2: Mycotoxins (toxins of fungi) [Biological-origin toxins]

MOULDS

Aflatoxins

Core data

Syndrome name: aflatoxicosis
Common sources: mycotoxins
- *Aspergillus flavus* growing in carbohydrate-rich feeds: peanuts, grain, bread

Animals affected: susceptibility:
- poultry > mammals (dog>pig>cattle>sheep)

Mode of action: suppresses messenger-RNA synthesis → inhibits protein synthesis
Poisoning circumstances:
- pre-harvest: drought & insect attack predisposes peanuts to *A. flavus* infection
- post-harvest: high moisture content of grain or water damage in storage
- distribution of aflatoxin *not* uniform in substrate

Main effects: dose & time dependant – descending order on intensity:
- generalised haemorrhage
- acute liver necrosis
- chronic liver damage with megalocytosis + fatty change

Diagnosis: pathology + assay feed, stomach contents, liver
Therapy: nil
Prevention:
- avoid predisposing environmental conditions
- screen feed for contamination
- add adsorbents to feed (bentonite)

Syndrome name: **aflatoxicosis**
Compounds:

Aflatoxins are difuranocoumarins. The most common is aflatoxin B_1. Other common aflatoxins are B_2, G_1, G_2 & M_1. [B = blue fluorescence under UV light, G = green fluorescence, M = milk (the site of its first isolation)]

Sources:

produced by the fungi growing in **carbohydrate-rich substrates**

fungi:

Aspergillus flavus*, A. parasiticus,* and *A. nomius* [and possibly some *Penicillium* spp.] produce the aflatoxins, *A.flavus* usually producing only B_1 & B_2 and *A. parasiticus* and *A. nomius* producing B_1, B_2, G_1 & G_2 (Cotty *et al.* 1994). As many as 20 species of *Aspergillus* including *A. nidulans* and species of *Bipolaris, Chaetomium, Farrowia* and *Monocillium* produce sterigmatocystin, a highly toxic intermediate in the aflatoxin B_1 synthesis pathway (sources cited by Meronuck & Xie 1999).

substrates:

peanuts
cotton seed
grains (e.g. sorghum, maize) (water-damaged wheat [Blaney 1986, Blaney *et al.* 1987])
other carbohydrate-rich feeds (e.g. bread, dry dog food)

dairy cows secrete 1.7% of their intake of aflatoxin B_1 intake as aflatoxin M_1 in milk (Frobish *et al.* 1986).

eggs of aflatoxin-fed poultry are contaminated with maximum concentrations 4-5 days after feeding starts (Wolzak *et al.* 1985)

Toxicity:

species susceptibility: poultry > mammals

duckling > turkey poult > chicken
dog > piglet > pregnant sow > calf > fattening pig > mature cattle > sheep

calves suffer some growth inhibition at 50-100 ppb aflatoxin
mature beef cattle can tolerate 200 ppb for periods of 2-3 months

it is possible to select for chickens resistant to aflatoxin effects

Mode of action:

suppression of messenger-RNA synthesis → inhibition of protein synthesis.

target organ: liver → periacinar necrosis, marked fatty change.

carcinogenesis demonstrated in rat & trout liver, suspected in other species (humans)

immunosuppression demonstrated (Silvotti *et al.* 1997; Azzam & Gabal 1998)

Conditions of poisoning:

pre-harvest aflatoxin production in peanuts is promoted by dry conditions during the late pod-filing stage of nut growth & soil temperatures of 26-32°C (i.e. **droughts**)

pre-harvest **insect infestation** of peanut pods & cotton seed heads promotes *A. flavus* infection.

post-harvest storage optimal *A. flavus* growth conditions: relative humidity 90%, temperature 30°C. Substrate moisture content 15-30% required for growth. Grains, peanuts, bread, dry dog food which are **water-damaged in storage** provide a suitable environment for aflatoxin production.

distribution of aflatoxins in feed is **not uniform**, e.g. individual peanut kernels with high toxin concentrations may be scattered through an otherwise toxin-free batch; water damage may affect only one part of a silo of grain

Clinical signs:

toxicity is dose & time dependent

acute → sudden death (e.g. Cockroft 1995)

subacute → lethargy, anorexia, dyspnoea, anaemia, ± epistaxis, ± melena, ± haematomata, ± jaundice

chronic → ↓ feed conversion efficiency, weight loss or ↓ weight gain, anaemia, jaundice → lethargy, anorexia, ↑ susceptibility to infections

Pathology:

acute → widespread **haemorrhage**, severe **liver necrosis**

subacute → liver necrosis & haemorrhagic gastroenteritis

chronic → **chronic liver lesions** with **megalocytosis**, fatty change, biliary retention, biliary ductular hyperplasia, fibrosis

Diagnosis:

pathology + detection of aflatoxins in feed, stomach contents, liver

assay methods include TLC, HPLC and ELISA

ELISA test kits for detecting and quantifying aflatoxins in grain are available in USA (Meronuck & Xie 1999).

dogs: differential diagnosis includes rare cases of hepatotoxicity associated with administration of diethylcarbamazine + cyromazine (Decaflea®) (*q.v.*)

Therapy: nil

Prevention & control:

mildly-affected animals recover

avoid predisposing environmental factors

peanut crop management (Graeme Wright, DPI Kingaroy, unpublished 1998: harvest on time, thresh within 2-3 days and artificially dry to safe moisture content → virtually aflatoxin-free peanuts) Rachaputi *et al.* (2002).

genetic resistance to fungal growth varies between peanut varieties ('Streeton' + shorter season types more resistant)

provide good nutrition and crop health to promote natural resistance to fungal growth/insect attack

minimise soil insect damage (white grub and etiella)

harvest at optimal maturity (or early)

optimum maturity predicted year-by-year on climatic variables

aflatoxin content increases with time after optimal maturity with maximum aflatoxin content in crops cut 2-3 weeks after optimum maturity and left for long periods in windrows

harvest up to 2 weeks before optimal maturity → minimal to almost no aflatoxins in nuts

minimise the cutting - thrashing interval (2-3 days best)

dry crop post-harvest efficiently and rapidly to below 15% moisture

thorough pre-cleaning, especially before & after drying

screening of susceptible food sources e.g. peanuts

ultraviolet light → infected grains fluoresce bright green-yellow (BGYF testing); misses about 15% of infected kernels (Walker 1999)

newer techniques under development

FTIR-PAS (Fourier Transform Infrared Photoacoustic Spectroscopy): infrared strobe light shone on kernels → rapid heating and cooling → emission of sound; sound is of slightly different wavelength in infected kernels; sounds recorded and analysed through a neural network → 96% accuracy in detecting infected corn kernels; not suitable for automated testing system because works on individual grains (Gordon *et al.* 1998, Walker 1999)

TIRES (Transient Infrared Emission Spectroscopy) may be useful for scanning bulk grain (Greene & Gordon 1992, Walker 1999)

adding adsorbents (bentonite, zeolite, other clay minerals) to rations to reduce absorption of aflatoxins (e.g. Kiran *et al.* 1998, Miazzo *et al.* 2000); adding soil (silty clay loam) to contaminated feed has reduced the adverse effects of aflatoxins on poultry (Madden *et al.* 1999); mycosorb, a product of *Saccharomyces cerevisiae* containing 10% mannan-oligosaccharide compound, reduces the effects of aflatoxins on poultry (Swamy & Devegowda 1998)

Ammoniation applied to feedstuffs such as cottonseed and maize in an industrialised process, applying ammonia (0.5-2.0%) at high temperatures (80-100°C) and pressures (45-55 psi) under controlled moisture conditions (12-16%) for 20-60 min, is capable of reducing aflatoxin concentrations from those of the order of 10,000 µg/kg to less than 10. Commercial application of ammoniation to whole cottonseeds, maize or peanuts under ambient temperature and atmospheric pressure conditions in Arizona resulted in concentrations less than 20 ppb in 42 days. This method is usually applied for 3-6 weeks. (Park & Price 2001)

Stock feed regulations (Qld) allow up to 20 ppb aflatoxin B_1 in grain and 50 ppb in complete feed. Contaminated feed should be removed for 2 weeks before slaughter to avoid residue violations.

US Food & Drug Administration aflatoxin action levels (= the concentration above which the commodity is condemned) (cited in Meronuck & Xie 1999)

Food or feed	**Action level (µg/kg or ppb total aflatoxins)**
Human foods (except milk)	20
Milk	0.5
Animal feeds (except as listed below)	20
Cottonseed meal (used for mature beef, swine & poultry rations)	20
Corn for breeding beef cattle, breeding swine, or mature poultry	100
Corn for finishing swine	200
Corn for feedlot beef cattle	300

References:

Review Literature:

Se160

Eaton DL, Groopman JD (eds.) (1994) *The Toxicology of Aflatoxins: Human Health, Veterinary and Agricultural Significance.* Academic Press, San Diego. xxvi +544 pp. ISBN 0 12 228255 8: [Miller DM, Wilson DM. Chapter 16. *Veterinary diseases related to aflatoxins.* pp.347-364.]

Park DL, Price WD (2001) Reduction of aflatoxin hazards using ammoniation. *Rev. Environ. Contam. Toxicol.* **171**:139-175.

General literature:

Azzam AH, Gabal MA (1998) Aflatoxin and immunity in layer hens. *Avian Path.* **27**:570-577.

Blaney BJ (1986) Mycotoxins in water-damaged and mouldy wheat from temporary bulk stores in Queensland. *Aust. J. Agric. Res.* **37**:561-565.

Blaney BJ, Moore, CJ, Tyler AL (1987) The mycotoxins 4-deoxynivalenol, zearalenone and aflatoxin in weather-damaged wheat harvested 1983-85 in south-eastern Queensland. *Aust. J. Agric. Res.* **38**:993-1000.
Blaney BJ, Kelly MA, Tyler AL, Connole MD (1989) Aflatoxin and cyclopiazonic acid production by Queensland isolates of *Aspergillus flavus* and *Aspergillus parasiticus*. *Aust. J. Agric. Res.* **40**:395-400.
Bryden WL, Rajion MA, Lloyd AB, Cumming RB (1975) Surveys of Australian feedstuffs for toxigenic strains of *Aspergillus flavus* and for aflatoxin. *Aust. Vet. J.* **51**:491-493.
Bryden WL, Lloyd AB, Cumming RB (1980) Aflatoxin contamination of Australian animal feeds and suspected cases of mycotoxicosis. *Aust. Vet. J.* **56**:176-180.
Cockcroft PD (1995) Sudden death in dairy cattle with putative acute aflatoxin B poisoning. *Vet. Rec.* **136**:248.
Cotty PJ, Bayman P, Egel DS, Elias DS (1994) Agriculture, aflatoxins and *Aspergillus.* In *The Genus* Aspergillus. Powell KA, Fenwick A, Peberdy JF (eds), Plenum Press, New York. pp.1-27.
Frobish RA, Bradley BD, Wagner DD, Long-Bradley PE, Hairston H (1986) Aflatoxin residues in milk of dairy cows after ingestion of naturally contaminated grain. *J. Food Prot.* **49**:781-785.
Gordon SH, Wheeler BC, Schudy RB, Wicklow DT, Greene RV (1998) Neural network pattern recognition of photoacoustic FTIR spectra and knowledge-based techniques for detection of mycotoxigenic fungi in food grains. *J. Food Prot.* **61**:221-230.
Greene RV, Gordon SH (1992) New non-destructive technology for evaluating corn. *Proc. Corn Utilization Conf., St.Lois, Missouri 24-26 June 1992.* National Corn Growers Assoc., St.Lois
Ketterer PJ, Williams ES, Blaney BJ, Connole MD (1975) Canine aflatoxicosis. *Aust. Vet. J.* **51**:355-357.
Ketterer PJ, Blaney BJ, Moore CJ, McInnes IS, Cook PW (1982) Field cases of aflatoxicosis in pigs. *Aust. Vet. J.* **59**:113-117.
Kiran MM, Demet O, Ortatath M, Oguz H (1998) The preventive effect of polyvinylpolypyrrolidone on aflatoxicosis in broilers. *Avian Pathol.* **27**:250-255.
Madden UA, Stahr HM, Stino FK (1999) The effect on performance and biochemical parameters when soil was added to aflatoxin-contaminated poultry rations. *Vet. Human Toxicol.* **41**:213-221.
McKenzie RA, Blaney BJ, Connole MD, Fitzpatrick LA (1981) Acute aflatoxicosis in calves fed peanut hay. *Aust. Vet. J.* **57**:284-286.
Miazzo R, Rosa CAR, De Queiroz Carvalho EC, Magnoli C, Chiacchiera SM, Palacio G, Saenz M, Kikot A, Basaldella E, Dalcero A (2000) Efficacy of synthetic zeolite to reduce the toxicity of aflatoxin in broiler chicks. *Poultry Sci.* **79**:1-6.
Rachaputi N, Wright GC, Krosch S (2002) Management practices to minimise pre-harvest aflatoxin contamination in Australian peanuts. *Aust. J. Exptl. Agric.* **42** (5): 595-605

Silvotti L. Petterino C, Bonomi A, Cabassi E (1997) Immunotoxicological effects on piglets of feeding sows diets containing aflatoxins. *Vet. Rec.* **141**:469-472.
Swamy HVLN, Devegowda G (1998) Ability of mycosorb to counteract aflatoxicosis in commercial broilers. *Indian J. Poultry Sci.* **33**:273-278. [Abstract 2050, *Nutr. Abs. Rev. B* **70**:354 (2000)]
Walker M (1999) Moaning mould. How can you tell when corn is fungus-ridden? Try listening. *New Scientist* **162**(2182) :11.
Wolzak A, Pearson AM, Coleman TH, Pestka JJ, Gray JI (1985) Aflatoxin deposition and clearance in the eggs of laying hens. *Food Chem. Toxicol.* **23**:1057-1061.

☑ *Fumonisins*

Core data

Syndrome name: equine leucoencephalomalacia
Common sources: mycotoxins
- *Fusarium verticillioides* [= *Fusarium moniliforme*] growing on maize kernels

Animals affected: horses
Mode of action: probably disrupt sphingolipid biosynthesis
Poisoning circumstances:
- humid late maize growing season; maize stored moist
- fed contaminated maize 3-4 weeks

Main effects:
- necrosis of subcortical cerebral white matter
- hepatic fibrosis

Diagnosis:
- brain pathology
- feed assay

Therapy: nil
Prevention: feed maize with low fumonisin content

Syndromes:
Horses: **equine leucoencephalomalacia** (LEM), blind staggers
Pigs: heart failure (pulmonary oedema)
Chemical structure:

Six fumonisins have been identified; fumonisin B_1 (FB_1), FB_2 and FB_3 are the major toxins in grain, while FB_4, FA_1 and FA_2 are produced in small amounts (Cawood *et al.* 1991)

Fumonisins are structurally similar to sphingosine, a constituent of sphingolipids in nervous tissue.

Sources:

Fumonisins are produced mostly by the fungus ***Fusarium verticillioides*** (Sacc.) Nirenberg [= *Fusarium moniliforme* Sheldon] growing on **maize kernels** (*Zea mays*) and producing pink discolouration of kernels (Gelderblom *et al.* 1988, Rheeder *et al.* 2002). ***Fusarium proliferatum*** is also capable of producing high yields of fumonisins (Meronuck & Xie 1999), and to date 15 *Fusarium* species and *Alternaria alternata* have been reported to produce fumonisins in culture (Rheeder *et al.* 2002).

N.B. Maize does not have to appear mouldy or discoloured to contain significant concentrations of fumonisins

Fumonisin-producing fungi and the maximum fumonisin yield (mg/kg) reported in culture from each (data from Rheeder 2002)

Fungal species	**FB_1**	**FB_2**	**FB_3**
Fusarium verticillioides [= *F. moniliforme*]	17,900	3,000	2,300
Fusarium sacchari	21	NT‡	NT
Fusarium fujikuroi	7	NT	NT
Fusarium proliferatum	31,000	17,000	5,700
Fusarium subglutinans	230	NT	NT
Fusarium thapsinum	30	5	5
Fusarium anthophilum	610	35	NT
Fusarium globosum	330	4	24
Fusarium nygamai	7,200	530	140
Fusarium dlamini	82	NT	NT
Fusarium napiforme	480	NT	NT
Fusarium pseudonygamai	Trace*	Trace	NT
Fusarium andiyazi	Trace	ND	NT
Fusarium oxysporum	300	6	0.9
Fusarium polyphialidicum	500	NT	NT
Alternaria alternata	+	+	+

* Trace = 1-4 ng/g
† ND = not detected (< 1 ng/g)
‡ NT = not tested

Toxicity:

Equine leucoencephalomalacia syndromes:

- **horses only**
- cases of equine leucoencephalomalacia are recorded from Southern Africa, North America, New Caledonia (Domenech *et al.* 1985), Australia – recently recognised in Vic & NSW (Robertson-Smith *et al.* 1985, Christley *et al.* 1993), South America (Mallmann *et al.* 1999)
- minimum toxic dietary concentration of fumonisin B_1 = 8 mg/kg

Porcine heart failure syndrome:

North America only to date (Harrison *et al.* 1990, Haschek *et al.* 1992, Osweiler *et al.* 1992, Colvin *et al.* 1993)

Deaths 4-10 days after feeding maize contaminated with fumonisins

Human toxicity:

Fumonisin B_1 has been assessed as a possible carcinogen for humans (IARC 1993). There is epidemiological evidence for a link with human oesophageal cancer in southern Africa (Sydenham *et al.* 1990) and China (Chu & Li 1994).

Mode of action:

- probably **disrupt sphingolipid biosynthesis** (Diaz & Boermans 1994)
- structurally related to sphinganine and sphingosine and inhibit sphinganine- and sphingosine-N-acyltransferase (ceramide synthase)
- classified as sphinganine analogue mycotoxins (SAMs) along with AAL toxins from *Alternaria alternata* f.sp. *lycopersici* (Caldas *et al.* 1998)
- sphingolipids are important for cell membrane integrity and intercellular communication
- sphingolipids occur in large amounts in nervous tissue; a major constituent of myelin
- SAMs induce changes in cellular homeostasis leading to either cell death (apoptosis) or proliferation. Signal transduction involving ceramide and sphingoid bases is an important lipid-based second messenger system in development, proliferation and degeneration of cells with links to apoptosis, carcinogenesis and degenerative diseases (Caldas *et al.* 1998)

Porcine heart failure syndrome:

- acute left-sided heart failure; increased pulmonary artery pressure but no effect on vascular permeability (Smith *et al.* 1994, 1996, 1999)
- heart failure probably related to increased plasma and myocardial sphingosine concentrations interfering with myocyte function through L-type Ca^{2+} channel blockade (Smith *et al.* 1999)
- damage to/necrosis of porcine pulmonary capillary endothelial cells only (Gumprecht *et al.*1998); probably of secondary significance (Smith *et al.* 1999)

Conditions of poisoning:

- outbreaks follow **heavy rains and high humidity during the latter part of the maize growing season** (growing season in Australia = spring-summer-autumn (October-May) with duration and harvest dates depending on location; both dryland crops and irrigated crops are produced)
- insect damage to cobs may promote fungal invasion.
- post-harvest fungal growth if kernel moisture content exceeds 15%

Clinical signs:

Equine leucoencephalomalacia syndromes:

- 2 syndromes - **neurological more common** than hepatotoxic
  - neurological signs occur after about **3-4 weeks of daily ingestion of toxic maize**.
  - hepatotoxic signs follow shorter term-higher dose exposure
- in both syndromes, signs appear abruptly and death usually follows in 2-3 days; **many horses are found dead** without signs being noticed
- **neurological** syndrome:
  - initial anorexia and lethargy
  - hypersensitivity, agitation
  - sweating
  - muscle tremor
  - ataxia, hypermetria, stumbling
  - apparent blindness
  - head pressing
  - circling
  - inability to swallow, flaccid paralysis of the lower lip and tongue (protrudes)
  - collapse, clonic-tetanic convulsions
- **hepatotoxic** syndrome:
  - oedematous swelling of the lips, nose, supraorbital fossae and lower legs
  - jaundice
  - cyanosis
  - mucosal petechiae
  - dyspnoea

Porcine heart failure syndrome:

- acute onset of dyspnoea
- paresis
- cyanosis
- moist rales

- bradycardia (Smith *et al*. 1999)
- rapid death
- ± abortions 1-4 days later in survivors

Abortion has been reported in sows clinically-affected by pulmonary oedema caused by fumonisins 1-4 days after onset of respiratory signs (Osweiler *et al.* 1992). It is uncertain if this was a direct effect on the uterus or the consequence of hypoxia secondary to the lung lesions. Placental necrosis and foetal resorption were induced in hamsters fed *Fusarium moniliforme* culture material containing fumonisins (Floss *et al.* 1994).

Pathology:

Equine leucoencephalomalacia syndromes:

- clinical pathology:
  - CSF yellow, ↑ protein, ↑↑ inflammatory cells
  - blood chemistry → ± hepatic damage.
- necropsy:
  - liquefactive **necrosis of subcortical cerebral white matter** (± grey matter) of one or both hemispheres ± extensive **haemorrhages**. Histologically, areas around the malacic lesions contain haemorrhage, oedema, plasma cell and eosinophil infiltrates, satellitosis and neuronophagia.
  - yellow **pigmentation** in white matter bordering the malacic cavities (→ green on fixation in formalin; lipofuscin-like granules histologically).
  - **hepatic centrilobular fibrosis** dominates
  - hepatocyte fatty change, multinucleation & enlarged asymmetrical hyperchromatic nuclei
  - yellow-brown pigment in hepatic sinusoidal macrophages

Porcine heart failure syndrome:

- hydrothorax
- **pulmonary oedema**
- pancreatic necrosis
- azotaemia, nephrosis (secondary to heart failure – Smith *et al.* 1999)

Diagnosis:

- assay feed for fumonisins

Equine leucoencephalomalacia syndromes:

- clinical differential diagnoses for the subcutaneous oedema of the head in the hepatotoxic syndrome include cardiotoxins such as persin, *Atalaya hemiglauca* and viral infections such as Hendra virus and African horse sickness
- characteristic brain lesions at necropsy

Therapy: no effective treatment

Prevention & control:

- it may be possible to salvage contaminated feed by feeding it to ruminants; for example, young goats have been fed 95 mg fumonisin B_1 /kg diet for up to 112 days without adverse clinical or production effects (Gurung *et al.* 1998)
- screening grain (see Prevention section under Aflatoxins) FTIR-PAS method applies to *F. verticillioides*-infected maize
- horse and pig feed should contain <10 μg fumonisin B_1/g (mg/kg)

References:

Se171

Caldas ED, Sadilkova K, Ward BL, Jones AD, Winter CK, Gilchrist DG (1998) Biosynthetic studies of fumonisin B_1 and AAL toxins. *J. Agric. Food Chem.* **46**:4734-4743.

Cawood ME, Gelderblom WCA, Vlegaar R, Behrend Y, Thiel PG, Marasas WFO (1991) Isolation of the fumonisin mycotoxins: a quantitative approach. *J. Agric. Food Chem.* **39**:1958-1962.

Christley RM, Begg AP, Hutchins DR, Hodgson DR, Bryden WL (1993) Leukoencephalomalacia in horses. *Aust. Vet. J.* **70**:225-226.

Chu FS, Li GY (1994) Simultaneous occurrence of fumonisin B_1 and other mycotoxins in mouldy corn collected from the People's Republic of China in regions with high incidences of esophageal cancer. *Appl. Env. Micro.* **60**:847-852.

Colvin BM, Cooley AJ, Beaver RW (1993) Fumonisin toxicosis in swine: clinical and pathological findings. *J. Vet. Diag. Invest.* **5**:232-241.

Diaz GJ, Boermans HJ (1994) Fumonisin toxicosis in domestic animals: a review. *Vet. Human Toxicol.* **36**:548-555.

D'Mello JPF, Placinta CM, Macdonald AMC (1999) *Fusarium* mycotoxins: a review of global implications for animal health, welfare and productivity. *Anim. Feed Sci. Technol.* **80**:183-205.
Domenech J, Boccas B, Pellegrin F, Laurent D, Kohler F, Magnol J, Lambert C (1985) Equine leucoencephalomalacia in New Caledonia. *Aust. Vet. J.* **62**:422-423.
Floss JL, Casteel SW, Johnson GC, Rottinghaus GE, Krause GF (1994) Developmental toxicity in hamsters of an aqueous extract of *Fusarium moniliforme* culture material containing known quantities of fumonisin B_1. *Vet. Human Toxicol.* **36**:5-10.
Gelderblom WCA, Jaskiewicz K, Marasas WFO, Thiel PG, Horak MJ, Vleggaar R, Kriek NPJ (1988) Fumonisins – novel mycotoxins with cancer promoting activity produced by *Fusarium moniliforme*. *Appl. Environ. Microbiol.* **54**:1806-1811.
Gumprecht LA, Constable PD, Smith GW, Simutis CA, Haschek WM (1998) Fumonisin-induced capillary endothelial alterations are organ and species specific: their potential role in porcine pulmonary edema. *Vet. Pathol.* **35**:455 (Abstract).
Gurung NK, Rankins DL Jr, Shelby RA, Goel S (1998) Effects of fumonisin B_1-contaminated feeds on weanling Angora goats. *J. Anim. Sci.* **76**:2863-2870.
Harrison LR, Colvin BM, Greene JT *et al.* (1990) Pulmonary edema and hydrothorax in swine produced by fumonisin B_1, a toxic metabolite of *Fusarium moniliforme*. *J. Vet. Diag. Invest.* **2**:217-221.
Haschek WM, Motelin G, Ness DK, *et al.* (1992) Characterisation of fumonisin toxicity in orally and intravenously dosed swine. *Mycopathologia* **117**:83-96.
IARC (International Agency for Research on Cancer) (1993) Toxins derived from *Fusarium moniliforme*: fumonisin B_1 and B_2 and Fusarium C. *IARC Monogr. Eval. Carcinog. Risk Chem. Humans* **56**:445-466.
Mallman CA, Santurio JM, Dilkin P (1999) Equine leukoencephalomalacia associated with ingestion of corn contaminated with fumonisin B_1. *Revista de Microbiologia* **30**:249-252. [Abstract 2438, *Nutr. Abs. Rev. B* **70**:412 (2000)]
Meronuck RA, Xie W (1999) Mycotoxins in feed. *Feedstuffs* **71**:123-130.
Osweiler GD, Ross PF, Wilson TM, Nelson PE, Witte ST, Carson TL, Rice LG, Nelson HA (1992) Characterization of an epizootic of pulmonary edema in swine associated with fumonisin in corn screenings. *J. Vet. Diagn. Invest.* **4**:53-59.
Rheeder JP, Marasas WFO, Vismer HF (2002) Production of fumonisin analogs by *Fusarium* species. *Appl. Environ. Microbiol.* **68**:2101-2105.
Robertson-Smith RG, Jeffcott LB, Friend SCE, Badcoe LM (1985) An unusual incidence of neurological disease affecting horses during a drought. *Aust Vet. J.* **62**:6-12. [1 case of LEM included]
Smith GW, Constable PD, Bacon CW, *et al.* (1994) Cardiovascular effects of fumonisins in swine. *Fundam. Appl. Toxicol.* **31**:169-172.
Smith GW, Constable PD, Haschek WM (1996) Cardiovascular responses to short-term fumonisin exposure in swine. *Fundam. Appl. Toxicol.* **33**:140-148.
Smith GW, Constable PD, Tumbleson ME, Rottinghaus GE, Haschek WM (1999) Sequence of cardiovascular changes leading to pulmonary edema in swine fed culture material containing fumonisin. *Am. J. Vet. res.* **60**:1292-1300.
Sydenham EW, Theil PG, Marasus WFO (1990) Natural occurrence of some *Fusarium* mycotoxins in corn from low and high esophageal cancer prevalence areas of the Transkei, Southern Africa. *J. Agric. Food Chem.* **38**:1900-1903.
Tyler CM, Davis RE, Begg AP, Hutchins DR, Hodgson DR (1993) A survey of neurological disease in horses. *Aust. Vet. J.* **70**:445-449. [3 cases recorded – those reported by Christley *et al.* 1993]

☑ Phomopsins

Core data

Syndromes:
- Lupinosis
- Lupinosis-associated myopathy (LAM)

Common source: hexapeptide mycotoxins
- *Diaporthe toxica* growing as a saprophyte in stubble of dead lupins (*Lupinus* spp.)
- WA, Vic, NSW

Animals affected: sheep, cattle (rarely horses)

Mode of action:
- cytoplasmic microtubular dysfunction in hepatocytes
- → abnormal mitosis, mitotic arrest
- pathogenesis of skeletal muscle lesions (LAM) undescribed

Poisoning circumstances:
- grazing infected dry lupin stubble
- fed infected lupin seed
- toxin cumulative

Main effects:
- Lupinosis:
  - weight loss, jaundice
  - chronic liver damage with
  - individual hepatocyte necrosis, numerous mitotic figures and fibrosis

- LAM: lupinosis +
  - stiff gait
  - skeletal muscle degeneration

Diagnosis:

- Lupinosis: lupin stubble or seed access + phomopsin assay + syndrome + liver histopathology
- LAM: differentiate from white muscle disease- LAM = not Se responsive, high liver Se, mostly skeletal muscle involved

Therapy:

- Lupinosis: nil
- LAM: ? Se + vitamin E

Prevention:

- immunisation
- *Diaporthe*-resistant lupin cultivars
- grazing & plant management to minimise stubble intake

Syndromes:

- **Lupinosis** (a mycotoxicosis). This syndrome should not be confused with lupin poisoning from isoquinoline alkaloids concentrated in seeds of lupin (*Lupinus* spp.) plants
- **Lupinosis-associated myopathy** (LAM)

Chemical structure:

Phomopsins are **linear hexapeptides** incorporating a 13-membered ring formed by an ether bridge linking the 5-hydroxy group of the phenylserine unit with the 3-hydroxyisoleucine unit.

Sources:

Phomopsins are produced by the fungus ***Diaporthe toxica*** (anamorph of *Phomopsis* sp.) (Williamson *et al.* 1994) previously referred to erroneously in the literature as *Phomopsis leptostromiformis* [see below] This organism is a **saprophyte on stubble from lupin crops** grown for green manure or seed.

Phomopsis leptostromiformis was the fungus originally shown to produce phomopsins. It has now been shown that there was an error in the original description of this fungus. The current situation is that lupinosis is caused by *Diaporthe toxica* (anamorph *Phomopsis* sp.) which is highly toxigenic. The fungus *Diaporthe woodii* (anamorph *Phomopsis leptostromiformis*) also infects lupins but has a very low capacity to produce phomopsins and is no longer regarded as the cause of lupinosis. *Phomopsis emecis*, which infects *Emex australis* (spiny emex, double-gee), has also been shown to produce large quantities of phomopsins when cultured in the laboratory but has not been incriminated in any field disease. [JG Allen, personal communication 1998]

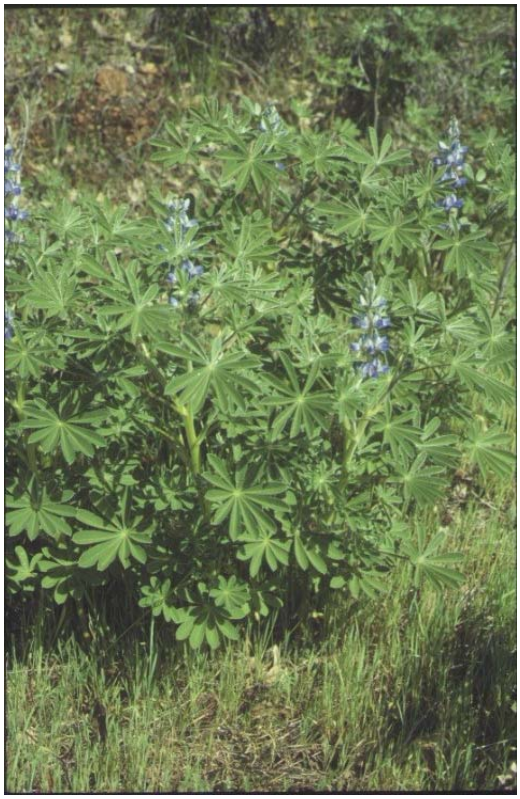
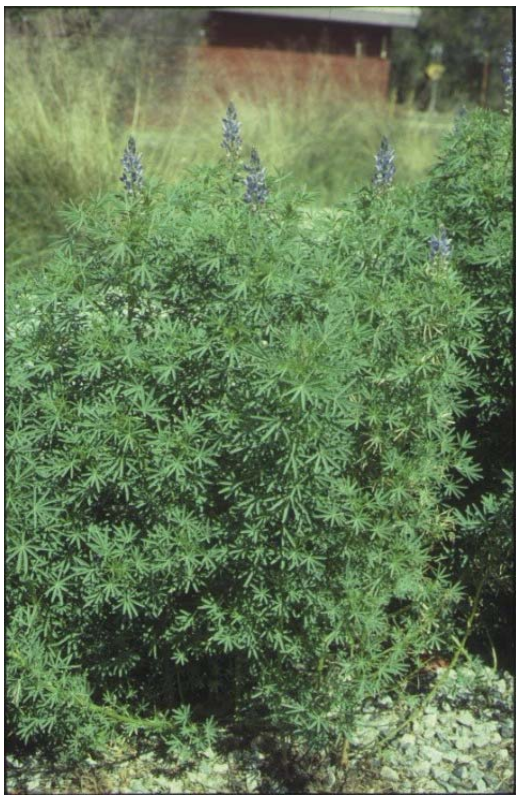
Plant host sources:

Family Fabaceae: mostly involved are

Lupinus angustifolius (New Zealand blue lupin)
Lupinus cosentinii (Western Australian blue or sandplain lupin)
Lupinus luteus (yellow lupin)

Family Polygonaceae:

Emex australis (spiny emex, double-gee)


Lupinus spp. : *L. cosentinii* (Western Australian blue or sandplain lupin) (top left); *L. angustifolius* (New Zealand blue lupin) (top right); *L. luteus* (yellow lupin) (below) [RAM Photos]

Toxicity:

Lupinosis:

- **sheep**, cattle (rarely horses)
- single sheep intraruminal LD_{50} = about 1 mg phomopsin A/kg live weight

- toxicity is **cumulative** - 20 consecutive intraruminal daily doses of 0.05 mg/kg lethal
- usually fatal in sheep

LAM:

- **sheep** in Western Australia
- LAM =
    - concurrent lupinosis (liver lesions)
    - high liver Se
    - not Se responsive
    - skeletal muscle mostly involved
    - sudden death not a feature (no cardiac muscle involvement)

Mode of action:

Phomopsins bind to tubulin and prevent formation of microtubules → cytoplasmic microtubular dysfunction in hepatocytes → abnormal mitosis, mitotic arrest & fatty infiltration (Edgar 1991)

LAM pathogenesis is undescribed.

Conditions of poisoning:

Lupinosis:

- Australia (WA, V, NSW)
- **infected dry lupin stubble** grazed/browsed.
- contaminated lupin **seed** may also cause poisoning

LAM:

- access to infected lupin stubble
- sheep with low vitamin E status (Smith & Allen 1997)

Clinical signs:

Lupinosis:

- Sheep
    - lethargy, inappetence
    - **weight loss**
    - **jaundice**
    - ± anaemia (Gardiner 1961, 1967, Allen & Cousins 1998)
    - ± photosensitisation

    Photosensitisation occurs less commonly than the degree of liver damage suggests. Possible explanation: Toxic lupin stubble available when there is little green feed to supply phylloerythrin & there is adequate excretory reserve left in the liver.

- Cattle (as for sheep OR)
    - **ketosis**
    - ± jaundice
    - ± photosensitisation
    - ± abortion
- Horses (*rare*)
    - lethargy, inappetence
    - jaundice
    - abdominal pain
    - haemoglobinuria
    - recumbency

LAM (additional to signs of lupinosis):

- reluctance to walk
- stiff gait
- stand with back arched, feet placed under body

Pathology:

Lupinosis:

- Necropsy
    - sheep
        - ↑ rumen fluid

- jaundice & swollen pale liver
- **or** no jaundice & fibrotic liver
- ± ascites, anasarca

- cattle
  - jaundice
  - swollen pale liver
  - **or** fibrotic liver
- horse
  - jaundice
  - pale liver

- histopathology of liver
  - **mitotic figures** in many hepatocytes
  - necrosis of individual hepatocytes (necrobiosis)
  - biliary ductular hyperplasia
  - portal fibroplasia
  - ± fatty infiltration & post-necrotic scarring

LAM:

degeneration and necrosis of skeletal muscle fibres

Diagnosis:

Various assay methods for phomopsins have been developed (nursling rat bioassay, sheep bioassay, HPLC, ELISA) and the currently-preferred method is the ELISA technique (Allen *et al.* 1998).

Lupinosis:

lupin stubble or seed access + phomopsin assay + syndrome + liver histopathology

LAM:

- pathology + access
- differentiate from white muscle disease (WMD = myopathy mostly affecting heart; liver Se <0.67μg/g d.m.; Se responsive)

Therapy:

Lupinosis:

nil

LAM:

Se + α-tocopherol together may be effective

Prevention & control:

Lupinosis:

- sheep

Immunisation with phomopsin-conjugate vaccine (CSIRO-WA Dept of Agriculture joint development) → protection; commercial product under development (Edgar *et al.* 1998)

***Diaporthe*-resistant lupin cultivars** (*Lupinus albus, L. angustifolius*)

Lupin **grazing management**:

- graze soon after harvest (early summer, not late autumn)
- sheep stocking rate <30/hectare
- train weaners to lupin seed diet before exposure → ↓ stubble intake

Lupin **plant management**:

- hay making (just after flowering on tertiary branches), fodder rolls
- mixed crops with oats, barley or wheat → ↓ lupin intake in summer grazing
- ↑ lupin stubble pH with strong alkali → ↓ fungal growth (experimental)

Zn dosing is *not* valuable for prevention; Zn dosing of sheep @ 0.5 g/day or more reduced the degree of liver damage, but induced Zn toxicity (Allen & Masters 1980)

LAM:

- general control of lupinosis should reduce occurrence
- supplement with vitamin E protects against LAM but not against liver damage (Smith & Allen 1997)

- the most effective supplementation is through **SC injection of selenomethionine + α-tocopherol** (vitamin E) (Smith & Allen 1997). Doses per sheep of 2000 IU α-tocopherol acetate + 0.1 selenium as selenomethionine / kg used by Smith & Allen (1997) were prepared as described by Hidiroglou & Charmley (1990): dissolve the required amount of selenomethionine into 10 ml of an emulsion of α-tocopherol acetate in an aqueous detergent solution (200 g α-tocopherol acetate / L).

References:

Se173

Alen JG (1978) The emergence of a lupinosis-associated myopathy in sheep in Western Australia. *Aust. Vet. J.* **54**:548-549.

Allen JG (1989) Studies of the pathogenesis, toxicology and pathology of lupinosis and associated conditions. PhD Dissertation, Murdoch University, Perth.

Allen JG, Wood PM, O'Donnell FM (1978a) Control of ovine lupinosis: experiments on the making of lupin hay. *Aust. Vet. J.* **54**:19-22.

Allen JG, Croker KP, Wilkinson FC, Wood PM (1978b) An investigation of the removal of coarse plant material from lupin stubble paddocks for the control of ovine lupinosis. *Aust. Vet. J.* **54**:521-524.

Allen JG, Wood PM (1979) The prevention of lupinosis by making lupin hay. *Aust. Vet. J.* **55**:38-39.

Allen JG, Masters HG (1980) Prevention of ovine lupinosis by the oral administration of zinc sulphate and the effect of such therapy on liver and pancreas zinc and liver copper. *Aust. Vet. J.* **56**:168-171.

Allen JG, Cousins DV (1998) Haematological changes in sheep with experimentally produced acute and chronic lupinosis. Chapter 14 in *Toxic Plants and Other Natural Toxicants*, edited by T Garland and AC Barr, CAB International, Wallingford UK, pp. 62-68.

Allen JG, Than KA, Speijers EJ, Ellis Z, Croker KP, McDonald CL, Edgar JA (1998) A comparison of a nursling rat bioassay and an ELISA to determine the amount of phomopsins in lupin stubbles. Chapter 39 in *Toxic Plants and Other Natural Toxicants*, edited by T Garland and AC Barr, CAB International, Wallingford UK, pp. 191-195.

Edgar JA (1991) Phomopsins: antimicrotubule mycotoxins. Chapter 18 in Keeler RF, Tu AT (eds) *Handbook of Natural Toxins. Vol.6. Toxicology of Plant and Fungal Compounds.* Marcel Dekker, Inc., New York. pp. 371-395.

Edgar JA, Than KA, Payne AL, Anderton N, Baell J, Cao Y, Cockrum PA, Michalewicz A, Stewart PL, Allen JG (1998) Towards a commercial vaccine against lupinosis. Chapter 40 in *Toxic Plants and Other Natural Toxicants*, edited by T Garland and AC Barr, CAB International, Wallingford UK, pp. 196-200.

Gardiner MR (1961) Lupinosis, an iron storage disease of sheep. *Aust. Vet. J.* **37**:135-140.

Gardiner MR (1967) Lupinosis. *Advances in Veterinary Science* **11**:85-138.

Hidiroglou M, Charmley E (1990)Vitamin E concentrations in blood plasma of sheep and in sheep tissues after a single intraperitoneal administration of dl-α-tocopherol acetate. *Res. Vet. Sci.* **48**:158-161.

Smith GM, Allen JG (1997) Effectiveness of α-tocopherol and selenium supplements in preventing lupinosis-associated myopathy in sheep. *Aust. Vet. J.* **75**:341-348.

Williamson PM, Highet AS, Gams W, Sivasithamparam K, Cowling WA (1994) *Diaporthe toxica* sp. nov., the cause of lupinosis in sheep. *Mycol. Res.* **98**:1364-1368.

Wood PM, Brown AGP, Meyer EP, Petterson DS (1975) Control of ovine lupinosis: experiments on the use of fungicides. *Aust. Vet. J.* **51**:381-384.

Wood PMcR, Petterson DS (1986) *Phomposis leptostromiformis* infection and phomopsin A content of lupin seed in Western Australia. *Aust. J. Exp. Agric.* **26**:583-586.

☑ *Sporidesmin*

Core data

Syndrome: facial eczema
Common source: spores of *Pithomyces chartarum* on *Lolium* sp. pasture litter
Animals affected: ruminants (alpacas > sheep, cattle > goats)
Poisoning circumstances: pasture spore counts high
Main effects: obliterating cholangitis
Diagnosis: spore counts, ↑GGT, liver pathology
Therapy: nil
Prevention:

- weather forecasts + spore count data
- zinc
- fungicide sprays
- genetic selection of resistant sheep, cattle

Syndrome name:

facial eczema (a secondary or hepatogenous photosensitisation)

Sources:

Sporidesmin is a mycotoxin produced by the fungus ***Pithomyces chartarum*** saprophytic on pasture litter, particularly *Lolium perenne* (perennial ryegrass) pastures. It is concentrated in the **spores** of the fungus. The spores, not entirely inappropriately, have the general appearance of Mills bombs (hand grenades used by allied forces in World Wars I and II).

Toxicity:

Ruminants (alpacas > sheep, cattle, deer > goats) (Smith & Embling 1991; Hartley 1993; Ross 1994; Smith *et al.* 1997)

Macropods (eastern grey kangaroo [Hum 2001])

Cases have been recorded in

New Zealand

Australia – Vic (Walsh 1966, Jubb 2001), NSW, WA (Gardiner & Nairn 1962), SA (Critchley 2001)

South Africa

USA (Hansen 1994)

Mode of action:

- damage to biliary tract → **obliterating cholangitis** → atrophy of left lobe, compensatory hypertrophy of remaining liver → distorted fibrotic liver
- sporidesmin catalyses generation of highly-toxic oxygen free radicals (Smith & Miles 1993)

Conditions of poisoning:

- pastures with heavy pasture litter component under weather conditions conducive to *Pithomyces chartarum* growth [minimum night temperatures greater than 15°C and relative humidity greater than 90% for some days about 10 days before an outbreak (BL Smith, personal communication VETTOX discussion group 5 July 2001)]

Clinical signs: hepatogenous photosensitisation

Pathology:

- liver: cholangitis, fibrosis
- severe chronic cases → complete atrophy of left liver lobe. Pathogenesis of this lesion probably results from there being a longer intrahepatic biliary system compared with that of the right lobe of ruminant livers. Cholestasis worse in left lobe → portal fibrosis → reduced blood flow to worst-affected parenchyma → deprivation of hepatotrophic factors → atrophy of left lobe >> right lobe (WR Kelly, personal communication 1996)

Diagnosis:

- spore count on pasture; hazardous = > 70,000 spores/g pasture litter
- spores may be detected in scrapings of the exudate from the gland just near the medial canthus of the eyes (BL Smith, personal communication VETTOX discussion group 5 July 2001)
- clinical pathology: ↑ plasma GGT concentration (Towers & Stratton 1978)
- hepatic lesions
- assay available for sporidesmin in pasture (Collin *et al.* 1995)

Therapy: no specific therapy

Prevention & control:

- *P. chartarum* spore counting + weather data → **forecast hazardous periods** (hazardous = > 70,000 spores/g pasture litter)
- **genetic selection** of more resistant sheep, cattle (Morris *et al.* 1998)
- spraying pastures with **fungicides** (benzimidazoles)
- **zinc supplementation** effective @ *ca.*20 mg Zn/kg/day [1 g Zn/day for a 50 kg sheep] provided that treatment starts before spore numbers increase (Munday *et al.* 1997)
  - Zn toxicity (supplementation rate x 3 - small error margin) → pancreatic necrosis
  - mode of action of Zn thought to be by formation of mercaptides with the dithiol moiety of reduced sporidesmin, thus reducing its ability to catalyse oxygen free radical formation, and by lowering hepatic copper concentrations (Smith & Miles 1993)
  - various delivery systems including intra-ruminal slow-release devices (Munday *et al.* 1997)
  - Cu deficiency may result from prolonged Zn dosage (Rounce *et al.* 1998).

Reference: Se178

Caple IW, Vandergraaff R, Malmo J (1976) Use of sulphobromophthalein liver function tests in cows with facial eczema. *Aust. Vet. J.* **52**:192-193.

Collin RG, Briggs LR, Towers NR (1995) Development and evaluation of an enzyme immunoassay for sporidesmin in pasture. *N.Z. J. Agric. Res.* **38**:297-302.
Critchley K (2001) Possible facial eczema in dairy cattle. *Animal Health Australia Animal Health Surveillance Quarterly Report 1 January - 31 March 2001.* **6** (1):13.
Gardiner MR, Nairn M (1962) Facial eczema in Western Australian sheep. *J. Agic. West. Aust.* **3**:85-92.
Hansen DE, McCoy RD, Hedstrom OR, Snyder SP, Ballerstedt PB (1994) Photosensitization associated with exposure to *Pithomyces chartarum* in lambs. *J. Am. Vet. Med. Assoc.* **204**:1668-1671.
Hartley MS (1993) Sporidesmin (facial eczema) toxicity in alpacas. *Post-Grad. Committee in Vet Science, University of Sydney: Control & Therapy Series*. Mailing 175, No.3467.
Hum S (2001) Suspect sporidesmin toxicity in an eastern grey kangaroo. *Vet. Path. Report (ASVP Newsletter)* No. 60, p. 9.
Jubb T (2001) Suspected facial eczema in dairy cattle in western Victoria. *Animal Health Australia Animal Health Surveillance Quarterly Report 1 January - 31 March 2001.* **6** (1):16.
Morris CA, Burton LJ, Towers NR, Cullen NG, Rendel JM, Johnson DL (1998) Genetic susceptibility to facial eczema in Friesian and Jersey cattle. *N. Z. J. Agric. Res.* **41**:347-357.
Munday R, Thompson AM, Fowke EA, Wesselink C, Smith BL, Towers NR, O'Donnell K, McDonald RM, Stirnemann M, Ford AJ (1997) A zinc-containing intraruminal device for facial eczema control in lambs. *N.Z. Vet. J.* **45**:93-98.
Ross AD (1994) Health problems in the alpaca industry. *Post-Grad. Committee in Vet Science, University of Sydney: Control & Therapy Series*. Mailing 179. No.3599.
Rounce JR, Knowles SO, Grace ND, Lee J (1998) Effect of zinc oxide treatment for facial eczema on the copper status of Romney sheep grazing ryegrass pastures. *Proc. NZ Soc. Anim. Prod.* **58**:199-201.
Smith BL (2000) Effects of low dose rates of sporidesmin given orally to sheep. *N. Z. Vet. J.* **48**:176-181.
Smith BL, Embling PP (1991) Facial eczema in goats: the toxicity of sporidesmin in goats and its pathology. *NZ Vet. J.* **39**:18-22.
Smith BL, Miles CO (1993) A letter to the editor: A role for *Brachiaria decumbens* in hepatogenous photosensitisation of ruminants? *Vet. Human Toxicol.* **35**:256-257.
Smith BL, Asher GW, Thompson KG, Hoggard GK (1997) Hepatogenous photosensitisation in fallow deer (*Dama dama*) in New Zealand. *N. Z. Vet. J.* **45**:88-92.
Towers NR, Stratton GC (1978) Serum gamma glutamyltransferase as a measure of sporidesmin-induced liver damage in sheep. *N. Z. Vet. J.* **26**:109-112.
Walsh AD (1966) Facial eczema of sheep in Victoria. *J. Agric. Vic. Dept. Agric.* **64**:519-522.

☑ *Furans - Mouldy sweet potatoes*

Core data

Common sources: Ipomoea batatus tubers infected with *Fusarium* sp.
Animals affected: cattle
Mode of action:

- tubers produce furanosesquiterpenes as phytoalexins
- fungus converts these to furanoterpenes, including 4-ipomeanol
- 4-ipomeanol metabolised by lung cells → pneumotoxicity

Poisoning circumstances: consumption of mouldy tubers
Main effects: atypical interstitial pneumonia
Diagnosis: access + pathology
Therapy: remove from access
Prevention: deny access

Syndrome names: atypical interstitial pneumonia
Chemical structure:

3-substituted furans (Ipomeanol from mouldy *Ipomoea batatus* tubers)

Sources:

- mouldy ***Ipomoea batatus*** (sweet potato) tubers infected with ***Fusarium solani*, *Fusarium oxysporum* or other *Fusarium* spp.**
- one case atypical interstitial pneumonia in cattle (bulls) browsing on *Leucaena leucocephala*, central Qld 1998; cause undetermined
- cases of atypical interstitial pneumonia have been reported in cattle grazing or hand-fed *Paspalum distichum* (water couch) in north-eastern NSW; investigations of pasture tryptophan (substrate for ruminal production of pneumotoxic 3-methylindole) were inconclusive (Gill 1996).
- atypical interstitial pneumonia in calves has been reported in association with perennial ryegrass staggers (lolitrems from endophyte *Acremonium lolii* in *Lolium perenne*) in Oregon USA (Pearson *et al.* 1996)

Toxicity:

- cases reported in cattle in North America (Peckham *et al.* 1972) & Australia (Hill & Wright 1992)
- cattle most susceptible species to 4-ipomeanol
- lesions have been reproduced in cattle drenched with 4-ipomeanol @ 6.0-14.0 mg/kg (Doster *et al.* 1978)

Mode of action:
- furanosesquiterpenes produced by damaged tuber tissue as phytoalexins (defense chemicals)
- converted by the fungus to other furanoterpenes (3-substituted furans), including 4-ipomeanol
- **4-ipomeanol** → pneumotoxicity *after* activation within lung cells by microsomal enzymes

Conditions of poisoning: consumption of **mouldy tubers** of sweet potato
Clinical signs:
- rapid onset
- dyspnoea
- abdominal breathing

Pathology: acute severe **interstitial pneumonia**, pulmonary oedema & emphysema
Diagnosis: access + pathology
Therapy:
- removal from the crop → recovery in all but the worst cases

Prevention & control:
- deny access to mouldy tubers
- experimental work suggests fermentation of affected tubers before feeding may prevent poisoning (Thibodeau *et al.* 1999)

References:

Review literature

Se78

Wilson BJ, Burka LT (1983) Sweet potato toxins and related toxic furans. Chapter 1 in Keeler RF, Tu AT (eds.) *Handbook of Natural Toxins. Volume 1-1. Plant and Fungal Toxins*. Marcel Dekker, Basel. pp.3-41.

General literature

Doster AR, Mitchell FE, Farrell RL, Wilson BJ (1978) Effects of 4-ipomeanol, a product from mold-damaged sweet potatoes, on the bovine lung. *Vet. Pathol.* **15**:367-375.

Gill P (1996) *Paspalum distichum*-associated pneumonia. *Vet. Path. Report (Newsletter Aust. Soc. Vet. Path.)* No.44, p.33-34.

Hill BD, Wright HF (1992) Acute interstitial pneumonia in cattle associated with consumption of mould-damaged sweet potatoes (*Ipomoea batatus*). *Aust. Vet. J.* **69**:36-37.

Pearson EG, Andraesen CB, Blythe LL, Craig AM (1996) Atypical pneumonia associated with ryegrass staggers in calves. *J. Am. Vet. Med. Assoc.* **209**:1137-1142.

Peckham JC, Mitchell FE, Jones OH, Doupnik B (1972) Atypical interstitial pneumonia in cattle fed mouldy sweet potatoes. *J. Am. Vet. Med. Assoc.* **160**:169-172.

Thibodeau MS, Rogers GM, Poore MH, Hagler WMJr (1999) Amelioration of the pulmonary toxic effects of 4-ipomeanol in mice by fermentation of mold-damaged sweet potatoes. In *Proc. 32nd Ann. Conf. Am. Assoc. Bov. Practit.*, Smith RA (ed.), American Association of Bovine Practitioners, Stillwater USA. p. 229 [*Nutrition Abstracts & Reviews (Series B)* 2000 **70**: Abstract 656]

☑ Zearalenone

Core data

Syndrome name: "vulvovaginitis" [sic]
Common sources:
- *Fusarium graminearum* growing on maize, sorghum and other grains

Animals affected: sexually-immature pigs
Mode of action: mimic oestrogen effects
Poisoning circumstances: moist storage of harvested grain
Main effects:
- vulval hyperaemia & swelling
- premature mammary development
- rectal prolapse
- preputial swelling, testicular atrophy

Diagnosis:
- syndrome + grain access
- feed zearalenone assay

Therapy:
- remove source from feed

- all signs reversible, no permanent effects

Prevention: apply correct grain storage conditions

Syndrome names: "vulvovaginitis" [sic]

Chemical structure:

Zearalenones are phenolic compounds with oestrogenic effects

Sources:

- fungus ***Fusarium graminearum*** (reproductive phase = *Gibberella zeae*) growing on maize, sorghum and other grains
- zearalenone is produced to regulate *F. graminearum* reproduction
- other *Fusarium* spp. can → zearalenone e.g. *Fusarium crookwellense* in maize stubble (Lopez *et al.* 1997)

Toxicity:

- pigs: effects in sexually-immature pigs (gilts 1-4 months) @ 1-5 mg zearalenone/kg ration
- suckling piglets have been affected (Dacasto *et al.* 1995)
- sheep & cattle: infertility in grazing sheep and cattle in New Zealand (Towers & Sprosen 1993, Towers 1996)

Mode of action: mimic oestrogen effects

Conditions of poisoning:

- *F. graminearum* → reddish-pink coloration to infected maize kernels
- *F. graminearum* requires at least 22-25% moisture in the substrate for growth
- hail damage to immature kernels predisposes to infection (Abbas *et al.* 1988)
- most zearalenone produced post-harvest under poor storage conditions (relative humidity about 45%, temperature 20-35^{o}C)

Clinical signs:

Sexually-immature pigs

- vulval hyperaemia & swelling ("vulvovaginitis")
- ↑ mammary development, rectal prolapse, preputial swelling, testicular atrophy

Adult sows fed > 10 mg zearalenone/kg ration →

- persistent corpora lutea, anoestrus, pseudopregnancy

→ recover 7-10 days after toxin removed

Cattle (rarely-affected)

- decreased fertility
- prolonged oestrus, some with oestrus during mid-cycle
- vulval swelling

Turkeys on feed containing 300 ppm for 4 days → greatly enlarged vents (Christensen *et al.* 1988)

Pathology: as above

Diagnosis:

- syndrome + access to grain
- assay feed for zearalenone

Therapy:

- remove from source
- all signs reversible & → no permanent negative effect

Prevention & control:

- apply correct storage conditions to grain
- use of bentonite as an adsorbent added to contaminated feed has **not** been effective (Williams *et al.* 1994)

References:

Se169

Abbas HK, Mirocha CJ, Meronuck RA, Pokorny JD, Kommedahl SL & T (1988) Mycotoxins and *Fusarium* spp. associated with infected ears of corn in Minnesota. *Appl. Env. Micro.* **54**:1930-1933.

Blaney BJ, Bloomfield RC, Moore CJ (1984) Zearalenone intoxication of pigs. *Aust. Vet. J.* **61**:24-27.

Christensen CM, Mirocha CJ, Meronuck RA (1988) Moulds and mycotoxins in feeds. *Minnesota Extension Services Bull.* AG-FO-3538 [cited by Meronuck RA, Xie W (1999) Mycotoxins in feed. *Feedstuffs* **71**:123-130.]

Dacasto M, Rolando P, Nachtmann C, Ceppa L, Nebbia C (1995) Zearalenone mycotoxicosis in piglets suckling sows fed contaminated grain. *Vet. Human Toxicol.* **37**:359-361.

di Menna ME, Lauren DR, Holland PT (1985) Presence of zearalenone in New Zealand pasture leaves. *N.Z. Vet. J.* **33**:193.

di Menna ME, Lauren DR, Sprosen JM, Maclean KS (1991) *Fusarium* and zearalenone on herbage fractions from short and from long pasture. *N.Z. J. Agric. Res.* **34**:193.

D'Mello JPF, Placinta CM, Macdonald AMC (1999) *Fusarium* mycotoxins: a review of global implications for animal health, welfare and productivity. *Anim. Feed Sci. Technol.* **80**:183-205.
Towers NR (1996) Oestrogenic fungal toxins affecting sheep and cattle production. *Proc. Sheep Sessions, 2nd Pan Pacific Veterinary Conference, Christchurch 1996*, pp.43-58.
Towers NR, Sprosen JM (1993) Zearalenone-induced infertility in sheep and cattle in New Zealand. *N.Z. Vet. J.* **41**:223-224.
Lopez TA, Escande A, Chayer R, Dosanto M, Gerpe O, Salomon ML (1997) *Fusarium crookwellense*-produced zearalenone in maize stubble in the field. *N.Z. Vet. J.* **45**:251-253.
Williams KC, Blaney BJ, Peters RT (1994) Pigs fed *Fusarium*-infected maize containing zearalenone and nivalenol with sweeteners and bentonite. *Livestock Prodn. Sci.* **39**:275-281.

Ochratoxins

Syndrome names:
- ochratoxicosis
- suspected association with Balkan endemic nephropathy (humans) (Stoev 1998)

Chemical structure:
Ochratoxins = dihydroisocoumarin derivatives linked to L-β-phenylalanine

Sources:
- produced by the fungi *Aspergillus alutaceus* [= *Aspergillus ochraceus*], other *Aspergillus* spp., *Penicillium viridicatum, P. verrucosum* & other *Penicillium* spp. growing on cereal grains (maize, rice, millet, wheat, barley), beans, peanuts, green coffee, olives, figs.
- not all strains are toxigenic
- significant variation between cultivars of crops in ochratoxin contamination rates (Axberg 1998)

Toxicity:
- species susceptibility: monogastrics (pigs, poultry) >> ruminants
- ruminants metabolise ochratoxin A in the rumen to non-toxic ochratoxin α; ochratoxin A half-life in rumen contents 0.17-1.84 hr (Müller *et al.* 1998)
- ochratoxicosis: Northern hemisphere
- toxigenic fungi are in Australia but no cases have been recorded
- associated with Balkan endemic nephropathy of humans (Stoev 1998)
- 5 ng ochratoxin A/g proposed maximum contamination of cereals for human consumption
- experimentally 1 mg ochratoxin A/kg feed fed to pigs for 2 years produced renal damage within a few weeks, but terminal kidney failure did not occur (Krogh *et al.* 1979)
- carcinogenic in rodents

Mode of action:
- possibly interferes with metabolism of phenylalanine (amino acid)

Conditions of poisoning:
- optimum conditions for toxin production by *A. ochraceus* in grain = moisture 19-22% & temperature 24°C.

Clinical signs:
- pigs
  - sudden onset polydipsia & polyuria
  - ± anorexia ± weight loss
- poultry
  - ↓ growth rate
  - tremors, convulsions

Pathology:
- pigs
  - serum ↑ creatinine & urea
  - glucosuria & proteinuria
  - **nephrosis**, perirenal oedema
  - ± gastrointestinal erosions
  - ± hepatocyte degeneration
- poultry
  - **nephrosis**
  - proventricular haemorrhage
  - visceral gout

Diagnosis: pathology + feed assay

Therapy:

- nil recognised
- phenylalanine prevents toxicity in mice

Prevention & control:

- ochratoxin A → significant residues in pig kidneys → 4 week withholding period before slaughter (Europe)

References:

Reviews

Se163

Marquardt RR, Frohlich AA (1992) A review of recent advances in understanding ochratoxicosis. *J. Anim. Sci.* **70**:3968-3988.

General literature

Axberg K, Jansson G, Hult K (1998) Ochratoxin A in rice cultivars after inoculation of *Penicillium verrucosum. Nat. Toxins* **6**:73-84.

Krogh P, Elling F, Friis C, Hald B, Larsen AE, Lillehøj EB, Madsen A, Mortensen HP, Rasmussen F, Ravnskov U (1979) Porcine nephropathy induced by long-term ingestion of ochratoxin A. *Vet. Pathol.* **16**:466-475.

Müller H-M, Lerch C, Müller K, Eggert W (1998) Kinetic profiles of ochratoxin A and ochratoxin α during *in vitro* incubation in buffered forestomach and abomasal contents from cows. *Nat. Toxins* **6**:251-258.

Stoev SD (1998) The role of ochratoxin A as a possible cause of Balkan endemic nephropathy and its risk evaluation. *Vet. Human Toxicol.* **40**:352-360.

Trichothecene mycotoxins

Trichothecene mycotoxins = 12,13-epoxytrichothecenes, a class of tetracyclic sesquiterpene lactones.
Trichothecenes are named after *Trichothecium roseum* [= *Fusarium graminearum*], the source of the first recognised compound in this group (Meronuck & Xie 1999).
Over 150 trichothecenes are known
Type A trichothecenes - non-ketone functional group at C-8
Type B trichothecenes - carbonyl function at C-8

General mode of action is inhibition of eucaryotic protein synthesis.
Six *Fusarium* spp. are known to produce trichothecenes worldwide (Lauren *et al.* 1987)

- *F. sporotrichioides* and *F. poae* → mainly T-2 toxin and diacetoxyscirpenol (DAS)
- *F. graminearum, F. crookwellense, F. culmorum* and *F. sambucinum* → mainly deoxynivalenol (DON) and DAS
- all are destructive pathogens attacking a wide range of plants

Main substrates for trichothecene production are cereal grains.
Low temperatures, high moisture and humidity tend to increase trichothecene production (Meronuck & Xie 1999).
Wide variety of toxic effects including

- gastrointestinal disturbance: vomiting, diarrhoea, inflammation
- feed refusal
- anaemia. leucopaenia
- dermal irritation
- abortion
- immunosuppression

References:

Cheeke 116; Os422

Buck WB, Côté L-M (1991) Trichothecene mycotoxins. Chapter 24 in Keeler RF, Tu AT (eds) *Handbook of Natural Toxins. Vol.6. Toxicology of Plant and Fungal Compounds.* Marcel Dekker, Inc., New York. pp. 523-555.

Desjardins AE, Hohn TM, McCormick SP (1993) Trichthecene biosynthesis in *Fusarium* species: chemistry, genetics and significance. *Micribiol. Rev.* **57**:594-604.

D'Mello JPF, Placinta CM, Macdonald AMC (1999) *Fusarium* mycotoxins: a review of global implications for animal health, welfare and productivity. *Anim. Feed Sci. Technol.* **80**:183-205.

Lauren DR, Asjley RA, Blackwell BA, Greenhalgh R, Miller JD, Neish GA (1987) Trichothecenes produced by *Fusarium crookwellense*. DAOM 193611. *J. Agric. Food Chem.* **35**:884-889.

Meronuck RA, Xie W (1999) Mycotoxins in feed. *Feedstuffs* **71**:123-130.

Trichothecenes (Type A)

Sources:

- late-harvested or over-wintered grain
- temperate zone countries of the northern hemisphere

- **T-2 toxin** and **diacetoxyscirpenol (DAS)** produced mostly by *Fusarium sporotrichoides*
- **satratoxin** produced by *Stachybotrys chartarum* [= *Stachybotrys atra, Stachybotrys alternans*] → stachybotryotoxicosis
- optimum toxin production conditions = alternating cool and warm temperatures (range 5-15°C)

Toxicity:

- **alimentary toxic aleukia** of humans in Russia during World War II (overwintered grain consumption)
- toxin stable in environment and resists heat & pressure of cooking, feed milling & processing
- inhibit protein, DNA & RNA synthesis; directly cytotoxic; suppress immunity
- voluntary feed refusal often prevents full expression of toxic potential
- trichothecenes rapidly metabolised and excreted
- cattle fed 0.64 ppm T-2 toxin for 20 days → death, dysentery, ruminal & abomasal ulcers (Pier *et al.* 1980)
- *S. chartarum* spore inhalation + tobacco smoke presumed cause of pulmonary haemorrhage (& pulmonary haemosiderosis) syndrome in children in Cleveland, Ohio, USA (Dearborn *et al.* 1999)
- dermatitis in cattle fed oat straw infected with *Fusarium sporotrichoides* (Wu *et al.* 1997)

Clinical signs:

- **feed refusal** → weight loss
- ± vomiting, diarrhoea (sometimes dysentery)
- ± dermal (feet, underline) and oral (tongue, forestomachs) irritation & necrosis (e.g. DAS → necrosis of oral mucosa/commissures of the mouth in poultry – Ademoyero & Hamilton 1991)
- ± haemorrhaging (?hypoprothrombinaemia, ?thrombocytopaenia)
- ± abnormal feathering (broilers)
- ↓ egg production + thin shells (20 ppm DAS in diet – Pier *et al.* 1980)
- ± abortion, infertility (pigs – Weaver *et al.* 1978a,b)

Pathology:

Acute

- stomatitis, dermatitis
- gastrointestinal ulceration (including lymphoid follicles)
- haemorrhagic enteritis & necrosis (DAS, pigs – Weaver *et al.* 1978c)

Chronic

- lymphoid depletion (thymus, spleen, bursa of Fabricius, intestinal lymphoid follicles)

Diagnosis: history, pathology, assay feed

Therapy: supportive

Reference:

Os422

Ademoyero AA, Hamilton PB (1991) Mouth lesions in broiler chickens caused by scirpenol mycotoxins. *Poultry Sci.* **70**:2082-2089.

Dearborn DG, Yike I, Sorenson WG, Miller MJ, Etzel RA (1999) Overview of investigations into pulmonary hemorrhage in infants in Cleveland, Ohio. *Environmental Health Perspectives* **107**(Supplement 3):495-499.

D'Mello JPF, Placinta CM, Macdonald AMC (1999) *Fusarium* mycotoxins: a review of global implications for animal health, welfare and productivity. *Anim. Feed Sci. Technol.* **80**:183-205.

Pier AC, Richard JL, Cysewski SJ (1980) The implication of mycotoxins in animal disease. *J. Am. Vet. Med. Assoc.* **176**:719-722.

Weaver GA, Kurtz HJ, Mirocha CJ, Bates FY, Behrens JC, Robinson TS, Gipp WF (1978a) Mycotoxin-induced abortions in swine. *Can. Vet. J.* **19**:72-74.

Weaver GA, Kurtz HJ, Mirocha CJ, Bates FY, Behrens JC, Robinson TS (1978b) Effect of T-2 toxin on porcine reproduction. *Can. Vet. J.* **19**:310-314.

Weaver GA, Kurtz HJ, Mirocha CJ, Bates FY, Behrens JC (1978c) Acute toxicity of the mycotoxin diacetoxyscirpenol in swine. *Can. Vet. J.* **19**:267-271.

Wu W, Cook ME, Chu FS, Buttles T, Hunger J, Sutherland P (1997) Case study of bovine dermatitis caused by oat straw infected with *Fusarium sporotrichoides. Vet. Rec.* **140**:399-400. [Cases in Wisconsin USA]

Trichothecenes (Type B)

Deoxynivalenol (DON, vomitoxin)

Sources:

DON is produced by various fungi of the genus *Fusarium* e.g. *F. graminearum* [= *Fusarium roseum*] growing on wheat & other grains. Sporadically, unseasonable winter rain in southern Qld increases the rate of infection of *F. graminearum* in wheat seed heads. Spoiled silage can also be a source of DON (Wilkinson 1999).

Toxicity:

Pigs are very sensitive compared to cattle, poultry, horses

- ↓ pig feed intake & growth rate occurs at feed concentrations > 2 mg vomitoxin/kg; vomiting at concentrations > 20 mg/kg (references cited by Trenholm *et al.* 1994)
- horses fed DON-contaminated barley (36-44 mg/kg feed) for 40 days were unaffected (Johnson *et al.* 1997)
- poultry unaffected by rations containing up to 18 mg/kg ; no residues in meat or eggs of poultry fed 9 mg/kg; turkeys unaffected by 5 mg/kg (Christensen *et al.* 1988 cited by Meronuck & Xie 1999)
- ruminal flora convert DON to deepoxydeoxynivalenol which is less toxic

Dogs and cats are susceptible to DON toxicity; similar degree of susceptibility to pigs (Hughes *et al.* 1999)

- conventional food processing methods used to produce extruded pet food do not degrade DON
- dog: food intake depressed by DON dietary concentrations > about 4.5 mg/kg; vomiting at 8 mg/kg or greater; dogs previously exposed to DON can select uncontaminated food
- cat: food intake depressed and vomiting induced by DON dietary concentrations > about 7.5 mg/kg;

Clinical signs (pigs, dogs, cats)

- **feed refusal**
- **vomiting**
- ↓↓ weight gain

Control

- feed material unsuitable for pigs to cattle/poultry/horses
- sweeteners added to feed have not overcome the effects of nivalenol (Williams *et al.* 1994)
- feed manufacturers screen consignments of grain for contamination; ELISA kits used for screening in USA
- US Food & Drug Administration guidelines (Meronuck & Xie 1999)

Feedstuff	Advisory level (ppm)
Finished wheat products (e.g. flour, bran, germ) that may be consumed by **humans**	1
Grain & grain by-products for ruminating beef and feedlot **cattle** > 4 months old	10; ingredients not to exceed 50% of diet
Grain & grain by-products for **poultry**	10; ingredients not to exceed 50% of diet
Grain & grain by-products for **swine**	5; ingredients not to exceed 20% of diet
Grain & grain by-products for **all other animals**	5; ingredients not to exceed 40% of diet

References:

Se181, Os422

Blaney BJ, Moore, CJ, Tyler AL (1987) The mycotoxins 4-deoxynivalenol, zearalenone and aflatoxin in weather-damaged wheat harvested 1983-85 in south-eastern Queensland. *Aust. J. Agric. Res.* **38**:993-1000.

D'Mello JPF, Placinta CM, Macdonald AMC (1999) *Fusarium* mycotoxins: a review of global implications for animal health, welfare and productivity. *Anim. Feed Sci. Technol.* **80**:183-205.

Hughes DM, Gahl MJ, Graham CH, Grieb SL (1999) Overt signs of toxicity to dogs and cats of dietary deoxynivalenol. *J. Anim. Sci.* **77**:693-700.

Johnson PJ, Casteel SW, Messer NT (1997) Effect of feeding deoxynivalenol (vomitoxin)-contaminated barley to horses. *J. Vet. Diagn. Invest.* **9**:219-221.

Meronuck RA, Xie W (1999) Mycotoxins in feed. *Feedstuffs* **71**:123-130.

Moore CJ, Blaney BJ, Spencer RA, Dodman RL (1985) Rejection by pigs of mouldy grain containing deoxynivalenol. *Aust. Vet. J.* **62**:60-62.
Trenholm HL, Foster BC, Charmley LL, Thompson BK, Hartin KE, Coppock RW, Albassam MA (1994) Effects of feeding diets containing *Fusarium* (naturally) contaminated wheat or pure deoxynivalenol (DON) in growing pigs. *Can. J. Anim. Sci.* **74**:361-369.
Tobin NF (1988) Presence of deoxynivalenol in Australian wheat and triticale – New South Wales Northern Rivers Region, 1983. *Aust. J. Exp. Agric.* **28**:107-110.
Wilkinson JM (1999) Silage and animal health. *Natural Toxins* **7**:221-232.
Williams KC, Blaney BJ, Peters RT (1994) Pigs fed *Fusarium*-infected maize containing zearalenone and nivalenol with sweeteners and bentonite. *Livestock Prodn. Sci.* **39**:275-281.

Trichothecenes – tibial dyschondroplasia of poultry

References:

Lee YW, Mirocha CJ, Schroeder DJ, Walser MM (1985) TDP-1, a toxic component causing tibial dyschondroplasia in broiler chickens and trichothecenes from *Fusarium roseum "graminearum"*. *Appl. Environ. Micro.* **50**:102-107.
Walser MM, Allen NK, Mirocha CJ, Hanlan GF, Newman JA (198) *Fusarium*-induced osteochondrosis (tibial dyschondroplasia) in chickens. *Vet. Pathol.* **19**:544-550.

Slaframine

Syndrome name: slobbers, salivary syndrome

Chemical structure:

Slaframine is a piperidine or indolizidine alkaloid, closely related chemically to swainsonine (also produced by *Rhizoctonia leguminicola*).

Source:

Mycotoxin produced by *Rhizoctonia leguminicola* growing on *Trifolium pratense* (red clover)

Toxicity:

Reported from only North America to date

Ruminants, horses

References:

Croom WJ Jr, Hagler WM, Froetschel MA, Johnson DA (1995) The involvement of slaframine and swainsonine in slobbers syndrome: a review. *J. Anim. Sci.* **73**:1499-1508.
Crump MH, Smalley EB, Nicjols RE, Rainey DP (1967) Pharmacologic properties of a slobber-inducing mycotoxin from *Rhizoctonia leguminicola*. *Am J. Vet. Res.* **28**:865-870.
Hagler WM Jr, Behlow RF (1981) Salivary syndrome in horses: identification of slaframine in red clover hay. *Appl. Env. Micro.* **42**:1067-1070.
Hagler WM Jr, Croom WJ Jr (1989) Slaframine: occurrence, chemistry, and physiological activity. Chapter 10 in Cheeke PR (ed) *Toxicants of Plant Origin. Volume 1. Alkaloids.* CRC Press Inc., Boca Raton, Florida. pp. 257-279.

Swainsonine

See the entry under Phytotoxins: Alkaloids

Mycotoxin produced by *Rhizoctonia leguminicola* (Schneider *et al.* 1983) and *Metarhizium anisopilae* (Hino *et al.* 1985).

Reference:

Hino M, Nakayama O, Tsurumi Y, Adachi K, Shibata T, Terano H Kohsaka M, Aoki H Imanaka H (1985) Studies of an immunomodulator, swainsonine: I. Enhancement of immune response by swainsonine *in vivo*. *J. Antibiot.* **38**:926-.
Schneider MJ, Ungemach FS, Broquist HP, Harris TM (1983) (1S,2R,8R,8aR)-1,2,8-trihydroxyoctahydroindolizidine (swainsonine), an α-mannosidase inhibitor from *Rhizoctonia leguminicola. Tetrahedron* **39**:29.

Roquefortine (dogs)

Roquefortine is a tremorgenic alkaloid mycotoxin produced by *Penicillium roquefortii* (and other *Penicillium* spp.)

Sources:

- over-ripe (mouldy) blue cheeses, including Roquefort
- mouldy garbage
- spoiled silage and grain (*P. roquefortii* isolated from these substrates) (Wilkinson 1999)

Conditions of poisoning: natural cases only in dogs that consumed over-ripe blue cheese (in Canada)

Clinical signs: similar to strychnine poisoning (see above)

- initial vomiting

- panting
- hyperaesthesia, **tetanic seizures**, opisthotonus, paddling
- nystagmus

Pathology: no significant necropsy lesions
Diagnosis: assay of vomitus, stomach contents or bile
Therapy:
- remove stomach contents
- apply barbiturate anaesthesia and general principles
- N.B. diazepam has been **ineffective** for control of seizures

Prevention & Control: prevent access to sources
References:

Lowes NR, Smith RA, Beck BE (1992) Roquefortine in the stomach contents of dogs suspected of strychnine poisoning in Alberta. *Can. Vet. J.* **33**:535-538.
Puls R, Ladyman E (1988) Roquefortine toxicity in a dog. *Can. Vet. J.* **29**:569-570
WilkinsonJM (1999) Silage and animal health. *Natural Toxins* **7**:221-232.

Penitrem A (dogs)

Penitrem A is a tremorgenic mycotoxin
Sources:

most commonly produced by *Penicillium crustosum,* but also by *Penicillium cyclopium, P. palitans* and *P. puberulum* (Os429)
Substrates: mouldy cream cheese, mouldy bread, mouldy walnuts (Os429)

Conditions of poisoning: ingestion of mouldy garbage by dogs
Clinical signs:
- severe muscle tremors
- tetanic seizures (similar to strychnine poisoning)

Pathology: no significant necropsy lesions
Diagnosis: assay of vomitus, stomach contents
Therapy:
- remove stomach contents
- apply barbiturate anaesthesia and general principles

Prevention & Control: prevent access to sources
References:

Arp LH, Richard TL (1979) Intoxication of dogs with the mycotoxin Penitrem A. *J. Am. Vet. Med. Ass.* **175**:565-566
Hocking AD, Holds K, Tobin NF (1988) Intoxication by tremorgenic mycotoxin (penitrem A) in a dog. *Aust. Vet. J.* **65**:82-85.

Aspergillus clavatus *tremorgenic mycotoxins*

Chemical structure:

The nature of the tremorgens involved is uncertain. The following have been suggested:
- tryptoquivaline, tryptoquivalone (Glinsukon *et al.* 1974;Clardy *et al.* 1975)
- patulin (*q.v.*) (Kellerman *et al* 1984)
- unidentified tremorgens (Kellerman *et al.* 1976)

Sources:
- sprouted grains infected with *Aspergillus clavatus*
  - barley (malt, distiller's culms) (Minciuna *et al.* 1977; Jiang *et al.* 1982; Gilmour *et al.* 1989; Shlosberg *et al.* 1991)
  - wheat (Moreua & Moreau 1960; Jaquet *et al.* 1963)
  - maize (Kellerman *et al.* 1984)
- sorghum beer residues (Kellerman *et al.* 1976)

Aspergillus clavatus infecting sprouted barley [Howard Prior Photo]

Toxicity:
- cattle, sheep

Mode of action: unrecorded

Conditions of poisoning: access to above sources

Clinical signs:
- high case fatality
- **muscle tremors**
- hypersensitivity
- stiff gait
- **ataxia** with knuckling of fetlocks, exacerbated by exercise
- recumbency
- ± excessive salivation
- ± dyspnoea after exercise
- ± anorexia
- ± lameness
- ± clonic convulsions

Pathology:
- no necropsy lesions
- **neuronal degeneration & necrosis in brainstem** (midbrain, medulla oblongata), **spinal cord & spinal ganglia**
  - larger neurones affected, often in groups
  - central to complete chromatolysis often with intense cytoplasmic eosinophilia
  - ± cytoplasmic vacuolation
  - nuclei frequently flattened, pyknotic and displaced peripherally
- Wallerian degeneration of spinal cord white matter tracts

Diagnosis: access + syndrome + pathology

Therapy: nil

Prevention & control: prevent access to mouldy sprouted grains

References:

Clardy J, Springer JP, Büchi G, Matsuo K, Wightman R (1975) Tryptoquivaline and tryptoquivalone, two tremorgenic metabolites of *Aspergillus clavatus*. *J. Am. Chem. Soc.* **97**:663-665.

Gilmour JS, Inglis DM, Robb J, Maclean M (1989) A fodder mycotoxicosis of ruminants caused by contamination of a distillery by-product with *Aspergillus clavatus*. *Vet. Rec.* **124**:133-135.

Glinsukon T, Yuan SS, Wightman R, Kitaura Y, Büchi G, Shank RC, Wogan GN, Christensen CM (1974) isolation and purification of cytochalasin E and two tremorgens from *Aspergillus clavatus*. *Plant Foods for Man* **1**:113-119.

Jaquet J, Boutibonnes P, Cicile JP (1963) Observations sur la toxicité d' *Aspergillus clavatus* pour les animaux. *Bulletin de l'Académie Vétérinaire de France* **36**:199-207.

Jiang CS, Huang SS, Chen MZ, Yu Z, Chen LH, Sang YZ (1982) Studies on mycotoxicosis in dairy cattle caused by *Aspergillus clavatus* from mouldy malt sprouts. *Acta Veterinaria et Zootechnica Sinica* **13**:247-254.

Kellerman TS, Pienaar JG, van der Westhuizen GCA, Anderson LAP, Naude TW (1976) A highly fatal tremorgenic mycotoxicosis of cattle caused by *Aspergillus clavatus. Onderstepoort J. Vet. Res.***43**:147-154.
Kellerman TS, Newsholme SJ, Coetzer JAW, van der Westhuizen GCA (1984) A tremorgenic mycotoxicosis of cattle caused by maize sprouts infested with *Aspergillus clavatus*. *Onderstepoort J. Vet. Res.* **51**:271-274.
Minciuna V, Mitroiu P, Donta C (1977) Severe intoxication in cows due to ingestion of mouldy malt sprouts. *Lucrarile Institutuliu de Cercetari Veterinare si Biopreparate "Pasteur"* **13**:81-84.
Moreau C, Moreau M (1960) Un danger pour le bétail nourri de plantules fouragéres cultivées en germoir: la pollution d'une moisissure toxique, l'*Aspergillus clavatus*, cause des accidents mortels. *Comptes Rendus de l'Académie d'Agriculture de France* **46**:441-445.
Nikov S, Simov I, Koroleva V, Zhelev V (1965) *Nauchni trudove. Vissh veterinarnomeditsinski institut "Prof. G. Pavlov"* **15**:169 [Abstract (1965) *Vet. Bull.* **36**:565]
Shlosberg A, Zadikov I, Perl S, Yakobson B, Varod Y, Elad D, Rapoport E, Handji V (1991) *Aspergillus clavatus* as the probable cause of a lethal mass neurotoxicosis in sheep. *Mycopathologia* **114**:35-39.
Tomova A (1965) *Veterinary Medicine Nauki, Sofia* **2**:997 [Abstract (1965) *Vet. Bull.* **36**:786]

Citrinin

See also citrus pulp under plant poisonings of uncertain cause.

Chemical structure:

Citrinin is a quinone methide. It is unstable and degrades with increased temperature (60-70^{o}C) and moisture content of substrate.

Sources:

The main producer of citrinin in animal feeds is ***Penicillium viridicatum***, but it is produced by several other *Penicillium* and *Aspergillus* spp. and was first identified as a product of *Penicillium citrinum*.

Substrates are concentrated carbohydrate sources such as feed grains and nuts including wheat, oats, barley, rye, corn and peanuts.

Citrinin production may occur from 5-12^{o}C reaching a maximum at 25^{o}C.

Citrinin is mainly a toxin of temperate climates.

Toxicity:

Natural poisoning of domestic animals is not well recorded. Experimental studies have confirmed **nephrotoxic** potential in pigs and poultry. Dogs are susceptible. Natural poisoning of ruminants is not recorded.

Toxic dietary citrinin concentrations: pigs > 20 mg/kg; poultry > 130 mg /kg; layer poultry > 250 mg/kg

Assessment of citrinin toxicity under natural conditions is complicated by its co-occurrence with other more potent mycotoxins including aflatoxins, ochratoxin A, patulin and penicillic acid. Thus it is thought that citrinin is a contributor to, rather than a primary cause of, porcine and avian nephroses.

Citrinin in feed rarely attains toxic concentrations (up to 80 mg/kg have been detected in Canadian wheat, 1200 mg/kg in peanuts under culture).

Mode of action: not understood

Conditions of poisoning: consumption of contaminated grains

Clinical signs:

Reduced growth rate
Increased water consumption
Polyuria, watery droppings (poultry)
diarrhoea

Pathology:

Nephrosis: coagulation necrosis of renal cortical tubules
Jejunal haemorrhage (poultry)
± liver damage

Diagnosis:

syndrome + access
feed assay
differential diagnosis or concurrent diagnosis to consider: ochratoxicosis

Therapy: nil

Prevention and control: general measures to prevent mycotoxin production in stored carbohydrate sources

References:

Cheeke 108

Cyclopiazonic acid

Chemical structure:

Cyclopiazonic acid (CPA) is an indole tetramic acid.

Sources:

Produced by many *Aspergillus* spp. and *Penicillium* spp. including many aflatoxin-producing strains of *Aspergillus flavus.*

CPA is known from a wide range of foods including corn, peanuts, cheese, eggs and meat.

Toxicity:

No intoxication of humans or other animals has been definitely attributable to CPA.

Poultry: CPA is now believed to be partly responsible for "turkey X disease", the investigation of which resulted in the discovery of aflatoxins.

Concern related to potential contamination of human food (milk, eggs, meat) through CPA-contaminated animal feed.

Mode of action:

Interacts with skeletal muscle sarcoplasmic reticulum vesicles

inhibition of Ca^{2+}-ATPase disrupting cellular Ca homeostasis

Conditions of poisoning: undefined

Clinical signs (experimental animals):

ataxia

spasms, opisthotonus

dyspnoea

Pathology:

Not fully defined

Associated with pancreatic lesions in birds (Balachandran & Patharsarthy 1995)

Diagnosis: undefined

Therapy: nil

Prevention and control: general measures to prevent mycotoxin production in stored carbohydrate sources

References:

Cheeke 110

Balachandran C, Patharsarthy KR (1995) Influence of dietary rice culture material containing cyclopiazonic acid on certain serum biochemical parameters of broiler chickens. *Mycopathologia* **132**:161-166.

Blaney BJ, Kelly MA, Tyler AL, Connole MD (1989) Aflatoxin and cyclopiazonic acid production by Queensland isolates of *Aspergillus flavus* and *Aspergillus parasiticus. Aust. J. Agric. Res.* **40**:395-400.

Kojic acid

Chemical structure:

Kojic acid = 2-hydroxymethyl-5-hydroxypyrone

Sources:

Many *Aspergillus* spp. and *Penicillium* spp.

Often produced in association with aflatoxin.

Toxicity:

Unlikely to pose a significant toxic hazard in itself.

Broiler poultry: toxic feed concentrations > 2000 mg/kg

References:

Cheeke 110

Diplodia maydis *neurotoxin*

This account is based largely on that in Kellerman *et al.* (1988).

Syndrome names: Diplodiosis – one of the earliest recognised mycotoxicoses (Mitchell 1919).

Chemical structure:

The neurotoxin responsible is unconfirmed. A toxin has been described from cultures of *Diplodia maydis* (Steyn *et al.* 1972), but its toxicity has not been tested in ruminants.

Sources:

Diplodia maydis (Berk.) Sacc. infecting *Zea mays* (maize, corn). *D. maydis* causes stem and ear rot of maize, producing a white mycelial mat and characterised by the black fruiting bodies (pycnidia) produced on affected plant structures towards the end of the growing season. The black

pycnidia allow differentiation from *Fusarium moniliforme* (*q.v.*) or other fungal infections of maize.

D. maydis infects maize in Australia, but is not prominent or widespread (Blaney 1996).

Toxicity:

Natural cases occur mostly in cattle, but sheep may also be affected. Goats are susceptible.

Diplodiosis has been reproduced experimentally by feeding ruminants on naturally-infected maize or pure cultures of *D. maydis*, but cultures incubated less than 8 weeks are not toxic.

Toxicity will survive 45°C for prolonged periods.

Toxic doses are of the order of 5 g/kg/day or 10-30 g/kg cultures, causing signs in 2-8 days (Kellerman *et al.* 1985)

Organ systems affected: CNS

Mode of action: undescribed

Conditions of poisoning:

Weather conditions conducive to *D. maydis* infection of maize are dry warm conditions in the early crop growth stage followed by damp cloudy period at flowering.

The syndrome is confined to southern Africa and affects cattle and sheep grazing maize crops in winter with damaged cobs remaining on the plants after harvest. Strains of *D. maydis* from beyond this region are toxigenic, but diplodiosis is not reported in their countries of origin (Kellerman *et al.* 1985).

New cases have been reported up to 10 days after animals have been removed from toxic maize crops and similar relapses have been seen in experimentally-induced diplodiosis. Virtually no natural cases have resulted from feeding maize that has been processed in any way, such as maize milled on the cob or ground maize used in compounded feeds (Kellerman *et al.* 1988).

There is one report of a possible case in Queensland, Australia (Darvall 1964). Feeding *D. maydis*-infected Australian maize to cattle and fowls did not induce disease (Blaney *et al.* 1981), but the *D. maydis* isolate from this material, when grown in culture, had a similar toxicity to chickens as isolates from southern Africa (H.McFadden, personal communication cited by Blaney & Williams 1991).

Clinical signs:

The syndrome is principally one of ataxia, paresis and paralysis without significant muscle tremor.

- reluctance to move
- wide-based stance
- incoordination
- walking with a stiff-legged, high-stepping gait
- frequent falling
- paresis/paralysis
- constipation
- excessive salivation (unrelated to any dysfunction of the swallowing mechanism)
- occasional muscle tremors
- about 10% become totally paralysed and consequently recumbent

Pathology:

No lesions are reported in natural cases.

In a few experimental animals, laminar cortical status spongiosis of the cerebrum and cerebellum was seen in badly-affected sheep and cattle.

Diagnosis:

syndrome + access to remnant maize cobs on standing crops after harvesting

Differential diagnoses should include botulism and *Paspalum* staggers.

Therapy:

Prognosis is good, with affected animals recovering after removal from toxic crops. Even recumbent animals recover with adequate nursing.

Prevention & control:

Effective disposal of maize crop residues, by prompt deep ploughing or burning, to prevent infection of crops in successive years is essential. Genetic selection for *D. maydis*-resistant maize may be effective in time.

References:

Review literature

Kellerman TS, Coetzer JAW, Naudé TW (1988) *Plant Poisonings and Mycotoxicoses of Livestock in Southern Africa.* Oxford University Press, Cape Town. pp. 47-49.

General literature

Blaney BJ (1996) Fungal toxins and animals. *Fungi of Australia* **1B**:225-238.

Blaney BJ, Williams KC (1991) Effective use in livestock feeds of mouldy and weather-damaged grain containing mycotoxins – case histories and economic assessments pertaining to pig and poultry industries of Queensland. *Aust. J. Agric. Sci.* **42**:993-1012.
Blaney BJ, Mannion PF, Tudor GD, McKenzie RA (1981) Examination of *Diplodia maydis* infected maize for toxicity to chickens and cattle. *Aust. Vet. J.* **57**:196.
Darvall PM (1964) Mouldy corn cobs, a danger to cows. *Qd. Agric. J.* **90**:692-693.
Kellerman TS, Rabie CJ, van der Westhuizen GCA, Kriek NPJ, Prozesky L (1985) Induction of the neuromycotoxicosis, diplodiosis, in domestic ruminants with cultures of indigenous and exotic isolates of *Diplodia maydis*. *Onderstepoort J. Vet. Res.* **52**:35-42.
Mitchell DT (1919) Poisoning of cattle by *Diplodia*-infected maize. *S. Afr. J. Sci.* **16**:446-452.
Steyn DG, Wessels PL, Holzapfel CW, Potgieter DJJ, Louw WKA (1972) The isolation and structure of a toxic metabolite from *Diplodia maydis* (Berk.) Sacc. *Tetrahedron* **28**:4775-4785.

Ustilago hordei-*infected wheat*

Ustilago hordei is the cause of covered smut of barley. This plant disease is readily controlled through seed treatment, but in most years some smutted barley becomes available for stock feed.
Pigs have been fed barley with 0.5% smutted grain with no ill effect (Williams *et al.* 1987). Cattle are frequently fed smutted barley without any ill effect being reported. There are some reports of dusty mould reducing palatability. This can be overcome by adding molasses to the ration (Blaney & Williams 1991).
References:

Blaney BJ, Williams KC (1991) Effective use in livestock feeds of mouldy and weather-damaged grain containing mycotoxins – case histories and economic assessments pertaining to pig and poultry industries of Queensland. *Aust. J. Agric. Sci.* **42**:993-1012.
Williams KC, Blaney BJ, Peters RT (1987) Nutritive value of smut-affected barley for pigs. In Barnett JL *et al.* (eds.) *Manipulating Pig Production.* Australasian Pig Science Association, Animal Research Institute, Werribee, Victoria. p.138.

Sclerotinia sclerotiorum *sclerotia*

Sclerotinia sclerotiorum is an important disease agent of mung beans, soya beans, navy beans, safflower and sunflower crops in northern Australia (Blaney & Williams 1991). The fungus invades stalks and seeds, forming sclerotia which contaminate the final harvested products. Removal of sclerotia is difficult, particularly from sunflower seeds because the sclerotia are very similar in size to these. *Sclerotinia sclerotiorum* also causes "pink rot" of celery (*q.v.*) and provokes the production of photosensitising furanocoumarins as phytoallexins (*q.v.*).
Toxicity: Pigs fed mung beans with a large proportion of *S. sclerotiorum* sclerotia had no ill effects (Williams & Daniels, unpublished data cited by Blaney & Williams 1991)
References:

Blaney BJ, Williams KC (1991) Effective use in livestock feeds of mouldy and weather-damaged grain containing mycotoxins – case histories and economic assessments pertaining to pig and poultry industries of Queensland. *Aust. J. Agric. Sci.* **42**:993-1012.

Pyrenofera tritici-repentis-*infected wheat*

Pyrenofera tritici-repentis is common in Australian wheat, causing discoloration of grain with a pale pink that may be confused with that caused by *Fusarium graminearum*.
Toxicity: Pigs have been reported to eat infected wheat without ill effect, but no controlled experiments are known which explore the toxic potential of this material (Blaney & Williams 1991).
References:

Blaney BJ, Williams KC (1991) Effective use in livestock feeds of mouldy and weather-damaged grain containing mycotoxins – case histories and economic assessments pertaining to pig and poultry industries of Queensland. *Aust. J. Agric. Sci.* **42**:993-1012.

YEAST

Ethanol (ethyl alcohol)

Syndrome name(s): drunk; tired & emotional, pissed, sloshed, under-the-weather, legless, *etc.*
Sources:
- alcoholic beverages with high alcohol content
- fermented fruit or flower nectar
- uncooked bread dough

Toxicity: dogs, cattle, pigs, sheep, birds (humans)
Conditions of poisoning:
- accidental access or deliberate administration (dogs) (Ratcliffe & Zuber 1977)
- ingestion of bread dough (dogs) (Thrall *et al.* 1984; Suter 1992)
- access to fermented fruit/vegetable waste (cattle) (Chamberlain & McKenzie 1993)
- calves fed milk replacer with high glucose content (18-60% glucose) leading to ethanol production through fermentation by the yeast *Torulopsis glabrata* in the gastrointestinal tract (Wijayasinghe *et al.* 1984)
- pigs fed diets containing 25-50% glucose (Wijayasinghe *et al.* 1984)
- birds feeding on fermented fruit or flower nectar (e.g. lorikeets feeding on flowers of *Schotia brachypetala*)

Clinical signs:
Dog
- ataxia
- vocalisation (incessant whining, crying)
- vomiting
- stupor
- ataxia, staggering gait
- unconsciousness
- dehydration
- diuresis

Cattle (Chamberlain & McKenzie 1993; Wijayasinghe *et al.* 1984)
- ataxia
- odour of alcohol on the breath
- ± distension of the left abdomen

Diagnosis:
- blood ethanol assay (human pathology laboratories) – serum sample collected in closed tube (Vacutainer® SST gel) required, minimum serum volume 1 ml required for colorimetric method, less for GC (S&N Pathology Biochemistry Department, Brisbane, personal communication 2001)
- fatally-intoxicated calves: 280 & 320 mg/100ml in jugular blood (Wijayasinghe *et al.* 1984)
- in humans, blood ethanol concentrations about 100 mg/100ml are associated with CNS depression and death may occur at concentrations over 400 mg/100ml

Prevention: include nystatin in milk replacers with high glucose content (Wijayasinghe *et al.* 1984)
References:

Chamberlain P, McKenzie RA (1993) Unpublished case in the records of the Yeerongpilly Veterinary Laboratory, Queensland Department of Primary Industries [93-135891: access to fermented pineapple & apple pulp, 2 adult Friesian cows; blood ethanol concentration in 1 cow = 0.23%]

Ratcliffe RC, Zuber RM (1977) Acute ethyl alcohol poisoning in dogs. *Aust. Vet. J.* **53**:48-49.

Suter RJ (1992) Presumed ethanol intoxication in sheep dogs fed uncooked pizza dough. *Aust. Vet. J.* **69**:20.

Thrall MA, Freemyer FG, Hamar DW, Jones RL (1984) Ethanol toxicosis secondary to sourdough ingestion in a dog. *J. Am. Vet. Med. Assoc.* **184**:1513-1514.

White RW, Lindsay DB, Ash RW (1972) Ethanol production from glucose by *Torulopsis glabrata* occurring naturally in stomachs of newborn animals. *J. Appl. Bacteriol.* **35**:631-646.

Wijayasinghe MS, Miranda M, Smith NE, Baldwin RL, Wijayasinghe C, Har SA (1984) A yeast related ethanol intoxication syndrome in experimental calves: prevention with nystatin. *Can. Vet. J.* **25**:251-253.

ERGOTS

☑ Ergot alkaloids (ergopeptide alkaloids)- ergotism

Core data

Syndrome types & names:

- hyperthermia (= bovine hyperthermia, summer slump, fescue summer toxicosis)
- gangrenous ergotism (= fescue foot, St.Anthony's fire [humans])
- agalactia / prolonged gestation / abortion

Common sources:

- *Claviceps purpurea* ergots in *Lolium rigidum* seed or grain crops
- *Claviceps africana* ergots in sorghum grain
- *Neotyphodium coenophialum* endophyte in *Festuca arundinacea*

Animals affected:

- Hyperthermia – cattle
- Gangrenous ergotism – cattle mainly
- Reproductive syndromes – cattle, pigs, horses

Mode of action:

- peripheral vasoconstriction → restricted heat loss
- pituitary dysfunction → ↓ circulating prolactin

Poisoning circumstances:

- feed grain or standing pasture contaminated with ergots OR
- grazing endophyte-infected tall fescue pasture

PLUS

- summer temperatures – hyperthermia
- winter temperatures – gangrenous ergotism

Main effects:

- Hyperthermia
  - pyrexia
  - salivation
  - dyspnoea
  - inappetence
- Gangrenous ergotism
  - Peripheral gangrene - distal limbs, tail, pinnae (ears)
- Reproductive syndromes
  - Agalactia + neonatal mortality – pigs, cattle
  - Prolonged gestation – horses
  - Abortion (rare)

Diagnosis:

- syndrome + access to sources
- alkaloid assay on feed

Therapy:

- remove source from diet
- hyperthermia - reduce body temperature

Prevention:

- screen ergots from grain
- hyperthermia - avoid handling affected cattle at ambient temperatures > 30 ^{o} C

Syndromes:

Ergotism is the general term for poisoning by ergot alkaloids. Three syndromes have been associated with their consumption, namely

- **hyperthermia** associated with high ambient temperatures and known by various names including
  - bovine hyperthermia
  - `summer slump'

  - `idiopathic (*sic*) hyperthermia'
  - fescue summer toxicosis
- **gangrenous ergotism** associated with low ambient temperatures and known by various other names including
  - fescue foot
  - St.Anthony's fire (humans) (Weaver *et al.* 1989; Magee 1991)
- and **reproductive disruption**, which may be concurrent with either of the former two, and manifest as
  - agalactia and neonatal mortality
  - prolonged gestation
  - abortion (Appleyard 1986)

A further syndrome, **nervous ergotism**, has been described, but its actual existence in domestic animals is disputed (Bourke 1994).

Human ergotism has a long history, originating as contamination of grain crops by *Claviceps purpurea,* causing syndromes including St.Anthony's fire and being associated by some scholars with accusations of witchcraft in Europe and North America in the 16th, 17th and 18th centuries (Matossian 1989).

Chemical structure:

The major ergot alkaloids responsible for toxicity are **ergovaline** in *C. purpurea* and *N. coenophialum* and **dihydroergosine** in *C. africana*.

Sources:

- sclerotia (ergots) of ***Claviceps purpurea*** (rye ergot) infecting seedheads of
  - *Lolium rigidum* (**annual ryegrass**) – NSW, hyperthermia of cattle; WA, gangrenous ergotism of cattle (Fraser & Dorling 1983)
  - grain crops (rye, barley, wheat, triticale, maize, rice)
  - *Cynodon dactylon* (couch grass, Bermuda grass [USA]) (Conway *et al.* 1992)
  - *Paspalum notatum* (bahia grass) – USA, cattle with gangrene (Nicholson S, personal communication VETTOX Discussion Group 22 May 1996)

  C. purpurea has been reported from Australia (NSW, WA), Europe, North & South America, Southern Africa
- sclerotia of ***Claviceps africana*** (sorghum ergot) infecting grain from *Sorghum bicolor* (**grain sorghum**) crops; Australia (Q) (Blaney *et al.* 2000a,b, Bhuiyan *et al.* 2002)
- sclerotia of *Claviceps cyperi* infecting *Cyperus esculentus* (nut sedge) cut with maize for silage → ergocryptine → hyperthermia; South Africa (TW Naude, personal communication 1999)
- fungal endophyte ***Neotyphodium (Acremonium) coenophialum*** in *Festuca arundinacea* (**tall fescue**) pasture grass leaves; Australia (NSW, V), North America
- fungal endophyte *Neotyphodium lolii* in *Lolium perenne* (perennial ryegrass) leaves; Australia (V) (Foot *et al.* 1994)

Toxicity:

Only the sclerotial (ergot) stage of the *Claviceps* spp. life cycle produces clinically-significant amounts of ergot alkaloids

Hyperthermia:

- cattle, sheep
- natural cases in Australia have been induced by feed containing 0.02-1.0% *C. purpurea* sclerotia; also from sorghum containing 5 mg dihydroergosine/kg (Taylor 2001)
- experimental work with broiler chickens fed sclerotia of *C. africana* in Australia resulted in significant mortality (Blaney BJ, unpublished data 1998), but in USA did not (Bailey *et al* 1999) indicating probable significant variation in alkaloid concentration for a given weight of sclerotia.

Gangrenous ergotism:

- cattle usually
- other species susceptible

Reproductive disruption:

- **pigs** (Lopez *et al.* 1997), cattle, sheep, horses

- ergopeptine alkaloids detected in *N. lolii*-infected *L. perenne* stubble; ergovaline and ergotamine comprised 70% of alkaloids detected (Rowan & Shaw 1987)
- horses in North America grazing tall fescue; ergot peptide alkaloids, mainly ergovaline

Mode of action:

Hyperthermia:

- peripheral vasoconstriction (reduced heat loss from skin)
  - increased activity of α_2 adrenergic receptors (not α_1) of peripheral blood vessels (Oliver *et al.* 1998)
- pituitary dysfunction → ↓ blood prolactin concentrations
- interact with dopamine receptors + increase release of dopamine from central nerve endings (Rowell & Larson 1999)
- reduced immune competence demonstrated in cattle grazing endophyte-infected tall fescue (Saker *et al.* 1998); endophyte-infected tall fescue has reduced Cu content and cattle grazing it may be Cu deficient – this may influence immune competence (Dennis *et al.* 1998; Saker *et al.* 1998)

Gangrenous ergotism:

- peripheral vasoconstriction → peripheral gangrene (limbs, tail, ears) under cold weather conditions
- *in vitro* experimentation suggests ergot alkaloids promote growth of vascular smooth muscle cells, thus contributing to restriction of peripheral blood flow [Strickland *et al.* 1996]

Reproductive disruption:

- mimic dopamine → pituitary dysfunction → **↓ circulating prolactin** → ↓ milk production (Blaney *et al.* 2000a,b,c)
- ↓ circulating prolactin concentrations in sheep on *L. perenne* pasture is unrelated to lolitrem B and an effect of ergot alkaloids (Fletcher & Barrell 1984)
- horses on tall fescue: ergot alkaloids → vasoconstriction → placental oedema, agalactia

Conditions of poisoning:

Hyperthermia:

- **↑ air temperature, exercise → ↑ severity of effect**
- cattle fed **grain contaminated with sclerotia** (ergots) during **summer** (Dec-Mar) (e.g. Taylor 2001)
- cattle grazing tall fescue, ergotised *L. rigidum* or ergotised forage/grain sorghum during summer (Dec-Mar)
- cattle fed silage (Hogg 1991; TW Naude, personal communication 1999)
- sheep grazing some *Lolium perenne* pastures during summer

C. purpurea

- sclerotia ingested directly from infected pasture
- infected *L. rigidum* seed contaminating grain fed to cattle (dairy, feedlot). [sclerotia mistaken for rodent faeces or weevils]
- grain grown and harvested in wet years → ↑*C. purpurea* occurrence
- herbicides not used to kill ryegrass in crops
- weed seeds not screened out of grain

C. africana

- late-planted (late summer-autumn) sorghum crops have the highest infection rates (infection occurs when plants are flowering during cool, humid weather)

Gangrenous ergotism:

- **↓ air temperature → ↑ severity of effect**
- cattle fed **grain contaminated with sclerotia** (ergots) during **winter**
- cattle grazing tall fescue or ergotised *L. rigidum* pastures during winter
- ergot alkaloids prescribed as medication for migraine in humans (Weaver *et al.* 1989, Magee 1991)

Reproductive disruption:

- pregnant or lactating pigs, cattle fed **grain contaminated with sclerotia** (ergots) (Lopez *et al.* 1997)

- pregnant or lactating cattle, horses grazing tall fescue or ergotised *L. rigidum* pastures
- sheep grazing some *Lolium perenne* pastures

C. purpurea
- sclerotia ingested directly from infected pasture
- infected *L. rigidum* seed contaminating grain fed to cattle (dairy, feedlot). [sclerotia mistaken for rodent faeces or weevils]
- grain grown and harvested in wet years → ↑*C. purpurea* occurrence
- herbicides not used to kill ryegrass in crops
- weed seeds not screened out of grain

C. africana
- late-planted (late summer-autumn) sorghum crops have the highest infection rates (infection occurs when plants are flowering during cool, humid weather)

Clinical signs:

Hyperthermia:
- high morbidity, effects persist for months
- **pyrexia** (rectal 41-2°C)
- **excessive salivation**
- ↑ respiratory rate, **dyspnoea**
- poor exercise tolerance
- **inappetence**
  - ↓↓ milk production
  - ↓ weight gain
- death in severe cases

Gangrenous ergotism:

Cattle
- **lameness**
- recumbency
- ± diarrhoea
- abortion (very rare)

Reproductive disruption:

Cattle, sheep, pigs:
- **agalactia**
- **neonatal mortality**
- ± abortion (Lopez *et al.* 1997)
- low lamb-marking percentages in some circumstances may have resulted from reduced milk production on *L. perenne* pasture (Foot *et al.* 1988)

Horses:
- prolonged gestation (by 2 weeks or more)
- placental thickening
- dystocia → ± death of mare
- abortion, stillbirth (chorioallantois very oedematous → no rupture at cervical star → membranes precede foetus through birth canal → premature separation from uterus → foetal anoxia)
- agalactia (no udder development or little or no milk produced)
- high perinatal foal mortality (weak foals, larger than normal, ± contracted legs)

Pathology:

Hyperthermia:

no specific lesions

Gangrenous ergotism:
- **gangrene of extremities** (cattle)
- ulcers of mouth, pharynx & rumen (sheep)

Reproductive disruption:

Pigs:

piglets dead of starvation

Horses:

- foetus large, dehydrated, slightly emaciated
- foetal thyroid: colloid goitre, ↓ plasma triiodothyronine (T_3) concentrations (Boosinger *et al.* 1995)
- placenta congested and very oedematous

Diagnosis:

- access + syndrome
- assay feed for alkaloid content (some labs only)

Detecting/assessing Claviceps africana *(sorghum ergot) infestation of grain* (Blaney 1997)

- General appearance of grain: lightweight, pale → possible fungal damage
- Stickiness: presence of honeydew indicates ergot infestation, but does not indicate toxicity
- *Cerebella* sp. (fungus super-infection): presence of large black bodies with highly folded surface (brain-like) → indicates ergot infection because grows on honeydew
- Presence of *Claviceps africana* sclerotia (ergots):
  Direct inspection (use a 10x hand lens)
  - Spread 100 g of grain on clean white paper and separate different types of grains
  - *Claviceps africana* sclerotia (ergots) = somewhat elongated grey-white bodies slightly smaller than mature sorghum grains; may be still emerging from glumes (plant parts surrounding developing seed); often with small black tip of developing *Cerebella* sp.
  - if > 20 sclerotia → possible significant infestation (approximately = > 0.3% ergots by weight)
  - *Cerebella* sp.-infected ergots are heavier but contain less alkaloid; about 30-40 of these = 20 sclerotia
  - Weigh the fractions to determine an accurate result

  Salt flotation
  - Dissolve 20g table salt in 200 ml tap water
  - Add 100 g grain and stir briskly
  - Take off floating material and blot dry with absorbent paper
  - Examine as above – floating material will contain sclerotia, *Cerebella* sp.-infected sclerotia, immature grain, weed seeds, glumes & chaff
- Commercial laboratories accepting grain samples for examination for sorghum ergot include (not an exhaustive list):
- Agritech Lab Services, 214 McDougall St., Toowoomba. Ph. (07) 4633 0599 Fax (07) 4633 0711
- Seed Testing Labs of Australia, 2/18 Devlan St., Mansfield. Ph (07) 3849 2744 Fax (07) 3849 2704

Therapy:

Hyperthermia:

-remove source from diet
- reduce body temperature (water sprays)
- possibly administer dopamine antagonist (domperidine, metoclopramide) (Samford-Grigsby *et al.* 1997)

Gangrenous ergotism:

- no specific therapy
- separate animals from source of toxin

Reproductive disruption:

remove source of toxin; possible use of dopamine antagonists such as metoclopromide (Samford-Grigsby *et al.* 1997)

Horses: agalactia may be treated with domperidone and reserpine (Evans TJ, personal communication VETTOX discussion group, 11 April 2000; 1999 Proceedings, American Assoc. Equine Practitioners):

- domperidone PO @ 1.1 mg/kg 4 times daily until in full lactation; side effects include excessive milk production (& dripping of colostrum following prepartum administration); domperidone does not cross the blood-brain barrier and does not produce CNS effects like other D2 receptor antagonists such as perphenazine
- reserpine PO @ 2.5-5.0 mg/day/450kg mare is helpful; side effects include sedation, diarrhoea, hypotension under general anaesthesia
- metoclopramide also useful (Hugnet C, personal communication, VETTOX discussion group, 11 April 2000)

Prevention & control:

General measures:

C. purpurea

- screen ergots from grain (< 0.1% *C. purpurea* ergot inclusion rate for cattle rations; Queensland Stock Feed Regulations → illegal to sell grain containing > 0.3% ergot)
- control *L. rigidum* infestations in grain crops (made difficult by herbicide resistance problem)

C. africana

- plant grain sorghum crops early-mid summer to avoid serious infections
- screen ergots from grain (< 0.1% *C. africana* ergot inclusion rate for cattle rations; Queensland Stock Feed Regulations → illegal to sell grain containing > 0.3% ergot; each 1% ergot = a maximum of about 10 mg total alkaloid, but there can be considerable variation in alkaloid content among batches of ergotised grain); < 0.2% *C. purpurea* ergot inclusion in sow rations (Digdean *et al.* 1986))
- results of experimental investigations in Queensland (BJ Blaney personal communication 4 Jan 2000) suggest concentrations of total alkaloid content of livestock feed contaminated with *C. africana* above which negative production effects occur are
  feedlot cattle: 1 mg/kg
  sows: 1 mg/kg
  grower pigs: 5 mg/kg
  broiler poultry: 10 mg/kg
- heavily-infected sorghum crops could be utilised by feeding off or ensiling at the honey-dew stage of infection

N. coenophialum

- endophyte-free fescue varieties available (but these are less resistant to insect attack)
- thiabendazole dosing of cattle before access to pasture
- ammoniation of hay

Hyperthermia:

- **avoid handling affected cattle at ambient temperatures > 30 ^{o} C** (high probability of deaths)

Reproductive disruption:

- domperidone (dopamine receptor antagonist) used successfully → circulating prolactin ↑ (Redmond *et al.* 1994)
- remove mares from tall fescue pasture by day 300 of gestation → prevention

References:

Se165, 166

Anderson JF, Werdin RE (1977) Ergotism manifested as agalactia and gangrene in sows. *JAVMA* **170**:1089-1091.

Appleyard WT (1986) Outbreak of bovine abortion attributed to ergot poisoning. *Vet. Rec.* **118**:48-49.

Bailey CA, Fazzino JJ Jr, Ziehr MS, Sattar M, Haq AU, Odvody G, Porter JK (1999) Evaluation of sorghum ergot toxicity in broilers. *Poultry Sci.* **78**:1391-1397.

Bhuiyan SA, Galea VJ, Ryley MJ, Tay D, Lisle AT (2002) Factors influencing the germination of macroconidia and secondary conidia of *Claviceps africana*. *Aust. J. Agric. Res.* **53**:1087-1094.

Blaney BJ (1997) Testing for sorghum ergot. *Pig Pen (Newsletter, Australasian Pig Institute)* No.14, p.20.

Blaney BJ, McKenzie RA, Walters JR, Taylor LF, Bewg WS, Ryley MJ, Maryam R (2000a) Sorghum ergot (*Claviceps africana*) associated with agalactia and feed refusal in pigs and dairy cattle. *Aust. Vet. J.* **78**: 102-107.

Blaney BJ, McKenzie RA, Josey BJ, Ryley MJ, Downing JA (2000b) Effect of grazing sorghum (*Sorghum bicolor*) infected with ergot (*Claviceps africana*) on beef cattle. *Aust. Vet. J.* **78**:124-125.

Blaney BJ, Kopinski JS, Magee MH, McKenzie RA, Blight GW, Maryam R, Dowding JA (2000c) Blood prolactin depression in growing pigs fed sorghum ergot (*Claviceps africana*). *Aust. J. Agric. Res.* **51**:785-791.

Boosinger TR, Brendemuehl JP, Bransby DL, Wright JC, Kemppainen RJ, Kee DD (1995) Prolonged gestation, decreased triiodothyronine concentration, and thyroid gland histomorphologic features in newborn foals of mares grazing *Acremonium coenophialum*-infected fescue. *Am. J. Vet. Res.* **56**:66-69.
Conway KE, Taliaferro CM, Shelby RA (1992) First report on formation of sclerotia of *Claviceps purpurea* on bermudagrass (*Cynodon dactylon*). *Plant Disease* **76**:1077.
Cross DL (1997) Fescue toxicosis in horses. Chapter 55 in *Neotyphodium/Grass Interactions*, edited by CW Bacon and NS Hill, Plenum Press, New York, pp.289-309.
Dennis SB, Allen VG, Saker KE, Fontenot JP, Ayad JYM, Brown CP (1998) Influence of *Neotyphodium coenophialum* on copper concentrations in tall fescue. *J. Anim. Sci.* **76**:2687-2693.
Dignean MA, Schiefer HB, Blair R (1986) Effect of feeding ergot-contaminated grain to pregnant and nursing sows. *J. Vet. Med.* **33**:757-766.
Fletcher LR, Barrell GK (1984) Reduced liveweight gains and serum prolactin levels in hoggets grazing ryegrass containing *Lolium* endophyte. *N. Z. Vet. J.* **32**:139-140.
Foot JZ, Heazlewood PG, Cummins LJ (1988) The effect of high endophyte perennial ryegrass pastures on reproduction in Merino ewes. *Aust. Adv. Vet. Sci.* p.146-147.
Foot JZ, Woodburn OJ, Walsh JR, Heazlewood PG (1994) Responses in grazing sheep to toxins from perennial ryegrass/endophyte associations. In Colegate SM, Dorling PR (eds) *Plant-associated Toxins*, CAB International, Wallingford UK, pp.375-380.
Fraser DM, Dorling PR (1983) Suspected ergotism in two heifers. *Aust. Vet. J.* **60**:303-305.
Hogg RA (1991) Poisoning of cattle fed ergotised silage. *Vet. Rec.* **129**:313-314.
Lopez TA, Campero CM, Chayer R, de Hoyos M (1997) Ergotism and photosensitization in swine produced by the combined ingestion of *Claviceps purpurea* sclerotia and *Ammi majus* seeds. *J. Vet. Diagn. Invest.* **9**:68-71.
Magee R (1991) Saint Anthony's fire revisited. Vascular problems associated with migraine medication. *Med. J. Aust.* **154**:145-149.
Matossian MK (1989) *Poisons of the Past. Molds, Epidemics, and History.* Yale University Press, New Haven & London.
Oliver JW (1997) Physiological manifestations of endophyte toxicosis in ruminant and laboratory species. Chapter 56 in *Neotyphodium/Grass Interactions*, edited by CW Bacon and NS Hill, Plenum Press, New York, pp.311-346.
Oliver JW, Strickland JR, Waller JC, Fribough HA, Linnabary RD, Abney LK (1998) Endophytic fungal toxin effect on adrenergic receptors in lateral saphenous veins (cranial branch) of cattle grazing tall fescue. *J. Anim. Sci.* **76**:2853-2856.
Redmond LM, Cross DL, Strickland JR, Kennedy SW (1994) Efficacy of domperidone and sulpiride as treatment for fescue toxicosis in horses. *Am. J. Vet. Res.* **55**:722-729.
Riet-Correa F, Mendez MC, Schild AL, Bergamo PN, Flores WN (1988) Agalactia, reproductive problems and neonatal mortality in horses associated with the ingestion of *Claviceps purpurea*. *Aust. Vet. J.* **65**:192-193
Rowan DD, Shaw GJ (1987) Detection of ergopeptine alkaloids in endophyte-infected perennial ryegrass by tandem mass spectrometry. *N. Z. Vet. J.* **35**:197-198.
Rowell PP, Larson BT (1999) Ergocryptine and other ergot alkaloids stimulate the release of [^{3}H]dopamine from rat striatal synaptosomes. *J. Anim. Sci.* **77**:1800-1806.
Saker KE, Allen VG, Kalnitsky J, Thatcher CD, Swecker WS Jr, Fontenot JP (1998) Monocyte immune cell response and copper status in beef steers that grazed endophyte-infected tall fescue. *J. Anim. Sci.* **76**:2694-2700.
Samford-Grigsby MD, Larson BT, Forcherio JC, Lucas DM, Paterson JA, Kerley MS (1997) Injection of dopamine antagonist into Holstein steers to relieve symptoms [*sic*] of fescue toxicosis. *J. Anim. Sci.* **75**:1026-1031.
Strickland JR, Bailey EM, Abney LK, Oliver JW (1996) Assessment of the mitogenic potential of the alkaloids produced by endophyte (Acremonium coenophialum)-infected tall fescue (Festuca arundinacea) on bovine vascular smooth muscle in vitro. *J. Anim. Sci.* **74**:1664-1671.
Taylor J (2001) Sorghum ergot poisoning in feedlot steers. *Vet. Path. Report (Newsletter ASVP)* No.61, p.24-25.
Vivrette S, Stebbins M, Martin O, Dooley K, Cross D (2001) Cardiorespiratory and thermoregulatory effects of endophyte-infected fescue in exercising horses. *Journal of Equine Veterinary Science* **21** (2):65–67.
Weaver R, Phillips M, Vacek JL (1989) St.Anthony's fire: A medieval disease in modern times: case history. *Angiology* **40**:929-932.

☑ *Paspalitrems (*Claviceps paspali *tremorgens)*

Core data

Syndrome name: paspalum staggers
Common sources: Claviceps paspali ergots in seedheads of *Paspalum* spp.
Animals affected: cattle, sheep, horses
Mode of action: undescribed
Poisoning circumstances: late summer-autumn access to ergotised pasture
Main effects: muscle tremor syndrome = lolitrem effects (see above)
Diagnosis: syndrome + access
Therapy: gentle removal from source
Prevention:

- heavy grazing of pasture in summer
- mow to remove seedheads

Syndrome names: ***Paspalum*** **staggers**

Chemical structure:

Paspalitrems = indole tremorgens

Sources:

- ***Claviceps paspali*** **(ergot of paspalum)** infecting seedheads of ***Paspalum*** **spp.** pasture grasses including:
  - *Paspalum dilatum* (paspalum, dallis grass [USA])
  - *Paspalum distichum* (*paspalodes)* (water couch, couch paspalum [S.Afr]) (Noble 1985, Botha *et al.* 1996)
  - *Paspalum notatum* (bahia grass)
  - *Paspalum scrobiculatum* (scrobic, ditch millet, mona grass)
  - *Paspalum urvillei* (vasey grass)
- Australia, New Zealand, North America, South Africa, Europe

The ergots (sclerotia) replace the seeds of the grass and are about the same size as a seed or slightly larger, grey-white or orange in colour. Invasion of the seedhead induces a flow of sap rich in sugars ("honeydew") which can be used as an energy source by non-toxic mould fungi which produce black spores and may cover and obscure the seedhead including any ergots present.

Toxicity:

- cattle, sheep, horses susceptible
- indole tremorgens isolated from fungal sclerotia (ergots)
- ergot alkaloids *not* responsible for syndrome
- *ca.* 1.0-5.0 kg ergots in 2-6 days → signs

Mode of action: undescribed

Conditions of poisoning:

- access to infected pasture
- seedheads contain fungal sclerotia (ergots) in late summer-autumn (February-April)

Clinical signs: tremorgenic syndrome very similar to lolitrem poisoning

- hypersensitivity, restless
- muscle tremors, head weaving/nodding
- incoordination, staggering, hypermetria → falling
- ± saliva drooling
- exercise exacerbates signs

Pathology: no significant lesions

Diagnosis: syndrome + ergotised pasture

Therapy:

- gentle removal from infected pasture → recovery in 2-10 days
- pasture may remain toxic for months

Prevention & control:

- deny access to ergotised pasture
- heavy grazing during summer → remove seedheads before fungal infection
- mow to remove seedheads

References:

Se165

Botha CJ, Kellerman TS, Fourie N (1996) A tremorgenic mycotoxicosis in cattle caused by *Paspalum distichum* (L.) infected by *Claviceps paspali*. *J. S. Afr. Vet. Assoc.* **67**:36-37.

Noble JW (1985) Suspected poisoning of cattle by *Claviceps* spp. on water couch. *Aust. Vet. J.* **62**:432-433.

GALL-FORMING FUNGI

Corallocytostroma ornicopreoides *toxicity (black soil blindness)*

Syndrome name: **black soil blindness**

Chemical structure:

Unknown toxins

preliminary isolation of the rumenitis-inducing component has been reported (Allen *et al.* 1998a)

Sources:

- ***Corallocytostroma ornicopreoides*** fungal growths ("corals"; sclerotia & conidiomata) on **Mitchell grasses (*Astrebla* spp.)** in the Kimberley (WA) & Victoria River (NT) districts. The fungus has also been seen on *Dicanthium* sp. (bundle bundle, blue grass) and *Iseilema vaginiflorum* (Flinders grass) (Jubb *et al.* 1998a).
- There is a possible association of the "corals" with galls induced by parasitic wasps (de Witte 1997)

Toxicity:

- cattle
- morbidity *ca.*5%, case fatality rate 100%
- the syndrome has been reproduced experimentally in cattle (Jubb *et al.* 1998) and sheep (Allen *et al.* 1998b)

Mode of action: unknown

Conditions of poisoning:

- conditions predisposing to large populations of the fungus in pasture = higher-than-normal rainfall in successive wet *and* dry seasons; these conditions occur on average about once in every 20 years
- cattle develop a taste for the growths
- growths (sclerotia) present in dry season; dissolved by heavy rain.

Clinical signs:

- blindness
- collapse & rapid death during mustering or in infested paddocks

Pathology:

- perirenal oedema
- nephrosis
- ruminoreticulitis
- "corals" (sclerotia) in reticulorumen
- ± jaundice & swollen liver
- ± individual hepatocyte necrosis
- no lesions of eyes, optic nerves or brain detected despite clinical blindness

Diagnosis: dry season + "corals" in pasture, rumen + pathology

Therapy: nil

Prevention & control: possibly reduce access to heavily infested pasture

References:

Allen JG, Colegate SM, Dorling PR, Jubb TF, Main DC, Mitchell AA, Shivas RG (1998a) Isolation of an extract of *Corallocytostroma ornicopreoides* sp. nov., which causes the rumenitis associated with black soil blindness. Chapter 94 in *Toxic Plants and Other Natural Toxicants.* eds Garland T, Barr AC. CAB International, Wallingford. pp. 483-486.

Allen JG, Main DC, Jubb TF, Shivas RG (1998b) Experimental black soil blindness in sheep. Chapter 97 in *Toxic Plants and Other Natural Toxicants.* eds Garland T, Barr AC. CAB International, Wallingford. pp. 497-503.

de Witte KW (1997) In Minutes of the AACV AGM. *Aust. Cattle Vet.* June Issue, p.15.

Jubb TF, Main DC, Mitchell AA, Shivas RG, de Witte KW (1996) Black soil blindness: A new mycotoxicosis of cattle grazing *Corallocytostroma* -infected Mitchell grass (*Astrebla* spp.) *Aust. Vet. J.* **73**:49-51.

Jubb TF, Main DC, Mitchell AA, Shivas RG, de Witte KW (1998) *Corallocytostroma ornicopreoides*: a new fungus causing a mycotoxicosis of cattle grazing Mitchell grass pastures in Australia. Chapter 95 in *Toxic Plants and Other Natural Toxicants.* eds Garland T, Barr AC. CAB International, Wallingford. pp. 487-492.

Shivas RG, Mitchell AA, Jubb TF (1997) *Corallocytostroma ornicopreoides* sp. nov., an unusual toxic fungus on *Astrebla* and *Dichanthium* in north-western Australia. *Mycol. Res.* **101**:849-852.

Yu Y, Zhang Z (1980) *Corallocytostroma* Yu et Zhang, gen. nov., a stromatic Coelomycete. *Acta Microbiological Sinica* **3**:230-235.

ENDOPHYTES

Fungal **endophytes** (endophytic fungi) live within the tissues of plants in a symbiotic relationship. The fungal hyphae inhabit the intercellular spaces of the host plant. Being symbiotic, no lesions result from the presence of the fungi and they can be detected only microscopically. No fruiting bodies are produced on the host plant and the fungus is transmitted between plant generations through infected seed. The fungi produce chemical products (e.g. peramine) that boost the plant's resistance to insect attack. Some chemical products are toxic to grazing mammals. The number of endophyte species in plants and their host range is very large and their study is a rapidly expanding field (Leuchtmann 1992, Redlin & Carris 1996, Saikkonen K *et al.* 1998, Withgott 2000). Nearly half the world's fungi may be endophytes (Withgott 2000). The classification of the endophytes formerly in the genus *Acremonium* and inhabiting grasses has been revised recently into the genus *Neotyphodium* (Glenn *et al.* 1996). Grass hosts include species of *Lolium, Festuca* and *Stipa*. See notes on reproductive syndromes under ergot alkaloids.

References:

Glenn AE, Bacon CW, Price R, Hanlin RT (1996) Molecular phylogeny of *Acremonium* and its taxonomic implications. *Mycologia* **88**:369-383.

Leuchtmann A (1992) Systematics, distribution, and host specificity of grass endophytes. *Natural Toxins* **1**:150-162.

Redlin S, Carris L (eds.) (1996) *Endophytic Fungi in Grasses and Woody Plants. Systematics, Ecology and Evolution.* APS Press (American Phytopathological Society), St.Paul, Minnesota.

Saikkonen K, Faeth SH, Helander M, Sullivan TJ (1998) Fungal endophytes: a continuum of interactions with host plants. *Annual Review of Ecology and Systematics* **29**:319-343.

Withgott J (2000) Inside story. *New Scientist* **166**(2236):36-39.

Ergot alkaloids (tall fescue endophyte)

See under Ergots (above)

Lysergic acid amide (ergot alkaloid)

Chemical structure:

- **ergot alkaloids**, mainly lysergic acid amide (similar in structure to LSD – lysergic acid diethylamide)

Sources:

- ***Stipa robusta*** (sleepy grass) infected with a *Neotyphodium* sp. [= *Acremonium* sp.] fungal endophyte (in North America: Colorado, Arizona, New Mexico, Texas)
- *Stipa inebrians* (in China)

Toxicity:

- cattle, horses

Mode of action: undefined

Conditions of poisoning: grazing the plants

Clinical signs:

- deep somnolence, stupor
- recumbency
- copious salivation
- frequent urination
- ± ↑ temperature

Pathology: nil

Diagnosis: access + syndrome

Therapy: nil

Prevention & control: deny access

References:

Cheeke 255

Petroski RJ, Powell RG, Clay K (1992) Alkaloids of *Stipa robusta* (sleepy grass) infected with an *Acremonium* endophyte. *Nat. Toxins* **1**:84-87.

☑ *Lolitrems*

Core data

Syndrome: perennial ryegrass staggers

Common sources:
- fungal endophyte *Neotyphodium lolii* in *Lolium perenne*
- lolitrem B concentrated in leaf sheath & seed

Animals affected: sheep, alpacas, horses, deer, cattle
Mode of action: undefined
Poisoning circumstances: well-cropped pastures under dry conditions
Main effects:
- muscle tremor, head weaving/nodding
- ataxia, brief collapse with spasms
- rapid recovery

Diagnosis:
- syndrome
- Poppi stain of leaf sheath
- lolitrem B assay

Therapy: gentle removal from source
Prevention: avoid grazing the lower part of the sward during the summer-autumn period

Syndrome name: **perennial ryegrass staggers**; a pasture mycotoxicosis caused by a tremorgen
Chemical structure:
- lolitrems = lipid-soluble complex substituted indoles.

Source:
- fungal endophyte ***Neotyphodium*** *(Acremonium)* ***lolii*** in temperate pasture grass ***Lolium perenne*** (perennial ryegrass) [DM52] (McLennan 1920)
- Lolitrem B concentrated in **leaf sheaths** near the base of the plant & in **seed**
- *N. lolii* mainly in leaf sheaths & flowering stems
  - mycelium confined to plant crown during winter
  - in spring, grows into leaf sheaths, leaves and inflorescences
  - → maximum density in late summer
  - > 70% of certified *L. perenne* seed sold in Australia contains *N. lolii* (Woodburn 1992)

Toxicity:
Lolitrem B → most toxicity
- alpacas (Holmes *et al.* 1999), sheep, horses, deer (Wapiti > red, fallow) (Hutton *et al.*1999), cattle; young more susceptible

Mode of action: undescribed
Conditions of poisoning:
- south-eastern Australia (southern Q, NSW, V, Tas, SA), New Zealand, North & South America, Europe (including UK – Pritchard & Lewis 1995, Holmes *et al.* 1999)
- mostly on **well-cropped pastures**, especially under unusually **dry conditions**
  - summer and autumn
  - livestock that closely crop the pasture are more susceptible
- rarely on fully irrigated unstressed pastures despite large amounts of endophyte being present and close grazing
- horses have been poisoned when fed **seed cleanings** of *L. perenne* (Munday *et al.* 1985)
- sporadic; greater-than-normal summer rainfall → widespread intoxication
- toxicity persists in **hay**

Clinical signs:
- nervous dysfunction reversible with low mortality (in contrast to corynetoxin poisonings)
- onset usually within 1-2 weeks of exposure to a toxic sward
- animals left undisturbed may appear normal
- fine **muscle tremor**, **head weaving**, **nodding** and swaying are the earliest signs
- forced exercise →
  - **stiff high-stepping gait**
  - ataxia
  - severe muscle spasms
  - **collapse with brief tetanic spasms and limb paddling**
  - **rapid recovery** if left alone
  - ± tenesmus in intensely affected horses

Pathology:

- usually no lesions
- sheep, deer: ± swollen Purkinje cell axons ("torpedoes") in cerebellar granular layer (significance unclear)
- atypical interstitial pneumonia has been associated with perennial ryegrass staggers in calves in Oregon USA (Pearson *et al.* 1996, Blyth *et al.* 1998)

Diagnosis:

- **Poppi stain** of leaf sheath → presence and density of endophyte: > 20 hyphae/mm leaf sheath width in toxic swards.

Poppi staining procedure for examination of Lolium perenne *plants for endophyte hyphae* (Smith 1987)

Reagents:

Poppi stain: 0.06 g aniline blue dissolved in 50 ml lactic acid with 250 ml distilled water. Add 50 ml glycerine and 50 g phenol.

Lactophenol: 20 g phenol, 16.7 ml lactic acid, 40 ml glycerine, 20 ml water

Procedure:

Discard outer drying leaves
Place the leaf sheath (below the ligule) in a test tube
Pour on Poppi stain
Boil 5 min and leave overnight
Mount next day in lactophenol

- **lolitrem B assay** (HPLC) of pasture: > 2mg/kg significant, > 4 mg/kg usually → clinical signs (Gallagher *et al.* 1985)

Therapy:

- careful removal from toxin source
- tranquillisers may be useful

Prevention & control:

- avoid grazing the lower part of the sward during the summer-autumn period
- endophyte → peramine → resistance to insect attack on the plant, thus endophyte-free grass is claimed not to be as productive, but data are somewhat conflicting (Thom *et al.* 1999)
- genetic resistance to lolitrem intoxication in sheep (NZ) (Morris *et al.* 1995)

References:

Se158 (note spelling error)

Blyth LL, Andreason CB, Pearson EG, Craig AM (1998). Atypical pneumonia associated with ryegrass staggers in calves. Chapter 15 in *Toxic Plants and Other Natural Toxicants*, edited by T Garland and AC Barr, CAB International, Wallingford UK, pp. 69-72.

Gallagher RT, Hawkes AD, Stewart JM (1985) Rapid determination of the neurotoxin lolitrem B in perennial ryegrass by HPLC with fluorescence detection. *J. Chromatography* **321**:217-226.

Giesecke PR, Lanigan GW, Payne AL (1979) Fungal tremorgens associated with ryegrass staggers in South Australia. *Aust. Vet. J.* **55**:444.

Holmes LA, Frame NW, Frame RK, Duff JP, Lewis GC (1999) Suspected tremorgenic mycotoxicosis (ryegrass staggers) in alpacas (*Llama pacos*) in the UK. *Vet. Rec.* **145**:462-463.

Hutton J, Arthur D, Bailey K (1999) Quarterly review of diagnostic cases – April to June 1999 (LabWorks Animal Health Ltd) *Surveillance* **26**(3):16-20.

McLennan E (1920) The endophytic fungus of *Lolium*. Part I. *Proc. Roy. Soc. Victoria* **32**:252-301. [cited by Hurst 1942]

Morris CA, Towers NR, Wheeler M, Amyes NC (1995) A note on the genetics of resistance or susceptibility to ryegrass staggers in sheep. *N.Z. J. Agric. Res.* **38**:367-371.

Munday BL, Monkhouse IM, Gallagher RT (1985) Intoxication of horses by lolitrem B in ryegrass seed cleanings. *Aust. Vet. J.* **62**:207.

Pearson EG, Andraesen CB, Blythe LL, Craig AM (1996) Atypical pneumonia associated with ryegrass staggers in calves. *J. Am. Vet. Med. Assoc.* **209**:1137-1142.

Pritchard GC, Lewis GC (1995) Ryegrass staggers. *Vet. Rec.* **137**:471-472.

Smith BL (1987) Mycotoxicoses of sheep in Australia and New Zealand. *Veterinary Clinical Toxicology. Proceedings No. 103. Post-Graduate Committee in Veterinary Science, University of Sydney.* pp. 279-286.

Thom ER, Clark DA, Waugh CD (1999) Growth, persistence, and alkaloid levels of endophyte-infected and endophyte-free ryegrass pastures grazed by dairy cows in northern New Zealand. *N. Z. J. Agric. Res.* **42**:241-253.

van Heeswijck R, McDonald G (1992) *Acremonium* endophytes in perennial ryegrass and other pasture grasses in Australia and New Zealand. *Aust. J. Agric. Res.* **43**:1683-1709.

Woodburn OJ (1992) The effect of perennial ryegrass endophyte on animal production. *Proc. Aust. Soc. Anim. Prod.* **19**:396-397.

Balansia *sp. in* Paspalidium jubiflorum *(Warrego summer grass)*

Hyperthermia syndrome recorded in cattle in north-western New South Wales associated with *Balansia* sp. endophyte in *Paspalidium jubiflorum* (Warrego summer grass) during investigation of the floodplain staggers syndrome (corynetoxin poisoning). (CA Bourke, unpublished data, cited in personal communication from S Slattery, Narrabri, June 1999).

MACROFUNGI (MYCETISM)

A general name for poisoning by macrofungi is mycetism.

Macrofungal peptides

Core data

Syndrome names: amatoxin or phalloides syndrome
Common sources: Amanita phalloides (death cap) macrofungi (mushrooms)
Animals affected: dogs (humans)
Mode of action: amatoxins inhibit RNA polymerase B
Poisoning circumstances: Amanita phalloides in Australia only associated with cultivated European tree species, e.g. oaks
Main effects: acute liver necrosis
Diagnosis: access + syndrome
Therapy:

- gastric lavage, activated charcoal + cathartic if presented within 6 hr of ingestion
- repeated activated charcoal PO
- fluid therapy to maintain good hydration and urine flow
- infuse penicillin G and silibinin (if available)

Prevention: deny access

Syndrome names:

Amatoxin syndrome
Phalloides syndrome (cyclopeptide poisoning)

Chemical structure:

Amatoxins, bicyclic octapeptides with an indole-(*R*)-sulphoxide bridge, are considered the principal toxins, capable experimentally of reproducing all the effects of poisoning by their parent fungus (Bresinsky & Besl 1990). These include amanitins, amanin and amaninamide as the most toxic components (Bresinsky & Besl 1990). **Phallotoxins**, bicyclic heptapeptides with an indole/thio-ether bridge, are toxins of lesser importance. These include phalloidin, phalloin, phallisin, phallacin and phallacidin as the most toxic components (Bresinsky & Besl 1990). **Virotoxins** are monocyclic heptapeptides. These include viroidin, alloviroidin, desoxoviroidin, viroisin and desoxoviroisin (Bresinsky & Besl 1990).

Sources of amatoxins: (Bresinsky & Besl 1990; Benjamin 1995)

Amanita spp.

Amanita phalloides (death cap mushroom, deadly amanita, deadly angel) – Europe (abundant), North America (patchy distribution on eastern and western seaboard: California, Washington, Oregon, Maryland, New York, Pennsylvania, Delaware, New Jersey, Vermont, Virginia, Rhode Island, Massachusetts), **Australia (Victoria, ACT)** (dog, Australia - Cole 1993a)
Amanita phalloides is described in Bresinsky & Besl (1990) as "A large, white-spored fungus with hanging ring on the stem and with a large sac-like, membranous sheath at the bottom of the stem. The gills are free, that is unattached to the stem, and white with a slight flesh-coloured tinge coming from the depths; they are never purplish. The convex to flattened convex cap is greenish olive, greyish olive, or yellowish green, with fine radially-arranged fibrils embedded in the surface, but no scales."

Amanita verna (spring amanita, white death cap, spring destroying angel, fool's mushroom) – Europe, North America (horse, USA - Frazier *et al.* 2000)
Amanita virosa (destroying angel, white amanita) – Europe, North America
Amanita ocreata – North America (California)
Amanita bisporigera (destroying angel) – North America
Amanita tenuifolia – North America
Amanita subalbiacea – North America
Amanita hygroscopia – North America
Amanita magnivelaris – North America

Galerina spp.

Galerina marginata (marginate pholiota) – Europe, North America
Galerina autumnalis (deadly galerina) – Europe, North America
Galerina venenata (deadly lawn galerina) – Europe, North America
Galerina unicolor – Europe, [North America?]
Galerina beinrothii – Europe, [North America?]
Galerina badipes – Europe, [North America?]
Galerina fasciculata – Japan, [North America?]
Galerina sulciceps – Indonesia , Europe (in greenhouses) tropical countries; toxin responsible for human cases thought not to be amatoxins (Benjamin 1995)

Lepiota spp.

Lepiota helveola – Europe, North America
Lepiota castanae – North America
Lepiota josserandii (deadly parasol) – Europe, North America
Lepiota heteri – North America
Lepiota subincarnata – Europe, North America
Lepiota brunneoincarnata – Europe, North America
Lepiota brunneolilacea - Europe
Lepiota scobinella – North America
Lepiota citrophylla – Sri Lanka, Europe (in greenhouses)
Lepiota clypeolarioides – Europe
Lepiota heimii – Europe
Lepiota pseudohelveola – Europe
Lepiota rufescens - Europe

Conocybe spp.

Conocybe filaris [=*Pholiotina filaris*] – North America (α-amanitin detected), Europe (non-toxic?)
Conocybe rugosa – North America
other *Conocybe* spp. may contain toxin – North America

Toxicity:

Animals affected – humans, dogs, horses

There can be wide variation in toxin content within a species of *Amanita*; in *A. phalloides* from North America, α-amanitin concentration varied from 0.5 to 1.5 mg/g of fungus. Toxin concentrations vary more widely between species (Benjamin 1995).

Human lethal dose of *Amanita phalloides* is less than 50 g fresh fungus (5-7mg amatoxins), that is equivalent to one fruiting body (Bresinsky & Besl 1990). Human estimated LD_{50} is about 0.1 mg/kg (Weiland 1968). Toxin concentration in *Galerina* spp. is less than in *Amanita* spp., with 100-150 g of mushroom caps (10-20 caps) being an estimated human lethal dose (Benjamin 1995). Mortality in human cases is of the order of 10-15%, reducing to 5-6% with aggressive intensive care.

Amatoxins do not cross the human placenta, but are excreted in human milk (Benjamin 1995).

Amatoxins are heat stable and resist freezing or drying (Benjamin 1995).

Mode of action:

- **amatoxins** (the principal toxins responsible for poisoning) inhibit RNA polymerase B (RNA polymerase II) thus completely blocking transcription of DNA through mRNA to protein and causing cell death
- phallotoxins alter cell membranes through their affinity for actin filaments, converting monomeric G-actin to polymeric F-actin and inhibiting the depolymerisation reaction which would reverse this effect, but they are not absorbed from the alimentary tract in a biologically-active form (Petzinger *et al.* 1982).
- virotoxins act similarly to phallotoxins

Conditions of poisoning:

Amanita phalloides grows in Australia only in association with European tree species, e.g. oaks, in cultivation, typically in Canberra and Melbourne. *Amanita phalloides* has been reported as the likely cause of death of a dog in Melbourne (Cole 1993a).

Human poisoning follows misidentification as edible species when collecting wild mushrooms for cooking. Poisoning of dogs may follow from these circumstances or from direct ingestion of the fungi in parks and gardens.

Amatoxin poisoning of humans (and domestic animals) mainly occurs in Europe and North America with sporadic cases reported elsewhere, e.g. Japan, Turkey, Israel, Chile.

Clinical signs:

As for acute hepatic necrosis (*q.v.*)

In humans, there is a very long latent period between ingestion and onset of signs – 6-24 hr, usually 8-12 hr – then a biphasic course dominated first by gastrointestinal signs and then hepatic and renal failure signs (Bresinsky & Besl 1990)

Pathology: As for acute hepatic necrosis (*q.v.*)

Diagnosis:

pathology + identification of fungus and/or identification of toxins in fungus, stomach contents or liver where suitable laboratory techniques are available

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Newspaper test of Wieland [incorrectly called the Meixner test] (Wieland 1978)

This test is a rapid screening test for amatoxins. Note its limitations (below).

- Squeeze a small piece of fungus out onto the unprinted edge of a sheet of newspaper (containing wood fibres)
- Dry the spot so obtained
- Moisten the spot with one or two drops of 6 to 8 N (*ca.* 25%) HCl
- After 5-10 minutes, the spot will turn green-blue to blue if it contains > 0.02 mg amatoxins/ml

Mechanism: Indole compounds (including amatoxins, phallotoxins) form coloured substances with aromatic aldehydes liberated by the action of strong acid on the lignin contained in the paper.

N.B. Other indoles occur in fungi (including bufotenine, psilocybin) and other classes of substances (including terpenes) give similar colour reactions, leading to false positives. False negatives also occur. A positive result is only preliminary information requiring laboratory methods for confirmation (e.g. chromatography).

Therapy:

As for acute hepatic necrosis (*q.v.*).

Interruption of the enterohepatic circulation is useful, e.g. with repeated doses of activated charcoal PO. Experimental interruption of enterohepatic circulation by surgical creation of bile fistulae in dogs was life saving (Faulstich & Fauser 1980). Infusions of penicillin G @ 0.5-1.0 x 10^6 IU/kg/day or silymarin or silibinin block excretion of amatoxins into bile and thus also interrupt enterohepatic circulation of toxin (Jahn *et al.* 1980). Silybinin/silymarin (from *Silybum marianum*) IV infusions @ 20-30mg/kg/day in 3-4 divided doses each of 2 hrs duration has been useful in humans (Bresinsky & Besl 1990) and experimentally in dogs (Vogel *et al.* 1984), but is unlikely to be available in veterinary practice.

Maintenance of adequate urinary output with good hydration (rather than forced diuresis) is indicated to reduce reabsorption of toxin from renal tubules. In dogs, 90% of an ingested dose of amatoxins was excreted by the end of 6 hrs (Faulstich *et al.* 1985).

Liver transplantation is an option employed in very severe human cases (<20%), but aggressive intensive care has been successful in these cases as well. (Benjamin 1995).

Prevention & control: As for acute hepatic necrosis (*q.v.*)

References:

Cole FM (1993a) A puppy death and *Amanita phalloides*. *Aust. Vet. J.* **70**:271-272.

Cole FM (1993b) *Amanita phalloides* in Victoria. *Med. J. Aust.* **158**:849-850.

Benjamin DR (1995) *Mushrooms: Poisons and Panaceas. A Handbook for Naturalists, Mycologists and Physicians.* W.H.Freeman & Co., New York

Bresinsky A, Bresl H (1990) *A Colour Atlas of Poisonous Fungi. A Handbook for Pharmacists, Doctors and Biologists.* [translated by N.G. Bisset] Wolfe Publishing, London. ISBN 0 7234 1576 5

Faulstich H, Fauser U (1980) The course of *Amanita* intoxication in beagle dogs. In *Amanita Toxins and Poisoning*. Faulstich H, Kommerell B, Weiland T (eds.), Gerhard Witzstrock, New York. pp. 115-123.

Faulstich H, Talas A, Wellhoner HH (1985) Toxicokinetics of labelled amatoxins in the dog. *Arch. Toxicol.* **56** (3):190-194.

Frazier K, Liggett A, Hines M, Styer E (2000) Mushroom toxicity in a horse with meningioangiomatosis. *Vet. Human Toxicol.* **42**:166-167. [*Amanita verna*; proposed that meningeal lesion altered behaviour causing mushroom ingestion]

Jahn W, Faulstich H, Weiland W (1980) Phamacokinetics of (^{3}H)methyldehydroxymethyl-α-amanitin in the isolated perfused rat liver. In *Amanita Toxins and Poisoning*. Faulstich H, Kommerell B, Weiland T (eds.), Gerhard Witzstrock, New York. pp. 79-87.

Petzinger E, Burckhardt J, Schrank M, Faulstich H (1982) Lack of intestinal transport of [H^3]-demethylphalloidin: comparative studies with phallotoxins and bile acids on isolated small intestinal cells and ileal brush borders. *Naunyn-Schmeidebergs Archives of Pharmacology* **320**:196-200.
Vetter J (1998) Toxins of *Amanita phalloides*. *Toxicon* **36**:13-24.
Vogel G, Tuchweber B, Trost W, Mengs V (1984) Protection by silibinin against *Amanita phalloides* intoxication in beagles. *Toxicol. Appl. Pharmacol.* **73**:355-362.
Weiland T (1968) Poisonous principles of mushrooms of the genus *Amanita*. *Science* **159**:946-952.
Weiland T (1978) Zeitungspapier-Test für Giftpilze. *Umschau Wiss. Technik* **78**:611.

Cortinarius *spp. macrofungi*

Toxins partly identified: **orellanine** (has a bipyridyl structure similar to herbicides paraquat and diquat) (*q.v.*) and possibly cortinarins (cyclic decapeptides).
All reported human cases have been in Europe (Danel *et al.* 2001). No cases are known from domestic animals. Species implicated in poisonings have been *Cortinarius orellanus, C. speciosissimus* and *C. splendens* (Danel *et al.* 2001). Species in which orellanine has been detected are *C. orellanus, C. orellanoides, C. speciosissimus, C. henrici, C. rainierensis, C. fluorescens* and *C. bruneofulvus* (Oubrahim *et al.* 1997).
Cortinarius spp occur in Australia, but their toxic status is unknown and no cases of toxicity are on record (Southcott 1996).
Delayed-onset (1-2 weeks) **renal failure** syndrome (nephrosis). Note that paraquat is also nephrotoxic.
References:

Benjamin DR (1995) *Mushrooms: Poisons and Panaceas.* WH Freeman, New York. pp.242-263.
Danel VC, Saviuc PF, Garon D (2001) Main features of *Cortinarius* spp. poisoning: a literature review. *Toxicon* **39**:1053-1060.
Lampe KF (1991) Human poisoning by mushrooms of the genus *Cortinarius*. Chapter 23 in Keeler RF, Tu AT (eds) *Handbook of Natural Toxins. Vol.6. Toxicology of Plant and Fungal Compounds.* Marcel Dekker, Inc., New York. pp. 497-521.
Michelot D, Tebbett IR (1990) Poisoning by members of the genus *Cortinarius* – a review. *Mycol. Res.* **94**:289-298.
Oubrahim H, Richard JM, Cantin-Esnault D, Seigle-Murandi F, Trécourt F (1997) Novel methods for identification and quantification of the mushroom nephrotoxin orellanine. Thin layer chromatography and electrophoresis screening of mushrooms with electron spin resonance determination of the toxin. *J. Chromatogr.* **A758**:145-157.
Southcott RV (1996) Mechanisms of macrofungal poisoning in humans. *Fungi of Australia* **1B**:297-313.

Gyromitra esculenta *(false morel)*

Exotic to Australia
Human cases occur in Europe and North America (Michelot & Toth 1991).
Fatal haemolysis reported in a 10 week-old dog in Ontario, Canada, with secondary nephrosis and hepatic necrosis (Bernard 1979).
The toxins are **gyromitrin**, the '*N*-methyl-*N*-formylhydrazone of acetaldehyde, and its hydrolysis product under acid conditions, ***N*-methyl-*N*-formylhydrazine** (Bresinsky & Besl 1990).
References:

Bernard MA (1979) Mushroom poisoning in a dog. *Can. Vet. J.* **20**:82-83.
Michelot D, Toth B (1991) Poisoning by *Gyromitra esculenta* – a review. *J. Appl. Toxicol.* **11**:235-243.

Ramaria flavo-brunnescens *(a coral fungus)*

Syndrome names:

Mal do eucalipto [Portuguese = eucalyptus sickness] (Brazil) – name coined because of the close association of the causative fungus with eucalypt woodlands in Brazil.

Chemical structure:

toxin unknown

selenium concentrations in the fungal fruiting bodies, the surrounding soil, and the hair and tissues of affected cattle are normal

Sources:

Ramaria flavo-brunnescens (a coral fungus: Family Clavariaceae) occurs in the south & south-eastern regions of Brazil and in Uruguay where toxicity is recognised. It is also known from Australia, North America, China and possibly Europe, but no cases have been reported from these localities.

Organ systems affected:

integument (hooves, horns, hair)

alimentary (including buccal cavity)

eyes

Toxicity:

cattle, sheep

syndrome reproduced experimentally in calves and sheep fed freshly-collected fungi. Fungi that were stored frozen were less toxic and those that were dried for 7-10 days lost toxicity. (Santos *et al.* 1975, Prucoli & Camargo 1965-66, Sallis *et al.* 1993, 2000). Season variation in toxicity has been detected with fungi collected in 1993 not toxic to sheep at 200-400 g/kg (Sallis *et al.* 2000).

calves fed 20 g fresh fungus/kg/day for 9-24 days developed disease after a few days (Kommers & Santos 1995)

sheep fed 166-430 g fresh fungus/kg over 3-10 days developed disease; minimum toxic dose 150 g/kg (Sallis *et al* 1993, 2000)

Mode of action:

Proposed interference in the metabolism of sulphur-containing amino acids, including cystine, responsible for the integrity of keratinised epithelium (Kommers & Santos 1995).

Proposed ergot alkaloid involvement with vascular integrity (Sallis *et al.* 1993)

Conditions of poisoning:

R. flavo-brunnescens fruiting bodies occur mid-autumn to early winter (April-June in southern hemisphere)

Cattle or sheep grazing in eucalyptus woodlands

Clinical signs:

Cattle (Kommers & Santos 1995):

onset after 3-6 days of experimental feeding; clinical course 8-30 days
anorexia, depression
drooling of saliva (ptyalism)
smoothness of the dorsum of the tongue
diarrhoea
lameness
loss of tail switch hair and hair of the dorsum
congestion of coronary bands of hooves
loosening leading to loss of hooves
loosening of horns
± haemorrhage into the eyes leading to blindness
± corneal opacity

Sheep (Sallis *et al.* 1993, 2000):

anorexia, depression
hyperthermia
drooling saliva (ptyalism)
ulcers of the borders of the tongue
wool loosening
congestion of coronary bands of hooves
polyuria
dyspnoea
nystagmus
ataxia
muscle tremors
seizures
haemorrhages in the anterior chamber of the eye

Pathology:

Cattle (Kommers & Santos 1995):

atrophy of lingual papillae
multifocal fibrinonecrotic lesions at the tongue margins and linear lesions in the oesophagus
vacuolation & irregular keratinisation of the laminar epidermis of hooves
degeneration of epidermis of tail switch hair follicles
decreased thickness of epithelium of the tongue with loss of papillae

Sheep (Sallis *et al.* 1993, 2000):

feet and tongue epithelium: endothelial degeneration and occasional thrombosis of arterioles followed by necrosis and ulceration of the mucosal epithelium.
eye: haemorrhage into the anterior chamber; severe congestion and haemorrhage of the iris, ciliary body.

Diagnosis:

access & syndrome

differential diagnoses include toxicity from selenium, mimosine

Therapy:

no specific therapy

deny further access; early cases or those without significant tissue damage (no eye damage or hoof loss) will recover

Prevention & control: deny access

References:

Bauer AG, Laranja RJ, Santos AG (1966) Sobre a etiologia do chamado "Mal do Eucalipto". *Arq. Inst. Pesq. Vet. Desiderio Finamor* **3**:85-90. [cited by Kommers & Santos 1995]

Barros SS (1958) Da possivel incidencia da toxicose pelo selenio em bovinos no Rio Grande do Sul. *Dipan* **11**(121-122):10-13. [cited by Kommers & Santos 1995] [First record of the syndrome, but without identification of the cause]

Fidalgo O, Fidalgo MEPK (1970)A poisonous *Ramaria* from southern Brazil. *Rickia* **5**:71-91. [cited by Kommers & Santos 1995]

Kommers GD, Santos MN (1995) Experimental poisoning of cattle by the mushroom *Ramaria flavo-brunnescens* (Clavariaceae): a study of the morphology and pathogenesis of lesions in hooves, tail, horns and tongue. *Vet. Human Toxicol.* **37**:297-301.

Prucoli O, Camargo WVA (1965-1966) Intoxicacao experimental em ovinos com *Clavaria* spp. *Bol. Ind. Animal* **23**:177-178. [cited by Kommers & Santos 1995]

Riet-Correa F, Schild AL, Méndez MC *et al.* (1983) *Laboratorio Regional de Diagnostico – relatorio de atividades e doencas da area de influencia no periodo de 1978-1982.* Universidade Federal de Pelotas, Pelotas. p. 98. [cited by Kommers & Santos 1995] [naturally occurring cases in sheep]

Sallis ES, Riet-Correa F, Méndez MC (1993) Experimental intoxication by *Ramaria flavo-brunnescens* in sheep. [Abstract] *N. Z. Vet. J.* **41**:224.

Sallis ES, Riet-Correa F, Raffi MB, Méndez MC (2000) Experimental intoxication by the mushroom *Ramaria flavo-brunnescens* in sheep. *Vet. Human Toxicol.* **42**:321-324.

Santos MN (1993) Intoxicacao por *Ramaria flavo-brunnescens.* In Riet-Correa F, Méndez MC, Schild AL (eds.) *Intoxicacao por Plantas e Micotoxinas em Animais Domesticos.* Editorial Agropecuaria Hemisferio Sur, Montevideo. pp. 309-318. [cited by Kommers & Santos 1995]

Santos MN, Barros SS, Barros CSL (1975) Intoxicacao em bovinos pelo cogumelo *Ramaria flavo-brunnescens. Pesq Agropec. Bras. Ser. Vet.* **10**:105-109. [cited by Kommers & Santos 1995]