Abdominal Intoxication - Our Experiences in USA (16-Dec-2003)

D. E. Freeman

College of Veterinary Medicine, University of Illinois, Urbana, IL, USA.

Poisonings pose diagnostic challenges in horses because they are so rare that few veterinarians have sufficient experience to recognize them, and signs can be subtle, non-specific, and easily confused with other diseases. Many cases are treated as colic, because the predominant signs fit that group of diseases more than any other. Although several plants do cause signs of abdominal disease, many that target other organs can cause tachycardia, tachypnea, patchy sweating, depression, inappetance, abnormal gait, and other signs that can be interpreted as colic. Conversely, horses that are presented as cases of suspected plant toxicity are often afflicted with another disease. Unfortunately, poisoning can be difficult to prove, which can complicate the handling of cases with legal ramifications. In suspect cases, history is critical, and samples of feed, pasture or hay must be examined closely for weeds and other contaminants. Other horses on the same premises should be examined for early signs of poisoning, and should receive different food until the suspect case is resolved. Post mortem diagnosis depends on careful sampling of tissues and gastrointestinal tract contents, combined with a detailed history and clinical signs.

Medications

Drugs discussed in this section are indispensable to daily equine practice, but they can be toxic if used in excessive doses or under inappropriate conditions. However, some horses can have an idiosyncratic sensitivity to commonly used agents that render them susceptible at low doses and with light treatment regimens. An example are nonsteroidal anti-inflammatory drugs, such as phenylbutazone, which have a wide margin of safety for many horses but very narrow for others. An awareness of these potential intoxications is essential, so owners can be warned, the drugs in question can be used judiciously, and intoxication can be recognized early and treated.

Laxatives -

Magnesium sulfate (1.0 g/kg in 2 to 6 L of water) is one of the oldest laxatives in use and may be given twice daily with little risk of a toxic effect (Freeman et al. 1992). However, repeated doses can cause weakness, collapse, and tachycardia from effects of the magnesium ion, which is absorbed more readily if magnesium sulfate is given with dioctyl sodium sulfosuccinate (DSS; Henninger and Horst 1997). Treatment of toxicosis is IV calcium and diuresis with IV fluids (Henninger and Horst 1997). Dioctyl sodium sulfosuccinate (10 to 20 mg/kg) is an ineffective laxative in human beings and of questionable value for horses at a dose of 50 mg/kg (Freeman et al. 1992). It can increase mucosal permeability, cause surface damage and inflammation, and delay gastric emptying, and a dose of 50 mg/kg can cause signs of colic that might be masked in a horse with existing signs of colic (Freeman et al. 1992). Toxic doses (650 mg to 1 g/kg) to horses can cause colic and severe watery diarrhea, which can be attributed to mucosal damage in the stomach and small intestine and fluid accumulation throughout the gastrointestinal tract (Moffat et al. 1975).

The active ingredient in castor oil, the C-18 hydroxy fatty acid, ricinoleic acid, has been used as an irritant laxative, particularly in a laxative cocktail for foals with nonresponsive meconium impaction at a dose of 2 oz, with 8 oz of mineral oil and 4 oz of milk of magnesia. At 2.5 ml/kg PO, castor oil causes a severe colitis in ponies, associated with surface epithelial disruption in the colon (Roberts et al. 1989). Linseed oil has been used successfully as a laxative in horses and has been proposed as a feed additive to depress synthesis of prostaglandins during endotoxemia (Schumacher et al. 1997). Linseed oil is produced from flaxseed as raw oil, but must not be used in any preparation in which it is included as a wood preservative. In one study, raw oil at 2.5 ml/kg (~ 1 quart per 1,000 lb) twice daily caused watery diarrhea, colic, depression, and signs of endotoxemia in clinically healthy horses (Schumacher et al. 1997). In the same study, mineral oil was safe. The toxicity of linseed oil was attributed to mucosal damage from saponification products in the intestinal lumen.
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Phenylbutazone toxicity in horses causes anorexia, depression, melena, diarrhea, weight loss, ventral edema, petechial hemorrhages, alimentary tract erosions and ulcers, renal papillary necrosis, and death (Collins and Tyler 1985; Meschter et al. 1990; MacAllister et al. 1993). Dehydration could increase the risk of renal damage. Hypoproteinemia and hypoalbuminemia are sensitive biochemical indicators of NSAID toxicity in horses. In healthy adult horses, phenylbutazone (4.4 mg/kg), flunixin meglumine (1.1 mg/kg), or ketoprofen (2.2 mg/kg), IV, q 8 hours for 12 days induced toxic effects in decreasing order of severity (MacAllister et al. 1993). In the stomach of adults and foals, phenylbutazone causes more extensive ulceration in the glandular mucosa and even the pyloric region than in the nonglandular mucosa (Meschter et al. 1990; MacAllister et al. 1993; Traub et al. 1983). Gastric mucosal injury by NSAIDs has been attributed to reduced mucus and/or bicarbonate production, decreased mucosal blood flow, neutrophil plugging of capillaries, and impaired healing (Wallace 1997). Right dorsal colitis is an insidious disease caused by diffuse and superficial necrosis with scattered erosions and ulcers attributed to NSAID toxicosis (Karcher et al. 1990). The chronic form has a high mortality from colonic stenosis, luminal impaction, and colonic rupture (Karcher et al. 1990). Topical irritant properties of NSAIDs are not as important contributors to their ulcerogenic effects as their ability to suppress prostaglandin synthesis (Wallace 1997).

Antimicrobial-associated Colitis

Antimicrobial-associated diarrhea is a well recognized iatrogenic disease in horses, and is considered to have a worse prognosis than other types of acute diarrhea (Cohen and Woods 1995). In one study, the risk of salmonellosis was 6.4 times greater in horses treated with antibiotics parenterally and 40.4 times greater in those treated with antibiotics orally and parenterally, compared with horses that did not receive antibiotics (Hird et al. 1986). In a recent study, horses with a history of receiving antimicrobials were 4.5 times less likely to survive from the resulting diarrhea than horses with diarrhea that did not receive these drugs (Cohen and Woods 1995). Antibiotics incriminated in antimicrobial-associated diarrhea are tetracyclines, lincomycin, erythromycin, trimethoprim-sulfonamides, ceftiofur sodium, and penicillin (Hird et al. 1986; Cohen and Woods 1995).

Antibiotic-associated colitis is well recognized in Sweden in mares of foals that are being treated with erythromycin ethylsuccinate, presumably through ingestion of minute quantities of the drug from contaminated surfaces (Gustafsson et al. 1997). The greatest concern for colitis might apply to those antibiotics that undergo enterohepatic circulation. Although Salmonella species are the organisms most commonly incriminated in antimicrobial-associated diarrhea, Clostridium difficile and other organisms could be involved also (Baverud et al. 1997).

Sedatives, Tranquillizers, Narcotics, and Others

A number of sedatives, tranquillizers, narcotics, and other drugs have been shown to inhibit gastrointestinal tract motility to some extent, and therefore have the potential to cause or predispose to impaction colics (Freeman 1999). Examples are detomidine, xylazine, morphine, fentanyl, meperidine (a synthetic narcotic), pentazocine (a synthetic narcotic agonist/antagonist), butorphanol (a synthetic opioid agonist/antagonist), loperamide, pethidine, atropine, glycopyrrolate, epinephrine, norepinephrine (α1-adrenergic agonist), isoproterenol (β-adrenergic agonist), phenylephrine (α1 agonists), salbutamol (β2 agonist), amitraz (a formamidine acaricide with probable α2-adrenergic effects), phenoxybenzamine, diphenoxylate, hyoscine, acepromazine, methadone, and common anesthetic regimens (Ducharme and Fubini 1983; Lester et al. 1992; Freeman 1999).

Miscellaneous

Mercury poisoning is rare in horses and application of organomercurial fungicides to grains has been banned since 1970 (Bailey 1992). The most common source of mercury for horses is in blisters, such as red iodide of mercury, applied as counterirritants to injured tendons, ligaments, and dorsal metacarpal periostitis. Although the treated limb is usually well protected, horses will lick and bite at the treated site if they can and thereby ingest the blister. This can cause severe oral and pharyngeal ulcers and inflammation throughout the gastrointestinal tract.

Iron toxicosis is rare in horses, although an "outbreak" of ferrous fumarate toxicosis with a high mortality has been described in neonatal foals that were given a Lactobacillus preparation called "Primapaste" (Divers et al 1983). Clinical signs were severe depression, icterus and other clinical and laboratory evidence of liver disease, and necropsy findings were marked liver atrophy and hepatocyte necrosis. Bile duct proliferation was so severe that the initial impression was that the process started in utero. The mechanism of toxicity is enhanced free radical damage, and disruption of normal mitochondrial
function and enzyme activities (Beasley 1999).

Poisonous Plants
Fortunately, horses rarely ingest poisonous plants. Many owners are aware of what plants are poisonous, and horses find most toxic plants to be unpalatable. However, some plants ingested over time can poison a horse insidiously, and others in small volumes can cause sudden death. The risk of poisoning increases under poor management conditions when lack of pasture forces horses to eat toxic weeds, or when horses are fed a poor quality hay with a high weed content.

Pyrrolizidine Alkaloid Poisoning
Senecio plants, such as Senecio jacobaea (tansy ragwort) and Senecio vulgaris (common groundsel; Fig. 1), are potentially hepatotoxic to horses if consumed over a period of weeks (Talcott 2003). After ingestion of the plants, the absorbed pyrrolizidine alkaloid is converted to highly reactive alkylating pyrroles that cause hepatocellular necrosis, biliary hyperplasia, fibrosis, and hepatocytomegaly. The liver becomes progressively smaller, and the prospects of any regeneration are poor by the time clinical signs of poisoning become evident. Most affected horses have chronic weight loss, weakness, depression, ataxia and icterus. Hepatoencephalopathy is responsible for the neurologic signs that follow. Signs can occur abruptly after a stressful event, such as transport and parturition. Diagnosis is made by indicators of liver disease in blood samples (elevated liver enzymes, bile acids, and ammonia and hypoalbuminemia) and evidence of the plant in grain, hay, haylage, and pasture. Treatment is supportive and aimed at ameliorating liver disease, but recovery is rare and then is not complete (Talcott 2003).

Figure 1. Common groundsel (Senecio vulgaris), similar to ragwort in Europe, is a source of pyrrolizidine alkaloids and is potentially hepatotoxic to horses. - To view this image in full size go to the IVIS website at www.ivis.org . -

The toxic principle of Crotalaria (Rattlebox) is also a pyrrolizidine alkaloid that causes similar clinical signs and lesions as Senecio (Beasley 1999). Poisoning can occur through ingestion of seed especially, but also the leaves and stem, all of which remain toxic when dry in hay. This plant is best known as the cause of Missouri bottom disease of horses, which occurs in low lying areas of the Missouri River (Beasley 1999).

Alsike Clover
Alsike and red clover are hardy and palatable plants that are often included in grass seed mixes for horses (Murphy and Reagor 1992; Murphy and Reagor 1997). Both grow tall and have flowers with globose heads that are pink/white (alsike) and rose, purple or red (red clover). The leaves of red clover (Fig. 2) have a characteristic chevron, and a more pointed tip than those of alsike clover (Fig. 3). Alsike clover causes photosensitization or "trifoliosis", colic, diarrhea, and liver disease, whereas red clover causes Slaframine toxicosis (see below). When alsike clover damages the liver, photoactive substances derived from chlorophyll accumulate in blood and become exposed to the sun in white areas, where they cause the typical lesions of photosensitization (Fig. 4). Poisoning with alsike clover can be associated with pasture or hay contamination, and the toxic agent is an unknown hepatotoxin, possibly a mycotoxin (Murphy and Reagor 1992; Murphy and Reagor 1997). Secondary photosensitivity produces some of the earlier signs, but later signs are the more neurologic form of severe hepatic disease. Less common signs are colic and blindness. Elevated liver enzymes support the diagnosis, but the absence of pathognomonic liver changes and variability of lesions can complicate necropsy confirmation. Prognosis is good for photosensitivity cases but poor for horses with other signs of hepatotoxicity.

Figure 2. Red clover flower and leaves, showing the chevron pattern on the leaves. - To view this image in full size go to the IVIS website at www.ivis.org . -
Red Clover
Slaframine is a toxic product of the fungus *Rhizoctonia leguminicola*, which can infest red clover (Murphy and Reagor 1992; Burger 1996; Murphy and Reagor 1997). It is called the "slobber factor", because hypersalivation is the most common clinical sign, but other signs of toxicity include anorexia, diarrhea, and frequent urination. Poisoning is caused by ingestion of second cutting hay with black patch on the leaves and stems.

White Snakeroot
Although horses that have ingested white snakeroot develop heart failure and myocardial degeneration, clinical signs such as sluggishness, trembling, dyspnea, slobbering, swallowing difficulties, unsteady gait, stiffness, and pronounced sweating (Murphy and Reagor 1997; Raisbeck 1992) can be interpreted as signs of alimentary tract disease, including colic. Toxicity is caused by tremetol, a mixture of alcohols, and the plant is toxic when dry or frosted, but especially when green. White snakeroot poisoning is most likely in wooded pastures when grass is covered by snow and the stalks above the snow are the only forage (Raisbeck 1992).

Black Walnut
Black walnut (*Juglans nigra*) is one of the best known toxic agents in horses in the eastern USA, and severe laminitis arises from contact with shavings or sawdust from the wood (Galey et al. 1991; Burger 1996), which is highly valued for furniture. A presumptive diagnosis can be made when a group of horses in a barn become acutely affected after arrival of a batch of contaminated shavings. Although the clinical signs are laminitis, this poisoning is of interest to those involved with gastrointestinal diseases, because so many cases are complicated by laminitis, and black walnut provides us with a means of studying this devastating disease.

Grasses
Kleingrass (*Panicum coloratum*) is a warm season perennial bunchgrass introduced into the USA from Africa, and is used for grazing and hay, particularly in Texas (Ocumpaugh et al. 1995). It has a fine stem, is leafy, and can reach heights of 3 to 4 feet. It is highly palatable and is safe for cattle, but causes hepatic necrosis and secondary photosensitization in horses (Burger 1996). Squirreltail grass grows abundantly in overgrazed pastures and the teeth on the flowering spike can cause ulcers and abscesses in the mouth and at the base of the tongue (Burger 1996), similar to those caused by foxtail.

Miscellaneous Plants
In one small handbook on toxic plants for horses (Burger 1996), colic was listed as a clinical sign for 28 plants, liver disease for 29, gastrointestinal disorders for 21, and diarrhea for 29, with some overlap between these signs and toxic agent. In many poisonings, the alimentary tract is not the major organ system affected, but its peripheral involvement can still lead to dramatic signs of gastrointestinal disease.

Cardiac-glycoside containing plants, such as foxglove and oleander, exert a digitalis-like action on the heart, but clinical signs can include colic (Burger 1996). Colic can be the initial sign of poisoning with nightshades (glycoalkaloid solanine) in
hay or pasture. Jimsonweed or thornapple contains solanaceous alkaloids that stimulate the autonomic nervous system and cause rapid onset of excitement, depression, colic, and diarrhea when fed in minute amounts to horses (Murphy and Reagor 1992; Murphy and Reagor 1997). Other members of the solanaceae family of plants that contain atropine or atropine-like substances that cause colic are the green parts of tomatoes, potatoes, ground cherry, and henbane (Beasley 1999).

Plants that contain saponins include pokeweed, bouncing bet, corn cockle (imported from Europe), and English ivy. Although horses find these plants to be unpalatable, saponins can irritate the digestive system and cause diarrhea and colic (Beasley 1999). Oak leaves and buds ingested when young, tender, and palatable, cause colic and bloody diarrhea in horses occasionally (Beasley 1999). Gallotannin is the possible toxic principle.

Colic can be a clinical sign of poisoning by any plant that causes oral ulcers, because the inflammation extends into the gastrointestinal tract. Weed seeds most likely to contaminate horse feed and cause colic in this way are mustard and corn cockle (Raisbeck 1992, 1997). The toxic agent in buttercup is a glycoside, ranunculin, that releases protoanemomin when crushed. Protoanemonin causes irritation on contact, red mucus membranes, colic and diarrhea, but is highly volatile and therefore does not pose a problem in hay (Beasley 1999). Castor bean (Fig. 5) contains ricin (not a component of castor oil), which causes hemorrhage in the gastrointestinal tract and bladder, and signs of colic (Burger 1996; Murphy and Reagor 1992; Murphy and Reagor 1997). Horses dislike the taste, but only a mouthful of beans incorporated into grain or forage is sufficient to kill a horse.

Figure 5. Castor bean, an ornamental plant and source of the highly toxic ricin. - To view this image in full size go to the IVIS website at www.ivis.org . -

Limb edema, laminitis, transient fever and diarrhea are signs that develop within a few days from consumption of hoary alyssum in pasture and hay grown in the northern part of the United States (Geor et al. 1992; Raisbeck 1992). The plant is tall, the flowers are very small and white, and the plant is unpalatable to horses. Lantana, an ornamental shrub that can grow wild in the USA (Fig. 6), causes hepatic necrosis and secondary photosensitization in horses (Burger 1996).

Figure 6. Lantana, an ornamental shrub that can grow wild in the USA and causes hepatic necrosis and secondary photosensitization in horses. - To view this image in full size go to the IVIS website at www.ivis.org . -

Feed Contaminants and Others
Feed contaminants are particularly dangerous because they are introduced into hay, grain, or processed feed in a way that leaves little opportunity for horses to avoid them or for horse owners to find them. Although many agents can be inadvertently included in horse feed, the following are the most notorious contaminants in the United States.

Monensin -
Monensin is a carboxylic ionophore that is added to rations for poultry, swine and cattle as a coccidiostat to improve feed utilization (Raisbeck 1992; Raisbeck 1997). It is extremely toxic for horses, and poisoning can arise from mixing horsefeed with equipment that is superficially contaminated by mixing monensin-containing rations for other animals. Signs include anorexia, abdominal pain, profuse intermittent sweating, tachycardia, hypotension, and posterior ataxia. Death early in the disease course is from hypovolemic shock and electrolyte losses, not unlike some forms of severe colic. Myocardial necrosis and scarring can be responsible for death weeks later (Stegelmeier 2003).
**Blister Beetle Toxicosis**

Ingestion of blister beetles incorporated into alfalfa hay causes poisoning by cantharadin, a vesicant produced by male beetles (Freeman and MacAllister 1998; Casteel and Evans 2003). Ingestion of 5 to 6 beetles can cause colic in horses (Casteel and Evans 2003). Cantharadin is heat stable and can survive the processing that produces dehydrated alfalfa pellets (Freeman and MacAllister 1998). Blister beetles tend to congregate in late summer for mating, especially around field margins and when alfalfa reaches full bloom. Cutting combined with crimping increases the risk of trapping beetles in the hay, and second and third cuttings, which are favored for horses, are at greatest risk of contamination because they are harvested during the period of greatest activity. Blister beetle poisoning might be more common in the Southwest, but has been reported in most of the eastern part of the United States (Freeman and MacAllister 1998). To prevent blister beetle poisoning, check borders to detect beetle swarms before harvesting, avoid field borders if necessary, spray infested areas, cut hay without crimping, avoid alfalfa hay cut between May and September from suspect fields, obtain hay from a reputable source, and check hay carefully, recognizing that beetle distribution in the crop will be very erratic.

Cantharadin disrupts cell membranes and causes inflammation, necrosis, ulceration, and erosions in the upper alimentary tract, and the excreted toxin causes severe urinary tract inflammation. The obvious presenting clinical sign is acute onset of colic, associated with elevated heart and respiratory rates, fever, hypersalivation, and frequent passage of small volumes of urine, which can be bloody. Mortality is 50%, less than 10% of affected horses have neurologic signs, affected horses can die quite suddenly, and death is preceded by signs of severe shock. Diagnosis is based on clinical signs, recent alfalfa hay ingestion, dead blister beetles in the hay supply, and marked and sustained hypocalcemia and hypomagnesemia. Recommended treatment is mineral oil and activated charcoal by stomach tube, analgesics, intravenous fluids, and calcium borogluconate. Prognosis is dose-related.

**Mycotoxins**

Aflatoxins are mycotoxins that form on carbohydrate feeds, such as cereal grains, peanuts, corn, and cottonseed, in the field or in storage, especially in the warm and humid conditions that prevail in the southeastern USA (Plumlee 1997; Hooser 2003). Because hepatocytes are the primary site of aflatoxin metabolism and undergo necrosis, along with centrilobular fatty change, perportal fibrosis, and bile duct proliferation, the major signs are related to liver damage and dysfunction. Chemical analysis of feed is recommended for suspect cases and serum biochemical analyses show expected changes in liver enzymes.

Fumonsin B1 is a mycotoxin produced from Fusarium moniliforme, a contaminant of corn and even pelleted feeds. High doses cause hepatosis, whereas low doses over long periods cause leukoencephalomalacia (Hooser 2003). Acute primary mycotoxicosis has been considered as a possible cause of duodentitis-proximal jejunitis (DPJ), because horses with aflatoxicosis or fusariotoxicosis can have necropsy lesions that include hemorrhagic enteritis (Schumacher et al. 1994). Fusarium moniliforme was fed to horses and caused intestinal lesions consistent with DPJ, but the predominant clinical signs were those of leukoencephalomalacia and not DPJ (Schumacher et al. 1995).

**Arsenic**

Arsenic poisoning is rare, but can arise when horses graze pasture contaminated with ashes from burnt wood that was pressure treated with an arsenic-containing preservative. Arsenic cannot be used anymore in pressure-treated wood, and any damaged wood that was treated with an arsenic compound must be collected for appropriate disposal. Unfortunately, burning remains a popular but dangerous means of disposal of such wood, and arsenic concentrated by burning in the ashes will remain in the environment indefinitely.

**Organophosphorous Insecticides**

Organophosphorous insecticides can achieve toxic levels in feed through misidentification, accidental contamination, or excessive application to forage crops (Beasley 1999). Organophosphate and carbamate insecticides competitively inhibit both acetylcholinesterases and pseudocholinesterases to cause muscarinic, nicotinic and central nervous system effects. The muscarinic effects in horses are characterized by salivation, colic, dehydration and severe diarrhea, and treatment includes atropine and protopam (2 PAM).
References


Beasley VR. A Systems Affected Approach to Veterinary Toxicology. Reference Notes VB320, University of Illinois, College of Veterinary Medicine, 1999.


