Trichothecenes

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Trichothecene Mycotoxins: Deoxynivalenol, T-2 Toxin, Diacetoxyscirpenol [DAS] Macrocyclic Trichothecenes
(als0 see Dermal Effects of Trichothecenes)

<table>
<thead>
<tr>
<th>Specific Agents</th>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Trichothecenes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deoxynivalenol (vomitoxin)</td>
<td>Swine, cattle, dogs, and poultry</td>
<td>Hours to days</td>
<td>Days; unlikely to be lethal</td>
<td></td>
</tr>
<tr>
<td>T-2 toxin, HT-2 toxin, diacetoxyscirpenol (DAS), related and macrocyclic trichothecenes</td>
<td>Cattle, swine, small animals, poultry</td>
<td>Hours to chronic</td>
<td>Days, potentially lethal</td>
<td></td>
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</tbody>
</table>

Introduction

Trichothecene mycotoxins: (12,13 epoxytrichothecenes) comprise a group of over 50 compounds of widely varying toxicity that are produced primarily by field fungi of the genus Fusarium.

Sources

- Trichothecenes tend to be produced in toxic concentrations in years of wet weather when harvests are delayed and prolonged.
- Trichothecenes known to cause problems in farm animals include: deoxynivalenol (vomitoxin), nivalenol, T-2 toxin, diacetoxyscirpenol (DAS), macrocyclic trichothecenes (roridin A verrucarin A satratoxins), as well as others. In the U.S. and Canada, deoxynivalenol appears to be the most significant member of the group despite its comparatively low toxicity. T-2 toxin has caused widespread epidemics in human beings in the Soviet Union and, as with DAS, is an occasional cause of outbreaks of important toxicoses in animals in North America.
- Deoxynivalenol is produced by Fusarium fungi, especially F. roseum (Giberella zeae, F. graminearum) with corn (Zea mays) and sometimes wheat (Triticum spp.) as well as other small grains being the most important sources of exposure to livestock.
  - Mild temperatures tend to encourage mold growth and cool temperatures increase toxin production by F. roseum. Therefore fluctuating warm to cool temperatures in the presence of high grain moisture concentrations increase the likelihood of deoxynivalenol and zearalenone poisoning. These toxins arise especially as a result of field infection, but occasionally improper storage can greatly magnify the problems.
- T-2 toxin is produced especially by F. sporotrichioides.
- Undulating temperatures on the cold side tend to be associated with contamination of cereal grains with T-2 toxin and diacetoxyscirpenol. Thus, T-2 toxin and diacetoxyscirpenol occur especially during years of delayed harvests when grains are left in the field over the winter and temperatures are highly fluctuant. These toxins, along with deoxynivalenol and zearalenone, were detected in specimens of the alleged chemical warfare agent, yellow rain. T-2 toxin may occur in corn but the highest concentrations generally occur in small grains such as barley and wheat. Forages are sometimes contaminated.
- Macro cyclic trichothecene toxins in plant tissues of the Baccharis genus cause severe toxicoses in herbivores in Brazil.
- Macro cyclics also are sometimes produced by Stachybotrys atro in wet forages and/or straw as well as in rain-damaged building materials and water-soaked air ducts. All these sources have resulted in clinical poisoning problems.

Mechanisms of Action

- Trichothecenes are potent inhibitors of peptidyl transferase a ribosomal enzyme that is essential for protein synthesis. Thus, the trichothecenes inhibit protein synthesis.
- Trichothecenes also inhibit uptake of amino acids.
- Trichothecenes promote uptake of calcium and this is believed to trigger apoptosis.
Some Trichothecene Mycotoxins

Toxicity

- Experimentally, 4 ppm deoxynivalenol has caused a 2% reduction in feed intake while at 40 ppm a 90% reduction was observed. In the field, however, concentrations of DON associated with feed refusal may be as low as 1 ppm.
- T-2 Toxin and DAS are far more acutely toxic than deoxynivalenol, T-2 and DAS infrequently cause major outbreaks of serious toxicosis in livestock and poultry.

Signs

- Deoxynivalenol (DON, Vomitoxin):
  - Swine appear to be most susceptible, but cattle, horses, dogs and poultry are all reported to be susceptible.
  - Though not among the more acutely toxic trichothecenes, deoxynivalenol, has caused great economic loss to the livestock industry.
  - The predominant sign associated with contaminated feed is reduced feed intake (or occasionally feed refusal) and decreased rate of gain.
  - Other signs may include soft stools, diarrhea, failure to thrive, and a predisposition to other disease entities and poor nutrition.
  - Vomiting is infrequently seen therefore the name vomitoxin seems inappropriate.
  - Animals may develop a resistance to deoxynivalenol and make compensatory gains.
  - Although a mild thickening of the squamous mucosa of the stomach has been noted experimentally, specific lesions may not be found.
- T-2 Toxin, Diacetoxyisocirpenol (DAS), and Macro cyclic Trichothecenes.
- Problems involving T-2 toxin, DAS, and macrocyclic trichothecenes occur mainly in cattle, hogs and poultry, and occasionally in horses, dogs, cats, and humans.
- Signs most often would include:
  - Increased incidence of infection.
  - Reduced feed intake or feed refusal.
  - Vomiting and diarrhea.
  - Necrosis of skin and oral mucosal damage.
- Less often one may see:
  - Hemorrhage and necrosis of GI mucosa (high doses).
  - Destruction of hemopoietic tissue and lymphoid necrosis (high doses).
Meningeal hemorrhage (massive doses).
Shock and death (massive doses).

Reproductive Effects
- At doses toxic to the dam, embryo toxicity and fetotoxicity, and possible abortion may occur.
- Testicular damage in males may occur with highly toxic levels of exposure.
- *Stachybotrys atia*, cause of stachbotryotoxicosis is a black mold that produces macrocyclic trichothecenes. These toxins in straw have poisoned horses and farm workers. When the mold grows in water-damaged homes or air ducts people become chronically affected.

Dermal Effects of Trichothecene Mycotoxins
- Only the more potent trichothecene mycotoxins are known for their effects on the skin. The local cytotoxic effects of these compounds may produce lesions on the snout, muzzle, lips and tongue. T-2 toxin, diacetoxyscirpenol and other trichothecenes, especially the macrocyclic toxins which have been recognized primarily in Europe, have dermal effects although other effects are more toxicologically important. The trichothecene believed to be of greatest importance in the USA, deoxynivalenol, also called vomitoxin, is less potent in most respects and is not known for any significant dermal effects.
- Stachbotryotoxicosis results from macrocyclic trichothecenes in Europe, especially in the eastern countries. The most severe outbreaks have occurred in large animals and are a result of contact with contaminated forages. Persons handling the affected forages have also experienced dermal and respiratory irritation. Affected animals experience the effects of the cytotoxic properties of the trichothecenes present. Perioral, pharyngeal and gastrointestinal irritation all result.
- Similar perioral, pharyngeal and gastrointestinal effects are seen with T-2 toxin and diacetoxyscirpenol.
- In calves dosed with T-2 toxin orally for up to 6 weeks, atrophy of the thymus was a consistent finding. Clotting disorders and reproductive problems have also been reported with T-2 toxin but the former have not been readily reproduced experimentally.

Diagnosis
- When a history includes feed refusal and failure to thrive, several mycotoxins should be included in the differential diagnosis.
- When mycotoxins are suspected, feed should be submitted for a mycotoxin screen.
- It may be wisest to submit some of the worst looking feed to account for "the worst case exposure" and a separate sample collected as to represent the balance of the feed on hand (a composite from several locations) to represent the feed as a whole. Ship at least 3 kg of each frozen or at a moisture concentration of 3% or less to the lab via priority mail or some even faster method.
- Testing for the presence of the trichothecene mycotoxins in feed is the most important means of arriving at a definitive diagnosis. Specific quantitative assays are available for a limited number of trichothecenes at most diagnostic laboratories. However, for the most comprehensive screen for trichothecenes, contact Dr. Howard Casper at the Toxicology Laboratory at North Dakota State University in Fargo, ND (telephone: 701/231-7529). Agri-Screen ELISA tests for DON and T-2 toxin are available.
- These mycotoxins are not found at very high concentrations in tissues, although stomach contents may contain detectable levels if the animals were eating prior to death.

Treatment
- There are no specific antidotes for trichothecene mycotoxins, therefore, supportive and symptomatic treatment are indicated.
- Questionable feed should be removed and replaced by good quality feed with additional protein supplementation.
- Stress should be reduced to a minimum.

Prevention
- These mycotoxicoses are best controlled by proper grain handling and avoidance of questionable feeds.
- When necessary, analyses may be performed on feed, however, a negative test result does not preclude the presence of mycotoxins in some other areas of the bulk feed.
- Test animals can also be fed suspected grain and monitored for feed refusal and other signs of trichothecene mycotoxicoses.

References

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