myonecrosis
  - Pulmonary edema, ascites
  - Passive hepatic congestion
- Skeletal muscle necrosis
- Delayed axonal degeneration

Slide 35

Diagnosis of Ionophore Toxicosis

- Hx of exposure
- Feed assays
- Tissue analysis
  - Confirm exposure
- Clinical signs
- Gross and histologic lesions
- Exclusion of other causes

Slide 36

Treatment of Ionophore Toxicosis

- Clean feed
- GI decontamination for recent ingestion
  - AC/cathartic
- Symptomatic & supportive
  - Hydration, electrolytes, K+
  - Stall rest, low stress for 6-8 wks

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Prognosis for Ionophore Exposure

- Dose dependent
- Guarded for myocardial damage
  - Exercise intolerance
  - Congestive heart failure

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Slide 39

What is the classic nervous system lesion of fumonisin poisoning?

A. Leukoencephalomalacia

B. Polioencephalomalacia

C. Nigropallidal encephalomalacia

D. Neuronal vacuolation

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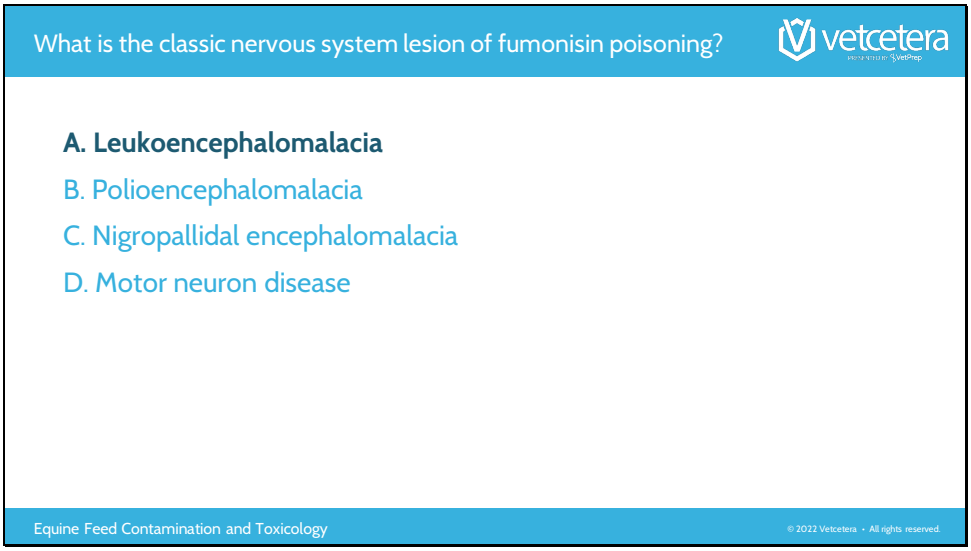
What is the classic nervous system lesion of fumonisin poisoning?
vetcetera
A. Leukoencephalomalacia
B. Polioencephalomalacia
C. Nigropallidal encephalomalacia
D. Motor neuron disease
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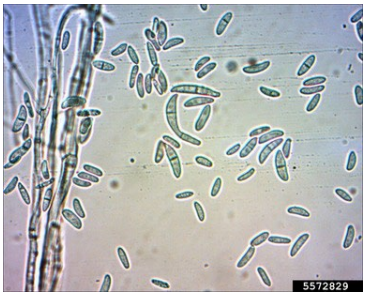
Slide 41

Mycotoxins

- *Fusarium* spp.
  - **Fumonisin**
  - DON, DAS, T-2, nivalenol, etc.
  - Zearalenone
- *Aspergillus* spp.
  - Aflatoxin



ipmimages.org

Slide 42

Fumonisin

- "Moldy Corn Poisoning"
  - One report in hay
  - Leukoencephalomalacia
  - Hepatopathy
- Onset - days to months of exposure

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Source of Fumonisins

- FB_1 most common
- *Fusarium verticillioides, F proliferatum*
  - Corn
    - Whole shelled, screenings, by-products
- Fungus doesn't guarantee fumonisin
  - Climatic factors
    - Midsummer drought & early, wet autumn
    - Temperature fluctuations

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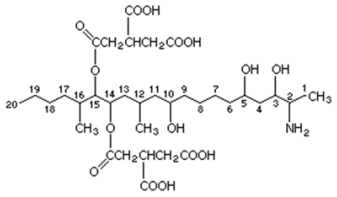
Fumonisin Toxicity

- 0.6 to 2.1 mg/kg fumonisin B1
  - Signs in 24-28d
- 10 ppm in feed
- FDA Guidelines
  - Horse feed <5 ppm



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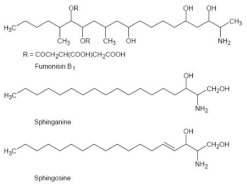
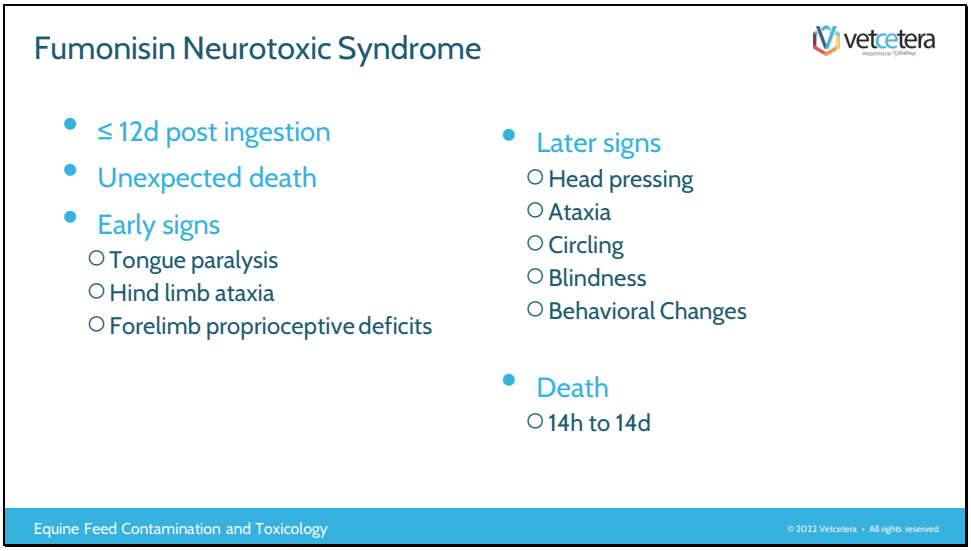
Fumonisin MOA

- Inhibit ceramide synthase
  - Sphingolipid synthesis
    - Precursor buildup
  - Role of sphingolipids
    - Cell membrane integrity
    - Cell membrane receptors
    - Cell messengers
    - Folate metabolism



Temp.biomin.net

Slide 46


Fumonisin Neurotoxic Syndrome
vetcetera
≤ 12d post ingestion
Unexpected death
Early signs
Tongue paralysis
Hind limb ataxia
Forelimb proprioceptive deficits
Later signs
Head pressing
Ataxia
Circling
Blindness
Behavioral Changes
Death
14h to 14d
Equine Feed Contamination and Toxicology
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Fumonisin Hepatotoxic Syndrome

- Less common
  - +/- concurrent with CNS form
- Decreased appetite
- Depression
- Edema of head
- Icterus
- Clinical pathology changes
  - Incr. AST, GGT, ALP, tBili, bile acids

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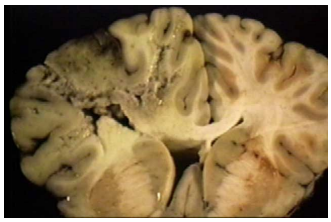
Lesions Associated with Fumonisin

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

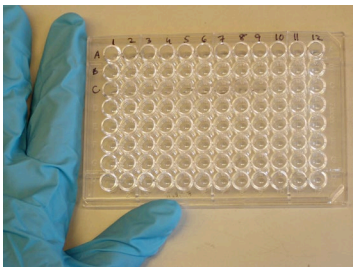


Courtesy deLahunta

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

Slide 50

Treatment of Fumonisin Toxicosis

vetcetera
www.lsuagcenter.com

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

Neuro horse photo by Dr. Rebecca McConnico

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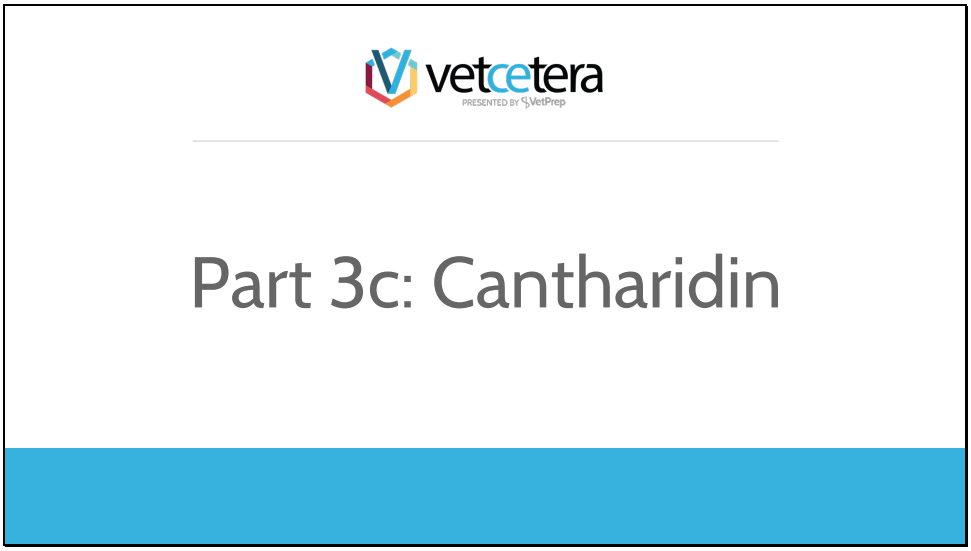
Preventing Fumonisin Toxicosis

- Avoid contaminated feed
  - Screen corn, remove damaged kernels
- Binders NOT FDA APPROVED!
  - Cholestyramine
  - Activated carbon
    - Ineffective in vivo?
  - Commercial mycotoxin binders
    - Efficacy?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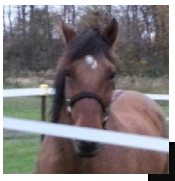
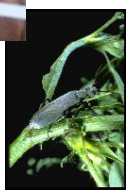
Part 3c: Cantharidin

Slide 53

Cantharidin

- Blister beetles ("Spanish Flies")
- Many other species susceptible
  - Cattle, sheep, rabbits, emu
  - Problem most common in OK, TX
- Clinical signs within hours
  - Last several days
  - Up to 100% mortality

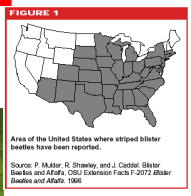




Slide 54

Source of Cantharidin

- *Epicauta* spp.
  - *E lemniscata, E pestifera, E pennsylvanica, E andersoni, E maculata*, etc.
- Other genera
  - *Lytta vesicatoria*: Spanish Fly



Slide 55

What organs are affected in blister beetle poisoning?

A. Urinary bladder

B. Heart

C. Gastrointestinal mucosa

D. All of the above

Slide 56

What organs are affected in blister beetle poisoning?

A. Urinary bladder

B. Heart

C. Gastrointestinal mucosa

D. All of the above

Slide 57

Conditions Associated with Infestation

- Insects aggregate in alfalfa fields
  - Swarm during the bloom
- Present at hay cutting
  - Crimping of alfalfa crushes insects into hay
- Variable concentration per beetle:
  - Zero to 5+% cantharidin

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Cantharidin Absorption, Elimination, & MOA

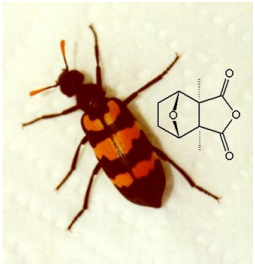
- Rapid GI absorption
- Urinary excretion
- MOA
  - Vesicant action
    - Acantholysis of epithelial cells
  - Inhibits protein phosphatase 2A
    - Affects cell proliferation
  - Direct necrotizing effect on cardiac myocytes

Entnemdept.ufl.edu

Slide 59

Signs of Cantharidin in Horses

- Colic
  - Restlessness
  - Perspiration
  - Increased pulse & respiration
  - Pollakiuria
  - Diarrhea
- High dose
  - Shock and death within hours
  - Found dead



Slide 60

Clinical Pathology Associated with Cantharidin

- Hypocalcemia
- Hypomagnesemia
- Increased PCV
- Increased CK

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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Diagnosis of Cantharidin Toxicosis

- History
- Clinical signs & clinical pathology
- Lesions
- Beetles in hay
- Analytical chemistries
  - Urine
  - GI content

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Treatment for Cantharidin Toxicosis

- Remove contaminated feed
- Intensive supportive care
  - 3 to 5d of treatment
- Detoxification
  - Mineral oil or AC

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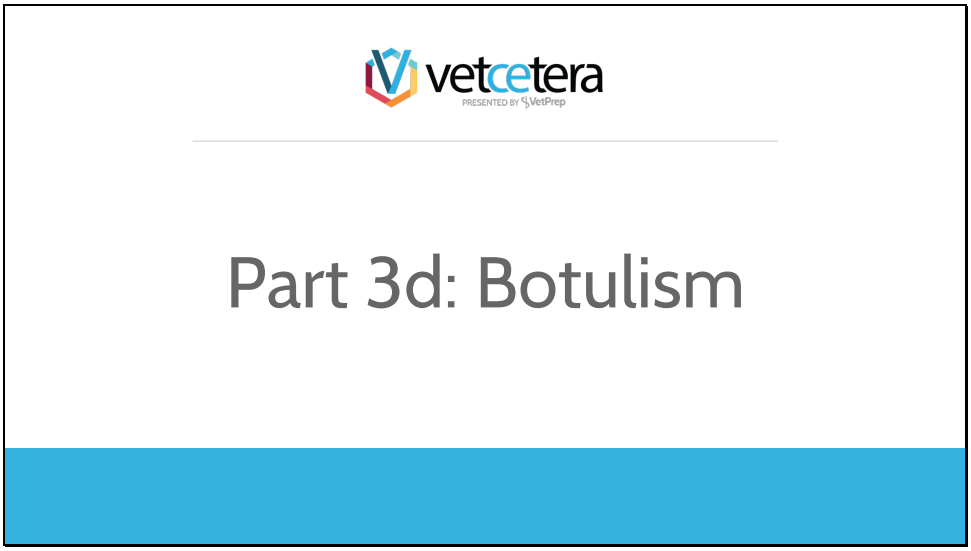
Symptomatic Treatment

- Pain relief
  - α_2-adrenergic agonists
    - Xylazine
    - NSAIDs are inadequate
- Fluid therapy
  - Diuresis
  - Rehydration, hypovolemic shock
  - Ca and Mg supplementation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Part 3d: Botulism

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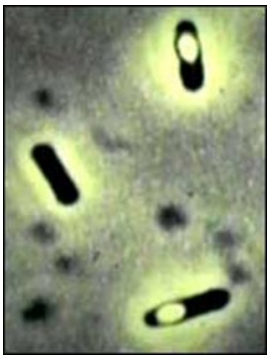
Botulism

- *C. botulinum* & related spp.
  - Soil, GIT of healthy animals
  - Common in GIT of cattle
- Most mammals, birds, fish affected
  - CDC Cat. A Bioterrorism Agent
  - Horses extremely susceptible
    - 100 horses in Florida 2008



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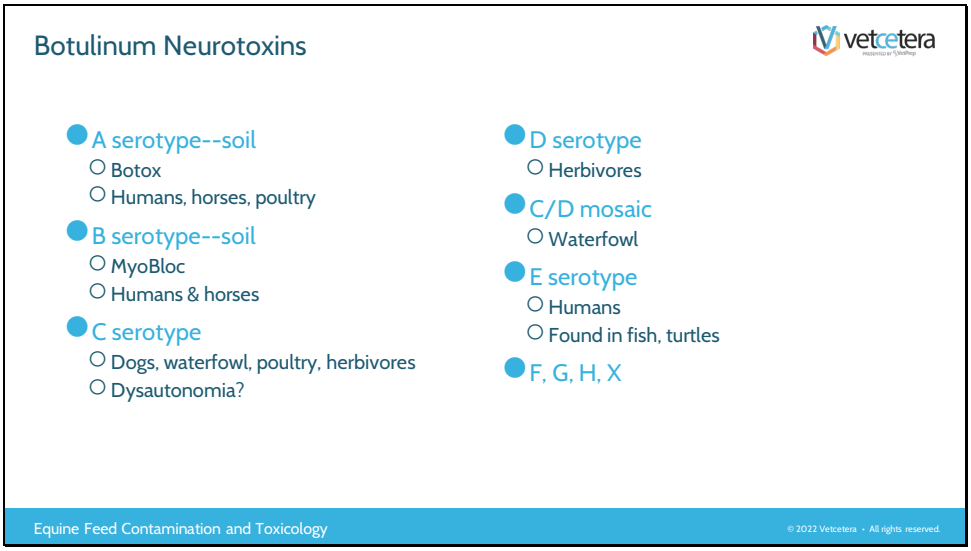
Botulinum Neurotoxins
vetcetera
A serotype--soil
Botox
Humans, horses, poultry
B serotype--soil
MyoBloc
Humans & horses
C serotype
Dogs, waterfowl, poultry, herbivores
Dysautonomia?
D serotype
Herbivores
C/D mosaic
Waterfowl
E serotype
Humans
Found in fish, turtles
F, G, H, X
Equine Feed Contamination and Toxicology
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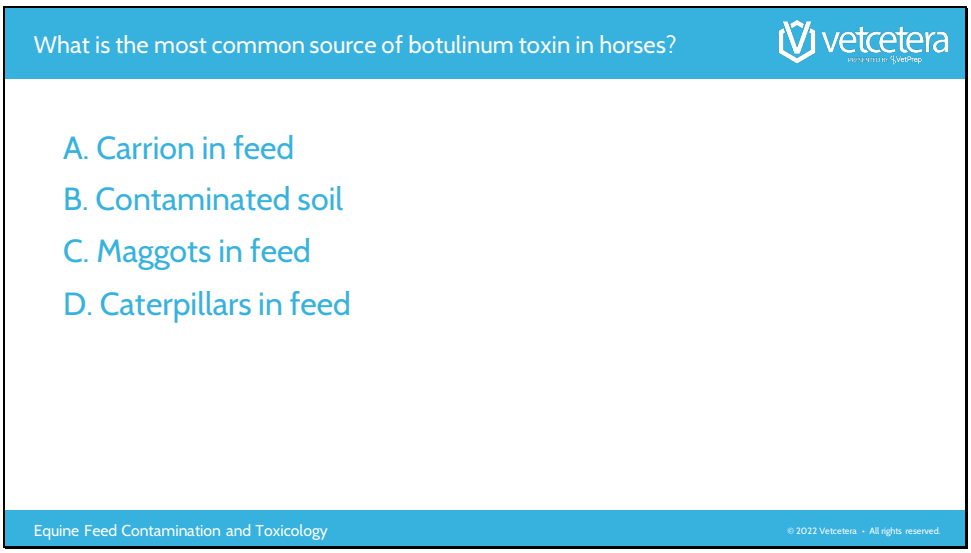
What is the most common source of botulinum toxin in horses?
vetcetera
A. Carrion in feed
B. Contaminated soil
C. Maggots in feed
D. Caterpillars in feed
Equine Feed Contamination and Toxicology
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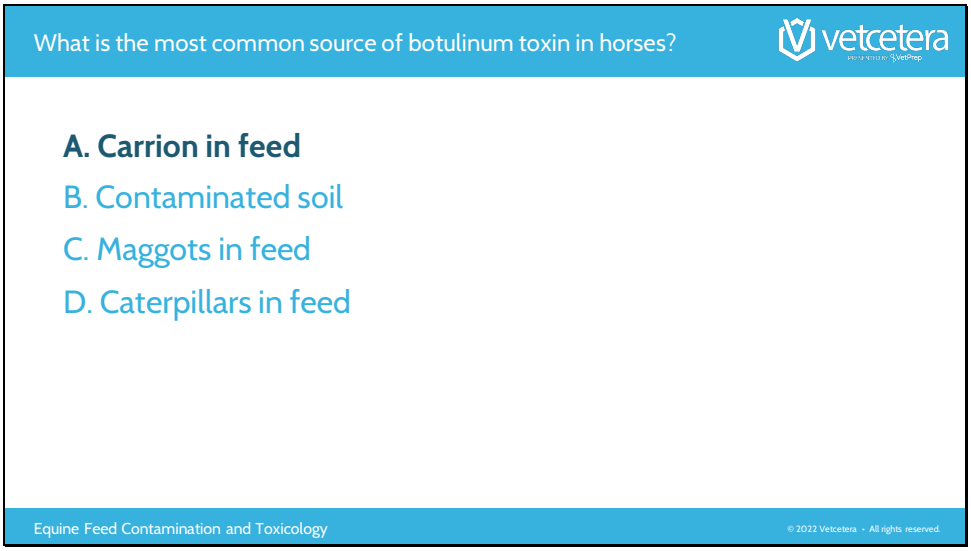
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Slide 70

Sources of BoNT

- Carrion–most common source
  - Haylage feeding in horses

CartoonStock.com

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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BoNT ADME

- Absorption
  - Resists gastric pH
  - SI mucosa
  - Devitalized tissue, not intact skin
- Distribution
  - Via blood
  - Does not cross bbb
  - Not reported to affect fetus

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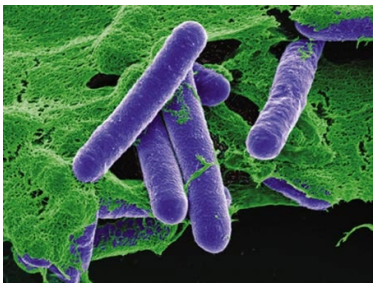
Toxicoinfectious & Wound Botulism

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



chinaaseansps.com

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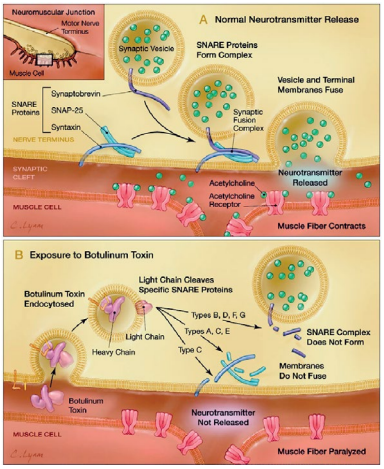
BoNT MOA



JAMA. 2001;285:1059-1070

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Botulism in Horses

- Dysphagia early
- Reduced tongue tone (tongue test)
- Head & neck edema
- Recumbence–delayed up to 5d
- Recovery > 21d
- Shaker foals
  - Tremors

The Horse

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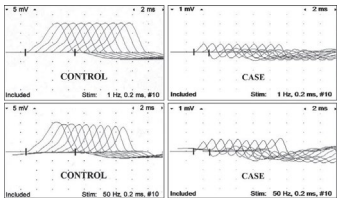
Diagnostic Assays for Botulism

- 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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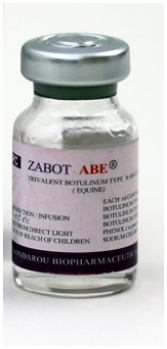
Treatment of Botulism

- $Antitoxin$ early, strains A, B, E
  - New Bolton Center
- Symptomatic & supportive
- Wound management
- Est 14-60d hospitalization



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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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

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Conclusions

- Feed related toxicants
  - Formulation errors
  - Natural contaminants
- Good diagnostic work-up essential
  - Clinical Signs
  - Clinical chemistry
  - Postmortem Lesions
  - Appropriate Toxicology Request

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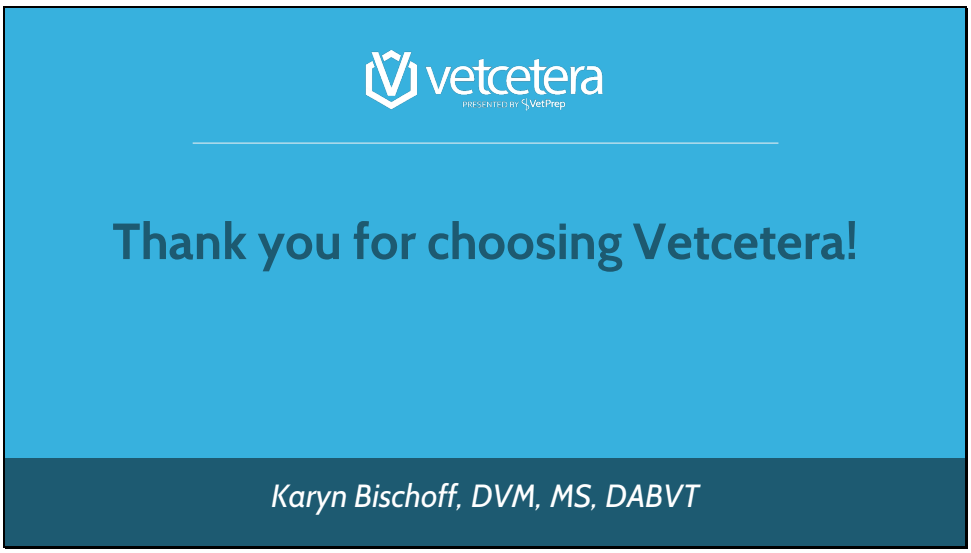
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Thank you for choosing Vetcetera!
Karyn Bischoff, DVM, MS, DABVT

References:

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