Mycotoxin Poisoning in Small Animals

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Overview

• Biology of fungi
• Signs of infestation
• Mycotoxins
• Management
Fungi are all around

• All conceivable habitats
• Incredible genetic diversity
  – Over 1-1.5 million species
    • Only about 70,000 species have been described
  – Many more genotypes/ecotypes/chemotypes
What are fungi?

• Mostly multicellular
  – Mycelium (mold) consists of branching hiphae (filaments)
  – Yeasts are exceptions
  – Usually chitin cell walls

• Aerobic

• Asexual/sexual reproduction
  – Spore-forming
  – Sexual reproductive structures/fruiting bodies are called mushrooms/puffballs/truffles etc.
Spore formation is key to reproductive success

- Imparts genetic variation through sexual reproduction
- Increases adverse condition survivability
- Small and light - easily spreads by wind/air currents

*Aspergillus flavus* (green) growing on a corn grain

*A. flavus* viewed under a microscope

Photos: Stella Marie M. Doyungan
What do they do?

• Mostly saprophytic (eat dead stuff)
  – Good at breaking down plant material
  – Often symbiotic with plants/insects
    • Mycorrhizae
    • Endophytes
  – Can be commensal/infectious/parasitic
    (eg Candida spp.)
  – But mostly COMPETITIVE

• Specialize in chemical warfare
  – Antibiotics eg penicillin
  – Mycotoxins
    • Human/animal poisoning is collateral damage!
Signs of mold

- **Heat**

\[ C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy} \]

(Carbohydrate)

- **Smell**
• Discoloration

*Aspergillus* spp.

[Image of corn with discolored kernels]

[Image of corn with Diplodia ear rot]

www.ipm.iastate.edu/.../images/aspercorn.jpg

www.ent.iastate.edu/.../diplodia_ear_rot.jpg
• Caking or clumping

• Slow movement out of bins
Mycotoxin production depends on:

- Genetic potential
- Environmental conditions
  - Aerobic conditions
  - Temperature and relative humidity
    - Generally warm and humid
  - Available water
  - Accessible nutrients
    - Crop damage!
- Growth stage/proliferation
Environmental fate of mycotoxins

• Resistant to decomposition by
  – cooking
  – freezing
  – digestion
    • May end up in milk (eg Aflatoxin M1)

• Breakdown is often slow
  – Contaminated crops/food/feed tend to remain contaminated
Regulation:
Action levels vs Advisory/Guidance levels

- **Action Levels**
  - Must be reported to FDA
    - Agencies such as GIPSA (Grain Inspection, Packers and Stockyards Administration – part of the USDA) has to report violative levels to the FDA if Action Levels are exceeded.
    - Lots are subject to FDA seizure

- **Guidance or Advisory Levels**
  - Provide an adequate margin of safety
  - Not subject to enforcement by FDA
Aflatoxins

• Seed crops; oilseeds; spices; nuts
  – A. flavus, A. paraciticus, A. nominus and others

• Rapid contamination
  – High levels within 2-7 days of inoculation

• Persistent – survives processing
  – Many potential sources of human/animal exposure
• Types
  – AB1, AB2
  – AG1, AG2
  – AM1, AM2
    • Metabolites of B1 and B2
    • Associated with milk

• Potent carcinogens; Hepatotoxic
  – Metabolized to reactive epoxides in the liver
  – Causes DNA alkylation
  – Trout are particularly sensitive (0.4 ppb)
  – Developmental problems in children??

• Tightly regulated due to health risks
Aflatoxin action levels in feeds

- **United States (regulated by the FDA)**
  - 20 parts per billion (ppb) - For corn and other grains intended for immature animals (including immature poultry) and for dairy animals, or when its destination is not known;
  - 100 ppb - For corn and other grains intended for breeding beef cattle, breeding swine, or mature poultry;
  - 200 ppb - For corn and other grains intended for finishing swine of 100 pounds or greater
  - 300 ppb - For corn and other grains intended for finishing (i.e., feedlot) beef cattle and for cottonseed meal intended for beef cattle, swine or poultry.
  - 20 ppb – All other animal feeds
Aflatoxin action levels in human food

- AM1 in milk: 0.50 ppb
  - Expected when AB1 in dairy cattle feed exceeds 40 ppb
- Other food: 20 ppb total

- Action levels in Europe are lower (but controversial)
  - 5 ppb for AB1
  - 4-10 ppb total depending on type of food
  - 0.05 ppb AM1 in milk
Treatment

• Remove the source
• There is no specific treatment
  – Provide supportive treatment depending on Sx
  – Animals are relatively non-responsive to treatment
• Good nutrition (high quality protein and carbohydrate)

Prognosis guardered: Even after removal of Aflatoxin, the liver’s return to normal function may be delayed
Penitrem A and Rocquefortine

- Penitrem A is associated with moldy nuts /cream/cheesecake
- Rocquefortine is often found in grass

**Neurotoxic**
- Inhibits glycine and GABA
- Promotes presynaptic acetylcholine release
- Dogs and cats are most sensitive.
- Acute onset of tremors (typically within 30 minutes)
- Death at high doses
Treatment

• Remove source
• Decontaminate
  – Emesis,
  – Activated charcoal + cathartic
• 0.5-5 mg/kg Diazepam to effect for seizures
  – Pentobarbital 14-30 mg/kg if ineffective.
• Fluid therapy as needed

Prognosis:
• Dogs that don’t respond to diazepam have a poor prognosis
• Otherwise guarded to fair prognosis, depending on dose
• Recovery is usually complete in 24-48 hours
Mycotoxins not originating in mold

- Mushrooms
- Fungus-metabolized phytochemicals
- Endophytes

A. *muscaria* (fly agaric)

(nmazca.com)
Amanita mushrooms (Amanita spp.)

- Responsible for most fatal mushroom poisonings in animals and humans

A. muscaria (fly agaric)
(nmazca.com)

A. phalloides (death cap)
(http://s3.amazonaws.com/lcp/revuyon/myfiles/Amanita_phalloides_1.JPG)
Description

• Universal veil often leaves a volva or other veil remnants

• Characterized by pale gills free from the stem

• White spore prints
Toxicity syndrome

- **Cyclopeptides**
  - Amatoxins, phallotoxins, virotoxins
  - Inhibit DNA and RNA transcription

- **Triphasic syndrome (useful in diagnosis)**
  - Gastroenteritis (lasts up to 24 hours)
    - Vomiting, hemorrhagic diarrhea
  - Latent phase (lasts 12-24 hours)
    - GI signs improve
    - Early signs of liver failure (enzyme elevations)
  - Liver and kidney failure (delayed up to 3-4 days after ingestion)
    - Progressive liver and kidney failure
    - Neurologic dysfunction
    - Death 3-7 days after ingestion