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2003

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Carlson, Michael P. and Ensley, Steve M., "G03-1513 Understanding Fungal (Mold) Toxins (Mycotoxins)" (2003). *Historical Materials from University of Nebraska-Lincoln Extension*. 1785.

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Understanding Fungal (Mold) Toxins (Mycotoxins)

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This NebGuide briefly discusses mycotoxins commonly encountered in grains and feeds used in Nebraska and the mycotoxicoses they cause. Mycotoxin sources and clinical signs, lesions, diagnostic aids and treatment for each mycotoxicosis are listed.

Mycotoxins are chemicals produced by fungi (molds) under certain conditions. They are not essential for fungal growth or reproduction, and are toxic to animals or humans. Scientists do not yet know how many mycotoxins may exist, even though more than 250 have been detected. They represent many different kinds of chemicals. For many, if not most, their toxicological characteristics have not been fully determined.

Diseases in animals caused by mycotoxins are called mycotoxicoses. There are many different kinds of mycotoxicoses because there are many different kinds of mycotoxins.

This NebGuide is not intended to allow animal owners to diagnose cases of mycotoxicoses without consulting a veterinarian. Diagnosing mycotoxicoses is not easy. Other diseases besides mycotoxicoses can cause similar clinical signs or lesions, and the expertise of a veterinarian is vital to accurate diagnoses. Otherwise, valuable resources may be worthlessly expended treating wrong diseases.

The medical vocabulary used here may not be familiar to some readers. Those words are used to minimize the size of this NebGuide. Definitions of unfamiliar words may be found in medical dictionaries.

Mycotoxicoses and Mycoses

Diseases called mycotoxicoses and mycoses are sometimes confused. They are not the same. Diseases caused by mycotoxins are called mycotoxicoses. Diseases caused by mold infections are called mycoses.

Mycotoxicoses occur when mycotoxins enter the body, usually by consumption of contaminated feed. Ill health is caused by actions of mycotoxins on cells in the body. Mycotoxicoses are not contagious, nor is there significant stimulation of the immune system.

Mycoses occur when molds infect tissues of the body. They can be contagious. Molds begin to grow in or on the body after the infections are established. There may be stimulation

of the immune system. Common mycoses include athlete's foot and ringworm.

Diagnosis and Treatment of Mycotoxicoses

Different mycotoxins cause different diseases. Although they all are called mycotoxicoses, they are very different from each other.

Modern agricultural practices make acute mycotoxicoses with high death loss (mortality) rare. Chronic mycotoxicoses are often suspected when clinical signs include poor performance, ill thrift, or increased incidence of infectious diseases. Establishing cause and effect relationships between consumption of mycotoxin-contaminated feed and vague chronic conditions is very difficult.

Diagnosis of mycotoxicoses is usually not very easy. Exposure cannot be established by detection of mycotoxins in tissues from animals suspected of being poisoned by mycotoxins because analytical services for detection of mycotoxins in animal tissues are not commonly available. We must rely on the detection of mycotoxins in grain or feed to help establish the diagnosis.

Investigation of suspected mycotoxicoses should begin by obtaining thorough histories. Clinical signs are very important because they can be used to select appropriate diagnostic tests to help confirm or refute mycotoxicoses. Investigation of suspected mycotoxicoses should include histopathological examination of tissues from affected animals whenever possible. Specific histopathological lesions may be evidence of mycotoxicoses. If there are no lesions in or evidence of pathology in organs known to be effected by mycotoxins, then likelihood of a mycotoxicosis is reduced.

Confirmation of suspected mycotoxicoses is assisted by either reproducing the clinical disease during a feeding trial using the suspected ration, or by detection of a known mycotoxin in the ration or tissues of animals consuming the ration. Feeding trials are not routinely performed because they are difficult to conduct, expensive, and slow to provide results. Detection of **known** mycotoxins in feeds is relatively easy with modern analytical chemical methods.

One of the most challenging aspects of diagnosing cases of suspected mycotoxicoses is collecting a feed sample that adequately represents the feed suspected of being contami-

nated. Mycotoxins are not evenly distributed in feeds, so the contaminated part of the feed may be consumed before disease is evident. Collection of meaningful feed specimens under such conditions is very difficult. More information about feed specimen collection and analysis for mycotoxins may be found in NebGuide G1515, *Sampling and Analyzing Feed for Fungal (Mold) Toxins (Mycotoxins)*.

Interpreting the significance of finding mycotoxins present in the ration is difficult. If a mycotoxin is detected in feed, the disease it causes should match the clinical syndrome observed for the case and its concentrations should be sufficient to cause a mycotoxicosis. If not, it is unlikely that the presence of the mycotoxin in the feed is significant.

Treatment of animals suffering from mycotoxicoses usually is supportive and often not very effective. Antidotes for mycotoxins are generally not available. Stopping and preventing further exposure by removing contaminated feed is important.

It is not uncommon for animals to improve after they quit eating feed suspected or known to be contaminated with mycotoxins. Such an occurrence supports the suspicion of the feed as a causal factor, but does not prove that the animals suffered from a mycotoxicosis.

Health effects, clinical signs, lesions and treatment for selected mycotoxicoses. (Reference: Osweiler, G.D. (1996) *Toxicology*, William & Wilkins, Media, PA: 416-432.)

Aflatoxicosis

Aflatoxicosis is caused by **aflatoxins**, produced by *Aspergillus flavus* and *Aspergillus parasiticus*. Aflatoxins are commonly found in corn, milo, cottonseed and peanuts. Aflatoxin concentrations in grains produced in Nebraska rarely contain enough aflatoxin to cause acute aflatoxicosis.

There are five important aflatoxins, called aflatoxin B₁, B₂, G₁, G₂, and M₁. Aflatoxin M₁ is a metabolite of aflatoxin B₁ found in milk and urine. It is formed after aflatoxin B₁ enters the body. It **is not** found in feed. Aflatoxin B₁ is found most frequently and in the highest concentrations in naturally contaminated feed.

Aflatoxin is a liver poison (hepatotoxin) in all species that consume it, however, ruminants tolerate it better than do monogastrics or poultry. It causes liver damage at higher doses and liver cancer at lower doses. Aflatoxin exposure can depress the immune system. It may cause abortions in some instances, however the circumstances necessary for abortions to occur are not well defined.

Clinical signs of aflatoxicoses:

Acute exposure, all species: Depression, anorexia, reduced gain or milk production, subnormal body temperature.

Chronic exposure, poultry: Decreased growth rate, reduced feed efficiency, steatorrhea (fat in feces), bruising.

Chronic exposure, swine: Anorexia, unthriftiness, slow growth, icterus, mild anemia, ascites, increased susceptibility to infection.

Chronic exposure, cattle: May slow rumen motility for 24 to 48 hours.

Lesions of aflatoxicosis:

Acute exposure: Hemorrhage, ascites.

Chronic exposure: Pale, soft, clay-colored liver, mild anemia, icterus, ascites.

Histopathological: Hepatocyte degeneration and necrosis; centrilobular hemorrhagic hepatic necrosis, fatty changes

and regeneration of hepatocytes; bile duct epithelial proliferation progressing to interlobular fibroplasia and extensive proliferation; Karyomegaly, atypical nuclei, hepatocytic vacuolization, bile retention.

Diagnostic aids for aflatoxicosis:

Blood workup: Check for anemia, elevated liver enzymes, serum bile acids, albumin:globulin ratio; prothrombin activity.

Tissue or fluid analysis: Aflatoxin M₁ present in milk or urine; parent compound may be present in kidney or liver.

Grain or feed analysis: Aflatoxins are most likely to be present in corn, peanuts or cotton seed. They are not likely to be present in forages or silage at significant concentrations. Dietary aflatoxin concentrations at which performance or clinical effects become noticeable depends upon species and effect. Decreased performance may occur at concentrations as low as 200 ppb in young, sensitive species. Immunity may become impaired at concentrations of about 200 ppb. Hepatic lesions may become noticeable at 200 to 400 ppb. Clinical illness may become obvious at about 400 ppb. Generally, ruminants are most resistant and swine and avian specimens least resistant to adverse effects. Violative residues in milk can occur at concentrations at or near 50 ppb aflatoxin.

Treatment for aflatoxicosis:

Stop exposure. Stop feeding contaminated ration and replace with noncontaminated ration.

Supportive treatment. Provide supportive treatment as clinical situation dictates.

Ergot Toxicosis

Ergot toxicosis is a disease caused by the ingestion of ergot alkaloids contained in the sclerotia of *Claviceps* spp. They are commonly found in cereal grains, especially rye. Tall fescue (*Festuca arundinaceae*) may contain the endophytic fungus *Neotyphodium coenophialumin* (*Acremonium coenophialum*), which can also make ergot alkaloids.

Sclerotia are dark brown, brownish-purple or black colored bodies that stick out from the seed heads of infected plants. They are visible to the naked eye and look similar to rodent droppings when removed from the seed heads. They may become quite large, up to an inch in length.

Several different ergot alkaloids may be present in sclerotia. They cause two syndromes: a central nervous system disorder and a peripheral vascular disorder. They can cause agalactia in lactating females.

Ergot alkaloids are potent smooth muscle stimulants. Any organ with smooth muscle in it may be affected, especially arterioles. Uterine contractions may be stimulated.

Clinical signs of ergot toxicosis:

Peripheral vascular syndrome: Lameness, swelling of feet and fetlocks; sharply demarcated necrosis of feet, ears or tail. In severe cases, hooves or feet, or tail may slough. Dry gangrene. These effects are due to ischemia resulting from constriction of arterioles in peripheral vascular beds.

Lactating females: Cessation of milk production; agalactia in post-partum females.

Central nervous system syndrome: Hyperexcitability, hypermetria, tremors; heat intolerance in cattle.

Lesions of ergot toxicosis:

Described above under clinical signs for peripheral vascular syndrome. Additionally, small and flaccid mammary glands of females in late pregnancy, with no evidence of secretions, are indications of probable agalactia.

Histopathological: Endothelial damage, thrombosis, coagulative necrosis.

Diagnostic aids for ergot toxicosis:

Analysis of stomach or rumen content for ergot alkaloids.

Detection of ergot alkaloids in stomach or rumen content is evidence of exposure.

Analysis of feed or grains for ergot alkaloids ingested by affected animals. Sclerotia may be visible if the feed has not been ground.

Treatment for ergot toxicosis:

Stop exposure. Remove contaminated grain or feed from ration.

Lactation may commence 5 to 7 days afterwards.

Control secondary infections in limbs suffering from dry gangrene.

Place animals in a warm, clean, stress-free environment.

Fumonisin Toxicosis

Fumonisin is produced by *Fusarium moniliforme* and *F. proliferatum*, and is found primarily in white and yellow corn. There are three kinds, called fumonisins B₁, B₂, and B₃. Fumonisin B₁ is most prevalent in naturally contaminated corn and it is the most toxic.

Horses and pigs are the most sensitive species. Equine leukoencephalomalacia (ELE) is a fatal disease of horses caused by fumonisins. Porcine pulmonary syndrome is the form of the disease in swine. The mechanism of action is believed to be the inhibition of enzymes involved in the production of sphingosine from sphinganine. Sphingosine is an important component of cell membranes, especially for neurons.

Clinical signs of fumonisin toxicosis:

Swine: Dyspnea, cyanosis, and weakness, which develop 4-7 days after fumonisin-contaminated feed begins. Death may occur within a few hours of onset of the syndrome.

Horses: Depression, blindness, ataxia, aimless wandering, facial paralysis, which may rapidly progress to coma and death. Death may occur 1 to 7 days after onset of signs.

Ruminants: May develop anorexia and suffer mild weight loss if fumonisin concentrations approach 200 ppm. Few other significant or persistent signs.

Poultry: Appear to be more resistant than other species. Inappetence and skeletal abnormalities may develop at concentrations of 200 - 400 ppm.

Lesions of fumonisin toxicosis:

Swine: Acute pulmonary edema characterized by marked to massive intralobular pulmonary edema and marked hydrothorax. Lungs are distended and turgid. Thoracic cavity is filled with straw-colored proteinaceous fluid. Microscopically, interstitial and interlobular edema. May include multiple areas of focal pancreatic necrosis and hepatic lesions characterized by disorganized hepatocytes, increased mitotic figures, necrosis of single hepatocytes and mild bile retention. Icterus.

Horses: Leukoencephalomalacia – massive softening and liquefaction of cerebral white matter, ranging from discrete focal areas to large cavitations and inward collapse of the cortical gray matter. Hemorrhage is prominent. Micro-

scopically, liquefaction and proliferation of macrophages in response to necrosis.

Diagnostic aids for fumonisin toxicosis:

Blood workup: Evidence of hepatic dysfunction.

Tissue analysis: Sphinganine:sphingosine ratio is increased. Analysis of tissues for sphinganine and sphingosine is not readily available.

Analysis of corn or corn-containing feed for fumonisins:

Concentrations in excess of 3 ppm fumonisin may be significant for horses. Concentrations above 5 ppm may be significant for pigs.

Treatment for fumonisin toxicosis:

Stop exposure. Remove contaminated feed from ration. Because of the long time between consumption of feed and onset of signs, oral detoxification is not recommended.

Supportive treatment – prognosis for horses and pigs suffering from advanced stages of the disease is poor.

Vomitoxin (Deoxynivalenol, DON) Toxicosis

Vomitoxin is produced by *Fusarium roseum* (*F. graminearum*) and *F. moniliforme*. It is found in corn, wheat, barley, milo and occasionally in oats. It is rarely found in hay or forages. *F. Roseum* also produces zearalenone, so DON may also be found with zearalenone.

Vomitoxin is a chemical that belongs to a group of mycotoxins called tricothecenes. There are at least 140 chemicals in that class, including T-2 toxin and diacetoxyscripenol (DAS). Tricothecenes other than vomitoxin are rarely, if ever, found in grain grown in Nebraska.

Vomitoxin is not very toxic, but it is associated with feed refusal and decreased feed consumption, which can affect animal performance. Concentrations ranging from 5 to 10 ppm are associated with vomiting in pigs, hence its name. Thresholds for decreased feed intake are about 1 ppm in swine and 10 to 20 ppm in ruminants.

The mechanism by which vomitoxin acts has not been elucidated. Other tricothecenes inhibit protein and nucleic acid synthesis.

Cattle are very resistant to the effects of vomitoxin. Pigs are more sensitive. There have been reports of health effects in dogs from pet foods contaminated with vomitoxin-containing grains.

Clinical signs of vomitoxin toxicosis:

Swine, dogs, cats – feed refusal, vomiting; cattle – usually none, however some reports of feed refusal may be found in the scientific literature; poultry – usually none.

Lesions of vomitoxin toxicosis:

No gross or histopathological lesions have been reported in animals consuming vomitoxin-contaminated feed.

Diagnostic aids for vomitoxin toxicosis:

Analysis of grains or feeds. Forages are seldom, if ever, contaminated with vomitoxin.

Analysis of tissues from affected animals: Not available.

Treatment for vomitoxin toxicosis:

Remove vomitoxin-contaminated grain/feed from ration.

Zearalenone Toxicosis

Zearalenone is produced by *Fusarium roseum* (*F. graminearum*) and *F. moniliforme*. It is found in corn, wheat,

barley, milo and occasionally in oats. *F. Roseum* also produces vomitoxin (deoxynivalenol, DON), so vomitoxin may also be found with zearalenone.

Zearalenone is a chemical that can act similarly to the female sex hormone estrogen. Excessive exposure does not cause death or abortions, but it can disrupt the estrus cycle in females, cause infertility and feminization in males, and precocious puberty in sexually immature females. Zearalenone content typically found in Nebraska grains is usually not enough to adversely affect animals, but unusual environmental conditions during the growing season, or insufficiently dried grain put up for storage may increase zearalenone production.

Clinical signs of zearalenone toxicosis:

Clinical signs vary with species, sex and age of the animal.

Swine, sexually immature gilts: Behavioral estrus, swollen and edematous vulva, enlarged mammary glands, tenesmus (spasmodic contraction of anal or bladder sphincter), sometimes vaginal or rectal prolapse; clinical signs appear 2-7 days after exposure begins and subsides 4 to 10 days after exposure ends.

Swine, mature sows: Exposure early in estrus cycle – suppression of ovulation and signs of estrus that are severe and prolonged; exposure mid-cycle – pseudopregnancy, anestrus which may persist for 40 to 60 days after exposure stops.

Swine, castrated boars: Enlarged prepuce and nipples.

Swine, immature boars: Reduced libido, retarded testicular development.

Swine, mature boars: Not effected unless dietary concentrations reach 200 ppm or higher. Such concentrations are rarely encountered in U.S. grains.

Lesions of zearalenone toxicosis:

Lesions are present only in the reproductive system.

Prepubertal gilts: Swollen and edematous vulva; enlarged mammary glands; enlarged, hypertrophic and edematous uterus. Histopathologically, uterine and vaginal metaplasia and follicular atresia.

Mature sows: Retained and functional corpora lutea with anestrus. Mammary alveolar development and ductular squamous metaplasia.

Diagnostic aids for zearalenone toxicosis:

Blood workup: Serum analysis for estrogen can help rule out an organic hormonal problem.

Tissue or fluid analysis: Not available.

Feed or grain analysis: Since clinical effects are delayed several days after ingestion, feed analysis may be of limited value. A specimen collected after the problem is noticed may not contain detectable amounts of zearalenone. Planned retention and dating of feed specimens aids in the identification of zearalenone-contaminated feed.

Differential considerations for zearalenone toxicosis:

Other estrogenic chemicals from plants (phytoestrogens) or other sources could also produce some of the signs of zearalenone toxicosis. An expensive, but possibly valuable estrogenic assay of feed is available to help assess

estrogenic activity of the feed. That assay detects any chemical with estrogenic activity that might be present in the feed.

Treatment for zearalenone toxicosis:

Stop exposure. Remove contaminated feed and replace with un-contaminated feed. Signs may persist for several days afterwards.

Decrease zearalenone absorption: Activated charcoal may help limit absorption of ingested zearalenone by individual animals. Several commercially available feed additives are advertised to bind zearalenone and help prevent excessive exposure. The efficacy of such additives may not have been adequately assessed. Thoroughly assess the evidence offered by manufacturers before using them. Such use may require approval by federal regulatory agencies before it can be used legally.

Prevention of Mycotoxins

Purchase grain or feed that are free of mycotoxins.

Have feed analyzed for mycotoxins before purchase or use. Make mycotoxin analysis a condition of sale. Require that the seller have the feed analyzed by a suitable laboratory before you accept delivery. However, it may be difficult to find feed free of mycotoxins sometimes because they occur naturally.

Remove grain or feed contaminated with mycotoxins.

Substitute grain or feed known not to be contaminated.

Use of feed additives to bind mycotoxins.

Mycotoxin binders are commercially available, but before purchase, determine if the product can be legally used for such purposes. Ask the seller if the product is approved under federal law or regulations for use as mycotoxin binder. If the seller claims such approval is not necessary, or if the seller cannot document approval, consult with staff at the Center for Veterinary Medicine (CVM) of the U.S. Food and Drug Agency. Its Web site address at the time this NebGuide was published is www.fda.gov/cvm/. Or, contact the regional office listed below:

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**Index: Plant Diseases
Field Crops**
Issued June 2003