



WEDNESDAY SLIDE CONFERENCE 2014-2015

Conference 23

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Guest Moderator:

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CASE I: NIAH2012-2 (JPC 4018762).

Signalment: 3-year-old female Holstein, *Bos Taurus*.

History: In a herd of 190 Holstein lactating cows, 9 cows died or were euthanized at 1 to 3 weeks after the onset of the clinical signs of fever, skin lesions, nasal discharge, decrease in milk production, and weight loss. Other characteristics of the skin lesions were multiple alopecia, dry scaling on the head, neck, vulva, and udder.

Gross Pathology: The lymph nodes, spleen, adrenal glands, kidneys, and liver were enlarged. The renal cortex was discolored and had multifocal to coalescing yellowish-gray nodules on both the capsular and cut surfaces.

Laboratory Results:

	At clinical onset	At necropsy (9 days after onset)
Temperature (°C)	38.1	39.3
Heart rate(/min)	84	90
Respiration rate (/min)	56	30
White blood cells (/ml)	9,100	12,300

	At clinical onset	At necropsy (9 days after onset)
Packed cell volume (%)	31	36
Plasma protein level (g/dl)	9.6	9.6

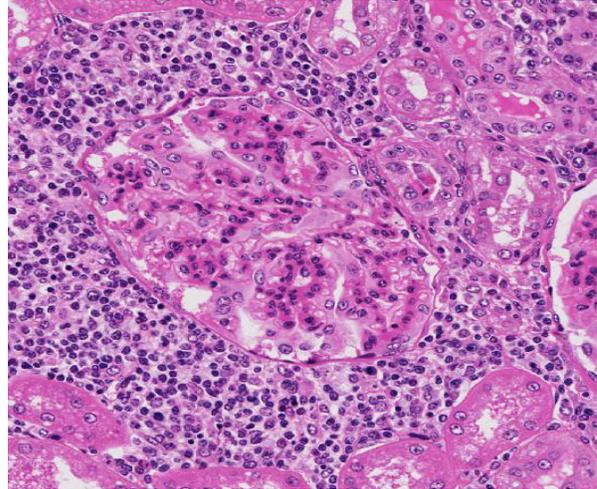
Flow cytometry analysis of the peripheral blood showed that the numbers of CD14+ monocytes (43.9%) and CD8 lymphocytes (19.1%) were significantly higher in the affected cows than in the normal lactating cows (CD14+ monocytes, $20.3 \pm 1.6\%$; CD8 lymphocytes, $10.9 \pm 1.3\%$). Further, the percentages of WC1 (3.5%) and IgM + lymphocytes (6.7%) were significantly lower in the affected cows than in the normal lactating cows (WC1+ cells, $12.7 \pm 2.5\%$; IgM+ cells, $15.9 \pm 2.6\%$).

No pathogens were isolated from the carcass.

Histopathologic Description: The interstitium throughout the renal cortex is replaced by multifocal to coalescing accumulations of inflammatory cells, mainly consisting of lymphocytes, macrophages, and multinucleated giant cells with moderate numbers of plasma cells. The arterioles are radially surrounded by the infiltrate. While some tubules are replaced with the infiltrate, other tubules throughout the cortex consist of diffuse mild vacuolation and contain



1-1. Ox, kidney: There are multiple foci of hypercellularity scattered through the cortex. (HE 5X)



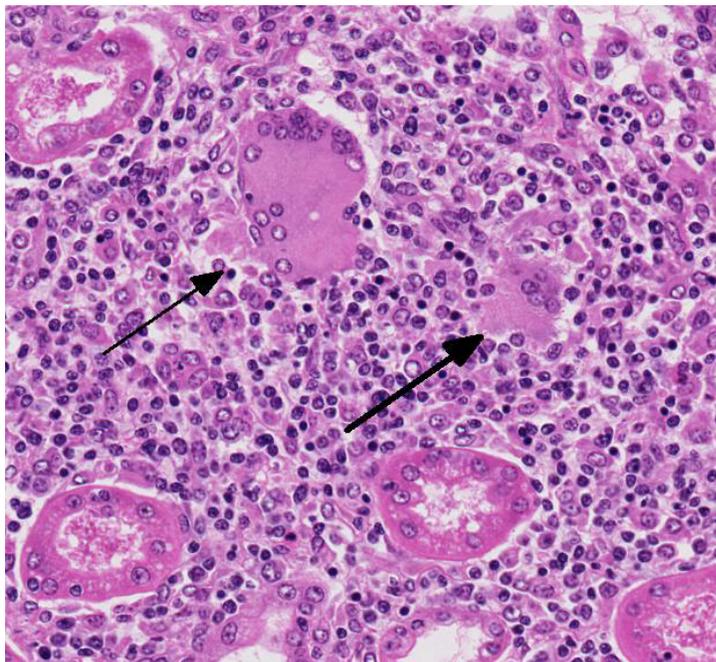
1-2. Ox, kidney: The cellular infiltrate throughout the kidney is composed of numerous macrophages, lymphocytes, and fewer plasma cells. (HE 152X)

eosinophilic stippled proteinaceous material. In addition, some areas show tubular and glomerular degeneration and necrosis, with protein casts and cellular debris in the tubular lumen.

Granulomatous inflammation with multinucleated giant cells was also detected in the adrenal glands, pancreas, thyroid, heart, mammary glands, liver, uterus, skin, and lymph nodes. The condition in the heart, mammary glands, and skin was accompanied with eosinophilic infiltration.

Contributor's Morphologic Diagnosis: Nephritis and diffuse, moderate to severe lymphogranulomatous inflammation.

Contributor's Comment: The outbreaks of the disease that were detected in various counties were characterized by systemic granulomatous inflammation; in cattle that is usually found to be induced by the ingestion of hairy vetch.



1-3. Ox, kidney: Scattered throughout the infiltrate are low numbers of large multinucleated macrophages ranging up to 100 μ m in diameter. (HE 185X)

The granulomatous inflammation with the presence of multinucleated giant cells and the distribution of the lesions on the tissues show similar characteristics to those reported in hairy vetch toxicosis,^{2,4,6} citrus pulp toxicosis,^{3,7} and di-ureido isobutane (DUIB) toxicosis^{1,5} in cattle. Various organs including the kidneys, heart, liver, spleen, adrenal glands, thyroid, lymph nodes, skin, and mammary gland are usually affected in these diseases.

Although the cause of the disease is an enigma, histopathological features suggest that a type 4 hypersensitivity reaction (key event) may play a role in the inflammatory reaction (pathogenesis).⁶ We suggest that a plant constituent absorbed by the cows acts as an antigen that evokes a type 4 hypersensitivity reaction and granulomatous response. Alternatively, lectins may act as immunostimulants that directly stimulate T lymphocytes to initiate the

inflammatory cytokine response that characterizes the disease. However, in this case, the diet that was fed to cows in the farm did not contain vetch, citrus pulp, or DUIB.

JPC Diagnosis: Kidney: Nephritis, granulomatous, multifocal, moderate, with tubular degeneration and necrosis.

Conference Comment: Hairy vetch toxicosis is a diagnosis of exclusion, and the provided history of multiple lactating cows being affected is a typical presentation. Holstein and Angus cattle are most susceptible; and while the granulomatous inflammation is disseminated throughout a wide range of tissues in most cases, the lesion seems to be most frequently seen in the skin and the most severe lesions are seen in the kidney.^{3,4} The heart is another common location in cattle, which distinguishes the disease from that in horses whom do not get myocardial involvement in addition to their lack of eosinophils in the granulomatous inflammation.³

The disease resembles a type 4 hypersensitivity reaction, although its pathogenesis is likely multifactorial as not all animals exposed develop lesions and lactating animals appear to be more susceptible.⁴ The toxic principle was originally identified as prussic acid which is found in the seeds of *Vicia villosa* Roth (hairy vetch),³ a forage commonly cultivated as winter cover or in row crop rotations due to its nitrogen-fixing ability. Other feed additives have been implicated (DUIB and citrus pulp), and this case serves as a reminder there are potentially other sources of a hapten or antigen capable of disease induction.

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CASE II: 50265 (JPC 4049053).

Signalment: 9-month-old male “sport horse”, *Equus caballus*.

History: This horse presented with a 6-week history of lesions involving the dorsal cervical and nasal skin.

Gross Pathology: The liver was small and diffusely pale, with a firm consistency. The surface was irregular and pitted and contained numerous 0.5-1 cm raised white nodules that extended throughout the parenchyma.

Laboratory Results: Blood bile acids were 62 umol/L (reference range 0-20 um/L).

Histopathologic Description: In the liver, the most prominent lesion is marked biliary hyperplasia that has resulted in distortion of hepatic cords and hepatocyte individualization. The biliary hyperplasia is associated with fibrosis that extends between portal areas (bridging fibrosis). Also throughout the parenchyma, there are multiple variably sized nodules of hepatic regeneration that are often separated by a thin rim of fibrous connective tissue. Within portal areas, large numbers of hepatocytes that are characterized by an enlarged nucleus (up to 4 times normal size) with frequent intranuclear cytoplasmic invaginations and abundant, irregularly shaped, granular or vacuolated eosinophilic cytoplasm (megalocytes) are visible. Scattered throughout the liver, there are small

numbers of hepatocellular mitotic figures. Additionally, Kupffer cells that often contain a greenish pigment that is interpreted as bile and few scattered lymphocytes are present.

Contributor’s Morphologic Diagnosis: Chronic severe biliary hyperplasia, bridging fibrosis and nodular regeneration with prominent megalocytosis.

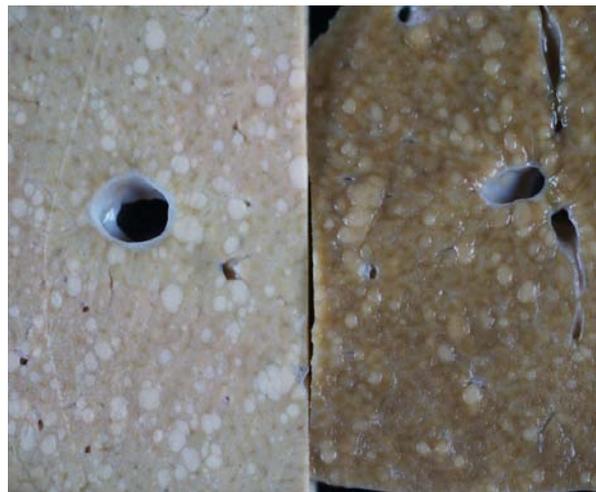
Contributor’s Comment: The gross and histological lesions in this case are consistent with pyrrolizidine alkaloid toxicity. Pyrrolizidine alkaloids (PA’s) are present in a wide variety of plants across the world. There are principally three families of plants that contain this toxin: Asteraceae (Compositae), Leguminosae (Fabaceae), and Boraginaceae.⁷

The most important genera are *Senecio*, *Cynoglossum*, *Amsinckia*, *Crotalaria*, *Echium*, *Trichodesma*, and *Heliotropium*. In New Zealand, PA toxicity in grazing animals is mostly associated with ragwort (*Senecio jacobaea*) poisoning. While ragwort is considered to be the most likely toxicant in this case, other possible causes of PA toxicity in New Zealand include: German ivy (*Senecio mikanooides*), groundsel (*Senecio vulgaris*), Paterson’s curse (*Echium plantagineum*), viper’s bugloss (*E. vulgare*), borage (*Borago officinalis*) and comfrey (*Symphytum* spp. & hybrids).¹

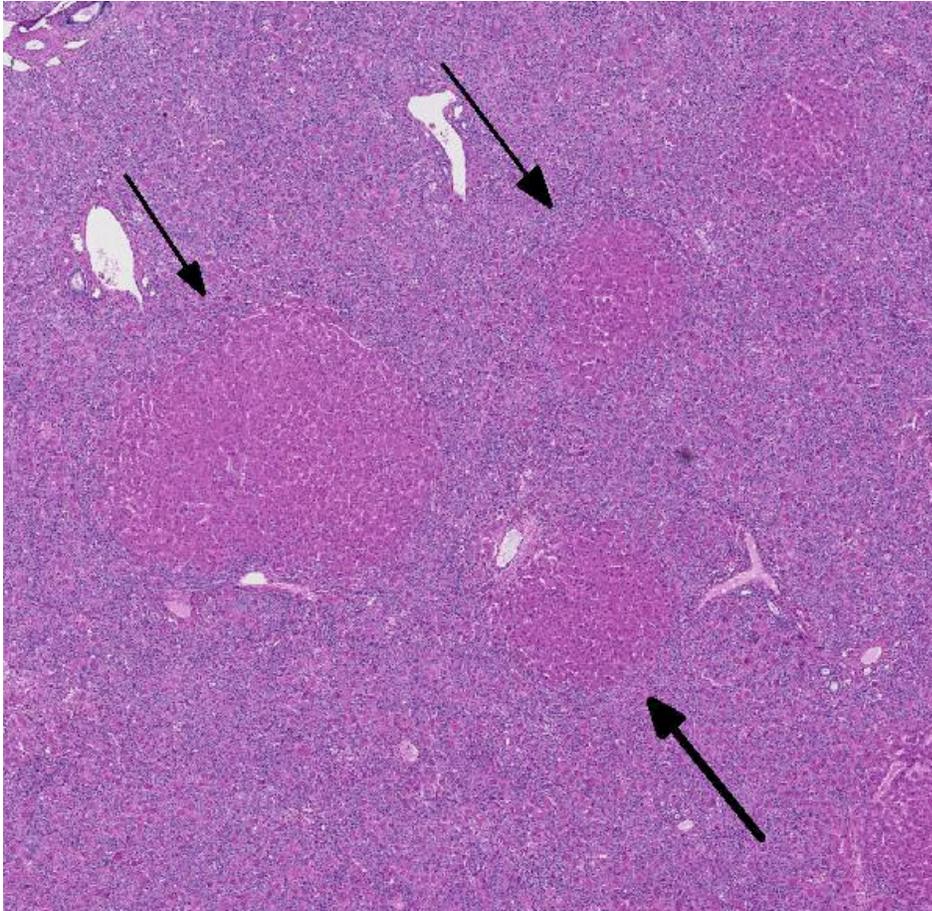
Pyrrolizidinosis is usually a chronic disease but acute toxicity may occur due to the variations in



2-1. Liver; horse: The liver is diffusely small, nodular, and pale. (Photo courtesy of: IVABS, Massey University, Palmerston North, New Zealand, <http://www.massey.ac.nz>)



2-2. Liver; horse: The surface was irregular and pitted and contained numerous 0.5-1 cm raised white nodules that extended throughout the parenchyma. (Photo courtesy of: IVABS, Massey University, Palmerston North, New Zealand, <http://www.massey.ac.nz>)



2-3. Liver, horse: Much of the hepatic parenchyma is lost, with scattered islands of regenerative hepatocytes remaining (arrows). (HE 22X)

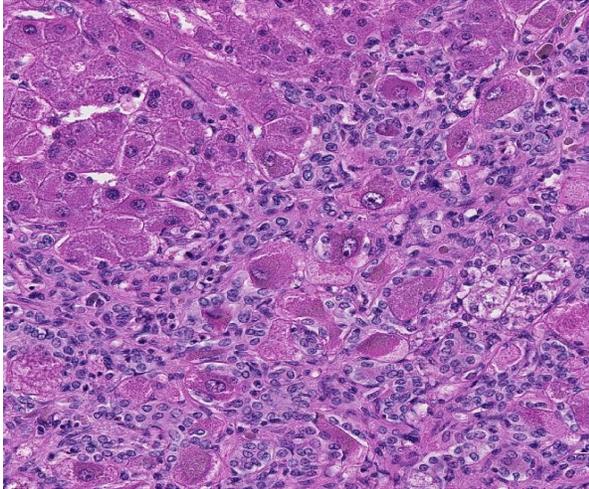
PA's content that can occur between seasons and years.¹ PA's are hepatotoxic, carcinogenic, genotoxic, teratogenic and sometimes pneumotoxic.⁷

PA exists in the plant in two molecular forms: the hydrophilic nontoxic N-oxide (amine-oxide) and the lipophilic pro-toxic free or tertiary bases (retroecine, heliotridine and otonecine). Toxicity occurs when these free bases are converted into highly reactive and unstable alkylating pyrroles or pyrrolic derivatives by liver microsomal enzymes (cytochrome P-450 monooxygenases mainly CYP3A and CPY2B6). Subsequently the C-7 or C-9 position of the pyrrolic ring system becomes highly electrophilic and capable of binding to proteins and/or nucleic acids, leading to altered cell function and cell damage or death.³ Individual animal variation in toxicity of PA's is mediated by the activity of the esterases that detoxify the alkylating pyrroles. Different PA's have different toxicity due to differences in total alkaloid

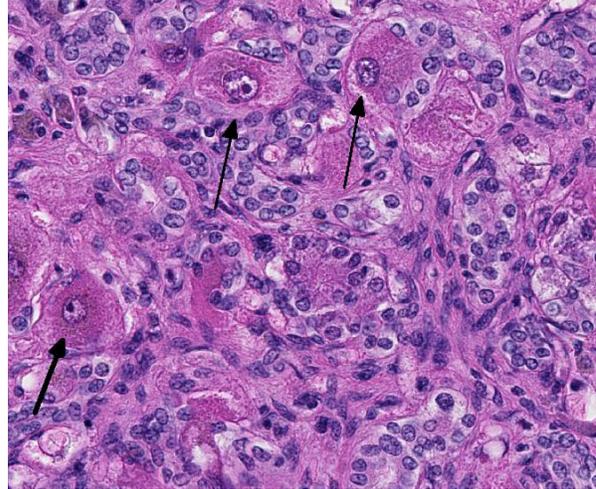
content, structural features of the amino alcohol and the presence of other substitutions on the chemical ring that modify the rate and extent of the toxicity. Toxicity of PA's is due to necrosis, antimetabolic action (crosslinks with DNA and inhibits mitosis with concomitant formation of megalocytes) and vascular damage mainly in the liver. Some alkylating pyrroles can escape the liver and reach the lung damaging capillaries and resulting in acute pulmonary edema and hydrothorax. Renal damage is also reported.¹

Ragwort (tansy ragwort, Saint James' wort) is a biennial, perennial or annual

weed with a diffuse root system. The alkaloids of ragwort include jacobine (major alkaloid), jaconine, jacoline, jacozone, senecionine and seneciphylline. All parts of the plants are toxic and animals normally eat the plant in small quantities either inadvertently or when forced due to lack of other food.¹ Pigs, horses, cattle, sheep, goats and chickens can be affected.^{1,2} In humans, certain liver and other diseases have been attributed to the consumption of foods and herbal medicines prepared from pyrrolizidine alkaloid-containing plants.⁶ Clinical signs in horses can be non-specific such as anorexia, weight loss, and diarrhea, photosensitization, icterus, or related to hepatic encephalopathy (depression, ataxia, circling, head pressing, blindness, collapse, coma and death).² There are three common histological patterns associated with pyrrolizidine poisoning: acute periportal zonal necrosis, hepatic atrophy with formation of regenerative nodules, and atrophy and fibrosis without nodular regeneration. Megalocytes are usually most prominent in the



2-4. Liver, horse: Remaining hepatocytes are separated by florid biliary hyperplasia. A regenerative hepatocellular nodule is at upper left. (HE 192X)



2-5. Liver, horse: Numerous hepatocytes contain nuclei that are 3-5X normal size (arrows), referred to as "megalocytes". (HE 250X)

second histological pattern. Megalocytosis is a progressive enlargement of liver cells to up to three times the normal diameter, with a proportionate increase in nuclear diameter. These are believed to be morphologically and functionally viable hypertrophic cells that are incapable of division due to the potent antimetabolic action of the pyrrolizidine alkaloids. Some enlarged nuclei have cytoplasmic invaginations that can become entrapped as intranuclear inclusions.⁶

JPC Diagnosis: Liver: Florid biliary hyperplasia, portal and bridging, diffuse, severe, chronic, with nodular hyperplasia and hepatocellular megalocytosis, necrosis, and loss.

Conference Comment: Pyrrolizidine alkaloids (PA) are produced by over 6,000 plants as a deterrent from consumption by herbivores.⁵ Most PA-producing plants are therefore unpalatable to grazing animals; however, when they invade pastures to the degree other forages are unavailable or their seeds contaminate prepared feeds, PA's become hepatotoxic by conversion to their metabolically activated form dehydropyrrolizidine.⁴ Horses and pigs are more susceptible than ruminants in part because the toxin can be degraded in the rumen.⁴

The contributor discusses the three types of patterns of hepatic lesions associated with PA's. The acute form results from ingestion of a large quantity of toxin, as can occur in starving animals grazing drought stricken pasture. In the second

form, likely present in the current case, repetitive prolonged exposure leads to the hepatic atrophy with megalocytosis. The third form, which lacks regenerative nodules, is due to prolonged exposure specifically to *Heliotropium* spp.⁴ The biliary hyperplasia is dramatic in this case, and often occurs in PA toxicosis. While this biliary reaction is commonly associated with bile duct obstructions or local portal inflammation and fibrosis, it is suspected to occur in toxicity cases such as PA, phomoposin, and aflatoxin due to sustained regenerative stimulus from an incapacitated atrophic liver.⁴

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CASE III: 090372-06 (JPC 4037988).

Signalment: Adult female New Zealand white rabbit, *Oryctolagus cuniculus*.

History: This rabbit was part of a study to determine the median lethal dose of aerosolized ricin. This rabbit was exposed to 4.41 ug/kg of aerosolized ricin and was found dead 24 hours after exposure. Research was conducted under an IACUC approved protocol in compliance with the Animal Welfare Act, PHS Policy, and other federal statutes and regulations relating to animals and experiments involving animals. The facility where this research was conducted is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, National Research Council, 2011.

Gross Pathology: The lungs were firm, bright red, edematous with rounded edges, mottled, and failed to collapse. The laryngeal and tracheal mucosa was dark red with multiple streaks of hemorrhage and blood tinged foam within the lumen. The connective tissue surrounding the organs within the mediastinum was gelatinous (edema). There was pleural effusion (20 ml of yellowish viscous fluid). There was blood staining of the hair on the face, and the nasal turbinates were slightly edematous and glistened on cut surface.

Laboratory Results: None.

Histopathologic Description: Lung: Diffusely, there are changes in all levels of the conducting, transitional, and exchange portions of the pulmonary parenchyma. The alveolar lumina are filled with large amounts of eosinophilic homogenous material (edema), eosinophilic finely fibrillar material (fibrin), sloughed necrotic

cellular debris, hemorrhage, and heterophils. There is disruption and loss of the alveolar septa with replacement by cellular and karyorrhectic debris (necrosis) or the septa are segmentally expanded by congestion and edema. The connective tissue surrounding the bronchi, bronchioles, blood vessels and within the pleura is expanded by increased clear space (edema), fibrin, hemorrhage, and viable and degenerate heterophils. The epithelium lining bronchi and bronchioles are segmentally or completely lost and replaced by fibrin, edema, and necrotic cellular debris (necrosis) which occasionally fills the



3-1. Lungs, rabbit: The lungs were firm, bright red, edematous with rounded edges, mottled, and failed to collapse. (Photo courtesy of: Pathology Division, USAMRIID, Building 1425, Fort Detrick, MD, 21702 <http://www.usamriid.army.mil/>)



3-2. Trachea, rabbit: The laryngeal and tracheal mucosa was dark red with multiple streaks of hemorrhage and blood tinged foam within the lumen. (Photo courtesy of Pathology Division, USAMRIID, Building 1425, Fort Detrick, MD, 21702 <http://www.usamriid.army.mil/>)

airway lumina. Lymphatics are moderately distended by fibrin and edema. Endothelial cells are often plump and protrude into the vascular lumen (reactive).

Contributor's Morphologic Diagnosis: Lung: Necrosis, interstitial and bronchiolar/bronchial epithelial, multifocal, moderate, with fibrin, peribronchovascular and pleural edema, hemorrhage, and acute inflammation.

Contributor's Comment: Ricin is a phytotoxin derived from the castor bean plant (*Ricinus communis*) that is found in all parts of the plant but is most highly concentrated in the seeds. It is listed as a Category B bioterrorism agent/toxin by the Centers for Disease Control and Prevention due to the potential use as a weapon of terrorism and as a biological warfare threat to military operations.¹

Ricin is a glycoprotein composed of two glycoprotein chains (A and B) that are weakly linked by disulfide bonds. The B chain facilitates entry into the cell by binding to cell surface glycoproteins. The ricin A chain induces cellular necrosis by inhibition of protein synthesis through enzymatic alteration of the 28S ribosomal RNA loop contained within the 60S subunit.^{1,3} The exotoxin, shiga toxin, produced by *Shigella dysenteriae* and *Escherichia coli* serotype O157:H7 have a similar mechanism of action.⁷ Ricin also induces inflammation through the activation of mitogen activated protein kinases (MAPK), synthesis of proinflammatory RNA

transcripts and production of increased levels of circulating cytokines and chemokines.⁸

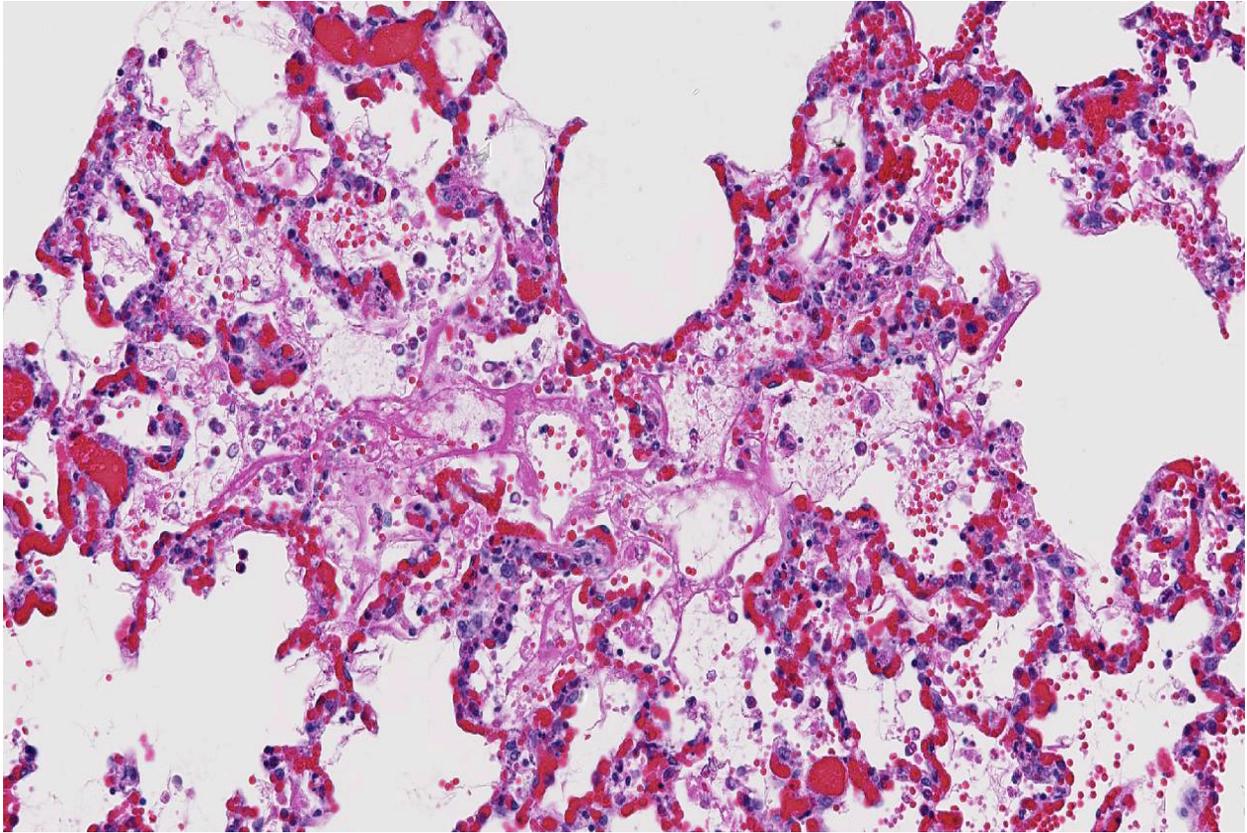
All animals are potentially susceptible to toxicosis with ricin. The horse is the most sensitive domestic species. In contrast, sheep, cattle and pigs are more resistant while ducks and chickens are the most resistant. Cases of poisoning have resulted from the accident or deliberate introduction of beans or castor-cake with other feedstuffs. Mixture of feed in a plant previously used for castor seeds has even resulted in poisoning.²

The clinical signs and pathological changes in ricin intoxication are route specific.³ The primary target of aerosolized ricin are the type I and II pneumocytes, and lesions following inhalation are primarily confined to the lungs and consist of intra-alveolar edema, acute alveolitis, and diffuse necrosis of the epithelium lining the lower respiratory tract.¹

The gross lesions reported from experimental inhalation studies in rhesus macaques consist of focal hemorrhage in the intestines, brain, myocardium, and pleura.⁷ Microscopic lesions consist of lymphocytic necrosis of lymphoid organs, hemorrhage, necrosis, hyaline droplets, and fibrin thrombi in the liver; hemorrhage and necrosis in the adrenal glands; tubular hyaline changes in the kidneys; degeneration and necrosis of the heart muscle; and congestion and hemorrhage of the gastrointestinal tract.⁷

Oral intoxication requires significantly more (up to 500X) material to reach toxic levels than by other routes of intoxication due to poor absorption in the digestive tract and possible enzymatic degradation in the digestive tract.^{2,3} A review of 751 cases of castor bean ingestion in humans found a death rate of 1.9%.³ The most common gross post-mortem findings reported in oral intoxication are multifocal ulceration and hemorrhages of the gastric and small intestinal mucosa. Findings in other organs systems are similar to parental introduction and include lymphoid necrosis in the mesenteric lymph nodes, gut-associated lymphoid tissue and spleen, as well as Kupffer cell and hepatocellular necrosis, diffuse nephritis and diffuse splenitis.³

In recent years, various extremist groups and individuals have used ricin in attacks or have been



3-3. Lung, rabbit: There is widespread septal necrosis. Alveoli contain variable amounts of hemorrhage, fibrin and edema, admixed with abundant cellular debris. In some areas, fibrin forms hyaline membranes. (HE 256X)

arrested for the possession of ricin. This is attributed to the ready availability of castor beans, ease of toxin extraction, and popularization on the Internet. None of these attacks resulted in human intoxications; however, they demonstrate that ricin is well known.^{3,6}

The ricin toxin is capable of inducing the formation of antibodies since it is a protein. Immunity in cattle and calves has been demonstrated by feeding increasing amounts of the bean.² Currently, there is no licensed vaccine available for use in humans; however, one is under development, and molecules that have been evaluated include a deglycosylated ricin A chain, formalin-inactivated toxoid, and recombinant ricin A chain.^{3,4} A vaccine candidate produced by the latter technique shows the most promise and is in more advanced stages of development in clinical trials.³

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Opinions, interpretations, conclusions, and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

JPC Diagnosis: Lung: Necrosis, interstitial, diffuse, with multifocal hyaline membrane formation.

Conference Comment: The contributor presents a rarely reported entity in the veterinary literature outside of experimental studies and delivers an excellent review of its pathogenesis and disease manifestations. Conference participants were struck by the widespread necrosis of Type I pneumocytes and largely unaffected septal capillaries in this case. The discussed differentials for toxic pneumonia in rabbits included paraquat toxicity and inhaled oxygen.

Aerogenous exposure is the most lethal form of ricin intoxication; however, a recent publication described two adult dogs that died 2-3 days following acute ingestion of fertilizer composed of residual castor bean plant material.⁵ The dogs exhibited similar clinical signs as described in

human ingestion cases, with vomiting and abundant hemorrhagic diarrhea due to ulcerative gastroenteritis. The most prominent histopathologic lesions were multifocal renal tubular degeneration and necrosis. Reports of such intoxication in dogs are rare, and only 9% ended in death or euthanasia in a retrospective review of 98 cases over a 11 year time period.⁵

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CASE IV: 14-2108 AFIP (JPC 4052872).

Signalment: Adult female Boer goat, *Capra hircus*.

History: Goats on a small holding with fair nutrition, Drenched with Q-drench 2 weeks ago. 25 goats, 2 sick, one found dead.

Gross Pathology: Generalised jaundice, liver swollen and finely mottled. Kidney swollen and moist with small (<1mm) white lesions scattered across surface. Lung, red with emphysema and foam in airways.

Laboratory Results: Gall bladder- profuse predominant growth of *Escherichia coli* (haemolytic).

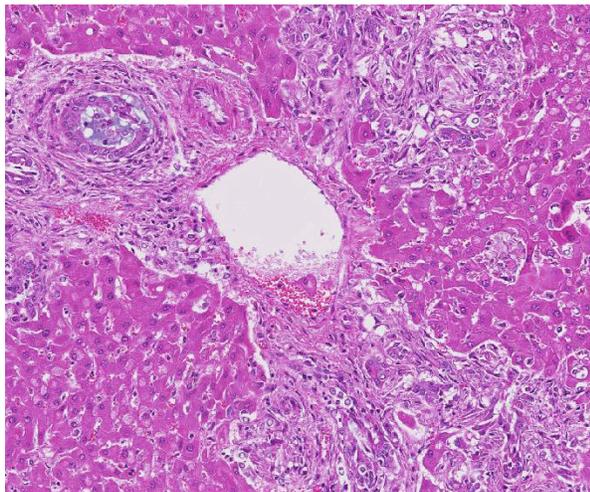
Histopathologic Description: Liver: The periportal areas are moderately expanded by fibrosis that is sometimes bridging, along with biliary hyperplasia and infiltration of occasional lymphocytes. Disrupting and effacing bile duct epithelium, obliterating bile ducts and extending into surrounding fibrous tissue are abundant negatively stained outlines of acicular crystals, shrunken, individualized, hypereosinophilic and sloughed epithelial cells, cellular debris and occasional neutrophils. Within occasional remaining intact bile ducts are non-viable neutrophils and cellular debris. Crystals are occasionally present in adjacent hepatocytes and there is hyperplasia of Kupffer cells. Occasional hepatocytes are lost, shrunken and

hypereosinophilic and replaced by neutrophils and cellular debris (necrosis). Remaining hepatocytes contain granular cytoplasm, often contain feathery vacuolation or occasionally contain variably sized, well defined cytoplasmic vacuoles (lipid), yellow-brown granular pigment (bilirubin) (cholestasis) and rare cytosomes.

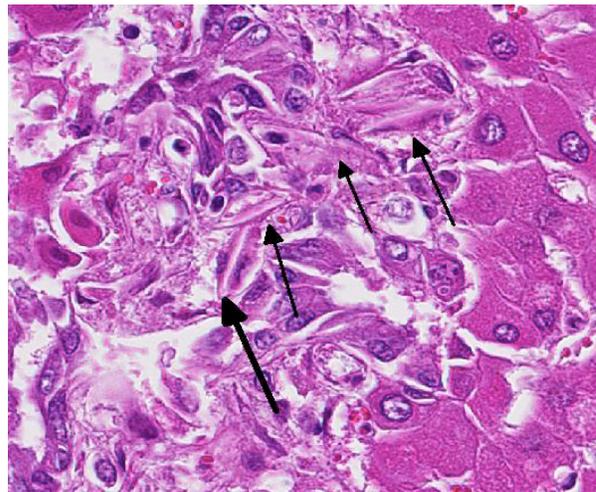
Contributor's Morphologic Diagnosis: Liver; Cholangiohepatitis, necrotizing, moderate, chronic with biliary crystals and bridging portal fibrosis.

Contributor's Comment: This is a spectacular case of crystal-associated cholangiohepatopathy, and although crystals are not seen, their outlines are readily apparent. Crystal-associated cholangiohepatopathy is a progressive disease seen with ingestion of plants containing steroidal saponins that form crystals in bile ducts and less commonly hepatocytes, Kupffer cells and renal tubules.^{1,4} Larger crystals are found with prolonged ingestion. This is a disease that primarily affects ruminants with sheep and goats being more commonly affected than cattle.¹

The crystals are composed principally of calcium salts of the steroidal saponins that are metabolised in the rumen and liver to form episapogenin glucuronides. In the presence of calcium they can precipitate and form crystals.⁵ Crystals can obstruct bile ducts and lead to icterus and secondary photosensitization.² It is still unclear whether the biliary crystals alone cause liver



4-1. Liver, goat: Portal areas are markedly expanded and often bridged by abundant fibrosis and moderate biliary hyperplasia. The fibrosis often breaches the limiting plate, effacing periportal hepatocytes. (HE 84X)



4-2. Liver, goat: Within portal areas, often effacing proliferating biliary epithelium, are numerous outlines of acicular crystals. (HE 292X)

damage or whether other toxins in the plants play a role.^{1,5}

Levels of saponins vary greatly with age of plant, location and size and the plants are thus not always toxic. Outbreaks commonly occur in summer when young plants become wilted, especially if rain is followed by hot dry weather.⁴

Plants that are known to cause crystal-associated cholangiohepatopathy are included in **Table 1**.

Many plants contain steroidal saponins, but have not yet been documented as causing biliary crystals. *Solanales*, *Primulales*, *Ranunculales*, *Fabales*, *Sapindales*, *Poales* and *Liliales* are all orders of plants that contain steroidal saponins¹, so should not be ignored when investigating the etiology of crystal associated cholangiohepatopathy.

In this case the significance of the *E.coli* is unclear. It may have been a post mortem contaminant, or a retrograde opportunist making use of the disrupted biliary epithelium.

JPC Diagnosis: Liver: Biliary hyperplasia, portal, diffuse, moderate, with intraductal crystal formation and periportal bridging fibrosis.

Conference Comment: Steroidal saponins are a type of glycoside, which, like alkaloids, are bitter and usually not readily consumed by domestic animals. Their metabolism to glucuronide conjugates result in the crystal formation evident in this case and subsequent hepatic disease secondary to biliary obstruction. Plants in early, rapid growth stages are most hazardous with the highest levels of saponins while mature plants can be grazed without incidence.³

Conference participants contrasted this entity with that of sporidesmin, the mycotoxin that causes biliary epithelial necrosis. Biliary hyperplasia with minimal inflammation is present in both entities and photosensitization is a common sequela, albeit through slightly different mechanisms. Saponins lead to biliary obstruction rather than necrosis, but both result in accumulation of phylloerythrin due to cholestasis inciting the characteristic skin manifestation of facial eczema when the affected animal is exposed to sunlight.²

Table 1

Scientific name	Distribution	Common name
<i>Tribulus terrestris</i>	South Africa, Australia, North America	Puncture Vine
<i>Nartheicum ossifragum</i>	Norway, UK	Bog asphodel
<i>Agave lecheguilla</i>	North America	Lecheguilla
<i>Nolina texana</i>	North America	Texan bear grass
<i>Brachiaria decumbens</i>	Brazil, Australia, Malaysia	Signal grass
<i>Panicum coloratum</i>	Australia, North America, Africa	Kleingrass
<i>Phytolacca octandra</i>	NZ, South America	Inkweed

The contributor outlined the most well-known steroidal saponin-producing plants, of which *Tribulus terrestris* may be most readily recognized since it has caused enormous loss of sheep in South Africa, where it is known as “yellow bighead” due to icterus and marked facial edema.⁵

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