

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 B₁. Other common aflatoxins are B₂, G₁, G₂ & M₁. [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 B₁ & B₂ and *A. parasiticus* and *A. nomius* producing B₁, B₂, G₁ & G₂ (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 B₁ 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 B₁ intake as aflatoxin M₁ 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 B₁ 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

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Se160

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☑ Fumonisin

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 B₁ (FB₁), FB₂ and FB₃ are the major toxins in grain, while FB₄, FA₁ and FA₂ 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 discoloration 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
<i>Fusarium verticillioides</i> [= <i>F. moniliforme</i>]	17,900	3,000	2,300
<i>Fusarium sacchari</i>	21	NT‡	NT
<i>Fusarium fujikuroi</i>	7	NT	NT
<i>Fusarium proliferatum</i>	31,000	17,000	5,700
<i>Fusarium subglutinans</i>	230	NT	NT
<i>Fusarium thapsinum</i>	30	5	5
<i>Fusarium anthophilum</i>	610	35	NT
<i>Fusarium globosum</i>	330	4	24
<i>Fusarium nygamai</i>	7,200	530	140
<i>Fusarium dlamini</i>	82	NT	NT
<i>Fusarium napiforme</i>	480	NT	NT
<i>Fusarium pseudonygamai</i>	Trace*	Trace	NT
<i>Fusarium andiyazi</i>	Trace	ND	NT
<i>Fusarium oxysporum</i>	300	6	0.9
<i>Fusarium polyphialidicum</i>	500	NT	NT
<i>Alternaria alternata</i>	+	+	+

* 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 B₁ = 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 B₁ 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 Ca²⁺ 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 B₁ /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 B₁/g (mg/kg)

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☑ 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]

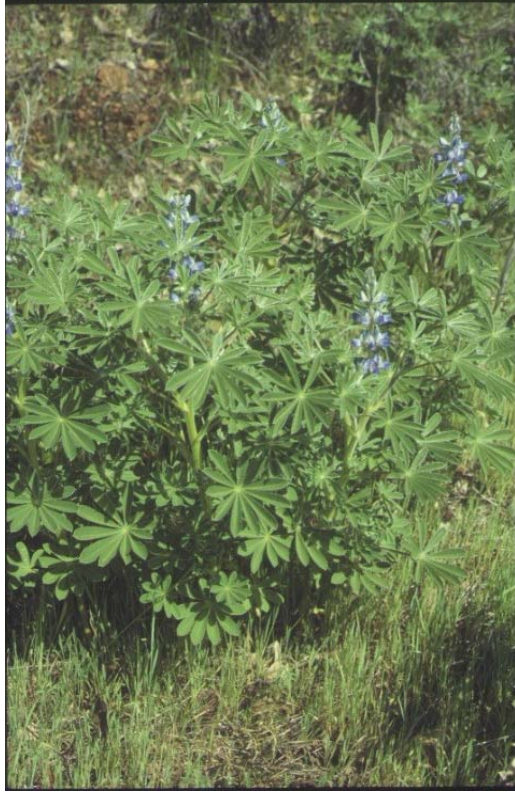
Plant host sources:

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 LD₅₀ = 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).

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Se173

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☑ 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, \uparrow 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).

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☑ **Furans - Mouldy sweet potatoes**

Core data

Common sources: *Ipomoea batatas* 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 batatas* tubers)

Sources:

- mouldy ***Ipomoea batatas*** (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)

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☑ 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°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)

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Se169

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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

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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) Trichothecene biosynthesis in *Fusarium* species: chemistry, genetics and significance. *Micribiol. Rev.* **57**:594-604.

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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, ?thrombocytopenia)
- ± 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.
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- 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.
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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.
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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.
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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.
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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-.
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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.
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- 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.
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- 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.
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- 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°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°C reaching a maximum at 25°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-hydroxypyrrone

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.

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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).

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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 phytoalexins (*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)

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- 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).

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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%]
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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 ° 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 (T₃) 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 (domperidone, 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 metoclopramide (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 parturition 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 ° 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

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☑ **Paspalitremis (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:

Paspalitremes = indole tremorgens

Sources:

- ***Claviceps paspali* (ergot of paspalum)** infecting seedheads of ***Paspalum* spp.** pasture grasses including:
 - *Paspalum dilatatum* (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

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GALL-FORMING FUNGI

Corallocytophthora 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:

- *Corallocytophthora ornicopreoides* fungal growths ("corals"; sclerotia & conidiomata) on **Mitchell grasses (*Astrelba* 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:

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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 (Leuchtman 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:

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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:

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☑ Lolitrem

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)

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***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 suballiacea – North America

Amanita hygroscozia – 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 LD₅₀ 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

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 10⁶ 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.*)

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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.

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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).

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Ramaria flavo-brunnescens (a coral fungus)

Syndrome names:

Mal do eucalypto [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 lamellar 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

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